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Comparison of percutaneous microwave/radiofrequency ablation liver partition and portal vein embolization versus transarterial chemoembolization and portal vein embolization for planned hepatectomy with insufficient future liver remnant

Tai-Wei Ye[1,2†], Tian-Wei Fu[1,2†], Cheng-Fei Du[1,2†], Ru-Chi Yue[3†], Qi-Tao Jiang[1], Zhi-Hang Zhong[1], Qin Zhao[4], Cheng-Wu Zhang[1], Jie Liu[1], Jun-Wei Liu[1], Zu-Yan Luo[1], Xiao-Ming Fan[1], De-Fei Hong[5], Jian Cheng[1*] and Zun-Qiang Xiao[1*]

Abstract

Background In China, both percutaneous microwave/radiofrequency ablation liver partition plus portal vein embolization (PALPP) and transarterial chemoembolization (TACE) plus portal vein embolization (PVE) have been utilized in planned hepatectomy. However, there is a lack of comparative studies on the effectiveness of these two techniques for cases with insufficient future liver remnant (FLR).

Methods Patients were categorized into either the PALPP group or the TACE + PVE group. Clinical data, including FLR growth rate, complications, secondary resection rate, and overall survival rate, were compared and analyzed for both groups retrospectively.

Results Between December 2014 and October 2021, a total of 29 patients underwent TACE + PVE ($n = 12$) and PALPP ($n = 17$). In the TACE + PVE group, 7 patients successfully underwent two-stage hepatectomy, while in the PALPP group, 13 patients underwent the procedure (two-stage resection rate: 58.3% vs. 76.5%, $P = 0.42$). There were no significant differences in postoperative complications of one-stage procedures (11.8% vs. 8.3%, $P > 0.05$) and second-stage resection complication (0% vs. 46.2%, $P = 0.05$) between the TACE + PVE and PALPP groups. However, the PALPP group demonstrated a shorter time to FLR volume growth for second-stage resection (18.5 days vs. 66 days, $P = 0.001$) and KGR (58.5 ml/week vs. 7.7 ml/week, $P = 0.001$).

†Tai-Wei Ye, Tian-Wei Fu, Cheng-Fei Du and Ru-Chi Yue these authors contributed equally to this work.

*Correspondence:
Jian Cheng
chengj0523@163.com
Zun-Qiang Xiao
zqxiao@zcmu.edu.cn
Full list of author information is available at the end of the article

Conclusions Compared with TACE + PVE, PALPP results in a more significant increase in FLR volume and a higher rate of two-stage resection without increasing postoperative complications.

Keywords Microwave/radiofrequency ablation, Liver partition, Planned hepatectomy, Transarterial chemoembolization, Portal vein mbolization, Future liver remnant

Introduction

Surgery remains the mainstay of curative treatment for liver-related malignant tumors, particularly primary hepatocarcinoma. Unfortunately, only a small percentage, ranging from 5–10%, of new cases of primary liver cancer annually are eligible for surgical resection [1]. Among those unable to undergo surgical resection, approximately 30% face inoperability due to insufficient future liver remnant (FLR), a condition predominantly contributing to postoperative liver failure [2, 3].

In addressing this challenge, Makuuchi et al. introduced portal vein embolization (PVE) in 1990. Subsequently, in 2012, Schnitzbauer et al. proposed the Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy (ALPPS) method to achieve compensatory liver enlargement and mitigate the risk of postoperative liver failure [2].

However, it is now understood that PVE typically takes 4–6 weeks to stimulate FLR growth, accompanied by an increased risk of tumor progression due to compensatory hepatic arterial blood flow. To address this, Gruttadauria et al. in 2006 proposed combining PVE with transcatheter arterial chemoembolization (TACE), aiming to enhance FLR volume to surgical standards within a shorter 4-week period [4]. While ALPPS significantly increases FLR volume, some studies have reported a rapid induction of liver hypertrophy within one week, reaching up to 93%. Nevertheless, its serious complications and high mortality compromise its clinical efficacy [5]. In 2015, Professor Gall TM and Cillo U introduced percutaneous radiofrequency ablation (PRA) and microwave ablation (PMA) to separate liver parenchyma. Hong et al. later refined this method, replacing portal vein ligation with the PVE method, resulting in percutaneous microwave ablation liver partition and portal vein embolization for planned hepatectomy (PALPP) [6–8], which achieves the surgical FLR requirement in about one week.

Despite the substantial enhancements in FLR growth efficiency and safety observed with these modified procedures, clinical selection remains contentious. Therefore, this study sought to compare FLR volume growth, safety, two-stage resection rates, and prognosis between the two surgical methods to inform future clinical practice.

Materials and Methods

Selection of patients

A retrospective study was conducted, including a total of 45 patients who underwent PVE at Zhejiang Provincial People's Hospital between December 2014 and October 2021. All interventional and surgical procedures were conducted at the same hospital.

Inclusion criteria: (I) age ≥ 18 years old; (II) Liver resection planned with insufficient FLR for primary surgical resection (FLR ≥ 25–30% is recommended for patients with a normal healthy liver and > 40% for those with severe cirrhosis or portal hypertension) [9–11]. (III) Liver function categorized as Child–Pugh class A, B, or per WHO criteria with performance status (PS) of 0, 1, or 2. (IV) No preoperative adjuvant therapy received.(V) All liver malignancies.

Exclusion criteria: (I) Non-malignant intrahepatic lesions. (II) PVE alone.

A total of 29 patients were enrolled in this study, including 12 patients treated with TACE + PVE. 17 patients were treated with PALPP(Fig. 1).

Procedure of operation

PVE: After administering general anesthesia, ultrasound-guided percutaneous portal vein puncture was performed. The hemihepatic portal vein, along with its branches in the segment where the lesion was located, were embolized with coils under transcatheter portal vein angiography by digital subtraction angiography (DSA) navigation. Following this procedure, appropriate embolization was carried out using a mixture of isobutyl cyanoacrylate (NBCA) and lipiodol in a 1:1 ratio until angiography demonstrated complete occlusion of the target vessels [12].

TACE: The main artery and its branches of the hepatic lesion were superselectively accessed through percutaneous femoral artery puncture under DSA navigation. Tumor vessels were embolized with ultra-liquefied lipiodol combined with epirubicin/cisplatin + famacin or drug-loaded microspheres and gelatin sponge particles [13].

Percutaneous microwave coagulation therapy (PMCT)/ Percutaneous radiofrequency ablation (PRFA): (I) PMCT: Ultrasound-guided PMCT was performed using a microcomputer cold circulation microwave therapeutic apparatus with a frequency of 2450 MHz and a maximum

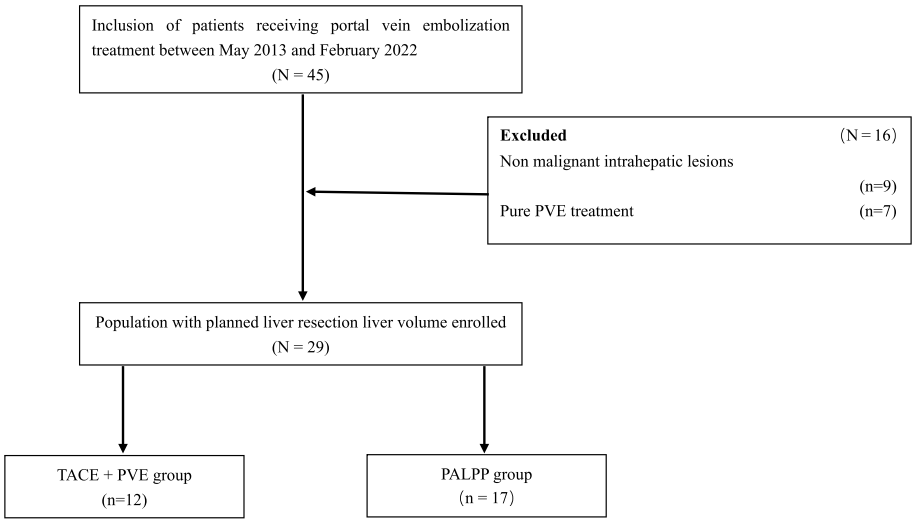

Fig. 1 Flow chart of enrolled patients. TACE + PVE, transarterial chemoembolization plus portal vein embolization; PALPP, percutaneous microwave/radiofrequency ablation liver partition and portal vein embolization

power of 100W (Fuzhong Medical High-tech Co., LTD., Jiangsu, China). A demarcation line in the hepatic parenchyma was delineated 2 cm from the primary hepatic vein, and this demarcation was conserved using real-time ultrasound guidance. The ablation line was ensured to be more than 1 cm away from the tumor boundary. Subsequently, the ablation needle was placed on the pre-tangent line during percutaneous puncture under ultrasound guidance, and the multi-point and multi-axis sector ablation method was used to separate the liver parenchyma. The ablation time was 2–3 min per point, the power was 50-60W, the temperature was around 90 °C, and the end of the needle track was coagulated to prevent bleeding.

As for the TACE + PVE cohort, PVE was performed 2 to 4 weeks after TACE in patients who underwent sequential therapy. Otherwise, PVE was performed immediately after successful TACE treatment, and then the second-stage resection was performed after about 4 weeks until the FLR reached the standard. For patients who underwent PALPP, a two-stage hepatectomy was performed as long as up to FLR requirement. All procedures were performed by the same team.

The liver volume measurement standard of the two groups was based on the liver-enhanced CT three-dimensional reconstruction before each intervention or operation. FLR was evaluated using three-dimensional visualization technology. The standard liver volume (SLV) was calculated according to the formula proposed by Urata and Bruix et al. (SLV (mL) = 706.2 × BSA (m^2) + 2.4). The kinetic growth rate (KGR) was calculated as the ratio of the degree of liver volume increase (%) to the time from baseline to the liver volume before the second stage hepatectomy (weeks) [14–16]. Due to the slow growth effect observed in the TACE + PVE group, tumor progression occurred during the waiting period, which was addressed by TACE treatment. After the first stage of surgery, the FLR was reviewed weekly, and if the FLR met the prespecified criteria, patients in the two groups underwent the second stage of surgery.

Treatment failure was considered if (I) tumor progression occurred while waiting, (II) complications caused the failure of the two-stage hepatectomy, or (III) treatment was abandoned by the patient after one-stage treatment. Patients who failed treatment received palliative care (chemotherapy, targeted therapy, intervention, etc.).

Outcomes and Follow-up

The primary outcomes were the rate of two-stage resection. Secondary outcomes included: (I) the growth rate of FLR, (II) postoperative complications, and mortality (complications were classified according to Clavien-Dindo) [17].

The surgical margin was defined as the shortest distance from the tumor edge to the resection plane, with R0 resection defined as a negative microscopic margin and R1 resection defined as a positive microscopic margin. Patients were followed up one month after surgical resection, and then serum AFP, enhanced CT, or enhanced MRI scans and liver function were reviewed every 3 months. Patients with recurrence or metastasis were treated with further therapy.

Data analysis

Continuous variables with a normal distribution were expressed as mean ± standard deviation (SD), and those with a skewed distribution were expressed as median and interquartile range (IQR). The Mann–Whitney U test was used for comparison. Categorical variables were expressed as frequencies and percentages and compared using Pearson's chi-square test or Fisher's exact test. Finally, multivariate COX regression analysis was included to determine the significant factors affecting the volume growth rate of FLR. All calculations were analyzed using standard software (SPSS Statistics 25.0). A two-tailed P-value < 0.05 was statistically significant.

Research methods and ethics

This study is a retrospective study on patients with liver malignancies who received TACE + PVE or PALPP treatment due to insufficient FLR. Our research was conducted in accordance with the principles outlined in the Helsinki Declaration, and all procedures involving human participants strictly adhere to the ethical standards of the Zhejiang Provincial People's Hospital Ethics Review Committee. Given the retrospective nature of this study, which involved the use and analysis of unverified data, the Ethics Review Committee of Zhejiang Provincial People's Hospital waived the requirement for written informed consent.

Result

A total of 45 patients who underwent PVE from December 2014 to October 2021 were included in this study. Nine patients with non-neoplastic lesions receiving PVE were excluded, along with 7 patients who underwent PVE alone. Finally, 29 patients were included in the study (Fig. 1).

Comparison of baseline data between the two groups

There were no significant differences between the two groups at baseline (Table 1).

Comparison of treatment outcomes and intraoperative variables between the PALPP group and TACE + PVE group

In the TACE + PVE group, 58.3% of patients ($n = 7$) underwent two-stage hepatectomy, while in the PALPP group, the proportion was higher at 76.5% ($n = 13$). The reasons for the failure to undergo a two-stage hepatectomy are detailed in Table 2. Importantly, there was no significant difference in the rate of two-stage hepatectomy completion between the two groups ($P = 0.42$). Within the PALPP group, all patients experienced sufficient FLR volume growth, and among those who did not undergo two-stage surgery, two patients underwent TACE due to tumor progression. Conversely, in the TACE + PVE group, two patients experienced insufficient FLR volume growth. One patient underwent TACE + PVE treatment again, but the growth effect was limited, leading the family to discontinue treatment. The other patient declined the second treatment and opted for conservative management. Among the two patients with tumor progression in this group, one chose to discontinue treatment, while the other received sorafenib. The choice of hepatectomy types varied between the groups, with right trisegmentectomy being the predominant approach in the PALPP group (69.2% vs. 14.3%, $P = 0.06$) and right hemihepatectomy being more common in the TACE + PVE group (57.1% vs. 15.1%). Although intraoperative blood loss was lower in the TACE + PVE group, and the operative duration was shorter in the PALPP group, there were no significant differences between the two groups ($P = 0.6$, $P = 0.38$).

FLR volume growth and FLR changes after stage 1 surgery

Two patients died after stage 1 surgery (one PALPP, one TACE + PVE) and were excluded from the analysis. The final FLR volume was comparable between groups (526.0 vs 502.2 mL, $P = 0.657$) (Table 3). However, the interstage interval was shorter for PALPP (18.5 vs 66 days, $P = 0.001$), with a faster FLR growth rate (43% vs 23%, $P = 0.026$) and higher weekly liver hypertrophy rate (58.5 vs 7.7 mL/week, $P = 0.001$). PALPP demonstrated superior FLR expansion over TACE + PVE (Fig. 2A), unaffected by portal hypertension (Fig. 2B). In addition, Table 4 shows the impact of different types of intrahepatic tumors on FLR proliferation.

Comparison of postoperative outcomes between the PALPP and TACE + PVE groups

Complications

All patients in both groups successfully completed the first stage operation, with only one case with complications above Grade II in the TACE + PVE group, specifically postoperative liver failure, which improved after comprehensive medical treatment. In contrast, the PALPP group encountered 2 cases of postoperative complications above Grade II: one patient succumbed during the perioperative period due to postoperative liver failure, and another developed postoperative pleural effusion, relieved after transthoracic puncture drainage. There was no significant difference in the incidence of complications exceeding Grade II after stage 1 surgery between the two groups (8.3% vs. 11.8%, $P > 0.05$) (Table 2). Among patients who underwent two-stage surgery (7 patients (58.3%) in the TACE + PVE group; 13 cases (76.5%) in the PALPP group), no complications exceeding Grade II were reported in the TACE + PVE group. In the PALPP group, however, 6 patients experienced complications higher

Table 1 Baseline characteristics between TACE + PVE and PALPP groups

Characteristic	Level	TACE + PVE group ($n=12$)	PALPP group($N=17$) PMA($n=8$) PRA($n=9$)	P
Age (year) (median [IQR])		50.5 (43.8, 57.0)	49.0 (46.0, 59.0)	0.76
Sex (%)	Male	10 (83.3)	14 (82.4)	1.00
	Female	2 (16.7)	3 (17.7)	
BMI (kg/m^2) (median [IQR])		23.0 (21.1, 23.6)	22.2 (20.5, 23.4)	0.35
ASA (%)	I	4 (33.3)	1 (5.9)	0.16
	II	7 (58.3)	14 (82.4)	
	III	1 (8.3)	2 (11.8)	
PS (%)	0	9 (75.0)	15 (88.2)	0.43
	1	2 (16.7)	2 (11.8)	
	2	1 (8.3)	0 (0.0)	
Tumor type (%)	HCC	11 (91.7)	13 (76.5)	0.65
	ICC	1 (8.3)	2 (11.8)	
	Other tumors	0 (0.0)	2 (11.8)	
Number of tumors (%)	Single tumor	8 (66.7)	7 (41.8)	0.26
	Multiple tumors	4 (33.3)	10 (58.8)	
Maximum tumor diameter (mm)		96.0 (47.5, 118.0)	80.0 (44.5, 112.5)	0.57
Macrovascular invasion (%)	No	6 (50.0)	8 (47.1)	1.00
	Yes	6 (50.0)	9 (52.9)	
TB (μmol/L) (median [IQR])		13.1 (11.3, 20.9)	20.1 (14.6, 25.7)	0.03
ALT (U/L) (median [IQR])		31.5 (24.5, 47.0)	42.0 (17.5, 72.5)	0.83
AST (U/L) (median [IQR])		47.0 (32.8, 72.5)	55.0 (34.5, 83.5)	0.72
AFP (%)	< 20 μg/L	2 (16.7)	6 (35.3)	0.41
	> 20 μg/L	10 (83.3)	11 (64.7)	
Cirrhosis (%)	No	1 (8.3)	4 (23.5)	0.37
	Yes	11 (91.7)	13 (76.5)	
HBV (%)	No	0 (0.0)	4 (23.5)	0.21
	Yes	12 (100.0)	13 (76.5)	
Protal hypertension (%)	No	7 (58.3)	7 (41.2)	
	Yes	5 (41.7)	10 (58.8)	0.59
Child–Pugh grade	1	12 (100.0)	14 (82.4)	0.36
	2	0 (0.0)	3 (17.7)	

BMI body mass index, *ASA* American Society of Anesthesiologists, *PS* performance status, *HCC* hepatocellular carcinoma, *ICC* intrahepatic cholangiocarcinoma, *PLT* platelet, *TB* total bilirubin, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *AFP* alpha-fetoprotein, *HBV* hepatitis B virus

than Grade II ($P=0.05$). The complications of abdominal bleeding and intestinal obstruction in the PALPP group were addressed by a second operation to relieve intestinal obstruction. Pneumothorax and pleural effusion were treated with closed thoracic drainage and thoracentesis drainage. Unfortunately, the family members of patients with postoperative liver failure chose to discontinue treatment.

Survival analysis

We further compared the prognostic impact of different surgical methods and pathological types.When the pathology is HCC, the TACE + PVE group had a median follow up period of 14.5 months, with a recurrence rate of 63.6% and a mortality rate of 45.5%. During the median folllow up period of 17.5 mongths; the recurrence rate of the PALPP group was 83.3%,and the mortality rate was 58.3%.

Discussion

ALPPS, as a revolutionary breakthrough in hepatobiliary surgery, offers a radical approach for resecting mid to late-stage liver cancer with insufficient FLR. However, its clinical application has faced challenges due to high complication and mortality rates. Consequently, alternative technologies like TACE + PVE and PALPP have gained

Table 2 Intraoperative and postoperative data of TACE + PVE and PALPP groups were compared

Index	TACE + PVE group	PALPP group	P
Data of first step	(*n* = 12)	(*n* = 17)	
Preoperative variables			
AST (U/L) (median [IQR])	47.0 (32.8, 72.5)	55.0 (34.5, 83.5)	0.72
ALT (U/L) (median [IQR])	31.5 (24.5, 47.0)	42.0 (17.5, 72.5)	0.83
AFP (> 20 μg/L) (%)	10 (83.3)	11 (64.7)	0.41
TB (μmol/L) (median [IQR])	13.1 (11.3, 20.9)	20.1 (14.6, 25.7)	0.03
Postoperative complications (Clavien Dindo) (%)			
> Grade II	1 (8.3)	2 (11.8)	1.00
Details	Liver failure (n = 1, 8.3%)	Perioperative mortality (*n* = 1, 5.9%), pleural effusion (*n* = 1, 5.9%)	
Data of second step	(n = 7)	(*n* = 13)	
Second step	Second step (n = 7, 58.3%)	Second step (*n* = 13, 76.5%)	0.42
Reasons for not proceeding to second step hepatectomy	Total:*n* = 5 (41.7%), Tumor progression (*n* = 2, 11.8%), Liver failure (*n* = 1, 8.3%), insufficient hypertrophy of FLR (*n* = 2, 16.7%)	Total:*n* = 4 (23.5%), Tumor progression (*n* = 2, 11.8%), Liver failure (*n* = 1, 5.9%), loss to follow-up (*n* = 1, 5.9%)	
Second step variables			
AST (U/L) (median [IQR])	30.0 (25.0, 37.0)	49.0 (27.5, 87.5)	0.19
ALT (U/L) (median [IQR])	24.0 (18.0, 47.0)	42.0 (23.0, 66.5)	0.23
AFP (> 20 μg/L) (%)	5 (71.4)	7 (53.8)	0.64
TB (μmol/L) (median [IQR])	16.6 (13.3, 18.5)	18.9 (12.3, 31.3)	0.38
Second step variables			
Operation time (min) (median [IQR])	300.0 (205.0, 350.0)	285.0 (245.0, 295.0)	0.38
Pringle maneuver (min) (median [IQR])	0.0 (0.0, 45.0)	12.0 (0.0, 29.0)	0.54
Blood transfusion (%)	5 (71.4)	10 (83.3)	0.60
Intraoperative blood loss (ml) (median [IQR])	700.0 (200.0, 1000.0)	800.0 (450.0, 1100.0)	0.84
Type of hepatectomy (%)			NA
Right hepatectomy	4 (57.1)	2 (15.4)	
Right trisegmentectomy	1 (14.3)	9 (69.2)	
Palliative hepatectomy	0 (0.0)	2 (15.4)	
2 segmental liver resection/tumor resection	2 (28.6)	0 (0.0)	
Sceond step complications (Clavien Dindo) (%)			
> Grade II	0 (0.0)	6 (46.2)	0.05
Details		Abdominal bleeding[a] (*n* = 1, 7.7%), Liver failure (*n* = 1, 7.7%), Intestinal obstruction (*n* = 1, 7.7%), pneumothorax (*n* = 1, 7.7%), Thoracic effusion requires puncture and drainage (*n* = 3, 23.1%)	
R0 (%)	7 (100.0)	11 (84.6)	0.52
Death 90 days after surgery (%)	0 (0.0)	2 (15.4)	
Cuase of death		Liver failure (*n* = 1, 7.7%), Tumor progression (*n* = 1, 7.7%)	
Postoperative tumor recurrence (%)	3 (42.9)	11 (84.6)	0.12
Treatment after recurrence	(*n* = 3)	(*n* = 11)	
Rehepatectomy (%)	0 (0.0)	2 (18.2)	
Ablation (%)	1 (33.3)	1 (9.1)	
TACE (%)	1 (33.3)	2 (18.2)	
Radiotherapy (%)	0 (0.0)	1 (9.1)	
Chemotherapy (%)	0 (0.0)	1 (9.1)[b]	
Targeted therapy (%)	0 (0.0)	0 (0.0)	
Chemotherapy + Targeted therapy (%)	1 (0.0)[c]	0 (0.0)	
Supportive treatment (%)	0 (0.0)	4 (36.4)	

[a] Abdominal bleeding requires secondary surgical hemostasis

[b] Chemotherapy (tegafur)

[c] Chemotherapy (FOLFOX) + Targeted therapy (sorafenib)

Table 3 Growth of FLR under two surgical methods

Index	TACE + PVE group ($n = 11$)	PALPP group ($n = 16$)	*P* value
SLV (ml) (median [IQR])	1147.9 (1068.6, 1251.5)	1192.8 (1133.4, 1241.7)	0.278
Liver volume growth time (day) (median [IQR])	66 (41.0, 118.0)	18.5 (12.5, 37.0)	0.001
FLR_1 (ml) (median [IQR])	383.3 (339.5, 447.0)	368.1 (308.3, 400.8)	0.43
FLR_2 (ml) (median [IQR])	502.2 (400.0, 586.8)	526.0 (456.6, 569.6)	0.657
FLR_3 (ml) (median [IQR])	83.1 (43.9, 182.8)	158.4 (95.5, 206.4)	0.043
FLR † (%) (median [IQR])	23 (12.0,47.0)	43 (29, 58.5)	0.026
KGR (ml/w) (median [IQR])	7.7 (3.2, 33.7)	58.5 (25.2 108.6)	0.001

SLV standard liver volume; Liver volume growth time, The waiting time between procedures or the time span from phase I surgery to treatment failure, FLR_1 First preoperative FLR, FLR_2 FLR before second surgery or FLR at the time of treatment failure, FLR_3 $FLR_3 = FLR_2\text{-}FLR_1$; FLR †, The increase in FLR between the two procedures was divided by the FLR before the first procedure (FLR † = FLR_3/ FLR_1); KGR, Degree of liver volume increase (%)/time elapsed from baseline to final volume before stage II hepatectomy (weeks)

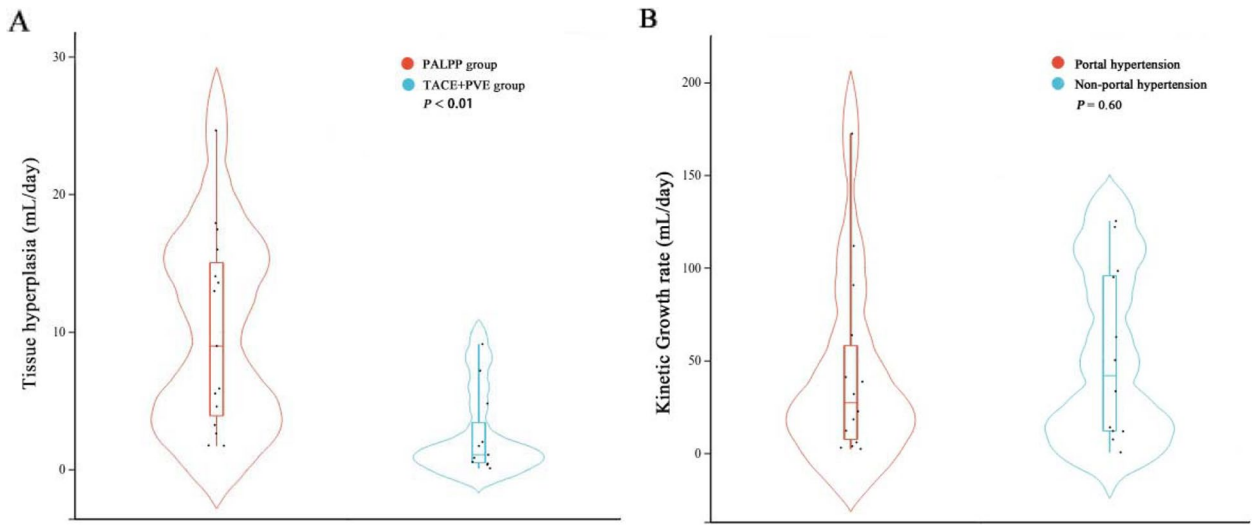

Fig. 2 Subgroup analysis of future liver volume growth. **A** The difference in daily hypertrophy volume of liver tissue under different operating methods; **B** The effect of portal hypertension on the increase of FLR

prominence in China, offering enhanced efficiency in promoting residual liver hyperplasia while maintaining minimally invasive and safe characteristics.

TACE + PVE serves as a safe strategy for increasing FLR volume, exhibiting a larger growth rate compared to PVE alone and mitigating the risk of tumor progression during the waiting period for liver volume growth [18]. However, the rate of secondary liver resection in patients with PVE + TACE has been reported at around 60% [19]. In contrast, PALPP is a novel strategy that has been associated with a remarkable 92% rate for increasing FLR volume after second-stage hepatectomy [20]. While both procedures demonstrate safety and clinical effectiveness, there remain controversies regarding their scope of use and clinical selection, and a direct comparison of their effects on insufficient FLR has not been reported.

The principle of TACE + PVE involves blocking blood flow to the tumor side of the liver, promoting regeneration of the residual liver tissue. Highly selective TACE is then employed to further block the tumor blood supply, inhibiting growth and reducing the time for recurrence and progression. PALPP, on the other hand, involves cutting off the tumor-side liver through PRA/PMA and combining it with PVE to block the blood flow further, promoting the proliferation of the residual liver volume and reducing the risk of complications like bile leakage and bleeding.

Table 4 Liver Volume Hyperplasia under Different Pathological Types

	TACE + PVE group (*n* = 11)			PALPP group (*n* = 16)		
	HCC (*n* = 11)	ICC (*n* = 0)	MLC (*n* = 0)	HCC (*n* = 12)	ICC[a] (*n* = 2)	MLC[a] (*n* = 2)
SLV (ml) (median [IQR])	1147.9 (1068.6, 1251.5)	NA	NA	1178.9 (1128.4, 1241.7)	(1232.7, 1268.6)	(1139.2, 1170.3)
Liver volume growth time (day) (median [IQR])	66 (41.0, 118.0)	NA	NA	19 (14.3, 40.8)	(11.0, 15.0)	(12.0, 15.0)
FLR1 (ml) (median [IQR])	383.3 (339.5, 447.0)	NA	NA	257.2 (199.8, 365.1)	(353.7, 367.4)	(367.4, 372.7)
FLR2 (ml) (median [IQR])	502.2 (400.0, 586.8)	NA	NA	523.4 (400.7, 576.7)	(508.5, 518.0)	(540.0, 558.5)
FLR3 (ml) (median [IQR])	83.1 (43.9, 182.8)	NA	NA	157.1 (89.3, 212.6)	(146.4, 150.6)	(162.0, 185.8)
FLR † (%) (median [IQR])	23 (12.0,47.0)	NA	NA	39.1(26.9, 78.7)	(38.4, 41.1)	(42.9, 49.9)
KGR (ml/w) (median [IQR])	7.7 (3.2, 33.7)	NA	NA	40.1(19.6, 107.8)	(54.0, 76.2)	(20.7, 92.6)

HCC hepatocellular carcinoma, *ICC* Cholangiocarcinoma, *MLC* Metastatic liver cancer, *SLV* standard liver volume; Liver volume growth time, The waiting time between procedures or the time span from phase I surgery to treatment failure, *FLR1* First pre-operative FLR, FLR_2 FLR before second surgery or FLR at the time of treatment failure, FLR_3 $FLR_3 = FLR_2\text{-}FLR_1$; FLR †, The increase in FLR between the two procedures was divided by the FLR before the first procedure (FLR † = FLR_3/ FLR_1); KGR, Degree of liver volume increase (%)/time elapsed from baseline to final volume before stage II hepatectomy (weeks)

[a] The column representation method is (minimum, maximum)

Modified TACE + PVE has been effective in reducing the growth time required for the remnant liver volume to reach a tolerable level for hepatectomy from the original 4–8 weeks to less than 4 weeks [4]. However, the median interval between the two operations at our center was 66 days, with a mean interval of 85.3 days, significantly longer than in previous studies. In response, we conducted an analysis to identify reasons for this prolonged interval in our study cases, which included severe postoperative complications, poor liver reserve function evaluation indicators and extended waiting intervals between surgeries due to patient-related reasons. In contrast, PALPP demonstrated superior results, achieving a median time of only 18.5 days and a mean time of 26.6 days ($P = 0.001$) to reach a resectable standard. Additionally, the surgical resection rate in the PALPP group was significantly higher than in the TACE + PVE group (76.5% *vs.* 58.3%, $P = 0.42$). In both groups, two patients each lost the opportunity for a second surgery due to tumor progression. In the TACE + PVE group, one case resulted in liver failure, while two cases developed dysplasia after the first step (Table 2). The liver growth rate per week was notably higher in the PALPP group (58.5 ml/w *vs.* 7.7 ml/w, $P = 0.001$). Similarly, when comparing the increase in liver volume between the two groups, the median increase in the TACE + PVE group was 23%, whereas, in the PALPP group, the median increase was 43% ($P = 0.026$) (Table 3), similar to the literature [21, 22].

The observed superior results of PALPP compared to TACE + PVE may be attributed to the similarity between PALPP and ALPPS in promoting residual liver hyperplasia. PALPP, like ALPPS, involves ablation and separation of liver parenchyma, replacing the disconnection of liver parenchyma. This process can effectively block the communicating branches of the portal veins on both sides of the preserved and resected liver, facilitating rapid growth of the FLR. The key distinction between PALPP and TACE + PVE lies in the absence of hepatic artery embolization chemotherapy in PALPP, minimizing the impact on the blood supply to the tumor-side liver. This avoids the potential complications associated with TACE + PVE, such as tumor-side liver ischemic necrosis, abscess formation, and even acute liver failure. Consequently, once the resectability criteria are met, PALPP allows timely liver resection.

To identify potential factors influencing growth, a stratified analysis was performed. The average growth of hepatocellular carcinoma, cholangiocarcinoma, and metastatic liver cancer using the PALPP method was 172.7 ml, 150.6 ml, and 185.8 ml, respectively. This variation may be associated with the absence of underlying liver diseases and better liver function reserves in patients with metastatic liver cancer compared to other types. Besides, portal hypertension was present in 41.7% and 58.8% of patients in the TACE + PVE group and PALPP group, respectively. In cases where both groups had portal hypertension, the median increase in liver volume in the TACE + PVE group was 14.7%, while in the PALPP group, it was 29.2% [23](Fig. 2). Factors influencing liver volume growth not only include portal hypertension but also encompass body reactions, inflammation levels, and liver hemodynamics. [24–26]

The incidence of complications and causes of death in both groups were reviewed (Table 2). After the initial surgery, the PALPP group experienced two cases of severe

complications (> Grade II). One case involved pleural effusion, which improved after thoracic puncture drainage, while the other resulted in perioperative death due to postoperative liver failure leading to gastrointestinal bleeding. In the TACE + PVE group, there was one case of severe complication (> Grade II), specifically liver failure, which improved after conservative treatment. Considering the occurrence of postoperative liver failure and considering patient medical history, it was noted that two cases with liver failure had severe cirrhosis and liver dysfunction before the operation. Although their liver function was corrected before the operation, the surgical procedure acted as a trigger, leading to postoperative liver failure. The incidence of severe complications (above Grade II) after the first step in the TACE + PVE group and PALPP group was 8.3% and 11.8%, respectively. These rates were lower than the incidence of complications after the initial surgery in radiofrequency-assisted ALPPS, as reported by Wang Q et al. [21].

In terms of prognosis, the overall mortality rates in the TACE + PVE group and PALPP group were 66.7% and 76.5% ($P = 0.85$) over a median follow-up time of 14 months. For the population undergoing the two-stage surgery, the overall mortality rate was 42.9% and 76.9% ($P = 0.32$) in the TACE + PVE group and PALPP group, respectively, at a median follow-up time of 18.8 months. The impact of PALPP on the prognosis of patients was explored, revealing a positive correlation between postoperative complications and prognosis in the PALPP group, especially with the extent of surgical resection. Among the patients who underwent two-stage surgery (n = 13), extended hemihepatectomy was performed in 77% of cases, compared to 14.3% in the TACE + PVE group. Additionally, the occurrence of postoperative complications, such as abdominal infection and pleural effusion, was directly related to the operation time and prognosis [26, 27]. However, further studies are warranted to ascertain whether PALPP has a direct effect on prognosis. Overall, our findings suggest that PALPP can improve the resection rate of secondary surgery without increasing the incidence of complications.

Based on the experience of our center, PALPP is considered appropriate for the following categories of the population: (1) Patients with liver malignant tumors, especially secondary liver malignant tumors; (2) Presence of cirrhosis or portal hypertension; (3) Liver function classified as Child–Pugh B; (4) Major liver resection (> 4 segments). PALPP can be performed to increase the remnant liver volume in planned hepatectomy when the liver volume is insufficient, with priority given to PALPP selection in the specified cases, though further verification by multiple centers is required.

Certain considerations should be noted during PALPP: (1) FLR volume growth can be accelerated by embolization of peripheral vessels during PVE [28]. (2) When selecting PRA and PMA, a safety margin of at least 10 mm around the outer edge of the lesion is recommended when choosing PMA, especially when the liver partition surface is small. PRA is suitable for various scenarios and can achieve the purpose of one-stage radical surgery for sub-lesions on the side of the liver. After PRA and PMA, the ablation margin is defined to ensure a 1-cm thick tumor-free margin, consistent with the tumor-free principle [29]. Once the tumor-free boundary of the liver parenchyma is established, an additional 50 to 80% of the liver tissue, typically to a depth of 2 to 4 cm, is cut off to facilitate the growth of the residual liver volume. In the meta-analysis conducted by Fadi et al., there was no significant difference between partial partition and complete partition in terms of liver volume increase ($P = 0.067$) and FLR increase ($P = 0.477$) [30]. In addition, the partial disconnection method reduced the incidence of postoperative complications ($P = 0.03$) and mortality ($P = 0.12$) [31].

Although two patients in the PALPP group included in our study lost the opportunity for the two-stage hepatectomy, they still survived for a significant period through remedial treatment measures such as TACE. Given that the primary pathway of Hepatocellular Carcinoma (HCC) metastasis is intrahepatic portal vein metastasis, PALPP effectively hinders tumor progression by severing the liver parenchyma through radiofrequency or microwave ablation methods. Additionally, PALPP blocks the portal vein communicating branch through PVE. PALPP exhibits better safety, a lower complication rate, less impact on liver injury, increased opportunities for remedial treatment, controlled tumor progression, and prolonged survival [32].

This study is subject to several limitations that should be acknowledged. First, the sample size was relatively small, and the findings are specific to the experience of our institution. Besides, the utilization of chemotherapy following inadequate liver volume hyperplasia, as opposed to remedial measures, diminished the exposure to factors associated with inadequate liver volume hyperplasia. Moreover, the exclusion of patients with benign liver lesions undergoing surgical treatment might obscure the method's efficacy in benign lesions' proliferation. Consequently, additional prospective studies or randomized controlled trials are warranted to assess the clinical efficacy of PALPP.

Conclusions

Overall, this study indicates that compared to TACE + PVE, PALPP can effectively shorten the proliferation time of future liver residues and improve proliferation efficiency. These findings indicate that PALPP is also a feasible method for improving FLR.

Abbreviations

PALPP	Percutaneous microwave/radiofrequency ablation liver partition plus portal vein embolization
TACE	Transarterial chemoembolization
PVE	Portal vein mbolization
FLR	Future liver remnant
BMI	Body mass index
ASA	American Society of Anesthesiologists
PS	Performance status
HCC	Hepatocellular carcinoma
ICC	Intrahepatic cholangiocarcinoma
MLC	Metastatic liver cancer
PLT	Platelet
TB	Total bilirubin
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AFP	Alpha-fetoprotein
HBV	Hepatitis B virus
SLV	Standard liver volume
KGR	Degree of liver volume increase (%)/time elapsed from baseline to final volume before stage II hepatectomy (weeks)

Supplementary Information

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Supplementary Material 1

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Authors' contributions

T-W Y, T-W F, C-F D and R–C Y contributed equally to this work. Dr. J C and Dr.Z-Q X had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: T-W Y, Z-Q X and J C. Acquisition, analysis, or interpretation of data: T-W F, C-F D, Z-H Z, Q-T J, Q Z, C-W Z, J L, J-W L. Drafting of the manuscript: T-W Y and T-W F. Critical revision of the manuscript for important intellectual content: J C and Z-Q X. Statistical analysis: T-W Y and T-W F. Obtained funding: None. Administrative, technical, or material support: C-W Z, X-M F, D-F H, Z-Y L, J C and Z-Q X. Study supervision: J C and Z-Q X.

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Availability of data and materials

Data is provided within the supplementary information files.

Declarations

Ethics approval and consent to participate

This retrospective study complies with the Declaration of Helsinki and was approved by the institutional ethical committee and the need for informed consent was waived.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]General Surgery, Department of Hepatobiliary & Pancreatic Surgery and Minimally Invasive Surgery, Zhejiang Provincial People's Hospital, Affiliated People's Hospital, Hangzhou Medical College, Cancer Center, Hangzhou, Zhejiang 310014, China. [2]The Second School of Clinical Medicine, Zhejiang Chinese Medical University, Hangzhou 310053, China. [3]Three Gorges University, Yichang, Hubei 443000, China. [4]Dalian Medical University, Dalian, Liaoning 116000, China. [5]Department of General Surgery, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine(DeFei Hong), No.3 East Qingchun Road, Hangzhou 310016, Zhejiang, China.

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