

## Current techniques for ABO-incompatible living donor liver transplantation

Silke Rummeler, Astrid Bauschke, Erik Bärthel, Heike Jütte, Katrin Maier, Patrice Ziehm, Christina Malessa, Utz Settmacher

Silke Rummeler, Heike Jütte, Katrin Maier, Patrice Ziehm, Institute of Transfusion Medicine, University Hospital Jena, 07747 Jena, Germany

Astrid Bauschke, Erik Bärthel, Christina Malessa, Utz Settmacher, Department of General, Visceral and Vascular Surgery, University Hospital Jena, 07747 Jena, Germany

**Author contributions:** Rummeler S and Bauschke A conducted the research and wrote the paper; Bärthel E, Jütte H, Maier K, Ziehm P and Malessa C collected and analyzed data; Settmacher U contributed important content-related arguments and revised the manuscript critically; Rummeler S and Bauschke A contributed equally.

**Conflict-of-interest statement:** The authors declare no conflict of interest.

**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/>

**Manuscript source:** Invited manuscript

**Correspondence to:** Astrid Bauschke, MD, Department of General, Visceral and Vascular Surgery, University Hospital Jena, Erlanger Allee 101, 07740 Jena, Germany. [astrid.bauschke@med.uni-jena.de](mailto:astrid.bauschke@med.uni-jena.de)  
**Telephone:** +49-3641-9322454  
**Fax:** +49-3641-9322602

**Received:** March 28, 2016  
**Peer-review started:** April 1, 2016  
**First decision:** May 23, 2016  
**Revised:** June 24, 2016  
**Accepted:** July 20, 2016  
**Article in press:** July 22, 2016  
**Published online:** September 24, 2016

### Abstract

For a long time, it was considered medical malpractice to neglect the blood group system during transplantation. Because there are far more patients waiting for organs than organs available, a variety of attempts have been made to transplant ABO-incompatible (ABOi) grafts. Improvements in ABOi graft survival rates have been achieved with immunosuppression regimens and plasma treatment procedures. Nevertheless, some grafts are rejected early after ABOi living donor liver transplantation (LDLT) due to antibody mediated rejection or later biliary complications that affect the quality of life. Therefore, the ABOi LDLT is an option only for emergency situations, and it requires careful planning. This review compares the treatment possibilities and their effect on the patients' graft outcome from 2010 to the present. We compared 11 transplant center regimens and their outcomes. The best improvement, next to plasma treatment procedures, has been reached with the prophylactic use of rituximab more than one week before ABOi LDLT. Unfortunately, no standardized treatment protocols are available. Each center treats its patients with its own scheme. Nevertheless, the transplant results are homogeneous. Due to refined treatment strategies, ABOi LDLT is a feasible option today and almost free of severe complications.

**Key words:** Living-donor liver transplantation; ABO-incompatible; Rituximab; Desensitization; Iso-titer; Biliary complications

© **The Author(s) 2016.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Due to refined treatment strategies, ABO-incompatible living donor liver transplantation (ABOi LDLT) is a feasible option today and almost free from severe complications, but biliary complications still affect the quality of life after ABOi LDLT. Until now, the best improvement could be reached with the prophylactic

use of rituximab more than one week before AB0i LDLT.

Rummler S, Bauschke A, Bärthel E, Jütte H, Maier K, Ziehm P, Malessa C, Settmacher U. Current techniques for AB0-incompatible living donor liver transplantation. *World J Transplant* 2016; 6(3): 548-555 Available from: URL: <http://www.wjgnet.com/2220-3230/full/v6/i3/548.htm> DOI: <http://dx.doi.org/10.5500/wjt.v6.i3.548>

## INTRODUCTION

Blood group antigens are expressed in almost every cell in the body, and an individual develops antibodies against blood group antigens (anti-A/B antibodies) absent in his or her own tissue. Grafts expressing foreign A/B antigens are usually hyperacutely rejected<sup>[1]</sup>. For a long time, it was considered medical malpractice to neglect the blood group system during cadaveric transplantation. Because there are far more patients waiting for organs than organs available, a variety of attempts have been made to transplant AB0-incompatible (AB0i) grafts. Most AB0i liver transplantations (AB0i LTs) have had a lower graft survival rate due to hepatic arterial thrombosis, various biliary complications or acute rejection episodes<sup>[2-4]</sup>. In those rejection episodes, the graft was damaged by necrosis or disseminated intravascular coagulopathy<sup>[4,5]</sup>. This susceptibility to rejection can be explained sufficiently by blood group antigens that are expressed on the vascular endothelium and in large bile ducts for up to 150 d after transplantation<sup>[6-10]</sup>.

Young children with an incompletely developed immune system seem to be an exception. In 1979, Starzl's group reported eleven human AB0i LTs without evidence of acute rejection after transplantation<sup>[11]</sup>.

Because AB0i LTs need a certain amount of prearrangement, we focus in this review on AB0i living donor liver transplantation (LDLT), which is conducted electively, and neglect cadaveric AB0i LT.

In Western Europe and the United States, few case reports of AB0i LDLT exist, even though new techniques are available to overcome the blood group barrier<sup>[6,12-17]</sup>. In Asia, Japan and South Korea, elective AB0i LDLT is performed with excellent results. Due to religious beliefs, fewer organs of deceased individuals are donated, and AB0i LDLT has become well established<sup>[18,19]</sup>. Patients demonstrate survival with an AB0i graft for nearly as long as patients with an AB0-compatible (AB0c) graft<sup>[18-21]</sup>. Improvements in AB0i graft survival rates have been achieved with immunosuppression and plasma treatment procedures (PTPs). The antibody titer (iso-titer) level cannot explain all clinical findings. However, hyperacute or acute antibody-mediated rejection (AMR) is closely related to hepatic necrosis or intrahepatic biliary complications<sup>[22]</sup>. Additionally, patients with a history of immunizations are at higher risk for AMR. Blood group incompatibility, recipient age, etiology of liver disease and transplant era were found

to be significant predictors of overall survival, too<sup>[23]</sup>.

Various treatment protocols have been used for iso-titer elimination in AB0i LDLT patients. They originate from AB0i kidney transplantation protocols and do not follow a common standard. The iso-titer itself has also not been standardized. The results as well as its interpretation depend on the examining laboratory. Therefore, this review compares several treatment possibilities and their effect on graft outcome from 2010 to the present.

## INDICATIONS FOR AB0i LDLT WITH SPECIAL REFLEXIONS

### *Pediatrics*

The younger the child, the fewer iso-titers have been developed. In the first month of life, children are able to tolerate an AB0i graft very well. Preformed antibodies are absent, and the immune system is highly tolerant<sup>[24]</sup>.

Gurevich *et al.*<sup>[25]</sup> examined 58 pediatric patients undergoing AB0i LDLT with a preoperative iso-titer of < 1:16. No graft rejection or death occurred and 93% survived beyond the first 10 years. Patients with biliary atresia had fewer rejection episodes in situations where the graft was donated by the mother (mother:father vs 40%:55%)<sup>[25-27]</sup>. Most data in children have been collected in Asia<sup>[25,28]</sup>. Okada *et al.*<sup>[29]</sup> described rituximab to be successful in pediatric AB0i LDLT. Kasahara *et al.*<sup>[23]</sup> analyzed 2224 pediatric transplantations, the largest cohort worldwide. They found 1-, 5-, 10- and 20-year patient survival rates of 88.3%, 85.4%, 82.8% and 79.6% in the 294 patients undergoing AB0i LDLT.

### *Acute liver failure*

In Europe and the United States, emergency AB0i LDLT is conducted only if no compatible donor can be acquired in time<sup>[8,30]</sup>. In Asia, this concept is more common. Shen *et al.*<sup>[31]</sup> for example, reported 3-year patient survival rates in AB0c vs AB0i LDLT of 83.1% vs 86%. The graft survival was 80% vs 86%. Two AB0i patients developed AMR, but no other patients had cellular rejection, biliary complications or infections. A model of end stage liver diseases (MELD) score > 30 put patients at high risk for mortality. For this reason, in the Asian Medical Center, the largest LDLT center in the world, Lee *et al.*<sup>[18]</sup> excluded high-urgency patients from AB0i LDLT. Shinoda *et al.*<sup>[32]</sup> in contrast, found no difference between AB0c and AB0i LDLT.

### *Hepatocellular carcinoma*

Living donation provides an alternative curative treatment option for patients with hepatocellular carcinoma (HCC) in cirrhosis if no offers for deceased donor organs exist. This can be due to low laboratory MELD scores or if the tumor burden is beyond the Milan criteria. There are only a few reports of successful AB0i LDLT in patients with HCC outside Milan<sup>[33]</sup>. After Lee *et*

**Table 1 Research regarding ABO-incompatible living donor liver transplantation published since 2010**

Ref.	Pat No.	Splenectomy local graft infusion	Rituximab	IVIg	PTP Target iso-titer	IS	AMR
Lee <i>et al</i> <sup>[59]</sup>	15	-/-	-14 d 300 mg/m <sup>2</sup>	+1, +4 d 0.8 g/kg bw	First -7 d 1:8	Triple	No
Shen <i>et al</i> <sup>[31]</sup>	35	n.s.	Z 375 mg/m <sup>2</sup>	Z 0.4 g/kg bw	Rescue	Quadruple	2
Lee <i>et al</i> <sup>[59]</sup>	15	-/-	-14 d, 300 mg/m <sup>2</sup> Z, +4 d, 200 mg/m <sup>2</sup>	No	TPE < 1:8	Triple	No
Kim <i>et al</i> <sup>[36]</sup>	14	-/-	-7 d 375 mg/m <sup>2</sup>	+1, +3, +5 d 0.6 g/kg bw	TPE 1:32	-3 d MMF 1.5 g triple	No
Song <i>et al</i> <sup>[52]</sup>	10	-/+	-14 d, 375 mg/m <sup>2</sup>	No	TPE 1:32	Triple with Cyc	No
Kim <i>et al</i> <sup>[20]</sup>	22	-/-	-14 d, 375 mg/m <sup>2</sup>	No	PP 1:32	PGE1 Triple	No
Lee <i>et al</i> <sup>[34]</sup>	20	-/-	-15 d 300 mg/m <sup>2</sup>	+1, +4 d 0.8 g/kg bw	TPE < 1.16	Quadruple	No
Song <i>et al</i> <sup>[66]</sup>	20	-/+	-21, -14 d 300, 375 mg/m <sup>2</sup>	No	TPE 1:8	Triple with Cyc	No
Song <i>et al</i> <sup>[66]</sup>	21-127	-/-	-21, -14 d 300, 375 mg/m <sup>2</sup>	No	TPE 1:8	Triple	No
Song <i>et al</i> <sup>[66]</sup>	128-235	+/-	-21, -14 d 300, 375 mg/m <sup>2</sup>	No	TPE 1:8	Triple	17
Yasuda <i>et al</i> <sup>[67]</sup>	5	+/-	-15, -3 d 500 mg/m <sup>2</sup>	No	TPE n.s.	Triple	4
Lee <i>et al</i> <sup>[35]</sup>	19	-/-	-10 d 300-375 mg/m <sup>2</sup>	No	TPE 1:32	-7 d Tac 0.1 mg/kg, quadruple	No
Lee <i>et al</i> <sup>[68]</sup> (Initial iso-titer < 1:64)	20	-/-	+1 d, 375 mg/m <sup>2</sup>	No	< 1:64	Quadruple	No
Lee <i>et al</i> <sup>[68]</sup> (Initial iso-titer > 1:64)	26	-/-	-21 d, 375 mg/m <sup>2</sup> +1 d, 187 mg/m <sup>2</sup>	No	TPE/PP < 1:64	Quadruple	No

Quadruple: Tacrolimus, mycophenolate mofetil, basiliximab, steroids; Triple: Tacrolimus, mycophenolate mofetil, steroids; TPE: Therapeutic plasma exchange; IS: Immunosuppression: 5 d before transplantation - 5 d, 5 d after TX - +5 d, day of TX - Z; Cyc: Cyclophosphamide; PP: Plasmapheresis, not otherwise specified; PGE1: Prostaglandin E1, gabexate mesilate; Tac: Tacrolimus.

*a*<sup>[34]</sup> experienced a recurrence of 57% in the first year after ABOi LDLT, they recommended refraining from transplanting HCC patients<sup>[34]</sup>.

Peter and Werny investigated a distinctly higher anti-A/B titer in patients with severe emaciating diseases compared to healthy blood donors<sup>[30]</sup>. HCC patients seem to have very high anti-A/B titers and a strong rebound. This increase could relate from altered expression of blood group antigens on the biliary tree in pathological conditions<sup>[23]</sup>. Neexpression or aberrant expression of A or B substances in malignant cells possibly boost the production of antibodies<sup>[24]</sup>. In this situation, the tumor bulk might define the antibody titer and rebound.

**Hepatitis B/C**

Lee *et al*<sup>[34]</sup> described ABOi LDLT in 20 patients. The etiology of liver diseases consisted mostly of HBV infections (*n* = 15) and one hepatitis C virus (HCV) infection. To prevent hepatitis C virus (HBV) recurrence, Lee *et al*<sup>[34]</sup> used entecavir or tenofovir with a high dose of intravenous (IV) HB-hyperimmune globulin. If HCV was confirmed by a liver biopsy or an abnormal liver function test with elevated HCV RNA loads, PEGylated-interferon and ribavirin were administered. Other authors describe ABOi LDLT in patients with HBV or HCV cirrhosis and in patients with HCC, as well. Unfortunately, they provide

no information about their hepatitis therapy or antibiotics (Table 1)<sup>[20,35,36]</sup>. No data are available on ABOi LDLT in HCV patients with the new antivirals.

**TREATMENT STRATEGIES TO OVERCOME BLOOD GROUP BARRIER**

ABOi LDLT requires careful planning and logistical preparation prior to surgery. As treatment regimens vary distinctly, we would like to present them in the following way. All regimens have the focus on antibody reduction in common. To reach this goal and to prevent antibody rebound as well, therapeutic apheresis is combined with immunosuppressive therapy. A good overview is given in a South Korean treatment schedule: Prior to transplantation rituximab and plasma exchange is started. When the anti-A/B titer has decreased to at least a titer of 1:8, transplantation takes place without local infusion or splenectomy. Afterward, immunoglobulins and quadruple immunosuppression are administered.

**Anti-A/B iso-titer**

As Warner *et al*<sup>[37]</sup> summarized, “The durable survival of ABOi solid organ allografts seems to be primarily dependent on 3 conditions: (1) the low expression of antigen on the graft, as in case of A2 positive organs; (2)

a low titer of anti-donor ABO antibodies in the recipient before transplantation; and (3) the ability to maintain low titers of antidonor ABO antibodies in the recipients after transplantation, at least for the first 3 to 6 week<sup>[37]</sup>. In the setting of ABOi LDLT, iso-titers naturally rise during the first two days after transplantation<sup>[38]</sup>. In addition to the natural rebound, de novo alloantibodies have the potential to develop. This alloimmune reaction induces a higher rebound and can lead to AMR, putting the graft at risk. This makes the first two weeks, or even four to six weeks, after ABOi LDLT critical for AMR<sup>[39]</sup>.

After this period, the graft has been mostly adapted to its new environment. This state is called accommodation.

Furthermore, the target titer for IgG and IgM in ABOi LDLT varies from center to center. Some centers estimate 1:8 to be appropriate, others 1:16<sup>[39]</sup>. However, a titer of 1:64 or above should be avoided due to an increased risk of complications during transplantation and AMR<sup>[30,40]</sup>. In the studies we compared in Table 1, titers of 1:64 or above were not accepted and lead to further PTPs (Table 1).

#### **Therapeutic apheresis**

Therapeutic apheresis is the most effective way to control the humoral antibody response to prevent rejection<sup>[41]</sup>. There are a variety of PTPs, which differ mainly in their selectivity toward immunoglobulin elimination.

**Therapeutic plasma exchange:** Therapeutic plasma exchange (TPE) is a widely accepted nonselective PTP to eliminate antibodies in patients with solid-organ transplants which are sensitive to HLA antigens or undergo ABOi transplantation. Still, no controlled studies of TPE in ABOi LDLT or therapy standards have been published. With TPE, usually 1.2 times (1.0-1.5) the patient's plasma volume is treated. The amount of treated plasma volume correlates with the removal of 63% to 72% of the original plasma constituents. At the end of a TPE procedure, IgM is very low. High levels of IgM are usually reduced with one or two TPE<sup>[42]</sup>. The American Society of Apheresis guidelines designate the perioperative use of TPE in ABOi LDLT as a category I with 1C recommendation<sup>[43]</sup>. Moreover, the use of double-volume TPE pre-transplant eliminated more than 90% of the antibodies, lead to an iso-titer of < 1:16 and decreased the episodes of rejection<sup>[44]</sup>. In the studies we reviewed, PTP was conducted before and after ABOi LDLT. Almost all centers used TPE to eliminate anti-A/B iso-titers (Table 1).

**Immunoabsorption:** Immunoabsorption (IA) is mainly performed in Western Europe. Controlled studies of IA are still lacking in the setting of ABOi LDLT. With IA, it is possible to deplete a large amount of circulating antibodies without considerable loss of essential plasma constituents. Two IA-methods are available to selectively reduce antibodies. The first is the blood group

antigen-specific apheresis (Glycosorb<sup>®</sup> ABO, Glycorex Transplantation, Lund, Sweden). This technique is preferred to reduce the iso-titer. Because the IA-column is highly selective for anti-A/B antibodies, other antibodies are not affected and no replacement fluid is required. With each plasma volume treated with Glycosorb<sup>®</sup>, the iso-titer of IgG and IgM is reduced by one titer. Compared to the baseline, a reduction to 59% for IgG iso-titer and to 30% for IgM iso-titer is considered average<sup>[45]</sup>.

The second is the semiselective antibody removal (Immunosorba<sup>®</sup>, Globaffin<sup>®</sup>, Fresenius Medical Care, Bad Homburg, Germany, Therasorb<sup>®</sup>, Miltenyi Biotec GmbH, Bergisch Gladbach, Germany). These columns mainly bind IgG and, to a lesser degree, IgM, regardless of their specificity. This unspecific removal is beneficial for transplant candidates with an additional sensitization. In ABOi kidney transplant patients, a single session of IA decreased anti-A/B IgG iso-titers more effectively than antigen-specific apheresis. IgG was reduced to 28% of the baseline value and IgM to 74%<sup>[45]</sup>. In the studies we compared, the use of IA was not reported, as IA is only common in Europe. Asian centers use TPE or double-filtration plasmapheresis instead (Table 1).

**Double-filtration plasmapheresis:** Outside of Japan, the use of double-filtration plasmapheresis for ABOi LDLT is very limited. The Evaflux<sup>™</sup> 2A (Kawasumi laboratories, Japan) eliminates IgG as well as IgM. After processing 1000 mL plasma, the ratio of solute returned to the patient, or the sieving coefficient, is 0.00 for IgM and 0.19 for IgG. As the value of 0.00 for IgM indicates, these pore-based filter columns are most effective for IgM depletion. The target iso-titer < 1:16 was reached with only 4 treatments, even in cases with very high initial iso-titers (> 1:2048)<sup>[46]</sup>.

#### **Intravenous immunoglobulin G**

Intravenous immunoglobulin G (IVIG) are suggested to be beneficial in immunoregulation because they block Fc receptors on mononuclear phagocytes and directly neutralize alloantibodies. They also inhibit the expression not only of CD19 on activated B cells and the complement system but also of alloreactive T cells<sup>[13]</sup>. In the field of transplantation, IVIG was used with PTPs in pre-sensitized recipients or to treat AMR<sup>[47,48]</sup>. IVIG can be used as a rescue therapy, in the case of severe AMR, if there is not enough time (three days) for rituximab to exert an effect<sup>[39]</sup>. When IVIG is part of the therapeutic protocol, graft survival is estimated to be greater than 87%<sup>[47,49,50]</sup>. Hanto *et al.*<sup>[44]</sup> compared ABOi recipients receiving TPE and IVIG with patients receiving only TPE during the post-transplant period. In this study, the patient group with IVIG did not develop AMR, but 27.3% of the patients in the other group did develop AMR post-transplant. Unfortunately, a transient increase of anti-A/B titers is observed after IVIG administration due to the passive transfer of anti-A/B. Thus, IVIG should not be administered prior to ABOi LDLT. All

centers that we have compared report using IVIG after ABOi LDLT (Table 1).

### Immunosuppression

Immunosuppression consists of steroids, calcineurin inhibitors and antimetabolites. In our center, we use quadruple immunosuppression: Monoclonal antibodies, calcineurin inhibitors, antimetabolites and steroids.

In 1998, Tanabe *et al.*<sup>[51]</sup> described a new protocol in which they, in addition to perioperative TPE and splenectomy, supplemented systemic immunosuppression with portal vein infusion therapy (PVIT). Methylprednisolone, prostaglandin E1 and gabexate mesilate were used in the PVIT. If PVIT causes portal vein thrombosis, Kozaki *et al.*<sup>[41]</sup>'s hepatic arterial infusion therapy (HAIT) could be conducted. The two most feared complications after PVIT or HAIT were thrombosis and bleeding.

In 2013, local graft infusion, in the form of hepatic arterial infusion (HAI) or portal vein infusion (PVI), with PGE1 was only performed by Kim *et al.*<sup>[20]</sup> and Song *et al.*<sup>[52]</sup>. Since 2010, only Song *et al.*<sup>[52]</sup> have also administered cyclophosphamide as immunosuppression. The therapeutic regimen after LDLT includes antifungal, antimicrobial and cytomegalovirus prophylaxis. However, dosage, medication and duration of the medication have not yet been standardized.

## MONOCLONAL ANTIBODIES

Rituximab is a monoclonal chimeric human-murine anti-CD20 antibody that depletes B cells. It acts by complement- and antibody-dependent cell-mediated cytotoxicity. The CD20 antigen is expressed on pre- and mature B cells, but not on long living plasma cells persisting in the bone marrow. Hence, rituximab does not directly affect antibody-producing plasma cells. A single dose of rituximab in ABOi LDLT suppresses B cells for more than six months after transplantation in the peripheral blood<sup>[4,50]</sup>. However, because B cells in the lymph node are unaffected, they are activated by the ABOi graft, and the anti-A/B titers rise for the first four to six weeks after transplantation<sup>[4,50,53]</sup>. But even if antibody production is possible at low levels, de novo production of antibodies is sufficiently delayed due to rituximab<sup>[28]</sup>. Monteiro *et al.*<sup>[54]</sup> reported the first case of ABOi LTX using rituximab in 2003. Usuda *et al.*<sup>[55]</sup> reported the first case of rituximab prophylaxis in ABOi LDLT in 2005. Egawa *et al.*<sup>[4]</sup> reported in 2014 that rituximab prophylaxis significantly decreased the incidence of AMR, especially severe AMR leading to hepatic necrosis ( $P < 0.001$ )<sup>[4]</sup>. However, other B cell desensitization therapies have shown no additional effects in the rituximab group. Multiple or large rituximab doses significantly increased the incidence of infection and early administration held no advantage<sup>[4]</sup>. All the transplantation centers we compared treated their ABOi LDLT patients with rituximab, with most of them administering it before transplantation. Two weeks before surgery tends to be an opportune time

(Table 1). Regarding the safety of rituximab in ABOi LDLT, pharmacodynamic studies have to be conducted to determine the safest dose. Currently, therapeutic regimens are adopted from the kidney transplantation protocols.

Basiliximab is a chimeric mouse-human monoclonal antibody to CD25 of the interleukin (IL)-2 receptor, located on the surface of activated T lymphocytes. It inhibits T cell proliferation and prevents cell-mediated rejection in liver transplantation<sup>[56,57]</sup>. It prevents T-helper cells from replicating, blocks the activation of B cells and restricts the production of antibodies, including anti-donor isoagglutinin antibody. Recently, the regimen that combines rituximab with basiliximab in ABOi LDLT has been questioned<sup>[4]</sup>.

### Splenectomy

The spleen is a major antibody reservoir, containing large amounts of B cells and plasma cells. Splenectomy before ABOi LDLT to prevent antibody rebound is becoming more controversial. Most Asian centers use protocols with splenectomy in addition to other immunosuppressive measures<sup>[18]</sup>. However, several reports have shown that splenectomy does not offer any immunological advantage in ABOi LDLT. For example, Raut *et al.* observed no statistically significant differences in anti-A/B IgM and anti-A/B IgG titers between "splenectomy" and "non-splenectomy" groups<sup>[58]</sup>. Several reports have also shown that splenectomy may not offer any immunological advantage in ABOi LDLT. The clinical outcomes, including AMR, biliary complications, infections and survival, were also similar in the two groups<sup>[52,59,60]</sup>. An exception to this general rule are patients with imminent "small for size" syndrome, who have better outcomes after splenectomy<sup>[4,61]</sup>. Only two centers of the ones compared carried out splenectomy. In these centers, 21 of 23 patients had AMR occurrence (Table 1).

### Complications after ABOi LDLT

Biliary complications, which are still a major issue in ABOi LDLT, are likely related to immunological mechanisms. Donor blood group antigens are expressed for up to 150 d on the bile duct's epithelium after transplantation<sup>[59,62-64]</sup>. Song *et al.*<sup>[7]</sup> reported a higher incidence of biliary strictures, especially diffuse intrahepatic biliary strictures (DIHBS), in ABOi LDLT than in ABOc grafts. These strictures significantly affected the overall survival<sup>[15]</sup>. In Lee *et al.*<sup>[18]</sup>'s study, 5.6% of the patients developed complications, such as DIHBS, 2.1-5.2 mo post-transplant. In 2005, Kozaki *et al.*<sup>[41]</sup> showed that high preoperative anti-IgM iso-titer led to bile duct complications. High preoperative anti-IgG iso-titer led to hepatic necrosis and high postoperative anti-IgM and anti-IgG iso-titers lead to hepatic necrosis as well. Once hepatic necrosis occurred, no patient survived.

Biliary complications developed in 54%-82% of the ABOi allograft recipients, compared to 6% in

ABO matched allografts. Hepatic artery thrombosis also occurred in 24% of ABOi allografts<sup>[3,28]</sup>. In 2011, the meta-analysis of Wu *et al*<sup>[64]</sup> showed increased complications and AMR in ABOi LDLT, as well.

Another complication, such as the “small for size” syndrome in ABOi LDLT, can be avoided *via* a new dual split technique from Asia<sup>[65]</sup>. Dual LDLT with ABOi and ABOc grafts is a feasible solution for simultaneously overcoming both the ABO blood group barrier and small-for-size graft.

## CONCLUSION

Since 2010, no new techniques in ABOi LDLT have been reported in medical journals, but the treatment options have been refined. The outcomes of ABOi LDLT are still inferior to those of ABO-compatible and identical LDLTs, and anti-A/B antibodies reappear after the transplant. However, due to refined treatment strategies, ABOi LDLT is a feasible option today and is almost free from severe complications. We compared the regimens of 11 transplant centers, as well as their outcomes from 2010 to the present. The best improvement in outcomes next to PTPs has been observed with the prophylactic use of rituximab more than one week before ABOi LDLT. Although each center treats its patients with its own scheme, the transplant results are homogeneous. In our center, we have had positive experiences starting quadruple immunosuppression with basiliximab before transplantation. We also use TPE or IA and reduce the iso-titer at least down to 1:8 prior to transplantation. If the iso-titer rises again afterward, we mainly perform TPE.

A new approach for overcoming both the ABO blood group barrier and small-for-size grafts seems to be the dual split LDLT with ABOi and ABOc grafts that has been conducted in Asia.

Still, ABOi graft survival in adults is poorly understood. Neither is the emergence of *de novo* anti-A/B, nor their impact. Graft accommodation gives a possible explanation for ABOi graft survival in the presence of donor specific antibody titers.

In the long term, iso-titer rebound prevention might be necessary to lower the risk of iso-titer mediated rejection even further. However, no specific medication is available yet to meet this need.

## REFERENCES

- Rydberg L. ABO-incompatibility in solid organ transplantation. *Transfus Med* 2001; **11**: 325-342 [PMID: 11532188 DOI: 10.1046/j.1365-3148.2001.00313.x]
- Gugenheim J, Samuel D, Reynes M, Bismuth H. Liver transplantation across ABO blood group barriers. *Lancet* 1990; **336**: 519-523 [PMID: 1975036 DOI: 10.1016/0140-6736(90)92082-S]
- Farges O, Kalil AN, Samuel D, Saliba F, Arulnaden JL, Debat P, Bismuth A, Castaing D, Bismuth H. The use of ABO-incompatible grafts in liver transplantation: a life-saving procedure in highly selected patients. *Transplantation* 1995; **59**: 1124-1133 [PMID: 7732558 DOI: 10.1097/00007890-199504270-00009]
- Egawa H, Teramukai S, Haga H, Tanabe M, Mori A, Ikegami T, Kawagishi N, Ohdan H, Kasahara M, Umehita K. Impact of rituximab desensitization on blood-type-incompatible adult living donor liver transplantation: a Japanese multicenter study. *Am J Transplant* 2014; **14**: 102-114 [PMID: 24279828 DOI: 10.1111/ajt.12520]
- Demetris AJ, Jaffe R, Tzakis A, Ramsey G, Todo S, Belle S, Esquivel C, Shapiro R, Markus B, Mroczek E. Antibody-mediated rejection of human orthotopic liver allografts. A study of liver transplantation across ABO blood group barriers. *Am J Pathol* 1988; **132**: 489-502 [PMID: 3046369]
- Goralczyk AD, Obed A, Schnitzbauer A, Doenecke A, Tsui TY, Scherer MN, Ramadori G, Lorf T. Adult Living Donor Liver Transplantation with ABO-Incompatible Grafts: A German Single Center Experience. *J Transplant* 2009; **2009**: 759581 [PMID: 20148072 DOI: 10.1155/2009/759581]
- Ravn V, Dabelsteen E. Tissue distribution of histo-blood group antigens. *APMIS* 2000; **108**: 1-28 [PMID: 10698081 DOI: 10.1034/j.1600-0463.2000.d01-1.x]
- Mendes M, Ferreira AC, Ferreira A, Remédio F, Aires I, Cordeiro A, Mascarenhas A, Martins A, Pereira P, Gloria H, Perdigoto R, Veloso J, Ferreira P, Oliveira J, Silva M, Barroso E, Nolasco F. ABO-incompatible liver transplantation in acute liver failure: a single Portuguese center study. *Transplant Proc* 2013; **45**: 1110-1115 [PMID: 23622639 DOI: 10.1016/j.transproceed.2013.02.012]
- Crew RJ, Ratner LE. ABO-incompatible kidney transplantation: current practice and the decade ahead. *Curr Opin Organ Transplant* 2010; **15**: 526-530 [PMID: 20613520 DOI: 10.1097/MOT.0b013e32833bfba]
- Reding R, Veyckemans F, de Ville de Goyet J, de Hemptinne B, Carlier M, Van Obbergh L, Moulin D, Reynaert M, Latinne D, Vraux H. ABO-incompatible orthotopic liver allografting in urgent indications. *Surg Gynecol Obstet* 1992; **174**: 59-64 [PMID: 1729752]
- Starzl TE, Koep LJ, Halgrimson CG, Hood J, Schroter GPJ, Porter KA, Weil R. Fifteen years of clinical transplantation. *Gastroenterology* 1979; **77**: 375-88
- Stewart ZA, Locke JE, Montgomery RA, Singer AL, Cameron AM, Segev DL. ABO-incompatible deceased donor liver transplantation in the United States: a national registry analysis. *Liver Transpl* 2009; **15**: 883-893 [PMID: 19642117 DOI: 10.1002/lt.21723]
- Broelsch CE, Malagó M, Testa G, Valentin Gamazo C. Living donor liver transplantation in adults: outcome in Europe. *Liver Transpl* 2000; **6**: S64-S65 [PMID: 11084088 DOI: 10.1053/jlts.2000.19015]
- Schumann A, Fiedler M, Beckebaum S, Cinnati VR, Herzer K, Lenz V, Witzke O, Paul A, Roggendorf M, Horn PA, Lindemann M. Donor- and recipient-derived immunity in ABO incompatible living-related liver transplantation. *Hum Immunol* 2015; **76**: 631-635 [PMID: 26394233 DOI: 10.1016/j.humimm.2015.09.008]
- Troisi R, Noens L, Montalti R, Ricciardi S, Philippé J, Praet M, Conoscitore P, Centra M, de Hemptinne B. ABO-mismatch adult living donor liver transplantation using antigen-specific immunoadsorption and quadruple immunosuppression without splenectomy. *Liver Transpl* 2006; **12**: 1412-1417 [PMID: 16528717 DOI: 10.1002/lt.20727]
- Yilmaz S, Aydin C, Isik B, Kayaalp C, Yilmaz M, Ara C, Kutlu R, Bayindir Y, Ersan V. ABO-incompatible liver transplantation in acute and acute-on-chronic liver failure. *Hepatogastroenterology* 2013; **60**: 1189-1193 [PMID: 23478144 DOI: 10.5754/hge11289]
- Soin AS, Raut V, Mohanka R, Rastogi A, Goja S, Balachandran M, Saigal S, Saraf N, Bhangui P, Sumana KR, Singla P, Srinivasan T, Choudhary N, Tiwari A, Raina V, Govil D, Mohan N, Vohra V. Use of ABO-incompatible grafts in living donor liver transplantation—first report from India. *Indian J Gastroenterol* 2014; **33**: 72-76 [PMID: 24369388 DOI: 10.1007/s12664-013-0424-0]
- Lee SG. A complete treatment of adult living donor liver transplantation: a review of surgical technique and current challenges to expand indication of patients. *Am J Transplant* 2015; **15**: 17-38

- [PMID: 25358749 DOI: 10.1111/ajt.12907]
- 19 **Egawa H**, Tanabe K, Fukushima N, Date H, Sugitani A, Haga H. Current status of organ transplantation in Japan. *Am J Transplant* 2012; **12**: 523-530 [PMID: 22054061 DOI: 10.1111/j.1600-6143.2011.03822.x]
  - 20 **Kim JM**, Kwon CH, Joh JW, Kang ES, Park JB, Lee JH, Kim SJ, Paik SW, Lee SK, Kim DW. ABO-incompatible living donor liver transplantation is suitable in patients without ABO-matched donor. *J Hepatol* 2013; **59**: 1215-1222 [PMID: 23928408 DOI: 10.1016/j.jhep.2013.07.035]
  - 21 **Tanabe M**, Kawachi S, Obara H, Shinoda M, Hibi T, Kitagawa Y, Wakabayashi G, Shimazu M, Kitajima M. Current progress in ABO-incompatible liver transplantation. *Eur J Clin Invest* 2010; **40**: 943-949 [PMID: 20636381 DOI: 10.1111/j.1365-2362.2010.02339.x]
  - 22 **Egawa H**, Ohdan H, Haga H, Tsuruyama T, Oike F, Uemoto S, Ozawa K. Current status of liver transplantation across ABO blood-type barrier. *J Hepatobiliary Pancreat Surg* 2008; **15**: 131-138 [PMID: 18392705 DOI: 10.1007/s00534-007-1298-2]
  - 23 **Kasahara M**, Umeshita K, Inomata Y, Uemoto S. Long-term outcomes of pediatric living donor liver transplantation in Japan: an analysis of more than 2200 cases listed in the registry of the Japanese Liver Transplantation Society. *Am J Transplant* 2013; **13**: 1830-1839 [PMID: 23711238 DOI: 10.1111/ajt.12276]
  - 24 **West LJ**. Antibodies and ABO-incompatibility in pediatric transplantation. *Pediatr Transplant* 2011; **15**: 778-783 [PMID: 22111997 DOI: 10.1111/j.1399-3046.2011.01579.x]
  - 25 **Gurevich M**, Guy-Viterbo V, Janssen M, Stephenne X, Smets F, Sokal E, Lefebvre C, Balligand JL, Pirotte T, Veyckemans F, Clapuyt P, Menten R, Dumitriu D, Danse E, Annet L, Clety SC, Detaille T, Latinne D, Sempoux C, Laterre PF, de Magnée C, Lerut J, Reding R. Living Donor Liver Transplantation in Children: Surgical and Immunological Results in 250 Recipients at Université Catholique de Louvain. *Ann Surg* 2015; **262**: 1141-1149 [PMID: 25563870 DOI: 10.1097/SLA.0000000000001094]
  - 26 **Sanada Y**, Kawano Y, Miki A, Aida J, Nakamura K, Shimomura N, Ishikawa N, Arai T, Hirata Y, Yamada N, Okada N, Wakiya T, Ihara Y, Urahashi T, Yasuda Y, Takubo K, Mizuta K. Maternal grafts protect daughter recipients from acute cellular rejection after pediatric living donor liver transplantation for biliary atresia. *Transpl Int* 2014; **27**: 383-390 [PMID: 24472036 DOI: 10.1111/tri.12273]
  - 27 **Nijagal A**, Fleck S, Hills NK, Feng S, Tang Q, Kang SM, Rosenthal P, MacKenzie TC. Decreased risk of graft failure with maternal liver transplantation in patients with biliary atresia. *Am J Transplant* 2012; **12**: 409-419 [PMID: 22221561 DOI: 10.1111/j.1600-6143.2011.03895.x]
  - 28 **Schukfeh N**, Lenz V, Metzelder ML, Paul A, Mathe Z, Kathemann S, Hoyer PF, Dohna-Schwake C, Gerner P. First case studies of successful ABO-incompatible living-related liver transplantation in infants in Germany. *Eur J Pediatr Surg* 2015; **25**: 77-81 [PMID: 25555094 DOI: 10.1055/s-0034-1387936]
  - 29 **Okada N**, Sanada Y, Hirata Y, Yamada N, Wakiya T, Ihara Y, Urahashi T, Miki A, Kaneda Y, Sasanuma H, Fujiwara T, Sakuma Y, Shimizu A, Hyodo M, Yasuda Y, Mizuta K. The impact of rituximab in ABO-incompatible pediatric living donor liver transplantation: the experience of a single center. *Pediatr Transplant* 2015; **19**: 279-286 [PMID: 25689881 DOI: 10.1111/petr.12445]
  - 30 **Maitta RW**, Choate J, Emre SH, Luczycki SM, Wu Y. Emergency ABO-incompatible liver transplant secondary to fulminant hepatic failure: outcome, role of TPE and review of the literature. *J Clin Apher* 2012; **27**: 320-329 [PMID: 22833397 DOI: 10.1002/jca.21244]
  - 31 **Shen T**, Lin BY, Jia JJ, Wang ZY, Wang L, Ling Q, Geng L, Yan S, Zheng SS. A modified protocol with rituximab and intravenous immunoglobulin in emergent ABO-incompatible liver transplantation for acute liver failure. *Hepatobiliary Pancreat Dis Int* 2014; **13**: 395-401 [PMID: 25100124 DOI: 10.1016/S1499-3872(14)60268-X]
  - 32 **Shinoda M**, Obara H, Kitago M, Hibi T, Abe Y, Yagi H, Matsubara K, Yamada Y, Fujino A, Hoshino K, Kuroda T, Tanabe M, Kitagawa Y. Emergency adult living donor liver transplantation using ABO-incompatible donor for acute liver failure, HPB. Conference: 5th Biennial Congress of the Asian-Pacific Hepato-Pancreato-Biliary Association Singapore Singapore; 2015: 206
  - 33 **Nakamura Y**, Hama K, Iwamoto H, Yokoyama T, Kihara Y, Konno O, Jojima Y, Shimazu M. Long-term recurrence-free survival after liver transplantation from an ABO-incompatible living donor for treatment of hepatocellular carcinoma exceeding Milano criteria in a patient with hepatitis B virus cirrhosis: a case report. *Transplant Proc* 2012; **44**: 565-569 [PMID: 22410070 DOI: 10.1016/j.transproceed.2012.01.029]
  - 34 **Lee SD**, Kim SH, Kong SY, Kim YK, Park SJ. Kinetics of B, T, NK lymphocytes and isoagglutinin titers in ABO incompatible living donor liver transplantation using rituximab and basiliximab. *Transpl Immunol* 2015; **32**: 29-34 [PMID: 25449537 DOI: 10.1016/j.trim.2014.11.216]
  - 35 **Lee J**, Lee JG, Lee JJ, Kim MS, Ju MK, Choi GH, Choi JS, Kim SI, Joo DJ. Results of ABO-incompatible liver transplantation using a simplified protocol at a single institution. *Transplant Proc* 2015; **47**: 723-726 [PMID: 25891718 DOI: 10.1016/j.transproceed.2015.02.004]
  - 36 **Kim JD**, Choi DL, Han YS. Fourteen successful consecutive cases of ABO-incompatible living donor liver transplantation: new simplified intravenous immunoglobulin protocol without local infusion therapy. *Transplant Proc* 2014; **46**: 754-757 [PMID: 24767341 DOI: 10.1016/j.transproceed.2013.11.100]
  - 37 **Warner PR**, Nester TA. ABO-incompatible solid-organ transplantation. *Am J Clin Pathol* 2006; **125** Suppl: S87-S94 [PMID: 16830960 DOI: 10.1309/8w4x9h6f8fclcgx]
  - 38 **Toso C**, Al-Qahtani M, Alsaif FA, Bigam DL, Meeberg GA, James Shapiro AM, Bain VG, Kneteman NM. ABO-incompatible liver transplantation for critically ill adult patients. *Transpl Int* 2007; **20**: 675-681 [PMID: 17521384 DOI: 10.1111/j.1432-2277.2007.00492.x]
  - 39 **Raut V**, Uemoto S. Management of ABO-incompatible living-donor liver transplantation: past and present trends. *Surg Today* 2011; **41**: 317-322 [PMID: 21365409 DOI: 10.1007/s00595-010-4437-3]
  - 40 **Haga H**, Egawa H, Fujimoto Y, Ueda M, Miyagawa-Hayashino A, Sakurai T, Okuno T, Koyanagi I, Takada Y, Manabe T. Acute humoral rejection and C4d immunostaining in ABO blood type-incompatible liver transplantation. *Liver Transpl* 2006; **12**: 457-464 [PMID: 16498648 DOI: 10.1002/lt.20652]
  - 41 **Kozaki K**, Egawa H, Kasahara M, Oike F, Yoshizawa A, Fukatsu A, Tanaka K. Therapeutic strategy and the role of apheresis therapy for ABO incompatible living donor liver transplantation. *Ther Apher Dial* 2005; **9**: 285-291 [PMID: 16076368 DOI: 10.1111/j.1744-9987.2005.00304.x]
  - 42 **Ward DM**. Conventional apheresis therapies: a review. *J Clin Apher* 2011; **26**: 230-238 [PMID: 21882233 DOI: 10.1002/jca.20302]
  - 43 **Schwartz J**, Winters JL, Padmanabhan A, Balogun RA, Delaney M, Linenberger ML, Szczepiorkowski ZM, Williams ME, Wu Y, Shaz BH. Guidelines on the use of therapeutic apheresis in clinical practice-evidence-based approach from the Writing Committee of the American Society for Apheresis: the sixth special issue. *J Clin Apher* 2013; **28**: 145-284 [PMID: 23868759 DOI: 10.1002/jca.21276]
  - 44 **Hanto DW**, Fecteau AH, Alonso MH, Valente JF, Whiting JF. ABO-incompatible liver transplantation with no immunological graft losses using total plasma exchange, splenectomy, and quadruple immunosuppression: evidence for accommodation. *Liver Transpl* 2003; **9**: 22-30 [PMID: 12514769 DOI: 10.1053/jlts.2003.50011]
  - 45 **Wahrmann M**, Schiemann M, Marinova L, Körmöczy GF, Derfler K, Fehr T, Stussi G, Böhmig GA. Anti-A/B antibody depletion by semiselective versus ABO blood group-specific immunoadsorption. *Nephrol Dial Transplant* 2012; **27**: 2122-2129 [PMID: 22086972 DOI: 10.1093/ndt/gfr610]
  - 46 **Tiwari AK**, Pandey P, Aggarwal G, Dara RC, Rawat G, Raina V, Soin AS. Cascade plasmapheresis (CP) as a preconditioning regime in ABO-incompatible live related donor liver transplants (ABOi-LDLT). *Transplant Res* 2014; **3**: 17 [PMID: 25232469 DOI: 10.1186/2047-1440-3-17]
  - 47 **Urbani L**, Mazzoni A, Bianco I, Grazzini T, De Simone P, Catalano G, Montin U, Petruccioli S, Morelli L, Campani D, Pollina L, Biancofiore

- G, Bindi L, Tascini C, Menichetti F, Scatena F, Filipponi F. The role of immunomodulation in ABO-incompatible adult liver transplant recipients. *J Clin Apher* 2008; **23**: 55-62 [PMID: 18186527 DOI: 10.1002/jca.20156]
- 48 **Ikegami T**, Taketomi A, Soejima Y, Yoshizumi T, Uchiyama H, Harada N, Iguchi T, Hashimoto N, Maehara Y. Rituximab, IVIG, and plasma exchange without graft local infusion treatment: a new protocol in ABO incompatible living donor liver transplantation. *Transplantation* 2009; **88**: 303-307 [PMID: 19667930 DOI: 10.1097/TP.0b013e3181adcae6]
- 49 **Morioka D**, Togo S, Kumamoto T, Takeda K, Matsuo K, Inayama Y, Yamanaka S, Tanaka K, Endo I, Maegawa J, Shimada H. Six consecutive cases of successful adult ABO-incompatible living donor liver transplantation: a proposal for grading the severity of antibody-mediated rejection. *Transplantation* 2008; **85**: 171-178 [PMID: 18212620 DOI: 10.1097/TP.0b013e31815e9672]
- 50 **Uchiyama H**, Mano Y, Taketomi A, Soejima Y, Yoshizumi T, Ikegami T, Shirabe K, Maehara Y. Kinetics of anti-blood type isoagglutinin titers and B lymphocytes in ABO-incompatible living donor liver transplantation with rituximab and plasma exchange. *Transplantation* 2011; **92**: 1134-1139 [PMID: 21946174 DOI: 10.1097/TP.0b013e318231e9f8]
- 51 **Tanabe M**, Shimazu M, Wakabayashi G, Hoshino K, Kawachi S, Kadomura T, Seki H, Morikawa Y, Kitajima M. Intraportal infusion therapy as a novel approach to adult ABO-incompatible liver transplantation. *Transplantation* 2002; **73**: 1959-1961 [PMID: 12131697]
- 52 **Song GW**, Lee SG, Hwang S, Ahn CS, Moon DB, Kim KH, Ha TY, Jung DH, Park GC, Namgung JM, Park CS, Park HW, Park YH. Successful experiences of ABO-incompatible adult living donor liver transplantation in a single institute: no immunological failure in 10 consecutive cases. *Transplant Proc* 2013; **45**: 272-275 [PMID: 23375314 DOI: 10.1016/j.transproceed.2012.06.079]
- 53 **Tyden G**, Donauer J, Wadström J, Kumlien G, Wilpert J, Nilsson T, Genberg H, Pisarski P, Tufveson G. Implementation of a Protocol for ABO-incompatible kidney transplantation--a three-center experience with 60 consecutive transplantations. *Transplantation* 2007; **83**: 1153-1155 [PMID: 17496528 DOI: 10.1097/01.tp.0000262570.18117.55]
- 54 **Monteiro I**, McLoughlin LM, Fisher A, de la Torre AN, Koneru B. Rituximab with plasmapheresis and splenectomy in abo-incompatible liver transplantation. *Transplantation* 2003; **76**: 1648-1649 [PMID: 14702545 DOI: 10.1097/01.TP.0000082723.02477.87]
- 55 **Usuda M**, Fujimori K, Koyamada N, Fukumori T, Sekiguchi S, Kawagishi N, Akamatsu Y, Enomoto Y, Satoh K, Satoh A, Ishida K, Moriya T, Satomi S. Successful use of anti-CD20 monoclonal antibody (rituximab) for ABO-incompatible living-related liver transplantation. *Transplantation* 2005; **79**: 12-16 [PMID: 15714163]
- 56 **Cai J**, Terasaki PI. Induction immunosuppression improves long-term graft and patient outcome in organ transplantation: an analysis of United Network for Organ Sharing registry data. *Transplantation* 2010; **90**: 1511-1515 [PMID: 21057388 DOI: 10.1097/TP.0b013e3181fecfcb]
- 57 **Rostaing L**, Saliba F, Calmus Y, Dharancy S, Boillot O. Review article: use of induction therapy in liver transplantation. *Transplant Rev (Orlando)* 2012; **26**: 246-260 [PMID: 22863028 DOI: 10.1016/j.tre.2012.06.002]
- 58 **Raut V**, Mori A, Kaido T, Ogura Y, Taku I, Nagai K, Sasaki N, Endo K, Hata T, Yagi S, Egawa H, Uemoto S. Splenectomy does not offer immunological benefits in ABO-incompatible liver transplantation with a preoperative rituximab. *Transplantation* 2012; **93**: 99-105 [PMID: 22094955 DOI: 10.1097/TP.0b013e318239e8e4]
- 59 **Lee SD**, Kim SH, Kong SY, Kim YK, Lee SA, Park SJ. ABO-incompatible living donor liver transplantation without graft local infusion and splenectomy. *HPB (Oxford)* 2014; **16**: 807-813 [PMID: 24467804 DOI: 10.1111/hpb.12215]
- 60 **Zhou J**, Ju W, Yuan X, Jiao X, Zhu X, Wang D, He X. ABO-incompatible liver transplantation for severe hepatitis B patients. *Transpl Int* 2015; **28**: 793-799 [PMID: 25630359 DOI: 10.1111/tri.12531]
- 61 **Ogura Y**, Hori T, El Moghazy WM, Yoshizawa A, Oike F, Mori A, Kaido T, Takada Y, Uemoto S. Portal pressure & It; 15 mm Hg is a key for successful adult living donor liver transplantation utilizing smaller grafts than before. *Liver Transpl* 2010; **16**: 718-728 [PMID: 20517905 DOI: 10.1002/lt.22059]
- 62 **Sanchez-Urdazpal L**, Batts KP, Gores GJ, Moore SB, Sterioff S, Wiesner RH, Krom RA. Increased bile duct complications in liver transplantation across the ABO barrier. *Ann Surg* 1993; **218**: 152-158 [PMID: 8342994]
- 63 **Nishida S**, Nakamura N, Kadono J, Komokata T, Sakata R, Madariaga JR, Tzakis AG. Intrahepatic biliary strictures after liver transplantation. *J Hepatobiliary Pancreat Surg* 2006; **13**: 511-516 [PMID: 17139424 DOI: 10.1007/s00534-005-1081-1]
- 64 **Wu J**, Ye S, Xu X, Xie H, Zhou L, Zheng S. Recipient outcomes after ABO-incompatible liver transplantation: a systematic review and meta-analysis. *PLoS One* 2011; **6**: e16521 [PMID: 21283553 DOI: 10.1371/journal.pone.0016521]
- 65 **Song GW**, Lee SG, Hwang S, Kim KH, Ahn CS, Moon DB, Ha TY, Kwon SW, Ko GY, Kim KW. Dual living donor liver transplantation with ABO-incompatible and ABO-compatible grafts to overcome small-for-size graft and ABO blood group barrier. *Liver Transpl* 2010; **16**: 491-498 [PMID: 20222051 DOI: 10.1002/lt.22016]
- 66 **Song GW**, Lee SG, Hwang S, Kim KH, Ahn CS, Moon DB, Ha TY, Jung DH, Park GC, Kim WJ, Sin MH, Yoon YI, Kang WH, Kim SH, Tak EY. ABO-Incompatible Adult Living Donor Liver Transplantation Under the Desensitization Protocol With Rituximab. *Am J Transplant* 2016; **16**: 157-170 [PMID: 26372830 DOI: 10.1111/ajt.13444]
- 67 **Yasuda M**, Ikegami T, Imai D, Wang H, Bekki Y, Itoh S, Yoshizumi T, Soejima Y, Shirabe K, Maehara Y. The changes in treatment strategies in ABOi living donor liver transplantation for acute liver failure. *J Med Invest* 2015; **62**: 184-187 [PMID: 26399345 DOI: 10.2152/jmi.62.184]
- 68 **Lee CF**, Cheng CH, Wang YC, Soong RS, Wu TH, Chou HS, Wu TJ, Chan KM, Lee CS, Lee WC. Adult Living Donor Liver Transplantation Across ABO-Incompatibility. *Medicine (Baltimore)* 2015; **94**: e1796 [PMID: 26496313 DOI: 10.1097/MD.0000000000001796]

P- Reviewer: Hilmi I, Karatapanis S S- Editor: Qi Y L- Editor: A  
E- Editor: Wu HL





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](mailto:bpgoffice@wjgnet.com)

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

<http://www.wjgnet.com>

