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ORIGINAL ARTICLE

Technical Aspects of Orthotopic Liver Transplantation—a Survey-Based Study Within the Eurotransplant, Swisstransplant, Scandiatransplant, and British Transplantation Society Networks

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Abstract

Background Orthotopic liver transplantation (OLT) has emerged as the mainstay of treatment for end-stage liver disease. However, technical aspects of OLT are still subject of ongoing debate and are widely based on personal experience and local institutional protocols.

Methods An international online survey was sent out to all liver transplant centers ($n = 52$) within the Eurotransplant, Swisstransplant, Scandiatransplant, and British Transplant Society networks. The survey sought information on center-specific OLT caseload, vascular and biliary reconstruction, graft reperfusion, intraoperative control of hemodynamics, and drain policies.

Results Forty-two centers gave a valid response (81%). Out of these, 50% reported piggy-back and 40.5% total caval replacement as their standard technique. While 48% of all centers generally do not apply veno-venous bypass (vvBP) or temporary portocaval shunt (PCS) during OLT, vvBP/PCS are routinely used in six centers (14%). Portal vein first reperfusion is used in 64%, followed by simultaneous (17%), and retrograde reperfusion (12%). End-to-end duct-to-duct anastomosis without biliary drain (67%) is the most frequently performed method of biliary reconstruction. No significant associations were found between the center caseload and the surgical approach used. The predominant part of the centers (88%) stated that techniques of OLT are not evidence-based and 98% would participate in multicenter clinical trials on these topics.

Conclusion Technical aspects of OLT vary widely among European centers. The extent to which center-specific variation of techniques affect transplant outcomes in Europe should be elucidated further in prospective multicenter trials.

Keywords Survey · Liver transplantation · Piggy-back · Reperfusion · Abdominal drain

Abbreviations

AFR	Artery first reperfusion
BTS	British Transplant Society
DCD	Donation following cardiac death
ECD	Extended criteria donors
EEDD	End-to-end duct-to-duct anastomosis
ET	Eurotransplant
MELD	Model for End-stage Liver Disease
OLT	Orthotopic liver transplantation
PB	Piggy-back
PCS	Portocaval shunt
PVFR	Portal vein first reperfusion
RCT	Randomized controlled trial

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RER	Retrograde reperfusion
ScaT	Scandiatransplant
SIR	Simultaneous reperfusion
SSDD	Side-to-side duct-to-duct anastomosis
ST	Swisstransplant
TCR	Total caval replacement
vvBP	Veno-venous bypass
WIT	Warm ischemia time

Introduction

Since Thomas Starzl's pioneering efforts in 1963, orthotopic liver transplantation (OLT) evolved as the standard treatment for patients with end-stage liver disease.[1] In an attempt to improve allograft allocation, transplantation networks such as the United Network for Organ Sharing, Eurotransplant (ET), Scandiatransplant (ScaT), Swisstransplant (ST), and the British Transplant Society (BTS) have been established. Better allocation and cross-border exchange of deceased donor organs as well as the wider use of dynamic preservation techniques have significantly improved the overall utilization of donor allografts.[2] Technical aspects of OLT are still widely based on personal experiences and institutional protocols. Although a fair amount of information is available on various aspects of organ retrieval and donor/recipient characteristics, there is still no national or international database available in Europe dedicated to surgical aspects of the transplantation procedure itself. While most clinical decisions in OLT are not supported by high-level evidence, several systematic reviews on surgical aspects of OLT remain inconclusive due to a lack of high-quality randomized controlled trials.[3–5]

We therefore conducted an international cross-sectional survey within all 52 liver transplant centers of the ET, ST, ScaT, and BTS networks to provide a comprehensive overview of clinical practices of adult whole-graft deceased donor OLT in these regions. Furthermore, we discussed the current level of evidence and attempted to identify factors relevant for future prospective clinical trials.

Methods and Analysis

Survey Development and Data Collection

An online survey instrument with open-ended multiple-choice questions (SurveyMonkey, Palo Alto, CA) investigating the surgical aspects of adult whole-graft deceased donor OLT was designed by the authors (ZC, GL) and an experienced computer scientist. Following domains were addressed: (I) center volumes, (II) techniques of liver transplantation: caval outflow reconstruction, use of veno-venous bypass (vvBP) for total caval replacement (TCR), or portocaval shunt (PCS) in piggy-back (PB); (III) graft reperfusion techniques; (IV) use of intra-abdominal drains; (V) approach of biliary reconstruction and drainage; and (VI) current evidence and need for further prospective trials. Where applicable, the opportunity to insert free-text statements was given. The original online survey is available as supplementary digital content (Text S1).

Content and face validity were initially pilot tested by five independent senior transplant surgeons. Survey items were updated based on initial feedback obtained. This manuscript was prepared according to available recommendations for reporting survey research.[6,7] This present survey study was formally endorsed by ET (Req 553-1.2016).

The survey was disseminated online containing a personalized link to the chairmen or clinical leads of each of the 52 transplant centers within the ET, ST, ScaT, and BTS networks. The survey was intended to reflect current first-line practices in the transplant unit rather than individual concepts and preferences of the respondents. The names of the program representatives were collected by written request from ET as well as using online resources. After the initial distribution, two reminders, each 2–3 weeks apart, were sent to non-responders. In a case of multiple responses from the same center, the first complete response was used for final analysis.

Data Analysis

Data was exported directly from SurveyMonkey into digital spreadsheets. For quantitative center caseload analysis, data was transferred to defined categories (< 25 OLT/year = category 1; 25–50 OLT/year = category 2; 50–100 OLT/year = category 3; > 100 OLT/year = category 4) and was compared using the Fisher's exact test. The level of significance was set to $p < 0.05$ and p values are given for two-sided testing. Statistical tests were performed using the IBM SPSS Statistics v24 software package (IBM Inc., Armonk, NY, USA).

Results

Characteristics

The online survey was sent out to all transplant centers (n = 52) on February 8, 2017 and was accessible until April 31, 2017. The median response time was 9 days (range 1–64 days). By April 2017, 42 out of the total 52 transplant centers (81%) gave a valid response to the survey. Transplantation case load of the participating centers were as follows: 10/42 centers (24%) < 25 OLT/year; 10/42 centers (24%) 25–50 OLT/year; 18/42 centers (43%) 50–100 OLT/year; 4/42 centers (9%) > 100 OLT/year. Further information on transplant network characteristics was obtained from the ET, ST, ScaT, and BTS annual activity reports Table 1.

Table 1 Transplant characteristics within Eurotransplant, Swisstransplant, Scandiatransplant, and British Transplant Society

	Eurotransplant	Swisstransplant	Scandiatransplant	British Transplant Society
Number of programs	37	3	5	7
Median patients on waiting list per numbers of programs in 2016	46	69	22	76
Total deceased donor OLTs last 5 years (median; range)	1537 (1468–1595)	109 (100–136)	377 (342–417)	780 (659–801)
Deceased donor OLTs 2016 per center (median; range)	39 (3–113)	37 (19–52)	92 (59–105)	102 (45–199)
Numbers of patients on waiting list during the last 5 years (median; range)	1918 (1704–2406)	161 (122–207)	108 (84–115)	521 (462–566)
Waiting list mortality last 5 years (median; range)	501 (471–674)	24 (21–33)	13 (11–20)	82 (80–105)
Waiting list mortality/waiting list last 5 years (%) (median; range)	27 (24–29)	15 (13–24)	12 (10–24)	16 (14–20)

Based on the Annual Activity Reports of ET, ST, ScaT, and BTS on adult OLT

Technical Aspects of Liver Transplantation

Seventeen centers (40.5%) reported TCR and 21 (50%) PB as their first-line technique for OLT, respectively. In four centers (9.5%), the decision for TCR or PB is based entirely on personal preference (Table 2). In 20 transplant centers, vvBP or PCS is completely avoided during transplantation. In summary, six centers stated their routine use of vvBP (7%, $n = 3/42$) or PCS (7%, $n = 3/42$). Sixteen centers (38%) reported the occasional usage of vvBP or PCS in selected cases (Table 2).

From all responding centers, the most frequent approach to first-line graft reperfusion in OLT was portal vein first (PVFR: 64.3% $n = 27/42$), followed by simultaneous (SIR: 17%, $n = 7/42$), retrograde (RER: 12%, $n = 5/42$), and artery first (AFR: 7%, $n = 3/42$) reperfusion, respectively (Table 2).

Within our survey population, the most frequent technique for biliary reconstruction was the end-to-end duct-to-duct anastomosis (EEDD) without (66.7%, $n = 28/42$) or with occasional biliary drain (T-tube or stent) placement in 19% ($n = 8/42$), followed by side-to-side duct-to-duct (SSDD) with biliary drain, used by six centers (14.3%) (Table 2). Regarding the routine use of biliary drains, our survey demonstrated that 66.7% ($n = 28/42$) of the centers do not use any kind of biliary drains. In 14.3% ($n = 6/42$), a biliary drain is routinely used (Table 2). Eight centers (19%) reported the use of biliary drainage in selected cases (Table 2).

The use of open-circuit (e.g., Easy-flow) (45%, $n = 19$) versus close-circuit (e.g., Robinson) (45%, $n = 19$) drains was equally distributed within the responding centers (Table 2). Four centers noted that they only use intra-abdominal drains in high-risk patients, such as patients with severe coagulopathy, complex biliary anastomosis, and/or high-MELD recipients.

No significant association have been found between the center caseload and the surgical approach concerning outflow reconstruction, use of vvBP or PCS, graft reperfusion, biliary reconstruction, and abdominal drainage ($p = .620$, .084, .352, .933, .392; Fisher's exact test; Table 3).

Discussion

The first human OLT in Europe was performed by Sir Roy Calne in Cambridge in 1968, only 1 year after the first successful human liver transplantation reported by Thomas Starzl in the USA.[8] While significant advancements have been made over the years, technical aspects of OLT are still widely based on personal experience and institutional protocols. This is mostly attributed to the overall low-quality clinical evidence from small sample size cohorts, heterogeneous study populations, and studies with high risk of bias.[3–5,9,10] The aim of the present survey was to depict a cross-sectional overview of the variation in current surgical practices of OLT in Europe.

In comparison to other online surveys, our study had an 81% response rate[10–14] with a median of 9 days until a response was given, suggesting a high relevance of these topics for transplant professionals. Piggy-back OLT or its modifications were reported by 21 (50%) centers compared to 17 (41%) centers that use TCR as their first-line outflow reconstruction approach.[15] Veno-venous bypass or PCS is routinely only used by the minority of the responding centers (14%, $n = 6$). Even though TCR- and PB-OLT are performed for decades, high-level clinical evidence supporting the use of one or the other as well as the effects of vvBP and PCS on complications and outcome after OLT are limited.[3,5] In addition, currently available data from prospective randomized controlled trials (RCTs) are outdated with some relevant methodological flaws.[3,5,16] Since Andreas Tzakis' introduction in 1989, OLT using the cava sparing PB technique and its modifications gained increasing popularity on a global scale.[17] Although current literature does not unambiguously support the beneficial effects of PB-OLT,[5,18–21] it tends to be the faster

Table 2 Survey results on the different technical aspects of orthotopic liver transplantation based on transplantation network

Transplant network:	All	Eurotransplant	Swisstransplant	Scandiatransplant	British Transplant Society
Responding centers/number of centers	42/52 (81%)	33/37 (89%)	2/3 (67%)	4/5 (80%)	3/7 (43%)
Center volume (based on 2016 data)					
< 25	10 (24%)	9 (27.3%)	1 (50%)	n.a.	n.a.
25–50	10 (24%)	10 (30.3%)	n.a.	n.a.	n.a.
50–100	18 (43%)	13 (39.4%)	1 (50%)	3 (75%)	1 (33.3%)
> 100	4 (9%)	1 (3%)	n.a.	1 (25%)	2 (66.7%)
Caval reconstruction					
TCR	17 (40.5%)	14 (42.4%)	1 (50%)	2 (50%)	n.a.
PB	21 (50%)	17 (51.5%)	1 (50%)	2 (50%)	1 (33.3%)
Individual decision	4 (9.5%)	2 (6.1%)	n.a.	n.a.	2 (66.7%)
vvBP or PCS					
No vvBP or PCS	20 (48%)	18 (54.5%)	1 (50%)	1 (25%)	n.a.
vvBP or PCS occasionally	16 (38%)	11 (33.3%)	1 (50%)	1 (25%)	3 (100%)
vvBP as first-line approach	3 (7%)	2 (6.1%)	n.a.	1 (25%)	n.a.
PCS as first-line approach	3 (7%)	2 (6.1%)	n.a.	1 (25%)	n.a.
Graft reperfusion					
AFR	3 (7%)	2 (6%)	n.a.	n.a.	1 (33.3%)
PVFR	27 (64%)	21 (64%)	1 (50%)	3 (75%)	2 (66.7%)
SIR	7 (17%)	7 (21%)	n.a.	n.a.	n.a.
RER	5 (12%)	3 (9%)	1 (50%)	1 (25%)	n.a.
Biliary reconstruction					
End-to-end without biliary drain	28 (66.7%)	21 (64%)	2 (100%)	3 (75%)	2 (66.7%)
End-to-end occasionally with biliary drain	8 (19%)	6 (18%)	n.a.	1 (25%)	1 (33.3%)
Side-to-side with biliary drain	6 (14.3%)	6 (18%)	n.a.	n.a.	n.a.
Side-to-side without biliary drain	n.a.	n.a.	n.a.	n.a.	n.a.
Abdominal drains					
No drain	n.a.	n.a.	n.a.	n.a.	n.a.
Open-circuit drain	19 (45.2%)	18 (55%)	n.a.	1 (25%)	n.a.
Closed-circuit drain	19 (45.2%)	14 (42%)	n.a.	3 (75%)	2 (66.7%)
Only in selected cases	4 (9.6%)	1 (3%)	2 (100%)	n.a.	1 (33.3%)

TCR total caval replacement, *PB* piggy-back, *vvBP* veno-venous bypass, *PCS* portocaval shunt, *AFR* artery first reperfusion, *PVFR* portal vein first reperfusion, *SIR* simultaneous reperfusion, *RER* retrograde reperfusion

technique with regard to warm ischemia time (WIT) as compared to TCR, with favorable effects on renal function, hemodynamic stability, blood loss, and concomitant avoidance of vvBP.[18] Exploring the effects of TCR and PB in a context of the preoperative clinical status of the recipient (e.g., preoperative hepato-renal syndrome, renal function, MELD) would be paramount to avoid biased conclusions.[18] Piggy-back, depending on the technical modification used (e.g., two vs. three hepatic veins vs. side-to-side cavo-caval anastomosis[22]), might also have deleterious effects like venous outflow occlusion due to venous kinking and outflow blockade.[18] Despite the relatively low incidence of this complication (1.5–8%), it may ultimately result in serious surgical complications such as graft-failure requiring re-OLT and/or death.[18,20,23] While bypass-related issues were mostly brought up by centers that routinely use the TCR without vvBP technique, the presumed absence of a clear benefit ($n = 30$), higher morbidity ($n = 7$), technical complexity ($n = 3$), and longer operating time ($n = 13$) were arguments against the routine use of vvBP. Centers that routinely or occasionally use vvBP or PCS for OTL emphasized a better control of hemodynamics ($n = 11$), less intraoperative bleeding ($n = 7$), and fewer overall complications due to the avoidance of splanchnic congestion ($n = 10$). Even though only three centers in our survey cohort routinely use PCS for PB, a recent meta-analysis by Pratschke et al. showed a clear benefit of PCS with regard to intraoperative blood loss, postoperative renal function, and hepatocellular injury in PB-OLT. It must be noted, however, that the conclusion drawn was based on five retrospective studies and one single-center RCT.[16]

Based on the findings from both of our survey, as well as from other studies, PVFR is currently regarded as the gold standard of

Table 3 Survey results on the different technical aspects of orthotopic liver transplantation based on center caseload

Center caseload	All	< 25 OLT	25–50	50–100	> 100	*p
Caval reconstruction						
TCR	17 (40.5%)	2 (20%)	4 (40%)	10 (56%)	1 (25%)	.620
PB	21 (50%)	7 (70%)	6 (60%)	6 (33%)	2 (50%)	
Individual decision	4 (9.5%)	1 (10%)	0 (0%)	2 (11%)	1 (25%)	
vvBP or PCS						
No vvBP or PCS	20 (48%)	8 (80%)	4 (40%)	7 (39%)	1 (25%)	.084
vvBP or PCS occasionally	16 (38%)	1 (10%)	6 (60%)	7 (39%)	2 (50%)	
vvBP as first-line approach	3 (7%)	n.a.	n.a.	3 (17%)	n.a.	
PCS as first-line approach	3 (7%)	1 (10%)	n.a.	1 (5%)	1 (25%)	
Graft reperfusion						
AFR	3 (7%)	n.a.	2 (20%)	n.a.	1 (25%)	.352
PVFR	27 (64%)	7 (70%)	6 (60%)	13 (72%)	1 (25%)	
SIR	7 (17%)	2 (20%)	2 (20%)	3 (17%)	n.a.	
RER	5 (12%)	1 (10%)	n.a.	2 (11%)	2 (50%)	
Biliary reconstruction						
End-to-end without biliary drain	28 (66.7%)	8 (80%)	7 (70%)	9 (50%)	4 (100%)	.933
End-to-end occasionally with biliary drain	8 (19%)	1 (10%)	n.a.	7 (39%)	n.a.	
Side-to-side with biliary drain	6 (14.3%)	1 (10%)	3 (30%)	2 (11%)	n.a.	
Side-to-side with biliary drain	n.a.	n.a.	n.a.	n.a.	n.a.	
Abdominal drains						
No drain	n.a.	n.a.	n.a.	n.a.	n.a.	.392
Open-circuit drain	19 (45.2%)	4 (40%)	7 (70%)	7 (39%)	1 (25%)	
Closed-circuit drain	19 (45.2%)	5 (50%)	3 (30%)	9 (50%)	2 (50%)	
Only in selected cases	4 (9.6%)	1 (10%)	n.a.	2 (11%)	1 (25%)	

*Fischer's exact test

TCR total caval replacement, *PB* piggy-back, *vvBP* veno-venous bypass, *PCS* portocaval shunt, *AFR* artery first reperfusion, *PVFR* portal vein first reperfusion, *SIR* simultaneous reperfusion, *RER* retrograde reperfusion

graft revascularization in adult deceased donor OLT.[10,14] There is, however, no high-level clinical evidence to support the superiority of PVFR in comparison to alternative approaches such as SIR, RER, or AFR.[10] Currently, there are five completed RCTs,[4,10] two meta-analyses,[4,10] and one comprehensive review elaborating different graft reperfusion techniques in adult deceased donor OLT.[24] In addition, further non-randomized and retrospective cohort studies have been published.

PVFR is used by the majority of centers due to practical reasons: the PV anastomosis is technically simple; henceforth, it is usually performed before arterial reconstruction.[10] Even though WIT is relatively shorter compared to other reperfusion techniques, it must be noted that due to the unique arterial blood supply of the bile duct with its peribiliary vascular plexus, composed of branches arising directly from the hepatic artery, the ischemic time of the biliary system itself is in fact prolonged.[10] Alternate techniques of allograft reperfusion such as AFR and SIR hold promise to improve arterial blood flow of the biliary vascular plexus but are generally less frequently used.[25] Retrograde reperfusion (RER) substantially reduces WIT of the liver parenchyma. Nevertheless, it must be emphasized that this effect comes at the price of a significant extension of the WIT of the biliary system, thus potentially aggravating biliary injury. This is attributed to an early venous retrograde but late anterior revascularization.[25] A recent meta-analysis by Manzini et al. suggests that SIR might result in slightly lower incidence of biliary complications compared to PVFR, especially when cold ischemia is prolonged.[10] It is hypothetically possible that certain subgroups of patients with long CIT, receiving extended criteria donation (ECD) allografts from brain dead donors, may benefit from a more rapid revascularization (RER or PVFR), in an attempt to reduce IRI and splanchnic congestion.[10,26] Meanwhile, other subgroups, such as recipients of donation after cardiac death (DCD) allografts, may benefit from an improved anterograde blood flow into the biliary plexus as provided by PVF, SIR, or alternatively by AFR.[27] These are clinically relevant research questions that should be addressed in future studies.

According to the results of our survey, abdominal drains are still routinely used by the majority of European centers (> 90%), which is in line with previous findings.[14] In contrast, there is also evidence from retrospective and case-matched

controlled studies, suggesting that prophylactic intra-abdominal drainage in major abdominal surgery may result in significant drain-related morbidity.[9,28,29] A systematic review on the routine intra-abdominal drainage in OLT remained inconclusive.[9] Although the quality of evidence is low, the majority of previous studies observed a lack of benefit for the routine use of abdominal drainage in OLT.[9,29] Most centers use passive open- or close-circuit drain systems. In an observational cohort study by Fernandez-Aguilar et al., an increased need for paracentesis due to ascites in the early post-OLT days was demonstrated for the no-drain group, while a higher incidence of peri-hepatic hematomas with the use of routine drainage was also noted.[30] In 2015, Weiss et al. compared open- and close-circuit drains in a retrospective analysis in OLT patients.[29] Although their results show an increased rate of abdominal infections, reoperations, and more intra-abdominal hematomas in the open-circuit drain group, these findings are yet to be confirmed in studies with lower risk of selection bias and systematic errors. In our survey cohort, centers that routinely use intra-abdominal drains justified doing so for diagnostic purposes ($n = 27$), removing intra-abdominal fluid ($n = 32$), and due to institutional standards ($n = 10$). Most centers with a more selective drain policy after OLT ($n = 3$) intend to avoid drain-related morbidity.

The preferred surgical technique for biliary reconstruction in our cohort was the EEDD (86%). The placement of a biliary drain in EEDD is performed in complex cases with donor-recipient size mismatch, re-do anastomosis, DCD donors, or in generally difficult bile duct anastomosis, as reported by 19% of all survey centers. Six centers use the side-to-side approach (SSDD) combined with a mandatory biliary drain. This correlates well with current evidence, as a recent systematic review including 3 RCTs, 6 prospective trials, and 48 further cohort studies suggests no difference of EEDD without drain versus SSDD with drain in risk of developing biliary complications.[31] The use of biliary drains was advocated in eight centers for physical support of the anastomosis to reduce complications (e.g., leakage, stenosis) and five centers stated diagnostic purposes behind the use of biliary drainage (e.g., bile quality and quantity, cholangiography). Two centers responded that the rationale for using biliary drains in OLT is only a matter of institutional protocol and center routine. In our assessments using Fisher's exact test, we could not find any significant association between center caseload and the implemented surgical approach. Although this supports the main message of our survey which demonstrates a substantial heterogeneity and lack of best practices regarding the utilization of various surgical techniques within Europe, our approach has certain limitations. Within our study, the caseload of centers has been divided into four categories (< 25, 25–50, 50–100, > 100 OLT/year); therefore, only ranges and no exact center-specific caseload numbers were used during the analysis. Furthermore, the lack of significant differences might also be attributed to the low sample sizes in certain technical subgroups. In this context, it should be emphasized that the surveyed transplant networks also show significant differences among each other. As such, the BTS and ScaT networks concentrate their OLT activity exclusively in few high-volume centers (Table 1).

Interestingly, only five respondents (12%) in our survey cohort believe there is overall enough evidence for the above-detailed technical aspects of OLT. The opinion of the rest of the responding representatives (88%) demonstrated a need for further well-designed multicenter trials and international standardization (Fig. 1). According to the feedback given, the overwhelming majority (98%, 41/42) of the sampled centers would agree to participate in multicenter RCTs on these topics (Fig. 1). Few centers, however, emphasized possible pitfalls in planning multicenter RCTs investigating clinical outcome in an imprecisely defined and heterogeneous OLT recipient population. Therefore, the feasibility of alternative prospective study designs (e.g., prospective case-matched analysis) should be explored in future clinical trials.

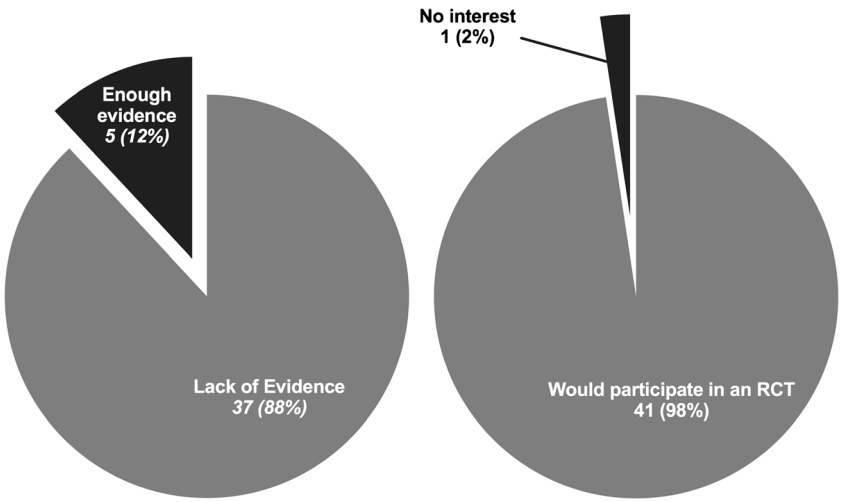

Fig. 1 Opinion of the respondents ($n = 42$) on current evidence and their interest in participating multicenter trials on the discussed surgical topics

In conclusion, the results of our survey demonstrate a significant heterogeneity in the first-line surgical approach for OLT among European centers. To ensure a high-response rate, the present survey was based on simple and easy to answer questions without the need of systematic data retrieval from the side of the respondent. Furthermore, the questions were designed to address key surgical aspects of adult whole-graft deceased donor OLT. To limit the number of possible answers, alternative first-line techniques used only in a subset of patients (e.g., hepatico-jejunostomy in PSC) as well as different technical modifications of the classical piggy-back technique (two vs. three hepatic veins vs. side-to-side cavo-caval anastomosis[22]) were not surveyed separately.

Although, the exact numbers slightly differ from previous survey cohorts[10,14] and our study is descriptive in nature, our results reflect the general practice in a large European collective of liver transplant centers with nearly 3000 OLTs performed in these centers every year (Table 1). Decision-making in OLT is insufficiently supported by evidence, and the need for well-designed multicenter RCTs is imminent. It should be noted, however, that the planning of a well-designed multicenter RCTs in this field is complicated by a number of confounding factors (open-label design, heterogeneous patient population, surgeon factor, graft, and recipient factors) that can significantly influence a single primary end-point and the final conclusion drawn. It is anticipated that the results of the present work will generate discussions, particularly between transplant surgeons as well as within the national and international associations, responsible for coordinating organ transplant activities. In addition, our findings may also promote collaborative multicenter research to generate high-level evidence and international consensus on technical aspects of liver transplantation. Further important questions such as a current status update on the utilization of clinical liver machine perfusion, aspects of donation after cardiac death or the use of rescue revascularization techniques, issues of living donor or split liver transplantation, as well as those of liver re-transplantation should be addressed in future surveys.

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Authors' Contribution The study was designed and the survey was distributed by the initiating study team (ZC, UPN, JB, GL). Data collection and analysis was performed by ZC, UPN, JB, and GL. Initial manuscript was drafted by ZC, GL, JB, UPN, and MNS. Further authors (JP, MG, SN, AM, GB, XR, JP, JL, ZM, PD, BE, MM, NH, WS) have substantially contributed to the final version of the manuscript. All authors have read and approved the final version of the manuscript.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Appendix

The Survey Study Group consists of:

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