Chirurgia. eCollection 2024 July

http://dx.doi.org/10.21614/chirurgia.119.eC.2987

Prognostic Factors in Liver Transplant with Marginal Grafts - Review of the Literature

Maria Serban[1], Irina Balescu[1#], Sorin Petrea[2,3#], Bogdan Gaspar[2,4#], Lucian Pop[5,6], Valentin Varlas[5,7], Adrian Hasegan[8], Gabriel Petre Gorecki[9,10#], Cristina Martac[11#], Marilena Stoian[12,13#], Nicolae Bacalbasa[2,14,15]*

[1]PhD Student, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[2]Department of Surgery, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[3]Department of Surgery, Ion Cantacuzino Clinical Hospital, Bucharest, Romania
[4]Department of Visceral Surgery, Clinical Emergency Hospital, Bucharest, Romania
[5]Department of Obstetrics and Gynecology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[6]Department of Obstetrics and Gynecology, National Institute of Mother and Child Care Alessandrescu-Rusescu, Bucharest, Romania
[7]Department of Obstetrics and Gynecology, Filantropia Clinical Hospital, Bucharest, Romania
[8]Department of Urology, Sibiu Emergency Hospital, Faculty of Medicine, University of Sibiu, Romania
[9]Department of Anesthesia and Intensive Care, CF 2 Clinical Hospital, Bucharest, Romania
[10]Faculty of Medicine, Titu Maiorescu University, 031593, Bucharest Romania
[11]Department of Anesthesiology, Fundeni Clinical Hospital, Bucharest, Romania
[12]Department of Internal Medicine and Nephrology, Dr Ion Cantacuzino Hospital, Bucharest, România
[13]Department of Internal Medicine and Nephrology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[14]Department of Visceral Surgery, Center of Excellence in Translational Medicine, Fundeni Clinical Institute, Bucharest, Romania
[15]Department of Visceral Surgery, Center of Digestive Diseases and Liver Transplantation, Fundeni Clinical Institute, Bucharest, Romania

*Corresponding author:
Nicolae Bacalbasa, M.D.
Department of Surgery
Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
E-mail: nicolaebacalbasa@gmail.com

#authors with equal contribution

Rezumat

Factori de prognostic în transplantul hepatic cu grefă marginală - review al literaturii

Transplantul hepatic reprezintă ultima soluție salvatoare de viață în cazul pacienților cu boală hepatică în stadiu terminal. Numărul scăzut al grefelor hepatice disponibile şi timpul de aşteptare tot mai lung pe listele de transplant au dus la extinderea criteriilor de donare şi apariția grefelor marginale, inițial considerate suboptimale. Alocarea grefelor şi identificarea celei mai potrivite "perechi donator-primitor" este încă în curs de dezvoltare. Cert este că apariția grefelor marginale a extins listele de donare şi pare să aibă prognostic cel puțin comparabil cu utilizarea grefelor ideale.

Cuvinte cheie: transplant hepatic, factori de prognostic, grefă marginală

Received: 09.05.2024
Accepted: 05.07.2024

Abstract
Liver transplantation is the last life-saving solution for patients with end stage liver disease. The low number of available liver grafts and the increasing waiting time on transplant lists have led to the appearance of extended donation criteria and the marginal grafs, initially considered suboptimal. Allocation of grafts and identification of the most suitable "donor-recipient" pair is still under development. The fact is that the appearance of marginal grafts has expanded the donation lists and seems to have a prognosis at least comparable to the use of ideal grafts.

Key words: liver transplantation, prognostic factors, marginal grafts

Introduction

In all areas of medicine, it is essential to acknowledge whether the patient can benefit or not from a certain treatment. In terms of organ transplantation and organ functionality, this knowledge is even more important, given the fact that organ disponibility is much lower than the need.

On the last decade, the waiting list for a transplant and the severity of the illness increased, whereas the donor pool didn't cover all the recipients (1). Although there have been proposed several extended criteria in order to decrease the mortality on the waiting list, the outcomes are still on debate. There have been proposed several risk scores for the evaluation of recipients and the urgency for transplantation (2).

There are four possible bases for organ allocation: medical urgency, pre-transplantation status, utility and transplant benefit.

In Europe, donors > 60 years have increased from less than 5 % in the early 1990s to approximately 30 % in the 2018, as the European Liver Transplantation Registry shows (3).

The perfect moment for a transplant in the evolution of liver disease is not well known, except for those patients with primary biliary cirrhosis and cholestatic disorders. Early in the 1992, Delmonico et al. noted that allocation policy should include the outcome of the procedure so that useless transplants could be avoided (4).

Physicians and candidates have become more and more aware that donor indicatives have a significant impact on liver transplantation outcomes. Although the qualitative effect of individual donor variables is understood, the quantitative risk associated with multiple characteristics is under question (5).

There have been made two important developments to ease the decision of liver transplantation: the model for end-stage liver disease (MELD score) and the use of high-risk donors (6).

The MELD system is a scoring system for assessing the severity of chronic liver disease and the 3 month survival on the waiting list. It was initially created to predict mortality within three months of surgery in patients who had undergone a transjugular intrahepatic portosystemic shunt (TIPS) procedure (7), and was subsequently found to be useful in determining prognosis and prioritizing for receipt of a liver transplant (8,9). MELD score had suffered modifications throughout the time, but remains still the main way to evaluate terminal liver disease, because it is an objective quantification of liver dysfunction by measuring 3 standard values: serum bilirubin, serum creatinine, and international normalized ratio (INR) (10).

The first report on the new system of the UNOS/OPTN liver transplantation committee revealed a significant 3.5% reduction on the waiting list mortality (11).

Usually, in the majority of transplant centers, standard livers are transplanted to low-risk recipients, while nonstandard ones are transplanted in high-risk recipients

(degradation of liver function by multiple causes), patients with a worse prognosis (acute liver failure) or patients with a borderline indication (advanced neoplastic disease) (10,12).

Material and Method

Literature on prognostic factors after liver transplantation was searched in multiple databases: Cochrane Library, PubMed, Embase, MedLine, Web of Science, Elsevier, Google Scholar. The literature that we reviewed consists of studies from 1990 to 2023, published in English, over 100 papers. The review analyzes primary completed studies as well as some ongoing studies with preliminary results. Key words we looked up for were liver transplant, marginal graft, prognostic, perfusion machines, living donor, steatosis, graft failure. We've excluded the papers that were written in other language than English and published before 1990.

Donor Risk Index and MELD Score

The donor risk index (DRI) includes several donor characteristics, which predict a high-risk of graft failure: donor age > 40 years (especially > 60 years), DCD (donation after cardiac death=1, otherwise=0), split or partial graft (split/partial=1, otherwise=0), race (Africa-American=1, others=0), height, DBD (donation after brain death=0, especially cerebrovascular accident=1), donor location (local, regional=0 or national sharing=1) (5,13).

The DRI formula is quite complex and is typically implemented using a statistical model. The original DRI calculation can be summarized as follows:

$$\begin{aligned}\text{DRI} = \exp(&0.154\times(\text{age in decades} - 4.5) + \\ &0.244\times(\text{African American}) + 0.616 \times \\ &(\text{DCD}) + 0.176\times(\text{height in meters} - \\ &1.70) + 0.310 \times (\text{CVA}) + 0.209 \times \\ &(\text{Partial/Split}) + 0.149\times(\text{national share})\end{aligned}$$

Increased DRI has been correlated with decreased graft and patient survival. While these nonstandard organs can be successfully used in the proper patient, they are at higher risk of graft dysfunction, graft failure and potentially decreased patient survival if mismatched (14,15).

A study performed by Axelrod et al. about the economic impact of high risk liver grafts showed a LOS (hospital length of stay) difference between standard donors (DRI <1.0) and very high risk donors (DRI > 2.5) was 10.6 days, for recipients with MELD < 15, while the average LOS increased from 23.2 to 41.8 days when very high-DRI donors were used with MELD >35 (16).

Furthermore, as shown by Schaubel et al., survival benefit depends not only on MELD score, but also on the quality of the graft (17). Transplants of high-DRI organs is suitable for high but not for low-MELD candidates; in other words, matching a high-DRI liver with a low-MELD candidate reduces the survival benefit and may deny the chance to life of a high-MELD candidate on the waiting list. Low-MELD patients have, in general, a limited or negative outcome after transplant, thus they have an even greater risk of death if transplanted with a high-DRI graft. Contrary to belief high-MELD recipients react better on a high-DRI graft with increased post-procedural survival (18).

But this doesn't mean that each high-MELD recipient should be offered a high-DRI liver or that every high-DRI liver is suitable for transplant; this is a decision that should be made by physicians after evaluating all the possibilities.

The Donor Risk Index is a valuable tool in liver transplantation, providing a quantitative measure of donor liver quality and helping to predict transplant outcomes. However, it is essential to use it as part of a broader assessment strategy.

MELD / D-MELD and Recipient Survival

As said before, MELD score suffered changes over the time. D-MELD score (which adds the donor age to the preoperative MELD) developed by Halldorson et al., is a convenient predictive way to estimate outcomes after

liver transplantation, meaning that avoiding donor age >60 with high-MELD recipients, the patient and graft survival cand be improved. (55)

D-MELD demonstrated the strongest association with progressively decreasing probability of survival as D-MELD increased.

As the study aforementioned shows, comparing mostly HCV (hepatitis C virus) patients survival with non-HCV pacients, survival was superior if D-MELD was < 1600. In HCV patients, D-MELD <1600 demonstrated a 4-year survival of 72.9% vs 54.4% if D-MELD ≥1600. For patients with non-HCV, 4-year survival was 82.9% for D-MELD <1600 and 68.5% for D-MELD ≥1600. For patients with cholestatic liver disease, 4-year survival was 85.3% for D-MELD <1600 and 64.1% for D-MELD ≥1600. For patients with other liver disease, 4-year survival was 75.1% for D-MELD <1600 and 67.3% for D-MELD ≥1600. All of those results were statistically significant (19).

D-MELD system could be useful to screen high-risk donor/recipient matches in order to better allocate a liver. Nowadays, liver allocation based on MELD system doesn't take into account postprocedural survival, therefor D-MELD system is a simpler method in predicting mortality on the waiting list that could eliminate, if used proper, donor/recipient misfit (20).

Merion et al. have studied the survival benefit after transplantation, more specifically if a recipient on the waiting list is better to be transplanted as soon as possible or is better to wait a suitable graft. They find out that significant transplant survival benefit was observed at MELD ≥ 18, and the magnitude of transplant benefit increased with increasing MELD score (21). As the MELD score rises, the mortality on the waiting list rises, but if transplanted the risk of mortality rises much more gradually (22).

In contrast, at MELD < 15, is better to remain on the waiting list, because the risk of mortality after transplantation is much higher (23).

Maluf et al demonstrated that patients with high-MELD scores may rather benefit from marginal grafts than waiting on the list (20). Amin et al also validates the statement mentioned above, patients with high-MELD scores should be transplanted with an available marginal graft rather than waiting for a standard one (18).

SOFT Score

The Survival Outcomes Following Transplantation (SOFT) score is a predictive tool used to estimate the risk of mortality following 3 month liver transplantation. It takes into account multiple factors related to both the donor and recipient, helping to assess the potential outcome and guiding decision-making in liver transplantation. The factors included are: recipient age, recipient hospitalization status, recipient life support status, MELD score, previous transplant, donor age, cause of death, graft condition, CIT. (53, 54)

The score is used for risk assessment, decision making and post-LT care.

Viral Infection

The most common type of cirrhosis is alcoholic cirrhosis, which is cirrhosis caused by chronic alcohol abuse. Hepatitis C-related cirrhosis is also significant, although its prevalence is decreasing with advancements in antiviral treatments. However, non-alcoholic steatohepatitis (NASH), a severe form of non-alcoholic fatty liver disease (NAFLD), is also becoming increasingly prevalent due to rising rates of obesity and metabolic syndrome, similar to trends observed in the United States. Advances in antiviral prophylaxy and treatment of post-transplantation hepatitis B (HBV) have significantly improved patient and graft survival infected recipients (24,25). The International Liver Transplantation Society Expert Panel Consensus Conference on Liver Transplantation and Hepatitis C identified risk factors for decreased survival or increased disease severity in patients infected with HCV, including recipient viral load,

female gender, recipient age, non-white race, recipient disease severity, donor age and cytomegalovirus (CMV) infection.

As a study from Lake et al. shows (26), 4-year graft survival rates were significantly lower in patients infected with HCV (hepatitis C virus) than in patients without viral hepatitis 71.3% vs. 75.1%, and 75.5% in patients with HBV (hepatitis B virus). No significantly different rates were noted between HBV patients and non-infected ones.

In addition to that, in patients with HCV an important role in graft failure and graft survival was the advanced donor age (mostly >60 years). Studies have demonstrated a relationship between accelerated progression of fibrosis after transplant in patients with HCV and donor graft > 60 years (27,28).

More than that, cumulative factors like ICU (intensive care unit) hospitalization or recipient comorbidities had a higher risk of graft loss.

Nemes et al concluded that high-MELD score recipients provided with a marginal graft had an increased risk of graft loss and post-transplant complications, reactivation of HCV and a bad response to antiviral therapy (29).

If we talk about immunosuppression, associating MMF (mycophenolate mofetil) to the therapy determined a decreased risk of graft failure and death in recipients with or without viral infection (26).

Donation after Cardiac Death (DCD)

Mateo et al. (30) studied the graft survival after DCD in comparison with DBD (donation after brain death).

Overall graft survival rates from DCD donors (71% at 1 year and 60% at 3 years) were significantly inferior to those from DBD donors (80% at 1 year and 72% at 3 years) (30).

They found a significantly risk of graft failure if recipients associated history of previous liver transplant, being on life support, ICU hospitalization, dialysis, serum creatinine > 2 mg/dl, age> 60 years or CIT > 10h (31).

DCD donors were then divided into two categories: low-risk (CIT ≤ 10h and WIT ≤ 30 min) and high-risk (CIT >10h, WIT > 30 min). The study showed that low-risk recipients receiving a low-risk graft had an increased survival graft rate, comparable with DBD grafts and low-risk recipients receiving high-risk grafts had a significantly decreased rate of graft survival, compared with DBD grafts.

Also, DCD grafts were associated with increased primary non-function rates and biliary tract complications, mostly because of the prolonged CIT and WIT (32,33).

However, in 2019, Croome et al found improved outcomes in DCD grafts that underwent simultaneous liver-kidney transplant (34).

Zhang et al. performed a study on 75 050 pacients, between 2002 and 2016, studying survival after transplantation (35). Between those years CIT decreased significantly, while recipient age, MELD score and the severity of illness have increased.

The study determined that CIT < 6 hours was a protective factor for graft survival, while donor age > 60 years, fatty livers and the necessity of hemodialysis after transplantation had worse outcomes (*Table 1*) (35,36).

Table 1. Risk factors

Factor	Donor		Recipient	
	DCD	DBD	DCD	DBD
Age	*	*	*	*
Race	*	*		
Sex	*	*	*	*
Cause of death	*	*		
Creatinine	*	*	*	*
Bilirubin	*	*	*	*
AST	*	*	*	*
ALT	*	*	*	*
PA	*	*	*	*
Albumin			*	*
PT			*	*
WIT	>30 min	>30 min		
CIT	>10h	>10h		
Hospitalization status			Y/N	Y/N
Regraft status			Y/N	Y/N
Dialysis			Y/N	Y/N

AST=aspartate aminotransferase, ALT=alanine aminotransferase, PA=phosphatase, PT=prothrombin time, WIT=worm ischaemia time, CIT=cold ischaemia time.

*=factors evaluated in every category

Abt et al. showed that NHBD (non-heart beating donor) recipients were most likely to develop primary nonfunction than HBD (heart beating donor), but survival rate wasn't significantly different (37). Also, graft failure was associated with increased CIT (every additional hour increased the risk with 17%), and age >60 years.

Steatosis

It is well known that transplantation of a liver with moderate or severe steatosis most of the time determines an early graft dysfunction. The mechanism appears to be the severe deterioration of the plasma membrane fluidity and mitochondrial functions due to cold preservation, as shown in the study of Fukumori et al (38).

Cameron et al. proposed an extended criteria donor score (EDS) that assigns 1 point for each individual risk factor (donor age > 55 years, donor hospital stay >5 days, CIT > 10 h, WIT > 40 min). The study showed that graft failure and patient mortality risk increased as the EDS increased, with a large increase as the EDS went from 2 to 3 (39).

Donor liver steatosis has been associated with increased rates of primary nonfunction (PNF) and initial poor function (40,41). While most authors agree that grafts with severe steatosis lead to a significant risk of graft failure and probably should be avoided, grafts with moderate steatosis (> 30% and < 60%) may lay a relative risk on posttransplant survival (39,42).

Zamboni et al discovered that macrovesicular steatosis ≥ 25% was significantly associated with shorter patient survival rates. Microvesicular steatosis on the other hand, in ≥45% of the liver was not significantly associated with a worse prognosis (43). There are others studies too that confirmed the fact that severe steatosis (microvesicular type) is compatible with adequate function, even if 60–100% of donor livers is intravesicular fat, they can be safely used without increasing the primary nonfunction of the graft (44).

There are several studies that evaluated the use of marginal grafts in liver transplantation. As shown below, Godora and Bacchella studied the postoperative complications and the postoperative survival in patients receiving a marginal graft vs a standard graft.

Godara also proposed a graft scoring system, described below. As the score increases, the graft survival decreases, significantly in first 30 days after transplant (47).

Goldaracena et al. concluded that extremely marginal liver grafts (with a score ≥ 3) could safely be used in expanding the donor pool, as they have a significantly higher mortality only in the first month after transplantation (48).

Feng et al. have discovered in their study that increasing age was associated with a significant increase in the risk of graft failure, donors over 60 years being the strongest risk factor, together with African-American donors that had a 19% higher risk of graft failure compared to those from white donors (*Table 2*) (5).

Table 2. Postoperative complications and survival rates (45,46)

		Godora et al.		Bacchella et al.	
		MGR n (%)	**NMGR n(%)**	**MGR n (%)**	**NMGR n (%)**
Wound infection		2 (10%)	1 (7.7%)	3 (4.6%)	1 (2.6%)
Vascular complications		5 (25%)	0	5 (7.6%)	2 (7.8%)
Acute rejection		5 (25%)	2 (15.4%)	7 (10.8%)	2 (5.2%)
PNF		2 (10%)	1 (7.7%)		
Survival	1 week	18/20 (90%)	12/13 (92.3%)	79%	85%
	1 month	17/20 (85%)	12/13 (92.3%)	80%	94.7%
	3 months	17/20 (85%)	12/13 (92.3%)		
	6 months	17/20 (85%)	11/13 (84.61%)		

PNF = primary nonfunction, MGR = marginal graft recipients, NMGR = nonmarginal graft recepients

Table 3. Graft score

	Marginal Graft	Ideal Graft	Score
Age > 60 years	Yes	No	1
ICU stay	> 4 days	None or < 4 days	1
CIT	>13h	< 13k	1
Steatosis	≥ 30%	< 30%	1
Bilirubin	> 2.0 mg/dl	< 2.0 mg/dl	1
ALT	>170 U/l	<170U/l	1
AST	>140 U/l	< 140U/l	1
Use of dopamine	>10 µg/kg/min	None or < 10 µg/kg/min	2
Serum sodium	>155 mEq/l	< 155 mEq/l	2

ICU = intensive care unit, CIT = cold ischaemia time, ALT = aspartate aminotranspherase, ALT = alanine aminotransferase

Regarding the cause of death, stroke was associated with 16% risk of graft failure, DCD with 51% and split/partial grafts a 52% of graft failure, in comparison with DBD grafts (*Table 3*)(49).

In addition to that, each hour of cold ischemia time (CIT) was associated with an additional 1% higher risk of graft loss. In extension, grafts within the local area had an 11% higher risk of graft loss, while grafts nationally shared had a 28% higher risk of graft failure (5,50).

Grafts with higher DRI were usually transplanted at for low MELD score recipients, rather than on Status 1 recipients (urgent cases). Graft survival differences between grafts with higher versus lower DRI are evident 3 months after transplantation and tend to increase over time (5,51).

Vitale et al showed a three-year survival rate of 93% for patients with MELD ≤ 17 and 85% for patients with MELD >17 (optimal livers), and 94% vs 72% in suboptimal livers group. Also, MELD >17 was significantly associated with early graft death rates (52).

Conclusions

In conclusion, all these studies show that marginal donors can be a good alternative to ideal donors, in order to shorten the waiting time on the list, and to extend the donor pool, but in order to have a similar post-transplant outcome to the ideal donor, there must be very well established allocation criteria, considering the recipient risk factors, the well of state at the moment of the transplant, as well as the comorbidities.

Conflict of Interests

The authors declared no potential conflicts of interest.

Ethics Statement

Fundeni Clinical Institute Ethics Committee approved the study (no 25/2024).

Author's Contributions

Conceptualization: S.P.; M.Se.; methodology: L.P.; validation: N.B.; formal analysis: A.H.; investigation: C.M.; resources: I.B.; data curation: G.P.G.; writing — original draft preparation: M. Se.; writing — review and editing: I.B.; visualization: B.G, V.V; supervision: L.P.; project administration: M.St. All authors have read and agreed to the published version of the manuscript.

References

1. Ghobrial RM, Gornbein J, Steadman R, Danino N, Markmann JF, Holt C, et al. Pretransplant model to predict posttransplant survival in liver transplant patients. Ann Surg. 2002;236(3):315-22; discussion 322-3.
2. Asrani SK, Saracino G, O'Leary JG, Gonzalez S, Kim PT, McKenna GJ, et al. Recipient characteristics and morbidity and mortality after liver transplantation. J Hepatol. 2018;69(1):43-50.
3. Annual report of the US Scientific Registry of Transplant Recipients and the Organ Procurement and Transplant Network, 2018.

4. Delmonico FL, Jenkins RL, Freeman R, Vacanti J, Bradley J, Dienstag JL, et al. The high-risk liver allograft recipient. Should allocation policy consider outcome? Arch Surg. 1992;127(5):579-84.
5. Feng S, Goodrich NP, Bragg-Gresham JL, Dykstra DM, Punchd JD, DebRoye MA, et al. Characteristics associated with liver graft failure: the concept of a donor risk index. Am J Transplant. 2006;6(4):783-90.
6. Halldorson JB, Bakthavatsalam R, Fix O, Reyes JD, Perkins JD. D-MELD, a simple predictor of post liver transplant mortality for optimization of donor/recipient matching. Am J Transplant. 2009;9(2):318-26.
7. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. Hepatology. 2000;31(4):864-71.
8. Bilbao I, Armadans L, Lazaro JL, Hidalgo E, Castells L, Margarit C. Predictive factors for early mortality following liver transplantation. Clin Transplant. 2003;17(5):401-11.
9. Merion RM, Schaubel DE, Dykstra DM, Freeman RB, Port FK, Wolf RA. The survival benefit of liver transplantation. Am J Transplant. 2005;5(2):307-13.
10. Avolio AW, Agnes S, Gasbarrini A, Nure E, Siciliano M, Castagneto M, Prognostic value of MELD score and donor quality in liver transplantation: implications for the donor recipient match. Transplant Proc. 2006;38(4): 1059-62.
11. Freeman RB Jr, Wiesner RH, Edwards E, Harper A, Merion R, Wolfe R, et al. Results of the first year of the new liver allocation plan. Liver Transpl. 2004;10(1):7-15.
12. Salizzoni M, Franchello A, Zamboni F, Ricchiuti A, Cocchis D, Fop F, et al, Marginal grafts: finding the correct treatment for fatty livers. Transpl Int. 2003;16(7):486-93.
13. Wiesner RH, McDiarmid SV, Kamath PS, Edwards EB, Malinchoc M, Kremers WK, Krom RA, Kim WR. MELD and PELD: application of survival models to liver allocation. Liver Transpl. 2001;7(7):567-80.
14. Manzarbeitia CY, Ortiz JA, Jeon H, Rothstein KD, Martinez O, Araya VR, et al. Long-term outcome of controlled, non-heart-beating donor liver transplantation. Transplantation. 2004;78(2):211-5.
15. Doshi MD, Hunsicker LG. Short- and long-term outcomes with the use of kidneys and livers donated after cardiac death. Am J Transplant. 2007; 7(1):122-9.
16. Axelrod DA, Schnitzler M, Salvalaggio PR, Swindle J, Abecassis MM. The economic impact of the utilization of liver allografts with high donor risk index. Am J Transplant. 2007;7(4):990-7.
17. Schaubel DE, Sima CS, Goodrich NP, Feng S, Merion RM. The survival benefit of deceased donor liver transplantation as a function of candidate disease severity and donor quality. Am J Transplant. 2008;8(2):419-25.
18. Amin MG, Wolf MP, TenBrook JA Jr, Freeman Jr RB, Cheng SJ, Pratt DS, et al. Expanded criteria donor grafts for deceased donor liver transplantation under the MELD system: a decision analysis. Liver Transpl. 2004;10(12): 1468-75.
19. Schaubel DE, Sima CS, Goodrich NP, Feng S, Merion RM. The survival benefit of deceased donor liver transplantation as a function of candidate disease severity and donor quality. Am J Transplant. 2008;8(2):419-25.
20. Maluf DG, Edwards EB, Kauffman HM. Utilization of extended donor criteria liver allograft: Is the elevated risk of failure independent of the model for end-stage liver disease score of the recipient? Transplantation. 2006;82(12): 1653-7.
21. Merion RM, Schaubel DE, Dykstra DM, Freeman RB, Port FK, Wolfe RA. The survival benefit of liver transplantation. Am J Transplant. 2005;5(2):307-13.
22. Schaubel DE, Guidinger MK, Biggins SW, Kalbfleisch JD, Pomfret EA, Sharma P, et al. Survival benefit-based deceased-donor liver allocation. Am J Transplant. 2009;9(4 Pt 2):970-81.
23. Strasberg SM, Howard TK, Molmenti EP, Hertl M. Selecting the donor liver: risk factors for poor function after orthotopic liver transplantation. Hepatology. 1994;20(4 Pt 1):829-38.
24. Vargas HE, Dodson FS, Rakela J. A concise update on the status of liver transplantation for hepatitis B virus: the challenges in 2002. Liver Transpl. 2002;8(1):2-9.
25. Lo CM, Fan ST, Liu CI, Lai CL, Wong J. Prophylaxis and treatment of recurrent hepatitis B after liver transplantation. Transplantation. 2003; 75(3 Suppl):S41-4.
26. Lake JR, Shorr JS, Steffen BJ, Chu AH, Gordon RD, Wiesner RH. Differential effects of donor age in liver transplant recipients infected with hepatitis B, hepatitis C and without viral hepatitis. Am J Transplant. 2005;5(3):549-57.
27. Machicao VI, Bonatti H, Krishna M, Aqel BA, Lukens FJ, Nguyen JH, et al. Donor age affects fibrosis progression and graft survival after liver transplantation for hepatitis C. Transplantation. 2004;77(1):84-92.
28. Wali M, Harrisson RF, Gow PJ, Mutimer D. Advancing donor liver age and rapid fibrosis progression following transplantation for hepatitis C. Gut. 2002;51(2):248-52.
29. Nemes B, Gelley F, Zádori G, Piros L, Perneczky J, Kóbori L, et al. Outcome of liver transplantation based on donor graft quality and recipient status. Transplant Proc. 2010;42(6):2327-30.
30. Mateo R, Cho Y, Singh G, Stapfer M, Donovan J, Kahn J, et al. Risk factors for graft survival after liver transplantation from donation after cardiac death donors: an analysis of OPTN/UNOS data. Am J Transplant. 2006;6(4): 791-6.
31. Tector AJ, Mangus RS, Chestovich P, Vianna R, Fridell JA, Milgrom ML, et al. Use of extended criteria livers decreases wait time for liver transplantation without adversely impacting posttransplant survival. Ann Surg. 2006; 244(3):439-50.
32. Miles CD, Schaubel DE, Jia X, Ojo AO, Port FK, Rao PS. Mortality experience in recipients undergoing repeat transplantation with expanded criteria donor and non-ECD deceased-donor kidneys. Am J Transplant. 2007;7(5):1140-7.
33. Abt P, Crawford M, Desai N, Markmann J, Olthoff K, Shaked A. Liver transplantation from controlled non-heart-beating donors: an increased incidence of biliary complications. Transplantation. 2003;75(10):1659-63.
34. Croome KP, Mao S, Yang L, Pungpapong S, Wadei HM, Taner CB. Improved national results with simultaneous liver-kidney transplantation using donation after circulatory death donors. Liver Transpl. 2020; 26(3): 397-407.
35. Zhang T, Dunson J, Kanwal F, Nguyen Galvan NT, Vierling JM, O'Mahony C, et al. Trends in outcomes for marginal allografts in liver transplant. JAMA Surg. 2020;155(10):926-932.
36. Renz JF, Kin C, Kinkhabwala M, Jan D, Varadarajan R, Goldstein M, et al. Utilization of extended donor criteria liver allografts maximizes donor use and patient access to liver transplantation. Ann Surg. 2005;242(4):556-63; discussion 563-5.
37. Abt PL, Desai NM, Crawford MD, Forman LM, Markmann JW, Olthoff KM, et al. Survival following liver transplantation from non-heart-beating donors. Ann Surg. 2004;239(1):87-92.
38. Fukumori T, Ohkohchi N, Tsukamoto S, Satomi S. Why is a liver with steatosis susceptible to cold ischemic injury? Transplant Proc. 1999;31(1-2):548-9.
39. Cameron AM, Ghobrial RM, Yersiz H, Farmer DG, Lipshutz GS, Gordon SA, et al. Optimal utilization of donor grafts with extended criteria: a single-center experience in over 1000 liver transplants. Ann Surg. 2006;243(6): 748-53; discussion 753-5.
40. Nacif LS, Pinheiro RS, Rocha-Santos V, Barbosa VM, de Moura Dias AP, Martino RB, et al. Better selection criteria with prognostic factors for liver transplantation. Transplant Proc. 2018;50(3):766-768.
41. Imber CJ, Peter SD St, Handa A, Friend PJ. Hepatic steatosis and its relationship to transplantation. Liver Transpl. 2002;8(5):415-23.
42. Verran D, Kusyk T, Painter D, Fisher J, Koorey D, Strasser S, et al. Clinical experience gained from the use of 120 steatotic donor livers for orthotopic liver transplantation. Liver Transpl. 2003;9(5):500-5.
43. Zamboni F, Franchello A, David E, Rocca G, Ricchiuti A, Lavezzo B, Rizzetto M, Salizzoni M. Effect of macrovescicular steatosis and other donor and recipient characteristics on the outcome of liver transplantation. Clin Transplant. 2001;15(1):53-7.
44. Fishbein TM, Fiel MI, Emre S, Cubukcu O, Guy SR, Schwartz ME, et al. Use of livers with microvescicular fat safely expand the donor pool. Transplantation. 1997;64(2):248-51.
45. Bacchella T, Ferreira Galvão FH, Jesus de Almeida JL, Figueira ER, de Moraes A, Cerqueira M, et al. Marginal grafts increase early mortality in liver transplantation. Sao Paulo Med J. 2008;126(3):161-5.

46. Godara R, Sudeep Naidu C, Rao PP, Sharma S, Banerjee JK, Saha A, et al. Use of marginal grafts in deceased donor liver transplant: assessment of early outcomes. Indian J Gastroenterol. 2014;33(2):136-40.
47. Ploeg RJ, D'Alessandro AM, Knechtle SJ, Stegall MD, Pirsch JD, Hoffmann RM, et al. Risk factors for primary disfunction after liver transplantation-A multivariate analysis. Transplantation. 1993;55(4):807-13.
48. Goldaracena N, Quiñonez E, Méndez P, Anders M, Orozco Ganem F, Mastai R, McCormack L. Extremely marginal liver grafts from deceased donors have outcome similar to ideal grafts. Transplant Proc. 2012;44(7):2219-22.
49. D'Alessandro AM, Kalayoglu M, Sollinger HW, Hoffmann RM, Reed A, Knechtle SJ, et al. The predictive value of donor liver biopsies for the development of primary nonfunction after orthotopic liver transplantation. Transplantation. 1991;51(1):157-63.
50. Gruenberger T, Steininger R, Sautner T, Mittlböck M, Mühlbacher F. Influence of donor criteria on postoperative graft function after orthotopic liver transplantation. Transpl Int. 1994:7 Suppl 1:S672-4.
51. Bilbao I, Armadans L, Lazaro JL, Hidalgo E, Castells L, Margarit C. Predictive factors for early mortality following liver transplantation. Clin Transplant. 2003;17(5):401-11.
52. Vitale A, D'Amico F, Brolese A, Zanus G, Boccagni P, Neri D, et al. Prognostic impact of model for end-stage liver disease score in patients undergoing liver transplantation with suboptimal livers. Transplant Proc. 2007;39(6):1907-9.
53. Rana A, Hardy MA, Halazun KJ, Woodland DC, Ratner LE, Samstein B, et al. Survival outcomes following liver transplantation (SOFT) score: a novel method to predict patient survival following liver transplantation. Am J Transplant. 2008;8(12):2537-46.
54. de Boer JD, Putter H, Blok JJ, Alwayn IP J, van Hoek B, Braat AE. Predictive capacity of risk models in liver transplantation. Transplant Direct. 2019; 5(6):e457.
55. Flores A, Asrani SK. The donor risk index: a decade of experience. Liver Transpl. 2017;23(9):1216-1225.