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REVIEW ARTICLE

A literature review of associating liver partition and portal vein ligation for staged hepatectomy (ALPPS): so far, so good

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Abstract Recently, associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) emerged as a novel surgical strategy to induce a rapid and large hypertrophy of the future liver remnant (FLR). We conducted a computerized search using PubMed and Google Scholar for reports published between March 2012 and July 2016 using mesh headings and key words relating to the ALPPS surgical procedure. The promising results obtained up to date are difficult to interpret due to the heterogeneous group of patients with different underlying pathologies and different chemotherapy schemes. The ALPPS appears as a feasible strategy to be included in the multimodal treatment menu of selected oncological patients. The ALPPS approach can be implemented with acceptable postoperative morbidity and mortality in experienced centers and only in carefully selected patients. This strategy might substitute classic 2-stage hepatectomy in certain patients if future evidence shows superior or equal long-term outcomes.

Keywords Liver resection · ALPPS · Liver failure · Hypertrophy · Liver regeneration

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Introduction

Surgical resection offers the only potential curative option for patients with malignant liver tumors. Major liver resections are frequently mandatory to achieve tumor-free surgical margins. In these circumstances, the volume and functional reserve of the future liver remnant (FLR) is essential, because posthepatectomy liver failure (PHLF) is an important cause of morbidity and mortality after extensive liver resection [1]. Since its description, portal vein occlusion (embolization or ligation) has become undoubtedly the gold standard strategy to induce hypertrophy of the FLR, minimizing the risk of PHLF and expanding the indications of resectability in liver tumors [2]. However, these surgical strategies have some drawbacks. Sufficient FLR hypertrophy is not always achieved and patients could experience tumor progression during the waiting time after portal vein embolization (PVE) [3, 4]. The cooperative German series introduced a novel strategy to induce a rapid and large hypertrophy of the FLR [5]. The procedure gains popularity around the world with the acronym "ALPPS" (Associating Liver Partition and Portal vein Ligation for Staged hepatectomy) [6].

Pathophysiological liver modifications

The liver has an intense regeneration capacity, which is achieved at the expense of both hyperplasia and cellular hypertrophy. Liver regeneration reaches its peak at 12 h after surgery by substantial changes in gene expression [7]. Studies have shown that liver cell replication after hepatectomy is mediated by hepatocyte growth factor, tumor necrosis factor, interleukin-6, epidermal, and transforming growth factors [8]. These mediators have been related in

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hepatic regeneration after partial hepatectomy and PVE [9]. ALPPS is associated with accelerated growth of the FLR, along with all markers of hepatocyte proliferation, when compared with portal vein ligation (PVL) alone [10]. A few data can elucidate the mechanisms that generate the accelerated and remarkable hypertrophy observed during ALPPS. However, among the potential mechanisms postulated, the redistribution of portal blood flow and hepatotrophic factors to the FLR induced by the portal ligation could play an important role [9, 11]; the arterialized disease hemiliver might act as an auxiliary liver, which allows the FLR to tolerate portal hyperafflux by modulating the double hepatic vascular inflow [12]; as well as the importance of parenchyma transection, which interrupts intrahepatic portal collaterals [13, 14] and may induce an inflammatory response with the release of putative growth factors that could itself be a regeneration stimulus [10].

The cooperative German series was the first to describe an increased proliferation activity and hyperplasia in the FLR, but in only one patient [5]. Another study analyzed biopsies in the FLR of 14 consecutive cases and showed a mean pre-regeneration Ki-67 index of 0 % and a post-regeneration index of 14 % [15]. Recently, it was found not only a significantly increased number of hepatocytes in the FLR but also significant morphological changes at the cellular level as well as upregulation of molecular markers of proliferative activity, all of which had direct correlation with volume gain in multidetector computed tomography (MDCT). Indicating that quiescent hepatocytes indeed enter the cell cycle and replicate during ALPPS [16]. Another study compared histologic findings in the FLR in ALPPS with those from hepatectomy after PVE and showed a greater hepatocyte cell density and smaller hepatocyte size in ALPPS than in PVE. They also confirmed that FLR hepatocytes in ALPPS were more immature than in PVE [17].

Experimental models

The ALPPS technique induces a rapid growth of the FLR, exceeding up to four times faster than PVO strategies. To better understand the basic principles of regeneration triggered by ALPPS, some animals models were develop during the last years. Schlegel et al. [10] described the first model of ALPPS in mice. The ALPPS group received 90 % PVL combined with parenchyma transection and controls underwent either transection or PVL alone. The result confirmed the unprecedented and rapid regenerative capacity of a small FLR after step I of the ALPPS procedure and provides evidence suggesting that the accelerated regenerative ability of the FLR is due to circulatory growth factors, rather than a discontinuity of the microcirculation after liver transection. Markers of hepatocyte proliferation were tenfold higher after ALPPS, when compared with controls. Similar results were described in rat's models [18–20]. Recently, a porcine model for ALPPS was introduced, with kinetic rate of growth similar to those seen in humans [21]. Histological and molecular studies in animal models represent a valuable tool to explain many of the mechanisms involved in the physiology of this complex surgical procedure. However, human patients who underwent the ALPPS strategy are complex patients with advanced oncological disease and prolonged chemotherapy schemes; situations that can be difficult to reproduce in animal models.

Patient selection

The ALPPS strategy was recently described; therefore, the precise indications for this surgery have not yet been clearly defined. Briefly, surgical candidates could be patients with marginally resectable or primarily non-resectable locally advanced liver tumors of any origin with an insufficient FLR, either by volume or quality conditions. Certainly, specific conditions can be indications for ALPPS: a tumor margin close to the FLR or its vascular pedicles; bilobar disease with contraindication for PVE; failure of PVE/PVL; unexpected tumor extension during surgical exploration with a larger than planned surgical resection; or the need for a large hypertrophy (>65 %) in an extremely small FLR [12]. From the pathology point of view, ALPPS for colorectal liver metastasis (CRLM) remains the indication of choice with the largest amount of data available. A call for caution must be considered in the use of ALPPS for hepatocarcinoma (HCC), intrahepatic cholangiocarcinoma, and perihilar cholangiocarcinoma in view of related higher morbidity and mortality [22, 23].

Surgical variants of the ALPPS procedure

The ALPPS is presented as one of the most revolutionary surgical procedures of the last decade in liver surgery and generated during the last years an extremely high interest in the HPB world community reflected by consensus, debates, and medical publications. To summarize this, we found 199 communications published in PubMed from 2012 onwards [24]. In 2007, Dr Hans Schlitt from Germany realized for the first time the surgical strategy that later was known worldwide by the acronym of ALPPS. The first official report was proposed, as a series of three cases, on a poster presented by Hauke Lang, during the ninth E-AHPBA meeting in Cape Town, South Africa [6, 25]. Later, Schnitzbauer et al. [5] communicate one of the

largest series of ALPPS, in a multicentric experience, including 25 patients with advanced liver malignancies. The technique can be resuming as follows: during the first surgical stage, the liver parenchyma is transected along the right side of the falciform ligament and PVL of the diseased hemiliver is applied. During this stage, the complete removal of those lesions in the left lateral segment or the right posterior segments (VI and VII) as part of the FLR must be done whenever bilateral disease is detected. Once appropriate hypertrophy of the FLR is achieved, the second stage is performed, usually as a right hepatectomy or trisectionectomy [26] or technical variations like the "left ALPPS," the "right ALPPS," and the "rescue ALPPS" in patients with failed portal vein embolization [27]. Moreover, another technique preserved only segments I and IV as the FLR [28]. Modern liver surgery argue that it was needed at least one anatomic section (2 continuous segments or more) representing at least 20 % of metabolic functional liver mass with the corresponding arterial and portal perfusion, and adequate biliary and venous drainage for a viable hepatic resection. However, ALPPS broke this paradigm, basing the FLR on only 1 Couinaud segment and permitting a safe and feasible monosegmental ALPPS hepatectomy [29]. Considering some technical aspects, Machado et al. [30] performed a successfully Stages 1 and 2—laparoscopy ALPPS, on a 69-year-old woman with multiple and bilobar liver metastases from colorectal origin and in the same Journal Issue they used the laparoscopic approach in a patient with failed portal vein embolization [31]. Furthermore, descriptions of Stage 2—laparoscopy ALPPS could be found [32].

During the first expert meeting on ALPPS celebrated on February 2015, the international faculty of 55 members expressed the necessity to develop a common language to adequately compare and further develop different variants of the original technique of ALPPS [22]. This was corroborated by a systematic review that showed a large variability in the techniques of ALPPS that limits statistical comparisons of outcomes, with a marked heterogeneity in the types of operations performed and the subtleties of operative technique [33]. Recently, Linecker et al. [34] proposed a consensus terminology of many variants of the ALPPS procedure. These variants were subsequently placed in form of prepositions before ALPPS following a defined order: strategy, stage of the procedure, access, portal vein embolization, if used, types of transection and hepatectomy.

Timing between first and second surgical stage

The knowledge of the liver functional reserve is essential, because liver failure is an important cause of mortality after major liver resection [1]. The majority of deaths and the development of PHLF in ALPPS appear after the completion hepatectomy in stage-2 [35]. Therefore, the timing between both surgical stages is essential. Volumetric studies do not always correlate with functionality. Some previous studies showed discrepancies between volumetric assessment, laboratory tests, and functional assessments [36, 37]. The FLR volume limit for safe resection varies from patient to patient. Expert consensus statement accepted cut-off values for proceeding to step 2 are FLR > 30 % or a future liver remnant to body weight ratio (FLR/BW) >0.5 % or >40 % (FLR/BW > 0.8 %) depending on liver quality [22, 38]. In terms of ALPPS safety, the quality of liver parenchyma and its function are clearly future directions to improve patient selection as well as timing of the second stage, both being important determining factors of outcomes [39]. Experts recommend that the first MDCT scan after step 1 should be done on days 8–10 and repeated weekly for 4 weeks, if FLR is insufficient [22]. The international ALPPS registry demonstrated that the majority of patients (86 %) tolerate rapid hypertrophy without developing liver dysfunction after stage-1. The use of liver function criteria proposed by the International Study Group for Liver Surgery (ISGLS) [40] defined liver failure at day 5 after stage-1 and MELD score at least 10 immediately before stage-2 are independent predictors of poor outcome after ALPPS stage-2 [23]. Furthermore, the group of the Hospital Italiano de Buenos Aires, Argentina, showed for the first time the use of hepatobiliary scintigraphy to determine regional FLR function expressed as percentage of total liver function (TLF) by quantifying 99mTc-dimethyl iminodiacetic acid (HIDA) uptake, in those patients with borderline sufficient FLR volume after the first stage or with doubts regarding

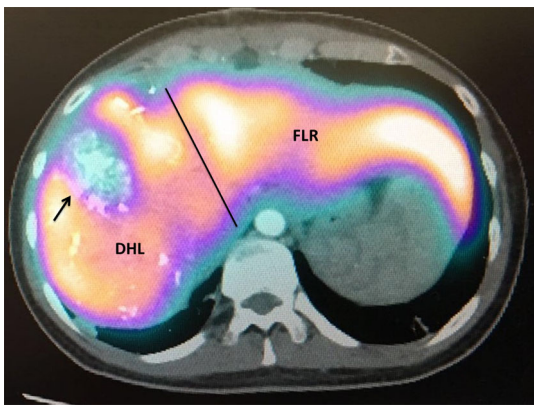

Fig. 1 Liver HIDA scintigraphy with SPECT CT fusioned image before the stage 2. Axial section in a 30-year-old patient with multiple liver metastases from sigmoid colon tumor. The *black arrow* showed tumor in the disease hemiliver (DHL). The *black line* showed the limits of the transection line. The future liver remnant (FLR) function was 41 %. sFLR (standardized future liver remnants): 31 %. FLR/BW (body weight): 0.69 %

Table 1 Patient's general characteristics, operative data, and outcomes in reports with ≥8 patients

Authors	Year	Country	*N*	Increase FLR (%)	Hospital stay, days Median (range)	Morbidity (%)	Major morbidity (%)	Mortality (%)	Follow-up, months Median (range)	OFS (%)	OS (%)
Schnitzbauer et al. [5]	2012	Multicenter Germany	25	74	NR	68	44[++]	12	6 (2–25.9)	80	86[a]
Machado et al. [30]	2012	Single Center Brazil	8	88[†]	NR	NR	NR	0[†]	NR	NR	NR
Donati et al. [44]	2012	Single Center Germany	8	NR	NR	NR	NR	NR	NR	NR	NR
Dokmak et al. [13]	2012	Single Center France	8	70	42 (25–56)	90	NR	NR	NR	NR	NR
Torres et al. [45]	2013	Multicenter Brazil	39	83	17.8 (13–40)	NR	59	12.8	NR	NR	NR
Li et al. [46]	2013	Single Center Germany	9	87.2	NR	100	31.2	22.2	NR	NR	NR
Robles et al. [47]	2014	Single Center Spain	22	61	16 (12–28)	NR	NR	9.1	6 (2–22)	95	100[*]
Nadalin et al. [14]	2015	Single Center Germany	15	87.2	NR	66.7	49.1[++]	28.7	17 (1–33)	NR	66.6[—]
Schadde et al. [23]	2015	Multicenter International ALPPS registry	320	NR	NR	7.2 (±1.9)[//]	NR	8.8–[^^]	3[b]	NR	NR
Truant et al. [48]	2015	Multicenter Franco-Belgian	62	48.6	29.2 (3–129)	80.6[^^]	40.3[^^]	12.9[^^]	NR	NR	NR
Hernández et al. [49]	2015	Single Center Canada	14	93	18 (23 ± 12)[c]	36	14[+]	0	9.4	85.7[d]	100
Ratti et al. [50]	2015	Multicenter Italy	12	47	24 (16–42)	NR	41.7	8.3	12 (6–18)	67[-]	92[-]
Lang et al. [51]	2015	Single Center Germany	16	85.5	30 (16–90)	81.2	31.3[+]	12.5	26.4 (3.2–54.3)	NR[e]	48.9[−]
Croome et al. [52]	2015	Multicenter USA-Canada	15	84.3	NR	NR	NR	0[^^]	NR	NR	NR
Alvarez et al. [12]	2015	Single Center Argentina	30	89.7	16 (11–62)	53	43	6.6	17 (1.5–33)[f]	40[^]	63[^]
Serenari et al. [53]	2016	Multicenter Italy	50	63	27 (15–127)	NR	54	20[^^]	12.1	55/45/62[***]	91/60/75[***]
Bjorsson et al. [54]	2016	Multicenter Sweden-Norway	23	64.3	9 (2–50)[**]	91	43.5	4.3[^^]	22.5	27[-]	59[^]
Vivarelli et al. [55]	2016	Single Center Italy	9	96	22 (13–5)	67	44	11.1[-]	17.1 (8.6–25.6)[F]	75[-]	89[-]

Table 1 continued

Authors	Year	Country	*N*	Increase FLR (%)	Hospital stay, days Median (range)	Morbidity (%)	Major morbidity (%)	Mortality (%)	Follow-up, months Median (range)	OFS (%)	OS (%)
Vennarecci et al. [56]	2016	Multicenter Italy	13	71.7–64.8[/]	22 (20–67) to 33 (26–66)[/]	NR[^^^]	NR[^^^]	23.1[^^]	15 (1–27)	42[-]	74[-]

FLR future liver remnant, *Major morbidity* Dindo–Clavien Classification was used (≥III): Total of complicated patients (≥III)/Total Patients), *OFS* overall free survival, *OS* overall survival, *NR* unreported

† Results reported in one patient

* Two postoperative deaths are excluded

** After the two-stage operation

*** Expressed for type of tumor. CLRM/Biliary tumors/HCC

[+] Expressed in severe morbidity (≥IIIb)

[++] Expressed as total of majors complications (≥III)/total of complications

- At 1 year of follow-up

^ At 2 years of follow-up

^^ At 90 day follow-up

^^^ Expressed by stages

– At 3 years of follow-up

/Liver Cirrhosis—normal livers

//Charlson Index (1–14), Mean (±SD)

— Ten of the 15 patients are still alive (survival rate: 66.6 %)

[a] 6 Months after resection

[b] Patient follow-up at least 90 days after stage-2

[c] (Mean ± SD)

[d] Recurrence developed in two patients

[e] Median disease-free survival (DFS) Was 14.6 months

[f] Expressed as mean

functional sufficiency (Fig. 1) [41]. It is remarkable that the HIDA scintigraphy was useful to decide the best timing of the second stage in 4 patients of this series. In this study, none of the patients with an FLR/TLF of 30 % or more before the second stage developed PHLF [12]. Some of these findings were confirmed recently [42, 43]. Routine use of HIDA scintigraphy before and after the first stage of ALPPS could contribute to a better evaluation of FLR functionality and, consequently, more appropriately identify the best time to complete the disease hemiliver resection.

Short-term outcomes

Currently, the main disadvantage of ALPPS is the high morbidity and mortality reported in most of the preliminary series (Table 1). These results could be explained as essentially two complex surgical procedures, which takes a 'learning curve' and which is carried out in patients with high tumor burden mostly underwent with extended chemotherapy regimens. It is noteworthy that these rates of morbidity and mortality related to ALPPS are similar than other recent publications in major liver resection [57].

Possibly, ALPPS outcomes will improve in the near future as a consequence of the learning curve, technical improvements, and better patient selection [39]. In fact, recently, it has been demonstrated that ALPPS can be achieved with similar perioperative results compared with classic 2-stage resections [12]. Schade et al. [35] described age (>60-year-old), intraoperative red blood cell transfusion, tumor type (other than CRLM) and duration of stage-1 surgery (>300 min) as independent predictors for severe complication and are also risk factors for mortality related to the ALPPS procedure [23]. Perhaps, elderly patients are at higher risk of poor outcome, and should be an important factor for patient selection and may justify longer intervals between stages 1 and 2 [22]. Recent analysis suggested that age had an inverse correlation with proliferating cell nuclear antigen expression, suggesting that older patients might have a decreased regenerative capacity [16]. Kremer et al. [58] showed that neoadjuvant chemotherapy significantly impairs hypertrophy of the FLR, without impact on patient outcome. The high rates of biliary complications observed in the first series suggest that this procedure should not be performed in patients requiring biliary reconstruction [13, 59]. The preservation of the middle hepatic vein with a minimal dissection of the hepatoduodenal ligament will minimize the risk of biliary or arterial complications and prevent complete devascularisation of segment 4 [49]. To minimize potential bile leaks, it was proposed that bile leak-tests may be useful after both steps 1 and 2 with a focus on the liver remnant [22]. In addition,

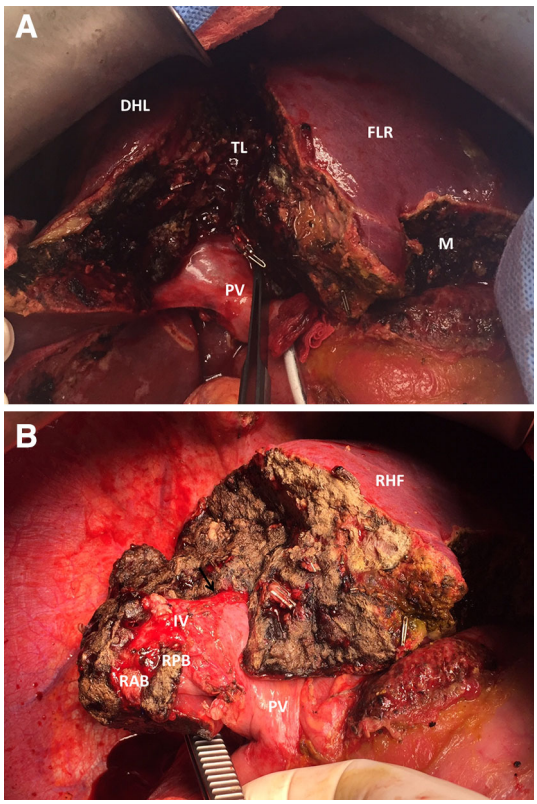

Fig. 2 **a** Stage 1 of the MINI-APPS approach in a 30-year-old patient with multiple liver metastases from sigmoid colon tumor. *DHL* disease hemiliver, *TL* transection line at the level of the middle hepatic vein, *PV* portal vein, *FLR* future liver remnant, *M* metastasectomy. **b** Stage 2 of the MINI-APPS approach. The disease hemiliver was resected as a right trisectionectomy. The *white arrow* showed the left hepatic pedicle. *VP* portal vein, *RAB* right anterior pedicle, *RPB* right posterior pedicle, *IV* ligated segment four branches, *RHF* functional hepatic remnant

the second stage should be delayed or even abandoned in case of compromised clinical status or liver function to avoid mortality [39].

Another important technical issue is that partial parenchymal transection (up to the middle hepatic vein) compared with complete partition (up to the inferior vena cava) was associated with a decrease in morbidity without unfavorable hypertrophy of the FLR [12]. Recently, the group of Zurich published similar results [60].

Assumed that the majority of deaths in most series occurred after the second stage of ALPPS, reducing the impact of the first stage would consequently seem rational to improve postoperative recovery and allow patients to reach properly the definitive procedure. Recently, a new surgical paradigm for ALPPS was introduced, aiming to maximally reduce the aggressiveness and surgical impact of ALPPS first stage. The proposal incorporates the combination of partial parenchymal transection with intraoperative portal vein embolization and minimum liver

Table 2 ALPPS versus 2-stage hepatectomy in series after 2010

2-Stage	*N*	Year of publication	Country	Completed 2nd stage (patients)	Resectability (%)	Major morbidity (%)	Liver failure (%)	Mortality (%)
Tsai et al. [71]	45	2010	USA	35	78	44.4**	8.6	8.8
Narita et al. [72]	80	2011	France	61	76.2	36.7**	12.5	0
Tsim et al. [73]	38	2011	Uk	33	87	NR*	NR	0
Brouquet et al. [70]	65	2011	USA	47	72.3	43.6**	6.1	4.6
Stella et al. [74]	56	2012	France	49	87.5	34.1**	13.8	1.8
Tanaka et al. [75]	24	2012	Japan	21	87.5	28.6**	NR	0
Muratore et al. [76]	47	2012	Italy	36	76.6	NR	4.2	0
Belghiti J et al. [13]	87	2012	France	87	NR	39	9	10
Turrini et al. [77]	42	2012	France	34	81	54.5**	NR[a]	4.8
Lam et al. [68]	459	2013	Australia	352	77	40	NR[b]	3
Cardona et al. [78]	40	2013	USA	35	88	45	NR	0
Abbot et al. [79]	82	2014	USA	56	68	44	NR	7.3
Giuliante et al. [80]	130	2014	Italy	102	78.5	58.3**	8.8[c]	3.1
Faitot et al. [81]	50	2015	France	38	76	16	NR	2
Imai et al. [82]	125	2015	France	81	64.8	NR	NR	2.4
Fuks et al. [83]	34	2015	France	26	76.4	38.7**	5.9	3
Ratti et al. [50]	36	2015	Italy	34	94.4	17.6	5.9	0
Levi Sandri et al. [84]	57	2015	Italy	46	80.7	17.8	NR	0
Passot et al. [85]	109	2016	USA	89	82	25.7	6.4	5.5
ALPPS (CRLM)								
Gauzolino et al. [27]	4	2013	Italy	4	100	25	0	0
Oldhafer et al. [65]	10	2013	Germany	7	70	14.3	NR	NR+
Hernandez et al. [15]	14	2015	Canada	14	100	14++	29	0
Ratti et al. [50]	12	2015	Italy	12	100	41.7	0	8.3
HOSPITAL ITALIANO DE BUENOS AIRES	26	2016	Argentina	26	100	42.3	23^^	0
Bjorsson et al. [54]	23	2016	Sweden	23	100	43.5	NR	4.3^

Major morbidity Dindo–Clavien classification was used (≥iii): total of complicated patients (≥iii)/total patients). *NR* unreported

* Reported the general and specific complications without clarifying treatment performed

** Reported as total of majors complications (≥ iii)/total of complications

+ According os (overall survival): 42.8 % (median follow-up: 15.5 months)

++ Expressed in severe morbidity (≥iiib)

^ At 90 day follow-up

^^ isgls (internacional study group of liver surgery)

[a] Two patients died 19 and 32 days after the second hepatectomy due to liver failure. it does not express overall % of liver failure

[b] 11 patients died due to liver failure. it does not express overall % of liver failure

[c] It includes transient liver failure and liver failure

mobilization minimizing the first stage impact to stimulate rapid patient recovery and leaving the main surgical procedure for the second stage (Fig. 2a, b) [61].

Long-term outcomes

The promising results obtained to date are difficult to interpret from the oncological point of view, due to the heterogeneous group of patients with different underlying pathologies and different chemotherapy schemes. The ALPPS appears as a feasible strategy to be included in the multimodal treatment menu of selected patients. Up to 40 % of patients with PVE are not candidates for liver resection, because of either tumor progression or insufficient FLR hypertrophy [62], especially in those patients with diabetes or severe sinusoidal injury [63]. Regarding the efficacy of ALPPS, a study showed that 80 % of the patients achieved a sufficient FLR hypertrophy in less than 10 days and a potentially complete oncologic resection (R0) in 93 % of the patients [12]. The results from a multicenter analysis revealed that 83 % of ALPPS patients achieved complete resection compared with 66 % in PVE/PVL ($p = 0.027$) [64]. Considering long-term oncological outcomes, undoubtedly the most essential question still unanswered is whether a better possibility of tumor resection, ultimately translates into better survival. CRLM represents the main indication for ALPPS in most series published in the present, especially in the existence of bilobar disease. Oldhafer et al. [65] revealed that ALPPS for patients with CRLM presented a high risk for recurrence and early tumor progression. Alvarez et al. [12] showed disease recurrence during follow-up in 11 from 19 patients with CRLM. Two patients with liver-only recurrence underwent for a repeated R0 hepatectomy. The group from Canada reported a 14.3 % recurrence after a median follow-up of 9.4 months [15]. Lang et al. [66] reported a 3-year overall survival of 56 % in both, patients with CRLM and those with either primary liver tumors or non-CRLM (CRLM 64.3 %, non-CRLM 50 %). Recently, a study reported intermediate oncological results with an 82 % recurrence rate after a median follow-up of 22.5 months from surgery, and an overall survival 1 year after stage-2 procedure of 83 and 59 % after 2 year. R0 operated patients had significantly better survival than R1 operated patients ($p = 0.037$) [54].

ALPPS versus two-stage hepatectomy

Adam et al. [67] first described two-stage hepatectomy for the treatment of colorectal bilobar metastatic disease that could not be resected in a single surgical procedure, to allow liver regeneration between both procedures. Over time there have been modifications of the technique. One major drawback of this strategy is that patient's failure to proceed to stage 2, due to insufficient FLR hypertrophy or tumor progression during the period of liver regeneration [68]. The ALPPS strategy emerged as a possible competitor in terms of resectability, safety and oncological outcomes for patients with advance liver tumors. Recent published series of two-stage hepatectomy reported rates of morbidity ranging from 49 to 59 % and mortality from 6.4 to 8.8 %, respectively [70–72], which are similar to those obtained with the ALPPS approach (Table 2). A recent multicenter case-match analysis demonstrated that the feasibility of tumor resection using ALPPS compared with two-stage hepatectomy was not significantly greater, with an increase in perioperative complications [50]. Contrary, cancer progression while waiting for the second stage hepatectomy after portal vein embolization is an important limitation for two-stage hepatectomy [86].

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval The article is in accordance with ethical standards.

Research involving human participants and/or animals This article does not contain any studies with human participants performed by any of the authors.

Informed consent For this type of study formal consent is not required.

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