Original Article

Short and Long-Term Outcomes Following Liver Transplantation: A Systematic Review and Meta-Analysis of Piggyback versus Conventional Approach

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ABSTRACT

Introduction: In adult liver transplantation (LT), Piggyback (PB-LT) and conventional (CON-LT) methods are the most commonly used approaches. However, the clinical outcomes of the two approaches and their survival rates have yet to be well examined. This study aimed to conduct a quantitative meta-analysis focused on the efficacy and safety of PB-LT and CON-LT procedures.

Methods: This systematic review and meta-analysis followed the PRISMA standards. The literature search was conducted on certain databases, including Cochrane Library, PubMed, Scopus, and EMBASE. The Newcastle-Ottawa Quality Assessment Scale and the risk of Cochrane Collaboration of bias tool were used to analyze eligible articles and evaluate their quality.

Results: The results showed that eight retrospective cohort studies and three RCTs were included. When PB-LT was used instead of CON-LT, perioperative red blood cells consumption decreased substantially (MD −1.49; 95% CI −2.53 to −0.45; p = 0.005), with significantly short hospital stay (MD −1.67; 95% CI −2.13 to −1.22; p = ＜0.001) and reduced warm (MD −8.7; 95% CI −14.93 to −2.48; p = 0.006) and cold (MD −48.32; 95% CI −61.03 to −35.61; p = ＜0.001) ischemia durations. Furthermore, there were no significant differences in primary graft nonfunction, total operation duration, hepatobiliary complication, length of ICU stay, 1-year mortality, and 1-year graft survival using either PB-LT or CON-LT.

Conclusions: This study found that PB-LT and CON-LT were viable options for adult LT. The PB-LT approach had different short-term outcomes. However, the two approaches had no significant differences in long-term clinical outcome indicators.

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KEYWORDS: liver transplantation, liver grafting, surgical procedures, approaches

Introduction

Liver transplantation (LT) is a life-saving surgery for patients experiencing severe liver dysfunction due to substantial loss of hepatic cells. This clinical condition is characterized by elevated bleeding and thrombosis risks, acid-base homeostasis alterations, a systemic inflammatory response, hemodynamic instability, and organ failure.[1, 2] Candidates awaiting transplantation face a terminal condition with significant needs, requiring comprehensive and com-

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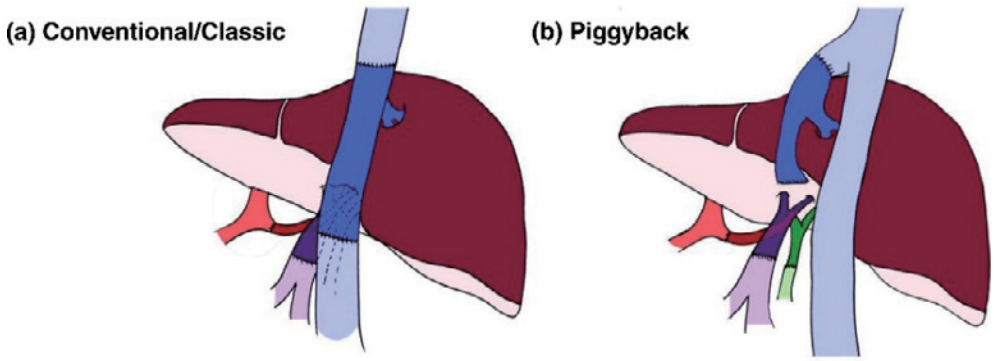


Fig. 1 Different Surgical Methods Used in Liver Transplantation[8)]

plex medical care even in the most advanced stages.[3, 4)] Since the first human liver transplantation was established in 1963, 98,989 patients who had end-stage liver diseases have had functional grafts.[5)] Between 2006 and 2010, Asia reported a constant increase in living donor liver transplantation (LDLT) rates, while Europe experienced a slight increase and the USA recorded a decline.[6, 7)] China is the only Asian country where deceased donor liver transplantation (DDLT) is more common than LDLT, with 95% of donated liver coming from deceased donors.[8)] DDLT program in Asia faces obstacles, such as a need for increased public awareness, religious issues, and proper laws. Consequently, most Asian countries fail to increase DDLT rates, with LDLT accounting for more than 90% of all transplants.[9, 10)]

The need for adult LT arises from severe diseases and conditions in which the function has critically deteriorated. For instance, Hepatocellular Carcinoma (HCC) typically develops due to liver cirrhosis, acting as a precancerous stage. Consequently, LT is used as the sole potentially curative approach for the underlying cirrhosis, aside from resection or local ablative treatments.[11, 12)] Patients with full recovery potential must be recognized, as it makes LT unnecessary and potentially harmful. Identifying those at a high risk of progression is crucial, as sepsis or irreversible organ failures may affect their suitability for transplantation and post-transplantation outcomes.[12)] Recurrent disease after a former transplant, including failed past non-liver transplants, might result in liver failure and necessitate retransplantation.[13)] Over the last decades, different surgical approaches have been performed to improve outcomes.

Piggyback (PB-LT) and conventional (CON-LT) methods are the most frequently used approaches (Fig. 1). In the CON-LT approach, the liver and the retrohepatic portion of the inferior vena cava (IVC) are completely removed, interrupting the venous return of the infradiaphragmatic bed. In contrast, the PB-LT approach preserves the recipient IVC side-to-side or the suprahepatic end anastomosed to the hepatic veins with the donor IVC still attached.[14–16)] Several studies comparing these two approaches have been conducted, with the results showing significant implications for short- and long-term outcomes. Most of these studies included patients with various liver diseases, providing homogenous data on overall mortality, intraoperative blood loss, total operation time, and length of hospital stay after LT surgery. However, the clinical outcomes and survival rates must be consistent and well-studied. Thus, these LT surgical approaches must be systematically compared. Therefore, this study aimed to compare the efficacy of CON-LT and PB-LT procedures from existing literature by quantitative meta-analysis. The results will provide clinicians with valuable information that can assist in making well-informed decisions regarding the most appropriate surgical approach for LT.

Methods

Data sources and search strategy

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines.[17)] All protocols were officially registered on The International Prospective Register of Systematic Reviews (PROSPERO) under the reference number CRD42023462283. This meta-analysis constituted a supplementary investigation built upon previously published data. Therefore, ethical clearance or specific informed consent was not required.

PubMed, Scopus, the Cochrane Library, and EMBASE

were the databases used to search for relevant Randomized Controlled Trials (RCTs) and observational studies comparing short- and long-term outcomes of LT using the two approaches. Search terms used were "conventional versus piggyback", "liver transplantation", and "surgical outcomes". Two authors, namely FM and NR, selected studies and extracted data, including evaluation following an established protocol. PB-LT and CON-LT procedures were compared to understand each approach's relative benefits and drawbacks. By combining data from various clinical studies, meta-analysis can improve statistical power and identify differences in clinically important outcomes.

Eligibility criteria

Studies focusing on adult (≥18 years old) human LT procedures that compare CON-LT and PB-LT approach outcomes were included. Eligible individuals were those with conditions, such as end-stage liver disease, acute liver failure, and liver cancer, who had exhausted medical treatment options and faced a considerable risk of death, necessitating a transplant. There were no gender, ethnicity, region, educational background, or economic status limitations. In the experimental group, adult patients received PB-LT, while patients in the control group received standard treatment. Papers without sufficient available data, other unrelated studies (such as non-comparative studies, meta-analyses, literature reviews, case reports, and animal studies), and those with poor approach quality were excluded from further analysis.

Data extraction and selection process

Two authors independently screened suitable titles, abstracts, and full-text articles. Subsequently, full-text articles for all listed studies were collected for further eligibility assessment. Information was systematically extracted regarding title, author, year of publication, and baseline characteristics of patients. As predictive parameters of short- and long-term surgical outcomes, the following were collected: blood product usage (red blood cells/RBC consumption), cold and warm ischemia, total operation time, hepatobiliary complication, length of intensive care unit (ICU) stay, length of hospital stay, primary graft nonfunction, 1-year graft survival, and 1-year mortality.

Statistical analysis

The comparisons were reported as the mean difference (MD) for continuous variables, risk ratio (RR) for dichotomous variables, and the 95% Confidence Interval (CI). An I2 value approaching 0% indicated low heterogeneity, while large values implied high heterogeneity. During the data analysis, a fixed effect model (I2 $<$50%) or a random effect model (I2 $>$50%) was used. Publication bias was visually evaluated by examining funnel plots, while pooled analyses were conducted using Review Manager (RevMan) software version 5.4.1 manufactured by The Cochrane Collaboration.

Risk of bias assessment

The risk of bias in trials was assessed with the components recommended by Cochrane Collaboration (CC)[18] for randomized control trials and the Newcastle-Ottawa Scale (NOS).[19] For the CC trial assessment, scores (up to 12 points) were assigned, with high scores representing low bias risks. The NOS was used to assess the observational studies, with a total maximum score of 9 points.

Results

Study selection

A total of 975 potentially relevant studies were identified, but 709 were removed after reviewing their titles and abstracts. Full-text articles from the remaining 33 references were assessed for eligibility. Among these, 22 studies were excluded, including 12 due to insufficient outcomes data, 7 being categorized as other study types (case series/report), and 3 for reporting irretrievable full-text articles. In this systematic review and meta-analysis, 11 selected studies published between 1997 and 2021 were considered, with 1,820 patients comprising 836 and 984 undergoing PB-LT and CON-LT, respectively. Moreover, the included studies comprise eight retrospective cohort studies and three RCTs fulfilling the criteria for data extraction. Details of study selection are listed in Fig. 2, showing the data from each cohort and trial using the current surgical outcomes parameter.

Study characteristics

The studies featured a large sample size, ranging from 37 to 384. Most were primarily centered on adults suffering from cirrhosis due to chronic diseases, malignancies, and acute liver failure, reflecting the predominant patient demographics for transplantation. All investigations were single-center based and conducted on adult patients above 18 years old across various countries, with the majority coming from Europe and Asia. Details of included studies regarding the number of patients, evaluated outcomes, and results are listed in Table 1.[4–14]

Risk of bias in studies

The overall quality assessment of the cohort and RCT

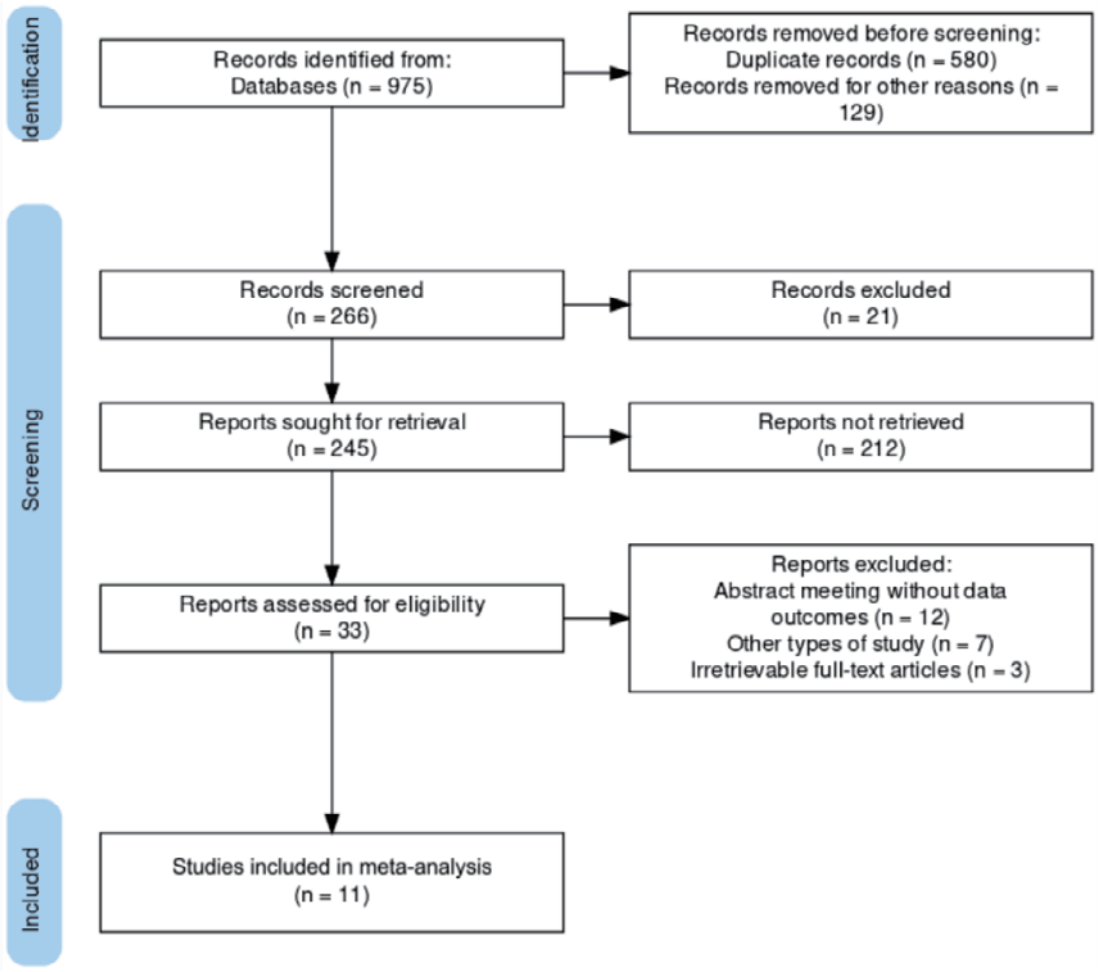


Fig. 2 PRISMA Flow Diagram

studies was considered suitable. In cohort studies, three[21, 25, 30] were classified as very good (9-10 points), four[22–24, 29] were good (7-8 points), and one[20] was satisfactory (5-6 points). The risk of bias in all RCT[26–28] was moderate, and a detailed summary is given in Fig. 3a, b.

Short-term surgical outcomes

When PB-LT was used instead of CON-LT, perioperative RBC consumption decreased substantially[21–28] (MD −1.49; 95% CI −2.53 to −0.45; p = 0.005), with significantly short total hospital stay[21, 23, 27, 28, 30] (MD −1.67; 95% CI −2.13 to −1.22; p = <0.001) and reduced warm[20, 22, 23, 25, 28] (MD −8.7; 95% CI −14.93 to −2.48; p = 0.006) and cold[22, 23, 25–27] (MD −48.32; 95% CI −61.03 to −35.61; p = <0.001) ischemia duration. Furthermore, both procedures' total operation time[21–23, 25–29] (MD −14.55; 95% CI −40.30 to 11.20; p = 0.27) and length of ICU stay[22, 23, 25, 29, 30] (MD −1.38; 95% CI −3.39 to −0.63; p = 0.18) did not exhibit statistically significant differences. The results of short-term surgical outcomes are illustrated in Fig. 4.

Long-term surgical outcomes

Long-term surgical outcomes using the PB-LT approach were similar to that of CON-LT. According to the pooled result, there was no significant difference in the risk of 1-year mortality[22–26, 30] (RR 1.00; 95% CI 0.51 to 1.95; p = 1.00), 1-year graft survival[22–25, 30] (RR 1.66; 95% CI 0.75 to 3.66; p = 0.21), primary graft nonfunction[21–23, 29] (RR 1.15; 95% CI 0.49 to 2.7; p = 0.74), and hepatobiliary complication[20–23, 25, 29, 30] (RR 0.95; 92% CI 0.67 to 1.27; p = 0.62). The results for long-term surgical outcomes are represented in Fig. 5.

Discussion

Several factors influence the success rate of LT, with approach-related parameters, such as operative duration, blood product usage, length of hospital stay, and post-surgical complications. This meta-analysis aimed to assess short- and long-term outcomes of LT using CON-LT and PB-LT approaches. An in-depth review of the available literature on RCT and cohort studies was conducted. The re-

Table 1 Summary of the Study Characteristics

Author (Year)	Study Design	Country	Study Period	Number of patients		Evaluated outcomes	Results
				CON-LT	PB-LT		
Ghazaly et al. (2014)	Retrospective cohort study	UK	2007–2008	93	27	• Hepatobiliary complication • Total hospital stay • ICU Stay • Graft failure • Long-term mortality	No significant differences between the CON-LT and PB-LT techniques regarding patient morbidity, graft survival, quality of life, and hospital stay
Saboor et al. (2006)	Retrospective cohort study	UK	2000–2003	138	246	• Total Operation time • Cold ischemia • Warm ischemia • ICU Stays • Total hospital stay • Blood product usage (RBC) • Hepatobiliary complication • Long-term mortality • Graft failure	No difference in short- or long-term graft or patient survival
Miyamoto et al. (2004)	Retrospective cohort study	Nether-lands	1994–2000	96	71	• Hepatobiliary complication • ICU Stay • Total Operation time • Cold ischemia • Warm ischemia • Blood product usage (RBC)	The total operation time was not different between both groups, but in the PB-LT group, cold and warm ischemia time (CIT and WIT), and revascularization time were significantly shorter. RBC use in the PB-LT group was lower than in the CON-LT group.
Vieira et al. (2011)	Retrospective cohort study	USA	1999–2008	125	70	• ICU stay • Length of hospital stay • Long-term mortality • Total Operation time • Cold ischemia • 1-year graft survival • Warm ischemia • Blood product usage (RBC)	There were no differences in relation to CIT; length of stay in the ICU; duration of hospital stay; renal function; graft function; the incidence of sepsis, biliary complications; and 1-year mortality
Zieniewicz et al. (2002)	Retrospective cohort study	Poland	1994–2001	68	11	• Hepatobiliary complication • Total Operation time • Warm ischemia time	There was a statistically significant difference in the intraoperative blood loss, total operation time, and WIT between the two methods
Zhitao et al. (2021)	Retrospective cohort study	People's Republic of China	2015–2019	282	101	• Hepatobiliary complication • ICU Stay • Total hospital stay • Total Operation time • Cold ischemia • Blood product usage (RBC)	The operation duration in the PB-LT group was significantly longer than that of CON-LT. The overall survival in the PB-LT group was better than in CON-LT
Reddy et al. (2000)	Retrospective cohort study	USA	1995–1998	40	36	• Long-term mortality • Blood product usage (RBC) • ICU Stay • Total hospital stay	Total operating time, blood product usage, graft survival, and length of hospital and ICU stay were significantly low in PB-LT patients
Hesse et al. (2000)	Retrospective cohort study	Belgium	Not described	75	15	• ICU Stay • Hepatobiliary complication • Graft failure • Operation time	No differences could be found in preoperative patient conditions, donor conditions, operating time, anastomosing time, or CIT.

Table 1 continued

Author (Year)	Study Design	Country	Study Period	Number of patients		Evaluated outcomes	Results
				CON-LT	PB-LT		
Jovine et al. (1997)	Randomized controlled trial	Italy	1995–1996	19	18	• ICU Stay • Hospital stay • Total Operation time • Blood product usage (RBC) • Graft failure • Warm ischemia time	No difference in the incidence of graft nonfunction or postoperative morbidity and mortality between the groups
Maria et al. (2004)	Randomized controlled trial	Brazil	1999–2001	34	33	• Total Operation time • Blood product usage (RBC) • Cold ischemia • Total hospital stay	No significant differences between the two groups regarding operative time, anesthesia time, graft CIT, duration of mechanical ventilation, length of hospital stay, and operative mortality
Marilia et al. (2015)	Randomized controlled trial	Brazil	1999–2006	15	17	• Total Operation time • Blood product usage (RBC) • Cold ischemia • Long-term mortality	No significant differences between the CON-LT and PB-LT techniques regarding perioperative data and survival rates

** Abbreviations: CON-LT: Conventional Liver Transplantation, PB-LT: Piggyback Liver Transplantation*

sults will assist clinicians in selecting the most suitable LT approach. In transplantation settings, there is a highly complex immune system. When the liver is transferred from a donor to a recipient, the alloantigen, primarily the allogeneic major histocompatibility complex or human leukocyte antigens in humans, is widespread and may potentially persist throughout the recipient's lifespan.[31, 32] This alloantigen can be delivered by professional and nonprofessional antigen-presenting cells at multiple sites.[31, 33, 34] Rejection in LT constitutes cellular and humoral alloimmune responses, which play crucial roles in regulating tolerance mechanisms.[34]

Regarding short-term surgical outcomes, the results showed a significant difference, favoring the PB-LT group rather than the CON-LT group. Preserving the recipient's IVC and partial liver in PB-LT may reduce the incidence of hepatic venous outflow blockage and improve the overall hemodynamics.[27, 35] Due to the underlying liver illness and hemostatic changes associated with the transplant, complex coagulation abnormalities may occur during transplantation.[36] Hemostatic changes are potentially caused by hemodilution, platelet consumption, thrombin dysfunction, and fibrinolysis.[36, 37] In three studies,[20, 21, 24] the PB-LT approach showed several advantages, including shorter operation time and lower estimated blood loss and complications during surgery than that of the CON-LT approach. In line with the results, PB-LT had a low intraoperative RBC loss, short length of hospital stay, and reduced warm (the period between the donor liver being removed from the ice until blood reperfusion in the recipient) and cold (the period between the aorta clamp in the donor and liver's release from ice for implantation in the recipient) ischemia duration in five studies.[20, 21, 24, 26, 28] However, another study stated that reduced cold ischemia duration does not significantly affect outcomes.[22]

According to Al-Kurd et al.,[38] significantly increasing trends were observed in transfusion demand, estimated blood loss, and high lactate levels with prolonged recipient warm ischemia duration. The duration of cold ischemia minimally impacted histological changes and correlated with hepatic injury, manifested by an elevation in blood ALT and total bilirubin levels.[39] RBC usage was lower in the PB-LT group than in the CON-LT group, and this concurred with a previous study on reduced hemodynamic instability.[40] The significant determinants affecting transfusion requirements include the severity of disease (evaluated by Child-Pugh Score or model for end-stage liver dis-

(a)

No.	First Author, Year	Selection				Comparability	Outcome			Quality Rating
		Representativeness of the sample	Selection of the non-exposed cohort	Outcome of interest was not present at the start of study	Ascertainment of the exposure		Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	
1.	Ghazaly et al., 2014	★	★	★	★	★★	★	★	★	9/10
2.	Hesse et al., 2000	★	★	★	★	★★		★		7/10
3.	Miyamoto et al., 2004	★	★	★	★	★★	★	★	★	9/10
4.	Reddy et al., 2000	★	★	★	★	★★			★	7/10
5.	Saboor et al., 2006		★	★	★	★★		★	★	7/10
6.	Vieira et al., 2011	★	★	★	★	★★	★	★		8/10
7.	Zhitao et al., 2021	★	★	★	★	★★	★	★	★	9/10
8.	Zieniewicz et al., 2002	★	★	★		★★		★		6/10

Very Good Studies: 9-10 points; Good Studies: 7-8 points; Satisfactory Studies: 5-6 points; Unsatisfactory Studies: 0 to 4 points

(b)

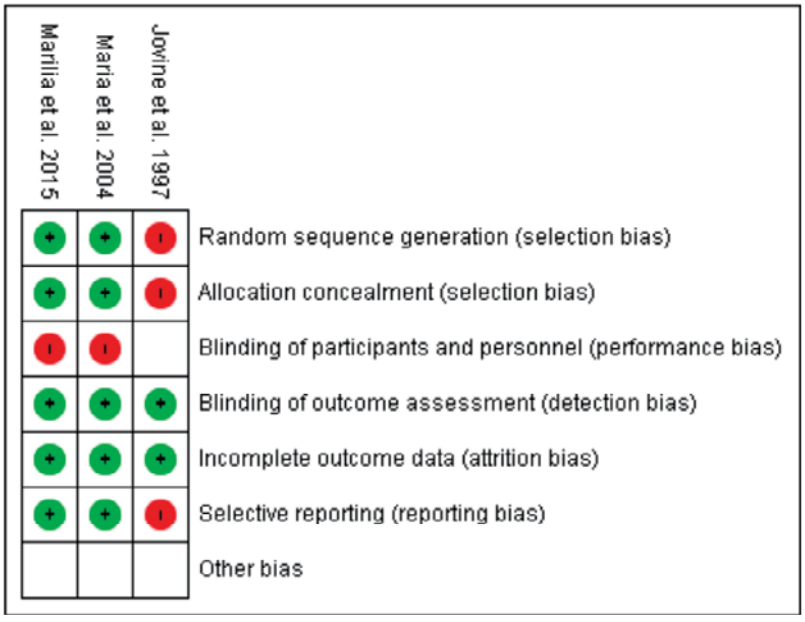


Fig. 3 Bias Summary Risk of (a) Cohort and (b) RCT studies

ease classification), preoperative prothrombin time, history of abdominal operations, and Factor V levels.[37, 41] The surgical team's experience was also reported as an independent predictor of transfusion.[42] According to Mehrabi et al.,[43] the PB approach reduces ICU and hospital stays.

Regarding long-term outcomes, the two surgical approaches did not significantly differ. The analysis results showed similar rates of 1-year mortality, 1-year graft survival, primary graft nonfunction, and hepatobiliary complication. A comparative study by Nikeghbalian et al. supported this result, showing no significant differences in survival rates between the two groups.[44] Outflow disruption or vena cava obstruction in the early post-liver transplant phase was associated with substantial morbidity and death.[19] Previous studies found that high recipient age, weight, and donor age decreased graft survival.[45, 46] Furthermore, primary nonfunction (PNF) demands emergency retransplantation as a life-saving surgery.[47–49] In a study conducted by Nanashima et al. on 93 patients, those who experienced early graft dysfunction had considerably increased in-hospital mortality (35% vs. 5%). Based on a previous report, mortality can reach approximately 90% in cases of PNF diagnosis.[47]

Our study did not emphasize the PB-LT method for LT as superior because it did not show a substantial effect on long-term outcomes, such as 1-year mortality and graft survival, the ultimate measures of transplantation success despite its short-term benefits. Reduced RBC use and hospital stays are beneficial, but without long-term benefits, their clinical value is secondary to patient survival and graft life. Furthermore, the substantial limitations in the data, such as retrospective designs, high heterogeneity,

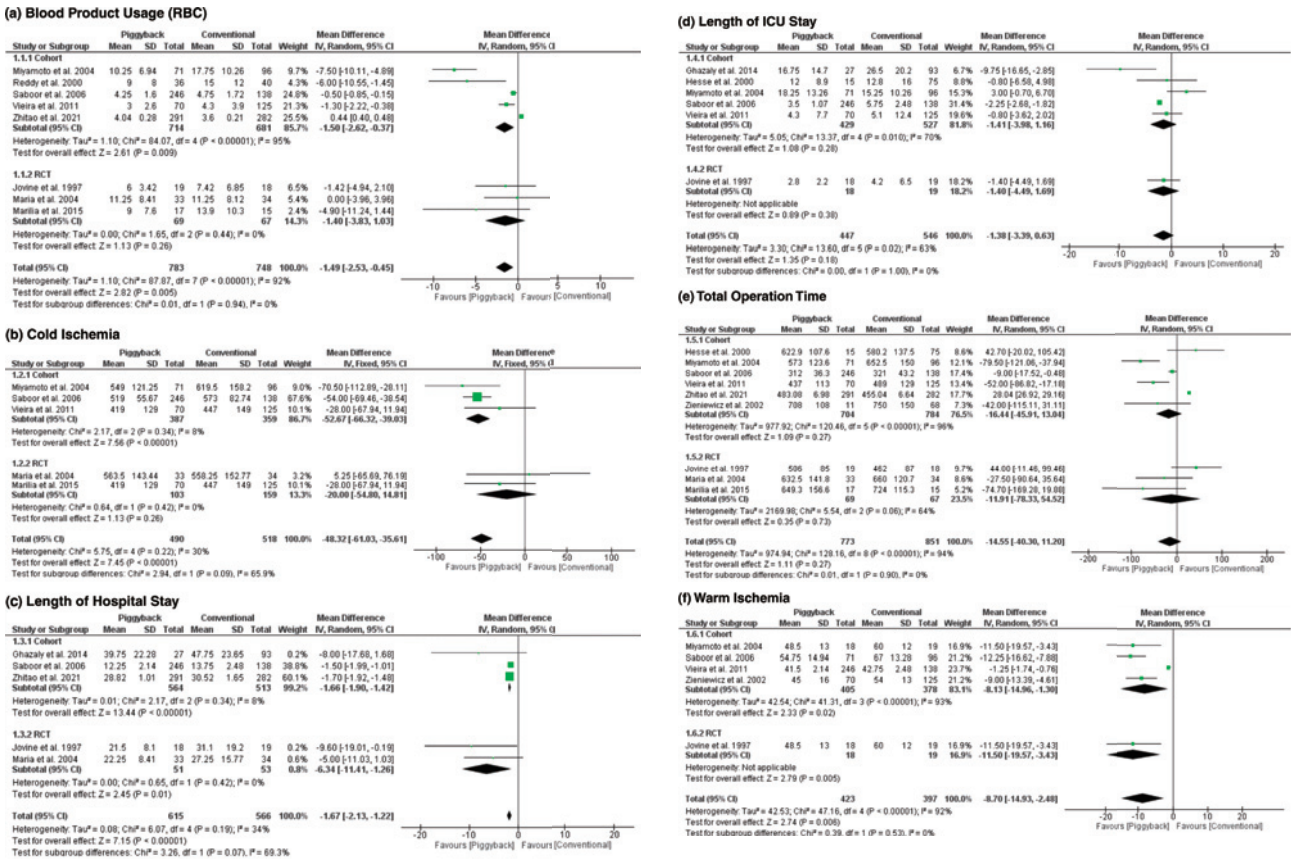


Fig. 4 a-f. Short-term Parameters Forest Plot

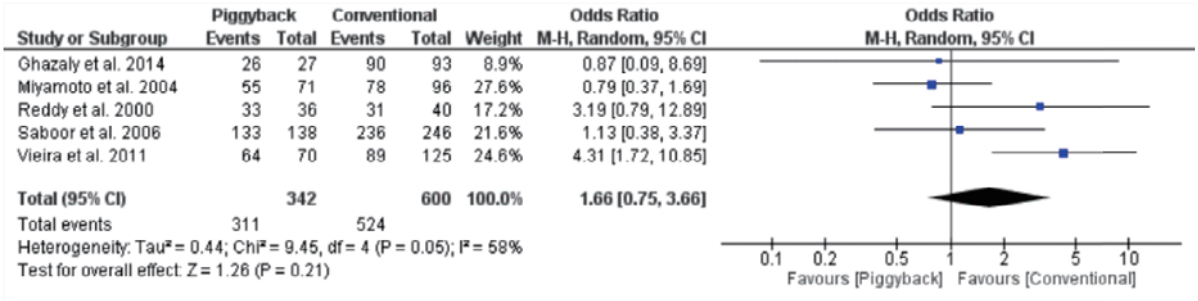
and potential biases, require a cautious interpretation of these findings. Aside from the surgical procedure, various factors influence LT success, including the recipient's immune system reactions, pre-existing health conditions, and postoperative care quality.[50, 51] Considering the importance of the surgical team's expertise and the protocols followed at various transplant centers, the short-term improvements associated with PB-LT may not be decisive in selecting it as the preferred method.

The lack of difference in long-term outcomes highlights the pivotal role of post-transplant care. Long-term success depends on the surgical procedure and postoperative management, particularly a strict regimen of immunosuppressants to prevent graft rejection, regular monitoring via blood tests and imaging to assess liver function and detect complications, and lifestyle modifications with dietary guidance and psychological support.[52] This comprehensive care is provided by a multidisciplinary team focused on personalized medication management, early complication intervention, and patient education on self-care. Moreover, the included studies predominantly feature developed countries with well-established transplant centers providing comprehensive care, which likely contributes to the similar long-term outcomes observed across different surgical procedures.

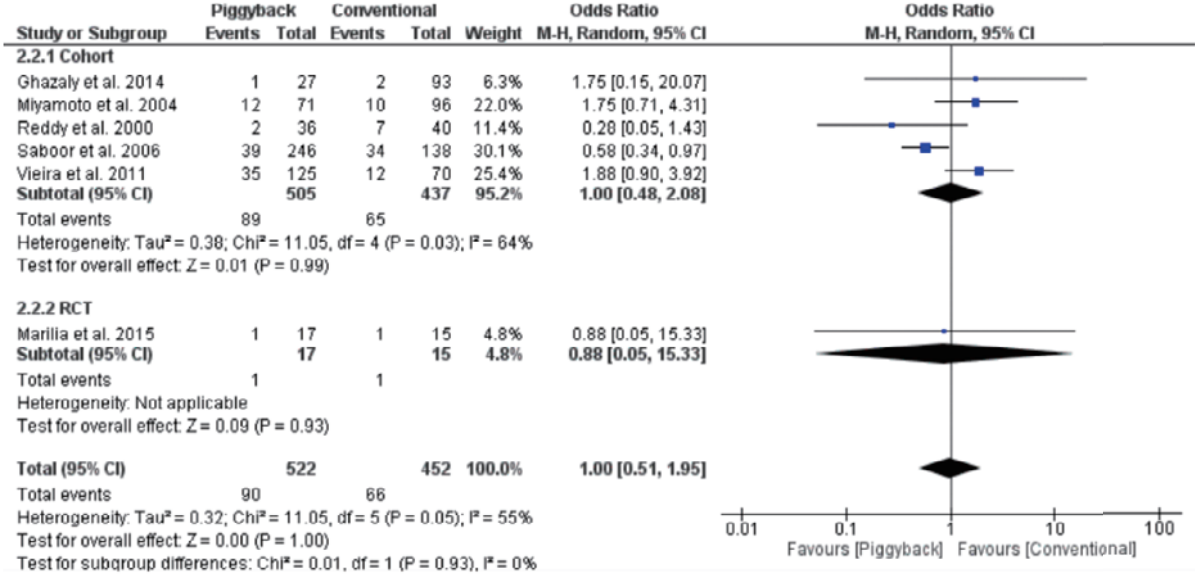
This meta-analysis had a few limitations. First, most of the included studies used a retrospective design, with only three RCTs found in the literature. Second, the results were based on a limited number of studies with high levels of heterogeneity. The underlying disparities in patient characteristics could have influenced the overall outcomes. Third, other factors potentially influencing LT results, such as comorbidities, nutritional status, and severity of liver disease, were not specifically addressed. Differences in surgical approaches and perioperative care practices between centers contributed to the unexamined outcomes variance in this study.

Based on the results, it was concluded that PB-LT and CON-LT were safe and feasible for short- and long-term outcomes after surgery. Although both approaches have equivalent long-term efficacy, the PB-LT approach can minimize early postoperative issues. The presence of a high bias risk emphasizes the significance of interpreting the results with caution. Further studies are required to

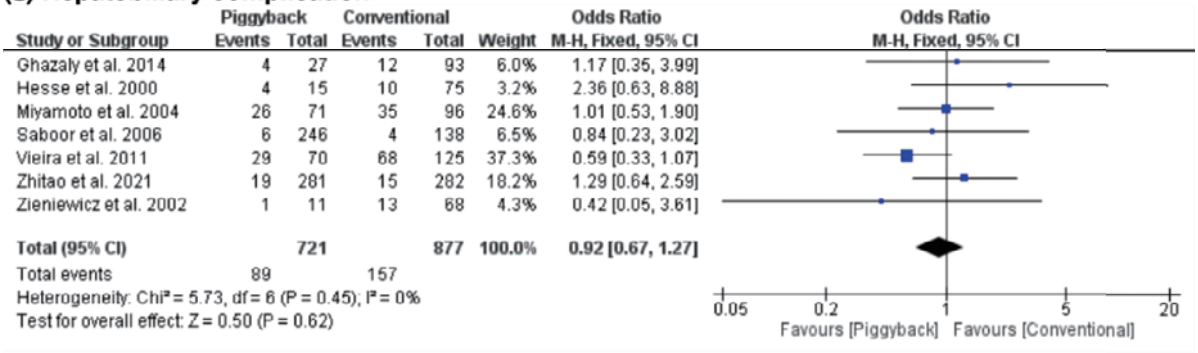
(a) 1-year graft survival



(b) 1-year mortality



(c) Hepatobiliary complication



(d) Primary graft nonfunction

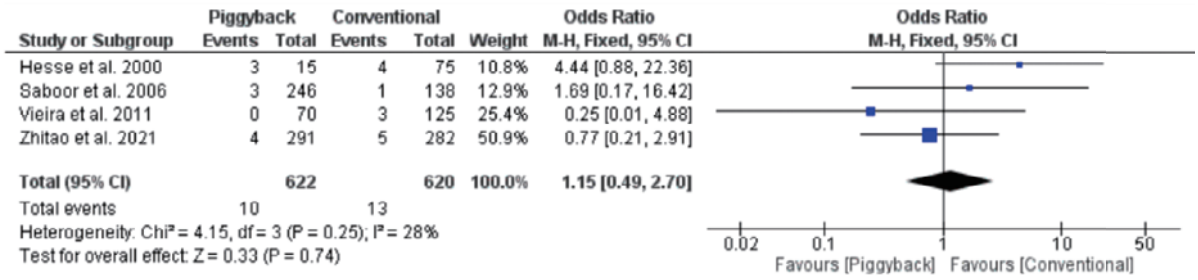


Fig. 5 a-d. Long-term Parameters Forest Plot

confirm the results and determine the optimal approach for LT depending on the clinical circumstances.

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Authors' contribution: F.M. designed the study; F.M. and A.N. analyzed the data; F.M. and A.N. wrote the manuscript.

Conflicts of interest: None declared.

References

1) Chamuleau RAFM, Hoekstra R. End-stage liver failure: Filling the treatment gap at the intensive care unit. J Artif Organs. 2020; 23 (2): 113-23. doi: 10.1007/s10047-019-01133-3.
2) Trovato FM, Rabinowich L, McPhail MJW. Update on the management of acute liver failure. Curr Opin Crit Care. 2019; 25 (2): 157-64. doi: 10.1097/MCC.0000000000000583.
3) Vieira Silva S, Freire E, Pessegueiro Miranda H. Palliative care in end-stage liver disease patients awaiting liver transplantation: Review. GE Port J Gastroenterol. 2020; 27 (6): 417-28. doi: 10.1159/000507336.
4) Patel AA, Walling AM, Ricks-Oddie J, May FP, Saab S, Wenger N. Palliative care, and health care utilization for patients with end-stage liver disease at the end of life. Clin Gastroenterol Hepatol. 2017; 15 (10): 1612-9.e4. doi: 10.1016/j.cgh.2017.01.030.
5) Kwong AJ, Ebel NH, Kim WR, et al. OPTN/SRTR 2020 annual data report: Liver. Am J Transplant. 2022; 22: 204-309.
6) Chen CL, Kabiling CS, Concejero AM. Why does living donor liver transplantation flourish in Asia? Nat Rev Gastroenterol Hepatol. 2013; 10 (12): 746-51. doi: 10.1038/nrgastro.2013.194.
7) Wertheim JA, Petrowsky H, Saab S, Kupiec-Weglinski JW, Busuttil RW. Major challenges limiting liver transplantation in the United States. Am J Transplant. 2011; 11 (9): 1773-84. doi: 10.1111/j.1600-6143.2011.03587.x.
8) Ozturk NB, Muhammad H, Gurakar M, Aslan A, Gurakar A, Dao D. Liver transplantation in developing countries. Hepatol Forum. 2022; 3 (3): 103-7. doi: 10.14744/hf.2022.2022.0014.
9) Shukla A, Vadeyar H, Rela M, Shah S. Liver transplantation: East versus West. J Clin Exp Hepatol. 2013; 3 (3): 243-53. doi: 10.1016/j.jceh.2013.08.004.
10) Hibi T, Wei Chieh AK, Chi-Yan Chan A, Bhangui P. Current status of liver transplantation in Asia. Int J Surg. 2020; 82S: 4-8. doi: 10.1016/j.ijsu.2020.05.071.
11) Graziadei I, Zoller H, Fickert P, et al. Indications for liver transplantation in adults: Recommendations of the Austrian Society for Gastroenterology and Hepatology (ÖGGH) in cooperation with the Austrian Society for Transplantation, Transfusion and Genetics (ATX). Wien Klin Wochenschr. 2016; 128 (19-20): 679-90. doi: 10.1007/s00508-016-1046-1.
12) Zanetto A, Shalaby S, Gambato M, et al. New indications for liver transplantation. J Clin Med. 2021; 10 (17): 3867. doi: 10.3390/jcm10173867.
13) Moreno R, Berenguer M. Post-liver transplantation medical complications. Ann Hepatol. 2006; 5 (2): 77-85. PMID: 16807513.
14) Chan T, DeGirolamo K, Chartier-Plante S, Buczkowski AK. Comparison of three caval reconstruction techniques in orthotopic liver transplantation: A retrospective review. Am J Surg. 2017; 213 (5): 943-9. doi: 10.1016/j.amjsurg.2017.03.045.
15) Kuramitsu K, Kido M, Komatsu S, et al. Standardization of the side-to-side cavo-caval anastomosis in orthotopic liver transplantation based on the causal analysis of outflow obstruction. Transplant Proc. 2021; 53 (10): 2934-8. doi: 10.1016/j.transproceed.2021.09.017.
16) Addeo P, Schaaf C, Noblet V, et al. The learning curve for piggyback liver transplantation: Identifying factors challenging surgery. Surgery. 2021; 169 (4): 974-82. doi: 10.1016/j.surg.2020.09.036.
17) Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ. 2021; 372: n71.
18) Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011; 343: d5928.
19) Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses, 2012. https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
20) Zieniewicz K, Krawczyk M, Nyckowski P, et al. Liver transplantation: Comparison of the classical orthotopic and piggyback techniques. Transplant Proc. 2002; 34 (2): 625-7.
21) Chen Z, Ju W, Chen C, et al. Application of various surgical techniques in liver transplantation: A retrospective study. Ann Transl Med. 2021; 9 (17): 1367.
22) Vieira de Melo PS, Miranda LE, Batista LL, et al. Orthotopic liver transplantation without venovenous bypass using the conventional and piggyback techniques. Transplant Proc. 2011; 43 (4): 1327-33.
23) Khan S, Silva MA, Tan YM, et al. Conventional versus piggyback technique of caval implantation; without extra-corporeal venovenous bypass. A comparative study. Transpl Int. 2006; 19 (10): 795-801.
24) Reddy KS, Johnston TD, Putnam LA, Isley M, Ranjan D. Piggyback technique and selective use of veno-venous bypass in adult orthotopic liver transplantation. Clin Transplant. 2000; 14 (4 Pt. 2): 370-4.
25) Miyamoto S, Polak WG, Geuken E, et al. Liver transplantation with preservation of the inferior vena cava. A comparison of conventional and piggyback techniques in adults. Clin Transplant. 2004; 18 (6): 686-93.
26) Brescia MD, Massarollo PC, Imakuma ES, Mies S. Prospective randomized trial comparing hepatic venous outflow and renal function after conventional versus piggyback liver transplantation. PLOS ONE. 2015; 10 (6): e0129923.
27) Isern MR, Massarollo PC, de Carvalho EM, et al. Randomized trial comparing pulmonary alterations after conventional with venovenous bypass versus piggyback liver transplantation. Liver Transpl. 2004; 10 (3): 425-33.
28) Jovine E, Mazziotti A, Grazi GL, et al. Piggy-back versus conventional technique in liver transplantation: Report of a randomized trial. Transpl Int. 1997; 10 (2): 109-12.
29) Hesse UJ, Berrevoet F, Troisi R, et al. Hepato-venous reconstruction in orthotopic liver transplantation with preservation of the recipients' inferior vena cava and veno-venous bypass. Langenbecks Arch Surg. 2000; 385 (5): 350-6.

30) Ghazaly M, Davidson BR. Conventional versus piggyback techniques: Do they have different outcomes? Prog Transplant. 2014; 24 (1): 51-5.
31) Lei H, Reinke P, Volk HD, Lv Y, Wu R. Mechanisms of immune tolerance in liver transplantation-crosstalk between alloreactive T cells and liver cells with therapeutic prospects. Front Immunol. 2019; 10: 2667. doi: 10.3389/fimmu.2019.02667.
32) Peruhova M, Peshevska-Sekulovska M, Velikova T. Interactions between human microbiome, liver diseases, and immunosuppression after liver transplant. World J Immunol. 2021; 11 (2): 11-6. doi: 10.5411/wji.v11.i2.11.
33) Ozaki M. Cellular and molecular mechanisms of liver regeneration: Proliferation, growth, death and protection of hepatocytes. Semin Cell Dev Biol. 2020; 100: 62-73. doi: 10.1016/j.semcdb.2019.10.007.
34) Gama JFG, Cardoso LMDF, Bisaggio RDC, Lagrota-Candido J, Henriques-Pons A, Alves LA. Immunological tolerance in liver transplant recipients: Putative involvement of neuroendocrine-immune interactions. Cells. 2022; 11 (15): 2327. doi: 10.3390/cells 11152327.
35) Calderon Novoa F, Mattera J, de Santibañes M, et al. Understanding local hemodynamic changes after liver transplant: Different entities or simply different sides to the same coin? Transplant Direct. 2022; 8 (9): e 1369. doi: 10.1097/TXD.0000000000001369.
36) Feltracco P, Brezzi M, Barbieri S, et al. Blood loss, predictors of bleeding, transfusion practice and strategies of blood cell salvaging during liver transplantation. World J Hepatol. 2013; 5 (1): 1-15. doi: 10.4254/wjh.v5.i1.1.
37) Pandey CK, Singh A, Kajal K, et al. Intraoperative blood loss in orthotopic liver transplantation: The predictive factors. World J Gastrointest Surg. 2015; 7 (6): 86-93. doi: 10.4240/wjgs.v7.i6.86.
38) Al-Kurd A, Kitajima T, Delvecchio K, et al. Short recipient warm ischemia time improves outcomes in deceased donor liver transplantation. Transpl Int. 2021; 34 (8): 1422-32. doi: 10.1111/tri.13962.
39) Freitas ACT, Matos DMN, Milsted JAT, Coelho JCU. Effects of cold ischemia time on hepatic allograft function. Arq Bras Cir Dig. 2017; 30 (4): 239-43. doi: 10.1590/0102-6720201700040003.
40) Feltracco P, Brezzi M, Barbieri S, et al. Blood loss, predictors of bleeding, transfusion practice and strategies of blood cell salvaging during liver transplantation. World J Hepatol. 2013; 5 (1): 1-15. doi: 10.4254/wjh.v5.i1.1.
41) Feltracco P, Brezzi M, Barbieri S, et al. Blood loss, predictors of bleeding, transfusion practice and strategies of blood cell salvaging during liver transplantation. World J Hepatol. 2013; 5 (1): 1-15. doi: 10.4254/wjh.v5.i1.1.
42) Hendriks HG, van der Meer J, Klompmaker IJ, et al. Blood loss in orthotopic liver transplantation: A retrospective analysis of transfusion requirements and the effects of autotransfusion of cell saver blood in 164 consecutive patients. Blood Coagul Fibrinolysis. 2000; 11 (Suppl 1): S87-93. doi: 10.1097/00001721-200004001-00017.
43) Mehrabi A, Mood ZA, Fonouni H, et al. A single-center experience of 500 liver transplants using the modified piggyback technique by Belghiti. Liver Transpl. 2009; 15 (5): 466-74. doi: 10.1002/lt.21705.
44) Nikeghbalian S, Toutouni MN, Salahi H, Aliakbarian M, Malekhosseini SA. A comparative study of the classic and piggyback techniques for orthotopic liver transplantation. Electron Physician. 2014; 6 (1): 741-6.
45) Jeffrey AW, Delriviere L, McCaughan G, et al. Excellent contemporary graft survival for adult liver retransplantation: An Australian and New Zealand registry analysis from 1986 to 2017. Transplant Direct. 2019; 5 (8): e 472. doi: 10.1097/TXD.0000000000000920.
46) Jain A, Reyes J, Kashyap R, et al. Long-term survival after liver transplantation in 4,000 consecutive patients at a single center. Ann Surg. 2000; 232 (4): 490-500. doi: 10.1097/00000658-200010000-00004.
47) Nanashima A, Pillay P, Verran DJ, et al. Analysis of initial poor graft function after orthotopic liver transplantation: Experience of an Australian single liver transplantation center. Transplant Proc. 2002; 34 (4): 1231-5. doi: 10.1016/s0041-1345(02)02639-8.
48) Zhang X, Zhang C, Huang H, et al. Primary nonfunction following liver transplantation: Learning of graft metabolites and building a predictive model. Clin Transl Med. 2021; 11 (7): e483. doi: 10.1002/ctm2.483.
49) Masior Ł, Grąt M. Primary nonfunction and early allograft dysfunction after liver transplantation. Dig Dis. 2022; 40 (6): 766-76. doi: 10.1159/000522052.
50) Parekh KN, Crowley JC, Liu LL. Postoperative care of the liver transplant recipient. Anesth Perioper Care Organ Transplant. 2016; 365-84. doi: 10.1007/978-1-4939-6377-5_29.
51) Moayed MS, Khatiban M, Nassiri Toosi M, Khodaveisi M, Soltanian AR, Ebadi A. Barriers to adherence to medical care programs in liver transplant recipients: A qualitative study. Int J Organ Transplant Med. 2019; 10 (3): 115-26.
52) Fuochi E, Anastasio L, Lynch EN, et al. Main factors influencing long-term outcomes of liver transplantation in 2022. World J Hepatol. 2023; 15 (3): 321-52. doi: 10.4254/wjh.v15.i3.321.