Optimizing associated liver partition and portal vein ligation for staged hepatectomy outcomes: Surgical experience or appropriate patient selection?

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Background: Early reports of associated liver partition and portal vein ligation for staged hepatectomy (ALPPS) outcomes have been suboptimal. The literature has confirmed that learning curves influence surgical outcomes. We have 54 months of continuous experience performing ALPPS with strict selection criteria. This study aimed to evaluate the impact of the learning curve on ALPPS outcomes.

Methods: We retrospectively compared patients who underwent ALPPS between April 2012 and March 2016. Patients were grouped into 2 24-month (early and late) periods. All candidates had a high tumour load requiring staged hepatectomy after chemotherapy response, a predicted future liver remnant (FLR) less than 30% and good performance status.

Results: Thirty-three patients underwent ALPPS during the study period: 16 in the early group (median age 65 yr, mean body mass index [BMI] 27) and 17 in the late group (median age 60 yr, mean BMI 25). Bilobar disease was comparable in both groups (94% v. 88%, $p > 0.99$). Duration of surgery was not statistically different. Intraoperative blood loss and need for transfusion were significantly lower in the late group (200 ± 109 mL v. 100 ± 43 mL, $p < 0.05$). The late group had a higher proportion of monosegment ALPPS (4:1). There were no deaths within 90 days in either cohort. Rates of postoperative complications were not statistically significant between groups. The R0 resection rate was similar. The entire 1-year disease-free and overall survival were 52% and 84%, respectively.

Conclusion: Excellent results can be obtained in innovative complex surgery with careful patient selection and good technical skills. Additionally, the learning curve brought confidence to perform more complex procedures while maintaining good outcomes.

Contexte : Les premiers résultats sur l'association de la partition hépatique et de la ligature portale pour l'hépatectomie en 2 temps (ALPPS) sont sous-optimaux. La littérature a confirmé que les courbes d'apprentissage influencent les résultats des interventions chirurgicales. Notre étude reposait sur 54 mois consécutifs d'utilisation de la technique ALPPS selon des critères de sélection rigoureux. Elle visait à évaluer l'effet de la courbe d'apprentissage sur les résultats liés à l'ALPPS.

Méthodes : Nous avons procédé à une comparaison rétrospective des patients traités par l'ALPPS entre avril 2012 et mars 2016. Nous avons divisé les patients en 2 groupes de 24 mois (précoce et tardif). Tous les candidats avaient une charge tumorale élevée nécessitant une hépatectomie en 2 temps après une réponse à la chimiothérapie, un volume estimé de futur foie résiduel (FFR) inférieur à 30 % et un indice fonctionnel favorable.

Résultats : Trente-trois patients ont été traités par l'ALPPS pendant la période de l'étude : 16 dans le groupe précoce (âge médian 65 ans, indice de masse corporelle [IMC] moyen 27) et 17 dans le groupe tardif (âge médian 60 ans, IMC moyen 25). Le taux de maladie bilobaire était comparable entre les 2 groupes (94 % c. 88 %, $p > 0,99$). La durée de la chirurgie n'était pas statistiquement différente. Les pertes de sang peropératoires et le besoin de transfusion étaient significativement inférieurs dans le groupe tardif (200 ± 109 mL c. 100 ± 43 mL, $p < 0,05$). Le groupe tardif avait une proportion plus élevée d'ALPPS mono-segmentaires (4:1). Il n'y a eu aucun décès dans les 90 jours parmi les 2 cohortes. Les taux de complications postopératoires n'étaient pas statistiquement significatifs entre les groupes. Le taux de résection R0 était similaire. Les taux de survie sans récurrence après une année complète et de survie globale étaient de 52 % et de 84 %, respectivement.

Conclusion : L'innovation dans le domaine des chirurgies complexes peut donner d'excellents résultats lorsqu'on sélectionne attentivement les patients et que l'on possède de bonnes habiletés techniques. De plus, la courbe d'apprentissage a eu pour effet d'accroître la confiance dans la capacité de réaliser des interventions complexes tout en produisant de bons résultats.

Associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) has been reported recently as a novel variant of 2-stage hepatectomy.^{1,2} It aims to increase the proportion of patients deemed operable by removing the tumour load in a shorter period of time than with other techniques.³ The first stage is performed by clearing the future liver remnant (FLR) from metastasis, ligating the portal vein and physically separating the FLR from the “deportalized” liver with an in situ split. The second stage follows with removal of the deportalized part of the liver after rapid hypertrophy of the FLR.⁴ The mechanism behind the accelerated hypertrophy in ALPPS is yet to be fully understood. Schlegel and colleagues⁵ described an elegant rodent study suggesting that the rapid hypertrophy of liver parenchyma may be associated with a systemic increase of circulating factors released as part of an inflammatory reaction to the parenchymal split in conjunction with portal vein ligation (PVL) and increased blood flow to the FLR.

An initially reported major complication rate (Clavien–Dindo grade III and higher) of 44% and mortality of 12% for ALPPS² led to concerns among the surgical community and raised questions regarding its role and indications.^{6,7} Recently published data from the international ALPPS registry indicate a perioperative 90-day mortality of 9% and a severe complication (Clavien–Dindo grade IIIb or higher) rate of 27%. The high morbidity associated with ALPPS is lower when treating patients younger than 60 years of age and those with colorectal liver metastases (CRLM).⁸ Patients who experience liver failure according to the International Study Group for Liver Surgery (ISGLS) criteria after stage 1 ALPPS and those with a model of end-stage liver disease (MELD) score of more than 10 before stage 2 ALPPS are at significantly greater risk of death within 90 days after stage 2 ALPPS.⁹ Nevertheless, few centres have documented initial good outcomes with ALPPS. We reported our initial experience with ALPPS, which had an overall complication rate of 36%, a severe complication rate of 14% and no deaths within 90 days.¹⁰ Recently, Alvarez and colleagues¹¹ reported high oncological feasibility with adequate patient safety. The morbidity in their series according to the Clavien–Dindo classification was 53% (43% for grade IIIa or higher and 31% for grade IIIb or higher) and mortality was 6.6%.

The learning curve effect describes practical improvement that comes with experience.¹² In hepato-pancreato-biliary (HPB) practice, this effect had been shown for pancreaticoduodenectomy/Whipple procedure, with improvements reported in duration of surgery and, more

importantly, in patient outcomes, including blood loss, complications and length of stay in hospital.^{13,14} However, data regarding centre-specific experience in ALPPS have yet to be established.

At our centre, we adopted ALPPS in April 2012 as a salvage procedure after failed portal vein embolization (PVE). The present study evaluates the impact of the learning curve on ALPPS complications and outcomes at our centre.

METHODS

Data from patients who underwent ALPPS at the London Health Sciences Centre (LHSC) in London, Ont., between April 2012 and March 2016 were recovered from a database established prospectively. All patients were reviewed by a multidisciplinary tumour board consisting of HPB and colorectal surgeons, medical oncologists, radiation oncologists, interventional radiologists, pathologists and radiologists and were deemed unresectable by a single-staged operation owing to high tumour load, bilobar disease and FLR less than 30%. Most of our patients had CRLM, for which careful patient selection has been established at our centre; we have developed specific inclusion and exclusion criteria. Inclusion criteria for CRLM are summarized in Box 1. The presence of 1 or more of the following was considered a contraindication for ALPPS: unresectable primary tumours, unresectable tumour in the FLR or extrahepatic metastases other than localized resectable CRLM, presence of clinical, laboratory or radiological signs of elevated pressures in the portal venous system, and/or poor functional capacity (Eastern Cooperative Oncology Group [ECOG] score ≥ 2).

Before surgery, routine blood tests, including serum tumour marker levels (carcinoembryonic antigen [CEA], cancer antigen [CA] 19.9, and/or α -fetoprotein [AFP]) were assessed. Preoperative radiologic investigations

Box 1: Associating liver partition and portal vein ligation for staged hepatectomy indication for colorectal liver metastases at London Health Sciences Centre

- Extensive bilobar CRLM necessitating an extended hepatectomy
- Predicted FLR < 30%
- Technically feasible resection (planned R0)
- No evidence of extrahepatic disease (except localized resectable lung metastasis)
- Good functional capacity (ECOG score of 0 or 1)
- Complete or partial morphology response, or absence of progression, after systemic chemotherapy (4–6 cycles)
- Biological response evident by CEA reduction

CEA = carcinoembryonic antigen; CRLM = colorectal liver metastases; ECOG = Eastern Cooperative Oncology Group; FLR = future liver remnant.

included thoracoabdominal computed tomography (CT) or magnetic resonance imaging (MRI). Selected patients with high tumour load also underwent positron emission tomography (PET) to evaluate the presence of extrahepatic disease.

We evaluated the following volumetric parameters: standardized total liver volume (sTLV) calculated according to the method used by Vauthey and colleagues,¹⁵ using the estimated body surface area (BSA) as described by Mosteller,¹⁶ future (remnant) liver volume (FLV), and future liver volume to total liver volume ratio (FLV:TLV). Volumetric measurements were performed preoperatively and after stage 1 of the procedure in order to plan stage 2. The percentage of FLR hypertrophy was calculated according to the following formula: $[(FLV2-FLV1)/FLV1] \times 100$.

We divided our patients into 2 groups: the early group consisted of patients who underwent the procedure in the first 2 years, and the late group consisted of those who underwent the procedure in the last 2 years. We collected the following data for each patient: demographic characteristics, site of the primary tumour, number of intrahepatic tumours and their distribution, timing of CRLM (synchronous or metachronous), presence of extrahepatic disease, use of perioperative chemotherapy and use of previous PVE. Operative details included duration of surgery, type of liver resection, rate of intraoperative blood transfusions and radicality of liver resection. When the surgical free margin was 0 mm or there was exposed tumour along the transection plane, liver resection was classified as R1. The following liver biochemistries were measured: international normalized ratio (INR), bilirubin, alkaline phosphatase (ALP) and transaminases (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]). Blood samples were taken before surgery, after stage 1 on postoperative days (POD) 1, 3, 5 and 7 and again after stage 2 on POD 1, 3, 5 and 7.

Primary outcomes for each group included postoperative morbidity and 90-day mortality. Secondary outcomes for the whole patient group included overall (OS) and disease-free survival (DS) rates. The types of liver resections performed were defined using the Brisbane 2000 nomenclature.¹⁷ Complications were scored according to the Clavien–Dindo grading system;¹⁸ we considered grade IIIa a major complication and grade IIIb or higher a severe complication. Mortality included deaths that occurred during the hospital stay or within 90 days after stage 2 ALPPS. Postoperative liver failure was defined according to the “50–50” criteria (prothrombin time [PT] < 50%, INR > 1.7 and a serum bilirubin level > 50 mmol/L on POD-5¹⁹) and the definition established by the International Study Group of Liver Surgery (ISGLS).²⁰

Procedure

The technical aspects of the procedure have been described previously.^{2,4,10} Overall, we distinguish the pro-

cedure into 2 major surgical stages and 1 interval phase. The key steps of stage 1 are as follows: 1) exploration and formal laparotomy to rule out any extrahepatic disease; 2) complete liver mobilization, including ligation and division of the retrohepatic veins draining into the inferior vena cava (IVC) and isolating and encircling both the right hepatic vein (RHV) and the middle hepatic vein with vessel loops; 3) intraoperative ultrasonography to determine resectability and mark the partition plane; 4) cholecystectomy; 5) complete tumour wedge resection (clearing) of the FLR if bilateral disease is present; and 6) isolation of the right portal vein behind the common hepatic duct followed by division of the portal supply of the diseased hemiliver. The hepatoduodenal ligament remains intact with no isolation of the main hilar structures, preserving the blood supply to segment 4.

In classical ALPPS, the in situ split of the parenchyma is achieved between the FLR and deportalized liver (between the left lateral sector and segment 4) using a vessel sealing device (Enseal, Ethicon Endo-Surgery Inc., Johnson & Johnson Medical Ltd.). The partition of the liver is continued until the retrohepatic IVC is visualized and the right hilar plate is identified and encircled with a vessel loop. Special attention is made to preserve the middle hepatic vein (MHV) to avoid congestion of segments 4, 5 and 8 of the deportalized right hemiliver. We believe this prevents congestion and subsequent ischemia during the interval phase between stage 1 and stage 2. A vessel loop is left around the MHV and RHV to avoid the need for dissection at the time of the second stage, which facilitates ALPPS completion. The right hepatic arterial inflow and biliary drainage to the deportalized hemiliver are maintained during this first stage to preserve the liver synthetic function. We place 2 round silicone drains (BLAKE, Ethicon Endo-Surgery Inc., Johnson & Johnson Medical Ltd.) in the surgical field: 1 in the partition plane and 1 in the retrohepatic area.

During our initial 4 cases, we used a bag on the deportalized hemiliver in an attempt to prevent adhesions for the stage 2 ALPPS and as a precaution of bile leak based on the initial ALPPS description.² We abandoned using the bag after our fourth case because no bile leak was noticed and this step might have increased a potential risk of infection. Furthermore, leaving a foreign body in situ necessitated a second operation to remove the plastic bag, regardless of the outcomes of stage 1. Vessel loops appear to be able to be left in the abdomen with no evident long-term consequences.²¹

During the interval phase, the patients are transferred to the high-acuity surgical unit for 24 h and then to the regular ward according to their postoperative course. To avoid overhydration and liver congestion, patients are placed on IV fluid for a day, followed by a clear liquid diet and finally a full diet advancement once oral intake is tolerated. We encourage early ambulation out of bed to a chair on POD-1 and ambulation at least 4 times daily. Blood work is repeated as previously mentioned. Within 7–10 days

after the operation, a contrast-enhanced abdominal CT scan is obtained. If adequate hypertrophy (FLR > 30%) is observed, stage 2 of the procedure is scheduled for the next available operative day, provided the patient is in stable condition (Fig. 1).

In stage 2, the diseased deportalized liver is usually removed by stapling through the hilar plate followed by stapling the right hepatic vein and then the middle hepatic vein. These sequences control the inflow first and allow rotating the diseased liver for better MHV visualization.

In 3 patients, we used a segment 4 modification of the above ALPPS technique. In these cases, the patients had a

high tumour load in the left lateral sector and in the right lobe. In stage 1, a left lateral sectionectomy preserving the segment 4 branch of the left portal vein, clean-up of the FLR, and right PVL were performed along with division of the parenchyma through the Cantile line. Stage 2 consisted of removal of the deportalized right lobe (Fig. 2). One patient had “segment 6 ALPPS,” where we preserved the inflow from the right posterior hepatic artery and right posterior portal vein as well as the outflow through the right inferior hepatic vein (Makuuchi vein). This was followed by ligation of the right anterior and left portal veins. Partition was then performed between segment 6 and 7 and across segment 5 to the hilar plate in stage 1. Stage 2 involved division of all 3 hepatic veins and completion of hepatectomy with resection of segments 1, 2, 3, 4, 5, 7 and 8.

Statistical analysis

Statistical analyses were performed using SPSS software version 21.0 (IBM Corp.). Categorical variables are described using percentages and compared using the χ^2 test or Fisher exact test, as appropriate. Continuous variables are expressed as means and standard deviations for symmetrically distributed data, as medians and interquartile ranges (IQR) for nonsymmetrically distributed data and compared using an unpaired *t* test or the Mann-Whitney *U* test, as appropriate. Actual OS and DS at 1 year is reported. We defined OS as the time from the first stage to death (all causes) and DFS as the time from the second stage to the first recorded evidence of recurrence on imaging (local or distant).

RESULTS

During the study period, a total of 39 patients were explored for ALPPS. The procedure was feasible in 33 patients (16 in the early and 17 in the late group). These procedures were performed in 2 patients with primary and 31 patients with secondary liver tumours. Six patients were deemed unresectable, and resection was abandoned before attempting stage 1 ALPPS. Of these, 2 patients were deemed technically unresectable after intraoperative ultrasonography, 2 patients had tumours abutting the left portal vein near the bifurcation, 1 had an unresectable primary tumour and 1 had severe steatohepatitis with 60% macrosteatosis in the FLR. The demographic and clinical characteristics of patients are summarized in Table 1. There were no significant differences in age, sex, body mass index (BMI) and American Society of Anesthesiologists (ASA) classification between the groups. A total of 31 (94%) patients had CRLM, and the remaining 2 patients had hepatocellular carcinoma (HCC) and cholangiocarcinoma. There were no significant differences in the indications for surgery between the groups. Bilobar disease was comparable (94% v. 88%, $p > 0.99$).

Fig. 1. (A) Preoperative computed tomography scan depicts small future liver remnant (FLR) before the first stage of associated liver partition and portal vein ligation for staged hepatectomy (ALPPS). (B) Scan after stage 1 ALPPS, showing the transection line for right trisectionectomy just to the right of the falciform ligament with complete parenchymal transection down to the inferior vena cava (IVC). There was a significant volumetric hypertrophy of the FLR 7 days after stage 1 ALPPS.

Thirty-two patients successfully underwent both stages of ALPPS (97% feasibility) during a single hospital stay. One patient in the early group experienced left portal vein thrombosis after stage 1 and did not reach the second stage. The metastasis was lying on and abutting the left portal vein; this was cleared from the vein and moved toward the right side during stage 1. The partition was completed as usual. Follow-up CT scan of the abdomen did not show evidence of hypertrophy of the left lateral segment owing to the presence of a partial clot in the left portal vein.

Intraoperative data are presented in Table 2. The median duration of surgery in the second stage decreased from 127 min in the early group to 90 min in the late group, but this decrease was not statistically significant.

Fig. 2. (A) Preoperative computed tomography scan depicts a small future liver remnant (FLR; segment 4) before the stage 1 associated liver partition and portal vein ligation for staged hepatectomy. (B) There was a significant volumetric hypertrophy of the FLR after stage 1. Only segment 4 is left behind.

Intraoperative clinically estimated blood loss and blood transfusion were similar in stage 1 and significantly lower in stage 2 in the late group (200 ± 109 mL v. 100 ± 43 mL, $p = 0.045$). The late group had a higher proportion of Monosegment ALPPS (4:1). There were no statistically significant differences between the groups in the number of extrahepatic simultaneous procedures, including abdominoperineal resection.

Thirty-two patients achieved a sufficient hypertrophy within 10 days (97% efficacy) after the stage 1. No patients had delayed hypertrophy. In the early experience, the mean ratio of FLR volume to TLV before ALPPS was $19.3\% \pm 4.7\%$. At 1 week after the procedure, the mean ratio increased to $36\% \pm 8.4\%$, with a median FLR hypertrophy of 90% (IQR 27%–107%). In the late group, the mean ratio of FLR volume to TLV before ALPPS was $21.9\% \pm 3.7\%$. At 1 week after the procedure, the mean ratio was $37.5\% \pm 6.6\%$, with a median FLR hypertrophy of 80% median (IQR 41%–140%).

Considering both groups, the overall morbidity of the study population was 58% (19 patients). Major complications (grade IIIa) occurred in 4 (25%) patients in the early group and 8 (47%) patients in the late group ($p = 0.70$). Two patients in each cohort had grade IIIb or higher complications. Four (25%) patients in the early group and 1 (6%) in the late group met the 50–50 criteria of postoperative liver failure ($p = 0.17$). Two of them required endoscopic retrograde cholangiopancreatography (ERCP) under general anesthesia. One patient in each group had

Table 1. Patient demographic and baseline clinical and tumour characteristics

Characteristic	Group; median (IQR) or no. (%)		
	Early, $n = 16$	Late, $n = 17$	p value
Age, yr	65 (31–74)	60 (41–75)	0.80
Sex			0.42
Male	68	82	
Female	32	18	
BMI	27.1 (21–33)	25 (19–35)	0.52
ASA class			0.46
< 3	6 (37)	4 (24)	
≥ 3	10 (63)	13 (88)	
Primary disease			0.48
CRC	16 (100)	15 (82)	
HCC	0	1 (6)	—
Cholangiocarcinoma	0	1 (6)	—
Timing (CRLM)			0.65
Synchronous	14 (87)	13 (76)	
Metachronous	2 (13)	4 (14)	
Bilobar distribution	15 (94)	15 (88)	> 0.99
PVE	1 (6)	1 (6)	> 0.99
Preoperative chemotherapy	16 (100)	16 (94)	> 0.99
≥ 6 cycles of chemotherapy	15 (94)	12 (71)	0.176

ASA = American Society of Anesthesiologists; BMI = body mass index; CRC = colorectal cancer; CRLM = colorectal liver metastasis; HCC = hepatocellular cancer; IQR = interquartile range; PVE = portal vein embolization.

abdominal wall dehiscence after stage 2 ALPPS that required repair. One patient with simultaneous ALPPS and colon resection in the early group had percutaneous drainage for an intra-abdominal abscess. Another patient in the late group had segment 6 ALPPS requiring diaphragmatic resection and mesh repair; a subphrenic abscess developed, and the patient was managed with IV antibiotics and percutaneous drainage. The remaining complications were postoperative wound infections. Rates of major and severe postoperative complications did not differ significantly between the groups (Table 1). There were no deaths within 90 days in either cohort.

The median interval between both surgeries was significantly shorter in the early than in the late group (8 d v. 10 d, $p = 0.010$). Negative resection margins (R0) were achieved in 14 of 15 patients in the early group and 15 of

17 patients in the late group ($p > 0.99$) who completed both stages. At 1-year follow-up, 14 of 15 patients in the early group and 12 of 16 patients in the late group were alive (93% v. 75%, $p = 0.33$). The 1-year DS was 53% in the early group and 50% in the late group ($p > 0.99$).

DISCUSSION

Our single-centre experience with ALPPS showed consistently acceptable morbidity and no perioperative mortality throughout the study period for 2-stage hepatectomy, with improvements in intraoperative blood loss and transfusion. We performed monosegment ALPPS in more patients in the late group, without any compromise in perioperative outcomes apart from a nonsignificant increase in major complications.

The ALPPS procedure has gained popularity for the treatment of patients requiring liver resection, with a very low predicted FLR. The ALPPS approach provides 2 perceived advantages. First, as a result of rapid liver kinetic growth, surgical resection of all disease can be achieved more promptly with ALPPS than with conventional 2-staged hepatectomy with portal vein embolization.²² Second, the completion rate of ALPPS significantly eclipses that of conventional 2-staged hepatectomy, with few patients failing to reach stage 2 of the procedure due to tumour progression.²³ Our results support the previous evidence of high feasibility of ALPPS. We found minimal interstage dropout, excellent FLR hypertrophy and a reduction in blood transfusion between stages in the late group without any compromise in perioperative outcomes.

These proposed advantages of ALPPS have been counterbalanced by reports of high perioperative morbidity and mortality. The first published cohort described a 12% perioperative mortality,² with other studies reporting similarly high perioperative mortality as well as severe morbidity in up to two-thirds of patients.²⁴ Our group has previously reported an early experience with ALPPS, showing no deaths within 90 days in a pilot series of 14 patients.¹⁰ In the present series, we again report no deaths within 90 days in 32 patients, which to our knowledge makes this study the largest single-centre cohort with no perioperative mortality.⁴ The largest available studies reporting on short-term outcomes of ALPPS are analyses of the International ALPPS Registry, with a published 90-day mortality of 9% and a severe complication (Clavien–Dindo $\geq$ IIIb) rate of 27%.^{8,9} This morbidity and mortality is further attenuated in patients with CRLM and in those older than 60 years.²⁴ This finding supports our centre's recommendation that selection criteria for ALPPS are the cornerstone of successfully improving perioperative outcomes, and, in addition to age and CRLM, we reiterate the importance of good functional status.

In addition to careful patient selection, we believe that several important technical considerations exist. Preservation

Table 2. Intraoperative data and short-term outcomes

Characteristic	Group; median [IQR], no. (%) or mean $\pm$ SD		<i>p</i> value
	Early, <i>n</i> = 16	Late, <i>n</i> = 17	
Duration of surgery, min			
Stage 1	388 [294–480]	440 [335–540]	0.70
Stage 2	127 [50–204]	90 [60–215]	0.13
Estimated blood loss, mL			
Stage 1	800 [500–2000]	1000 [400–2500]	0.17
Stage 2	200 [50–400]	100 [50–200]	0.045
RBC transfusion	9 (56)	4 (24)	0.15
No. RBC packs per patient			
Stage 1	0.75 [0–3]	0.7 [0–4]	0.43
Stage 2	0.67 [0–3]	0	0.044
Type of liver resection			
Right trisectionectomy	15 (94)	13 (76)	0.042
Monosegment ALPPS	1 (6)	4 (24)	0.042
Reversed approach	2 (12)	0	0.16
Extrahepatic simultaneous procedures	4 (25)	5 (29)	0.16
Colon resection	2	1	—
LAR	2	3	—
APR	0	1	—
Plastic bag used	4 (25)	0	0.021
Interval phase, d	8 [7–10]	10 [7–12]	0.010
%FLR/TLV	19.27 $\pm$ 4.7	21.94 $\pm$ 3.7	0.11
%FLR/TLV after stage 1	36 $\pm$ 8.4	37.5 $\pm$ 6.6	0.84
Complications			
Any complication	6 (37)	13 (76)	0.44
Major (IIIa)	4 (25)	8 (47)	0.70
Severe ($>$ IIIb)	2 (12)	2 (11)	$>$ 0.99
90-d mortality	0	0	$>$ 0.99
LOS, d	17 [13–49]	16 [14–33]	0.35
Curability			
R0	15 (94)	15 (88)	$>$ 0.99
R1	1 (6)	2 (11)	$>$ 0.99

ALPPS = associated liver partition and portal vein ligation for staged hepatectomy; APR = abdominoperineal resection; FLR = future liver remnant; IQR = interquartile range; LAR = low anterior resection; LOS = length of stay; RBC = red blood cells; SD = standard deviation; TLV = total liver volume.

of the middle hepatic vein in order to reduce the incidence of segment 4 venous congestion and subsequent necrosis should be mandatory.²⁵ Although some centres have adopted variations of the initial technique,^{26,27,28} we continue to perform complete parenchymal transection and show that this can be performed with acceptable perioperative morbidity and a 90-day mortality of 0%. Complete parenchymal transection during stage 1 facilitates a quicker and more straightforward stage 2. Finally, we recommend minimizing dissection of the hepatoduodenal ligament to reduce the risk of biliary or arterial complications. Refinements in these aspects of the surgical technique are underscored by a reduction in intraoperative blood loss and the need for blood transfusion in our cohort's later group.

Limitations

Some limitations arise as a consequence of the study design. As a single-centre series with a small sample size (despite being relatively large when compared with the existing literature), the conclusions reached by our group may not be generalizable to other centres. Furthermore, potential biases and confounders arise from the retrospective nature of the study. Although unrecognized confounding variables may be the underlying cause of the improved intraoperative characteristics and interstage interval in the later experience, we performed more monosegment ALPPS in the later stage, which should bias the analysis against the later group.

CONCLUSION

The ALPPS technique continues to generate considerable controversy in the hepatobiliary community. We have previously hypothesized that the morbidity and mortality associated with ALPPS can be reduced with careful patient selection and surgical technique.² In the present study, we showed that acceptable morbidity and mortality can be sustained over a larger cohort of 32 patients, despite the inclusion of more patients requiring monosegment ALPPS. Improvements in intraoperative blood loss and reduction in interstage interval suggest refinement in surgical technique and perioperative, multidisciplinary care. Surgical team experience, in conjunction with greater understanding and participation from medical oncologists, radiation oncologists, radiologists, nurses and other members of the patient care team has contributed to the learning curve shown at our centre. We acknowledge that further data are necessary before any conclusions can be drawn regarding the safety of ALPPS and that few data exist on long-term oncological outcomes and quality of life. Based on our results, we continue to believe that with careful patient selection and refinement in surgical technique, the initial concerns regarding poor perioperative outcomes can be assuaged and the ALPPS can gain greater

acceptance as a surgical option for patients with extensive, bilobar disease and a very small predicted FLR.

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