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META-ANALYSIS

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Intraoperative Surgical Portosystemic Shunt in Liver Transplantation: Systematic Review and Meta-Analysis

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Data Collection B
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Manuscript Preparation E
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Background: Expanded clinical and surgical techniques in liver transplantation can markedly improve patient and graft survival. The main purpose of this study was to evaluate the efficacy of intraoperative portocaval shunts in liver transplantation.

Material/Methods: Searches were conducted in Cochrane, MEDLINE, and EMBASE databases, and updated in January 2018. The following specific outcomes of interest were defined and evaluated separated using 2 different reviews and meta-analyses for 1) hemi-portocaval shunt (HPCS) and 2) temporary portocaval shunt (TPCS). Comparative studies were analyzed separately for both surgical portocaval shunt modalities.

Results: Only 1 well-designed randomized controlled trial was found. Most studies were retrospective or prospective. Initially, we found 1479 articles. Of those selected, 853 were from PubMed/MEDLINE, 32 were from Cochrane and 594 were from EMBASE. Our meta-analysis included a total of 3232 patients for all the included studies. Results found that 41 patients with HPCS experienced increased 1-year patient survival (OR 16.33; *P*=0.02) and increased 1-year graft survival (OR 17.67; *P*=0.01). The TPCS analysis with 1633 patients found patients had significantly shorter intensive care unit length of stay (days) (*P*=0.006) and hospital length of stay (*P*=0.02) and had decreased primary nonfunction (PNF) (OR 0.30, *P*=0.02) and mortality rates (OR 0.52, *P*=0.01).

Conclusions: Intraoperative surgical portosystemic shunt in relation to liver transplantation with TPCS was able to prevent PNF, decrease hospital length of stay and unit care length of stay. Furthermore, in analyzing data for patients with HPCS, we observed increases in the 1-year graft and patient survival rates. More prospective randomized trials are needed to arrive at a more precise conclusion.

MeSH Keywords: **Liver Transplantation • Portasystemic Shunt, Surgical • Review**

Abbreviations: **LT** – liver transplantation; **OLT** – orthotopic liver transplantation; **LDLT** – living donor liver transplantation; **TPCS** – temporary portocaval shunt; **HPCS** – hemi-portocaval shunt; **TIPS** – transjugular intrahepatic portosystemic shunt; **SFSS** – small-for-size syndrome

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Background

Liver transplantation (LT), whether deceased donor (DDLT) or living donor (LDLT), is the most appropriate approach in adult and pediatric patients to treat end-stage liver disease and it is an effective therapeutic modality to increase patient survival time [1]. Nowadays, we observe an important improvement in medical (drugs) to prevent or treat transplant rejections and infections, better intensive care, and improved anesthetic, hemodynamic, and surgical approaches [1,2].

For an extended period, the "classical technique" has been the most common surgical strategy in the LT, which involves dissection and cross-clamping of the infra-hepatic inferior vena cava and portal vein. Thus, this approach can lead to stasis in splanchnic circulation, which can introduce the creation of venous bypass to tributaries of the superior vena cava during the clamp technique [3,4]. The "piggyback technique" was described in 1989 to maintain cardiac venous return and reduce pressure in the inferior vena cava, obtained through anastomosis of the suprahepatic vena cava of the graft with the hepatic veins, but without the need for a cross-clamp of the portal vein during LT [3,4].

A temporary bypass, the temporary portocaval shunt (TPCS), can be used and is associated with the use of the piggyback technique during hepatectomy to reduce pressure in the portal system and facilitate dissection of the retrohepatic vena cava [1]. The TPCS can have different anastomosis: end-to-side or passive portocaval tubing shunt. TPCS reports in the literature indicate some improvement in hemodynamic stability, maintenance of renal function preserved, and less blood transfusion.

Another intraoperative venous bypass technique is the hemi-portocaval shunt (HPCS), which has no relationship with the TPCS. The HPCS is a permanent shunt developed to regulate the pressure and flow in the portal system in special cases of LDLT or for cases with differences in graft and recipient weight, as there is a great concern regarding the development of small-for-size syndrome (SFSS) [5,6].

The scientific hypothesis of this study was to evaluate the real benefits of surgical portosystemic shunt in both modalities and indications: 1) TPCS (all types of intraoperative anastomosis or portal shunt) and 2) HPCS with liver transplantation. The specific outcomes of interest were defined and evaluated separated, with 2 different reviews and meta-analyses. The aim of this study was to systematically review and analyze separately current articles that used different surgical techniques of portocaval shunts for liver transplantation.

	Terms search PubMed database
Patients OR/AND	Liver transplantation OR liver transplant OR kepatic transplantation OR liver grafting
Intervention OR/AND	AND (portosystemic shunt, surgical OR portacaval shunt, surgical OR portacaval anastomosis OR portacaval bypass)
Exclusion NOT	NOT (postoperative period)

Figure 1. The terms used for the PubMed database search were developed using patient, intervention, comparison or control, and outcome (PICO) structure.

Material and Methods

Study identification and selection

A systematic review of the literature was examined for the management of the intraoperative portocaval shunts in liver transplantation. The Cochrane Library, EMBASE, and MEDLINE-PubMed databases were electronically searched and updated to January 2018. The MESH-terms used were "Liver Transplantation," "Portosystemic Shunt," "Surgical," and "Portocaval Shunt, Surgical."

The terms and MESH-terms for the PubMed database search were developed with based on PICO (patient, intervention, comparison, or control, outcome) structure. The terms for each group were combined with the "OR" operator. The results of the search terms forming the "P" (patients) group were merged with the result forming the "I" (intervention) group with "AND", and for the exclusion terms with "NOT" (Figure 1).

This systematic review was registered in the International Database of Prospectively Registered Systematic Reviews (PROSPERO, registration number = CRD42017081906). The review protocol can be accessed online via the PROSPERO website (*https://www.crd.york.ac.uk/prospero/*). The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) checklist were adhered to when structuring this article [7,8]. The review methodology followed recommendations published by PRISMA (2009). The study was carried out using the instructions of no preference in report items for systematic review and meta-analysis protocols [7–9].

The quality and selection of the studies were evaluated by 3 independent researchers (LSN, LYZ, and VFS). In the case of disagreement, the researchers held a consensus meeting to reach a final decision.

The MEDLINE search was performed through PubMed *(www.ncbi.nlm.nih.gov/pubmed)* and was adapted using the basic terms and Mesh-terms: (Liver Transplantation" [Mesh]" AND

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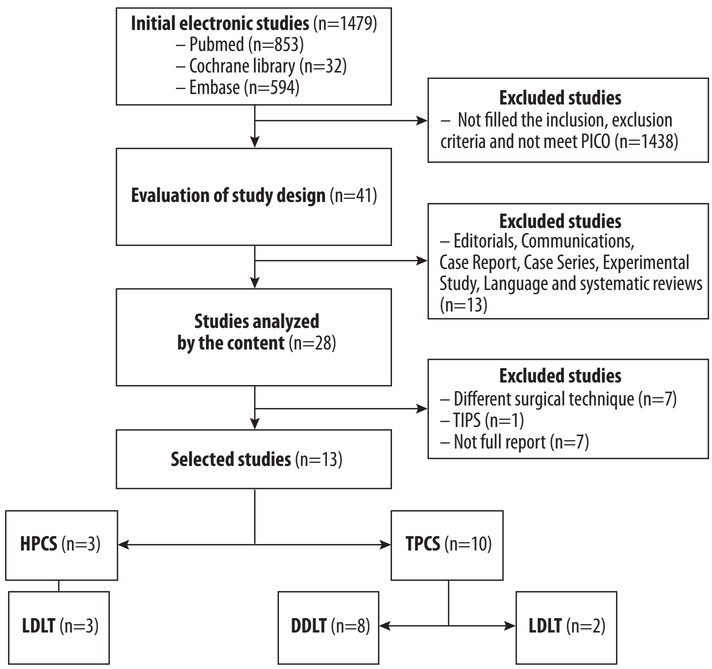

Figure 2. Flow diagram of systematic literature search according to the PRISMA statement.

"Portosystemic Shunt, Surgical" [Mesh]). The same strategy was used in the EMBASE (*www.embase.com*). The Cochrane Library Database (*http://www.cochrane.org*) was searched for both registered and recently published systematic reviews (CDSR), as well as clinical trials (CCTR) with "Liver Transplantation" and "Portocaval Shunt" terms.

The specific outcomes of interest were defined and evaluated separated, in 2 different reviews and meta-analyses: 1) HPCS: graft to body weight ratio (GBWR), 1-year patient and graft survival, SFSS; and 2) TPCS: hepatic injury [alanine aminotransferase (ALT) and primary nonfunction (PNF)], time of surgical intervention, unit care time, and hospital length of stay, transfusion [packed red blood cell (RBC) requirements, fresh frozen plasma requirements (FFP), platelets], and renal function (creatinine) on the third day.

Inclusion and exclusion criteria

Selection criteria were performed within the research question of the PICO structure. Only randomized controlled trials, nonrandomized controlled trials, and comparative clinical studies were included. All studies evaluated were written in English and all studies evaluated the portosystemic shunt in liver transplantation.

Data synthesis and statistical analysis

Data were extracted from text, tables, and figures of the original published articles. The measures of effectiveness for each treatment were expressed in absolute numbers and respective frequencies, i.e., the absolute risk. For the meta-analyses, the data were synthesized using Review Manager Version 5.3 software provided by the Cochrane Collaboration (RevMan; The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark). The results from the included papers were compared with the differences seen in absolute risks. Continuous data were expressed as mean difference and 95% confidence intervals (CI).

Heterogeneity and sensitivity analysis in the studies

Heterogeneity was examined with I^2 statistics, in which I^2 values of 70% or more represented an indicator of substantial heterogeneity. In the absence of this heterogeneity, we pooled data with a fixed-effect model ($I^2<50\%$); otherwise we used a random effects model ($I^2>50\%$) [10]. Results were considered statistically significant at $P<0.05$. Publication bias was evaluated with a funnel plot.

Data analysis and critical evaluation

Study quality assessment included design, level of evidence, New Castle score (Ottawa Quality Assessment Cohort Studies) (accessed February 2018) for nonrandomized clinical trials [11] and Jadad Scale for randomized clinical trials [12].

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Results

Study selection

Initially, we found 1479 articles. Of these articles, 853 were from PubMed/MEDLINE, 32 were from Cochrane, and 594 were from EMBASE. Of these systematic reviews, we selected 28 cases to further assess. We analyzed all articles regarding liver transplantation [1,4–6,13–24], 3 articles describing HPCS [4–6], and 10 articles describing TPCS [1,13–18,20,23,24]. In Figure 2 we show the flow diagram of the systematic literature search, according to PRISMA statement.

Only 1 well-designed randomized control trial was found. Most studies were retrospective or prospective in design. All parameters and study characteristics are shown in Table 1. Moreover, the specific evaluation and quality of the studies are shown in Table 2.

Meta-analysis

In the meta-analysis of portocaval shunt following liver transplantation, we separately evaluated HPCS and TPCS. The specific outcomes of interest were defined and evaluated separated as 2 different reviews and meta-analyses.

We utilized the Forest plot for meta-analysis, as the size of the squares also indicates the weight of the studies and the diamond indicates the overall effect size. First, the meta-analysis calculations involved the HPCS group with 3 articles selected (3 LDLT included); a different analysis and evaluation of TPCS included 8 articles of the 10 selected articles (8 DDLT articles included and 2 LDLT articles excluded [22–24]).

HPCS

The meta-analysis of HPCS in liver transplantation evaluated the GBWR (Figure 3), 1-year patient survival (Figure 4), 1-year graft survival (Figure 5), and SFSS (Figure 6).

GBWR

GBWR data from 3 studies [4–6] evaluated 34 patients with HPCS and 11 patients without HPCS. The mean difference in GBWR (Figure 3) assessed was not significant (*P*=0.23).

One-year patient survival

For 1-year patient survival, data from 2 studies [5,6] evaluated 18 patients with HPCS and 6 patients without HPCS. We observed significant improvement in the 1-year patient survival in cases using HPCS (OR 16.33; *P*=0.02) (Figure 4).

One-year graft survival

For 1-year graft survival, data from 2 studies [5,6] evaluated 18 patients with HPCS and 6 patients without HPCS. We observed significant improvement in the 1-year graft survival in cases with HPCS (OR 17.67; *P*=0.01) (Figure 5).

SFSS

For SFSS, data from 2 studies [4,6] evaluated 24 patients with HPCS and 10 patients without HPCS. We observed no significant differences between groups, either with or without HPCS (OR 0.27; *P*=0.19) (Figure 6).

TPCS

The meta-analysis of TPCS was evaluated to align with surgery time (Figure 7), unit care length of stay (Figure 8), hospital length of stay (Figure 9), ALT (Figure 10), PNF (Figure 11), liver re-transplantation (Figure 12), mortality (Figure 13), and postoperative renal function (creatinine) on the third postoperative day (Figure 14), and transfusion in the operative room: RBCs (Figure 15), FFP (Figure 16), and platelets (Figure 17).

Surgery time

For surgery time, data from 6 studies [1,13–17] evaluated 1054 patients with TPCS and 796 patients without TPCS. The mean difference was –9.76 [–42.96–23.44] (Figure 7) and was not significantly different (*P*=0.43).

Unit care length of stay

For length of stay in unit care, data from 3 studies [1,15,17] evaluated 543 patients with TPCS and 572 without TPCS. The mean difference was –1.38 [–2.38–0.39] (Figure 8) with a significant difference (*P*=0.006).

Hospital length of stay

For hospital length of stay, data from 5 studies [1,13,15–17] evaluated 698 patients with TPCS and 751 patients without TPCS. The mean difference was –2.37 [–4.33–0.41] (Figure 9) which showed a significant difference (*P*=0.02).

Hepatic injury

Alanine aminotransferase (ALT)

For hepatic injury, ALT data from 2 studies [16,18] evaluated 305 patients with TPCS and 264 patients without TPCS. The mean difference was –192.01 [–801.19–417.17] (Figure 10) without a significant difference (*P*=0.54).

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Table 1. Demographic and overall characteristics of all selected studies analyzed.

Study	Type	N	Population	Intervention	Comparison	Outcomes
Arzu et al., 2008 [13]	Retrospective	186	Patients underwent DDLT	TPCS (n=97)	LT without TPCS	TPCS improves the hemodynamic status and the duration of each LT phases
Botha et al., 2010 [4]	Retrospective	21	LDLT (with left lobe grafts)	HPCS (n=16)	LDLT without HPCS	Diversion of the portal flow prevents small for size syndrome
de Cenarruzabeitia et al., 2007 [14]	Retrospective	401	Patients underwent DDLT	TPCS (n=356)	LT without TPCS	TPCS enhanced hemodynamic status
Figueras et al., 2001 [15]	Prospective randomized	80	Patients underwent DDLT	TPCS (n=40)	LT without TPCS	TPCS improve hemodynamic status, reduces intraoperative transfusions and preserves renal function
Ghinolfi et al., 2010 [16]	Retrospective	148	Patients underwent DDLT	TPCS (n=58)	LT without TPCS	Survival at 3 months was higher when performed TPCS
Suárez-Munoz et al., 2006 [17]	Retrospective	349	Patients underwent DDLT	TPCS (n= 160)	LT without TPCS	PCS provided reduction in the intraoperative use of blood-derived products, especially platelet transfusion
Kim et al., 2015 [24]	Retrospective	116	Patients underwent LDLT	TPCS (n=33)	LT without TPCS	Improvement of hemodynamic status and postoperative outcomes
Muscari et al., 2005 [20]	Prospective	156	Patients underwent DDLT	TPCS (n=0)	Data of previous studies	TCPS doesn't demonstrated better results
Pratschke et al., 2012 [19]	Retrospective	448	Patients underwent DDLT	TPCS (n=274)	LT without TPCS	TPCS improves survival
Rayar et al., 2017 [1]	Retrospective	686	Patients underwent DDLT	TPCS (n=343)	LT without TPCS	TPCS should be recommended especially when considering the use of an ECD
Troisi et al., 2005 [6]	Prospective	13	Patients underwent LDLT	HPCS (n=8)	LT without HPCS	HPCS improves overall patient and graft survival, and also prevents small-for-size syndrome
Yamada et al., 2008 [5]	Prospective	11	LDLT (with small-for-size graft)	HPCS (n=10)	LT without HPCS	HPCS is excellent for graft survival and to avoid small-for-size syndrome
Son et al., 2016 [23]	Retrospective	67	Patients underwent LDLT	TPCS (n=16)	Case-control study in 67 consecutive LDLT	TPCS offers more favorable hemodynamic conditions during the anhepatic phase

N – number; LT – liver transplantation; DDLT – deceased donor liver transplatation; LDLT – living donor liver transplantation; PCS – temporary portocaval shunt; HPCS – hemi-portocaval shunt; PCS – portocaval shunt.

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Table 2. The Jadad Scale for randomized clinical trials and Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies.

Study Score	
Randomized clinical trial	
Figueras et al., 2001 [15]	Jadad: 4
Non-randomized clinical trial	
Arzu et al., 2008 [13]	NOS: 7
Botha et al., 2010 [4]	NOS: 7
de Cenarruzabeitia et al., 2007 [14]	NOS: 8
Ghinolfi et al., 2010 [16]	NOS: 7
Kim and Choi, 2015 [24]	NOS: 7
Muscari et al., 2015 [20]	NOS: 6
Pratschke et al., 2012 [18]	NOS: 7
Rayar et al., 2017 [1]	NOS: 8
Suárez-Munoz et al., 2006 [17]	NOS: 7
Troisi et al., 2005 [6]	NOS: 7
Yamada et al., 2008 [5]	NOS: 7
Son et al., 2016 [23]	NOS: 8

Studies according the Jadad Scale for randomized clinical trials [12] and Newcastle-Ottawa Scale (NOS) – instrument tool for quality assessment of non-randomized studies to be used in a systematic review [11].

PNF

For PNF, data from 3 studies [15,16,18] evaluated 372 patients with TPCS and 304 patients without TPCS. The OR was 0.30 [0.11–0.86] (Figure 11) and was significantly different (*P*=0.02).

Liver re transplantation

For liver re-transplantation, data from 2 studies [16,18] evaluated 332 patients with TPCS and 264 patients without TPCS. The OR was 0.83 [0.30–2.34] (Figure 12) and was not significantly different (*P*=0.73).

Mortality

For mortality, data from 3 studies [1,13,16] evaluated 498 patients with TPCS and 522 patients without TPCS. The OR was 0.51 [0.30–0.87] (Figure 13) and there was a significantly different (*P*=0.01).

Postoperative renal function

Creatinine on the third postoperative day

For creatinine on the third postoperative day, data from 4 studies [13,14,16,18] evaluated 785 patients with TPCS and 398 patients without TPCS. The mean difference was –0.19 [–0.48–0.10] (Figure 14) and was not significantly different (*P*=0.20).

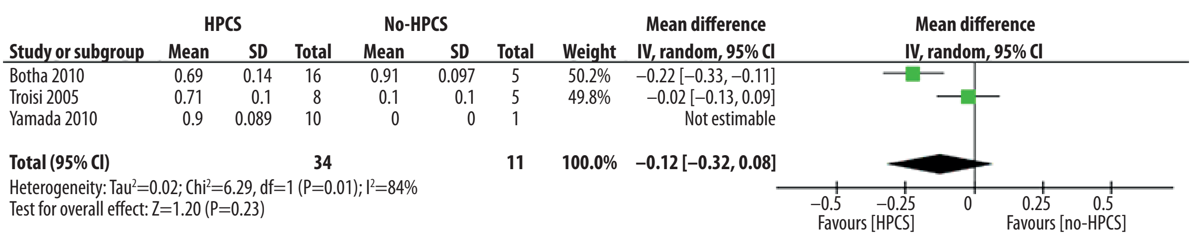

Figure 3. Forest plot for the meta-analysis of studies examining the effect of hemi-portocaval shunt (HPCS) on the graft to body weight ratio (GBWR).

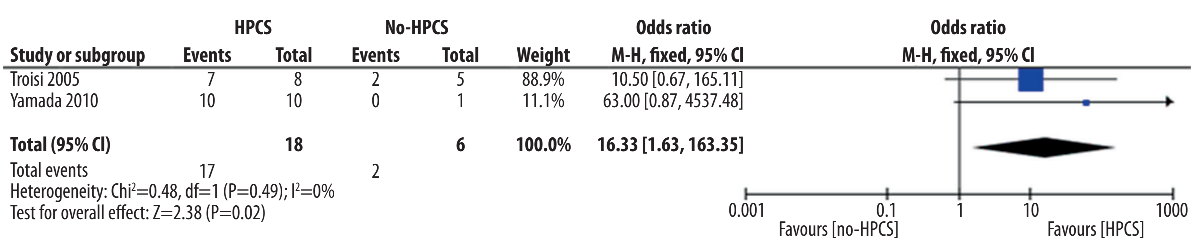

Figure 4. Forest plot for the meta-analysis of studies examining the effect of hemi-portocaval shunt (HPCS) on 1-year patient survival.

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Study or subgroup	HPCS Events	HPCS Total	No-HPCS Events	No-HPCS Total	Weight	Odds ratio M-H, fixed, 95% CI
Troisi 2005	6	8	1	5	88.9%	12.00 [0.80, 180.97]
Yamada 2010	10	10	0	1	11.1%	63.00 [0.87, 4537.48]
Total (95% CI)		**18**		**6**	**100.0%**	**17.67 [1.78, 175.49]**
Total events	16		1			

Heterogeneity: Chi²=0.42, df=1 (P=0.52); I²=0%
Test for overall effect: Z=2.45 (P=0.01)

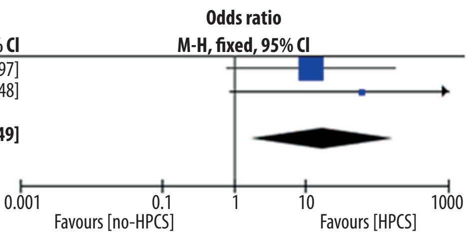

Figure 5. Forest plot for the meta-analysis of studies examining the effect of hemi-portocaval shunt (HPCS) on 1-year graft survival.

Study or subgroup	HPCS Events	HPCS Total	No-HPCS Events	No-HPCS Total	Weight	Odds ratio M-H, fixed, 95% CI
Botha 2010	1	16	0	5	19.2%	1.06 [0.04, 30.20]
Troishi 2005	0	8	2	5	80.8%	0.08 [0.00, 2.19]
Total (95% CI)		**24**		**10**	**100.0%**	**0.27 [0.04, 1.94]**
Total events	1		2			

Heterogeneity: Chi²=1.15, df=1 (P=0.28); I²=13%
Test for overall effect: Z=1.30 (P=0.19)

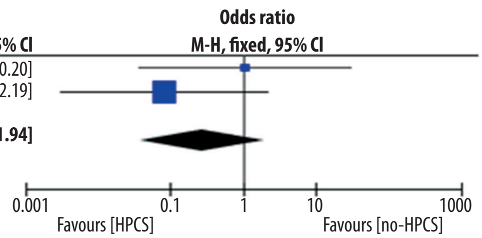

Figure 6. Forest plot for the meta-analysis of studies examining the effect of hemi-portocaval shunt (HPCS) on small-for-size syndrome (SFSS).

Study or subgroup	TPCS Mean	TPCS SD	TPCS Total	No-TPCS Mean	No-TPCS SD	No-TPCS Total	Weight	Mean difference IV, random, 95% CI
Arzu 2008	504	108	97	511	110	89	16.2%	−7.00 [−38.37, 24.37]
Cenarruzabeitia 2007	338.37	73.95	356	332.56	69.22	45	17.6%	5.81 [−15.82, 27.44]
Figueras 2001	403	77	40	387	56	40	16.5%	16.00 [−13.51, 45.51]
Ghinolfi 2010	416	134	58	431	124	90	14.4%	−15.00 [−57.96, 27.96]
Rayar 2017	404.25	141.4553	343	387.25	145.7883	343	17.6%	17.00 [−4.50, 38.50]
Suárez-Munoz 2006	361	82.92	160	435	110.58	189	17.7%	−74.00 [−94.34, −53.66]
Total (95% CI)			**1054**			**796**	**100.0%**	**−9.76 [−42.96, 23.44]**

Heterogeneity: Tau²=1511.56; Chi²=48.80, df=5 (P<0.00001); I²=90%
Test for overall effect: Z=0.58 (P=0.56)

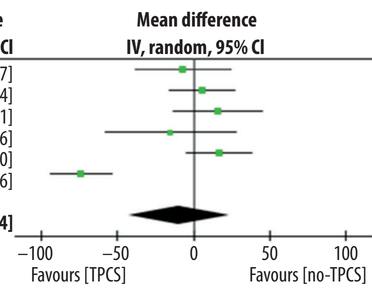

Figure 7. Forest plot for the meta-analysis of studies examining the effect of temporary portocaval shunt (TPCS) on surgery time (minutes).

Study or subgroup	TPCS Mean	TPCS SD	TPCS Total	No-TPCS Mean	No-TPCS SD	No-TPCS Total	Weight	Mean difference IV, fixed, 95% CI
Figueras 2001	2.9	1.4	40	4.9	5.7	40	30.0%	−2.00 [−3.82, −0.18]
Rayar 2017	20.5	20.82	343	21.25	21.68	343	9.8%	−0.75 [−3.93, 2.43]
Suárez-Munoz 2006	3.98	4.9	160	5.16	7.25	189	60.3%	−1.18 [−2.46, 0.10]
Total (95% CI)			**543**			**572**	**100.0%**	**−1.38 [−2.38, −0.39]**

Heterogeneity: Chi²=0.69, df=2 (P=0.71); I²=0%
Test for overall effect: Z=2.72 (P=0.006)

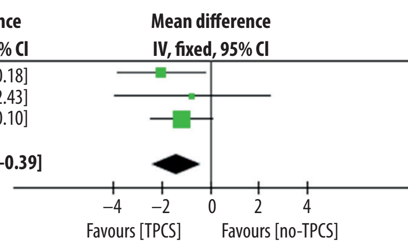

Figure 8. Forest plot for the meta-analysis of studies examining the effect of temporary portocaval shunt (TPCS) on unit care length of stay (days).

	TPCS			No-TPCS				Mean difference
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, fixed, 95% CI
Arzu 2008	16.5	22.7	97	17.8	22.4	89	9.2%	−1.30 [−7.79, 5.19]
Figueras 2001	15.6	11.0	40	17.9	13.4	40	13.3%	−2.30 [−7.67, 3.07]
Ghinolfi 2010	17.5	17.7	58	20.3	19.6	90	10.4%	−2.80 [−8.89, 3.29]
Rayar 2017	68.25	66.71	343	35.75	29.18	343	6.5%	32.50 [24.79, 40.21]
Suárez-Munoz 2006	12.7	7.94	160	18.9	15.42	189	60.7%	−6.20 [−8.72, −3.68]
Total (95% CI)			**698**			**751**	**100.0%**	**−2.37 [−4.33, −0.41]**

Heterogeneity: Chi²=87.67, df=4 (P<0.00001); I²=95%
Test for overall effect: Z=2.37 (P=0.02)

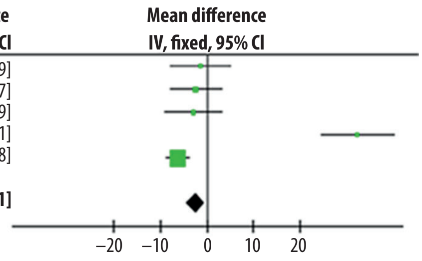

Figure 9. Forest plot for the meta-analysis of studies examining the effect of temporary portocaval shunt (TPCS) on length of hospital stay (days).

	TPCS			No-TPCS				Mean difference
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, random, 95% CI
Ghinolfi 2010	696.7	1,041.8	58	568.5	621.5	90	48.5%	128.20 [−169.07, 425.47]
Pratschke 2013	694.2	689.4	247	1,187.9	1,290.2	174	51.5%	−493.70 [−703.80,−283.60]
Total (95% CI)			**305**			**264**	**100.0%**	**−192.01 [−801.19, 417.17]**

Heterogeneity: Tau²=176,131.99; Chi²=11.21, df=1 (P=0.0008); I²=91%
Test for overall effect: Z=0.62 (P=0.54)

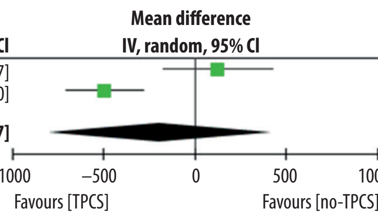

Figure 10. Forest plot for the meta-analysis of studies examining the effect of temporary portocaval shunt (TPCS) on hepatic injury – alanine aminotransferase (ALT).

	TPCS		No-TPCS			Odds ratio
Study or subgroup	Events	Total	Events	Total	Weight	M-H, fixed, 95% CI
Figueras 2001	0	40	1	40	9.7%	0.33 [0.01, 8.22]
Ghinolfi 2010	3	58	7	90	34.2%	0.65 [0.16, 2.61]
Pratschke 2013	1	274	7	174	56.1%	0.09 [0.01, 0.72]
Total (95% CI)		**372**		**304**	**100.0%**	**0.30 [0.11, 0.86]**
Total events	4		15			

Heterogeneity: Chi²=2.48, df=2 (P=0.29); I²=19%
Test for overall effect: Z=2.25 (P=0.02)

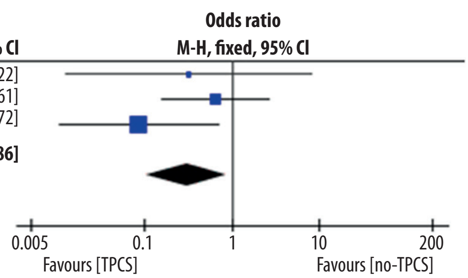

Figure 11. Forest plot for the meta-analysis of studies examining the effect of temporary portocaval shunt (TPCS) on primary nonfunction.

	TPCS		No-TPCS			Odds ratio
Study or subgroup	Events	Total	Events	Total	Weight	M-H, fixed, 95% CI
Ghinolfi 2010	10	58	11	90	44.7%	1.50 [0.59, 3.79]
Pratschke 2013	20	274	23	174	55.3%	0.52 [0.27, 0.97]
Total (95% CI)		**332**		**264**	**100.0%**	**0.83 [0.30, 2.34]**
Total events	30		34			

Heterogeneity: Chi²=0.40, df=1 (P=0.06); I²=71%
Test for overall effect: Z=0.35 (P=0.73)

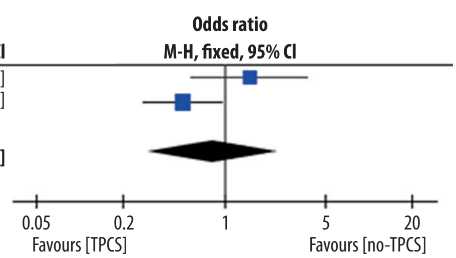

Figure 12. Forest plot for the meta-analysis of studies examining the effect of temporary portocaval shunt (TPCS) on liver re-transplantation.

Study or subgroup	TPCS Events	TPCS Total	No-TPCS Events	No-TPCS Total	Weight	Odds ratio M-H, fixed, 95% CI
Arzu 2008	6	97	10	89	24.7%	0.52 [0.18, 1.50]
Ghinolfi 2010	2	58	9	90	17.2%	0.32 [0.07, 1.54]
Rayar 2017	14	343	24	343	58.1%	0.57 [0.29, 1.11]
Total (95% CI)		**498**		**522**	**100.0%**	**0.51 [0.30, 0.87]**
Total events	22		43			

Heterogeneity: Chi^2=0.42, df=2 (P=0.81); I^2=0%
Test for overall effect: Z=2.46 (P=0.01)

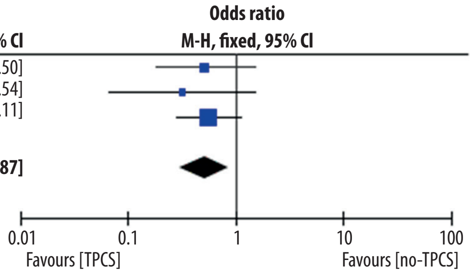

Figure 13. Forest plot for the meta-analysis of studies examining the effect of temporary portocaval shunt (TPCS) on mortality.

Study or subgroup	TPCS Mean	TPCS SD	TPCS Total	No-TPCS Mean	No-TPCS SD	No-TPCS Total	Weight	Mean difference IV, random, 95% CI
Arzu 2008	1.21	0.9	97	1.42	0.89	89	32.0%	−0.21 [−0.47, 0.05]
Cenarruzabeitia 2007	1.15	0.52	356	1.48	0.86	45	32.0%	−0.33 [−0.59, −0.07]
Ghinolfi 2010	70	39.4	58	92.5	64.1	90	0.0%	−22.50 [−39.18, −5.82]
Pratschke 2013	1.64	0.82	274	1.67	1.09	174	36.0%	−0.03 [−0.22, 0.16]
Total (95% CI)			**785**			**398**	**100.0%**	**−0.19 [−0.48, 0.10]**

Heterogeneity: Tau^2=0.05; Chi^2=10.53, df=3 (P=0.01); I^2=72%
Test for overall effect: Z=1.27 (P=0.20)

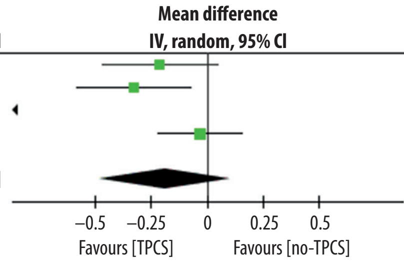

Figure 14. Forest plot for the meta-analysis of studies examining the effect of temporary portocaval shunt (TPCS) on creatinine (Cr) on third postoperative day.

Study or subgroup	TPCS Mean	TPCS SD	TPCS Total	No-TPCS Mean	No-TPCS SD	No-TPCS Total	Weight	Mean difference IV, random, 95% CI
Arzu 2008	1,145	1.023	97	3,534	3,249.21	89	0.0%	−2,389.00 [−3,064.04, −1,713.96]
Cenarruzabeitia 2007	4.37	3.03	356	5.91	3.84	45	20.7%	−1.54 [−2.71, −0.37]
Figueras 2001	2.3	2.5	40	3.3	2.9	40	20.7%	−1.00 [−2.19, 0.19]
Ghinolfi 2010	7.5	5.8	58	12.2	14.2	90	17.5%	−4.70 [−7.99, −1.41]
Pratschke 2013	5.0	4.0	274	4.4	5.0	174	20.9%	0.60 [−0.28, 1.48]
Rayar 2017	11.5	10.416	343	13.0	11.574	343	20.2%	−1.50 [−3.15, 0.15]
Suárez-Munoz 2006	1,586	1,389,23	160	3,534	3,249.21	189	0.0%	−1,948.00 [−2,458.80, −1,437.20]
Total (95% CI)			**1328**			**970**	**100.0%**	**−1.66 [−4.92, 1.60]**

Heterogeneity: Tau^2=13.00; Chi^2=121.06, df=6 (P<0.00001); I^2=95%
Test for overall effect: Z=1.00 (P=0.32)

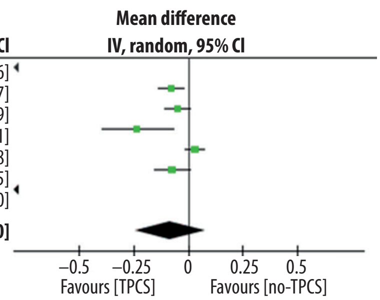

Figure 15. Forest plot for the meta-analysis of studies examining the effect of temporary portocaval shunt (TPCS) on red blood cell (RBC).

Transfusion in the operative room

RBCs

For RBCs, data from 7 studies [1,13–18] evaluated 1328 patients with TPCS and 970 patients without TPCS. The mean difference was –1.66 [–4.92–1.60] (Figure 15) and was not significantly different (*P*=0.32).

FFP

For FFP, data from 6 studies [1,13,15–18] evaluated 936 patients with TPCS and 925 patients without TPCS. The mean difference was –0.68 [–4.47–3.12] (Figure 16) and was not significantly different (*P*=0.73).

Platelets

For platelets, data from 4 studies [1,15–17] evaluated 601 patients with TPCS and 662 patients without TPCS. The mean difference was –3.62 [–9.35–2.11] (Figure 17) and was not significantly different (*P*=0.22).

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	TPCS			No-TPCS				Mean difference
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, random, 95% CI
Arzu 2008	715.0	552.0	97	917.0	872.0	89	0.0%	−202.00 [−413.87, 9.87]
Figueras 2001	1.6	2.4	4	1.4	2.7	40	24.1%	0.20 [−2.30, 2.70]
Ghinolfi 2010	7.9	6.8	58	10.4	10.3	90	23.5%	−2.50 [−5.26, 0.26]
Pratschke 2013	21.1	1.2	274	19.6	1.1	174	26.8%	1.50 [1.28, 1.72]
Rayar 2017	11.75	10.7053	343	13.0	11.574	343	25.5%	−1.25 [−2.92, 0.42]
Suárez-Munoz 2006	1,830	1,299	160	3,049	1,883.87	189	0.0%	−1,219.00 [−1,554.63, −883.37]
Total (95% CI)			**936**			**925**	**100.0%**	**−0.68 [−4.47, 3.12]**

Heterogeneity: Tau²=13.95; Chi²=73.39, df=5 (P<0.00001); I²=93%
Test for overall effect: Z=0.35 (P=0.73)

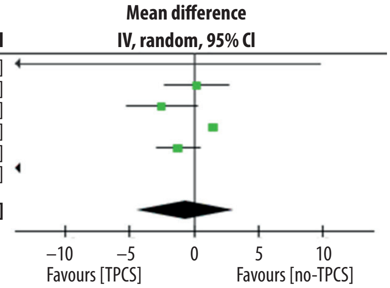

Figure 16. Forest plot for the meta-analysis of studies examining the effect of temporary portocaval shunt (TPCS) on frozen fresh plasma (FFP).

	TPCS			No-TPCS				Mean difference
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, random, 95% CI
Figueras 2001	9.2	13.0	40	9.6	8.5	40	22.5%	−0.40 [−5.21, 4.41]
Ghinolfi 2010	2.5	6.4	58	3.8	9.8	90	25.3%	−1.30 [−3.91, 1.31]
Rayar 2017	2.0	2.35	343	2.5	2.91	343	26.7%	−0.50 [−0.90, −0.10]
Suárez-Munoz 2006	5.0	6.93	160	17.0	14.43	189	25.6%	−12.00 [−14.32, −9.68]
Total (95% CI)			**601**			**662**	**100.0%**	**−3.62 [−9.35, 2.11]**

Heterogeneity: Tau²=32.03; Chi²=91.83, df=3 (P<0.00001); I²=97%
Test for overall effect: Z=1.24 (P=0.22)

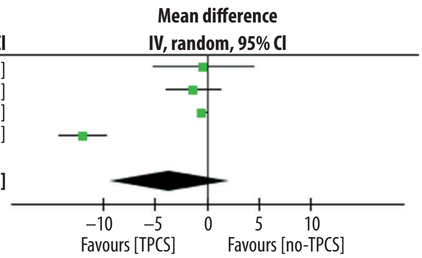

Figure 17. Forest plot for the meta-analysis of studies examining the effect of temporary portocaval shunt (TPCS) on platelets.

Discussion

This present study demonstrated specific outcomes of interest that were defined and evaluated separated: 2 different reviews and meta-analyses of the literature in which we assessed the intraoperative surgical portosystemic shunt in relation to liver transplantation. Among the several factors studied and evaluated, we observed that each modality, HPCS and TPCS, had specific benefits and indications that were completely different.

The meta-analyses evaluated 3232 patients in all selected studies. Of these, 41 patients with HPCS had more than 1-year patient survival (OR 16.33; *P*=0.02) and 1-year graft survival (OR 17.67; *P*=0.01). For TPCS the analysis evaluated 1633 patients and found significantly shorter unit care length of stay (days) (*P*=0.006) and hospital length of stay (*P*=0.02), and a decrease in PNF (OR 0.30, *P*=0.02) and mortality rate (OR 0.52, *P*=0.01).

Pratschke et al. (2016) [19] showed different findings compared to our review findings. However, Pratschke et al. only evaluated TPCS, and showed a reduction for blood loss, with improved postoperative transaminases and renal function [19]. In our review, we were able to include more studies with more TPCS patients for evaluation. Furthermore, we did not find a significant difference in relation to renal failure, transfusions, and postoperative transaminases. Our important finding for TPCS was the decrease in PNF, hospital length of stay, and unit care length of stay.

Rayar et al. (2017) [1] studied 686 patients for TPCS and recommended (especially when considering an extended criteria for donor's graft) demonstrating survival analysis. This revealed that TPCS improved 3-month graft survival (94.2% *vs.* 88.8%, *P*=0.01) as well as long-term survival of the elderly (i.e., age >70 years) donor grafts (*P*=0.02) [1]. This important finding agreed with our study, in that we observed decreased mortality rate with TPCS (OR 0.52, *P*=0.01).

TPCS has important recipient technical attributes that have been discussed recently [1,15,18,20]. First, it has been shown to be an important technique associated with the piggyback technique, mainly in severe patients, with better reported results in these cases. Other relevant factors include vena cava clamping (partial or total) and preservation, in addition to the technique being used in liver implants, which can be side-by-side anastomosis, or union of the 3 hepatic veins, or closing the right hepatic vein and using anastomosis with the medial-left trunk of the hepatic vein, or conventional anastomosis with a total clamp [15,18,20,21]. These variations in relation to the vena cava may influence its benefit in TPCS cases.

HPCS is an important method and technique for flow modulation and has been demonstrated using several approaches, mainly in the handling of SFSS [4–6]. Kinaci et al. [21] described an interesting study with positive benefits among too small grafts for liver transplant modulates with portosystemic shunt [21]. The present meta-analysis reaffirms the relevance and importance in cases of small-for-size, pediatric grafts, and living donors.

Botha et al. [4] studied data from 2 centers and demonstrated that small grafts with portal modulation with HPCS might prevent SFSS [4]. However, in this systematic review, SFSS was evaluated for 24 patients with HPCS and 10 patients without HPCS; no significant difference was seen (OR 0.27; P=0.19). HPCS has the potential for positive patient results for graft survival.

Regarding hepatic hemodynamic, portal modulation and liver regeneration is a hot topic nowadays, mainly related to LDLT, split livers, and major hepatectomy. The portal venous modulation aims to prevent SFSS and liver failure after major hepatectomy [25–28]. This hemodynamic procedure is based on the portal flow and the portal pressure that directly influences the shear stress in hepatocytes and sinusoidal endothelial cells triggering them to perform optimal liver regeneration. So, some surgical procedures such as splenectomy or portocaval shunt (side-to-side, end-to-side, stent, tube, or using donor vessels) can be used for portal modulation and to reduce portal flow and portal pressure in liver transplantation [25–28].

The limitations of this study were that we found only 1 well-designed randomized controlled trial in our literature search. Our study had other limitations. The number of patients with HPCS was very small. The failure to demonstrate a difference in SFSS (OR=0.27) but a demonstrated definite effect on patient and graft survival (OR >16) was problematic, as this operation was designed to reduce SFSS. This most likely reflects the small number of patients analyzed. The specific outcomes of interest were defined and evaluated separated; 2 different reviews and meta-analyses were performed as HPCS has no relationship with TPCS as the indications for both are different. The last major limitation was that we evaluated together the types of TPCS being used (end-to-side portocaval anastomotic surgical shunts), while others utilized a passive portocaval tubing shunt. The majority of studies found were retrospectively. One study was registered on Clinicaltrial.gov recruiting patients for the "Effect of Temporary Portocaval Shunt during Liver Transplantation on Function of Liver Graft from Extended Criteria Donor" (*https://clinicaltrials.gov/ct2/show/NCT02784119?term=porto+caval+shunt&recrs=ab&cond=Liver+Transplant&rank=1*). Only this review was completely registered in PROSPERO (*https://www.crd.york.ac.uk/prospero/*). In this area, more prospective randomized clinical trials are needed to focus on adequate conclusions.

The benefit of our systematic review and meta-analysis was to evaluate more patients with important risk factors in both modalities of intraoperative portocaval shunt. This information might help to increase survival and decrease complications and hospitals costs. This meta-analysis found HPCS had an increased 1-year patient survival (OR 16.33; P=0.02) and 1-year graft survival (OR 17.67; P=0.01); and TPCS had significant decreased unit care length of stay (days) (P=0.006), hospital length of stay (P=0.02), PNF (OR 0.30, P=0.02), and mortality (OR 0.52, P=0.01).

Conclusions

An intraoperative surgical portosystemic shunt regarding liver transplantation using TPCS was able to prevent PNF, decrease the length of hospital stay, unit care stay, and mortality. In analyzing HPCS, we observed increases in the 1-year graft and patient survival. More prospective randomized clinical trials are needed for precise conclusions.

Conflict of interest

None.

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