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REVIEW ARTICLE

Expanding the living donor pool using domino liver transplantation: a systematic review

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Abstract

Introduction: To this day, a discrepancy exists between donor liver demand and supply. Domino liver transplantation (DLT) can contribute to increasing the number of donor livers available for transplantation.

Methods: The design of this systematic review was based on the Preferred Reporting Items for Systematic Reviews (PRISMA). A qualitative analysis of included studies was performed. Primary outcomes were mortality and peri- and postoperative complications related to DLT.

Results: Twelve studies met the inclusion criteria. All included studies showed that DLT outcomes were comparable to outcomes of deceased donor liver transplantation (DDLT) in terms of mortality and complications. One-year patient survival rate ranged from 66.7% to 100%. Re-transplantation rate varied from 0 to 12.5%. Most frequent complications were related to biliary (3.7%–37.5%), hepatic artery (1.6%–9.1%), portal vein (12.5–33.3%) and hepatic vein events (1.6%), recurrence of domino donor disease (3.3%–17.4%) and graft rejection (16.7%–37.7%). The quality of the evidence was rated as moderate according to the Newcastle–Ottawa scale (NOS).

Conclusion: DLT outcomes were similar to DDLT in terms of mortality and complications. Even though DLT will not solve the entire problem of organ shortage, transplant programs should always consider using this tool to maximize the availability of liver grafts.

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Abbreviations

Anti IL2RA	basiliximab
CIT	cold ischemia time
CNI	calcineurin inhibitor
CNS1	Crigler-Najjar syndrome
Cort	corticosteroids/steroids/glucocorticoid
CSA	cyclosporine A
DDLT	deceased donor liver transplantation
DLT	domino liver transplantation
ESLD	end stage liver disease
FAP	familial amyloid polyneuropathy
FK	Tacrolimus
GRWR	graft recipient weight ratio
HA	hepatic artery
HCC	hepatocellular carcinoma
ICU	intensive care unit
IQR	inter quartile range
LDLT	living donor liver transplantation
LT	liver transplantation
MMF	mycophenolate mofetil/purine inhibitor
MSUD	maple syrup urine disease
N/A	not available
OKT3	muromonab-CD3
OTCD	ornithine transcarbamylase deficiency
PV	Portal vein
SD	standard deviation
WIT	warm ischemia time

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Introduction

Liver transplantation (LT) is the only cure for patients with End Stage Liver Disease (ESLD). The increasing number of indications for LT aggravates the common problem of organ shortage. Both the number of patients on the waiting list and the average waiting time have increased over the last years.[1] Eurotransplant reports a yearly wait list mortality of 19% with an average waiting time of 3 years. Moreover, 7% of these patients are delisted while waiting for a liver graft. The problem is that on one hand, patients have to reach higher MELD scores in order to get a liver allocated, while on the other hand, they pay for getting this chance with the closing window of being transplantable.[2] Minimizing the waiting time will decrease mortality in patients with ESLD.[3] It might also lead to better outcomes as patients undergo surgery in better medical condition. Organ shortage is a contributing factor to a longer waiting time.[4] To diminish the discrepancy between organ demand and supply, more suitable liver grafts are needed. The latter is motivation to explore possibilities in increasing the donor pool. Established techniques are split liver transplantations and living donor liver transplantations (LDLT).[5]

Domino liver transplantation (DLT) uses explanted livers from transplant recipients as graft for other patients. This re-use of explanted livers from transplant patients is possible in a limited number of diseases, which are an indication for LT. In these cases, development of the donor's disease in the domino recipient does not happen or takes longer than posttransplant life expectancy. Otherwise, the post LT graft function is normal. Typical examples are livers from metabolic disease patients re-used in elderly recipients with cancer as underlying indication for LT. Examples of the metabolic diseases forming an indication for domino liver transplantation are: Familial amyloid neuropathy, fibrinogen A2 chain amyloidosis, maple syrup urine disease, familial hypercholesterolemia, and neurogenic intestinal pseudo-obstruction. The domino donor can receive a liver from a deceased or a living donor.[6] For patients with a ESLD, who are mostly in a lower position on the waitlist, a domino liver transplantation can be considered.

Because of the lower chance of receiving a liver through the transplantation waitlist and the fact that these patients often have lower life expectancy, DLT can be a good option.

Safety is fundamental in order to re-use explanted livers of selected diseases. This systematic review assesses the peri- and postoperative outcomes of domino liver transplantation.

Methods

Search strategy

The criteria and guidelines as described in the Preferred Reporting Items for Systematic Reviews (PRISMA) were used for the design of this systematic review. Together with the help from a clinical librarian, we searched Embase, Medline, Web of Science, Cochrane and Google Scholar database. A search was conducted to identify studies on domino transplantation procedures. The search was performed on the on the 27th of October 2020. The exact search terms used are mentioned in the appendix.

Inclusion and exclusion criteria

All studies were firstly screened on title and abstract by two independent reviewers (MSB and JBLM). Studies describing cases of domino transplantation and patient characteristics (e.g., age, sex, comorbidities) and outcomes or complications (e.g., mortality, recurrence of disease) were included. Predefined exclusion criteria were non-English language and specific types of articles (e.g., editorials, letters to the editor, replies). Furthermore, studies not conducted in humans, reviews, and case reports were excluded. Regarding studies with overlapping patient populations, it was decided to include the study with the largest cohort. The reference lists of the included studies were examined to identify the studies that might have been missed during the search.

Disagreements or concerns regarding eligibility of different studies were resolved by consensus between both reviewers and, if necessary, consulted with a third party (RM and MUB).

Data extraction

The data extraction was performed independently by two reviewers. The extracted data from the included studies were patient characteristics: donor age, donor disease, recipient age, recipient sex and recipient disease. The extracted intraoperative characteristics were graft weight, graft-to-recipient weight ratio, second warm ischemia time, cold ischemia time, operative time, blood loss, blood transfusion and intraoperative complications. The second warm ischemia time was defined as the time between taking the liver out of the ice and reperfusion (anastomotic time). The extracted postoperative characteristics were postoperative complications, follow-up time, immunosuppressive regime, graft rejection, 1-year survival and 5-year survival.

Quality assessment

An adjusted version of the Newcastle–Ottawa Scale for observational studies (NOS)[7] was used to assess the quality of the included studies. The included articles were scored on seven different criteria, divided into three sections. Studies were graded based on selection of study groups, generalisability and ascertainment of exposure and outcomes. MSB and JBLM assessed the articles independently. A maximum of eight points could be obtained. Studies with more than seven points were considered of good quality. Studies with 4–6 points were considered as moderate quality and studies with less than 4 points were considered poor quality. MSB and JBLM assessed the studies independently.

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Results

Study selection

A total number of 576 potentially relevant studies were identified. Fig. 1 presents the PRISMA flow diagram. Twelve studies met the inclusion criteria and were included in the eventual analysis. Of these, seven studies were retrospective cohort studies,[8–14] three studies were prospective cohort studies[15–17] and one study was a retrospective case control study.[18] The baseline demographics of all included studies are given in Table 1. Table 2 shows the perioperative results of domino liver transplantation. Postoperative results are divided over two tables. Table 3 shows the survival rates and Table 4 shows the postoperative complications.

Donor disease

Eleven studies reported the disease of the domino donor, one study did not.[18] In eight studies, the domino donor was diagnosed with familial amyloid polyneuropathy (FAP).[8,9,11,12,14–17] In 2 studies, maple syrup urine disease (MSUD) was the primary disease of the domino donor.[10,13] These results are shown in Table 1.

Living/deceased donor

The studies included in this systematic review used living and deceased donor grafts for the transplantation of the domino donors (Table 1). Three studies included living donors (N = 147,[11,13,18] and four studies included deceased donors (N = 197).[10,12,14,15] Four studies (N = 117) did not report whether the first donor was a deceased or living donor.[8,9,16,17]

MELD score domino donor and recipient

The mean MELD score of domino donor patients was reported in one study. Marín Gomèz et al. reported a mean MELD score of 6±0.[12] The mean MELD score of domino liver recipients was described in four studies. These were respectively 15 ± 5,[18] 10.8 ± 4,[15] 13.4,[10] and 15.5 ± 2.7.[12] The mean MELD scores are shown in Table 1.

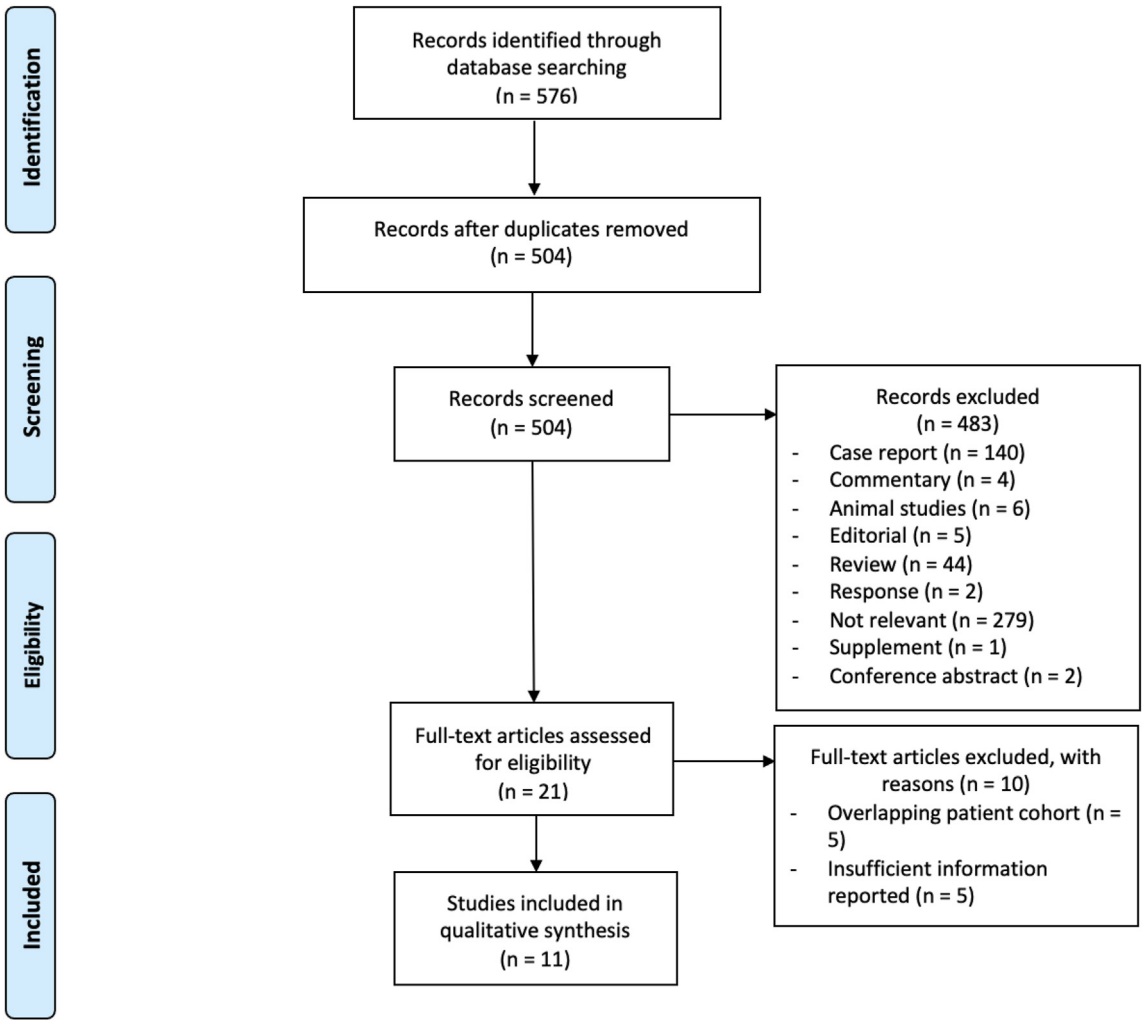

Figure 1 Flowchart study selection

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Table 1 Demographics of 10 included studies

Reference	Country	Number of domino transplants	Living/ deceased donor	Age domino donor (years)	Age domino recipient (years)	Male to female ratio domino recipient	Donor disease	Recipient disease	MELD score domino donor	MELD score domino recipient	Follow up duration
Geyer 2018	USA	126	Living	46 ± 17 (mean SD)	57 ± 14 (mean SD)	81:45	N/A	65 (51.6%) Miscellaneous 25 (19.8%) Hepatitis 18 (14.3%) Alcoholic Cirrhosis 18 (14.3%) HCC	N/A	15 ± 5 (mean SD)	120 months
Marques 2015	Portugal	114	Deceased	33.5 (median)	56 (median)	35:3	FAP	114 (100%) HCC	N/A	10.8 ± 4 (mean SD)	45 months (median)
Bolte 2013	Germany	61	N/A	45 ± 11.3 (mean SD)	58 ± 6.7 (mean SD)	46:15	FAP	46 (75.4%) HCC 11 (18%) Miscellaneous 2 (3.3%) Alcoholic Cirrhosis 2 (3.3% Hepatits)	N/A	N/A	46 months (median)
Tincani 2011	France	61	Deceased	45.3 ± 12.9 (mean SD)	54.6 ± 9.9 (mean SD)	53:8	FAP	N/A	N/A	N/A	N/A
Yamamoto 2007	Japan	27	N/A	47.1 ± 12.2 (mean SD)	52.4 ± 10.2 (mean SD)	14:13	FAP	12 (42.8%) HCC 10 (35.7%) Hepatitis 4 (14.8%) Miscellaneous 2 (7.4%) Biliary	N/A	N/A	36 months
Vollmar, 2018	Germany	23	N/A	41.5 ± 9.07 Range: 36-61	59 ± 5.97 (mean ± SD) Range: 46-69	18:5	FAP	19 (82.6%) HCC 2 (8.7%) Alcoholic Cirrhosis 2 (8.7%) Miscellaneous	N/A	13.3 (±9)	11.66 years (mean)
Herden 2019	Germany/ Belgium	14	Deceased	27 (mean)	29.6 (mean)	3:5[a]	MSUD	4 (28.6%) Miscellaneous 3 (21.4%) Biliary 1 (7.1%) Hepatitis	N/A	13.4[a]	23 months (median)
Roda, 2019	Brazil	11	Living	38 months (median) Range: 24–79 months	18 months (median) Range: 6–68 months	4:7	MSUD	10 (90.9%) Biliary 1 (9.1%) Miscellaneous	N/A	N/A	8 months
Marín Gómez 2010	Spain	8	Deceased	45.2 ± 12.9 (mean SD)	59.4 ± 8.7 (mean SD)	5:3	FAP	3 (37.5%) Miscellaneous 3 (37.5%) Hepatits 2 (25%) Alcoholic Cirrhosis	6 ± 0	15.5 ± 2.7	24 months
Y. Inomata 2007	Japan	8	Living	34.8 (mean)	41.1 (mean)	N/A	FAP	N/A	N/A	N/A	8–40 months
Figueras 2002	Spain	6	N/A	38 ± 15.4 (mean SD)	65.5 (±2.3 (mean SD)	5:1	FAP	4 (66.7%) HCC 1 (16.7%) Alcoholic Cirrhosis 1 (16.7%) Miscellaneous	N/A	N/A	4.8 months (mean)

Abbreviations: CNS1 = Crigler-Najjar Syndrome, FAP = Familial Amyloidotic Polyneuropathy, HCC = Hepatocellular carcinoma, MSUD = Maple Syrup Urine Disease, N/A = Not Available, SD = Standard Deviation.
[a] Patients from this study were from different hospitals, data only available from 8/14 patients.

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Table 2 Peri-operative characteristics of domino recipient transplantations

Reference	Graft weight (g) (mean)	GRWR (%) (mean)	2nd WIT (min) (mean)	CIT recipient (min)	Operative time	Blood transfusion	ICU stay (days)	Hospital stay (days)	Immunosuppressive regime	Intra-operative complications
Geyer 2018	N/A	N/A	N/A	270 ± 234 (mean SD)	N/A	N/A	N/A	N/A	N/A	N/A
Marques 2015	N/A	N/A	N/A	481 ± 140 (mean SD)	347.3 ± 79.4 (mean SD)	N/A	4[3] (median IQR)	20[17] (median IQR)	CSA or FK and Cort, MMF	N/A
Bolte 2013	N/A	N/A	N/A	400 (median)	344 (median)	N/A	N/A	N/A	CNI (n = 30) MMF (n = 26) Monotherapy (CNI) or combination therapy Cort (n = 7)	N/A
Tincani 2011	N/A	1.7 ± 0.4 (mean SD)	53.2 ± 38.7 (mean SD)	436 ± 201 (mean SD)	424 ± 113 (mean SD)	6.7 ± 8.8 (blood units)	12.2 ± 7.5	34.7 ± 13.9	N/A	N/A
Yamamoto 2007	N/A	N/A	N/A	N/A	N/A	14.7 ± 11.1 including cell saver blood, units (mean SD)	N/A	N/A	FK and Cort (n = 8) FK, Cort and MMF (n = 8), additional OKT3 for steroid resistant rejection (n = 2) CSA, Cort and Anti IL2RA (n = 6) CSA and Cort (n = 5),	N/A
Vollmar, 2018	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Herden 2019	720[a]	2.11[a]	N/A	N/A	N/A	N/A	8 (median) Range: 2–35[a]	29 (median) Range: 16–52[a]	N/A	N/A
Roda 2019	437 ± 105.5	4.8 ± 1.8	27 (median) 24-30 (range)	240 (median) 98-328 (range)	350 (median) 255-540 (range)	14 (Packed red blood cell transfusion volume (ml/kg))	N/A	N/A	N/A	1 intraoperative HA and PV thrombosis
Marín Gómez 2010	N/A	N/A	N/A	N/A	N/A	N/A	N/A	27.4 ± 17.2 (mean SD)	FK, MMF and Cort	N/A
Y. Inomata 2007	660–1100 (range)	1.53 (mean)	>60 min	481-764 (range)	N/A	N/A	N/A	N/A	N/A	2 PV thrombosis 2 late biliary stenosis
Figueras 2002	N/A	N/A	N/A	502 (mean)	363.3 (mean)	N/A	4 (mean)	17 (mean)	N/A	N/A

Abbreviations: Anti IL2RA = basiliximab, CIT = Cold Ischemia Time, CNI = calcineurin inhibitor, Cort = corticosteroids/steroids/glucocorticoid, CSA = cyclosporine A, FK = Tacrolimus, GRWR = Graft to Recipient Body Weight Ratio, HA = Hepatic Artery, ICU = Intensive Care Unit, IQR = Inter Quartile Range, MMF = mycophenolate mofetil/purine inhibitor, N/A = Not Available, OKT3 = Muromonab-CD3, PV = Portal Vein, SD = Standard Deviation, WIT = Warm Ischemia Time.
[a] Patients in this study were from different hospitals, data only available from 8/14 patients.

Cold ischemia time

The mean cold ischemia time (CIT) of the recipients was reported in four studies,[9,14,15,18] two studies reported the median CIT,[8,13] one study reported a range of CIT's[11] (Table 2). The mean CIT ranged from 240 min up to 764 min.[11,13] Two out of three studies using living donors for liver transplantation to the domino donor,[13,18] and reported the lowest mean and median CIT, these were 240 and 270 min respectively. One study reported a higher CIT range (481–764 min). This is likely due to the fact that the procedure of the domino graft recipient did not start until the domino liver graft was completely retrieved.[11]

Mortality and re-transplantation

The follow-up time ranged from eight months to ten years. One-year patient survival rate ranged from 66.7% to 100%. Five studies reported a 5-year patient survival rate.[8,15–18] This survival rate varied from 15% to 70%. The incidence of re-transplantation is reported in six studies.[8,12,13,15–17] This varied from 0%[13] to 12.5%.[15] The survival rate and incidence of re-

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Table 3 Postoperative outcomes

Reference	Graft failure	1-year patient survival (%)[a]	5-year patient survival	Re-transplantation of domino liver
Geyer, E.D.	37%	77[b]	42.1[b]	N/A
Marques, H.P. 2015	N/A	71.1	59	6 (5.8%)
Bolte, F.J. 2013	N/A	81.6	68.8	3 (4.9%)
Tincani, G. 2011	N/A	98.4	N/A	N/A
Yamamoto, S. 2007	N/A	67	15	1 (3.7%)
Vollmar, 2018	N/A	82	70	1 (4.3%)
Herden, U. 2019	N/A	**93**	N/A	N/A
Roda, K.M.O. 2019	0	100	N/A	0
Marín Gómez, L.M. 2010	1 (12.5%)	75	N/A	1 (12.5%)
Y. Inomata 2007	N/A	100[a]	N/A	N/A
Figueras, J. 2002	N/A	66.7	N/A	N/A

Abbreviations: N/A = Not Available.
*Patients in this study were from different hospitals, data only available from 8/14 patients.
[a] 1 year or the given mean follow up when less than 1 year.
[b] Survival is censored for follow up.

transplantation are shown in Table 3. Patients from cases in which the first donor was a living donor had 1-year patient survival rates between 77% and 100%.[11,13,18] Patients from cases in which the first donor was a deceased donor had a 1-year patient survival rate between 71% and 98.4%.[10,12,14,15]

Postoperative complications

Table 4 shows the incidence of postoperative complications. The most common complications were biliary,[11,14,15,17] hemorrhagic,[10,13–15,17] recurrence of domino donor disease in recipient,[8,15,17] and graft rejection.[8,9,12–14]

Four studies reported biliary complications which varied from 3.7% to 33.3%.[11,14,15,17] Two studies reported complications with the hepatic artery. Both reported this in one patient, which lead to 1.6% and 9.1% hepatic artery complications.[13,14] One study reported on a patient with a portal vein complication.[12] One study reported a patient (1.6%) with hepatic vein complication. Marques et al. reported 14% overall vascular complications.[15] Furthermore, the most common complications were recurrence of domino donor disease in recipient,[8,15,17] and graft rejection.[8,9,12–14]

De novo amyloidosis

Occurrence of de novo amyloidosis in domino liver recipients was reported in three studies.[8,15,17] Marques et al. reported occurrence of amyloidosis in the domino recipient in thirteen cases (11.4%).[15] Bolte et al. reported this in two cases (3.3%).[8] Yamamoto et al. found de novo amyloidosis in three cases (11.1%).[17]

Comparison *DLT and* deceased donor liver transplantation *(DDLT)*

Two studies compared patient survival in DLT to DDLT.[14,18] Geyer et al. compared 126 DLT's to 126 DDLT's. They found no statistically significant difference in survival between the two groups (p = 0.273).[18] Tincani et al. compared the survival of 61 FAP DLT's to 61 DDLT's as well. In this study, no difference in patient survival was found between the two groups (p = 1.0).[14]

Quality assessment

The results of the quality assessment are given in supplementary Table 5. Five studies were rated as good quality.[8,11,13,15,16] The quality of the remaining six studies was considered moderate.[9,10,12,14,17,18]

Discussion

This systematic review shows that domino liver transplantation is a safe option for increasing the donor pool. Peri- and postoperative outcomes are comparable to DDLT. Domino liver transplantation is mainly an option for older patients with ESLD with anticipated long waiting time due to their lower MELD score.

Patients placed lower on the liver transplantation waiting list are often older patients and patients with extensive comorbidities. These patients can qualify for domino liver transplantation. Moreover, in older patients, it is highly unlikely for the recipient to develop the original domino donor's disease.[19,20]

None of the DLT studies showed any disadvantage for the domino donor or domino recipient compared with conventional liver transplant procedures. Two studies compared the survival of DLT to DDLT and showed no statistical difference.[14,18]

DLT, however rarely performed, is a valid method for increasing the donor pool and can consecutively help reduce the waitlist mortality. Grafts used for DLT come from donors with a metabolic disease originating in the liver. This implies that the liver is functionally good, except for one metabolic deficiency. When this liver is transplanted into a recipient who does not have

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Table 4 Complications

Reference	Vascular				Biliary	Hemorrhagic	Recurrence domino disease in recipient	Recurrent primary disease recipient	Graft rejection episodes
	Hepatic artery	Portal vein	Hepatic vein	Vascular overall					
Geyer 2018	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Marques 2015	–	–	–	16 (14%)	20 (17.5%)	35 (30.7%)	13 (11.4%)	16 (14%)	N/A
Bolte 2013	–	–	–	–	–	–	2 (3.3%)	5 (8.2%)	23 (37.7%)
Tincani 2011	1 (1.6%)	–	1 (1.6%)	–	3 (4.9%)	3 (4.9)	–	–	14 (22.9%)
Yamamoto 2007	–	–	–	–	1 (3.7%)	1 (3.7%)	3 (11.1%)	7 (25.9%)	N/A
Vollmar, 2018	N/A	N/A	N/A	N/A	N/A	N/A	4 (17.4%)	N/A	N/A
Herden 2019	–	–	–		–	2 (14.3%)	–	1 (7.1%)	N/A
Roda 2019	1 (9.1%)	–	–	–	–	1 (9.1%)	–	–	N/A
Marín Gómez 2010	–	1 (12.5%)	–	–	–	–	–	–	2 (25%)
Y. Inomata 2007	–	–	–	–	3 (37.5%)	–	–	1 (12.5%)	–
Figueras 2002	–	–	–	–	–	–	–	N/A	1 (16.7%)

Abbreviations: N/A = Not Available.

this disease, the 'healthy' body will compensate for the disease and thus the patient will, in theory, not become ill.[21,22] In some cases, the recipient will develop the metabolic disease of the donor after a certain period of time. If this would be the case, it is important to take the life expectancy of the domino recipient into consideration. The life expectancy should not exceed the projected time for the recipient to develop the donors' disease. The authors are aware that previously published studies mention higher recurrence rates of the donors' disease in DLT recipients. However, these studies often have longer follow-up periods in which the disease recurrence occurs and identified. The included studies mentioning disease recurrence rates in this systematic review have follow-up times up to 46 months maximum, with the exception of Vollmar et al.[16] These shorter follow up periods may have resulted in lower disease recurrence rates than expected based on the literature on this subject.[23]

Domino liver transplantation has several advantages compared to DDLT. The domino liver is a living donor graft, consequently, the procedure has the advantages of living donation, which include a plannable procedure if possible, a shorter CIT and the possibility of transplanting patients before they become critically ill.[24,25] The latter is highly dependent on the number of grafts available for transplantation.

However, outcomes vary between different centers. Geyer et al. performed the most DLT's and was experienced in living donation. This study also had the lowest CIT and a one-year survival comparable to DDLT survival. They had a 5-year survival of 42.1%. However, these survival rates are based on patients still participating in the study. This would indicate that 42.1% of patients are still alive and taking part in the study, and the remaining 57.9% includes deceased patients as well as patients lost to follow up. Studies do indicate that the condition of the domino recipient before surgery should be taken into consideration when assessing outcomes, since many domino graft recipients have severe comorbidities such as HCC.

The study with the second most DLT's was relatively inexperienced with living donation (Marques et al.).[15] They had a long CIT and a lower patient survival than studies with experience in living donation. This systematic review showed slightly better survival in patients transplanted in transplantation centres where the first domino transplantation was with a living donor. These studies also had the lowest CIT. This is probably due to the fact that these centres have more experience in living liver donation and are familiar with working with multiple teams. These factors contribute to making CIT as short as possible. A prolonged CIT is correlated with biliary and hepatic artery complications, as well as with primary nonfunction of the liver and reduction of graft and patient survival.[26,27]

Two studies[14,15] reported that working with multiple teams would improve the outcomes because of logistical advantages. When multiple teams are working simultaneously, it reduces the CIT because the liver can be implanted almost directly, rather than having to wait for the first surgery to finish. However, Marques et al. reported that, for logistic reasons, the second LT was frequently performed immediately after the first LT.[15]

While the overall impact of DLT on organ shortage will be limited, little is known on whether this resource is used sufficiently and efficiently. Further research is needed to assess whether the domino technique is being used to its full potential in patients needing a LT and what measures can be taken to optimize it.

Our study has several limitations. Only 11 studies, all observational, were included due to the highly specialized procedure that DLT is, which introduces a risk of bias for which it was not possible to correct. Furthermore, the included studies used both living and deceased donors as primary donor in the domino chain. In living donor liver transplantation, vascular complications occur more often because of the necessary reconstruction

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of the hepatic vein outflow. This makes the outcomes of living and deceased donor liver transplantation difficult to compare. Another risk of bias is that living donor liver transplant surgeons are more experienced surgeons, possibly performing better with lower complication rates. All studies included in this systematic review did not correct for case selection.

Conclusion

In conclusion, DLT is a safe procedure and provides similar outcomes compared with DDLT. The field of LT is significantly guided by the problem of organ shortage. The number of possible DLT procedures will remain a very low percentage of the overall LT numbers. Therefore, the usage of this option will not have a statistical effect on the waitlist mortality in a country or region. Nevertheless, every life which can be saved is worth saving; domino liver transplantation remains a beautiful option in the field of transplantation.

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Conflict of interest

None to declare.

References

1. Busuttil RW, Goss JA. (1999) Split liver transplantation. *Ann Surg* 229: 313–321.
2. *Annual report 2019 eurotransplant*. (2019). International Foundation, 03-12-2020.
3. Lo CM, Fan ST, Liu CL, Chan JK, Lam BK, Lau GK *et al*. (1999) Minimum graft size for successful living donor liver transplantation. *Transplantation* 68:1112–1116.
4. Wall SP, Plunkett C, Caplan A. (2015) A potential solution to the shortage of solid organs for transplantation. *JAMA* 313:2321–2322.
5. Merion RM. (2010) Current status and future of liver transplantation. *Semin Liver Dis* 30:411–421.
6. Celik N, Squires JE, Soltys K, Vockley J, Shellmer DA, Chang W *et al*. (2019) Domino liver transplantation for select metabolic disorders: expanding the living donor pool. *JIMD Rep* 48:83–89.
7. Institute. (2017) *TOHR*. Available from: http://www.ohri.ca/programs/clinical_epidemiology/nosgen.pdf.
8. Bolte FJ, Schmidt HH, Becker T, Braun F, Pascher A, Klempnauer J *et al*. (2013) Evaluation of domino liver transplantations in Germany. *Transpl Int* 26:715–723.
9. Figueras J, Parés D, Munar-Qués M, Torras J, Fabregat J, Rafecas A *et al*. (2002) Experience with domino or sequential liver transplantation in familial patients with amyloid polyneuropathy. *Transplant Proc* 34: 307–308.
10. Herden U, Grabhorn E, Santer R, Li J, Nadalin S, Rogiers X *et al*. (2019) Surgical aspects of liver transplantation and domino liver transplantation in maple syrup urine disease: analysis of 15 donor-recipient pairs. *Liver Transplant* 25:889–900.
11. Inomata Y, Zeledón ME, Asonuma K, Okajima H, Takeichi T, Ishiko T *et al*. (2007) Whole-liver graft without the retrohepatic inferior vena cava for sequential (domino) living donor liver transplantation. *Am J Transplant* 7:1629–1632.
12. Marín-Gómez LM, Gómez-Bravo MA, Barrera-Pulido L, Bernal-Bellido C, Alamo-Martínez JM, Suárez-Artacho G *et al*. (2010) Outcomes of domino liver transplantation: a single institution's experience. *Transplant Proc* 42:644–646.
13. Roda KMO, Vincenzi R, Fonseca EA, Benavides M, Turine P, Afonso RC *et al*. (2019) Domino liver transplant in maple syrup urine disease: technical details of cases in which the first surgery involved a living donor. *Transplantation* 103:536–543.
14. Tincani G, Hoti E, Andreani P, Ricca L, Pittau G, Vitale V *et al*. (2011) Operative risks of domino liver transplantation for the familial amyloid polyneuropathy liver donor and recipient: a double analysis. *Am J Transplant* 11:759–766.
15. Marques HP, Ribeiro V, Almeida T, Aniceto J, Silva S, Sobral M *et al*. (2015) Long-term results of domino liver transplantation for hepatocellular carcinoma using the "double piggy-back" technique: a 13-year experience. *Ann Surg* 262:749–756. discussion 56.
16. Vollmar J, Schmid JC, Hoppe-Lotichius M, Barreiros AP, Azizi M, Emrich T *et al*. (2018) Progression of transthyretin (TTR) amyloidosis in donors and recipients after domino liver transplantation-a prospective single-center cohort study. *Transpl Int* 31:1207–1215.
17. Yamamoto S, Wilczek HE, Iwata T, Larsson M, Gjertsen H, Söderdahl G *et al*. (2007) Long-term consequences of domino liver transplantation using familial amyloidotic polyneuropathy grafts. *Transpl Int* 20:926–933.
18. Geyer ED, Burrier C, Tumin D, Hayes D, Jr., Black SM, Washburn WK *et al*. (2018) Outcomes of domino liver transplantation compared to deceased donor liver transplantation: a propensity-matching approach. *Transpl Int* 31:1200–1206.
19. Ericzon BG, Larsson M, Wilczek HE. (2008) Domino liver transplantation: risks and benefits. *Transplant Proc* 40:1130–1131.
20. Wilczek HE, Larsson M, Yamamoto S, Ericzon BG. (2008) Domino liver transplantation. *J Hepatobiliary Pancreat Surg* 15:139–148.
21. Kitchens WH. (2011) Domino liver transplantation: indications, techniques, and outcomes. *Transplant Rev* 25:167–177.
22. Qu W, Wei L, Zhu ZJ, Sun LY, Liu Y, Zeng ZG. (2019) Considerations for use of domino cross-auxiliary liver transplantation in metabolic liver diseases: a review of case studies. *Transplantation* 103:1916–1920.
23. Adams D, Lacroix C, Antonini T, Lozeron P, Denier C, Kreib AM *et al*. (2011) Symptomatic and proven de novo amyloid polyneuropathy in familial amyloid polyneuropathy domino liver recipients. *Amyloid* 18(Suppl 1): 174–177.
24. Humar A, Ganesh S, Jorgensen D, Tevar A, Ganoza A, Molinari M *et al*. (2019) Adult living donor versus deceased donor liver transplant (LDLT versus DDLT) at a single center: time to change our paradigm for liver transplant. *Ann Surg* 270:444–451.
25. Mc Kiernan PJ. (2017) Recent advances in liver transplantation for metabolic disease. *J Inherit Metab Dis* 40:491–495.
26. Nunes F, Valente M, Pereira R, Amil M. (2004) Domino liver transplant: influence on the number of donors and transplant coordination. *Transplant Proc* 36:916–917.

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27. Schielke A, Conti F, Goumard C, Perdigao F, Calmus Y, Scatton O. (2015) Liver transplantation using grafts with rare metabolic disorders. *Dig Liver Dis* 47:261–270.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.hpb.2023.03.006.