

Split liver transplantation: What's unique?

Aparna R Dalal

Aparna R Dalal, Department of Anesthesiology, Icahn School of Medicine at Mount Sinai, New York, NY 10029, United States

Author contributions: Dalal AR authored the paper.

Conflict-of-interest statement: The author declares that there is no conflict of interests regarding publication of this paper.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Aparna R Dalal, MD, Assistant Professor, Department of Anesthesiology, Icahn School of Medicine at Mount Sinai, 1428 Madison Avenue, New York, NY 10029, United States. aparna.dalal@mssm.edu
Telephone: +1-216-2722545
Fax: +1-206-4864610

Received: August 23, 2014
Peer-review started: August 25, 2014
First decision: December 17, 2014
Revised: December 26, 2014
Accepted: June 18, 2015
Article in press: June 19, 2015
Published online: September 24, 2015

Abstract

The intraoperative management of split liver transplantation (SLT) has some unique features as compared to routine whole liver transplantations. Only the liver has this special ability to regenerate that confers benefits in survival and quality of life for two instead of one by splitting livers. Primary graft dysfunction may result from small for size syndrome. Graft weight to recipient body weight ratio is significant for both trisegmental

and hemiliver grafts. Intraoperative surgical techniques aim to reduce portal hyperperfusion and decrease venous portal pressure. Ischemic preconditioning can be instituted to protect against ischemic reperfusion injury which impacts graft regeneration. Advancement of the technique of SLT is essential as use of split cadaveric grafts expands the donor pool and potentially has an excellent future.

Key words: Graft to recipient body weight ratio; Split liver transplantation; Small for size syndrome; Hemiliver grafts; Portal hyperperfusion

© **The Author(s) 2015.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The liver has a special ability to regenerate that confers benefits in survival and quality of life for two instead of one by splitting livers. Primary graft dysfunction may result from small for size syndrome. Graft weight to recipient body weight ratio is significant for both trisegmental and hemiliver grafts. Intraoperative surgical techniques aim to reduce portal hyperperfusion and decrease venous portal pressure. Ischemic preconditioning can be instituted to protect against ischemic reperfusion injury which impacts graft regeneration.

Dalal AR. Split liver transplantation: What's unique? *World J Transplant* 2015; 5(3): 89-94 Available from: URL: <http://www.wjgnet.com/2220-3230/full/v5/i3/89.htm> DOI: <http://dx.doi.org/10.5500/wjt.v5.i3.89>

INTRODUCTION

Liver parenchyma is able to regenerate. Additionally, the liver vasculature has lobar and segmental distributions. Thus, the liver is considered to be a double organ and offers benefits in survival and quality of life for two instead of one recipient, by means of dividing or

splitting a graft.

SMALL-FOR-SIZE-SYNDROME

Primary graft dysfunction can result from the use of partial livers despite the absence of other causes such as vascular obstruction or sepsis. This increasingly recognized phenomenon is termed as "small-for-size-syndrome (SFSS)"^[1].

The graft exhibits signs of primary graft dysfunction within the first postoperative week. This dysfunction is in absence of other diagnosis such as vascular obstruction, biliary leak, sepsis and immune rejection. Coagulopathy, bilirubinemia and ascitis are typical manifestations of SFSS^[2]. SFSS has been studied extensively in both, humans as well as animals.

It has been suggested that portal hyperperfusion of the graft combined with poor venous outflow and reduced arterial flow might cause sinusoidal congestion and endothelial dysfunction, resulting in SFSS. Graft related factors such as graft to recipient body weight ratio < 0.8, impaired venous outflow, steatosis > 30% and prolonged warm/cold ischemia time are positively predictive of SFSS^[1].

Another study states that the lower limit of the graft weight to recipient weight ratio can be safely reduced to 0.6% in adult-to-adult living donor liver transplant, if portal pressure control is used^[3].

GRAFT ALLOCATION

Though a split liver maybe obtained from a standard criteria donor, splitting it creates two extended criteria grafts, thus increasing the risk of graft failure^[4,5]. There are also ethical dilemmas associated with ownership and stewardship of the organs. Is it ethical for a patient to request for an entire organ rather than a split component^[6]? There is increased risk of biliary complications with a split liver, and a recipient may wish to thus decline it. Would it be considered coercion if the patient on the top of the waiting were told that if they declined to a splitting of the liver it would be given to the next on the list^[6]?

Other considerations include use of the unassigned part of the graft. As per the United Network for Organ Sharing allocation policy, the unassigned part has to be allocated according to the waiting list and cannot be used by the center performing split liver transplantation (SLT). If an incentive is created by allowing the unassigned part of the liver to be retained by the organization, then the number of split livers in the United States will increase^[7].

INTRAOPERATIVE FEATURES

The liver can be split *in situ*, on the back table or in the donor hospital before the donor cross-clamp. Notable advantages are a decrease the total ischemia time and increase in the possibility of inter-center sharing. It may

take an additional 1-2 h to perform cholangiogram, hilar dissection and parenchymal division. Cholangiogram can be performed to assess surgical splitability^[8].

Contrast enhanced computed tomography could be used to perform a virtual resection and volume analysis. Prior to an *in situ* split, one can determine the segmental volume and delineate surgical planes. The anatomy of the hepatic vasculature and biliary structures can be determined. The anticipated graft and remnant liver volumes post resection can be calculated. The severity of portal hypertension can be assessed using a triphasic computer tomographic scan^[9]. Liver grafts are then perfused and preserved with Histidine-Tryptophan-Ketoglutarate solution (Custodiol Solution; Essential Pharmaceuticals, Newtown, PA)^[8].

Excellent results have been reported with split livers. These are a right tri-segmental graft that includes segments I, IV, V, VI VII, and VIII; and a left graft consisting of the left lateral lobe including segments II and III. Pediatric recipients are usually transplanted with the left lateral lobe. The right tri-segmental graft is usually transplanted into an adult recipient^[1].

The liver's regeneration capacity is compromised by aging. Therefore acceptable donor age is usually less than 50 years^[10]. However, the major challenge in the field of liver transplantation is organ shortage^[11-14].

The split liver technique has been further expanded to use two hemiliver grafts: a left lobe and a right lobe, which effectively expands the donor pool. Unfortunately, however, many challenges have surfaced^[7,15-17]. Some challenges and unfavorable outcomes have made many transplant centers reluctant to use hemiliver grafts^[16,17]. Since the model for end-stage liver disease (MELD) allocation uses the sickest first policy, livers amenable to splitting are most often allocated to patients unsuitable for SLT.

The middle hepatic vein (MHV) is considered "dominant" in drainage of the hemiliver in 27% of cases^[18]. A right hepatectomy without the MHV or reconstruction can induce congestion of the paramedian segments V and VIII, reducing functional capacity of the graft. When graft survival was analyzed, no significant difference was found with or without harvest of the MHV, as long as a vein interpositional graft was used for anastomosis^[19,20]. The MHV primarily drains the right anterior lobe and segment IV. On the other hand, a meta-analysis discovered that there was better functional recovery of patients who received the right lobes with MHV^[21].

It maybe beneficial to maintain a low central venous pressure (CVP) to minimize graft hyperperfusion. Additionally, low CVP decreases backflow bleeding from the hepatic veins and decrease bleeding during parenchymal transection^[22]. An analysis stated that patients with a CVP < 5 cm H₂O had a median blood loss of 200 mL, whereas those with CVP > 5 cm H₂O had a median blood loss of 1000 mL^[23]. Low CVP facilitates safe dissection of the retro-hepatic vena cava and major hepatic veins and produces decreased postoperative morbidity and reduction of hospital stay^[24]. The potential

disadvantages of low CVP anesthesia are chances of perioperative embolism, need for pressor agents and postoperative renal dysfunction.

The partial clamp inserted in the piggyback method allows some venous return, thereby preventing an acute reduction in the preload during inferior vena cava cross clamping. When the patient is unable to tolerate the test cross clamp, it may be prudent to consider venovenous bypass. Presently, in the United States, temporary portocaval shunt is routine practice in 29% of programs, and a low CVP technique is practiced in 54% of centers^[25].

The liver weight can be estimated as 2% of donor's body weight, divided into approximate weights of 35% for the left lobe and 65% for the right lobe^[8]. It is important to note that since small-for-size grafts require vigorous and immediate hepatocyte proliferation, regeneration is critically required for the success of SLT. In rats, remnant liver of 10% maybe enough. However, in humans, more volume is required for transplantation^[26]. Though at three months after partial liver transplantation (50%, 60% size) liver volume slightly exceeds 100% of the standard liver volume in recipients. The graft increase ratio is higher in 50% partial liver transplantation as compared to 30% partial LT^[27].

The liver receives approximately 25% of the cardiac output, of which 75% is supplied by the portal vein and the other 25% by the hepatic artery. Hepatic blood flow is reduced by all anesthetic agents and techniques *via* reductions in hepatic blood flow and hepatic oxygen uptake^[28].

Intraoperative factors that decrease hepatic blood flow are mechanical ventilation, hypercarbia, positive end expiratory pressure, hypotension, hemorrhage, hypoxemia and surgery. If the decrease in hepatic blood flow is significant, it can result in parenchymal centrilobular necrosis^[28]. Etomidate, ketamine and propofol are induction agents. Etomidate decreases hepatic blood flow^[29]. Ketamine has little impact on hepatic blood flow. Propofol has a vasodilator effect, ultimately increasing total hepatic blood flow^[30,31]. Midazolam has a longer half-life, a reduced clearance, reduced protein binding, a longer duration of action and an enhanced sedative effect. Dexmedetomidine, an alpha-2 adrenergic agonist, with sedative and analgesic properties, is primarily metabolized in the liver^[32]. All volatile anesthetics decrease the mean arterial pressure and portal blood flow. Desflurane and sevoflurane have very little or no effect on total hepatic blood flow^[33].

The elimination half-life of morphine is prolonged in cirrhosis. The sedative and respiratory depressant effects are exaggerated. Fentanyl has a short duration of action and its elimination is not appreciably altered in patients with cirrhosis^[34]. However, unlike fentanyl, plasma clearance and elimination of alfentanil is increased in patients with cirrhosis^[35]. Remifentanyl is a short acting synthetic opioid that is hydrolyzed by blood and tissue esterases. Its pharmacokinetics is unaltered

in patients with severe liver disease^[36].

Vecuronium and rocuronium are steroidal muscle relaxants that are metabolized by the liver. In cirrhotic patients, they have decreased clearance, prolonged half-lives, and prolonged neuromuscular blockade. In living donor liver transplantation, requirements of vecuronium were least in the neohepatic phase^[37]. Sugammadex can reverse rocuronium rapidly^[38]. Cisatracurium undergoes ester hydrolysis and cisatracurium infusions during liver transplantation require increased dosages and result in prolonged recovery^[39].

Ischemic preconditioning protects against ischemic reperfusion injury (IRI) in liver transplantation. Lower aspartate aminotransferase levels and significant reduction of moderate-severe hepatocyte swelling is seen^[40]. In rat liver, morphine preconditioning protects against IRI. This involves opioid receptors, phosphatidylinositol-3-kinase, and Akt^[41]. IP protected against hepatic IRI under isoflurane anesthesia in rats. The mechanism of protection appeared to involve upregulation of Bcl-2 expression resulting in inhibited apoptosis^[42]. Human studies have revealed that patients preconditioned with sevoflurane experienced a reduction in peak transaminase levels, an improvement in clinical outcomes, and enhanced benefit in those with steatotic livers. Inducible nitric oxide synthase mRNA was significantly increased in the preconditioned group suggesting a role for nitric oxide^[43].

Unfortunately, ischemic preconditioning significantly enhances the extent of split liver graft injury and hinders hepatic regeneration in SFS liver transplant models^[44]. Interestingly, rather than IRI, a shift in regeneration ability is more likely to cause liver graft dysfunction and failure following small-for-size transplantation.

Portal hyperperfusion has been cited as one of the causes for SFSS. Thus the most important step is prevention of SFSS through perioperative treatment strategies include reduction of portal blood flow^[45]. Lowering the graft perfusion pressure is vital. Hepatic venous congestion due to insufficient vascular orifices or mechanical stenosis and kinking should be prevented^[45].

Surgical approaches to prevent SFSS fall into two categories. The first targets portal hyperperfusion by reducing inflow to the graft, including splenic artery modulation and portacaval shunts. The second aims to relieve parenchymal congestion^[1]. Adenosine washout maintains the hepatic arterial buffer response (HABR) that maintains constant total blood flow to the liver. Portal blood flow removes adenosine that has a local vasodilator effect on the arterial system^[46,47]. However, an exaggerated HABR may contribute to ischemic injury in states of portal hyperperfusion, as seen in small for size grafts^[48,49]. Prophylactic splenic artery modulation^[50,51] produced a significant reduction in portal flow causing a significant reduction in incidence of SFSS.

SFSS grafts are also at least partly associated with persistent elevation of portal venous pressure^[52]. Vasopressin infusions have been used in certain insti-

tutions to decrease portal pressures and flow prior to the anhepatic phase^[53].

CONCLUSION

The following factors such as changes in recipient and donor selection and matching, changes in allocation and logistics, and improved technical proficiency have influenced outcomes. The risk of graft failure is now similar between split and whole-liver recipients^[54].

There are several challenges, and routine application of the hemiliver technique is still controversial, but can achieve excellent outcomes under the model for end-stage liver disease allocation^[8]. The 5-year graft survival for hemilivers is comparable to whole livers^[8]. Split liver transplantation, which is based on this unique ability of the liver to regenerate, is an excellent idea to increase the donor grafts. Through the expansion of split-liver transplantation, the transplant community might be able to both increase the organ pool and bridge the liver demand-supply gap.

REFERENCES

- Gonzalez HD**, Liu ZW, Cashman S, Fusai GK. Small for size syndrome following living donor and split liver transplantation. *World J Gastrointest Surg* 2010; **2**: 389-394 [PMID: 21206720 DOI: 10.4240/wjgs.v2.i12.389]
- Dahm F**, Georgiev P, Clavien PA. Small-for-size syndrome after partial liver transplantation: definition, mechanisms of disease and clinical implications. *Am J Transplant* 2005; **5**: 2605-2610 [PMID: 16212618 DOI: 10.1111/j.1600-6143.2005.01081.x]
- Kaido T**, Mori A, Ogura Y, Hata K, Yoshizawa A, Iida T, Yagi S, Uemoto S. Lower limit of the graft-to-recipient weight ratio can be safely reduced to 0.6% in adult-to-adult living donor liver transplantation in combination with portal pressure control. *Transplant Proc* 2011; **43**: 2391-2393 [PMID: 21839274 DOI: 10.1016/j.transproceed.2011.05.037]
- Feng S**, Goodrich NP, Bragg-Gresham JL, Dykstra DM, Punch JD, DeRoy MA, Greenstein SM, Merion RM. Characteristics associated with liver graft failure: the concept of a donor risk index. *Am J Transplant* 2006; **6**: 783-790 [PMID: 16539636 DOI: 10.1111/j.1600-6143.2006.01242.x]
- Burroughs AK**, Sabin CA, Rolles K, Delvart V, Karam V, Buckels J, O'Grady JG, Castaing D, Klempnauer J, Jamieson N, Neuhaus P, Lerut J, de Ville de Goyet J, Pollard S, Salizzoni M, Rogiers X, Muhlbacher F, Garcia Valdecasas JC, Broelsch C, Jaeck D, Berenguer J, Gonzalez EM, Adam R. 3-month and 12-month mortality after first liver transplant in adults in Europe: predictive models for outcome. *Lancet* 2006; **367**: 225-232 [PMID: 16427491]
- Split vs whole liver transplantation. OPTN/UNOS Ethics Committee White Paper. Available from: URL: <http://optn.transplant.hrsa.gov/resources/bioethics.asp?index=8>
- Emre S**, Umman V. Split liver transplantation: an overview. *Transplant Proc* 2011; **43**: 884-887 [PMID: 21486620 DOI: 10.1016/j.transproceed.2011.02.036]
- Hashimoto K**, Quintini C, Aucejo FN, Fujiki M, Diago T, Watson MJ, Kelly DM, Winans CG, Eghtesad B, Fung JJ, Miller CM. Split liver transplantation using Hemiliver graft in the MELD era: a single center experience in the United States. *Am J Transplant* 2014; **14**: 2072-2080 [PMID: 25040819 DOI: 10.1111/ajt.12791]
- Aucejo FN**, Hashimoto K, Quintini C, Kelly D, Vogt D, Winans C, Eghtesad B, Baker M, Fung J, Miller C. Triple-phase computed tomography and intraoperative flow measurements improve the management of portosystemic shunts during liver transplantation. *Liver Transpl* 2008; **14**: 96-99 [PMID: 18161777]
- Schlitt HJ**. Which liver is splittable? In: Rogiers X, Bismuth H, Busuttil RW, DC, Broering D. Azoulay: Split-liver transplantation-theoretical and practical aspects. Darmstadt, Germany: Steinkopff Verlag, 2002: 63
- Broering DC**, Topp S, Schaefer U, Fischer L, Gundlach M, Sterneck M, Schoder V, Pothmann W, Rogiers X. Split liver transplantation and risk to the adult recipient: analysis using matched pairs. *J Am Coll Surg* 2002; **195**: 648-657 [PMID: 12437252 DOI: 10.1016/S1072-7515(02)01339-X]
- Yersiz H**, Renz JF, Farmer DG, Hisatake GM, McDiarmid SV, Busuttil RW. One hundred in situ split-liver transplantations: a single-center experience. *Ann Surg* 2003; **238**: 496-505; discussion 506-507 [PMID: 14530721 DOI: 10.1097/01.sla.0000089852.29654.72]
- Merion RM**, Rush SH, Dykstra DM, Goodrich N, Freeman RB, Wolfe RA. Predicted lifetimes for adult and pediatric split liver versus adult whole liver transplant recipients. *Am J Transplant* 2004; **4**: 1792-1797 [PMID: 15476478 DOI: 10.1111/j.1600-6143.2004.00594.x]
- Wilms C**, Walter J, Kaptein M, Mueller L, Lenk C, Sterneck M, Hillert C, Fischer L, Rogiers X, Broering DC. Long-term outcome of split liver transplantation using right extended grafts in adulthood: A matched pair analysis. *Ann Surg* 2006; **244**: 865-872; discussion 872-873 [PMID: 17122611 DOI: 10.1097/01.sla.0000247254.76747.f3]
- Ferla F**, Lauterio A, Di Sandro S, Mangoni I, Poli C, Concione G, Cusumano C, Giacomoni A, Andorno E, De Carlis Luciano L. Split-liver full-left full-right: proposal for an operative protocol. *Transplant Proc* 2014; **46**: 2279-2282 [PMID: 25242768 DOI: 10.1016/j.transproceed.2014.07.066]
- Giacomoni A**, Lauterio A, Donadon M, De Gasperi A, Belli L, Slim A, Dorobantu B, Mangoni I, De Carlis L. Should we still offer split-liver transplantation for two adult recipients? A retrospective study of our experience. *Liver Transpl* 2008; **14**: 999-1006 [PMID: 18581461 DOI: 10.1002/lt.21466]
- Zambelli M**, Andorno E, De Carlis L, Rossi G, Cillo U, De Feo T, Carobbio A, Giacomoni A, Bottino G, Colledan M. Full-right-full-left split liver transplantation: the retrospective analysis of an early multicenter experience including graft sharing. *Am J Transplant* 2012; **12**: 2198-2210 [PMID: 22578214 DOI: 10.1111/j.1600-6143.2012.04071.x]
- Radtke A**, Sotiropoulos GC, Sgourakis G, Molmenti EP, Schroeder T, Saner FH, Beckebaum S, Broelsch CE, Broering DC, Malago M. Hepatic venous drainage: how much can we learn from imaging studies? Anatomic-functional classification derived from three-dimensional computed tomography reconstructions. *Transplantation* 2010; **89**: 1518-1525 [PMID: 20410853 DOI: 10.1097/TP.0b013e3181dd6bac]
- Kasahara M**, Takada Y, Fujimoto Y, Ogura Y, Ogawa K, Uryuhara K, Yonekawa Y, Ueda M, Egawa H, Tanaka K. Impact of right lobe with middle hepatic vein graft in living-donor liver transplantation. *Am J Transplant* 2005; **5**: 1339-1346 [PMID: 15888039 DOI: 10.1111/j.1600-6143.2005.00817.x]
- Adham M**, Dumortier J, Abdelaal A, Sagnard P, Boucaud C, Boillot O. Does middle hepatic vein omission in a right split graft affect the outcome of liver transplantation? A comparative study of right split livers with and without the middle hepatic vein. *Liver Transpl* 2007; **13**: 829-837 [PMID: 17539013 DOI: 10.1002/lt.21133]
- Zhang S**, Dong Z, Zhang M, Xia Q, Liu D, Zhang JJ. Right lobe living-donor liver transplantation with or without middle hepatic vein: a meta-analysis. *Transplant Proc* 2011; **43**: 3773-3779 [PMID: 22172845 DOI: 10.1016/j.transproceed.2011.08.100]
- Bismuth H**, Castaing D, Garden OJ. Major hepatic resection under total vascular exclusion. *Ann Surg* 1989; **210**: 13-19 [PMID: 2742411 DOI: 10.1097/0000658-198907000-00002]
- Jones RM**, Moulton CE, Hardy KJ. Central venous pressure and its effect on blood loss during liver resection. *Br J Surg* 1998; **85**: 1058-1060 [PMID: 9717995 DOI: 10.1046/j.1365-2168.1998.00795.x]

- 24 **Chen H**, Merchant NB, Didolkar MS. Hepatic resection using intermittent vascular inflow occlusion and low central venous pressure anesthesia improves morbidity and mortality. *J Gastrointest Surg* 2000; **4**: 162-167 [PMID: 10675239 DOI: 10.1016/S1091-255X(00)80052-9]
- 25 **Schumann R**, Mandell MS, Mercaldo N, Michaels D, Robertson A, Banerjee A, Pai R, Klinck J, Pandharipande P, Walia A. Anesthesia for liver transplantation in United States academic centers: intraoperative practice. *J Clin Anesth* 2013; **25**: 542-550 [PMID: 23994704 DOI: 10.1016/j.jclinane.2013.04.017]
- 26 **Kiuchi T**, Kasahara M, Uryuhara K, Inomata Y, Uemoto S, Asonuma K, Egawa H, Fujita S, Hayashi M, Tanaka K. Impact of graft size mismatching on graft prognosis in liver transplantation from living donors. *Transplantation* 1999; **67**: 321-327 [PMID: 10075602]
- 27 **Fu WY**, Yan JQ, Shi MM, Ma D, Peng CH, Li HW. Suppression of liver regeneration affects hepatic graft survival in small-for-size liver transplantation in rats. *Hepatol Res* 2013; **43**: 300-310 [PMID: 22882432 DOI: 10.1111/j.1872-034X.2012.01071.x]
- 28 **Dalal A**, Lang JD. Anesthetic considerations for patients with liver disease, hepatic surgery. Abdeldayem H, editor. Available from: URL: <http://www.intechopen.com/books/hepatic-surgery/anesthetic-considerations-for-patients-with-liver-disease>
- 29 **van den Heuvel I**, Wurmb TE, Böttiger BW, Bernhard M. Pros and cons of etomidate—more discussion than evidence? *Curr Opin Anaesthesiol* 2013; **26**: 404-408 [PMID: 23743556 DOI: 10.1097/ACO.0b013e328362a84c]
- 30 **Meierhenrich R**, Gauss A, Mühlhng B, Bracht H, Radermacher P, Georgieff M, Wagner F. The effect of propofol and desflurane anaesthesia on human hepatic blood flow: a pilot study. *Anaesthesia* 2010; **65**: 1085-1093 [PMID: 20860555 DOI: 10.1111/j.1365-2044.2010.06504.x]
- 31 **Suh SJ**, Yim HJ, Yoon EL, Lee BJ, Hyun JJ, Jung SW, Koo JS, Kim JH, Kim KJ, Choung RS, Seo YS, Yeon JE, Um SH, Byun KS, Lee SW, Choi JH, Ryu HS. Is propofol safe when administered to cirrhotic patients during sedative endoscopy? *Korean J Intern Med* 2014; **29**: 57-65 [PMID: 24574834 DOI: 10.3904/kjim.2014.29.1.57]
- 32 **Wang ZX**, Huang CY, Hua YP, Huang WQ, Deng LH, Liu KX. Dexmedetomidine reduces intestinal and hepatic injury after hepatectomy with inflow occlusion under general anaesthesia: a randomized controlled trial. *Br J Anaesth* 2014; **112**: 1055-1064 [PMID: 24771805 DOI: 10.1093/bja/aeu132]
- 33 **Kang JG**, Ko JS, Kim GS, Gwak MS, Kim YR, Lee SK. The relationship between inhalational anesthetic requirements and the severity of liver disease in liver transplant recipients according to three phases of liver transplantation. *Transplant Proc* 2010; **42**: 854-857 [PMID: 20430189 DOI: 10.1016/j.transproceed.2010.02.057]
- 34 **Bosilkovska M**, Walder B, Besson M, Daali Y, Desmeules J. Analgesics in patients with hepatic impairment: pharmacology and clinical implications. *Drugs* 2012; **72**: 1645-1669 [PMID: 22867045 DOI: 10.2165/11635500-000000000-00000]
- 35 **Höhne C**, Donaubaueer B, Kaisers U. [Opioids during anesthesia in liver and renal failure]. *Anaesthesist* 2004; **53**: 291-303 [PMID: 15074320]
- 36 **Zhang LP**, Yang L, Bi SS, Lu W, Zhang XH, Zhai SD, Duan LP. Population pharmacokinetics of remifentanyl in patients undergoing orthotopic liver transplantation. *Chin Med J (Engl)* 2009; **122**: 1032-1038 [PMID: 19493437]
- 37 **Kim WH**, Joo HS, Ko JS, Gwak MS, Lee SK, Kim GS. Vecuronium requirements according to the operative phase during living donor liver transplantation under desflurane anesthesia. *Transplant Proc* 2013; **45**: 1920-1923 [PMID: 23769073 DOI: 10.1016/j.transproceed.2012.10.064]
- 38 **Fujita A**, Ishibe N, Yoshihara T, Ohashi J, Makino H, Ikeda M, Setoguchi H. Rapid reversal of neuromuscular blockade by sugammadex after continuous infusion of rocuronium in patients with liver dysfunction undergoing hepatic surgery. *Acta Anaesthesiol Taiwan* 2014; **52**: 54-58 [PMID: 25016508 DOI: 10.1016/j.aat.2014.04.007]
- 39 **Cammu G**, Bossuyt G, De Baerdemaeker L, Den Blauwen N, Struys M, Mortier E. Dose requirements and recovery profile of an infusion of cisatracurium during liver transplantation. *J Clin Anesth* 2002; **14**: 135-139 [PMID: 11943528 DOI: 10.1016/S0952-8180(01)00370-1]
- 40 **Franchello A**, Gilbo N, David E, Ricchiuti A, Romagnoli R, Cerutti E, Salizzoni M. Ischemic preconditioning (IP) of the liver as a safe and protective technique against ischemia/reperfusion injury (IRI). *Am J Transplant* 2009; **9**: 1629-1639 [PMID: 19519822 DOI: 10.1111/j.1600-6143.2009.02680.x]
- 41 **Wang Y**, Wong GT, Man K, Irwin MG. Pretreatment with intrathecal or intravenous morphine attenuates hepatic ischaemia-reperfusion injury in normal and cirrhotic rat liver. *Br J Anaesth* 2012; **109**: 529-539 [PMID: 22745352 DOI: 10.1093/bja/aes209]
- 42 **Ko JS**, Gwak MS, Kim GS, Shin YH, Ryu S, Kim JS, Kim SJ, Kim ST. The protective effect of ischemic preconditioning against hepatic ischemic-reperfusion injury under isoflurane anesthesia in rats. *Transplant Proc* 2013; **45**: 1704-1707 [PMID: 23769028 DOI: 10.1016/j.transproceed.2012.08.026]
- 43 **Beck-Schimmer B**, Breitenstein S, Urech S, De Conno E, Wittlinger M, Puhon M, Jochum W, Spahn DR, Graf R, Clavien PA. A randomized controlled trial on pharmacological preconditioning in liver surgery using a volatile anesthetic. *Ann Surg* 2008; **248**: 909-918 [PMID: 19092335 DOI: 10.1097/SLA.0b013e31818f3dda]
- 44 **Yao A**, Li X, Pu L, Zhong J, Liu X, Yu Y, Zhang F, Kong L, Sun B, Wang X. Impaired hepatic regeneration by ischemic preconditioning in a rat model of small-for-size liver transplantation. *Transpl Immunol* 2007; **18**: 37-43 [PMID: 17584601]
- 45 **Umeda Y**, Yagi T, Sadamori H, Fujiwara T. Small-for-size syndrome after living donor liver transplantation. In: Liver transplantation—technical issues and complications. Abdeldayem H, editor. Available from: URL: <http://www.intechopen.com/books/liver-transplantation-technical-issues-and-complications/small-for-size-syndrome-after-living-donor-liver-transplantation>
- 46 **Lautt WW**. Regulatory processes interacting to maintain hepatic blood flow constancy: Vascular compliance, hepatic arterial buffer response, hepatorenal reflex, liver regeneration, escape from vasoconstriction. *Hepatol Res* 2007; **37**: 891-903 [PMID: 17854463 DOI: 10.1111/j.1872-034X.2007.00148.x]
- 47 **Lautt WW**, Legare DJ, Ezzat WR. Quantitation of the hepatic arterial buffer response to graded changes in portal blood flow. *Gastroenterology* 1990; **98**: 1024-1028 [PMID: 2311859 DOI: 10.1016/0016-5085(90)90029-Z]
- 48 **Demetris AJ**, Kelly DM, Eghtesad B, Fontes P, Wallis Marsh J, Tom K, Tan HP, Shaw-Stiffel T, Boig L, Novelli P, Planinsic R, Fung JJ, Marcos A. Pathophysiologic observations and histopathologic recognition of the portal hyperperfusion or small-for-size syndrome. *Am J Surg Pathol* 2006; **30**: 986-993 [PMID: 16861970 DOI: 10.1097/00000478-200608000-00009]
- 49 **Smyrniotis V**, Kostopanagiotou G, Kondi A, Gamaletsos E, Theodoraki K, Kehagias D, Mystakidou K, Contis J. Hemodynamic interaction between portal vein and hepatic artery flow in small-for-size split liver transplantation. *Transpl Int* 2002; **15**: 355-360 [PMID: 12122512 DOI: 10.1111/j.1432-2277.2002.tb00178.x]
- 50 **Troisi R**, Cammu G, Militerno G, De Baerdemaeker L, Decruyenaere J, Hoste E, Smeets P, Colle I, Van Vlierberghe H, Petrovic M, Voet D, Mortier E, Hesse UJ, de Hemptinne B. Modulation of portal graft inflow: a necessity in adult living-donor liver transplantation? *Ann Surg* 2003; **237**: 429-436 [PMID: 12616129 DOI: 10.1097/01.SLA.0000055277.78876.B7]
- 51 **Umeda Y**, Yagi T, Sadamori H, Matsukawa H, Matsuda H, Shinoura S, Mizuno K, Yoshida R, Iwamoto T, Satoh D, Tanaka N. Effects of prophylactic splenic artery modulation on portal overperfusion and liver regeneration in small-for-size graft. *Transplantation* 2008; **86**: 673-680 [PMID: 18791439 DOI: 10.1097/TP.0b013e318181e02d]
- 52 **Kiuchi T**, Tanaka K, Ito T, Oike F, Ogura Y, Fujimoto Y, Ogawa K. Small-for-size graft in living donor liver transplantation: how far should we go? *Liver Transpl* 2003; **9**: S29-S35 [PMID: 12942476 DOI: 10.1053/jlts.2003.50198]

Dalal AR. Split liver transplantation

- 53 **Wagner G**, Gubitosa G, Renz J, Kinkhabwala M, Brentjens T, Guarrera JV, Emond J, Lee HT, Landry D. Vasopressin decreases portal vein pressure and flow in the native liver during liver transplantation. *Liver Transpl* 2008; **14**: 1664-1670 [PMID: 18975276 DOI: 10.1002/lt.21602]
- 54 **Cauley RP**, Vakili K, Fullington N, Potanos K, Graham DA, Finkelstein JA, Kim HB. Deceased-donor split-liver transplantation in adult recipients: is the learning curve over? *J Am Coll Surg* 2013; **217**: 672-684.e1 [PMID: 23978530 DOI: 10.1016/j.jamcollsurg.2013.06.005]

P- Reviewer: Arshad R, Rodriguez-Castro KI, Sumi S
S- Editor: Gong XM **L- Editor:** A **E- Editor:** Jiao XK





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>

