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ORIGINAL ARTICLE

The ALPPS procedure: hepatocellular carcinoma as a main indication. An Italian single-center experience

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Abstract
The ALPPS is a technique that allows achieving hepatic resection by a rapid future liver remnant hypertrophy. The aim of this study was to report the experience of an Italian center with ALPPS in patients with liver tumors. A retrospective analysis of patients undergoing ALPPS between 2012 and 2017 was performed. Patients' characteristics and disease presentation, increase in future liver remnant (FLR) as well as intraoperative and postoperative short- and long-term outcomes were evaluated. A total of 24 patients underwent the ALPPS procedure: 17 procedures for hepatocarcinoma (HCC), 5 for colorectal liver metastases (CRLM), 1 for cholangiocarcinoma (CC) and 1 for Merkel Cell Carcinoma liver metastasis (MCCLM). Macrovascular invasion (MVI) was recorded in 10 (41.6%) patients: 8 (33.3%) patients with HCC had invasion of portal vein (5), middle hepatic vein (2) and inferior vena cava (1). One patient with CRLM had involvement of middle hepatic vein and one patient with CC had involvement of right portal vein and middle hepatic vein. A p-ALPPS in 14 cases (58.3%), 10 t-ALPPS (41.6%) and hanging maneuver in 19 patients (80%) were performed. Median postoperative stay was 26 days (range 16–68 days). 90-day mortality was 8.3% (two patients, one with CC and one with HCC), 90-day mortality for HCC was 5.8%. After stage 1, we counted 15 complications all of grade I; after stage 2 the number of complications was increased to 37:33 were of grade I and 4 were of grade IV. R0 resection was achieved in all patients with 100% oncology feasibility. After a median follow-up of 10 months (range 2–54), disease recurrence has been recorded in 6 patients with HCC and in 2 with CRLM. Eleven patients died, nine affected by HCC, one by CRLM, and one by CC. 2-years OS and disease-free survival (DFS) for the entire group were 47.3% and 47.5%, respectively. Concerning patients operated on for HCC, the 2-years OS and DFS were 38.5% and 60%, respectively. The ALPPS procedure is an interesting approach for large primary or secondary liver tumor with small FLR above all for large HCC associated with MVI, with acceptable OS and DFS.

Keywords Hepatic resection · ALPPS · HCC · Cirrhosis · Metastases

Introduction

Surgical liver resection has to be considered as the only potential curative treatment for primary and secondary liver malignancies and major liver resections are frequently required to achieve complete tumor removal, with disease-free surgical margins. One of the most life-threatening complications after major liver resection still remains the posthepatectomy liver failure (PHLF), a particularly felt condition when resections are performed on cirrhosis. In this setting, the evaluation of the future liver remnant (FLR) after hepatectomy is of crucial importance as inadequate liver remnant volume after resection is directly related to the development of PHLF [1, 2]. After 35 years from its introduction in the clinical practice, portal vein occlusion, with surgical ligation or embolization, is still the gold standard technique to induce hypertrophy of the FLR, though some drawbacks have emerged over time. Firstly, failure in achieving sufficient liver hypertrophy can be experienced. Moreover, tumor progression between surgical stages can determine patient dropout, with negative impact on survival [3–5]. Furthermore, in the case of portal vein tumor

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thrombosis or hepatic vein thrombosis, a classic two-staged hepatectomy is not feasible and a different approach should be considered. In these circumstances, a recently launched technique called Associating Liver Partition and Portal Vein Ligation for Staged hepatectomy (ALPPS) can induce rapid hypertrophy within a shorter period of time between stages than the classic two-staged hepatectomy, providing a chance for resection in patients otherwise eligible for ablation or palliative treatment, according to the staging system of the Barcelona Clinic Liver Cancer (BCLC). This novel strategy has been successfully used for locally advanced malignancies risen on a healthy liver, such as cholangiocarcinoma (CC) and colorectal liver metastases (CRLM), or on cirrhotic liver, such as hepatocarcinoma (HCC) [6, 7]. Experiences of ALPPS performed for HCC with macrovascular invasion (MVI) on cirrhotic liver are still limited though encouraging. Nevertheless, noteworthy, ALPPS is associated with higher morbidity and perioperative mortality rates; so, careful selection of patients is mandatory [8–11].

In this paper, we report our experience on ALPPS performed for CC, CRLM, and HCC focusing especially on the outcomes in patients with cirrhotic liver with HCC and MVI.

Materials and methods

This is a retrospective and observational study. Between September 2012 and September 2017, a total of 24 patients underwent two-staged hepatectomy with the ALPPS procedure which represents 1.4% of 1724 liver resections performed over 17 years of activity. We performed 17 procedures for HCC, 5 for CRLM, 1 for CC and 1 for merkel cell carcinoma liver metastasis (MCCLM).

All patients had locally advanced liver tumors which were judged not resectable by a classic two-stage hepatectomy. MVI was recorded in 10 (41.6%) patients: 8 (33.3%) patients with HCC had invasion of a major branch of portal vein (5), middle hepatic vein (2), and inferior vena cava (1).

One patient with CRLM had involvement of middle hepatic vein and one patient with CC had involvement of right portal vein and middle hepatic vein.

Four (17%) patients had bile duct involvement, two with HCC, one with CC, and one with MCCLM, and three of them had preoperative obstructive jaundice.

The goal of the study was to report the 90-day mortality, disease-free survival (DFS), overall survival, postoperative complications (POC), length of hospital stay, FLR volumes and increase in FLR volume after the first stage was recorded.

All patients with locally advanced liver cancers were discussed by a multidisciplinary panel of hepatologists, liver surgeons, interventional radiologists, anesthetists, and oncologists. Patients with liver cirrhosis (LC) were considered eligible for surgical resection if they had preserved liver function (serum bilirubin level < 1.5 mg/dl, INR < 1.3, and no signs of liver decompensation), esophageal varices $<$ grade 1, platelets count $> 80 \times 10^3$/dl, and absence of ascites. Child–Pugh, model for end-stage liver disease (MELD), and Eastern Cooperative Oncology Group Score were calculated. No metabolism and/or hemodynamic tests were performed before surgery (i.e., indocyanine green clearance test, hepatic venous pressure gradient). All patients underwent preoperative radiological evaluation with volumetric computed tomography (VCT) or magnetic resonance imaging (MRI) to exclude extrahepatic disease. The presence of tumor thrombosis in a major branch of PV, hepatic veins, or bile duct was not considered as an exclusion criteria for the procedure.

A VCT was performed in each patient before stage 1 to assess FLR. A future liver remnant sufficient to perform a major liver resection during second stage was 40% in case of liver cirrhosis and 30% in case of healthy liver. Accordingly, a liver remnant-to-bodyweight ratio (LBWR) of 0.8 in liver cirrhosis and of 0.5 in healthy livers should be achieved before completion surgery. VCT scan of the liver was repeated after the first stage starting from postoperative day (POD) 6. Correlation between the FLR volume at the baseline (vol_0) and after the first stage (vol_1) was calculated using the formula: %FLR volume increase $= (vol_1 - vol_0)/vol_0$ x 100 to evaluate the FLR volume increment.

Liver resections and anatomy were defined according to the Brisbane Conference nomenclature and Couinaud's segmentation of the liver. Informed consent was obtained from all patients before the procedures. The surgical techniques for ALPPS have been described elsewhere [6]. Whenever possible, liver parenchymal transection was performed using the anterior approach with hanging maneuver.

Hematoxylin–eosin-stained slides and immunohistochemical analysis from surgical specimens were reviewed and fibrosis was scored according to the Metavir Scoring System. A score of 0–4 was given according to the degree of fibrosis: 0 (no fibrosis), 1 (mild fibrosis), 2 (moderate fibrosis), 3 (severe fibrosis), and 4 (cirrhosis). Grading of PHLF was defined according to the international study group of liver surgery (ISGLS) classification. POC were defined according to the Clavien–Dindo classification. Tumor recurrence was assessed by clinical examination, laboratory parameters, and radiological examination (MRI, CT scan, and PET scan). Descriptive statistics were used on the characteristics of patients. The Kaplan–Meier method was used to estimate survival curves. The SPSS software (SPSS version 21.0, SPSS Inc., Chicago, IL, USA) was used for all statistical evaluations.

Results

Between September 2012 and August 2017, in our institution, a total of 24 patients underwent two-staged hepatectomy with the ALPPS procedure. The median age of the group at the moment of surgery was 61 (range 36–79). 79% of patients were men. The median BMI was 26 kg/m^2 (range 21–33). The procedures performed for HCC were 17. The remaining patients underwent ALPPS for CRLM (= 5), CC (= 1), and MCCLM (1). Among those affected by HCC, 15 patients had a cirrhotic liver (88.2%). 11 patients (64.7%) were affected by HCV infection, whilst only 3 patients were positive for HBV infection (17.6%). The median MELD value was 9 with a range between 7 and 17. The median value of αFP among cirrhotic patients with HCC was 7.312 ng/ml (range 2–92,000). In one patient with HCC, the ALPPS procedure was unplanned due to the progression of the disease, requiring a right hepatectomy. In 8 (47%) patients with HCC an involvement of a major vessel was recorded: portal vein (= 5), middle hepatic vein (= 2), portal vein and middle hepatic vein (= 1), suprahepatic inferior vena cava (= 1). Involvement of right hepatic bile duct was recorded in two patients with HCC. The median HCC dimension was 7 cm (range 3–20 cm) and the median number of lesions was one (range 1–4). In the group of patients affected by HCC, a recurrence rate of 35.3% (six patients) was recorded. After a median follow-up of 10 months (2–54 months), eight HCC patients are alive (47%) and seven patients died by progression of the disease, and two by other causes (ischemic ictus and infection). All the cases affected by CRLM had synchronous multiple bilobar liver metastases from colorectal cancer. In three cases, the ALPPS procedure was unplanned for: unknown liver fibrosis ($n = 1$), disease progression in the left liver after PVE ($n = 1$), and tumor invasion of the middle hepatic vein ($n = 1$). The remaining two cases were planned due to insufficient liver hypertrophy after PVE. All of them had previously undergone neoadjuvant chemotherapy (Folfiri + Cetuximab = 3; Folfox + Bevacizumab = 1). The preoperative median level of CEA was 12.7 (1–208). One patient had intrahepatic CC with macroscopic involvement of the right bile duct and MVI of right portal vein and middle hepatic vein. Biliary drainage was performed to achieve a normal preoperative serum concentration of bilirubin. The patient underwent neoadjuvant chemotherapy with Capecitabin + Cisplatin. The preoperative median value of Ca 19.9 was 30 U/ml (3–205). One patient affected by MCCLM, previously treated with chemotherapy with Etoposide + Cisplatin, underwent ALPPS for unsatisfactory liver hypertrophy after PVE. All patients with CRLM, CC, and MALM had normal preoperative liver function tests except one patient who had liver fibrosis (Tables 1, 2).

Table 1 Preoperative characteristics of the study patients

	ALPPS $n = 24$
Male/female	19/5
Age, years (range)	61 (36–79)
Body mass index (range)	26 (21–33)
ASA 1–2	20
ASA 3	4
Preoperative Child–Pugh	
A	16
B	1
Preoperative MELD Score (range)	9 (7–17)
Comorbidity	
Cardiovascular	6
Pulmonary	2
Diabetes	6
Renal dysfunction	2
Diagnosis	
HCC	17
Colorectal metastases	5
Cholangiocarcinoma	1
Merkel cell carcinoma metastases	1
Failed portal vein embolization	3
Preoperative chemotherapy	
Oxaliplatin-based	3
Iritnotecan-based	2
Cisplatin-based	2
Previous abdominal surgery	
Colorectal resection	5
Nephrectomy	2
Preoperative tumor markers	
AlfaFP (range)	7.315 (2–92,000)
CEA (range)	12 (1–208)
CA 19.9 (range)	30 (3–205)
Cirrhosis	
F4	15
F3	0
F2	1
F1	0
F0	8
Preoperative viral status	
HCV	11
HBV	3

Liver volumetry

An average TLV of 1800 cm^3 was calculated radiologically among patients of the whole group. A median preoperative

Table 2 Preoperative characteristics of tumor of the study patients

HCC	17
No. of nodules (range)	1 (1–4)
Size of largest lesion (cm)	20
Tumor location	
Right lobe-segment 4	17
Vascular involvement	8
Portal vein	5
Hepatic vein	2
Inferior vena cava	1
Bile duct involvement	2
Hepaticojejunostomy	2
Liver metastases	6
No. of nodules (range)	6 (1–15)
Size of largest lesion (cm)	5.5
Tumor location	
Bilobar	4
Right lobe	2
Vascular involvement	1
Hepatic vein	1
Bile duct involvement	1
Hepaticojejunostomy	1
Cholangiocarcinoma	1
No. of nodules	1
Size of largest lesion (cm)	15
Tumor location	
Right lobe	1
Vascular involvement	
Hepatic vein	1
Portal vein	1
Bile duct involvement	1
Hepaticojejunostomy	1

FLR of 539.5 cm^3 was recorded with a FLR/TLV and a FLR/BW ratio of 32.5% and 0.7%, respectively. After a median time of 5 days since first stage, VCT managed to show a median FLR of 730.5 cm^3 in the whole group with a FLR/BW ratio of 0.99%. The median percentage of FLR increase after 1 week was 68.4% in the whole group.

Intraoperative data for the first and second stage and postoperative complications are shown in Table 3

All patients underwent stage II of the ALPPS procedure (100% feasibility) in a median time after stage I of 7 days (range 4–12 days). We performed 14 right hepatectomies (82%) and three right trisectionectomies (18%) in the HCC patients. In the CRLM group, we performed six right hepatectomies (80%) and one right trisectionectomy with caudate lobe resection (20%). In total, four hepaticojejunostomies were performed: two in HCC group, one in CC and MCCLM, respectively. 85% of our ALPPS procedures were planned.

For the first phase, median operative time was 229 min (range 120–349), while the median duration for the second stage was 203 min (range 120–360), for the overall record. In the HCC group, median operative time for first and second stages were 228 and 190 min (range 120–349 and 120–270), respectively . Median blood loss during

Table 3 Operative data, postoperative complications, and clinical outcome of the study patients

Variable		ALPPS $n=24$
Surgery		
Right hepatectomy		20
Right trisegmentectomy		3
Right trisegmentectomy extended to segment 1		1
Step 1		
Operative time	Min.	229 (120–349)
Blood loss	cc	220 (100–550)
RBC transfusion		0
Step 2		
Operative time	Min.	203 (120–360)
Blood loss	cc	150 (100–250)
RBC transfusion		5
Total parenchymal transection		10
p-ALPPS		14
Hanging maneuver		19
Pringle maneuver		2
ALPPS efficay	%	100
Plastic bag use	%	0
Planned	%	83.3
R0 resection	%	100
Relaparotomy rate	%	4.1
ICU stay (step 1 + 2)	Days	2 (0–6)
Postoperative complications		33 + 17 = 52
Liver failure after step 1		0
Liver failure after step 2		2
Clavien I–II		15 + 33 = 48
Clavien III		0
Clavien IV		4
Clavien V		0
Postoperative stay (step 1 + 2)	Days	29 (15–68)
30-Day mortality	%	0
90-Day mortality	%	8,3
Recurrence rate	%	33
2-Years overall survival	%	47.3
2-Years disease-free survival	%	47.5
Follow-up	Months	10 (2–54)

stages I and II of the ALPPS procedure were 220 ml (range 100–550 ml) and 150 ml (range 100–250 ml), respectively.

We performed a p-ALPPS in 14 cases (58.3%) and 10 t-ALPPS (41.6%) in the remaining ones. Among patients with HCC, a major proportion underwent p-ALPPS ($n = 11$; 65%), whilst total parenchymal transection was performed in 35% of cases. Hanging maneuver was performed in 19 patients (80%). In the remaining ones, the anterior approach was not doable for tumor burden on the retrohepatic IVC or for tight adhesions which made the hanging maneuver unsafe. A similar figure was recorded in the HCC group (88%). Pringle maneuver was performed in two cases, one of which was in a HCC patient (10 and 18 min).

In nine (37.5%) patients, an associated procedure was required to achieve an R0 resection: four common bile duct resections, two portal vein thrombectomies during first stage (HCC patients), two partial vein resections of IVC, one for HCC and one for CRLM, and one diaphragmatic resection. In three (12.5) cases the ALPPS procedures were classified as salvage for FLR insufficient regeneration after PVE.

Among patients with bile duct tumor thrombosis, one had CC, two had HCC, and one had MCCLM. In the case with CC, common bile duct resection followed by hepaticojejunostomy was performed to achieve an R0 resection. In the two cases with HCC, two bile duct exereses were performed followed by hepaticojejunostomy.

Only one (4%) relaparotomy was required in a patient affected by CRLM for portal vein thrombosis after stage II.

Postoperative outcomes

Median postoperative stay was 26 days (range 16–68 days). Two patients died of PHLF within 90 days from surgery (90-day mortality = 8.3%), one had CC, and one HCC. 90-day mortality for HCC was 5.8%. After step I, we counted 15 complications, all of grade I, whilst after stage II the number of complications increased to 37: 33 were of grade I and 4 were of grade IV according to Clavien–Dindo classification. R0 resection was achieved in 24 patients (complete resection = 100% oncology feasibility).

After a median follow-up of 10 months (range 2–54), disease recurrence has been recorded in six patients with HCC (recurrence rate = 35%) and in two other patients with CRLM (overall recurrence rate = 33%) (Table 3).

So far, in the series, 11 patients died, 9 affected by HCC, 1 by CRLM, and 1 by CC. Overall, seven deaths were due to recurrence and progression of the disease, one to infection, one to ischemic ictus, and two to PHLF. Two-years overall survival and disease-free survival for the entire group were 47.3% and 47.5%, respectively (Fig. 1). Concerning patients operated on for HCC, the 2-years OS and DFS were, respectively 38.5% and 60% (Fig. 2).

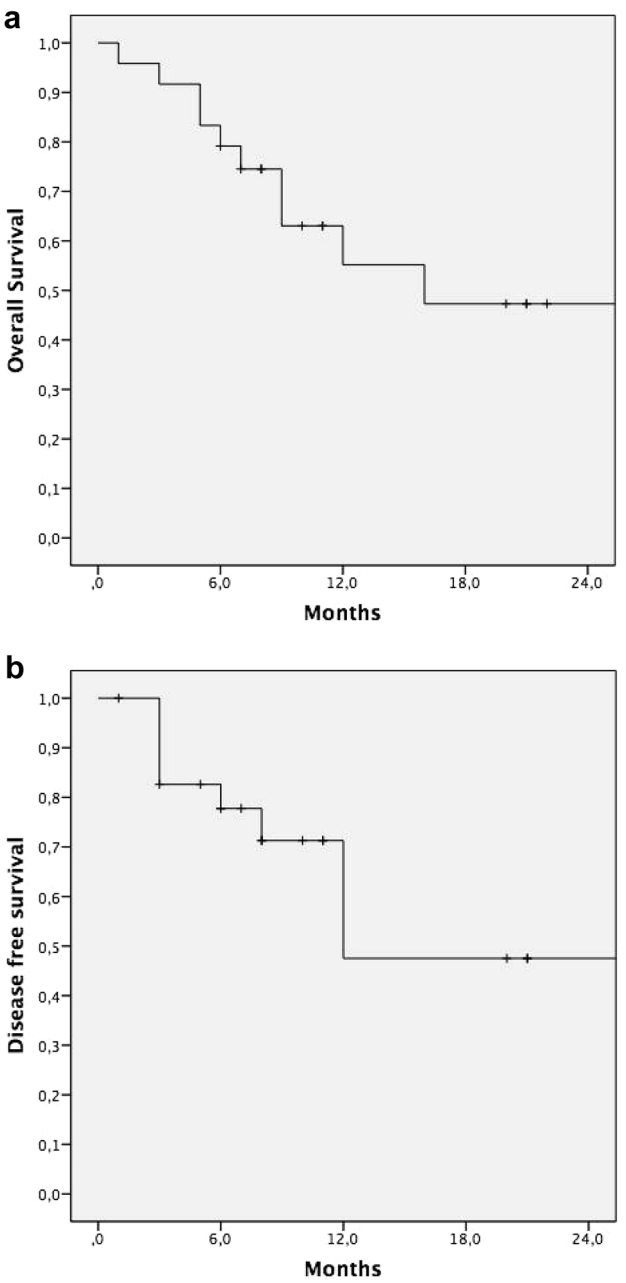

Fig. 1 **a** Overall survival and **b** disease-free survival of the entire series

Discussion

The introduction of the ALPPS procedure has been one of the most interesting innovations in liver surgery introduced over the 5 years. Up to now, the vast majority of studies conducted in this field have focused on the indications, the technical aspects and the feasibility of the procedure, highlighting the high morbidity and mortality rates related. However, as ALPPS is mostly performed in borderline situations, such a prevalence of adverse events can be justified by the

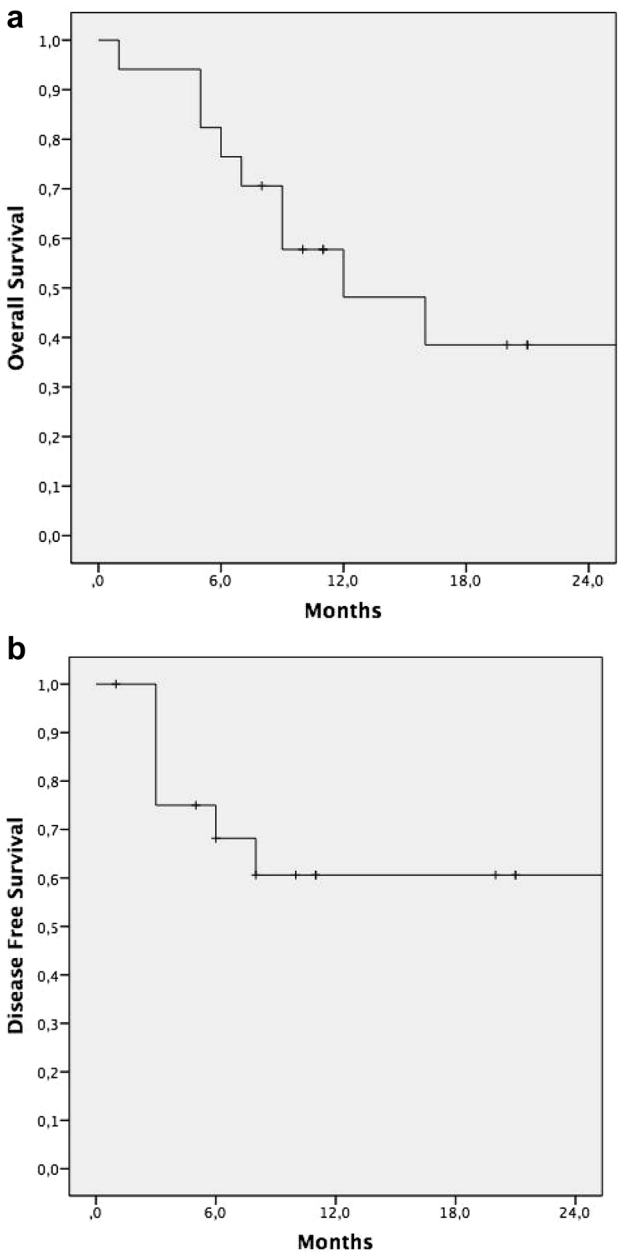

Fig. 2 **a** Overall survival and **b** disease-free survival of patients with HCC

extremely unfavorable conditions in which it is carried out—advanced liver fibrosis or cirrhosis, extensive chemotherapy, locally advanced neoplastic, often bilobar, disease—and by the fact that patients with extreme tumor burden undergo two consecutive complex procedures over a short period of time. Accordingly, careful selection of patients, adequate indications, evaluation of risk factors, and accurate and standardized surgical technique are mandatory to reduce the rate of drawbacks [12]. As far as long-term outcomes are concerned, in different series, ALPPS has been proven to be a burden by a high complication rate—59–64%—and a mortality rate ranging from 12% to 16%. When compared to the classic two-staged hepatectomies, ALPPS seems to be less feasible for the higher morbidity and mortality rates [13, 14]. Recent reports have shown similar results for ALPPS when compared with classical two-staged hepatectomies even though some risk factors for poor outcomes have been identified. Elderly patients (age >60) are considered at high risk for morbidity and mortality as their regenerative capacity has been proven to be inferior to that of younger patients. Inverse correlation between age and nuclear antigen expression has been revealed, thus justifying the reduced capacity to perform liver hypertrophy and the need for increased time between the two stages to reach adequate FLR. The need for blood transfusion and an operative time greater than 300 min for the first stage procedure are independent factors for poor outcome [15–18]. Moreover, it has been shown that partial liver transection (above middle hepatic vein) can lead to adequate hypertrophy (not statistically different when compared with total parenchyma transection up to inferior vena cava) though minimizing morbidity related to complication due to improper management of the raw surface (bile leaks and bleeding) [19]. Furthermore, a combination of partial hepatic transection and minimal mobilization of the liver with the use of hanging maneuver and anterior approach can probably minimize the impact of the first stage and grant a rapid recovery of the patient. This technical aspect is determinant as it can lead to reduced operative time and blood loss, decreasing the need for blood transfusion, hence providing better chances for minimal morbidity and mortality [20].

Our series of 24 ALPPS procedure is rather peculiar as it is characterized by a large number of procedures for HCC. This is due to the fact that our center is also a liver transplant center and therefore has a great attractiveness for HCC. Furthermore, HCC is a disease in which are present different clinical scenarios which may favor the ALPPS strategy for the following reasons: (1) it is often localized locally with neoplasms that invade the portal vein, which prevents portal embolization and a classic two-stage hepatectomy; (2) in some cases portal embolization fails to generate an adequate FLR in a cirrhotic liver; (3) in other cases, the massive neoplasia with aggressive behavior does not leave time to perform a classic two-stage hepatectomy. As our experience demonstrates, it is no doubt true that the ALPPS procedure allows resection of tumors that would not be otherwise operable but only amenable of medical or palliative treatment, as stated by BCLC guidelines. Consequently, with the advent of the ALPPS procedure, we have expanded the indications to liver resections for HCC and a greater number of patients can benefit from a radical surgical intervention that can provide the greater chances of cure.

However, this study confirms again that early morbidity and mortality after ALPPS is slightly higher than that

reported in the literature for major liver resections. Allegedly, this would seem to be attributable to a combination of factors such as the complexity of procedure, a cirrhotic liver, and locally advanced disease. These results are in line with that reported from the international ALPPS registry which showed an overall 90-day mortality rate of 8.8% in 320 patients mainly with CRLM and postoperative liver failure in 75% of patients as predominant cause of death. Our series is, however, different as it is predominantly formed by cirrhotic patients who had, in a high proportion of cases, a macrovascular involvement of portal vein and/or hepatic vein, thus requiring complex operations. Nevertheless, it shows a good profile regarding postoperative complications, operative times, blood loss, and need of perioperative blood transfusions underlying that the procedure in our unit is not only feasible, but now standardized. In $>80\%$ of cases, ALPPS is performed with anterior approach and hanging maneuver, two technical aspects extremely useful in case of locally extended tumors with involvement of vital hepatic structures.

Our experience confirms previous studies and highlight that patients, with CRLM in healthy livers or with HCC in cirrhotic ones, undergo a significant increase in FLR volume after liver partitioning [21]. Liver cirrhosis, per se, is not a reason to not perform the ALPPS procedure and liver partitioning. However, our experience points out an early and frequent tumor recurrence in HCC and CRLM patients and this is not a surprise since the ALPPS procedure is applied to patients with extensively locally advanced oncologic liver disease and poor oncologic prognosis. One-third of patients tend to recur after 1 year and at 2 years post-ALPPS surgery 50% of patients have died of tumor recurrence. Thus, in the majority of cases, the ALPPS strategy would not change the natural history of the disease if not associated with effective adjuvant regimen able to prolong survival.

This is particularly true for patients with CLRM and infact, a study, from Oldhafer et al., reported an early tumor recurrence rate of 86% in patients who underwent ALPPS for CRLM despite R0 resection was achieved in all patients and chemotherapy was administered in the perioperative phase [22]. This was also true for our series of patients with HCC, characterized by a high proportion of macrovascular involvement which subsequently resulted in an early postoperative relapse of the disease outside the liver to the lungs and bones which had a negative impact on survival. Nevertheless, ALPPS, inducing an unprecedented liver hypertrophy in a shorter period of time, enables major liver resections of otherwise unresectable liver tumors offering a hope of cure for many patients. In this regard, it would be desirable to combine surgery with an adjuvant therapy capable of prolonging patient survival. Unfortunately, studies on the use of sorafenib in adjuvant therapy have given disappointing results indicating that there is no convincing evidence of sorafenib as an effective adjuvant therapy in patients with HCC after resection [23]. The ALPPS procedure for HCC is still restricted to a limited number of prevalently Asian centers but, after initial experiences, the number of cases treated is increasing. An increasing trend of ALPPS performed for CRLM from 55 to 77% and a reverse trend for biliary tumors from 24 to 9% has been reported. This adjustment of patients' selection resulted in a drop of early and postoperative complications [24–29]. Postoperative results for HCC after ALPPS do not seem to be very different from those for CRLM although the experience in this context is still limited and further studies are needed to confirm these initial impressions.

Given the preliminary results of this study, it remains to ask whether, in the subgroup of patients with MVI, there is any clinical advantage to perform the ALPPS procedure. For HCC patients, according to international guidelines, sorafenib is the only recommended therapy when HCC is associated with MVI [30, 31]. However, considering the limited efficacy and tolerance of sorafenib, the management of HCC with MVI and without extra-hepatic spread is regularly questioned. Retrospective surgical studies have reported prolonged survival in this situation. Kokudo et al. reported the results of surgery in a large cohort of more than 2000 HCC patients with MVI of portal vein. Mean survival times were 2.67, 1.51, 0.78, and 0.50 years in patients with PVTT classified as Vp1, Vp2, Vp3, and Vp4, respectively [32]. However, a recent French study, reviewed retrospectively a total of 143 patients with HCC and MVI (70% with major extension vp3/vp4 of portal thrombosis) without extra-hepatic spread and treated with surgical resection or sorafenib: the overall survival of patients with HCC and MVI undergoing surgical resection was similar to that achieved with sorafenib, with a 90-day mortality rate in the whole surgical cohort of 16% [33].

Our preliminary experience shows that the ALPPS procedure for HCC occurring on cirrhotic liver is feasible with resultant acceptable perioperative results. In our view, the ALPPS procedure could further expand the number of patients undergoing major radical liver resections for HCC with BCLC stage B and C. Furthermore, the poor life expectancy of these patients should be considered, as well as high-rate recurrence, which could be amenable of treatment. However, all these observations require external validations to be confirmed. Although the results of the present study are interesting, this is a retrospective study and includes a small sample of patients that yields a selection bias without a follow-up long enough to report long-term oncologic results.

In conclusion, the ALPPS procedure is an interesting approach for large primary or secondary liver tumor with small FLR above all for large HCC associated with extended portal thrombosis, with acceptable OS and DFS.

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Compliance with ethical standards

Conflict of interest Authors do not have conflict of interest. The manuscript has not been submitted to other journals for simultaneous consideration.

Research involving human participants and/or animals All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from the study patients.

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