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Order of liver graft revascularization in deceased liver transplantation: A systematic review and meta-analysis

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ABSTRACT

Background: The ideal order for liver graft revascularization during liver transplantation remains unknown. The majority of liver transplant centers prefer portal venous reperfusion followed by arterial reperfusion to shorten the warm ischemia time. The aim of this study was to review the different revascularization techniques used in clinical liver transplantation to identify any potential clinical benefits.

Methods: A systematic search of 5 databases was performed to identify all available original articles that reported liver transplantation and compared different techniques of reperfusion. The primary outcomes were patient and graft survival. Secondary outcomes were defined by postreperfusion syndrome, primary nonfunction, vascular complications, biliary complications, and retransplantation.

Results: A total of 1,160 patients undergoing liver transplantation from 15 studies were included in this review and meta-analysis. There were no differences regarding the 1-year patient and graft survival for the revascularization techniques. The incidence of primary nonfunction, vascular complications, and retransplantation did not differ between the groups. Although there were no differences regarding biliary complications between the different groups, there were more nonanastomotic strictures in patients with initial portal revascularization (9%) compared with those with simultaneous revascularization (2%; risk ratio 1.07; 95% confidence interval, 1.00–1.14; $P = .05$; $I^2 = 51\%$).

Conclusion: The order of liver graft revascularization does not influence patient and graft survival. Each revascularization technique offers potential benefits that can be used under specific clinical situations.

Liver transplantation (LTx) has become an accepted form of treatment for end-stage liver disease, acute liver failure, and certain types of liver tumors since the early 1980s.[1] Since the operative techniques used for LTx have evolved over time, it has now become relatively standardized[2]; however, unresolved questions remain regarding the order of revascularization of the liver graft during LTx.

Introduction

Although several experimental studies have analyzed various revascularization protocols using different animal models,[3–5] the results are not unequivocal, and the endpoints differ between studies. Another important limitation of animal studies is the lack of portal hypertension, which can substantially affect different revascularization techniques.

In the first report of human LTx, the liver graft was reperfused via the hepatic artery (initial arterial revascularization [IAR]) followed by portal venous reperfusion.[6] Since then, the majority of liver transplant centers have preferred portal venous reperfusion (initial portal revascularization, IPR) followed by arterial reperfusion to shorten the warm ischemia time (WIT).[7,8] To achieve this

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Table I
Types of revascularization techniques used in clinical liver transplantation

Sequential revascularization (SeqR)
Anterograde reperfusion via:
Portal vein: IPR
Hepatic artery: IAR
Retrograde reperfusion via the inferior vena cava: ICR
Simultaneous re-vascularization (SimR) via portal vein and hepatic artery

goal, retrograde reperfusion was also proposed, in which the graft is reperfused via the inferior vena cava (initial caval revascularization [ICR]) with a subsequent reconstruction of the portal vein and hepatic artery.[9,10] All aforementioned techniques represent sequential revascularization (SeqR), either in an anterograde (IAR and IPR) or retrograde (ICR) fashion.[11]

A potential disadvantage of the IPR and ICR techniques is that portal or caval venous blood alone in a progressively rewarming graft may induce damage to the biliary tract, which depends almost solely on the oxygenated hepatic artery blood supply.[12–14] To avoid this issue, some liver transplant centers have advocated either IAR or simultaneous reperfusion.[15] In simultaneous revascularization (SimR), both the portal vein and arterial anastomosis are created first, followed by simultaneous reperfusion via the portal vein and hepatic artery. Although there are 4 different revascularization techniques used in LTx (Table I), no consensus exists regarding the optimal sequence for revascularization, which has been also shown in a survey of 28 European liver transplant centers.[16] Moreover, differences in the quality of the donor population may alter the order of revascularization during LTx, especially the broad use of donors after circulatory death (DCD) in some countries.

Thus, the purpose of this study was to review the different techniques of revascularization used in the clinical setting of LTx to systematically describe and identify the possible clinical benefits of each revascularization technique.

Materials and Methods

A systematic database search was performed on August 15, 2018, to identify all available original articles reporting a comparison between different reperfusion techniques during LTx. The search was limited to English articles. Review articles, registry data, conference abstracts, comments, case reports, case series, letters to the Editor, and animal studies were excluded.

Search methodology

Data sources

A comprehensive Embase, Medline Ovid, Cochrane CENTRAL, Web of Science, and Google scholar search was performed with the use of relevant queries. The queries were constructed based on suitable terms corresponding with liver transplantation and revascularization (Table S1, Supplementary Content). All abstracts were entered into EndNote Version X8.0.1 (Clarivate Analytics, Philadelphia, PA) and duplicate records were removed. Two independent investigators (P.D. and K.T.) determined which articles were eligible for additional analysis based on the title and abstract. The third investigator (W.P.) resolved any discrepancies between the 2 reviewers. The full-text articles were obtained and inquired to meet the criteria used for the review. The guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses was applied.[17]

Data extraction

The data were independently extracted from the selected reports (P.D. and K.T.). Discrepancies in opinion were resolved through discussion. The extracted data included among others, the publication year, the country of the study, the type of the study, number of participants, the type of revascularization, the study period, the follow-up time, and the defined outcome variables.

Criteria used for the review

Inclusion and exclusion criteria

The included studies reported adult patients (≥18 years) undergoing deceased LTx. Only studies describing a comparison between ≥2 different techniques of revascularization in clinical LTx from deceased donors were included in the review. When multiple articles were published from the same institution using the identical patient cohort, the one containing the most complete information was selected.

Outcome variables

The primary outcomes were patient and graft survival. The secondary outcomes were defined by primary nonfunction (PNF), vascular complications (VC), biliary complications (BC), liver retransplantation (re-LTx), and postreperfusion syndrome (PRS). PRS was defined according to the authors of the analyzed studies. The definition of PNF included an initial lack of function or very poor function, leading to the need for early retransplantation or death. BC was defined by the authors of the studies and consisted primarily of bile leakage and stricture. VC was defined by the authors study and consisted mainly of hepatic artery thrombosis and portal vein thrombosis.

Meta-analysis

The meta-analysis was performed according to the available data. Only studies with data that was possible to extract were included in the meta-analysis.

Quality assessment

The quality of the studies included in the meta-analysis was assessed using the Jadad score[18] for randomized controlled trials (studies with scores <3 were classified as low quality and studies with score of ≥3 were classified as high quality) and the Newcastle-Ottawa scale for cohort studies (studies scored <3 were considered as poor quality, those scored between 4 and 6 were classified as fair quality studies, and studies scoring ≥7 were considered good quality).[19]

Statistical analysis

Outcomes were presented according to the original articles. Review Manager software (RevMan, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark, version 5.3) provided by the Cochrane Collaboration was used to perform the meta-analysis.[20] The meta-analysis was performed for a single variable if it was possible to extract the data from ≥3 studies describing the same revascularization technique. The results were presented as the risk ratio (RR) with a corresponding 95% confidence interval (CI). The heterogeneity of the studies was determined by the term I^2. The random-effect model was used for reporting the outcomes.

Results

A systematic search of the literature revealed 3,422 titles that were independently screened as described above. After excluding studies based on the title and abstract, 21 full-text articles were analyzed (Fig 1). There were 15 comparison studies eligible for this

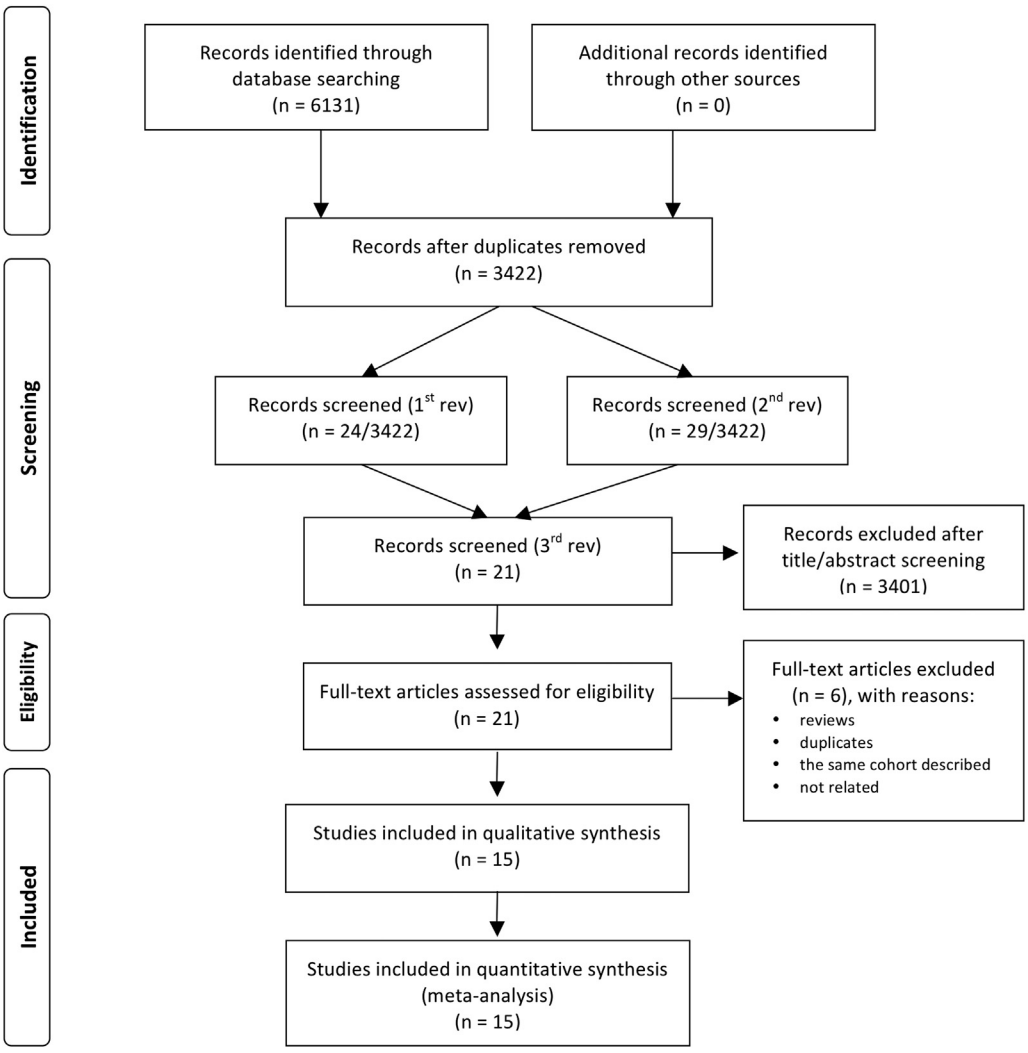

Fig 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart: selection of articles for the review.

review: 10 studies from Europe, 2 from China, 2 from the United States, and 1 from Brazil.[21–35]

General characteristics of the included studies

Among the 15 articles, 6 were randomized prospective studies,[24,28–31,34] 2 were prospective cohort studies,[27,33] and 7 were retrospective cohort studies[21–23,25,26,32,35] (Table II). Seven studies compared IAR with IPR,[22,24,25,27,28,30,34] 5 studies compared SeqR with SimR,[21,23,26,31,32] 2 studies compared SimR with ICR,[29,33] and 1 study compared ICR with SeqR.[35] It is important to note that all studies comparing SeqR with SimR or ICR used the IPR technique. A total of 1,160 patients were included in the analysis with study sample sizes ranging from 20 to 177 subjects. All the 15 identified studies were included in the meta-analysis because it was possible to extract at least 1 outcome parameter from each study. Forest plots were performed if at least 2 studies comparing the same 2 revascularization techniques reported the same outcome.

Donor parameters, recipient characteristics, and operative techniques

There were no significant differences between the donor parameters in the compared groups in the analyzed studies (data not presented). There was a limited variety of donor parameters presented in each of the studies. There were no significant differences in the donor age and type of donor compared between the groups in the analyzed studies, in which the data were presented. The available characteristic parameters of the recipients and operative techniques are summarized in Tables III and IV.

Outcome parameters

There was substantial heterogeneity in the reported outcome parameters among the 15 studies. Eight studies assessed graft function,[21,22,24–27,29,31–35] 6 studies presented graft survival,[23,25,26,29,31,32] 10 studies reported the incidence of BC,[21–26,28,29,31,32] 8 studies revealed the incidence of VC,[22,24–27,29,31,32] 7 studies focused on the hemodynamic/cardiovascular changes after different types of revascularization,[22,24,27,28,31,32,34] and 1 study evaluated the plasma concentration of *Rocuronium*.[30]

Influence of the revascularization techniques on the operative parameters

The summary of the operative parameters from the included studies is presented in Table IV. In almost all the included studies, the cold ischemia time (CIT) was mentioned; however, no

Table II
Study characteristics

Reference	Year	Country	Type of study	No. of patients	Study period	Follow-up	Choice of revascularization technique
SimR vs IPR							
Sankary et al[21]	1995	US	Retrospective, cohort	45 SimR vs 83 IPR	N/A	6 mo	N/A
Massarollo et al[23]	1998	Brazil	Retrospective, cohort	50 SimR vs 26 IPR	1992–1995	N/A	N/A
Polak et al[26]	2005	NL	Retrospective, cohort	31 SimR vs 71 IPR	1998–2001	38 mo (0–72)	Decision made by the staff surgeon
Baccarani et al[31]	2012	Italy	Prospective, randomized	42 SimR vs 38 IPR	2008–2011	17 vs 19 mo	Randomization 1:1 prior to transplantation
Lu et al[32]	2014	China	Retrospective, cohort	121 SimR vs 56 IPR	2007–2010	40 mo (24–61)	Until February 2008 all patients IPR, from February 2008 all patients SimR
IAR vs IPR							
Millis et al[34]	1997	US	Prospective, randomized	40 IAR vs 60 IPR	1993–1994	12 mo	N/A
Noun et al[22]	1997	France	Retrospective, cohort	15 IAR vs 14 IPR	1993–1994	24 mo (18–30)	N/A
Ducerf et al[24]	2000	France	Prospective, randomized	29 IAR vs 30 IPR	1995–1996	34 mo	N/A
Sadler et al[25]	2001	UK	Retrospective, cohort	26 IAR vs 26 IPR	1995–2000	12 mo	N/A
Walsh et al[27]	2002	UK	Prospective, cohort	10 IAR vs 10 IPR	N/A	3 mo	Decision made by the surgeon (IAR was influenced by arterial anatomy)
Moreno et al[28]	2006	Spain	Prospective, randomized	30 IAR vs 30 IPR	2001–2002	N/A	Randomization prior to reperfusion
Sabaté et al[30]	2010	Spain	Prospective, randomized	14 IAR vs 16 IPR	N/A	N/A	Randomization after completion of both anastomosis
SimR vs ICR							
Heidenhain et al[29]	2006	Germany	Prospective, randomized	66 SimR vs 65 ICR	2001–2004	27 mo (12–36)	Randomization prior to transplantation
Cai et al[33]	2016	China	Prospective, cohort	21 SimR vs 21 ICR	2013–2014	7 days	N/A
ICR vs IPR							
Kniepeiss et al[35]	2003	Austria	Retrospective, cohort	53 ICR vs 21 IPR	1998–2003 1989–1998	8 days	Implementation of new technique in comparison to the historical group

NA, not available.

Table III
Recipient and operative characteristics

Reference	No. of patients	Age	UNOS/Child-Pugh/MELD/diagnosis	Surgical technique
Sankary et al[21]	45 SimR vs 83 IPR	48.7 vs 46.6	N/A	N/A
Massarollo et al[23]	50 SimR vs 26 IPR	39.7 vs 40.3	N/A	Classical with VVB
Polak et al[26]	31 SimR vs 71 IPR	46 vs 46	No differences in Child-Pugh classification and diagnosis	PB TPCS 2/31 vs 5/71
Baccarani et al[31]	42 SimR vs 38 IPR	56 vs 56	No differences in MELD and diagnosis HCC 24% vs 39% HCV 43% vs 32%	PB
Lu et al[32]	121 SimR vs 56 IPR	48 vs 47	No differences in Child-Pugh classification, MELD and diagnosis Malignancy 46% vs 56%	PB
Millis et al[34]	40 IAR vs 60 IPR	50 vs 51	No differences in UNOS status	Classical with VVB
Noun et al[22]	15 IAR vs 14 IPR	41 vs 45	No difference in diagnosis	PB
Ducerf et al[24]	29 IAR vs 30 IPR	51 vs 49	No differences in Child-Pugh classification and diagnosis	PB with TPCS
Sadler et al[25]	26 IAR vs 26 IPR	53 vs 52.5	No difference in diagnosis (ALF excluded)	PB TPCS 21/26 vs 9/26 ($P < .001$)
Walsh et al[27]	10 IAR vs 10 IPR	45 vs 51	No differences in diagnosis	PB TPCS 8/10 vs 6/10
Moreno et al[28]	30 IAR vs 30 IPR	55 vs 53	No differences in UNOS status, Child-Pugh classification, MELD and diagnosis	PB with TPCS
Sabaté et al[30]	14 IAR vs 16 IPR	55 vs 54	No differences in Child-Pugh classification, MELD and diagnosis	PB with TPCS
Heidenhain et al[29]	66 SimR vs 65 ICR	51 vs 52	No differences in diagnosis ALD 33% vs 38%	Classical with VVB (100% vs 91%*)
Cai et al[33]	21 SimR vs 21 ICR	49 vs 47	N/A	N/A
Kniepeiss et al[35]	53 ICR vs 21 IPR	55 vs 48	HBV and HCV 29% vs 19% ALD 29% vs 43%	PB

ALD, alcoholic liver disease; *ALF*, acute liver failure; *HBV*, hepatitis B; *HCC*, hepatocellular carcinoma; *HCV*, hepatitis C; *NA*, not available; *MELD*, model for end-stage liver disease; *NL*, The Netherlands; *PB*, piggy-back; *TPCS*, temporary portacaval shunt; *UNOS*, United Network for Organ Sharing; *VVB*, venovenous bypass.
* $P < .05$.

differences in CIT duration were found except in 1 study,[29] irrespective of the type of the compared revascularization technique. A similar trend was found for the operation time, in which all studies but 2[22,29] were comparable between the different revascularization techniques; however, all studies comparing SimR with IPR in which WIT was reported found that WIT was significantly less in IPR. In one study comparing SimR to ICR, WIT was found to be significantly greater for SimR.[29] In all studies but 1 comparing IAR with IPR and presenting WIT, no differences in the duration of WIT were found. Only Sadler et al found significantly lesser WIT when IAR was used.[25] Use of blood products was described in 8 studies; in 6, there were no differences in red blood cell use between the 2 different revascularization techniques. One study showed significantly greater red blood cell use for IAR compared with IPR[22] and the other for SimR compared with IPR.[26]

Primary nonfunction and post-transplant liver function

There were no significant differences in the incidence of PNF in the 4 studies that compared SimR with IPR (Fig S1, Supplementary

Table IV
Perioperative parameters

Reference	No. of patients	CIT (min)	WIT (min)	Operation time (min)	Blood products use during LTx
Sankary et al[21]	45 SimR vs 83 IPR	636 vs 606	82 vs 62*	N/A	RBC 21 vs 25
Massarollo et al[23]	50 SimR vs 26 IPR	800 vs 852	N/A	N/A	N/A
Polak et al[26]	31 SimR vs 71 IPR	537 vs 547	64 vs 49*	556 vs 584	RBC 5.5 vs 2*
Baccarani et al[31]	42 SimR vs 38 IPR	455 vs 486	61 vs 39*	371 vs 400	RBC 6 vs 7 FFP 2,121 vs 2,097
Lu et al[32]	121 SimR vs 56 IPR	577 vs 561	N/A	378 vs 404	N/A
Millis et al[34]	40 IAR vs 60 IPR	N/A	N/A	N/A	N/A
Noun et al[22]	15 IAR vs 14 IPR	401 vs 405	N/A	472 vs 590*	RBC 5.4 vs 7.6* FFP 6.9 vs 7.2 PLT 3.2 vs 3.1 Antifibrinolytic agents 2 (13%) vs 7 (50%)*
Ducerf et al[24]	29 IAR vs 30 IPR	682 vs 741	35 vs 33	N/A	RBC 4 vs 3 FFP 9 vs 11
Sadler et al[25]	26 IAR vs 26 IPR	657.5 vs 711.5	40 vs 51*	N/A	RBC 4 vs 4 FFP 4 vs 4 PLT 1 vs 1
Walsh et al[27]	10 IAR vs 10 IPR	N/A	N/A	N/A	N/A
Moreno et al[28]	30 IAR vs 30 IPR	477 vs 494	53 vs 57	362 vs 368	RBC 2.1 vs 2.5 FFP 1 vs 1.5 PLT 4.7 vs 6.2
Sabaté et al[30]	14 IAR vs 16 IPR	535 vs 524	89 vs 110	N/A	RBC 1.9 vs 1.4 FFP 1 vs 0.9
Heidenhain et al[29]	66 SimR vs 65 ICR	557 vs 511*	49 vs 32*	303 vs 286*	N/A
Cai et al[33]	21 SimR vs 21 ICR	583 vs 575	N/A	487 vs 481	N/A
Kniepeiss et al[35]	53 ICR vs 21 IPR	288 vs 275	85 vs N/A	N/A	N/A

FFP, fresh frozen plasma; *N/A*, not available; *PLT*, platelets; *RBC*, red blood cells.
* $P < .05$.

Table V
Post-transplant liver function

Reference	No. of patients	PNF	Liver function
Sankary et al[21]	45 SimR vs 83 IPR	N/A	No differences in peak AST
Massarollo et al[23]	50 SimR vs 26 IPR	5/50 vs 3/26	N/A
Polak et al[26]	31 SimR vs 71 IPR	1/31 vs 1/71	No differences in peak AST and in PT
Baccarani et al[31]	42 SimR vs 38 IPR	0	No differences in AST, ALT, bilirubin, GGT, ALP and coagulation ≤90 d post-transplant
Lu et al[32]	121 SimR vs 56 IPR	1/121 vs 1/56	No differences in AST, ALT, bilirubin, INR, GGT, and ALP ≤30 d post-transplant Increased albumin concentration on day 1 in SimR compared to IPR*
Millis et al[34]	40 IAR vs 60 IPR	2/40 vs 3/60	No differences in liver function
Noun et al[22]	15 IAR vs 14 IPR	N/A	No difference in AST (day 1 and 5), factor V (day 1 and 5), and bile flow (day 1 and 5)
Ducerf et al[24]	29 IAR vs 30 IPR	0	Peak AST 721 vs 1,205*
Sadler et al[25]	26 IAR vs 26 IPR	1 vs 0	No difference in lactate concentrations at 1- and 12-h postreperfusion No difference in ALT at 24 h or peak during first 48 h No difference in PT at 12 and 24 h
Walsh et al[27]	10 IAR vs 10 IPR	N/A	No differences in ALT concentration 24-h post-transplant
Moreno et al[28]	30 IAR vs 30 IPR	0	N/A
Sabaté et al[30]	14 IAR vs 16 IPR	N/A	N/A
Heidenhain et al[29]	66 SimR vs 65 ICR	5/66 vs 0	No differences in bile production, PT and bilirubin concentration ALT significantly elevated in SimR on day 0, 1, 3, and 5
Cai et al[33]	21 SimR vs 21 ICR	0	Lower AST, ALT, GGT and bilirubin in ICR group
Kniepeiss et al[35]	53 ICR vs 21 IPR	0 vs 3	Lower AST, ALT, GGT and bilirubin in ICR group

ALT, alanine aminotransferase; *AST*, aspartate aminotransferase; *GGT*, gamma-glutamyl transpeptidase; *INR*, international normalized ratio; *N/A*, not available; *PT*, prothrombin time.
* $P < .05$.

Content; RR 1.00; 95% CI, 0.98–1.03; $P = .86$; $I^2 = 0\%$),[23,26,31,32] in 4 studies that compared IPR with IAR (Figure S2, Supplementary Content; RR 0.99; 95% CI, 0.96–1.03; $P = .80$; $I^2 = 0\%$),[24,25,28,34] and in 2 studies that compared SimR with ICR (Figure S3, Supplementary Content; RR 0.96; 95% CI, 0.88–1.04; $P = .29$; $I^2 = 47\%$).[29,33] There were also no differences in PNF observed in one study that compared ICR with IPR.[35]

In a study performed by Heidenhain et al, SimR was associated with a significantly higher alanine aminotransferase post-LTx compared with ICR.[29] A study performed by Ducerf et al that compared the differences between IAR and IPR revealed significantly greater peak serum aspartate aminotransferase levels in the IPR group.[24] In a study performed by Lu et al, an increased serum albumin concentration was observed early post-LTx in the SimR group compared with IPR.[32] All of the other studies showed no differences in the postoperative liver function as evaluated by several parameters irrespective of the type of revascularization technique. Post-transplant liver function and the incidence of PNF are summarized in Table V.

Patient and graft survival

There were no differences in the 1-year patient (Fig 2, *A*) and graft (Fig 2, *B*) survivals in the 3 studies that compared SimR with IPR (RR 0.91; 95% CI, 0.51–1.65; $P = .76$; $I^2 = 28\%$ and RR 0.83; 95% CI, 0.51–1.35; $P = .45$; $I^2 = 0\%$, respectively).[26,31,32] It was not

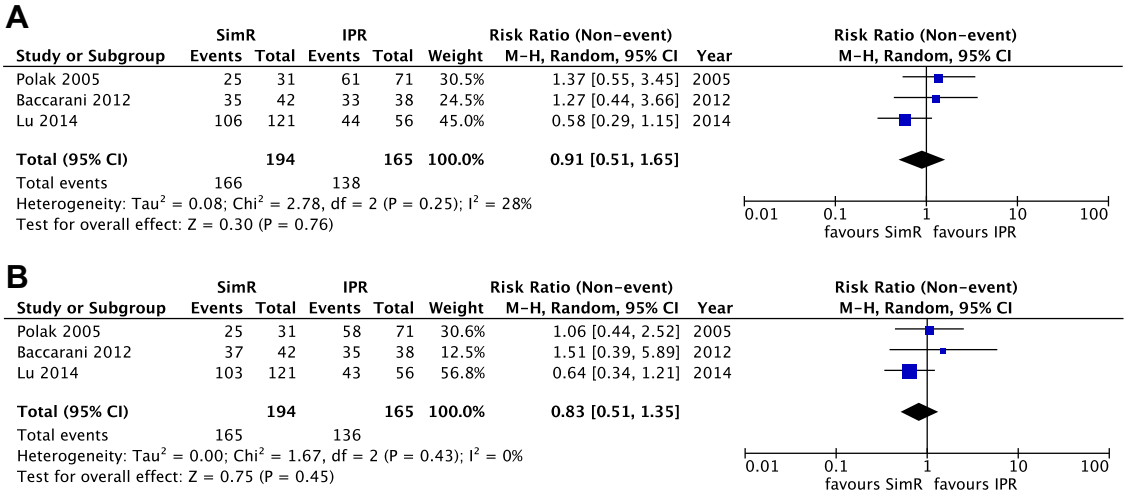

Fig 2. Comparison of first year patient (*A*) and graft survival (*B*) used for liver grafts reperfused with SimR and IPR.

Table VI
Outcome and complications

Reference	No. of patients	Patient survival	Graft survival	Vascular complications	Biliary complications	Late re-LTx
Sankary et al[21]	45 SimR vs 83 IPR	N/A	N/A	N/A	1/45 (NAS) vs 7/83 (NAS)*	N/A
Massarollo et al[23]	50 SimR vs 26 IPR	86% vs 73% at 1 mo	76% vs 69% at 1 mo	N/A	1/50 vs 9/26* Leak 1/50 vs 1/26 AS 0/50 vs 7/26 NAS 0/50 vs 1/26	N/A
Polak et al[26]	31 SimR vs 71 IPR	81% vs 86% at 1 y	80% vs 82% at 1 y	2/31 (1 PVT and 1 HAT) vs 4/71 (2 PVT and 2 HAT)	7/ 31 vs 6/71 AS 4/31 vs 2/71 NAS 3/31 vs 4/71	2/31 vs 6/71
Baccarani et al[31]	42 SimR vs 38 IPR	83% vs 88% at 1 y	87% vs 93% at 1 y	1/42 (HAT) vs 1/38 (HAT)	8/42 vs 15/38* Leak 2/42 vs 3/38 AS 4/42 vs 5/38 NAS 0 vs 9/38*	1/42 vs 1/38
Lu et al[32]	121 SimR vs 56 IPR	88% vs 79% at 1 y 79% vs 71% at 2 y 76% vs 68% at 3 y	85% vs 76% at 1 y 76% vs 69% at 2 y 73% vs 66% at 3 y	4/121 (2 HAT) vs 4/56 (2 HAT)	11/121 vs 14/56* Leak 2/121 vs 2/56 AS 5/121 vs 7/56 NAS 2/121 vs 5/56* Stones 4/121 vs 2/56	5/121 vs 2/56
Millis et al[34]	40 IAR vs 60 IPR	N/A	N/A	N/A	N/A	4/40 vs 8/60
Noun et al[22]	15 IAR vs 14 IPR	N/A	N/A	0 vs 1/14 (HAT)	1/15 (AS) vs 1/14 (AS)	N/A
Ducerf et al[24]	29 IAR vs 30 IPR	93% vs 93% at 2 y	N/A	3/29 (HA narrowing) vs 3/30 (HAT, HA stricture, PV stricture)	2/29 (leak) vs 2/30 (leak)	1/29 vs 3/30
Sadler et al[25]	26 IAR vs 26 IPR	85% vs 96% at 1 y	85% vs 88.5% at 1 y	0 vs 2 (HAT)	1 vs 0	0 vs 2/26
Walsh et al[27]	10 IAR vs 10 IPR	90% vs 100% at 3 mo	N/A	1/10 (PVT and HAT) vs 0	N/A	N/A
Moreno et al[28]	30 IAR vs 30 IPR	97% vs 97% at 1 mo	N/A	N/A	5/30 (strictures) vs 4/30 (strictures)	0
Sabaté et al[30]	14 IAR vs16 IPR	N/A	N/A	N/A	N/A	0 vs 2/16
Heidenhain et al[29]	66 SimR vs 65 ICR	95% vs 94% at 1 y 92% vs 89% at 3 y	88% vs 89% at 1 y 84% vs 86% at 3 y	3/66 (1 PVT and 2 HAT) vs 2/65 (HAT)	2/66 (NAS) vs 8/65 (NAS)	6/66 vs 3/65
Cai et al[33]	21 SimR vs 21 ICR	N/A	N/A	N/A	N/A	N/A
Kniepeiss et al[35]	53 ICR vs 21 IPR	94% vs 95% at 8 d	N/A	N/A	N/A	N/A

AS, anastomotic strictures; *HA*, hepatic artery; *HAT*, hepatic artery thrombosis; *N/A*, not available; *NAS*, nonanastomotic strictures; *PVT*, portal vein thrombosis; *PV*, portal vein.
* $P < .05$.

possible to perform forest plots comparing IAR with IPR and SimR with ICR techniques regarding patient and graft survival owing to a lack of reported outcomes or differences in the follow-up period. None of the analyzed studies presented independently significant differences regarding patient or graft survival. Patient and graft survival are summarized in Table VI.

Vascular complications, biliary complications, and liver retransplantation

There were no differences in VC in the 3 studies that compared SimR with IPR (Fig S4, Supplementary Content; RR 1.01; 95% CI, 0.97–1.06; $P = .57$; $I^2 = 0\%$)[26,31,32] or in the 4 studies comparing IAR with IPR (Fig S5, Supplementary Content; RR 1.04; 95% CI, 0.95–1.13; $P = .40$; $I^2 = 0\%$).[22,24,25,27] There was no difference in VC in the study that compared SimR with ICR.[29]

In 4 of the 5 studies that compared SimR with IPR, the incidence of BC was significantly greater in the IPR group as reported in each of the studies.[21,23,31,32] In the meta-analysis of these 5 studies (Fig 3, *A*), there was no difference in the BC rate (RR 1.14; 95% CI, 0.97–1.35; $P = .11$; $I^2 = 76\%$), although a trend was observed (10% vs 19% of BC for SimR versus IPR, respectively). Regarding the fact that there were differences in the type of BC reported by different authors and in 3 studies comparing SimR with IPR,[21,31,32] significant

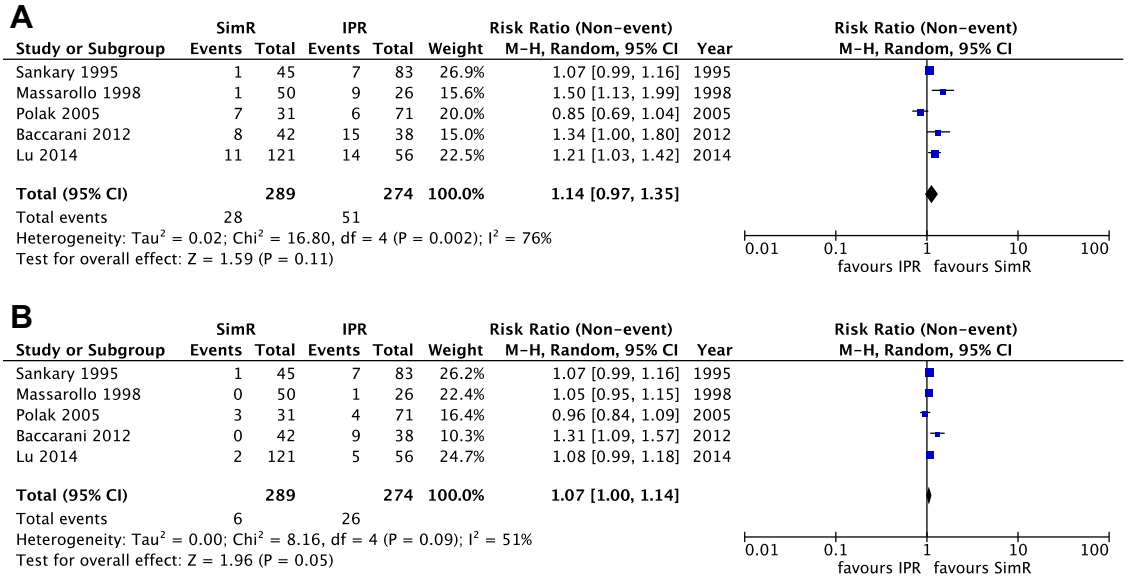

Fig 3. Comparison of biliary complications (*A*) and nonanastomotic strictures (*B*) for liver grafts reperfused with SimR and IPR.

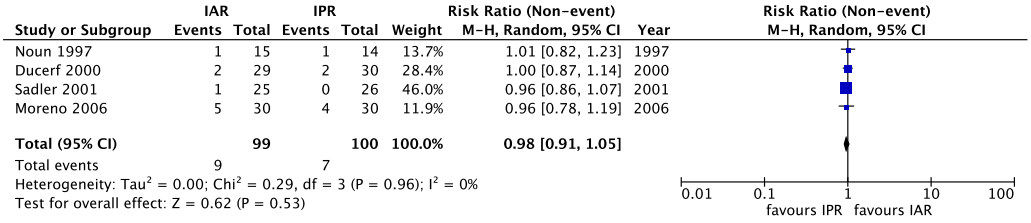

Fig 4. Comparison of biliary complications for liver grafts reperfused with IAR and IPR.

differences were observed in the incidence of nonanastomotic strictures, and a separate subanalysis was performed (Fig 3, *B*). There was a significant difference in the rate of nonanastomotic strictures between the SimR and IPR groups (2% vs 9%, respectively), although moderate heterogeneity between studies was observed (RR 1.07; 95% CI, 1.00–1.14; $P = .05$; $I^2 = 51\%$). In the 4 studies comparing IAR with IPR, no differences were found regarding the incidence of BC (Fig 4; RR 0.98; 95% CI, 0.91–1.05; $P = .53$; $I^2 = 0\%$).[22,24,25,28] In a study comparing SimR with the ICR technique, there were no differences in BC.[29]

There were no differences in re-LTx in 3 studies comparing SimR with IPR (Fig S6, Supplementary Content; RR 1.00; 95% CI, 0.96–1.05; $P = .96$; $I^2 = 0\%$)[26,31,32] and in the 5 studies comparing IAR with IPR (Fig S7, Supplementary Content; RR 1.03; 95% CI, 0.98–1.08; $P = .23$; $I^2 = 0\%$).[24,25,28,30,34] There was also no significant difference in re-LTx in a study comparing SimR with the ICR technique.[29] VC, BC, and re-LTx are summarized in Table VI.

Hemodynamic and metabolic changes

Two studies comparing SimR with IPR found no differences in the incidence of PRS or intra- and postoperative vasopressor requirements.[31,32] In 3 studies, hemodynamic changes and the cardiovascular status were compared between the IAR and IPR techniques.[22,27,28] Two studies demonstrated more homogenous reperfusion when IAR was used.[22,24] There were no differences in the incidence of PRS in the 2 studies that compared IAR with IPR (Fig S8, Supplementary Content; RR 1.02; 95% CI, 0.73–1.44; $P = .89$; $I^2 = 6\%$).[22,28]

The tissue oxygenation and metabolic changes after IAR and IPR were assessed in 2 studies. A study by Moreno et al demonstrated that a decrease in gastric and arterial pH was more accentuated in IAR compared to IPR, whereas oxygen delivery and consumption was significantly greater in the IPR group.[28] Walsh et al[27] also reported greater oxygen consumption in the IPR group compared to IAR, although no differences in the lactate and bicarbonate concentration were observed. In 1 study, the *Rocuronium* profile was compared between IAR and IPR, revealing a significant decrease in the concentration of *Rocuronium* after portal unclamping, irrespective of the order of unclamping (IAR versus IPR).[30] Hemodynamic and metabolic changes are summarized in Table S2 (Supplementary Content).

Quality assessment

The quality of the analyzed studies was assessed as low (3 studies) and high (3 studies) for the randomized trials (Table VII). In the cohort studies, the quality was assessed as either fair (3 studies) or good (6 studies).

Discussion

This systematic review summarizes all currently available data from the literature regarding the different techniques of revascularization used in clinical LTx. In our review, the outcome

Table VII
Quality assessment of the studies included in the meta-analysis according to the Jadad score and Newcastle-Ottawa scale

Reference	Quality points by outcome			Sum
	Randomized controlled trials			
	Randomization (0–2)	Double blinding (0–2)	Withdrawals and dropouts (0–1)	
Baccarani et al[31]	0	0	1	1/5
Millis et al[34]	0	0	1	1/5
Ducerf et al[24]	0	0	1	1/5
Moreno et al[28]	2	0	1	3/5
Sabaté et al[30]	2	0	1	3/5
Heidenhain et al[29]	2	0	1	3/5

	Cohort studies								
	Selection (0–4)				Comparability (0–2)	Outcome (0–3)			
Sankary et al[21]	1	1	1	1	1	1	0	0	6/9
Massarollo et al[23]	1	1	1	1	2	1	0	0	7/9
Polak et al[26]	1	1	1	1	1	1	1	0	7/9
Lu et al[32]	1	1	1	1	2	1	1	0	8/9
Noun et al[22]	1	1	1	1	1	1	1	0	7/9
Sadler et al[25]	1	1	1	1	1	1	0	0	6/9
Walsh et al[27]	1	1	1	1	1	1	0	0	6/9
Cai et al[33]	1	1	1	1	2	1	1	0	8/9
Kniepeiss et al[35]	1	1	1	1	1	1	1	0	7/9

parameters included patient and graft survival, retransplantation rate, biliary and vascular complications, intraoperative parameters, post-transplant liver function, and hemodynamic and metabolic changes. This approach allowed us to perform a more extensive analysis of the possible benefits or drawbacks of each technique of revascularization.

An online survey of 28 of 37 liver transplant centers within the Eurotransplant International Foundation region showed that most of the centers used IPR as a preferred technique (46%), followed by SimR (39%), and ICR (11%).[16] IAR was the preferred method of revascularization at only 1 center (4%). In 75% of the centers, the revascularization technique was standardized; however, in most of the cases, this standard was based only on personal or institutional experience rather than on hard data. In the remaining centers, the surgeon performing LTx selected the revascularization technique. A recent international online survey among all liver transplant centers ($n = 52$, with an 81% response rate) within the Eurotransplant, Scandiatransplant, Swisstransplant, and British Transplant Society networks confirmed that IPR was the most common revascularization technique (64%) followed by the SimR (17%), ICR (12%), and IAR (7%) techniques.[36]

IPR is the preferred technique at the majority of LTx centers, and some data in this review confirmed the superiority of IPR. IPR is simple and rapid and allows for the use of portal blood as a flush to remove the preservation solution from the liver, if necessary.[37] Indeed, an analysis of the studies in this review showed that IPR results in a lesser WIT than in the SimR group and was comparable to the IAR group, except for the study performed by Sadler et al.[25]

According to the presented results, the incidence of PNF in IPR did not differ from SimR and IAR. The same was found for postoperative liver function, which was generally comparable between IPR and other revascularization techniques, except for 1 study in favor of IAR.[24] The incidence of PRS did not differ between IPR and the other revascularization techniques. Despite similar patient and graft survival between all revascularization techniques, IPR was associated more often with BC compared with SimR. The meta-analysis of all BC showed that there was a nonsignificant trend of a more frequent incidence of BC and a significantly greater rate of nonanastomotic strictures for the IPR technique, which favored the SimR technique. One possible explanation could be that the time for arterial reperfusion in SimR is less than in IPR; therefore, bile duct ischemia is less pronounced. Surprisingly, there was no difference in the rate of BCs between IPR and IAR, in which the time to arterial reperfusion in IAR is even less than with SimR. Unfortunately, there are no studies that compared IAR with SimR, which could clarify this potential difference.

The second most common revascularization technique appears to be SimR, which is also favored in 1 of the studies.[16] A study performed by Polak et al displayed significantly greater requirement for blood products when using SimR compared with IPR.[26] Possible explanations for this finding include a prolonged anhepatic phase in SimR resulting in an increase in tissue-type plasminogen activator with a consecutive increase in fibrinolysis after reperfusion and intraoperative problems with bleeding after SimR.

Although IAR was used infrequently in the survey, LAR has gained attention at many centers.[15] The results of this systematic review indicate that IAR offered more homogenous reperfusion, fewer changes in hemodynamics, but also less oxygen delivery and oxygen consumption compared with IPR. This finding may be extremely important if the recipient is hemodynamically unstable or has pulmonary hypertension. The second clinical scenario when IAR can offer greater benefit than IPR or SimR is the use of extended criteria livers, especially from donors after DCD. These grafts are prone to pronounced hemodynamic variations at the time of reperfusion and postoperative BCs. Unfortunately, there was insufficient data regarding the liver donors in the studies included in this systematic review to confirm this speculation. Moreover, based on the available data and study period, it can be presumed that majority of the donors were standard and not extended criteria donors.

Gurusamy et al and Manzini et al each performed a meta-analysis on the revascularization techniques in clinical LTx based on 6 and 11 studies, respectively.[16,38] No differences in patient survival, graft survival, and postoperative complications were found; however, owing to the heterogenous nature of the analyzed studies, both of these meta-analyses have some limitations in their interpretation. Based on the incomplete donor data, an important difference in the mean donor age was clearly observed. For

Table VIII
Benefits and drawbacks of revascularization techniques with possible application in specific clinical situations

Revascularization technique	Benefits	Drawbacks	Potential use
IPR	Short WIT Favorable immediate perfusion of the liver parenchyma	Acute overload of the pulmonary circulation Prolonged ischemia to bile ducts	Standard donor liver, old liver Hemodynamically stable recipient with cardiopulmonary reserve In case of predicted technically difficult arterial anastomosis
IAR	Prevents acute overload of the pulmonary circulation Short WIT (also for bile ducts)	Less overall blood flow to the graft	Extended criteria livers (DCD) Recipient with poor cardiopulmonary reserve Recipient with portal vein thrombosis
ICR	Very short WIT Beneficial for hepatocytes (less IPF, low transaminases)	Prolonged warm ischemia to bile ducts (risk for nonanastomotic strictures)	Liver with very low risk for nonanastomotic strictures (short CIT, young, DBD)
SimR	Physiologic restoration of blood flow to the liver parenchyma and the bile ducts	Significantly prolonged warm ischemia	Standard donor liver (young, DBD)

IPF, initial poor function.

example, in a study conducted by Sankary et al, the median donor age was 33 years, whereas the liver donors were 23 years older (median age: 56 years) in the study performed by Baccarani et al.[21,31] The same was found for the different operative techniques in the analyzed studies that include both the piggy-back technique with or without a temporary portocaval shunt and the classic techniques with or without a venovenous bypass (Table II). In our opinion, the latest meta-analysis performed by Wang et al contains at least 2 methodologic errors[39]: (1) the authors included 2 studies from the same center that described the same patient cohort,[31,40] and (2) the investigators did not avoid an error in data extraction and replaced SimR with the IPR group when reporting one of the studies.[26] Thus, the conclusion that the SimR technique decreases the incidence of BCs does not seem to be justified.

We agree with Manzini et al that an adequately performed randomized controlled trial (RCT) comparing the different revascularization techniques could determine which technique is superior.[16] In our opinion, however, it will be extremely difficult to set up a well-designed RCT to address this issue. First, such an RCT would require a large number of patients in each of the arms of the study to have sufficient statistical power and provide any relevant conclusions. Second, the outcome parameters that should be taken as the primary endpoint and the secondary endpoints (eg, graft survival, PNF or early graft dysfunction, BC, or hemodynamic stability after reperfusion) need to be determined. Although each of these endpoints are extremely important, they can be influenced by several confounding factors related to the donor, transplant procedure, and the recipient. The question remains as to whether the data from this systematic review could be used to draw some conclusions regarding the benefits and drawbacks of each revascularization technique. It is not possible to answer the question of whether any one revascularization technique was superior over the other without a proper RCT. Thus, the ongoing RTC from Belarus that is comparing the ICR and IPR techniques for revascularization may provide fresh insight into this issue.[41]

We strongly maintain that each revascularization technique can provide some benefit when it is used in a specific clinical situation.[11] Challenging situations regarding the recipient can be overcome with a use of proper techniques of revascularization. The ICR technique leads to an extremely short WIT (which is an advantage for hepatocytes), but prolongs the ischemia time to the bile ducts (which can cause nonanastomotic biliary strictures). This technique can be applied to good liver grafts with an extremely low risk for nonanastomotic biliary strictures, such as young livers from donors after brain death (DBD) with a short CIT. The SimR technique is the most physiologically beneficial regarding the restoration of blood flow through the liver, although the WIT is prolonged. This technique can be applied to standard grafts and young livers from DBD. The IPR technique can be used in most clinical scenarios for LTx because it allows for lessening of the WIT; however, this technique is associated with a sudden overload in the pulmonary circulation and prolonged ischemia time to the bile ducts. This technique is also recommended when a technically difficult arterial anastomosis is predicted. The IAR technique prevents an acute overload of the pulmonary circulation and decreases the WIT for the liver as a whole organ, including biliary tree, which might be an important benefit in the DCD grafts. This revascularization technique may also be recommended in recipients with a poor cardiopulmonary reserve and in cases of unexpected or extensive portal vein thrombosis, when an additional portal vein thrombectomy is required. All DCD liver grafts can supposedly also benefit from the performance of IAR. The benefits and drawbacks of 4 different revascularization techniques based on this review are summarized in Table VIII.

The revascularization technique seems to be further complicated in the upcoming era of liver storage by perfusion (both hypothermic and normothermic concepts). It is likely that new studies regarding the sequence of liver revascularization should be performed when liver machine perfusion becomes a standard procedure in clinical practice.

This systematic review and meta-analysis are associated with limitations. There are differences in the study type, population, techniques, and follow-up period. This review included 15 studies, 6 of which were RCTs and 9 were cohort studies. Surprisingly, only 4 studies of the 6 reported the method of randomization. This obviously creates heterogeneity between studies and may implicate proper conclusions. Significant or moderate heterogeneity was present for the analysis of BC and nonanastomotic strictures (Fig 3, *A* and *B*) when the SimR and IPR techniques were compared. Data regarding the donor characteristics including organ steatosis were limited. According to the available data, there were no differences between the donors regarding the age, sex, duration of stay in the intensive care unit, or the use of catecholamines intraoperatively. It can be presumed that the majority of livers in the analyzed studies were retrieved from DBD and relatively young donors during the study period. A significant increase was observed regarding the use of old liver grafts and grafts procured from DCD during the past 2 decades. This situation implicates that a comparison of the different revascularization techniques may bring alternative results after LTx. Finally, the analyzed recipient population was awkward to compare because the number of patients in the reviewed articles ranged from between 20 and 176; neither of the compared groups, however, exceeded more than 100 in 11 of the 15 studies. There were no differences between the age and sex of the recipients. The rest of the recipient characteristics were descriptive and difficult to compare. In 11 studies, no differences in the diagnosis of liver disease were reported. In 5 studies, the Child-Pugh classification

was compared, and the MELD score was used in 4 studies. We agree that these scales do not present comorbidities and do not completely reflect the recipient status; however, it is difficult to present more objective and comparable scales that can be used to evaluate patients with end-stage liver disease. To further complicate this issue, the recipient population has also changed recently as an increasing number of individuals on the waiting list for LTx have hepatocellular carcinoma and nonalcoholic steatohepatitis disease. All of these concerns limit our review and meta-analysis and lead us to be cautious with our present conclusions.

In conclusion, the knowledge regarding optimal revascularization techniques in LTx is growing gradually. Based on available studies, it can be concluded that the order of revascularization does not influence patient and graft survival. Moreover, each revascularization technique offers potential benefits that can be used in specific clinical situations. Based on changes in the donor and recipient population, there appears to be a need to design and conduct an RCT to compare the different revascularization techniques.

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Conflict of interest

The authors have indicated that they have no conflict of interest regarding the content of this article.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.surg.2019.03.024.

References

1. Liver transplantation. National Institutes of Health Consensus Development. *Natl Inst Health Consens Dev Conf Summ*. 1983;4:15.
2. Polak WG, Peeters PMJG, Slooff MJH. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant*. 2009;23:546–564.
3. Hickman R, Innes CR. The relevance of the order of revascularization in liver grafting. *Hepatology*. 1990;11:471–476.
4. van As AB, Lotz Z, Tyler M, et al. Effect of early arterialization of the porcine liver allograft on reperfusion injury, hepatocellular injury, and endothelial cell dysfunction. *Liver Transpl*. 2001;7:32–37.
5. Post S, Palma P, Gonzalez AP, et al. Timing of arterialization in liver transplantation. *Ann Surg*. 1994;220:691–698.
6. Starzl TE, Marchioro TL, Kaulla KNV. Homotransplantation of the liver in humans. *Surg Gynecol Obstet*. 1963;117:659–676.
7. Piratvisuth T, Tredger JM, Hayllar KA, et al. Contribution of true cold and rewarming ischemia times to factors determining outcome after orthotopic liver transplantation. *Liver Transpl Surg*. 1995;1:296–301.
8. Platz KP, Mueller AR, Schafer C, et al. Influence of warm ischemia time on initial graft function in human liver transplantation. *Transplant Proc*. 1997;29:3458–3459.
9. Kniepeiss D, Iberer F, Grasser B, et al. A single-center experience with retrograde reperfusion in liver transplantation. *Transplant Int*. 2003;16:730–735.
10. Kniepeiss D, Zink M, Iberer F, et al. Influence of retrograde flushing via the caval vein on the post-reperfusion syndrome in liver transplantation. *Clin Transplant*. 2004;18:638–641.
11. Polak WG, Porte RJ. The sequence of revascularization in liver transplantation: it does make a difference. *Liver Transpl*. 2006;12:1566–1570.
12. Noack K, Bronk SF, Kato A, et al. The greater vulnerability of bile duct cells to reoxygenation injury than to anoxia. Implications for the pathogenesis of biliary strictures after liver transplantation. *Transplantation*. 1993;56:495–500.
13. Terblanche J, Allison HF, Northover JM. An ischemic basis for biliary strictures. *Surgery*. 1983;94:52–57.
14. Slieker JC, Farid WR, van Eijck CH, et al. Significant contribution of the portal vein to blood flow through the common bile duct. *Ann Surg*. 2012;255:523–527.
15. Bartlett A, Rela M, Heaton N. Reperfusion of the liver allograft with blue blood: Is it still the royal perfusate? *Am J Transplant*. 2007;7:1689–1691.
16. Manzini G, Kremer M, Houben P, et al. Reperfusion of liver graft during transplantation: techniques used in transplant centres within Eurotransplant and meta-analysis of the literature. *Transpl Int*. 2013;26:508–516.
17. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg*. 2010;8:336–341.
18. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials*. 1996;17:1–12.
19. Wells GSB, O'Connell D, Peterson J, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed April 12, 2019.
20. Collaboration TC. RevMan 2014. Available from: https://community.cochrane.org/help/tools-and-software/revman-5/revman-5-download. Accessed April 12, 2019.
21. Sankary HN, McChesney L, Frye E, et al. A simple modification in operative technique can reduce the incidence of nonanastomotic biliary strictures after orthotopic liver transplantation. *Hepathol*. 1995;21:63–69.
22. Noun R, Sauvanet A, Belghiti J. Appraisal of the order of revascularization in human liver grafting: A controlled study. *J Am Coll Surg*. 1997;185:70–73.
23. Massarollo PCB, Mies S, Raia S. Simultaneous arterial and portal revascularization in liver transplantation. *Transplant Proc*. 1998;30:2883–2884.
24. Ducerf C, Mechet I, Landry JL, et al. Hemodynamic profiles during piggyback liver grafts using arterial or portal revascularization. *J Am Coll Surg*. 2000;190:89–93.
25. Sadler KM, Walsh TS, Garden OJ, et al. Comparison of hepatic artery and portal vein reperfusion during orthotopic liver transplantation. *Transplantation*. 2001;72:1680–1684.
26. Polak WG, Miyamoto S, Nemes BA, et al. Sequential and simultaneous revascularization in adult orthotopic piggyback liver transplantation. *Liver Transplant*. 2005;11:934–940.
27. Walsh TS, Garden OJ, Lee A. Metabolic, cardiovascular, and acid-base status after hepatic artery or portal vein reperfusion during orthotopic liver transplantation. *Liver Transplant*. 2002;8:537–544.
28. Moreno C, Sabaté A, Figueras J, et al. Hemodynamic profile and tissular oxygenation in orthotopic liver transplantation: Influence of hepatic artery or portal vein revascularization of the graft. *Liver Transplant*. 2006;12:1607–1614.
29. Heidenhain C, Heise M, Jonas S, et al. Retrograde reperfusion via vena cava lowers the risk of initial nonfunction but increases the risk of ischemic-type biliary lesions in liver transplantation–a randomized clinical trial. *Transplant Int*. 2006;19:738-748.
30. Sabaté A, Ferreres E, Valcárcel M, et al. Rocuronium profile during orthotopic liver transplantation: effect of changing the order of vascular clamp release at reperfusion of the hepatic graft. *Transplant Proc*. 2010;42:1760–1762.
31. Baccarani U, Rossetto A, Lorenzin D, et al. Protection of the intrahepatic biliary tree by contemporaneous portal and arterial reperfusion: results of a prospective randomized pilot study. *Updates Surg*. 2012;64:173–177.
32. Lu D, Xu X, Wang J, et al. The influence of a contemporaneous portal and hepatic artery revascularization protocol on biliary complications after liver transplantation. *Surgery*. 2014;155:190–195.
33. Cai Q, Li S, Jiang Y, et al. Alleviating graft injury during liver transplantation by improving retrograde perfusion in standard orthotopic liver transplantation. *Int J Clin Exp Med*. 2016;9:4364–4371.
34. Millis JM, Melinek J, Csete M, et al. Randomized controlled trial to evaluate flush and reperfusion techniques in liver transplantation. *Transplantation*. 1997;63:397–403.
35. Kniepeiss D, Iberer F, Schaffellner S, et al. Feasibility of a new technique of reperfusion in liver transplantation. *Langenbecks Arch Surg*. 2003;15:47–50.
36. Czigany Z, Scherer MN, Pratschke J, et al. Technical aspects of orthotopic liver transplantation-a survey-based study within the eurotransplant, swisstransplant, scandiatransplant, and british transplantation society networks. *J Gastrointest Surg*. 2019;23:529–537.
37. Emre S, Schwartz ME, Mor E, et al. Obviation of prereperfusion rinsing and decrease in preservation/reperfusion injury in liver transplantation by portal blood flushing. *Transplantation*. 1994;57:799–803.
38. Gurusamy KS, Naik P, Abu-Amara M, et al. Techniques of flushing and reperfusion for liver transplantation. *Cochrane Database Syst Rev*. 2012;3:CD007512.
39. Wang JZ, Liu Y, Wang JL, et al. Sequential vs simultaneous revascularization in patients undergoing liver transplantation: a meta-analysis. *World J Gastroenterol*. 2015;21:7036–7046.
40. Adani GL, Rossetto A, Bresadola V, et al. Contemporaneous portal-arterial reperfusion during liver transplantation: preliminary results. *J Transplant*. 2011;2011:251656.
41. A Study of Retrograde rEperfusion in Dbd Donor LIver Transplantation (REDLIT) 2015. Available from: https://www.clinicaltrials.gov/ct2/show/NCT02423941. Accessed April 12, 2019.