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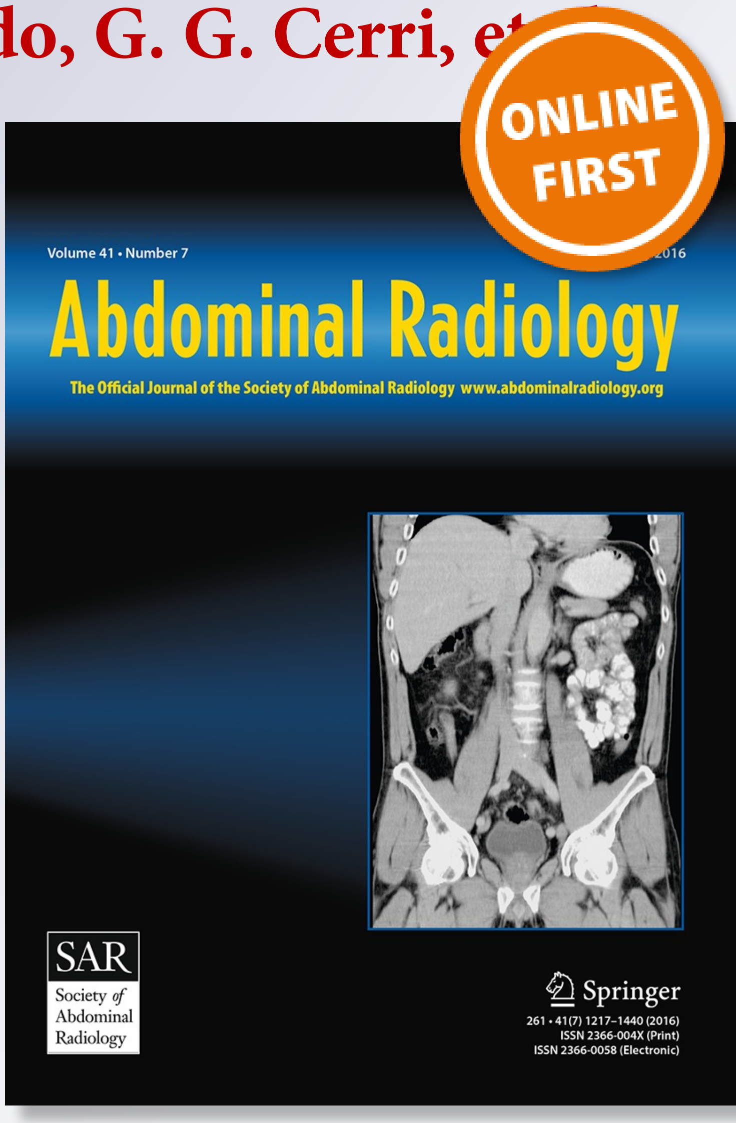

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Associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) in colorectal liver metastasis: the radiologist's perspective

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Abstract

Purpose: Hepatic resection is the only potentially curative treatment for patients with colorectal liver metastasis (CRLM). Many multidisciplinary approaches, including the associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) procedure, have been proposed to increase the resectability rate in these patients. ALPPS is the most recently described staged liver resection technique, representing an advantageous strategy to induce a rapid and marked increase in the future liver remnant (FLR) volume. The aim of this article is to describe the radiological evaluation of this procedure and its variation.
Methods: This retrospective study included 9 patients with CRLM who underwent the ALPPS procedure. Abdominal imaging studies were reviewed, with an emphasis on a rational radiological approach. The number of liver metastases, the FLR volume (pre- and postportal vein ligation), anatomical variations, potential pitfalls related to disease progression, and postoperative complications were evaluated.
Results: The types of hepatic resection included 4 classical ALPPS cases, 3 right ALPPS variations, and 2 left ALPPS variations. The mean FLR volume calculated in the initial evaluation was 453 mL (213–790 mL). Following the first surgery, the mean FLR volume increased to 634 mL (410–957 mL), which indicated a mean volume increase of 181.1 mL (95% CI 149.7–212.5 mL; $p < 0.001$) and a mean absolute volume increase of 48% (19%–88%).
Conclusion: The ALPPS procedure is an emerging form of two-stage hepatectomy. In this context, radiologists should provide crucial preoperative and perioperative information that may change surgical planning and contribute to an improvement in the oncologic outcome.

Key words: Hepatectomy—Metastases—Surgical technique—Magnetic resonance imaging—Tomography

Abbreviations

ALPPS	Associating liver partition and portal vein ligation for staged hepatectomy
CRLM	Colorectal liver metastasis
FLR	Future liver remnant
IM1	First imaging evaluation (staging imaging)
IM2	Second imaging evaluation (recalculation of the FLR)
IM3	Third imaging evaluation (complication assessment)
MDCT	Multidetector computed tomography
PHLF	Posthepatectomy liver failure
PVL	Portal vein ligation
TLV	Total liver volume

Hepatic resection is the only potentially curative treatment for patients with colorectal liver metastasis (CRLM). In recent years, it has become the standard of

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care for patients with CRLM and a sufficient amount of future liver remnant (FLR) following surgery [1–5].

It is well known that the safety of liver resection is determined by both the function and the volume of the FLR which can help to avoid posthepatectomy liver failure (PHLF) [2, 3, 6–8]. In general, for patients with normal liver function, an FLR of 25%–30% is sufficient. However, resections associated with chemotherapy-related injury or cirrhosis have increased morbidity and require an FLR of at least 35%–40% [9–12].

A multidisciplinary approach has been proposed to increase the resectability rate in patients with initially nonresectable CRLM [1–3]. Many surgical strategies have been described to increase the FLR, including portal vein occlusion (PVO), which is attempted to redistribute the portal venous flow and consequently cause compensatory hypertrophy of the FLR [10, 13–15].

To minimize the risk of PHLF in patients with a borderline FLR, two-stage surgeries with portal vein ligation (PVL) or preoperative percutaneous portal vein embolization combined with improved systemic chemotherapy have been widely used. As a result, the number of surgical candidates for resection of multiple colorectal hepatic metastases has increased [2–4].

Associating liver partition and PVL for staged hepatectomy which is also referred to as the ALPPS procedure is the most recently described liver resection technique; in particular, it represents an advantageous strategy to induce a rapid and marked increase in the FLR volume [2, 8, 11, 16–20].

ALPPS has been performed in different surgical scenarios with at least three major variations, and the initial experience of specialized oncologic centers has recently been reported with promising results [2, 8, 11, 16–19].

However, the imaging particularities of the ALPPS technique and its variations remain unfamiliar to the majority of radiologists, including gastrointestinal specialists. Therefore, the aim of this article is to describe the radiological evaluation of the ALPPS procedure and its variations in the context of multinodular CRLM.

Methodology

The institutional review board approved this HIPAA-compliant study and waived the need for informed consent. This retrospective study included 9 patients with CRLM who underwent the ALPPS procedure between January 2012 and June 2014, following a multidisciplinary oncologic board discussion. All patients had a borderline FLR and a good performance status.

Digital medical records were analyzed to obtain patient demographics and clinical data.

Multidetector computed tomography (MDCT) and magnetic resonance imaging (MRI) studies of the abdomen were reviewed to assess the number of liver metastases, the volume of the FLR, anatomical variations and their impact on surgical decisions, potential pitfalls related to disease progression, and postoperative complications.

All patients underwent a radiological evaluation with the following three steps:

1. Prior to the first surgery (S1), to stage the hepatic disease, to calculate the FLR and to exclude extra-hepatic metastasis;
2. Between procedures, to recalculate the FLR;
3. Following the second surgery (S2), to evaluate complications.
4. A routine oncologic follow-up was performed for all patients to determine recurrence.

ALPPS technique

The ALPPS technique was first performed on a hilar cholangiocarcinoma in 2007 [1, 15, 18]. The technique is applied when a two-stage hepatectomy is necessary and the FLR is considered inadequate (FLR $<$ 30%) [15, 18].

1. In the first surgery (S1), the liver parenchyma is transected along the intended line of the resection, and PVL is performed. Additionally, the FLR is cleaned via metastasis enucleations and/or intraoperative radiofrequency ablations [1, 3, 10, 21] (Fig. 1).
2. In the second surgery (S2), following a period of 1–2 weeks, the excluded liver is removed along with the residual metastatic disease. The surgical strategies include right classical ALPPS (trisectionectomy), left ALPPS variation, and right ALPPS variation, which are based on the number and location of the hepatic lesions [1, 3, 10, 21] (Figs. 2, 3).

Imaging evaluation

MDCT images were obtained using a dual-source 256-MDCT scanner (Somaton Definition Flash, Siemens Healthcare, Forchheim, Germany). A multiphase protocol was used which included pre- and postcontrast images (arterial, venous, and delayed phase) following the administration of 1.5 mL of nonionic contrast material per kilogram of body weight. MRI was performed using 1.5 T scanners (Magnetom Avanto, Siemens Medical Systems), and the protocol included diffusion-weighted imaging (DWI) and hepatobiliary contrast-enhanced imaging (Gd-EOB-DTPA, Primovist ®).

First imaging: staging imaging (IM1)

The IM1 assessment was performed before S1 to stage the disease and emphasize the number of liver nodules, anatomical variations, and FLR calculation, in addition to excluding extra-hepatic metastasis (Fig. 4).

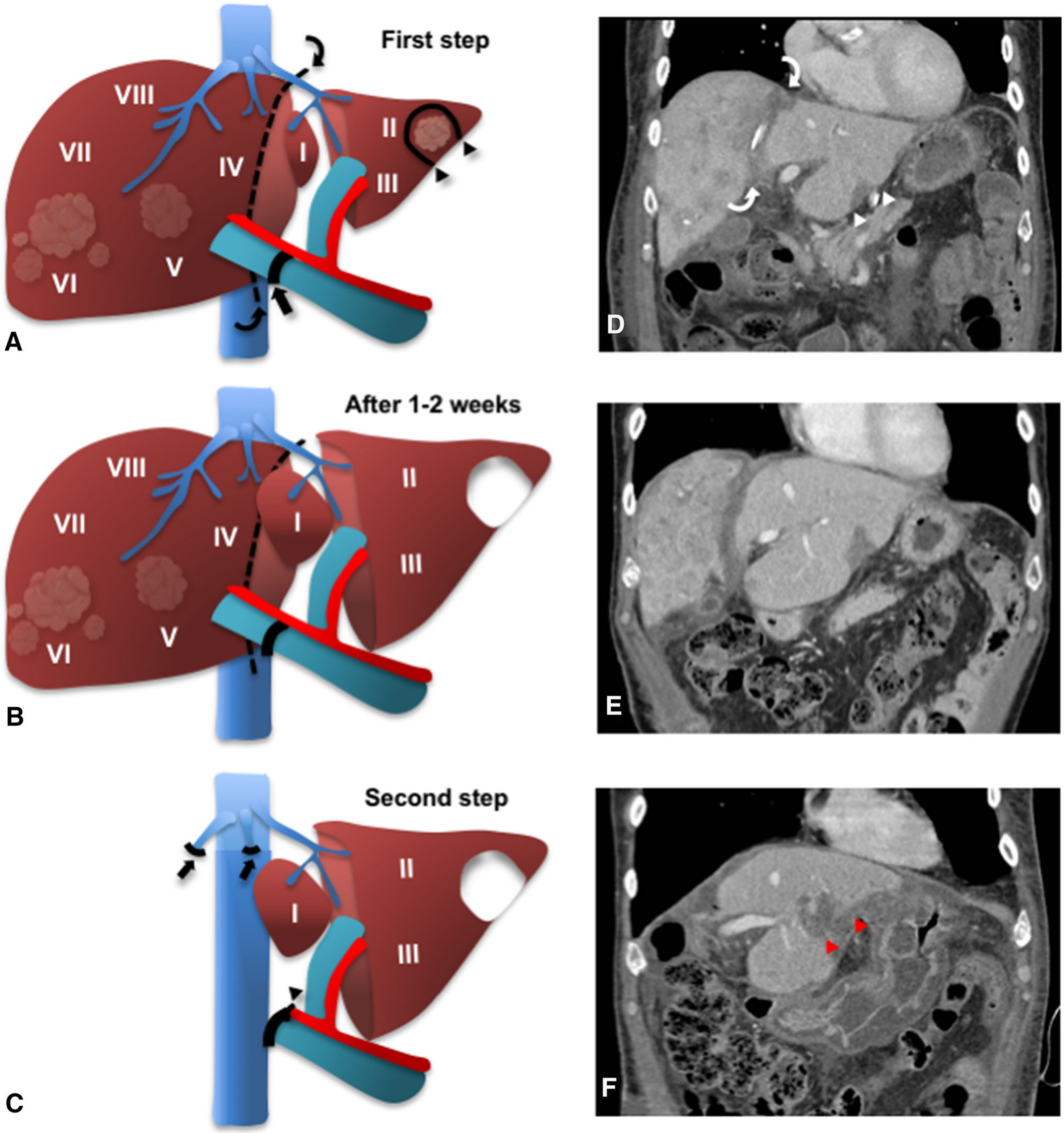

Fig. 1. ALPPS technique: right classical ALPPS (trisectionectomy). *First step* **A** The liver parenchyma is transected along the intended line of the resection (*dotted line*/*curved arrows*), and the future liver remnant is cleaned via metastasis enucleations (*black arrowheads*). Portal ligation of the larger liver lobe is also performed (*arrow*). **D** Coronal-enhanced CT scan shows both the liver partition (*curved arrows*) separating the left lateral segments and multiple nodulectomies in the left lobe (*arrowheads*). Following a period of 1–2 weeks (**B**), the future liver remnant increases in volume. **E** Coronal CT images two weeks after the first surgery. The remnant liver (segments I, II, and III) increased in volume from 479 to 570 cm^3 (an increase of 19%, which represents 31% of the total liver volume). *Second step* **C** The excluded liver is removed along with the residual metastatic disease. **F** Coronal-enhanced CT 7 days after a right hepatectomy. Coronal images demonstrate the remnant liver (segments I, II, and III) and nodulectomy areas (*arrowheads*).

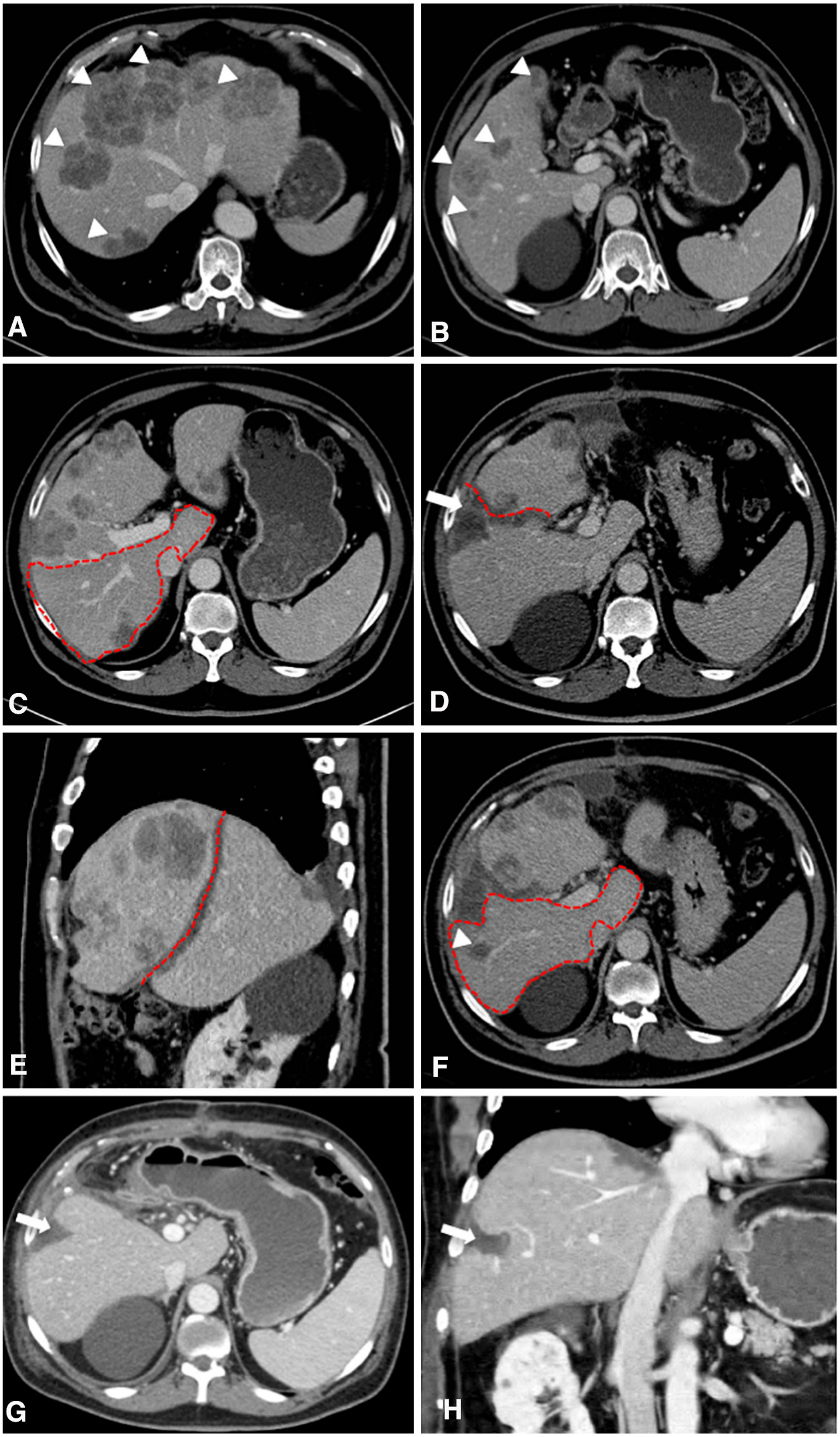

Fig. 2. ALPPS variation: left ALPPS variation: A 58-year-old man with sigmoid colon cancer with multiple liver metastases. **A** In the preoperative images (IM1), there were 14 nodules, including **B** 4 nodules within segments VI, V, and IV (*arrowheads*). Prior to ALPPS (IM1) (**C**), the total liver volume was 2030 cm^3, and segments I, VI, and VII were 540 cm^3 in volume (25% of the total volume). Axial- (**D**) and sagittal (**E**)-enhanced CT images following ALPPS S1 indicate both the liver partition (*red dotted line*) separating segments I, VI, and VII from the remaining liver and a nodulectomy at segment VI (*arrow*). **F** Axial-enhanced CT images after the first surgery (IM2); the *red dotted lines* indicate segment I and the transition of segments VI and VII. Twelve days after the first surgery, the right lateral segments increased in volume from 540 to 625 cm^3 (an increase of 15%, which represents 30% of the total liver volume). There was still a lesion adjacent to right hepatic vein (*arrowhead*). Axial (**G**) and coronal (**H**) follow-up-enhanced CT images 4 weeks after hepatectomy demonstrate the remnant liver (segments I, VI, and VII) and the nodulectomy areas (*arrow*).

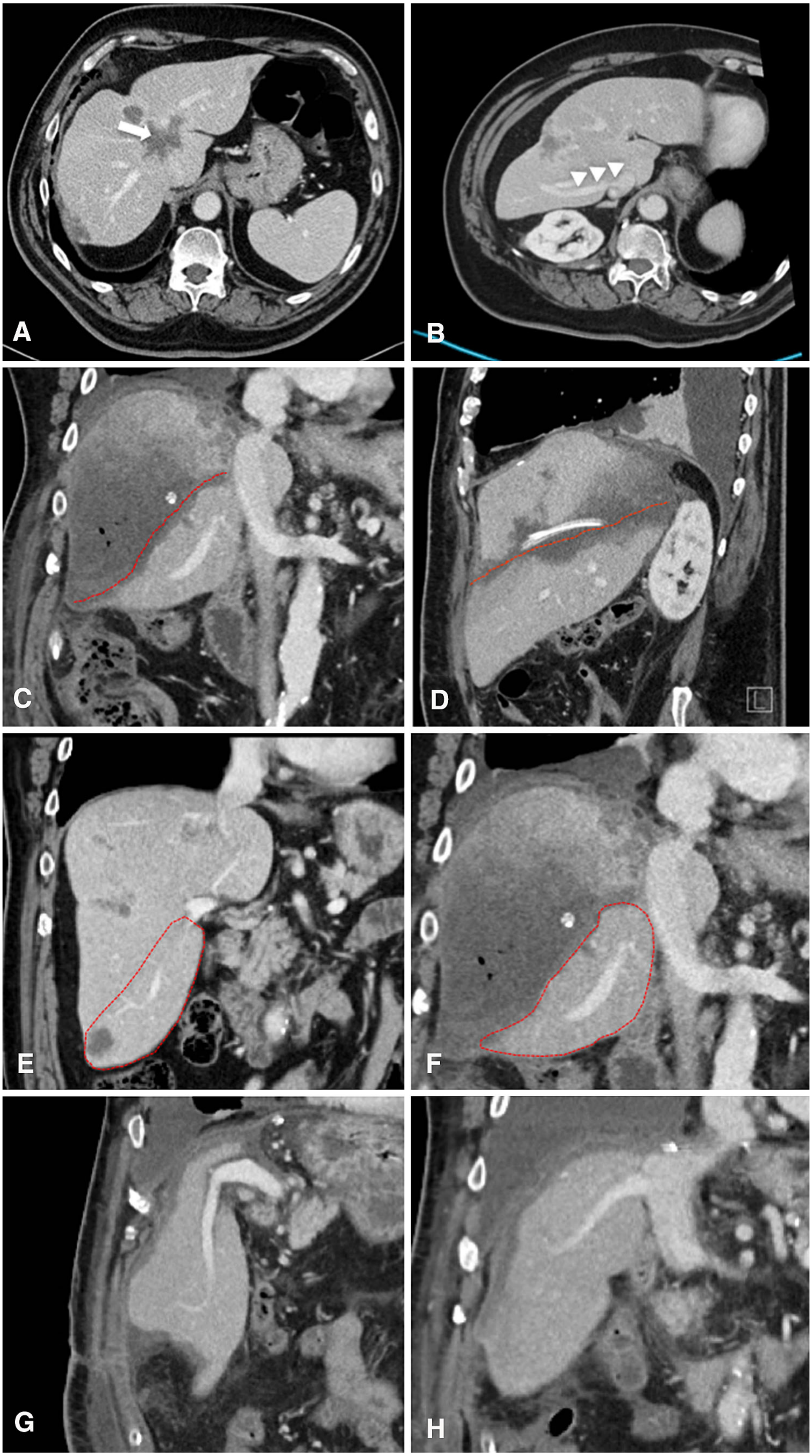

Fig. 3. ALPPS variation: monosegment ALPPS: A 66-year-old man with colon cancer with multiple liver metastases. **A** In the preoperative images, there were 18 nodules, one of which had infiltrated the 3 hepatic veins (*arrow*). **B** Preoperative images also indicated a venous anatomical variant (*arrowheads*) in which segment VI was drained by an accessory vein directly into the inferior vena cava (accessory right hepatic posterior vein). Segment VI had 3 nodules. Because of this variant, the ALPPS procedure was performed to isolate part of segment VI. Coronal- (**C**) and sagittal (**D**)-enhanced CT images indicate the liver partition (*red dotted line*) separating part of segment VI from the rest of the liver. **E** Prior to ALPPS (IM1), the total liver volume was 1560 cm^3, and the remnant liver (*red dotted lines*; segment VI) was 370 cm^3 in volume (23% of the total liver volume). **F** Coronal CT images 12 days after S1. Segment VI increased in volume (*red dotted lines*) from 370 to 520 cm^3 (an increase of 40%, which represents 33% of the total liver volume). Coronal images from follow-up-enhanced CT 4 weeks after hepatectomy demonstrate the remnant liver (segment VI), with its portal branch (**G**) and accessory right hepatic posterior vein (**H**).

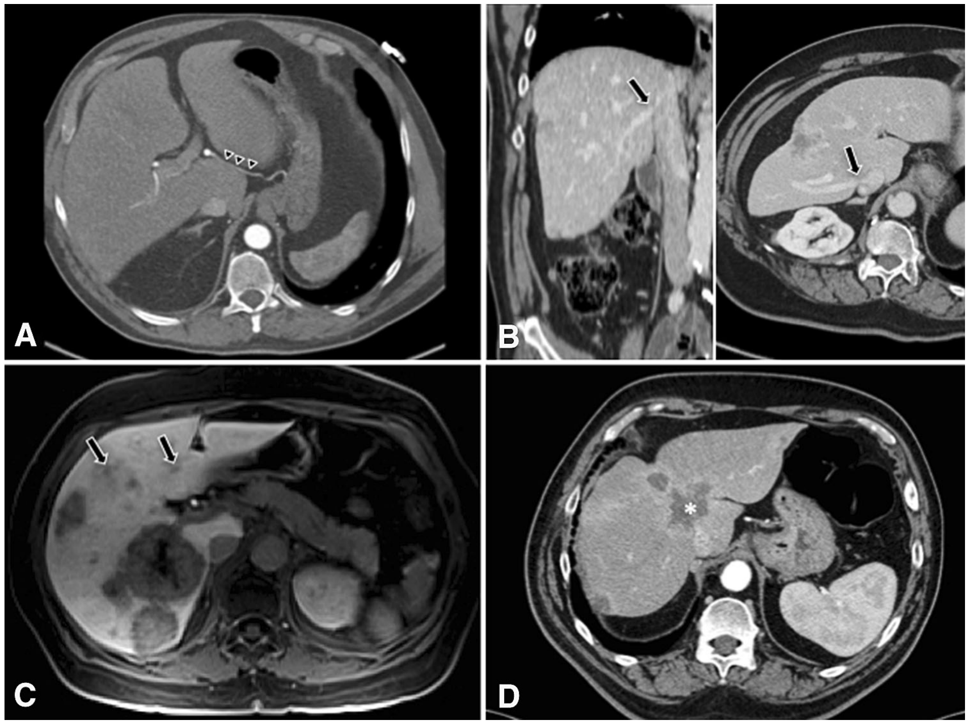

Fig. 4. First imaging (IM1): preoperative/staging imaging: Preoperative CT scans are performed before the first surgery to reveal the anatomical variations: **A** A 23-year-old-woman with a right hepatic artery that arose from the left gastric artery and extended into the fissure for the ligamentum venosum (*arrowheads*). **B** Sagittal- and axial-enhanced CT images of a 66-year-old male with colon cancer with multiple liver metastases and a venous anatomical variant. Segment VI drained via an accessory venin (*black arrow*) directly into the inferior vena cava (accessory right hepatic posterior vein). An additional reason for preoperative CT is to stage the liver disease by determining the number and distribution of the nodules: **C** Axial MRI T1 FAT with a hepatospecific contrast image for a 58-year-old man with sigmoid colon cancer with multiple liver metastases. The image indicates 2 small nodules in the segments IV and V that were not identified in the axial-enhanced CT image (*black arrow*). **D** A 66-year-old man with colon cancer with multiple liver metastases. A total of 18 nodules were identified, including one nodule that had infiltrated the 3 hepatic veins (*asterisks*). It is also important to stage the global disease by excluding extra-hepatic metastasis such as pulmonary metastasis identified in the thoracoabdominal transition and peritoneal disease.

A multiphase abdominal computed tomography (CT) scan and Gd-EOB-DTPA-enhanced MRI for liver evaluation were performed on all patients.

A radiologist with 10-year experience in abdominal imaging performed a volumetric analysis of all patients using the imaging postprocessing software iNtuition® (TeraRecon, Houston, TX).

Second imaging: recalculation of FLR (IM2)

Prior to S2 and typically 14 days after S1, a second imaging study (IM2) was performed. The total liver volume (TLV) and the FLR volume were recalculated, and the FLR volume was expressed in terms of the percentage of the TLV.

The portal venous phase was used for CT volumetry and assessment of the resected areas; the ablation zones and inferior vena cava were not taken into account in the regions of interest (ROIs) (Fig. 5).

Third imaging: complication assessment (IM3)

An abdominal CT scan was performed at the first sign of complications or prior to hospital discharge. The ALPPS postoperative complications were reported according to the Clavien–Dindo classification [22]; these may include bile leaks, biliary fistulas and bilomas, anemia, encephalopathy, fever, pleural effusion, ascites, pneumonia, wounds, intraabdominal infections, or liver insufficiency (s peak total bilirubin level greater than 7 mg/dL and/or typical clinical manifestations of hepatic insufficiency, including massive ascites or encephalopathy) (Fig. 6).

Results

Nine patients with isolated liver metastasis of colorectal cancer underwent ALPPS as the preferred surgical approach. Six patients were male, and the mean age was 57 years (29–66). There was no mortality among the 9

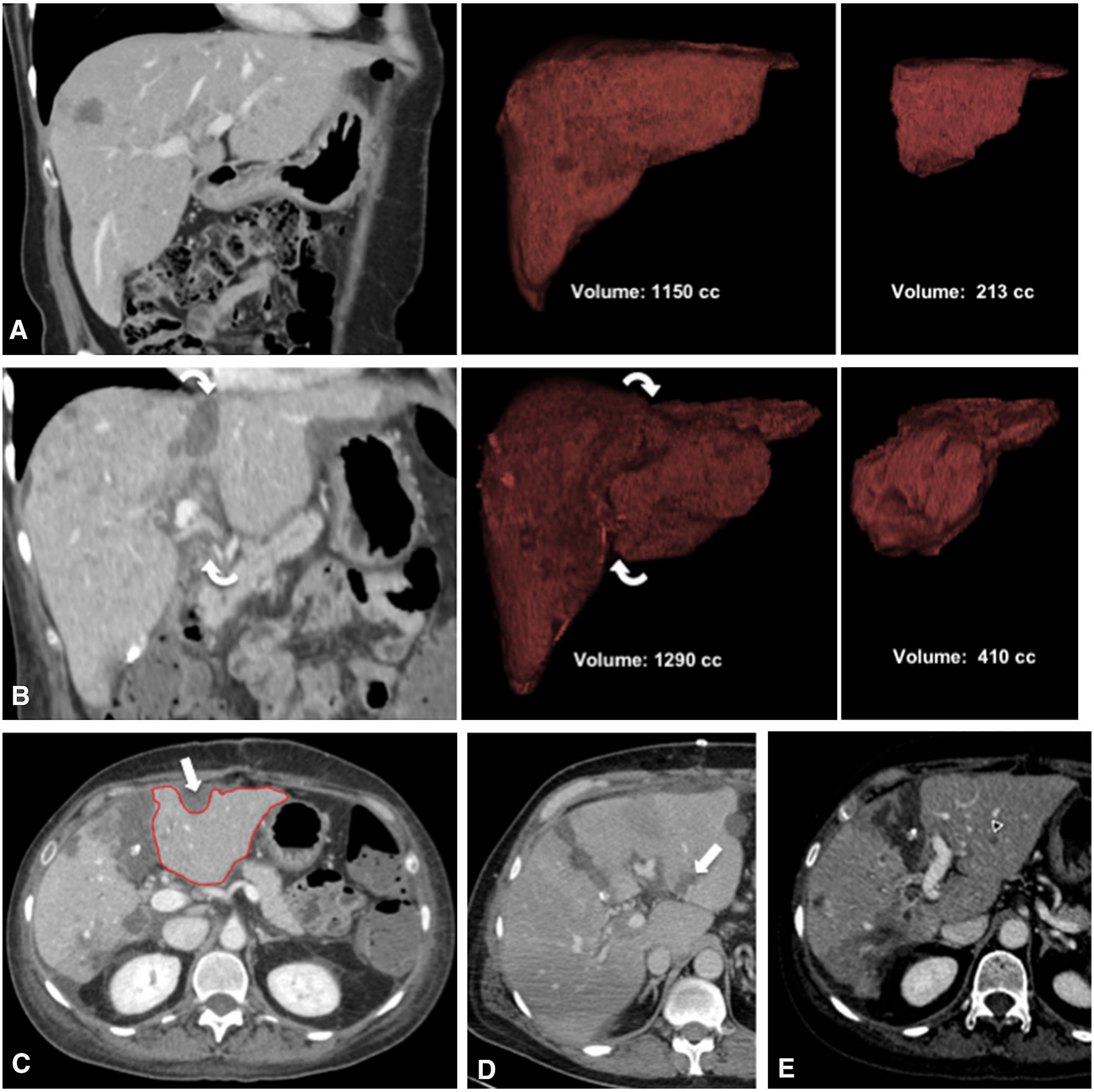

Fig. 5. Second imaging (IM2): recalculation of FLR and pitfalls: Prior to the second step, typically after 14 days, a second CT scan is performed. The total liver volume and the future liver remnant (FLR) volume are calculated, always in the portal venous phase. **A** Coronal image (A1) and 3D reconstructions indicate the total liver volume (A2) and FLR volume (A3) prior to ALPPS (IM1); here, the total liver volume was 1150 cm^3, and the remnant liver segments were 213 cm^3 in volume (19% of the total volume). **B** Coronal image (B1) and 3D reconstructions 14 days after ALPPS S1 (IM2) indicate an increase in the FLR volume, from 213 to 410 cm^3 (an increase of 92%, which represents 32% of the total liver volume). **C** Contours of the FLR segments (*red line*) with nodulectomies (*black arrow*) manually traced by a radiologist using a free-hand region of interest (ROI) method. **D** Axial CT-enhanced image with an ablation zone in the left lobe (*black arrow*). **E** Axial images indicate the progression of disease with the detection of a single lesion in the FLR. This patient was excluded from S2.

patients, and the average length of hospitalization was 10 days (7–15) for S1 and 14 days (6–16) for S2 (Table 1).The types of hepatic resection included 4 classical ALPPS cases, 3 right ALPPS variations, and 2 left ALPPS variations (Table 1). The number of liver lesions varied from 14 to 40 nodules, and all patients had 3–10 lesions in the remnant liver. All lesions were cleared in the first procedure through nodulectomies, and intra-

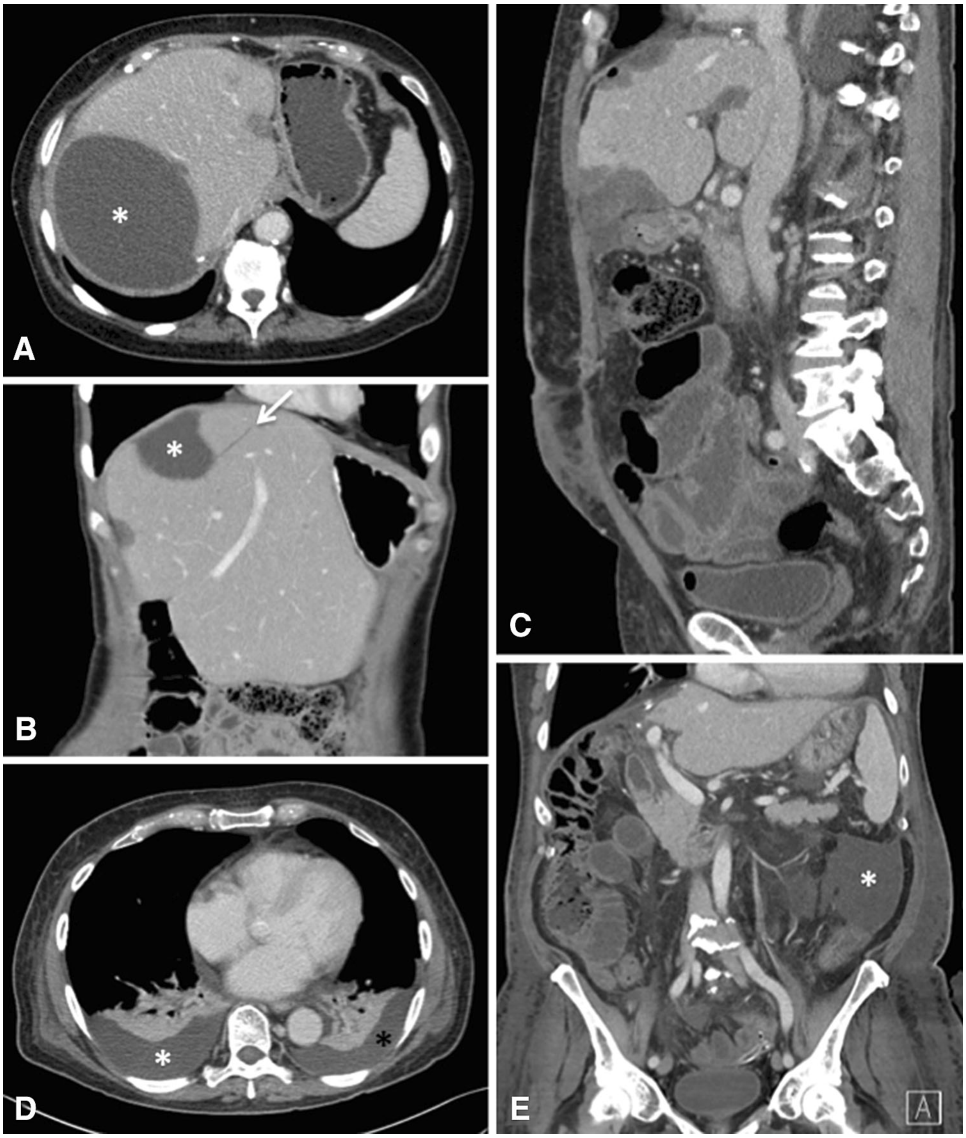

Fig. 6. Third imaging (IM3): complication assessment: postoperative CT scans are performed after the second surgery to identify potential complications: **A** axial-enhanced CT image of a 66-year-old woman with a biloma (*asterisk*). **B** Coronal-enhanced CT image of a 29-year-old woman with a biloma (*asterisk*) and a biliary fistula (*black arrow*). **C** Sagittal-enhanced image of a 66-year-old male with an adynamic ileum. **D** Axial-enhanced image of a 55-year-old woman with bilateral pleural effusion. **E** Coronal image of a 64-year-old female with ascites.

operative radiofrequency ablation was also used in two patients (Table 1).

The mean FLR volume calculated in IM1 was 453 mL (213–790 mL). Following the first surgery, the mean FLR volume increased to 634 mL (410–957 mL), which indicated a mean volume increase of 181.1 mL (95% CI 149.7–212.5 mL; $p < 0.001$) and a mean absolute volume increase of 48% (19%–88%) (Table 2).

One patient had progression in IM2, with the detection of a single lesion in the FLR; thus, the patient was excluded from S2 (Fig. 5D).

Following the completion of two surgical procedures in 8 patients (88%), all resections were considered R0.

The patients experienced grade I–IIIA complications, according to the Clavien–Dindo classification. Specifically, all patients had bilateral pleural effusion after S1. Moreover, after S2, one patient (11%) had an adynamic ileum, one patient (11%) had ascites, and there were 3 biliary fistulas (33%) (Fig. 6).

Discussion

The ALPPS technique has changed the resectability criteria for CRLM in recent years by enabling the removal of an extensive part of the liver in only two steps [1, 15, 18].

This method provides a strategy to induce faster and more marked FLR hypertrophy as well as a way to avoid PHLF following borderline liver resections [2, 8, 11, 16–19].

Despite initial promising results, a limited number of series and reports have been published regarding ALPPS, and most studies have comprised observational studies with small numbers of patients [1–3, 7, 8, 11–13, 15, 16, 18, 23]. The conclusions of a recent systematic review highlighted the importance of developing clear indications for ALPPS and the lack of consensus regarding technical aspects, which hampers reproducibility among centers [2]. None of these reports has emphasized a rational radiological approach for these patients, including patients undergoing classical ALPPS or its variations.

Table 1. Background characteristics of 9 ALPPS patients

Age, median (range), years	57 (29–66)
Sex, male, *n* (%)	5 (55%)
History of chemotherapy, yes, *n* (%)	9 (100%)
Hepatic lesions, median (range), *n*	
Remnant lobe	5 (3–10)
Total liver	26 (14–40)
Resections type	
Classical ALPPS, *n* (%)	4 (44%)
Right ALPPS variation, *n* (%)	3 (33%)
Left ALPPS variation, *n* (%)	2 (22%)
Time between ALPPS steps, median (range), weeks	3 (1–5)
Hospital stay, median (range), days	
First ALPPS First step	11 (7–12)
Second ALPPS Second step	16 (6–46)
Complications	
Pleural effusion, *n* (%)	9 (100%)
Adynamic ileum, *n* (%)	1 (11%)
Ascites, *n* (%)	1 (11%)
Biliary fistula, *n* (%)	3 (33%)

Table 2. Liver volume measurements for 9 ALPPS patients

Patient	IM1		IM2		FLR volume increase (%)
	Total liver volume	FLR volume	Total liver volume	FLR volume	
1	1910	562 (29%)	2240	790 (35%)	41
2	1599	323 (20%)	1710	520 (30%)	61
3	2034	547 (27%)	2160	747 (35%)	37
4	2800	790 (28%)	2901	957 (33%)	21
5	1797	479 (27%)	1850	570 (31%)	19
6	1352	241 (18%)	1563	453 (29%)	88
7	1150	213 (19%)	1290	410 (32%)	92
8	1567	520 (33%)	1550	708 (46%)	36
9	1562	400 (26%)	1650	550 (33%)	38
Median	1752	453 (25%)	1879	634 (34%)	48

The radiological report from IM1 is crucial to determine the surgical strategy [4]. In our series, there were 4 cases of classical ALPPS, which is considered a major surgery, with resection of segment IV and the right lobe. The first surgery in classical ALPPS consists of splitting the liver along the umbilical fissure, right PVL, and clearance of the lateral segments of the left lobe [1, 3, 10, 21]. A volumetric analysis should be conducted according to these parameters, and the main hallmark for calculating the preoperative FLR volume in IM1 is the left hepatic vein. One important issue in the postoperative FLR volume calculation in IM2 is that resected areas should not be considered in the ROIs, given that they are not considered as viable parenchyma. In classical ALPPS, the second surgical step is completed with a right trisectionectomy, and the FLR consists of segments I, II, and III [19, 23].

The right ALPPS variation consists of a right hepatectomy, with segments V, VI, VII, and VIII resected. The main difference compared with the classical ALPPS procedure is the sparing of segment IV. The radiological evaluations are basically the same; however, the hallmark for the volume calculation in IM1 is the middle hepatic vein. The second surgical step is completed with a right hepatectomy, and the FLR consists of the whole left lobe and caudate. This procedure is typically performed when there are many lesions within the left lateral segments and no lesion in segment IV [11, 18].

In our series, there was 1 left ALPPS variation, in which the remaining segments are VI and VII; this is also referred to as a left trisegmentectomy. This variation is performed as an exception when the left hilum or left hepatic vein is encased by the tumor [11, 18]. The margin of resection is wide, and a biloma is more likely than with a right trisegmentectomy.

In one case, the patient had multiple liver lesions and a single nodule that encased all three hepatic vein confluences. The patient was not initially considered a surgical candidate. However, the liver presented an anatomical variation, including an accessory portal branch to segment VI and an accessory right hepatic posterior vein that drained directly to the inferior vena cava. Following a new radiological evaluation, the clinical decision changed, and the patient underwent a successful modified ALPPS approach (monosegment ALPPS) [24] (Fig. 3).

In our study, the mean FLR hypertrophy percentage was 4%, which is significantly lower than the mean reported in a recent review by Hasselgren et al. (range between 65% and 110.3%); however, this value was sufficient to enable a definitive resection in 8 patients (88%). In the same review, the reported mortality rate was 9% which was higher than that observed in our series (0%) [25].

In the series presented here, only one patient did not undergo complete resection (S2) because IM2 detected a new small (0.5 cm) single lesion in the FLR, which was considered progression of the metastatic disease. Following PVO in a patient with bilateral liver metastasis, the risk of tumor progression is increased in the FLR, which results in an overall 52%–80% resection rate for traditional two-stage hepatectomy [26].

Therefore, the identification of new lesions in the FLR is a major concern in IM2 evaluation because tumor progression represents the main cause of an incomplete two-stage procedure [1, 4, 18]. However, this assessment may be challenging because there is a potential pitfall related to postoperative changes (nodulectomies and/or radiofrequency ablations). Consequently, the radiologist must be aware of the surgical planning to avoid misinterpretations.

In an initial study, Chan et al. demonstrated that liver MRI with hepatobiliary contrast-enhanced agents has a superior sensitivity (96%) and positive predictive value (PPV) (0.91) compared with MDCT or positron emission tomography (PET)/CT in patients with CRLM who are eligible for liver resection. Other studies have supported that enhanced MRI has superiority even for lesions smaller than 1 cm. In our series, all patients underwent liver MRI in IM1 following the MDCT evaluation to increase the detection of small lesions in the FLR. The ALPPS procedure is only recommended if R0 resection is possible; therefore, this approach is very useful and may potentially change the surgical strategy once peripheral lesions are resected, and the central nodules near the major vessels are treated via radiofrequency ablation (Fig. 5D). However, the cost–benefit ratio for performing a single evaluation of the whole abdomen with P-MRI remains unclear [27–29].

Volumetric calculation is operator dependent and crucial to prevent PHLF postsurgery. Therefore, this calculation must be performed only after the multidisciplinary oncology board establishes the surgical approach. The radiologist must precisely trace the ROIs according to the hallmarks for each strategy [2, 30, 31].

The present study was limited by the small number of cases. The number was small in part because ALPPS is an emerging technique performed at a limited number of oncology centers worldwide and is indicated only for a specific group of patients. However, in this series of CRLM cases, we demonstrated the major radiological aspects of classical ALPPS and its main variations.

Conclusion

In conclusion, the ALPPS procedure is an emerging two-stage hepatectomy, and the interpreting radiologist should provide crucial preoperative and perioperative information that may change the surgical planning and contribute to an improvement in the oncologic outcome.

Compliance with ethical standards

Conflict of interest All authors declare this that there is no conflict of interest in relation to this manuscript.

Disclosures The authors of this manuscript declare that they have no relationships with any companies, whose products or services may be related to the subject matter of the article. The authors also state that this work has not received any funding. Institutional Review bBoard approval was obtained. W, and the need for written informed consent was waived by the Institutional Review Board.

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Informed consent The institutional review board approved this HIPAA-compliant study and waived the need for informed consent.

Research involving animal and human rights 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. For this type of study, formal consent is not required. This article does not contain any studies with human participants or animals performed by any of the authors.

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