

# Adult Living Donor Liver Re-Transplant Following Late Pediatric Liver Transplant Failure: A Case Report

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
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**Conflict of interest:** None declared

**Patient:** Male, 14  
**Final Diagnosis:** Primary sclerosing cholangitis  
**Symptoms:** Abdominal and/or epigastric pain • jaundice  
**Medication:** —  
**Clinical Procedure:** Liver transplantation twice • splenic artery embolization  
**Specialty:** Transplantology

**Objective:** Unusual clinical course  
**Background:** Re-transplant of a late failing living donor liver graft using another graft from another living donor is a rare occurrence and is associated with high mortality due to the complexity of the procedure. There are only a few such case series reported in the literature, mainly from South Asia and Japan, where living donor liver transplant is commonly performed, and there are no such reports from Western countries.  
**Case Report:** This is a case of living donor liver re-transplant for a 28-year-old recipient whose graft failed 14 years after his primary living donor transplant for primary sclerosing cholangitis. The second transplant was a right-lobe graft obtained from a living donor. The presence of portal vein thrombosis in the setting of high Model for End-Stage Liver Disease (MELD) score added to the complexity of the case. The procedure was concluded successfully with an uneventful post-operative course. The patient was discharged 3 weeks after the procedure. One-year follow-up showed a normally functioning graft.  
**Conclusions:** Successfully re-transplanting a patient with a failing living donor liver graft from a living donor is possible if sufficient surgical expertise is available and the risk and benefit are carefully considered. This is especially important in countries where a cadaveric graft is difficult to obtain due to organ scarcity.

**MeSH Keywords:** Graft Rejection • Liver Transplantation • Living Donors

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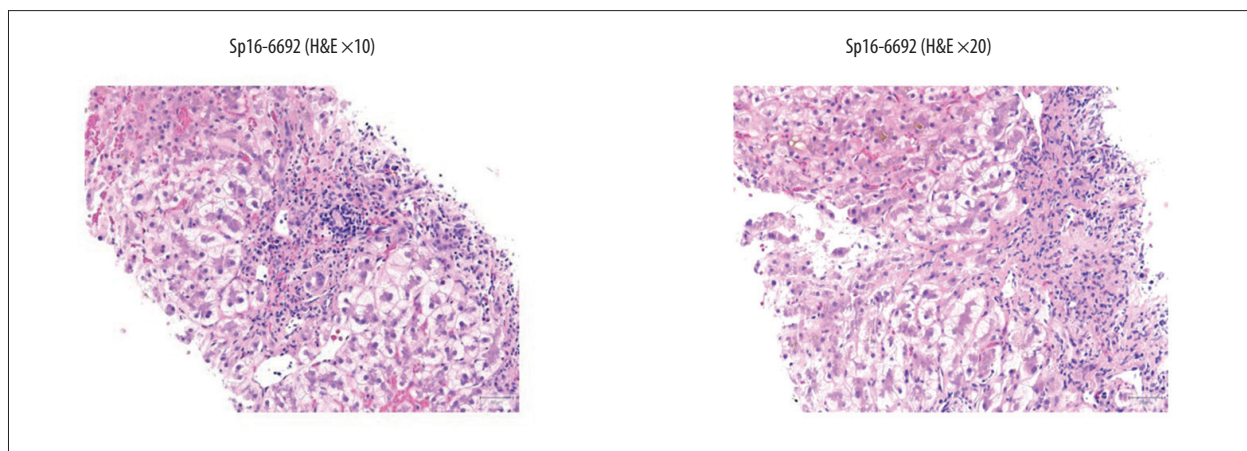
## Background

Liver transplantation (OLT) became the standard of care for patients with end-stage liver disease (ESLD) since its introduction in 1967. Despite all the technical pre- and post-operative advances, graft failure following OLT occurs in 10–20% of cases, necessitating re-transplantation [1–3]. Although re-transplantation (re-OLT) can be successful [4], the outcome is inferior to primary OLT [5]; which poses an ethical dilemma in the era of cadaveric organ shortage [6,7]. The remarkable advances in living donor liver transplant (LDLT) partially alleviated the organ shortage crisis, especially in countries where deceased donor liver transplant (DDLT) is done on a small scale as a result of organ scarcity. Re-transplantation utilizing an organ from a living donor (LDLT) avoids the ethical dilemma of depriving a liver from the donor pool and giving it to a recipient who may have inferior outcome; however, this is associated with technical difficulties which translate into a poor outcome, especially if done in the setting of high MELD score (model for end-stage liver disease). As a result, re-transplanting for a late failure of LDLT utilizing a living donor is a rare occurrence. In one of the biggest LDLT centers, with a total of 1312 LDLTs performed over 25 years, there were only 14 re-OLTs after primary LDLT; of which 3 were with a living allograft. Outcomes were poor, with a 1-year mortality rate of 43.5% [8,9]. In this report we describe a case of living donor liver re-transplant for late liver failure secondary to liver fibrosis, progressive cholestasis, and acute portal vein thrombosis in a patient who underwent LDLT 14 years earlier. The degree of adhesion was unexpectedly not severe, permitting safe re-OLT, contrary to what was reported in the literature.

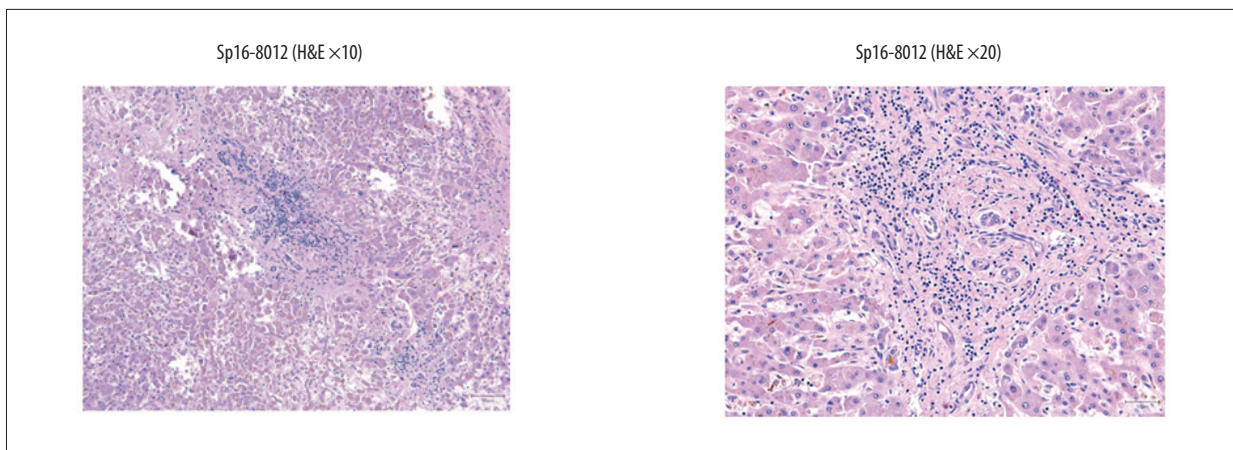
## Case Report

The patient was 28-year-old man who underwent living unrelated liver transplant in 2003 at the age of 14 at Prince Sultan Military Medical City (PSMMC). His original disease was progressive failure secondary to primary sclerosing cholangitis (PSC). The graft implanted was a left lateral segment with Roux-en-Y hepaticojejunostomy. He had an uneventful early post-operative course, with stable graft function on Tacrolimus-based immunosuppressive regimen and low-dose steroids. In 2009 (6 years after his transplant), he started to have a persistent rise in his liver enzymes; mainly cholestatic enzymes. Doppler ultrasound showed a normal, well-perfused graft with patent vessels. He was diagnosed with acute cellular rejection (AC) and was treated with adjustment of his immunosuppression, which resulted in normalization of his liver enzymes. In 2012 (9 years after his transplant), he presented with persistent hyperbilirubinemia with elevated liver enzymes. At that time, magnetic resonance imaging (MRI) and Doppler ultrasonography showed intra-hepatic biliary dilatation with focal stenosis at the level of hepaticojejunostomy anastomosis, which was managed with temporary percutaneous transhepatic biliary dilatation and subsequent surgical revision of the anastomosis. An intra-operative liver biopsy showed mild portal fibrosis (Figure 1). His graft was subsequently stable, based on liver enzyme follow-up data.

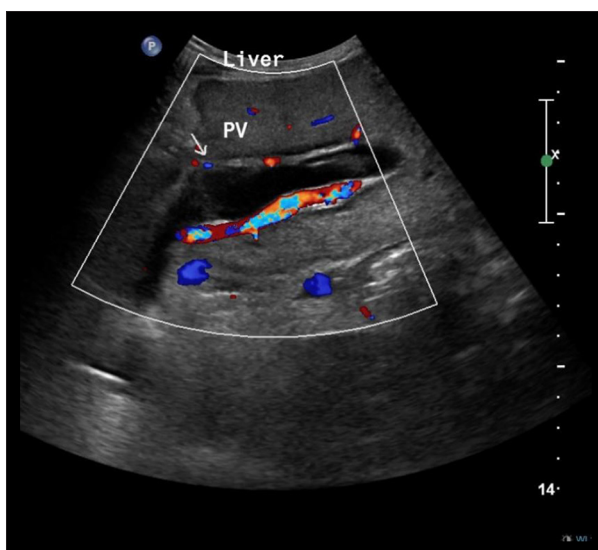
At follow-up in 2015 (12 years after his initial transplant), his liver enzymes were elevated, with pancytopenia. Doppler sonography revealed an enlarged graft with presence of large splenomegaly, indicative of portal hypertension. Because of his severe pancytopenia, he underwent splenic artery embolization; consequently, he had abdominal pain and deterioration of his clinical condition, associated with marked elevation in liver enzymes. A liver biopsy showed progressive portal



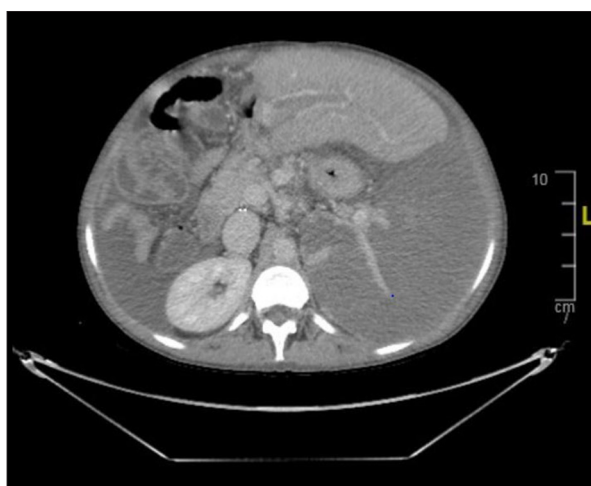
**Figure 1.** Sections showing liver tissue with portal fibrosis, inflammation, and ductular reaction. There are canalicular bile plugs and periportal hydropic swelling of hepatocytes with cytoplasmic clumping and Mallory bodies. No significant lobular inflammation is seen.



**Figure 2.** Portal fibrosis and bile ductular reaction with lymphoplasmacytic portal inflammation. There is an extensive hepatocanicular cholestasis with mild lobular inflammation.



**Figure 3.** Doppler ultrasound showing intra-hepatic portal vein thrombosis.



**Figure 4.** Computerized tomography (CT) scan of the liver in the venous phase showing intra-hepatic portal vein thrombosis in the graft with enlarged spleen and splenic vein thrombosis with multiple collaterals.

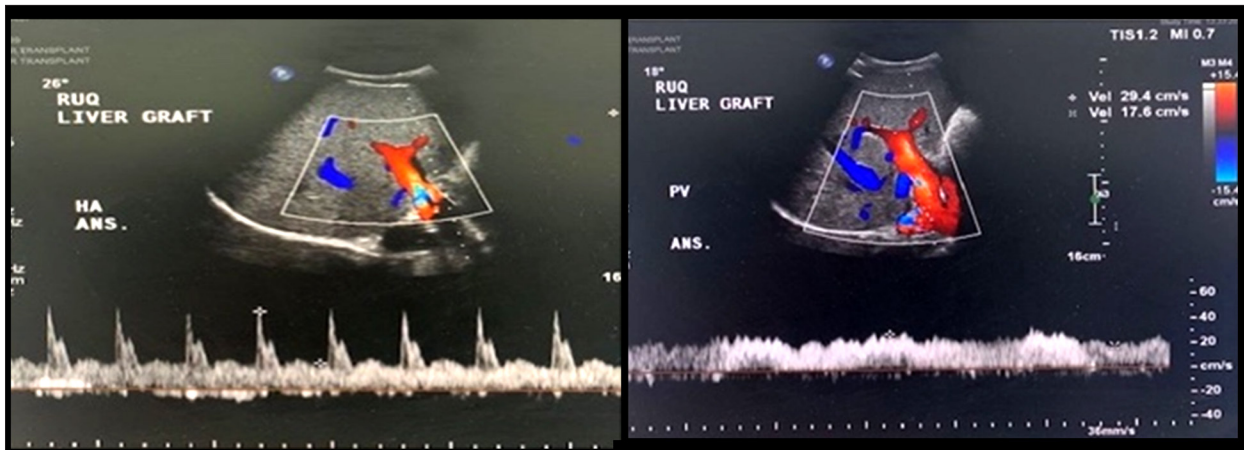
fibrosis and severe cholestasis (Figure 2). Doppler ultrasound and computed tomography showed a complete intra-hepatic portal vein thrombosis (Figures 3, 4), but the extra-hepatic portal vein was patent (Figure 5). Based on the clinical presentation and derangement of liver function, allograft failure was diagnosed and the decision was made to proceed with liver transplant. His MELD score at that time was above 30 (bilirubin: 989  $\mu\text{mol/l}$ , INR 2.3, and creatinine 90  $\mu\text{mol/l}$ ).

An ABO-compatible living donor was evaluated and was suitable for right liver lobe donation. Seven months after the failure of his first graft, the patient underwent liver transplant on July 2016. The graft obtained from the donor was a right lobe without middle hepatic vein, weighing 750 grams, with a graft-to-patient weight ratio of 1.1. As expected, in the recipient side there were dense adhesions in the epigastric region,



**Figure 5.** CT scan of the graft showing extra-hepatic portal vein patency with intra-hepatic left portal vein thrombosis. The spleen is enlarged with splenic vein thrombosis.





**Figure 6.** Doppler ultrasound of the second graft showing normal flow and velocities of portal vein and hepatic artery.

**Table 1.** Laboratory investigations before and after second liver transplant.

Date	Bilirubin	ALP	ALT	INR	Creatinine	Comments
23/7/2016	804	107	96	3.3	81	Immediately pre-transplant
24/7/2016	432	97	97	4.2	89	
25/7/2016	341	38	194		159	Immediately post-transplant
26/7/2016	263	36	148	2.2	210	
23/7/2017	10	163	31	1.1	91	1-year post-transplant

ALP – alkaline phosphatase; ALT – alanine aminotransferase; INR – international normalization ratio.

right upper quadrant, and liver hilum. There were mostly grade 2 adhesions (dense, non-vascularized) which needed sharp dissection, with resulting blood loss of around 1.4 L, requiring transfusion of 4 units of blood. The hepatectomy was completed and portal vein patency was ascertained. The graft was then implanted with portal to portal anastomosis, right hepatic vein to cava anastomosis, and right hepatic artery to right hepatic artery anastomosis. Biliary reconstruction was done with a fresh hepaticojejunostomy. The duration of surgery was 9 h. The cold ischemia time was 153 min and the warm ischemia was 37 min.

The patient had a stable immediate post-operative course and was extubated on the 3rd day after surgery. His immunosuppression regimen consisted of Tacrolimus (Prograf®) starting with 1 mg twice daily orally, and increasing the dose to maintain drug level at 8–10 ng/ml. Methylprednisolone 500 mg was given during the anhepatic phase, followed by 100 mg, tapered over 5 days to 20 mg of Prednisone (Delatstone®) orally. Infection prophylaxis was started with Valganciclovir hydrochloride (Valcyte®), Fluconazol (Diflucan®) and Cefoxitin (Mefoxin®) for viral, fungal, and bacterial infections, respectively. Other medications used during his stay in the ICU included midazolam, fentanyl, omeprazole, and albumin. There were no noticeable adverse effects related to these medications. Surveillance of

tissue and fluid cultures was done daily for the first 5 days and as clinically indicated. He stayed 3 weeks in the hospital, with subsequent outpatient follow-up. His post-operative Doppler study showed patent vessels with normal flow waves (Figure 6). One year after his re-transplant, he had a normally functioning graft (Table 1). The patient's compliance with immunosuppression was ascertained by stable Tacrolimus drug level and normal liver function test. Follow-up 2 years after his transplant showed satisfactory quality of life, as evident by his return to work as an office employee. The relevant events in this case are summarized in (Figure 7).

### Ethics approval

Both living donors were unrelated. Consent for donation was obtained as per the protocol of the liver transplant program at the Multi-Organ Transplant Center at PSMMC and in accordance with the regulations of the Saudi Center of Organ Transplantation (SCOT), which is the official body regulating organ transplantation and organ donation in the Kingdom of Saudi Arabia. Consent was obtained from the patient for reporting the case. Approval was obtained from the Institutional Research Board (IRB) of PSMMC.

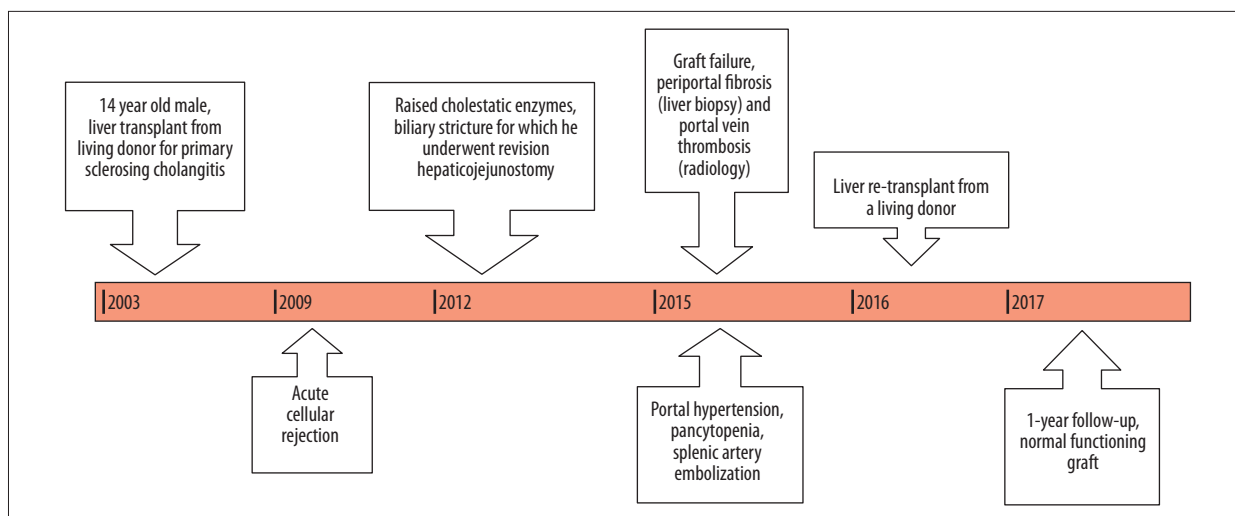


Figure 7. The patient's progress.

## Discussion

Most of the data we have on re-OLT are in the setting of DDLT [4–6]. Re-transplant with a deceased graft for failed living donor transplant was explored using data from the Organ Procurement and Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS). This retrospective analysis showed similar outcome when re-OLT was done from cadaveric donor, regardless of whether the first graft was from a living or a cadaveric donor [8].

In Asia, where LDLT is commonly practiced, re-OLT is not common. The 2 largest LDLT centers worldwide reported small number of cases over a long period of time. Re-transplantation for a late failure of a living donor graft utilizing a living donor is associated with inferior results [9], with a 1-year mortality rate of 43.5% [10]. This was attributed to the complexity of surgery as a result of severe adhesions formed after extended time from the primary surgery.

In a more recent study from Asan Medical Center, Korea, which is the largest LDLT center in the world, over 20 years only 55 cases were re-transplanted, of which 33 were done for late graft failure. The 1-year survival rate was only 50%. A significant mortality risk factor for late primary transplant failure was high bilirubin. The operative procedures were associated with longer operative time and more blood loss in the late primary graft failure patients [11].

In our case, re-OLT was performed 14 years after the initial surgery. Portal vein thrombosis, high bilirubin, and high MELD score added to the complexity of the case. The young age of the patient and the preservation of his renal function were

positive predictors of survival, which, among other factors, encouraged the surgical team to proceed with the re-OLT despite the potential risk.

In contrast to what is reported in the literature, the transplant was completed within a reasonable operative time with acceptable blood loss. Severe adhesions are the main factor increasing the complexity re-OLT. In our case, the adhesions encountered were mostly grade 2, which contributed to the success of the surgery. It follows that re-OLT should always be considered and that concerns about adhesion should not be a reason to deny patients from undergoing re-OLT. Being the first and only re-OLT in our program is a limitation to our recommending this approach. Assertion of the safety of re-OLT in this setting may be strengthened with more cases. The other limitation to this approach is availability of surgical expertise and set-up in such complicated cases.

## Conclusions

Re-transplant for a living donor liver transplant failing graft is associated with inferior survival, especially when done from a living donor. High MELD score, high bilirubin, and late graft failure are potential risk factors for mortality. Proceeding with living donor liver re-OLT can be successful, but risk factors should be considered carefully. Fear of encountering severe adhesions should not be a barrier to performing re-OLT.

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