

Split Liver transplantation: Early experience at public sector hospital in western India

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Abstract

Context: Split liver transplantation (SLT) is well established method to increase organ donor pool in developed nations. It is not routinely being practiced in India due to nascent deceased donation program and well-established living donor liver transplant across country. Here in, we present our early experience with SLT at public sector hospital with emerging liver transplant unit.

Aims: To understand the logistics and application of split liver transplantation in Indian context.

Settings and Design: The study is conducted from a developing liver transplant unit in a tertiary centre,

which is government funded and affiliated to a state university.

Methods and Material: It is a retrospective analysis of all split liver transplantation performed between March 2013 to October 2021.

Statistical analysis used: Demographic data of recipients and donors are analysed in MS excel and Kaplan Mayer survival curve is obtained for the recipients.

Results: Ten SLT were done in 6 years of study. We had three perioperative mortalities and one late mortality while six patients survived and alive with stable graft function. One-month graft and patient

survival was 66 percent while one-year patient and graft survival were 53 percent.

Conclusions: Split liver transplantation is technically demanding and resource intensive exercise but it is the need of the hour to increase organ donor pool.

Keywords: Model of end stage liver disease (MELD), Standard criteria donor, Split liver transplantation, primary non function, early allograft dysfunction, biliary leak.

Introduction

Liver transplantation has become definite modality of treatment for patients suffering from decompensated chronic liver disease and early stage small HCC^{1,2}. There is a wide gap between number of deceased donor donation and need of organs in both adult and paediatric patients which leads to high waitlist mortality. Especially, paediatric end stage liver disease patients are at disadvantage due to scarcity of size matched organ donation³. Though living donor liver transplant is well established option for paediatric patients, there is always a situation and rather more often when no group matched voluntary donor available or willing to donate. There is no available data from India but extrapolating from other database (UNOS)⁴, approximately 5-10 % of total waitlisted patients were of paediatric age group. To increase organ donor pool, it is useful to split a suitable cadaver donor to right extended and left lateral or full right/full left split³. Split liver transplant is a highly demanding procedure in term of technical complexity, logistic and resource utilization of both human and material. Liver can be divided into two halves either at back table in cold phase (ex situ split) or at operating table during donor operation before cross clamping (in situ split)⁵. In situ split has advantage of lower cold ischemia and

warm ischemia time, better delineation of hilar biliary anatomy, clipping of smaller vessels and biliary ductules during parenchymal transection⁵. SLT is routinely being performed in developed country to increase organ donor pool with acceptable outcome but it is not a routine procedure in our country, here in we have shown our experience of in situ split liver transplantation at public sector hospital.

Subjects and Methods:

It is a retrospective analysis of patients who underwent split liver transplantation between March 2013 to October 2021. The study protocol was approved by institution ethics and review board. Informed consent was taken from all recipient and deceased donor family for collection of data. The study was conducted according to declaration of Helsinki. The recipient age, weight, aetiology of liver disease, MELDNa score, cold ischemia time, operative time, complication grade according to Clavien-Dindo classification and outcomes were recorded. All the deceased donor was brain dead declared by competent hospital brain dead declaration committee. Our donor selection criteria for consideration for splitting are, age up to 50 years age, no ultrasonographic evidence of fatty liver, ICU stay less than 3 days, haemodynamically stable with no or minimal vasopressor, normal LFT or minimal deranged LFT and serum Na less than 160 meq/L. All suitable potential cadaver donors were considered for split if appropriate paediatric recipient is in waiting list according to **G-DOT** guidelines.

Recipient selection: Allocation policy for left lateral section or left lobe grafts were based on Paediatrics end stage liver disease (PELD) score. Right lobe or right extended lobe graft were allocated according to MELD Sodium score. Urgent liver transplantation indications

like acute liver failure are avoided & patients with severe portal hypertension and a deteriorated clinical status were not considered for split transplants. Standard liver volume of cadaver liver donor was calculated by estimated weight-based formula and approximate left/right distribution was based on equation.⁶

Methodology of splitting and procurement: After inspection of abdominal cavity and assessment of liver texture, Extended Cattell-Braasch manoeuvre was performed. Infrarenal aortal and IVC were controlled. Left lobe of liver is mobilised. Right crus of diaphragm identified and supra-celiac aorta was controlled with umbilical tape. Liver hilar dissection and splitting will start after above steps to do rapid cold perfusion in case donor develop cardiac arrest during in situ splitting procedure. Though no patients developed sudden cardiac arrest in our series.

We used a living donor hepatectomy technique for splitting of liver. After cholecystectomy, Intra-operative cholangiogram done to reveal hilar biliary anatomy or alternately CBD can be probed after cutting LHD away from bifurcation to know the anatomy. Left duct was divided away from bifurcation after marking with radiopaque marker to avoid injury to hilar bile duct and CBD was kept with right lobe. Main hepatic artery trunk was kept with left lateral graft or left lobe graft. Main portal vein was kept with LLS or left lobe graft. IVC was kept with right lobe graft and in full right/full left split, MHV was kept with left lobe and segment 5/8 branch on right lobe was re constructed with cadaver iliac artery graft.

Two recipient operations: Selection of recipient for right extended graft was MELD based policy. Both recipient operations were started simultaneously to

decrease cold ischemia time as much as possible. Once cold perfusion started at donor place, recipient was wheeled in to operation theatre. During implantation, left lateral and left lobe graft was implanted first followed by right lobe graft implantation. Implantation was done by single surgeon.

Immunosuppression protocol: Patients was induced with methylprednisolone 10 mg per kg around half an hour before reperfusion followed by 5 mg per kg on post-operative day 1 and 2.5 mg per kg on post-operative day 2 then kept on maintenance oral prednisolone. Tacrolimus started once urine output was established irrespective of absolute value of serum creatinine. Tacrolimus trough level was maintained between 10-12 ng/ml from 1st week till 4-week post LT. Trough level was maintained between 6-8 ng/ml for first 3 month followed by 3-5 ng/ml till 1 year. MMF was introduced once leukocyte counts are above 4000 and continued till 6 months unless not tolerated by patients. Steroids are tapered and stopped once 3 months completed unless aetiology of original disease was autoimmune. Target was to keep the patients on tacrolimus mono therapy after 6 month of liver transplant.

Results

Donor -A total of five split liver procurements were commenced and all five were completed in hemodynamically stable condition. One donor required 2 units of PCV transfusion during procurement to maintain haematocrit. Median donor splitting and procurement duration was 4 hours and 18 min. Median donor age was 35 years, four were male and one female. Cause of death was head injury in four donors and neurotoxin related brain injury in one. Liver function tests were within normal limits in all donors.

Two donors were on single low dose vasopressor and median ICU stay was 2 days. Median distance between donor organ procurement centre and recipient centre was 185 km. HTK solution was used as cold perfusion agent. There was no anatomic variability in both arterial and portal anatomy during hilar dissection, inflow (hepatic artery, Portal vein) was kept with left lobe graft and outflow (bile duct and IVC) with right lobe graft.

Recipient - The median age of recipient was 13.5 years. 5 were male and 5 were females. The median weight and BMI were 36 kg and 17.13 kg/m² respectively. Aetiology of liver disease and type of graft was depicted in table no 1. The median MELD score, Cold ischemia time and Warm ischemia time were 21, 550 min and 33 min respectively. We have four perioperative mortality, six patients survived and are alive with stable graft function. Three months & one-year patients and graft survival was 53 percent as most complication occurred in perioperative period. Complications were graded according to Clavien Dindo classification and depicted in detail in table 1.

Discussion

These case series are unique in a way as only few centres perform split liver transplantation in India. These series is only second publication on split LT in india⁷ and first to report from public sector hospital in India. Even though the highest number of patients suffering from end stage liver disease is being treated at public sector hospital, there are only few government institutes doing liver transplantation due to various reasons like short of skilled manpower, short of proper infrastructure and unwillingness or least priority in eyes of administrator^{8,9}. Though one month survival is 66 percent & 1 year survival of 53 % which is quite lower

in current era/series⁸ but our last 5 consecutive recipients are alive with stable graft function. These series may bring hope for public sector hospitals to delivery such technically advanced surgical procedure to a deserving patient.

First requirement for successful split liver transplantation is identification of probable donor who can undergo splitting procedure safely without compromising the quality of graft³. Only young hemodynamically stable donors with healthy liver were considered for in situ split. In our series median donor age was of 35 years and fatty liver was ruled out by ultrasonography screening. Four in situ splits was done at state level medical college and small private hospital which were far from transplant centre. In only one instance splitting was done at transplant centre. The median distance between procurement centre and transplant centre was 185 km. Liver parenchymal transection was done with CUSA, which was not available at procurement centres so additional logistics for transport of vascular instruments and experienced staff and surgeons needed to be carried out. a strong administrative will and support is a must for such endeavour. In western country DBD organ donors are older and due to cerebrovascular accident while in our country majority of DBD donors are young and due to road traffic accident⁷. In our series, Cause of brain death in most donors was head injury due to road side accident. So if all potentially splittable organs are used then organ pool can be increased substantially³.

Partial graft is considered as marginal graft so to reduce a risk of non-function or dysfunction a cold ischemia time management is required. Once perfusion started at donor centre, both recipients were induced for transplants. In surgery, hilar structures are dissected but

not divided, liver mobilised by diving right & left triangular ligament. Once organ arrived at transplant centre and bench surgery started then hilum was taken down and IVC dissection done. First left lateral section/left lobe with MHV was implanted followed by right extended lobe or right lobe with MHV reconstruction. In our series, median cold ischemia time was 9 hour & 16 min. One left lateral section patient developed graft failure due to portal vein thrombosis and died on first post-operative day due to multiple organ failure, Rest all grafts functioned well in immediate post operative period.

There is no central or local registry which maintained data on patients suffering from end stage liver disease in India. Extrapolating data from UNOS, out of all transplantation activity, approximately 10 % of total liver transplantation are done on paediatrics patients⁴. It means around 3000 procedures per year are needed to meet the requirement while around 150/year paediatrics LT are being done in India^{8,9,10}. In a developing nation of ours, parents of children who end up in government hospital are mostly daily wage workers and lower middle class family. Most parents of such patients consent for only DDLT but not LDLT. Concurrently the availability of cadaveric paediatric donor is a rare event, hence the split liver transplant programme has been started. Paediatric population are future productive population worth saving, with transplant giving excellent long term quality of life. So if regular split liver transplantation is being performed in tertiary medical college then mismatch between supply and demand of organ can be reduced.

Our series has 1-month patient survival of 66% and three months & one-year graft patient survival is 53%. The reason for inferior survival was technical

complication related to split liver transplantation but as experience increases it will decrease as evident by last five cases who have survived and doing well with good quality of life. Liver transplantation activity in our country grew in 2nd decade of 21st century while it was started 20 years earlier in western country. On literature review, Early series from Europe, France & US were showing inferior outcomes when compared to recent series which implies as experience increase, survival can be improved^{11,12,13}. For example in a study by Emond JC et al¹¹, nine of 18 patients are alive with good function of the primary split graft after a postoperative follow-up from 2 to 12 months. Three additional patients are alive with a second graft which leads to overall patient survival to 67 percent. In our setup, there is least possibility to get graft for retransplant which is a limitation to manage serious complication like primary non function. All four mortalities are due to technical complications notably bile leak related sepsis in left lateral graft, perforation peritonitis due to inadvertent injury to bowel during adhesiolysis in left lateral graft, donor IVC thrombosis leading to graft dysfunction & persistent right hydrothorax in right extended graft and first left lateral split recipient developed graft necrosis due to portal vein thrombosis. These technical complications were due to humble experience during early part of programme which can be overcome as experience increase with time. As the living donor liver transplant program has simultaneously developed at institute, anterior sector vein reconstruction and complex biliary reconstructions can now be done with lesser complication rates and thus benefitting outcomes of split liver transplant as well.

Table 1: Demographic detail, graft type & complication of case series

Sn.	Age	Weight	Aetiology	MELD PELD	Type of Graft	Complications	Outcome
1	7	15	Primary hyperoxaluria	16	Left lateral	Portal vein thrombosis graft necrosis	Dead
2	52	47	Cryptogenic CLD	21	Right extended	Transient AKI	Alive
3	14	32	Autoimmune hepatitis	28	Left lateral	Early allograft dysfunction Perforation peritonitis Sepsis with MODS	Dead
4	33	46	Wilson disease	21	Right extended	Intra hepatic IVC thrombosis Sepsis with MODS	Dead
5	7	20	ACLF-Wilson	30	Left lateral	Early allograft dysfunction Bile leak with sepsis	Dead
6	13	42	Autoimmune hepatitis	24	Right extended	No complication	Alive
7	14	40	Cryptogenic with severe HPS	21	Left lobe with MHV	Anastomotic bile duct stricture-PTBD f/b internal stenting	Alive
8	13	29	Budd Chiari syndrome	19	Right lobe with anterior venous reconstruction	No complication	Alive
9	6	14	ACLF- wilson disease related	37	Left lateral	Persistent Ascitis	alive
10	53	50	NASH –Cirrhosis	20	Right extended	No complication	Alive

Conclusion

Split liver transplantation is complex surgical exercise requiring highly trained manpower and robust infrastructure to support emergency surgeries of extreme grade of complexity. It is need of hour to perform SLT for providing timely transplants to

paediatric patients as well as to increase donor pool for liver transplantation.

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