MedCrave
Step into the World of Research

Journal of Liver Research, Disorders & Therapy

Review Article

Open Access

CrossMark

Combined heart and liver transplantation

Abstract

Combined heart and liver transplantation (CHLT) is a common procedure beneficial to the patients suffering from various cardiac and liver ailments, the most common being familial amyloidosis. The success rates of CHLT have been comparable but more sustainable over the heart only or liver only transplantation. Although there are many complications involving the dual organ transplantation, a critical choice of donors and recipients, correct timing of the transplantation with accurate surgical methodology, and sustained pre and post-operative care of the patients can determine the efficacy of the outcomes.

Keywords: combined heart, liver transplantation, familial hypercholesterolemia, simultaneous transplantation, end-stage liver, cardiac disease.

Volume 2 Issue 2 - 2016

Tasleem SH,[1] Jalal PK[2]
[1]Fellow in Hepatology and Liver Transplantation, USA
[2]Division of Gastroenterology and Hepatology and Liver Transplantation, USA

Correspondence: Syed H Tasleem, Fellow in Hepatology and Liver Transplantation, Baylor College of Medicine, Houston, 6620 Main Street, Suite 1450, Houston, TX, USA, 77030, Tel 281-854-8390, Fax 713-610-2479, Email dr.syedtasleem@gmail.com

Received: March 01, 2016 | **Published:** June 07, 2016

Abbreviations: CHLT, combined heart and liver transplantation; FAP, familial amyloid poly neuropathy; OLT, orthotopic liver transplant; OHT, orthotopic heart transplant; UNOS , united network for organ sharing; OPTN, organ procurement and transplantation network; HLT, heart-liver transplant; HRT, heart transplant; LIV, liver transplant; ECMO, extracorporeal membrane oxygenation; CHD, congenital heart disease; CAV, coronary allograft vasculopathy; DSA, donor-specific antibody; HLAs, human leukocyte antigens

Introduction

Combined heart and liver transplantation (CHLT) is a life saving surgical procedure that can potentially treat a variety of conditions such as familial amyloidosis, hemo chromatosis, restrictive cardiomyopathy and congenital heart disease with associated cardiac cirrhosis.[1–3] In the current medical scenario, although it is quite a common procedure, it is limited to only few centres around the globe (Table 1).[4] CHLT was first successfully performed in 1984 on a 6-year old girl with familial hypercholesterolemia and coronary artery disease with her unfortunate death after 10weeks.[5] There was another setback due to the demise of 2patients at the time of admission with complications of familial hypercholesterolemia and coronary artery disease in one and biliary hypoplasia and cardiomyopathy in another. Therefore, these findings led to the conclusion that the size of the organs might contribute to the risk of the recipient. Moreover, it was also suggested that simultaneous transplantation of the two organs from the same donor might have successful outcomes.[6] Since then, multi organ transplantation such as CHLT has seen tremendous success over the years, and often patients with Familial Amyloid Polyneuropathy (FAP) are treated with liver transplantation with successful outcomes. However, it should be pointed out that cardiac amyloidosis can lead to poor cardiac function, which ultimately can hamper the progress of liver transplantation. Therefore, these insights led to the simultaneous transplantation of heart and liver in order to avoid graft rejection.[7] In this review, we aim to update the findings from the past studies on CHLT to outline the current status of simultaneous heart and liver transplantation.

Table 1 Combined heart and liver transplants: survival and complications.[4]

Reporting year	No. of patients	Patients age (in years) and gender	Patients pre-operative health	Patients post-operative complications	Survival time/ survival rate	Reference
1984	1	6 (F)	FH	None	10 weeks	[5]
		(a) 6.5 (F)	(a) FH	(a) None	(a) 1 year until publication	
1985	3	(b) 2 (F)	(b)Cardiomyopathy and biliary hypoplasia.	(b) Low	(b) Died Post-operation	[6]
		(c) 17 (F)	(c) FH and bacterial endocarditis	(c) Cardiac output and acidosis Inferior wall infarction.	(c) Died Post-operation	
1990	3	6,17,2	FH, CAD, BH	NA	5 years and two <5 months	[8]
1995	2	33,61	FH, CAD, Congestive heart failure	NA	3.7 years, 1.7 years	[7]

Table Continued.....

Reporting year	No. of patients	Patients age (in years) and gender	Patients pre-operative health	Patients post-operative complications	Survival time/ survival rate	Reference
1996	4	21–35 (2F, 2M)	CF, BC	Pulmonary rejection and intrathoracic bleeding	1 death; 1.6-8.3 years	[9]
1999	3	39–47 (1F, 2M)		Hepatic and cardiac failure	1,3,and 4 years	[10]
1999	3	(a) 47 (M) (b) 39 (F) (c) 45 (M)	(a) DC and cirrhosis (b) DC and ACLD (c) DC and cirrhosis	None	4 months–2.3 years	[11]
2004	4	M	FAP	Heart rejection; bleeding, renal failure, sepsis, heart failure, and colon ischemia.	2 alive at 1 month and 38 months; 2 dead at 2 months and 20 months	[1]
2007 (Data from 1998–2005 in USA)	36	NA	NA	Sepsis, multiple organ system failure, cardiovascular complications, intracranial hemorrhage, and metastatic adenocarcinoma.	1-year SR 88%; 5-year SR 78%	[12]
2008 (Data from 1987–2005 in USA)	47	22–65 years (1)6 F,31 M	30% had amyloidosis		1-year SR 84.8% 5-year SR 75.6%	[13]
2009 (Data from 1992–2007 in USA)	13	NA	11 had amyloidogenic cardiomyopathy	3 patients with end-stage renal failure	SR at 1, 5, and 10 years were 100, 75, and 60%, respectively	[2]
2010	4	48–57 (M)	FH, HRCM, right heart failure, and congestive cirrhosis, HBV cirrhosis		Patients reportedly did well 25–38 months post-operatively	Hennessey et al.
2011	1	21 (M)	Failed Fontan circulation and secondary end-stage liver failure in a patient with dextrocardia	None	2 years	[14]
2011	1	32 (M)	right heart failure and refractory ascites with biopsy proven cirrhosis	None	100%	[15]
2012	3	14 (F), 17 (F), and 17 (M)	Cardiomyopathy, cardiac cirrhosis, heterotaxy syndrome, and multiple ventricular septal defects	None	100% 1 and 4-year post-operation	[16]

Table Continued.....

Reporting year	No. of patients	Patients age (in years) and gender	Patients pre-operative health	Patients post-operative complications	Survival time/ survival rate	Reference
2012	1	34 (M)	FH and ischemic heart failure	None	16 months	[17]
2012 (Data from 1987–2010 in USA)	97	Mean age: 43.7 29 (F), 68 (M)	Familial amyloidosis, porto pulmonary hypertension	NA	SR at 1, 5, and 10 years was 84.4, 73.9, and 72.3%, respectively	[18]
2013 (Data from 1998–2009 in Denmark)	7	Mean age: 48.3 years (3F, 4M)	FAC, peripheral poly neuropathy	Multi-organ failure, infection, cardiac rejections, mild liver rejection	2 died at 3 months and 9 months, 5 survived in 4.5 years	[19]
2013 (Data from 2006–2012 in Cleveland, USA)	5	Mean age: 49 years (1F, 4M)	Amyloidosis, hepatitis C	None	3-year SR 100%	[3]
2014 (Data from 1990–2012 in Mayo clinic, USA)	2	53 (F), 46 (M)	CHD	None	100%	[20]

Survival rate of the patients undergoing CHLT

Since the report of Shaw et al.[6] there has been significant improvement in the success rate of CHLT. For example, a successful CHLT case was reported in 1995 on 2patients with their survival time of 3.7 and 1.7years at the time of publication.[7] In another study, a Kaplan Meier survival analysis of 36patients with CHLT from 1998-2005 reported that 84% of the patients survived first year and 74% of the patients survived third year of post transplantation.[8] Recently, Barbara et al.[9] carried out perioperative management of patients undergoing CHLT and reported low mortality of CHLT patients.[9] Therefore, it was thought that the unsuccessful cases could be due to the low tolerance of heart with end stage injury along with the hemodynamic changes occurring during Orthotopic Liver Transplant (OLT). It was, therefore, suggested that Orthotopic Heart Transplant (OHT) needs to be performed before OLT.[8] Another analysis of 1 and 3-year patient survival rates at 84.8 and 79.5%, respectively, suggested that CHLT treatment needs less immunosuppression than the individual transplantation.[10] According to the study by Atluri et al.[11] CHLT patients showed success rates with short-term survival of 1year (87.7%) and excellent long-term survival after 5year post transplantation (83.8%). Analysis of the database of the United Network for Organ Sharing (UNOS)/Organ Procurement and Transplantation Network (OPTN) from February 27, 2002 to December 31, 2012 included a transplant cohort comprising of 76,803 adults of which 19,555 subjects underwent isolated Heart Transplant (HRT), 98 subjects underwent Heart-Liver Transplant (HLT) and 57, 150 underwent isolated Liver Transplant (LIV).[12] It is found that although the post-transplant outcomes of CHLT recipients are comparable to those receiving OHT and OLT (P=0.01; 7% vs. 4% and 24% vs. 9%)[10,13] there were more deaths listed for CHLT patients in the wait-list than in OHT and OLT wait-list, which could be due to dual vital organ failure.[12] Cannon et al.[13] in their study reviewed 97cases of CHLT in the United States based on the data reported by UNOS between 1987 and 2010.[13] During this time span, 96,033 OLTs and 67,852 OHTs were performed in the United States.[13] In their review, Cannon et al.[13] found that the most common reason for the need of heart and liver transplantation appeared to be amyloidosis, which can affect both heart (26.8%) and liver (27.8%).[13] They also found that liver graft survival in the CHLT cohort at 1, 5, and 10years was 83.4, 72.8, and 71.0%, which was almost similar to the survival of cardiac allograft (83.5, 73.2, and 71.5%, respectively). Furthermore, the graft survival rates of CHLT were similar to isolated heart and isolated liver transplantation with the difference that patients with CHLT had lower graft rejection rates than that undergoing isolated heart transplantation alone.[13] The better graft survival rate in CHLT patients is seen because of the shedding of human leukocyte antigens providing an immuno protective effect.[2] According to the Organ Procurement and Transplantation Network National Data Transplantation Reports from December 11, 2013, 163 CHLT (141 CHLTs, 13 combined heart-liver-kidney, and 12 combined heart-liver-lung transplantation) cases have been reported in the United States. Moreover, graft survival after CHLT was >70% at 10years, similar to isolated liver or heart transplantation.[8,13] Another study reported a successful en bloc CHLT in three pediatric transplant recipients of Hispanic origin with end-stage heart and liver disease (2 females aged 14 and 17years and 1male aged 7years), with a 100% survival rate at the time of its publication.[14] Furthermore, a study of CHLT showed a 3-year survival rate of 100% between January 2006 and December 2012.[3] In a recent study by Careddu et al.[15] simultaneous CHLT was performed on patients with end-stage heart-liver disease. They found 93, 93, and 82% of survival rates at 1month and 1 and 5years, respectively.[15] Survival rates of 5 CHLT patients in Cleveland clinic was 100% suggesting that there is a growing requirement to perform dual organ transplantation in cases of dual organ failure due to various reasons.

CHLT performed on patients diagnosed with critical abnormalities has been successful over the years. For example, the first report describing CHLT performed to treat congenital heart defects and end-stage liver disease diagnosed with situs ambiguous, was of a 21year old man. In the same study, a successful case of CHLT performed to treat failed Fontan circulation and secondary end-stage liver failure in a patient with dextrocardia was reported.[16] In another case of CHLT of a 32year-old man diagnosed with transient heart graft failure, a central

Extracorporeal Membrane Oxygenation (ECMO) was used to support hepatic and renal functions.[15] Furthermore, another study reported 7 patients diagnosed with Familial Amyloidotic Cardiomyopathy (FAC) (mean age: 48.3±4.2years) including four men and three women received CHLT between 1998 and 2009 with a 71% survival rate at 4.5years.[17] Also, from 1990-2012, a total of 45patients with end-stage Congenital Heart Disease (CHD) underwent cardiac transplantation in Mayo clinic, with a patient survival rate at 1, 5, and 10years was 89, 89, and 72%, respectively, while graft survival rate at 1, 5, and 10years was 89, 89, and 61% respectively.[18] Furthermore, 3patients underwent multi-organ transplantation with two of them receiving CHLT with a survival rate of 100%.[19] A 34year old man underwent CHLT for end-stage ischemic heart failure with severe left ventricular dysfunction and heterozygous familial hypercholesterolemia. At the time of publication, he did not experience any post transplantation complications after 16months of follow up period.[18] In Asia, the first case of combined heart and liver transplantation for Familial Amyloid Polyneuropathy was reported by Marriott et al.[19] They continued the patient on cardiopulmonary bypass during liver transplantation to provide hemodynamic support to the cardiac graft and to protect it from the impending reperfusions that accompanies liver transplantation.[20] Table 1 summarizes the information regarding the survival rates and pre and post-operative complications of CHLT patients in the past years.

Complications during pre and post-operative period

Although a large number of successful cases of CHLT were reported during the 1990s with a survival rate from 9months to 8.3years, there were complications including hepatic and cardiac failure.[21–23] Other complications, if a combined heart-lung-liver-Transplantation is performed, included early pulmonary rejection and intrathoracic bleeding with survival rate from 1.6-8.3years.[24] In late 1990s, the patient survival rate significantly increased to 80%,[10] but non survival of patients in the wait-list also increased, raising the question on the patient's selection criteria. Mortality was high in patients waiting for CHLT than the patients waiting for OHT and OLT.[12] Furthermore, another study showed that simultaneous thoracic and abdominal transplantation candidates had higher risk of wait-list mortality compared to single organ candidates. Therefore, prioritizing simultaneous double organ transplantation does not affect the candidates awaiting single organ transplantation.

There are various reasons for graft rejection and mortality that are gradually coming into light with the progress in organ transplantation and follow up study of patients. For some, shortage of organ donors, longer waiting times, and non availability of simultaneous organs for transplantation may be limiting factors.

Graft Vasculopathy is one factor that limits graft survival; its detection and treatment is a major challenge. Studies have consistently shown that the older donors increase the risk after heart transplantation.[25] Therefore, specific donor criteria should be defined to minimize the risks obtained in all types of organ transplantation.[11] for example, age of the donor and size of the organ. Moreover, there could be excessive blood loss during hepatectomy and implantation. Some of the other complications include prolonged donor operation, splitting of diaphragm, and injury to the phrenic nerve during surgical operation.[14] Immunosuppression is one major problem with organ transplantation and should be monitored carefully. Moreover, the patients are given induction therapy, calcineurin inhibitor, or corticosteroids.[18] Organ rejection is a major determiner for the transplantation procedure. Cardiac rejection can be monitored by endomyocardial biopsies. Liver rejection monitoring can be performed by observing liver function tests (ALT, AST, and bilirubin). Liver biopsy can also be performed. Coronary Allograft Vasculopathy (CAV) can be monitored and cardiac angiograms should be performed annually.[18]

Factors determining the success of an organ transplant

There are a number of criteria that can impact successful organ transplantation. For example, low levels of Donor Specific Antibody (DSA) titers at the time of grafting can avoid an immediate graft rejection and maintaining them low during the first post operative weeks.[26] However, there is a possibility of failure of such treatments and there are some significant side effects related to this. The use of intravascular ultrasound has proven to be extremely useful to visualize the vessel walls.[27] Heart transplant recipients may be more difficult to desensitize. Furthermore, organizing the organ donation and organ transplantation timely to patients undergoing desensitizing protocols can minimize the risks.[28] There are certain criteria to be met for successful organ transplantation, including an appropriate donor selection. A donor organ should be healthy with a size of 90-160% of recipient's.[14] The size of heart should be suitable and the liver should be small enough to circumvent any kind of size reduction to prevent leakage of bile or any infection after operation. Health of the donor should be stable. Early diagnosis and critical selection of transplant candidates is a prerequisite especially with patients having complicated conditions such as non cardiac amyloidosis before transplantation.[18] Recipients should also be evaluated properly for critical cardiac and liver dysfunction that may follow a CHLT procedure immediately.[14] Nevertheless, it is recommended to avoid extended preservation of liver for long time in order to avoid graft rejection. Also, cardiopulmonary bypass reduces any reperfusion effect from liver.[14] With CHLT en bloc, the ischemia time in the liver graft is reduced, and the cytokine injury to the heart is also reduced.[14] En bloc CHLT on cardiopulmonary bypass is known to assist in circulating cytokines, decreasing ischemia time, and improving oxygenation of the organ grafts.[14] Furthermore, the concomitant liver transplantation is thought to have immuno protective effect on the cardiac allograft thereby increasing the success rate of CHLT.

Implications

Allograft transplants may result in chronic rejection as a result of immunosuppressive changes and obstructive changes in the arterial vessels. Immuno suppressive measures or agents such as cytokines have been temporarily effective in the survival of such allografts but are inefficient for long term effects. Most of the heart transplant recipients suffer from Cardiac Allograft Vasculopathy (CAV), which is the major cause of mortality in the recipients.[29] Multi organ transplant is associated with less cardiac rejection and CAV.[30]A group identified a total of 10recipients of CHLT from January 2004 to April 2009 with no CAV cases, 2 whereas the isolated heart transplant group was diagnosed with CAV in 38% of the patients. In contrast to the CHLT patients, patients in the isolated heart transplantation had a higher prevalence of ischemic cardiomyopathy, which is a risk factor for accelerated CAV.[31]

This eventually results in accelerated plaque progression in the isolated heart transplant patients as compared to the CHLT group. Moreover, the CHLT group had lower triglyceride levels and lower incidence of hypertension before transplant, which minimized the

risk for vasculopathy. The reason for less allograft rejections or attenuated CAV in CHLT is the migration of donor myeloid cells into recipient's T dependent areas of lymphoid tissue.[32] This migration induces donor leukocyte chimerism, which causes elimination of cells in thymus that are reactive to donor antigen.[33] Another possibility may be regulation of T cells.[33] It is also suggested that donor liver sheds soluble Human Leukocyte Antigens (HLAs), which have immune tolerogenic properties by modulating the functions of several immune effectors. Furthermore, the concomitant liver transplantation confers immuno protective effect on the cardiac allograft. Overall, patients with a number of complications such as homozygous familial hypercholesterolemia and severe ischemic cardiomyopathy have experienced excellent long-term outcomes with CHLT.[34]

Conclusion

Although CHLT facility is limited to a few centres, the clinical outcomes are similar to those of isolated heart or liver transplantation. Still the sustainability and success rates are high.[10] CHLT with first liver and then heart transplantation is a positive approach that protects the heart from antibody mediated graft rejection, as the DSA may be absorbed or neutralized by the liver allograft.

Currently, CHLT is suggested only for patients with end stage liver and cardiac disease or for patients with familial amyloidosis, thereby limiting its clinical use. The planning of complex organ transplantations should be detailed and include contingency plans. In procurement of deceased-donor organs or tissues, variations of the implantation procedure should be anticipated.[35] Size of the organs is one of the major contributing factors and should be from the same donor.[6] It is important to characterize the outcomes of CHLT in the patients in order to ascertain a critical patient selection and operative technique or immunosuppressive treatments post-transplantation.[22] Pre and post-transplant decision making, management, and critical and timely selection of donors and recipients can determine the successful outcomes.[3]

Acknowledgements

None.

Conflict of interest

Author declares that there is no conflict of interest.

References

1. Nardo B, Beltempo P, Bertelli R, et al. Combined heart and liver transplantation in four adults with familial amyloidosis: Experience of a single center. *Transplant Proc*. 2004;36(3):645–647.
2. Raichlin E, Daly RC, Rosen CB, et al. Combined heart and liver transplantation: A single-center experience. *Transplantation.* 2009;88(2):219–225.
3. Nagpal AD, Chamogeorgakis T, Shafii AE, et al. Combined heart and liver transplantation: The Cleveland Clinic experience. *Ann Thorac Surg.* 2013;95(1):179–182.
4. Giakoustidis A, Cherian TP, Antoniadis N, et al. Combined cardiac surgery and liver transplantation: three decades of worldwide results. *J Gastrointestin Liver Dis*. 2011;20(4):415–421.
5. Starzl TE, Bilheimer DW, Bahnson HT, et al. Heart-liver transplantation in a patient with familial hyper cholesterolaemia. *Lancet.* 1984;1(8391):1382–1383.
6. Shaw BW, Bahnson HT, Hardesty RL, et al. Combined transplantation of the heart and liver. *Ann Surg.* 1985;202(6):667–672.
7. Rela M, Muiesan P, Heaton ND, et al. Orthotopic liver transplantation for hepatic-based metabolic disorders. *Transpl Int*. 1995;8(1):41–44.
8. Barshes NR, Udell IW, Joyce DL, et al. A pooled analysis of post transplant survival following combined heart-liver transplantation. *Transplantation*. 2007;83(1):95–98.
9. Barbara DW, Rehfeldt KH, Heimbach JK, et al. The perioperative management of patients undergoing combined heart-liver transplantation. *Transplantation.* 2015;99(1):139–144.
10. Te HS, Anderson AS, Millis JM, et al. Current state of combined heart-liver transplantation in the United States. *J Heart Lung Transplant*. 2008;27(7):753–759.
11. Carrier M, Lizé JF, Québec-Transplant Programs. Impact of expanded-criteria donors on patient survival after heart, lung, liver and combined organ transplantation. *Transplant Proc*. 2012;44(7):2231–2234.
12. Schaffer JM, Chiu P, Singh SK, et al. Combined heart-liver transplantation in the MELD era: do waitlisted patients require exception status? *Am J Transplant.* 2014;14(3):647–659.
13. Cannon RM, Hughes MG, Jones CM, et al. A review of the United States experience with combined heart-liver transplantation. *Transpl Int*. 2012;25(12):1223–1228.
14. Hill AL, Maeda K, Bonham CA, et al. Pediatric combined heart-liver transplantation performed en bloc: a single-center experience. *Pediatr Transplant*. 2012;16(4):392–397.
15. Careddu L, Zanfi C, Pantaleo A, et al. Combined heart-liver transplantation: a single-center experience. *Transpl Int*. 2015;28(7):828–834.
16. Horai T, Bhama JK, Fontes PA, et al. Combined heart and liver transplantation in a patient with situs ambiguous. *Ann Thorac Surg*. 2011;91(2):600–601.
17. Eyraud D, Vaillant JC, Ionescu C, et al. Early primary cardiac graft failure and combined heart-liver transplantation: need for an uncommon double bypass. *Br J Anaesth*. 2011;107(2):280–281.
18. Nelson LM, Penninga L, Sander K, et al. Long-term outcome in patients treated with combined heart and liver transplantation for Familial Amyloidotic Cardiomyopathy. *Clin Transplant*. 2013;27(2):203–209.
19. Robinson JA, Driscoll DJ, O'Leary PW, et al. Cardiac and multiorgan transplantation for end-stage congenital heart disease. *Mayo Clin Proc*. 2014;89(4):478–483.
20. Marriott AJ, Hwang NC, Lai FO, et al. Combined heart-liver transplantation with extended cardiopulmonary bypass. *Singapore Med J.* 2011;52(3):e48–e51.
21. Bahnson HT, Gordon RD. Transplantation of other organs with the heart. *Cardiovasc Clin.* 1990;20(2):237–248.
22. Befeler AS, Schiano TD, Lissoos TW, et al. Successful combined liver-heart transplantation in adults: report of three patients and review of the literature. *Transplantation*. 1999;68(9):1423–1427.
23. Tazbir JS, Cronin DC. Indications, evaluations, and postoperative care of the combined liver-heart transplant recipient. *AACN Clin Issues*. 1999;10(2):240–252.
24. Dennis CM, McNeil KD, Dunning J, et al. Heart-lung-liver transplantation. *J Heart Lung Transplant.* 1996;15(5):536–538.
25. Weiss ES, Allen JG, Kilic A, et al. Development of a quantitative donor risk index to predict short-term mortality in Orthotopic heart transplantation. *J Heart Lung Transplant*. 2011;31(3):266–273.

26. Stegall MD, Gloor JM. Deciphering antibody mediated rejection: new insights into mechanisms and treatment. Curr Opin *Organ Transplant*. 2010;15(1):8–10.
27. Topilsky Y, Hasin T, Raichlin E, et al. Sirolimus as primary immunosuppression attenuates allograft Vasculopathy with improved late survival and decreased cardiac events after cardiac transplantation. *Circulation*. 2012;125(5):708–720.
28. Daly RC, Topilsky Y, Joyce L, et al. Combined heart and liver transplantation: protection of the cardiac graft from antibody rejection by initial liver implantation. *Transplantation*. 2013;95(2):e2–e4.
29. Miller LW, Schlant RC, Kobashigawa J, et al. 24th Bethesda conference: Cardiac transplantation. Task Force 5: Complications. *J Am Coll Cardiol.* 1993;22(1):41–54.
30. Raichlin E, Kushwaha SS, Daly RC, et al. Combined heart and kidney transplantation provides an excellent survival and decreases risk of cardiac cellular rejection and coronary allograft Vasculopathy. *Transplant Proc*. 2011;43(5):1871–1876.
31. Taylor DO, Stehlik J, Edwards LB, et al. Registry of the International Society for Heart and Lung Transplantation: Twenty-sixth Official Adult Heart Transplant Report-2009. *J Heart Lung Transplant.* 2009;28(10):1007–1022.
32. Thomson AW, Lu L, Wan Y, et al. Identification of donor-derived dendritic cell progenitors in bone marrow of spontaneously tolerant liver allograft recipients. *Transplantation*. 1995;60(12):1555–1559.
33. Kawai T, Cosimi AB, Spitzer TR, et al. HLA mismatched renal transplantation without maintenance immunosuppression. *N Engl J Med.* 2008;358(4):353–361.
34. Patel SR, D'alessandro D, Shin JJ. Combined heart and liver transplantation in an adult with familial heterozygous hypercholesterolemia and severe ischemic cardiomyopathy. *J Heart Lung Transplant.* 2012;31(2):229.
35. Chan SC, Cheng LC, Ho KL, et al. Improvising hepatic venous outflow and inferior vena cava reconstruction for combined heart and liver and sequential liver transplantations. *Asian J Surg*. 2013;36(2):89–92.