Published in final edited form as:

J Gastrointest Surg. 2015 January ; 19(1): 133–141. doi:10.1007/s11605-014-2617-y.

Volume Regeneration of Segment 2 and 3 after Right Portal Vein Embolization in Patients Undergoing 2-Stage Hepatectomy

Yoshihiro Mise¹, Thomas A. Aloia¹, Claudius Conrad¹, Steven Y. Huang², Michael J. Wallace², and Jean-Nicolas Vauthey¹

¹Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

²Department of Diagnostic Radiology, The University of Texas MD Anderson Cancer Center, Houston, TX

Abstract

Corresponding Author: Jean-Nicolas Vauthey, MD, Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Unit 1484, Houston, TX 77030. Tel: (713) 792-2022; Fax: (713) 745-1921; jvauthey@mdanderson.org.

Discussant: Dr. Chad G. Ball (Calgary, AB Canada)

Dr. Vauthey and his esteemed HPB team have provided the SSAT members with yet another detailed and technical approach to individualized hepatic oncology. More specifically, they outline the role of portal vein embolization (PVE) within the spectrum of 2-stage hepatectomies for colorectal metastases. The importance of this paper lies in 3 dominant conclusions: (1) the dynamics of liver regeneration are impaired in patients undergoing a 2-stage hepatectomy, (2) volume increases were negatively impacted following depending on the magnitude of the first-stage resection, and (3) a PVE that includes segment 4 buffers the inhibitory effect on hypertrophy of the first-stage resection.

This paper supports the importance of segment 4 embolizations, and continues to refine the dance we all find ourselves within regarding 2-stage resections. I have 3 questions:

1. Please discuss the mechanics of your team interaction with the interventional radiologists. Do you have a select IR team that does these interventions? What is their complication rate?
2. What percentage of patients at your center do not proceed to the second-stage despite interval PVE+4? Can we predict these patients in a reliable manner?
3. Does your team have any insight or further commentary on patients who have 'impaired' liver function (i.e. chemotherapy damage, fatty liver,...) in these scenarios?

Closing Discussant: Dr. Mise

Thank you, Dr. Ball, for your important questions. Our answers follow.

1. We now have 6 skilled interventional radiologists who can perform PVE, including right PVE extended to segment 4 (RPVE+4). Whether to perform segment 4 embolization is discussed in a multidisciplinary team conference; the decision is based on tumor distribution and future liver remnant volume. Complications following PVE occurred in 6 patients (5%) undergoing single-stage hepatectomy and 1 patient (2%) undergoing 2-stage hepatectomy ($p = 0.43$).
2. In this study, 12 of 28 patients (43%) who underwent interval right PVE+4 did not complete second-stage hepatectomy. However, in only 1 patient (4%) did insufficient volume increase preclude the second-stage procedure; the majority of failures were due to short-interval progression of disease. It is certainly important to prevent patient dropout due to insufficient volume regeneration by technical refinements such as RPVE+4. However, we still believe that the test of time to optimize patient selection is one of the advantages of two-stage hepatectomy, considering the high short-term recurrence rate observed with the ALPPS (associating liver partition and portal vein ligation for staged hepatectomy) approach (Oldhafer et al. *World J Surg* 2014; 38: 1504-1509, Sala S et al. *Updates Surg* 2012;64: 167-172).
3. Volumetric analysis has dramatically improved the safety of liver surgery. However, as Dr. Ball points out, we now need to care for patients with various causes of liver impairment, and the conventional static volume assessment may not be adequate because the degree of liver impairment has yet to be clarified based on the causes of impairment. We recently reported that the magnitude and speed of liver growth after PVE (kinetic growth rate [KGR]) predicted postoperative outcomes in patients undergoing major hepatectomy better than static volume assessment did. Further investigation of reliable volumetric benchmarks may be needed to catch up with the changing causes of liver impairment.

Background—The impact of first-stage resection on volume regeneration of segment 2 and 3 (2+3) after right portal vein embolization (RPVE) in patients undergoing 2-stage right hepatectomy has not been investigated.

Method—Volume data for segments 2+3 were compared between 44 patients undergoing 2-stage hepatectomy and 116 undergoing single-stage hepatectomy after RPVE.

Results—Degree of hypertrophy (difference between standardized volume of segments 2+3 before and after RPVE) and kinetic growth rate (degree of hypertrophy at initial volume assessment divided by the number of weeks elapsed after RPVE) were significantly lower in patients undergoing 2-stage hepatectomy (median 8.6% vs 10.5% [$p=0.01$] and 1.7% vs 2.4% [$p<0.01$], respectively). Resection volume during first-stage resection was negatively correlated with standardized volume increase from the volume before first-stage resection (R^2 : 0.546, $p<0.01$). In patients undergoing 2-stage hepatectomy after RPVE with segment 4 embolization, degree of hypertrophy and kinetic growth rate were similar to those in patients undergoing single-stage hepatectomy ($p=0.17$ and $p=0.08$, respectively).

Conclusion—In patients undergoing 2-stage hepatectomy, first-stage resection impairs the dynamics of volume regeneration of segments 2+3 after RPVE. When 2-stage extended right hepatectomy is planned, additional embolization of segment 4 provides volume hypertrophy similar to that in patients undergoing single-stage hepatectomy.

Keywords

Liver Regeneration; Colorectal Neoplasms; Hepatectomy

Introduction

Liver resection is the mainstay of treatment for colorectal liver metastases (CLM), providing long-term survival and in some cases cure of the disease. However, the majority of patients with CLM present with unresectable disease at diagnosis.[1, 2] The current issue in the treatment of CLM is how to refine multidisciplinary approaches to expand the proportion of patients who are candidates for liver resection.

Two-stage hepatectomy is a modern strategy for resection of extensive bilateral CLM that cannot be resected by conventional single-stage resection.[1, 3-8] An interval between first-stage tumor clearance in the future liver remnant (FLR) and staged resection expands technical resectability in patients with insufficient FLR by inducing hypertrophy of FLR. To accelerate the interval hypertrophy, portal vein occlusion technique plays an important role in 2-staged major resection. Recent reviews demonstrated that more than 70% cases of 2-stage hepatectomy combine this technique, preferring portal vein embolization (PVE) after first-stage resection,[7] which enables additional embolization of segment 4 when performing 2-stage extended right hepatectomy.[4, 7, 9-11]

Increasing evidence has demonstrated the safety and efficacy of PVE in patients undergoing 2-stage hepatectomy.[4, 6, 7, 12, 13] However, it remains uncertain how first-stage resection for tumor clearance in the FLR influences the dynamics of volume regeneration of the FLR after PVE. We previously reported that the magnitude and speed of liver growth after PVE

are good predictors of postoperative outcomes in patients undergoing liver resection following PVE.[14, 15] The impact of first-stage resection on liver volumetric change in patients undergoing 2-stage hepatectomy needs to be clarified to improve not only the technical resectability but also the overall safety of the aggressive surgical approach.

The aim of this study was to determine the impact of first-stage resection on the dynamics of volume regeneration of the FLR after right PVE (RPVE) in patients undergoing 2-stage right hepatectomy (RH). We compared volumetric data for segment 2 and 3 (S2+3) between patients undergoing 2-stage RH after RPVE and patients undergoing single-stage RH after RPVE.

Patients and Methods

The Institutional Review Board of The University of Texas, MD Anderson Cancer Center approved this study protocol. The prospectively maintained liver resection database of the Department of Surgical Oncology was queried to identify 208 patients who underwent RPVE prior to liver resection for CLM during the period from September 1999 through August 2012. Of these 208 patients, 47 did not have volumetric data available for S2+3, either because single-stage RH was planned and the volume of S2+3 was not separately calculated ($n = 21$), or because computed tomography (CT) imaging was not performed after first-stage resection in 26 patients undergoing 2-stage RH. One patient who underwent complete resection of S2+3 prior to 2-stage RH was also excluded. The remaining 160 patients constituted the study cohort. Forty-four patients underwent RPVE after first-stage resection as part of 2-stage RH and 116 underwent RPVE prior to planned single-stage RH.

Right Portal Vein Embolization

All patients with potentially resectable disease underwent liver volumetry based on CT imaging, and standardized total liver volume (sTLV) was estimated according to the method described previously.[16, 17] PVE was considered when standardized FLR was less than 20% in patients with normal liver or less than 30% in patients with impaired liver function. All embolizations were performed with the ipsilateral percutaneous transhepatic approach using tris-acryl microspheres. When extended right hepatectomy was planned, RPVE extended to segment 4 branches (RPVE+4) was performed.

Two-Stage Right Hepatectomy

2-stage RH was planned in patients with advanced bilateral CLM in whom first-stage limited resection could clear the tumors in the left liver before the patient underwent a planned right hepatectomy. In patients undergoing 2-stage RH, RPVE was performed after first-stage resection, and then RH was performed when sufficient volume regeneration was confirmed without tumor progression. To avoid the risk associated with extended chemotherapy, interval chemotherapy was not used routinely.[1] In patients undergoing 2-stage RH, baseline CT volumetry was conducted after first-stage resection.

Volumetric Analysis (Figure 1)

1) Post-RPVE evaluation of hypertrophy—All patients underwent 3 dimensional CT volumetry 2 to 8 weeks after RPVE to assess the extent of liver hypertrophy. Degree of hypertrophy (DH) of S2+3 was defined as the percentage-point difference between volume of S2+3 / sTLV before and after RPVE. Kinetic growth rate (KGR) of S2+3 was calculated using the following formula: $KGR = \text{DH at first post-RPVE volume assessment (\%)} / \text{time elapsed since RPVE (weeks)}$ at first post-RPVE volume assessment (Figure 1). Hypertrophy rate of S2+3 was also calculated using the following formula: $\text{Hypertrophy rate} = (\text{post-RPVE volume of S2+3} - \text{pre-RPVE volume of S2+3}) / \text{pre-RPVE volume of S2+3 (\%)}$. If hypertrophy at the volume assessment was insufficient to the above-mentioned criteria, serial volumetry and assessment of disease progression were performed based on CT imaging.

2) Impact of resection volume during first-stage resection on liver regeneration after RPVE—To assess the impact of resection volume during first-stage resection on liver regeneration after RPVE, the correlation between resection volume of S2+3 during first-stage resection and DH was analyzed. Resection volume during first-stage resection was calculated by the following formula: $\text{Resection volume} = \text{volume of S2+3 before first-stage resection} - \text{volume of S2+3 before RPVE}$. The tumor volume was excluded from volume of S2+3 before first-stage resection. Degree of hypertrophy of S2+3 from the status prior to first-stage resection (DH_0) was defined as the percentage-point difference between the volume of S2+3 / sTLV before first-stage resection and after RPVE (Figure 1).

Statistical Analysis

Background patient characteristics and volumetric data were compared between patients undergoing 2-stage RH and single-stage RH. Categorical variables were compared using the chi-squared test. Continuous variables were compared using the Mann–Whitney U test and expressed as median (range). $P < 0.05$ was considered statistically significant.

To identify predictors of DH and KGR, the following clinicopathological variables were evaluated in a univariate proportional hazards models: age (< 65 years vs > 65 years), sex, body surface area (< 2.0 vs ≥ 2.0 m²), body mass index (< 25 vs ≥ 25 kg/m²), American Society of Anesthesiologists score (< 3 vs ≥ 3), the presence of diabetes mellitus, the presence of hepatitis B or C, administration of 2-stage RH, administration of RPVE+4, the presence of RPVE complication, duration of pre-RPVE chemotherapy (≤ 12 weeks vs > 12 weeks), administration of cytotoxic drug (oxaliplatin, irinotecan), administration of targeted agents (bevacizumab, cetuximab or panitumumab), history of previous hepatectomy for CLM, and the presence of background liver damage (fibrosis [F1-4], $> 30\%$ steatosis, or moderate to severe sinusoidal injury). All variables associated with $p \leq 0.1$ in the univariate analysis were subsequently entered into a Cox multivariate regression model with backward elimination. The Student t test and Pearson correlation coefficient were used to investigate the impact of resection volume during first-stage resection on liver regeneration after RPVE. $P < 0.05$ was considered statistically significant.

Results

Clinicopathologic Characteristics

Clinicopathologic characteristics of the single-stage and 2-stage RH groups are summarized in Table 1. No patients in the 2-stage RH group had diabetes mellitus, whereas 12% of patients in the single-stage RH group did ($p=0.01$). The presence of background liver damage was not available in 14 patients in the single-stage RH group who did not undergo liver resection. In the 2-stage RH group, for first-stage resection, the median number of limited resections performed was 2 (range, 1-5). The median hospital stay was 6 days (range, 3-13 days). One patient developed a postoperative pleural effusion that necessitated thoracentesis. No other patient had a major complication as defined by Dindo classification ($>$ grade II) after first-stage resection.[18]

Volumetric Data

Volumetric data for S2+3 are presented in Table 2. DH and KGR values for both groups are plotted in Figure 2. The interval between RPVE and final CT volumetry assessment was significantly longer in the 2-stage RH group than the single-stage RH group ($p<0.01$). Although the pre-RPVE volumetric data for S2+3 were similar for the 2 groups, DH and KGR were significantly lower in the 2-stage RH group than in the single-stage RH group ($p=0.01$ and $p<0.01$, respectively).

Predictors of the Dynamics of Volume Regeneration

Table 3 summarized the results of multivariate analysis of predictors of the dynamics of volume regeneration of S2+3 in 146 patients whose background liver status was available. 2-stage hepatectomy was found to be a significant predictor of low DH ($p<0.01$, HR: 1.90, CI: 1.27-2.82) and low KGR ($p<0.01$, HR: 1.85, CI: 1.24-2.73). Segment 4 embolization was a significant predictor of both higher DH and higher KGR ($p<0.01$, HR: 2.44, CI: 1.61-3.71, and $p<0.01$, HR: 2.49, CI: 1.64-3.78, respectively).

Impact of Segment 4 Embolization in Patients Undergoing 2-stage RH

Volumetric data of patients in the 2-stage RH group with and without segment 4 embolization were compared to those of the single-stage RH group (Figure 3). In patients in the 2-stage RH group who underwent RPVE+4 ($n=28$), median DH and KGR were not significantly different from those in patients in the single-stage RH group (8.8% vs 10.5% [$p=0.17$], 1.6% vs 2.4% [$p=0.08$], respectively). In contrast, in patients in the 2-stage RH group who underwent RPVE without segment 4 embolization, both DH and KGR were lower than those in the single-stage RH group (7.7% vs 10.5% [$p=0.02$], 1.4% vs 2.4% [$p<0.01$], respectively). No significant differences were found in DH and KGR between patients in the 2-stage RH group with or without segment 4 embolization ($p=0.26$ and $p=0.30$, respectively).

Relationship between Resection Volume during First-Stage Resection and Volume Regeneration

Resection volume during first-stage resection is plotted against DH_0 and DH in Figure 4. A negative correlation was found between resection volume and DH_0 in the 2-stage RH group overall (R^2 : 0.546, $p < 0.01$, $y = -0.842x + 7.87$). The gradient in the correlation between resection volume and DH_0 was double in patients without segment 4 embolization (R^2 : 0.811, $p < 0.01$, $y = -1.357x + 8.74$), what it was in patients with RPVE+4 (R^2 : 0.479, $p < 0.01$, $y = -0.677x + 7.74$). No significant correlation was found between resection volume and DH in the 44 patients in the 2-stage RH group overall (R^2 : 0.048, $p = 0.16$, $y = 0.145x + 6.44$) and in the 16 patients without segment 4 embolization (R^2 : 0.229, $p = 0.07$, $y = -0.307x + 7.34$). However, a positive correlation between resection volume and DH was found in patients with RPVE+4 (R^2 : 0.200, $p = 0.02$, $y = 0.292x + 6.25$).

Discussion

We investigated the impact of first-stage partial hepatectomy on volume regeneration of S2+3 after RPVE in patients undergoing 2-stage RH. The following 3 findings were observed in this study. First, the dynamics of volume regeneration estimated by DH and KGR were impaired in patients undergoing 2-stage RH, compared with those in patients undergoing single-stage RH. Second, pure volume increase from the volume before first-stage resection was negatively correlated with first-stage resection volume. Third, in patients undergoing 2-stage RH, RPVE+4 compensated for the negative impact of first-stage resection, inducing hypertrophy similar to that in patients undergoing single-stage RH. These findings indicate that a parenchymal-sparing approach should be used during first-stage resection and that additional embolization of segment 4 needs to be performed when 2-stage extended right hepatectomy is planned to achieve favorable growth of S2+3.

Although it is well established that partial hepatectomy induces hypertrophy of the liver, [19-28] we found that partial hepatectomy of the FLR prior to PVE did not accelerate but rather impaired hypertrophy induced by PVE. This finding can be explained by 3 separate findings previously reported in the literature. First, the effect of liver regeneration after hepatectomy is to revert the volume to the preoperative status, not to surpass the original volume.[19, 21, 23, 24] Second, complete regeneration of the resected liver generally takes 6 months [23, 28] to 1 year [25, 26] after surgery. Finally, a positive correlation has been found between resection volume and hypertrophy of the liver after hepatectomy, and a small resection does not trigger liver hypertrophy.[21-23, 29, 30] On the basis of these previously reported findings, the reported interval of 3 months between first-stage and second-stage hepatectomy may not be sufficient to allow the liver to fully recover from the previous hepatectomy in terms of volume regeneration,[4, 7] and the small resection volume during first-stage resection, generally less than 10% of sTLV (Figure 4), does not trigger hypertrophy after liver resection nor accelerate the effect of PVE. Further investigation at a molecular level needs to be conducted to clarify the mechanism of impairment of volume regeneration after PVE in patients undergoing 2-stage RH because sound hypertrophy after PVE is the key to completing the procedure and lowering morbidity.

Our finding that resection volume during first-stage resection negatively correlated with degree of hypertrophy estimated from the status before first-stage resection in patients undergoing 2-stage RH has a clinical implication. Specifically, when we plan the strategy for 2-stage procedures, we anticipate the volume increase induced by RPVE on the basis of the imaging before first-stage resection. If large parenchymal loss is inevitable because of the need to remove centrally located tumors or multiple tumors, we need to estimate less volume increase induced by RPVE. Furthermore, during first-stage resection, a parenchymal-sparing approach needs to be used to maximize the effect of portal vein manipulation.

Additional segment 4 embolization during RPVE offset the negative impact of first-stage resection, inducing volume regeneration of S2+3 similar to that in patients undergoing single-stage RH. The trophic effect of RPVE+4 on volume regeneration of S2+3 has been clarified previously.[9, 10, 31] The current study went a step further by focusing on patients undergoing 2-stage hepatectomy, and revealed that the additional embolization halved the negative effect of the resection volume during first-stage resection on DH_0 (Figure 4A). In addition, volume increase from the status after first-stage resection can be boosted by RPVE +4 with a positive correlation with resection volume (Figure 4B). The boosting effect becomes important when first-stage hepatectomy entails large parenchymal loss to accomplish radical clearance of tumors in the FLR. Although the pure increase from the status before first-stage resection (DH_0) diminishes according to resection volume, RPVE+4 compensates for the loss of liver volume by accelerating hypertrophy induced by RPVE. On the basis of these findings, additional embolization of segment 4 needs to be performed when 2-stage extended right hepatectomy is planned and when first-stage resection removes large parenchyma in the FLR to achieve favorable growth of S2+3. We previously reported the safety of segment 4 embolization both in single- and 2-stage hepatectomy.[9, 12] However, specialized expertise is needed to accurately embolize segment 4 branches while preserving non-targeted portal vein. Technological advances may overcome this problem. We have recommended the use of C-arm CT to help with the acquisition of angiographic and 3-dimensional images.[9, 32]

Multivariate analysis in patients undergoing RPVE revealed that 2-stage hepatectomy and RPVE without embolization of segment 4 were procedure-related risk factors impairing DH and KGR of S2+3 after RPVE. Several authors have reported factors predictive of liver regeneration following PVE, such as pre-PVE FLR volume,[20, 29] receipt of chemotherapy,[33] and functional hepatic reserve.[33, 34] However, their analyses were based on the hypertrophy rate of the FLR (increase of FLR/pre-PVE FLR). In contrast, we investigated predictors including administration of 2-stage hepatectomy based on DH (increase of standardized volume of S2+3) and KGR (DH at first assessment/time elapsed since PVE) because these kinetic profiles are able not only to evaluate the trophic effects of PVE but also to predict postoperative morbidity and mortality after major hepatectomy.[14, 15] In the clinical setting, assessment of volume regeneration after PVE is based on the pure increase in the volume of the FLR, not on the rate of the increase. Hence, the prediction of these kinetic profiles would be clinically relevant to optimize the strategy for 2-stage RH combined with PVE.

The limitations of this study include its retrospective nature and the small number of patients in the 2-stage RH group (n = 44). Differences in tumor burden between single- and 2-stage RH groups, which were not assessed in this study, may have affected volume regeneration after RPVE. In addition, comparison between RPVE and RPVE+4 in the 2-stage RH group did not show significant differences in volumetric parameters because of the small number of patients in each group as we previously reported.[12] This study focused on investigating the impact of first-stage resection on volume regeneration after PVE, comparing parameters between patients with and without first-stage resection. Then, sub-analysis of the 2-stage RH group revealed the effect of RPVE+4, which is one of the key procedures in 2-stage RH. Further investigation needs to be conducted to confirm the findings of this study because the effect of RPVE+4 demonstrated in this study can increase the completion rate of 2-stage extended right hepatectomy, which provides an excellent prognosis in patients with extensive bilateral CLM.[1, 8]

Conclusion

In conclusion, first-stage partial hepatectomy had a negative impact on volume regeneration of S2+3 after RPVE in patients undergoing 2-stage RH. When 2-stage extended right hepatectomy is planned, additional embolization of segment 4 provides volume regeneration similar to that in patients undergoing single-stage hepatectomy.

Acknowledgments

The authors would like to recognize Ms. Ruth Haynes for administrative support in the preparation of this manuscript.

Sources of Support: This paper was presented at the 54th annual meeting of the Society for Surgery of the Alimentary Tract, May 3-6, 2014, Chicago, IL, USA.

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Figure 1.

Volumetric analysis in patients undergoing 2-stage right hepatectomy RPVE = Right portal vein embolization, DH_0 = Degree of hypertrophy estimated from the volume before 1st-stage hepatectomy, DH = Degree of hypertrophy, KGR = Kinetic growth rate

Figure 2.
Degree of hypertrophy (A) and kinetic growth rate (B) of segment 2+3 in patients undergoing single-stage and 2-stage right hepatectomy (RH).

Figure 3.

Degree of hypertrophy (A) and kinetic growth rate (B) of segment 2+3 in patients undergoing single-stage and 2-stage right hepatectomy (RH) with right portal vein embolization (RPVE) or RPVE extended to segment 4 branches (RPVE+4).

Figure 4.

Correlation between resection volume during first-stage hepatectomy and liver regeneration after portal vein embolization (PVE) in patients undergoing 2-stage right hepatectomy (RH) with right portal vein embolization (RPVE) or RPVE extended to segment 4 branches (RPVE+4).

A) Correlation between resection volume and degree of hypertrophy after PVE estimated from the status before first-stage hepatectomy (DH₀). 2-stage RH = overall 44 patients who underwent 2-stage right hepatectomy (R^2 : 0.546, $p < 0.01$). RPVE = 16 patients who underwent right portal vein embolization (R^2 : 0.811, $p < 0.01$), RPVE+4 = 28 patients who underwent right portal vein embolization and additional segment 4 embolization (R^2 : 0.479, $p < 0.01$).

B) Correlation between resection volume and degree of hypertrophy estimated from the status before PVE (DH). 2-stage RH group (R^2 : 0.048, $p = 0.16$), RPVE (R^2 : 0.229, $p = 0.07$), RPVE+4 (R^2 : 0.200, $p = 0.02$).

Table 1
Background characteristics of patients undergoing single-stage and 2-stage right hepatectomy after RPVE

	Single-stage n=116	Two-stage n=44	p value
Patient-related			
Age, median (range), y	57 (34-81)	53 (33-86)	0.02
Male, n (%)	86 (74)	27 (61)	0.14
Body height, median (range), cm	172 (149-192)	172 (141-188)	0.86
Body weight, median (range), kg	84 (47-127)	81 (55-131)	0.88
Body surface area, median (range), m ²	2.0 (1.4-2.5)	2.0 (1.6-2.5)	0.99
Body mass index, median (range), kg/m ²	27.0 (17.1-46.5)	26.0 (20.2-42.5)	0.82
ASA score >2, n (%)	95 (82)	37 (84)	0.74
Diabetes mellitus, n (%)	14 (12)	0 (0)	0.02
HBs antigen, n (%)	1 (1)	0 (0)	0.54
HCV antibody, n (%)	1 (1)	0 (0)	0.54
Treatment-related			
Segment 4 embolization, n (%)	74 (64)	28 (64)	0.99
PVE complication, n (%)	6 (5)	1 (2)	0.43
Duration of chemotherapy, median (range), wk	12 (0-56)	12 (0-48)	0.58
Oxaliplatin, n (%)	85 (73)	35 (80)	0.41
Irinotecan, n (%)	24 (21)	10 (23)	0.78
Bevacizumab, n (%)	74 (64)	36 (82)	0.03
Cetuximab or Panitumumab, n (%)	7 (6)	5 (11)	0.25
Previous hepatectomy, n (%)	7 (6)	1 (2)	0.32
Background liver status ^a			
Fibrosis, F1-4, n (%)	14 (14)	2 (5)	0.10
Steatosis>30%, n (%)	11 (11)	6 (14)	0.67
Sinusoidal injury, moderate to severe, n (%)	7 (7)	2 (5)	0.55

RPVE, right portal vein embolization; ASA, American Society of Anesthesiologists; HBs Ag, hepatitis B surface antigen; HCV, hepatitis C virus.

^aThe presence of background liver damage was not available in 14 patients in the single-stage right hepatectomy group who did not undergo liver resection.

Table 2
Volumetric data for segment 2 and 3 (S2+3) in patients undergoing single-stage and 2-stage right hepatectomy after RPVE

	Single-stage (n=116)	Two-stage (n=44)	<i>p</i> value
Pre-RPVE S2+3 volume, median (range), mL	258 (71-556)	224 (31-474)	0.11
Pre-RPVE S2+3 volume/ sTLV, median (range), %	15.5 (8.9-31.9)	13.0 (5.9-28.4)	0.08
Interval between RPVE and final CT, median (range), wk	4.4 (2.6-36.3)	5.4 (2.7-37.0)	<0.01
Degree of hypertrophy of S2+3, median (range), %	10.5 (0.1-43.9)	8.6 (0.8-19.6)	0.01
Kinetic growth rate of S2+3, median (range), %/wk	2.4 (0.1-7.8)	1.7 (0.2-4.5)	<0.01
Hypertrophy rate, median (range), %	61.9 (0.6-168.1)	54.3 (3.7-394.7)	0.24

RPVE, right portal vein embolization; sTLV, standardized total liver volume

Table 3

Factors influencing volume regeneration after RPVE

		DH, median(range)	Univariate	Multivariate		KGR, median (range)	Univariate	Multivariate				
				HR	95%CI			HR	95%CI			
Two-stage hepatectomy	-	11.0	0.1-43.9	<0.01	1.90	1.27-2.82	2.5	0.1-7.8	<0.01	1.85	1.24-2.73	
	+	8.6	0.8-19.6				1.6	0.2-5.5				
Body surface area	<2.0	10.7	1.8-43.9	0.04			2.4	0.4-7.8	<0.01	1.67	1.13-2.49	
	2.0	8.5	0.1-28.3				2.0	0.1-5.4				
Segment 4 embolization	+	11.0	0.1-43.9	<0.01	2.44	1.61-3.71	2.6	0.1-7.8	<0.01	2.49	1.64-3.78	
	-	7.6	0.8-19.4				1.8	0.2-5.3				
Previous hepatectomy	-	9.9	0.1-43.9	0.08	0.04	2.50	1.02-5.24	2.2	0.1-7.8	0.33		
	+	7.3	5.1-11.1				2.3	1.3-3.1				
Mod-severe sinusoidal injury	-	9.7	0.1-43.9	0.08	0.02	2.63	1.18-5.29	2.2	0.1-7.8	0.04	2.85	1.29-5.58
	+	6.0	1.6-14.4				1.0	0.4-3.3				

RPVE, right portal vein embolization; DH, degree of hypertrophy of segment 2+3; HR, hazard ratio; KGR, kinetic growth rate of segment 2+3