Preoperative Locoregional Therapy With Portal Vein Embolization Does Not Increase the Risk of Postoperative Complications After Hepatectomy

Andrew R. Kolarich, MD[1]; Ved Tanavde, BS[2]; Alex Solomon, MD[3]; Matthew Weiss, MD[1]; Benjamin Philosophe, MD, PhD[1]; Christos S. Georgiades, MD, PhD[3]; Kelvin Hong, MD[3]

Abstract

Purpose. Prior analyses of the National Surgery Quality Improvement Program (NSQIP) as well as single-institution studies have resulted in differing post-hepatectomy complication rates after portal vein embolization (PVE), including liver failure. We sought to determine if PVE, either alone or combined with locoregional treatment (LRT) (ablation, arterial infusion/chemoembolization, etc) increases post-hepatectomy complications. **Methods.** NSQIP standard data files from 2014-2016 were combined with hepatectomy procedure-targeted datasets. A matched propensity-score analysis was constructed utilizing age, gender, principal procedure, pathologic indication, preoperative systemic chemotherapy, hepatitis status, preoperative platelets and bilirubin, operative approach, biliary reconstruction, Pringle maneuver, drains left during the procedure, and liver texture. Finally, patients who underwent PVE alone vs PVE in addition to locoregional therapy (LRT) were compared. **Results.** A total of 11,243 patients underwent hepatic resection. Of these patients 427 (3.9%) underwent PVE, 157 (1.4%) underwent LRT alone, and 35 (0.3%) underwent PVE + LRT. There was no significant difference in the no-PVE and PVE groups in likelihood of postoperative liver failure (12.8% vs 17.1%; P=.15) or 30-day mortality (2.7% vs 2.6%; P=.90). Additionally there was no difference in acute renal failure, deep vein thrombosis, sepsis, days until discharge, return to the operating room, or unplanned readmissions. However, PVE was associated with an increased likelihood of postoperative transfusion (33.3% vs 23.7%; P=.01). There were no significant differences in any postoperative complications including transfusion in the PVE group vs the PVE + LRT group. **Conclusion.** Utilizing a large national database, our analysis suggests that postoperative PVE is not associated with significantly increased rates of postoperative liver failure or 30-day mortality. However, there was a slightly higher risk of blood transfusion in patients undergoing PVE vs those who did not. There does not appear to be an added increased risk of complications with the addition of LRT prior to PVE.

IO LEARNING 2022(10):E20-E29. Epub 2022 August 12.

Key words: hepatectomy, locoregional therapy, NSQIP, portal vein embolization

Liver resection for hepatic tumor was first performed in 1888.[1] Mortality rates remained high for almost a century, with operative mortality of more than 20% as late as the 1980s.[2] In recent decades, hepatic resection has emerged as an effective and much safer treatment for primary and metastatic liver malignancies, with mortality rates of less than 5%.[2,3] However, post-hepatectomy liver failure (PHLF), the most severe complication, has been shown to be associated with mortality as high as 50% and is the main cause of mortality following hepatic resection.[4-6]

The risk of PHLF is associated with both decreased volume and decreased function of future liver remnant (FLR).[7,8] Smaller or dysfunctional liver remnant prevents sufficient liver regeneration and places patients at increased risk for serious complications. In patients without chronic liver disease, PHLF occurs in roughly 5% of patients, rising to more than 20% in cirrhotic patients.[9,10] The minimum safe volume of FLR is considered to be between 20% and 30% in patients without chronic liver disease, with minimum FLR of

40% recommended for patients with cirrhosis or prolonged biliary obstruction.[6,8,11]

For patients who would have FLR volume below these recommended values post hepatectomy, portal venous embolization (PVE) may be utilized before resection in order to induce regrowth or "hypertrophy" of the liver remnant. This involves the introduction of microbeads via catheterization of the portal vein by an interventional radiologist on the side of the liver containing the greatest margins of tumor, redirecting blood to and resulting in hyperplasia of the contralateral lobe. Although increased FLR volume after PVE has been well established, with a clinical success rate of 96.1%, there is controversy over short-term safety and whether this increased volume is associated with improved liver function.[12-14] Previous studies have shown PVE to be associated with increased albumin uptake and enhanced biliary excretion.[15,16] A 2008 meta-analysis of 37 studies and 1088 patients demonstrated an overall morbidity rate of 2.2%, although other smaller-scale studies have reported rates as high as 12% and 15%, and 0% mortality rate.[11,13,17-19]

The addition of locoregional therapy (LRT), such as chemoembolization and image-guided ablation, has been utilized to provide the combined benefits of antitumor effect and liver hypertrophy. As liver tumors typically draw their blood supply from the hepatic artery, chemoembolization involves transcatheter delivery of chemotherapy through the hepatic artery of the lobe containing hepatic tumor.[20] A 2011 study by Yoo et al showed significantly increased FLR and decreased incidence of hepatic failure in patients receiving combination therapy as opposed to PVE alone, although there is a paucity of literature comparing outcomes of PVE alone vs PVE in combination with LRT prior to hepatic resection.[21]

The National Surgical Quality Improvement Program (NSQIP) Participant User Files (PUFs) contain deidentified clinical data and quality measures from millions of cases across more than 500 hospitals. Our retrospective study is the largest to date for the evaluation of clinicodemographic differences and postoperative outcomes in patients who received PVE vs patients who did not prior to hepatic resection. Additionally, we report results after comparing demographic and clinical data in patients who received PVE + LRT and patients who received only PVE prior to hepatic resection.

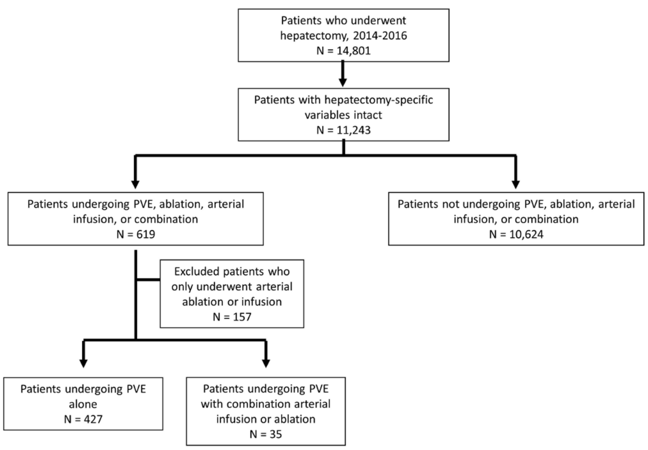

FIGURE 1. CONSORT diagram.

Methods

The NSQIP standard PUFs from 2014-2016 were obtained along with hepatectomy procedure-targeted datasets for retrospective review. Patients were first selected by their hepatectomy-specific CPT codes for wedge resection (47120), trisegmentectomy (47122), total left lobectomy (47125), and total right lobectomy (47130). We refer to trisegmentectomy as extended lobectomy, which by convention can refer to either left extended hepatectomy or right extended hepatectomy. The 2 datasets were subsequently merged using the unique patient identification number, resulting in 14,801 cases. Patients with missing hepatectomy-specific variables were then excluded, resulting in a total of 11,243 patients. Finally, patients were stratified by receiving preoperative PVE, and later stratified further if they underwent PVE along with either ablation or chemoembolization as recorded in the neoadjuvant therapy type variable. The study's CONSORT diagram is illustrated in **Figure 1**.

Next, a population analysis of clinical and preoperative factors on patients undergoing PVE preoperatively vs those who did not was performed; for this analysis patients who received both PVE and LRT were excluded. Throughout the analysis, missing variables were excluded by variable recoding. Because there were significant differences in preoperative factors suggestive that certain preoperative factors were more likely to predispose to PVE, a propensity-score analysis was constructed using all variables that were determined to be significantly different between patients who underwent PVE vs those who did not. Subsequently, the same clinicodemographic factors were compared using the new matched propensity cohort, demonstrating no significant difference between the groups (defined as $P<.05$). Following this, the following postoperative variables were isolated: days from operation to discharge; intraoperative or postoperative transfusion requirement; acute renal failure; deep venous thrombosis (DVT); septic shock; unplanned return to the operating room; unplanned readmission after discharge; PHLF; and 30-day mortality.

Next, only patients who underwent PVE were isolated and those who underwent both PVE and preoperative LRT were identified again using the neoadjuvant therapy type variable. Locoregional treatment types were identified as "locoregional arterial infusion" and "locoregional ablation" and combined; patients who only underwent LRT without PVE were excluded. Clinicodemographic variables were compared. Because no significant differences between patients undergoing PVE alone vs PVE with preoperative LRT were found, propensity-score matching

TABLE 1. Comparison of clinicodemographic data in patients who underwent preoperative PVE vs those who did not.

Characteristics	No-PVE Patients (n = 10624)[a]	PVE Patients (n = 427)[a]	*P*-Value Prior to Matching	*P*-Value After Matching
Age				
<45 years	1717 (16.2%)	48 (11.2%)	<.01	.69
45-65 years	4962 (46.7%)	228 (53.4%)		
>65 years	3935 (37.1%)	151 (35.4%)		
Gender				
Male	5118 (48.2%)	165 (38.6%)	<.001	.41
Female	5506 (51.8%)	262 (61.4%)		
Principal procedure				
Wedge resection	7214 (67.9%)	71 (16.6%)	<.001	.09
Total left lobectomy	1016 (9.6%)	8 (1.9%)		
Total right lobectomy	1682 (15.8%)	183 (42.9%)		
Extended lobectomy	712 (6.7%)	165 (38.6%)		
Pathologic indication				
Benign	2370 (23.2%)	17 (4.0%)	<.001	.49
Primary HPB cancer	2888 (28.3%)	164 (39.0%)		
Metastatic tumor	4937 (48.4%)	240 (57.0%)		
Surgery type				
Non-elective	696 (6.6%)	22 (5.2%)	.25	.68
Elective	9925 (93.4%)	405 (94.8%)		
Ascites				
No	10558 (99.4%)	422 (98.8%)	.16	.83
Yes	66 (0.6%)	5 (1.2%)		
Preoperative systemic chemotherapy				
No	7912 (74.5%)	253 (59.3%)	<.001	.48
Yes	2712 (25.5%)	174 (40.7%)		
Hepatitis status				
None	8491 (88.6%)	322 (85.9%)	.11	.33
Hepatitis B, C, or both	1094 (11.4%)	53 (14.1%)		
Preoperative platelets				
<150,000/mm^3	1403 (13.5%)	87 (20.6%)	<.001	.40
>150,000/mm^3	8994 (86.5%)	335 (79.4%)		
Preoperative international normalized ratio				
<1.5	9063 (98.5%)	403 (98.5%)	.96	.31
≥1.5	138 (1.5%)	6 (1.5%)		
Preoperative bilirubin				
<1.2 mg/dL	8962 (91.7%)	373 (90.5%)	.42	.28
>1.2 mg/dL	815 (8.3%)	39 (9.5%)		

Continued

TABLE 1. Comparison of clinicodemographic data in patients who underwent preoperative PVE vs those who did not.

Characteristics	No-PVE Patients (n = 10624)[a]	PVE Patients (n = 427)[a]	*P*-Value Prior to Matching	*P*-Value After Matching
Operative approach				
Laparoscopic	2470 (23.7%)	36 (8.4%)	<.001	.48
Open	7941 (76.3%)	391 (91.6%)		
Biliary reconstruction				
No	9843 (93.7%)	358 (84.6%)	<.001	.62
Yes (hepaticojujenostomy)	661 (6.3%)	65 (15.4%)		
Pringle maneuver used				
No	8043 (75.7%)	285 (66.7%)	<.001	.83
Yes	2581 (24.3%)	142 (33.3%)		
Drain(s) left during procedure				
No	5912 (55.8%)	151 (35.4%)	<.001	.33
Yes	4685 (44.2%)	276 (64.6%)		
Liver texture				
Cirrhotic	3001 (54.5%)	110 (45.8%)	.04	.67
Congested	1015 (18.4%)	48 (20.0%)		
Fatty	193 (3.5%)	13 (5.4%)		
Normal	1295 (23.5%)	69 (28.7%)		

Data presented as number (%). PVE = portal vein embolization.
[a]Missing variables: age 10 (0.1%), gender 0 (0.0%), principle procedure 0 (0.0%), pathologic indication 435 (3.9%), elective status 0 (0.0%), ascites 0 (0.0%), systemic chemoembolization 0 (0.0%), hepatitis status 1091 (9.9%), preoperative platelets 232 (2.1%), preoperative international normalized ratio 1441 (13.0%), preoperative bilirubin 862 (7.8%), operative approach 213 (1.9%), concurrent intraoperative ablation 57 (0.5%), biliary reconstruction 124 (1.1%), Pringle maneuver 0 (0.0%), drains left during procedure 27 (0.2%), liver texture 5307 (48.0%).

was not performed on this population. Postoperative complications as described above were again calculated for the 2 groups.

Statistical analysis. Statistical analysis was performed using SPSS, version 25 (2017; IBM Corp). Categorical variables were compared using χ^2 tests, and continuous variable means were compared using the Student's *t* test. Propensity-score matching was performed using the SPSS Propensity Score Matching function, with a separate data file of 646 matched cases. Throughout the analysis, all *P*-values calculated were 2 sided and *P*-values <.05 were considered statistically significant.

Results

Clinicodemographics for patients undergoing PVE vs those who did not. We analyzed 11,243 patients in the NSQIP who underwent hepatic resection. Of these patients, 427 (3.9%) underwent PVE, 35 (0.3%) underwent PVE with ablation or infusion preoperatively, and 157 (1.4%) underwent ablation or arterial infusion without PVE. Clinicodemographic data of patients who had PVE and those that did not have PVE before hepatic resection are presented in **Table 1**. A total of 11,051 patients were analyzed, with patients undergoing ablation or infusion excluded from analysis. Propensity-score matching was performed to control for these differences and assess the association between PVE and several postoperative outcomes. Prior to matching, there was a significant association between age and receiving PVE, with a statistically significantly higher proportion of patients under the age of 45 years in the group of patients not undergoing PVE (16.2% vs 11.2%; *P*<.01). There was a significant association between gender and receiving PVE, with a higher proportion of females in the group of patients undergoing PVE (61.4% vs 51.8%; *P*<.001). The principal procedure was significantly associated with the proportion undergoing PVE, with a higher proportion of wedge resection in patients not undergoing PVE (67.9% vs 16.6%) and a higher proportion of extended lobectomy in patients who had preoperative PVE (38.6% vs 6.7%; *P*<.001). Pathologic indication had a significant association with undergoing PVE, with a higher proportion of metastatic tumor in patients undergoing PVE (57.0% vs 48.4%) and a higher proportion of benign tumor in patients not undergoing PVE (23.2% vs 4.0%; *P*<.001). Preoperative systemic chemotherapy was significantly associated with

TABLE 2. Postoperative outcome variables between patients who underwent PVE vs those who did not, controlled by propensity-score matching.

	No-PVE Patients (n = 646)[b]	PVE Patients (n = 646)[b]	*P*-Value
Time from operation to discharge (days)	8.64 ± 7.95	9.01 ± 0.61	.29
Intraoperative or postoperative blood transfusions			
No	167 (76.3%)	285 (66.7%)	.01[a]
Yes	52 (23.7%)	142 (33.3%)	
Acute renal failure			
No	212 (3.2%)	421 (1.4%)	.12
Yes	7 (96.8%)	6 (1.4%)	
Deep vein thrombosis			
No	210 (95.9%)	408 (95.6%)	.84
Yes	9 (4.1%)	19 (4.4%)	
Sepsis			
No	210 (95.9%)	405 (94.8%)	.56
Yes	9 (4.1%)	22 (5.2%)	
Unplanned return to operating room			
No	207 (94.5%)	407 (95.3%)	.66
Yes	12 (5.5%)	20 (4.7%)	
Unplanned readmission			
No	186 (85.0%)	359 (84.1%)	.86
Yes	33 (15.0%)	68 (15.9%)	
Post-hepatectomy liver failure			
No	191 (87.2%)	354 (82.9%)	.15
Yes	28 (12.8%)	73 (17.1%)	
30-day mortality			
Alive	213 (97.3%)	416 (97.4%)	.90
Deceased	6 (2.7%)	11 (2.6%)	

Data presented as mean ± standard error of the mean or number (%), where appropriate.
PVE = portal vein embolization.
[a]Denote statistical significance.
[b]Missing variables: days from operation to discharge 2 (0.4%), required blood transfusion 0 (0.0%), acute renal failure 0 (0.0%), deep vein thrombosis 0 (0.0%), unplanned return to operating room 0 (0.0%), unplanned readmission 0 (0.0%), post-hepatectomy liver failure 0 (0.0%), 30-day mortality 0 (0.0%).

receiving PVE, with a higher proportion receiving preoperative systemic chemotherapy in the group undergoing PVE (40.7% vs 25.5%; *P*<.001). Preoperative platelet levels were significantly associated with PVE, with patients not undergoing PVE more likely to have >150,000 platelets/mm^3 (86.5% vs 79.4%; *P*<.001). Several operative variables were also significantly associated with receiving PVE, namely operative approach, biliary reconstruction, Pringle maneuver use, and drains left during the procedure (**Table 1**). After propensity-score matching, there was no significant association between any of the clinicodemographic variables and receiving PVE (**Table 1**).

A comparison of postoperative outcome variables after propensity-score matching of patients receiving PVE and patients not receiving preoperative PVE is presented in **Table 2**. There was no significant difference between the PVE and no-PVE groups in the likelihood of acute renal failure, deep venous thrombosis, sepsis, and PHLF. Additionally, there was no significant difference in days from operation to discharge, proportion with unplanned return to the operating room, and unplanned readmission. Patients undergoing PVE had 30-day mortality of 2.7%, which was not significantly different from the 30-day mortality of 2.6% in patients not undergoing preoperative PVE (*P*=.90). Undergoing PVE was significantly associated with requiring intraoperative or postoperative blood transfusion, with increased likelihood of transfusion in patients who underwent PVE vs patients who did not undergo PVE (33.3% vs 23.7%; *P*=.01).

Postoperative complication rate for PVE alone vs PVE + LRT. Patients receiving PVE were further stratified if they underwent PVE as well as locoregional therapy, such as arterial chemoembolization or image-guided ablation pre-operatively. In total, 427 (92.4%) patients underwent PVE alone while 35 (7.6%) underwent PVE in combination with locoregional therapy. Comparison of clinico-demographic data of patients receiving PVE alone and patients receiving PVE with LRT is presented in **Table 3**. There were no significant differences in clinicodemographic data between patients who received PVE alone and patients who received PVE with LRT. Postoperative outcome variables were compared between patients receiving PVE alone and patients receiving PVE with LRT and are presented in **Table 4**. There was no significant association between any postoperative outcome variable and receiving PVE alone or PVE with LRT. Of patients receiving PVE alone, 33.3% required intraoperative or postoperative blood transfusions, and of patients receiving PVE with LRT, 40.0% required intraoperative or postoperative blood transfusions, showing no

Table 3. Comparison of clinicodemographic data in patients who underwent locoregional ablation and preoperative PVE vs those who only underwent PVE.

Preoperative Factors	Patients Undergoing PVE Without Locoregional Therapy (n = 427)[a]	Patients Undergoing PVE With Locoregional Therapy (n = 35)[a]	*P*-Value
Age			
<45 years	48 (11.2%)	6 (17.1%)	.28
45-65 years	228 (53.4%)	14 (40.0%)	
>65 years	151 (35.4%)	15 (42.9%)	
Gender			
Male	165 (38.6%)	11 (31.4%)	.40
Female	262 (61.4%)	24 (68.6%)	
Principal procedure			
Wedge resection	71 (16.6%)	4 (11.4%)	.69
Total left lobectomy	8 (1.9%)	0 (0.0%)	
Total right lobectomy	183 (42.9%)	17 (48.6%)	
Extended lobectomy	165 (38.6%)	14 (40.0%)	
Pathologic indication			
Benign	17 (4.0%)	0 (0.0%)	.27
Primary HPB cancer	164 (39.0%)	17 (50.0%)	
Metastatic tumor	240 (57.0%)	17 (50.0%)	
Elective surgery			
Non-elective	22 (5.2%)	0 (0.0%)	.17
Elective	405 (94.8%)	35 (100%)	
Ascites			
No	422 (98.8%)	35 (100%)	.52
Yes	5 (1.2%)	0 (0.0%)	
Preoperative systemic chemotherapy			
No	253 (59.3%)	20 (57.1%)	.81
Yes	174 (40.7%)	15 (42.9%)	
Hepatitis status			
None	322 (85.9%)	29 (82.9%)	.63
Hepatitis B, C, or both	53 (14.1%)	6 (17.1%)	
Preoperative platelets			
<150,000/mm^3	87 (20.6%)	4 (11.4%)	.19
> 150,000/mm^3	335 (79.4%)	31 (88.6%)	
Preoperative international normalized ratio			
<1.5	403 (98.5%)	34 (100%)	.48
≥1.5	6 (1.5%)	0 (0.0%)	

Continued

TABLE 3. Comparison of clinicodemographic data in patients who underwent locoregional ablation and preoperative PVE vs those who only underwent PVE.

Preoperative Factors	Patients Undergoing PVE Without Locoregional Therapy (n = 427)[a]	Patients Undergoing PVE With Locoregional Therapy (n = 35)[a]	*P*-Value
Preoperative bilirubin			
<1.2 mg/dL	373 (90.5%)	34 (97.1%)	.19
>1.2 mg/dL	39 (9.5%)	1 (2.9%)	
Operative approach			
Laparoscopic	36 (8.4%)	1 (2.9%)	.24
Open	391 (91.6%)	34 (97.1%)	
Biliary reconstruction			
No	358 (84.6%)	33 (94.3%)	.12
Yes (hepaticojujenostomy)	65 (15.4%)	2 (5.7%)	
Pringle maneuver used			
No	285 (66.7%)	22 (62.9%)	.64
Yes	142 (33.3%)	13 (37.1%)	
Drain(s) left during procedure			
No	151 (35.4%)	11 (31.4%)	.64
Yes	276 (64.6%)	24 (68.6%)	
Liver texture			
Cirrhotic	110 (45.8%)	6 (46.2%)	.25
Congested	48 (20.0%)	5 (38.5%)	
Fatty	13 (5.4%)	1 (7.7%)	
Normal	69 (28.7%)	1 (7.7%)	

Data presented as number (%). PVE = portal vein embolization.
[a]Missing variables: age 0 (0.0%), gender 0 (0.0%), principal procedure 0 (0.0%), pathologic indication 7 (1.5%), ascites 0 (0.0%), preoperative systemic chemotherapy 0 (0.0%), hepatitis status 52 (11.3%), preoperative platelets 5 (1.1%), preoperative bilirubin 15 (3.2%), preoperative international normalized ratio 19 (4.1%), operative approach 0 (0.0%), intraoperative ablation 2 (0.4%), biliary reconstruction 4 (0.9%), Pringle maneuver 0 (0.0%), operative drain 0 (0.0%), liver texture 209 (45.2%).

significant difference (P=.42). There was no significant difference in PHLV (17.1% vs 14.3%; P=.67) or 30-day mortality between patients undergoing PVE alone and patients undergoing PVE + LRT (2.6% vs 0.0%; P=.34).

Discussion

PVE does not significantly increase risk of postoperative complications. Apart from transplantation, hepatic resection is considered the definitive curative therapy for primary and metastatic liver malignancies. Postoperative liver failure is an important complication of hepatectomy and is directly related to the volume of FLR after surgery.[13,22] Other common major complications include bile leak, pulmonary edema or embolism, DVT, bleeding, and renal failure.[23,24] Our study is the largest to date for the evaluation of PVE and postoperative outcomes.

Our results demonstrate significant clinical differences in patients who received PVE and patients who did not receive PVE prior to hepatectomy. These differences seem to underscore the indication for PVE in patients who would have lower FLR volume after hepatectomy and hence are likely to have more advanced cancer. We report a higher proportion of benign tumor in patients without PVE and a higher proportion of primary hepato-pancreato-biliary cancer and metastatic tumor in patients undergoing PVE. This is likely borne out in the increased use of wedge resection for patients without PVE and greater use of extended lobectomy in patients with PVE. Additionally, decreased use of preoperative chemotherapy in the population without PVE further suggests that those receiving PVE have more advanced cancer. Consequently, we expect an increased used of

TABLE 4. Postoperative outcome variables between patients undergoing PVE with or without locoregional therapy without propensity-score matching.

Postoperative Outcome Variables	Patients Undergoing PVE Without Locoregional Therapy (n = 427)[a]	Patients Undergoing PVE With Locoregional Therapy (n = 35)[a]	*P*-Value
Time from operation to discharge (days)	9.01 ± 0.61	9.29 ± 1.32	.73
Intraoperative or postoperative blood transfusions			
No	285 (66.7%)	21 (60.0%)	.42
Yes	142 (33.3%)	14 (40.0%)	
Acute renal failure			
No	6 (1.4%)	35 (100%)	.48
Yes	421 (98.6%)	0 (0.0%)	
Deep vein thrombosis			
No	408 (95.6%)	33 (94.3%)	.56
Yes	19 (4.4%)	2 (4.8%)	
Sepsis			
No	393 (92.0%)	32 (91.4%)	.90
Yes	34 (8.0%)	3 (8.6%)	
Unplanned return to operating room			
No	407 (95.3%)	32 (91.4%)	.31
Yes	20 (4.7%)	3 (8.6%)	
Unplanned readmission			
No	359 (84.0%)	27 (77.1%)	.55
Yes	68 (15.9%)	8 (22.9%)	
Post-hepatectomy liver failure			
No	354 (82.9%)	30 (85.7%)	.67
Yes	73 (17.1%)	5 (14.3%)	
30-day mortality			
Alive	416 (97.4%)	35 (100)	.34
Deceased	11 (2.6%)	0 (0.0%)	

Data presented as mean ± standard error of the mean or number (%), where appropriate.
PVE = portal vein embolization.
[a]Missing variables: days from operation to discharge 2 (0.4%), required blood transfusion 0 (0.0%), acute renal failure 0 (0.0%), deep vein thrombosis 0 (0.0%), unplanned return to operating room 0 (0.0%), unplanned readmission 0 (0.0%), post-hepatectomy liver failure 0 (0.0%), 30-day mortality 0 (0.0%).

open approach, biliary reconstruction, Pringle maneuver, and abdominal drainage in those who received PVE with associated larger resections, as is demonstrated in our results (**Table 1**).

In a recent study, Huiskens et al showed no significant difference in T-stage or N-stage of primary tumor in 745 patients who had hepatectomy with or without preoperative PVE, although they found PVE patients had significantly higher American Society of Anesthesiologists (ASA) physical classification and more and larger metastases.[14] After propensity-score matching, they found similar outcomes overall, with a significant difference in rate of complications, with 48% in the PVE group and 24% in the no-PVE group, although it should be stated that each group had only 46 patients. They also reported a 90-day mortality of 11% in the PVE group and 0% in the no-PVE group (P=.056). We show similar outcomes between patients with PVE (n = 427) and patients without PVE (n = 219) prior to hepatectomy, with no significant difference in 30-day mortality or in several complications, including acute renal failure, DVT, sepsis, and PHLF.

We report a 30-day mortality of 2.7% in patients without PVE and 2.6% in patients with PVE after hepatectomy, which is comparable to the 30-day mortality rate of 1.7% reported by Abulkhir et al in a meta-analysis of 37 studies.[13] In a cohort of 576 patients who received hepatectomy, Guglielmi et al reported that 11% had subsequent PHLF.[8] In an analysis of 95 patients who received PVE followed by hepatectomy, Alizai et al similarly found an 11% incidence of PHLF.[25] In the present analysis, the incidence of PHLF was 12.8% in patients who had hepatectomy without PVE and 17.1% in patients who had hepatectomy with PVE, again with no significant difference between the groups.

We demonstrate a significant difference in requiring intraoperative or postoperative blood transfusions, with a higher proportion of patients with PVE requiring transfusion, which suggests a difference in blood loss during or following hepatectomy. Overall, our analysis of 11,051 patients demonstrates that PVE is a safe procedure, with no increase in posthepatectomy complications, readmission, or mortality when compared with patients who did not receive PVE.

LRT does not significantly improve postoperative outcomes. LRT typically refers to chemical or thermal percutaneous ablation or transarterial chemoembolotherapy (TACE). LRTs are utilized for unresectable cancers, with the specific therapy depending on the stage of disease. Early-stage hepatocellular carcinoma is often treated with radiofrequency ablation and intermediate-stage disease is managed with TACE.[20] As liver parenchyma is supplied primarily by the portal vein, delivery of chemotherapeutic agents to the hepatic artery results in minimal toxicity, whereas malignant tissue grows primarily from hepatic arterial blood flow and can be directly targeted.[20] It has been suggested that the combination of TACE and PVE could improve liver hypertrophy; whereas PVE leads to apoptosis, TACE results in necrosis, which results in increased rates of liver regeneration.[11]

A review of the literature found no studies examining the efficacy of PVE in combination with LRT for hepatic tumors. A study on rabbit VX2 liver tumor models showed that the combination of TACE and PVE had significantly more suppressive effect on tumor growth than TACE or PVE alone.[27] We report the first comparison of patients receiving PVE alone (n = 427) and patients receiving PVE with LRT (n = 35). We found no clinicodemographic differences between these groups, eliminating the need for matching. We demonstrate similar postoperative outcomes in both groups, with no significant difference for any variable. Similar outcomes in PHLF and 30-day mortality suggest that there is no significant benefit or risk to liver function with the addition of LRT, although these results are not sufficiently granular to draw any conclusions on tumor control.

Study limitations. These data have some important limitations related to the data source. The NSQIP database does not provide detailed information on specific patient charts and there is no way to ensure the use of standardized definitions for variables like PHLF, which has several definitions utilizing different criteria in clinical practice. Data on 90-day morbidity and mortality are not provided, with all data presented for 30-day morbidity and mortality. Additionally, the lack of data on future liver remnant volume prevents analysis of how PVE affects liver hypertrophy and how liver growth correlates with PHLF. Finally, the order in which PVE and preoperative locoregional intervention is offered is not recorded, so conclusions regarding timing cannot be drawn.

Conclusion

This retrospective study utilizes the American College of Surgeons NSQIP to produce the largest analysis of patients undergoing PVE, establishing the relative safety of PVE prior to hepatic resection. After controlling for clinicodemographic variables, we demonstrate that PVE has postoperative outcomes comparable to those in patients who did not receive PVE. Additionally, we show that the addition of LRT does not produce any significant change in postoperative outcomes as compared with the use of PVE alone. Prior studies of PVE have been smaller scale, and no prior study has looked at postoperative outcomes for the combination of PVE and LRT. Additional research into the effects of PVE on FLR volume and liver function may provide further insight into the overall efficacy of the procedure in the management of hepatic malignancies. A randomized, controlled trial could conclusively show the superiority or inferiority of the procedure for hepatic regrowth and function as compared with hepatectomy alone.

References

1. Langenbuch C. Ein Fall von Resection eines Linksseitigen Schnurlappens der Leber. *Berl Klin Wochenschr.* 1888;25:37.
2. Dudeja V, Fong Y. The liver. In: *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice.* 20th ed. Townsend JR Jr, Beauchamp CM, Evers DR, Mattox MB, eds. Philadelphia, PA: Elsevier; 2017:1418-1481.
3. Mullen JT, Ribero D, Reddy SK, et al. Hepatic insufficiency and mortality in 1,059 noncirrhotic patients undergoing major hepatectomy. *J Am Coll Surg.* 2007;204(5):854-862; discussion 862-864. Epub 2007 Feb 15. doi:10.1016/j.jamcollsurg.2006.12.032
4. Balzan S, Belghiti J, Farges O, et al. The "50-50 criteria" on postoperative day 5: an accurate predictor of liver failure and death after hepatectomy. *Ann Surg.* 2005;242(6):824-828, discussion 828-829. doi:10.1097/01.sla.0000189131.90876.9e
5. Nagino M, Kamiya J, Uesaka K, et al. Complications of hepatectomy for hilar cholangiocarcinoma. *World J Surg.* 2001;25(10):1277-1283. doi:10.1007/s00268-001-0110-8
6. Shirabe K, Shimada M, Gion T, et al. Postoperative liver failure after major hepatic resection for hepatocellular carcinoma in the modern era with special reference to remnant liver volume. *J Am Coll Surg.* 1999;188(3):304-309. doi:10.1016/s1072-7515(98)00301-9
7. Rassam F, Olthof PB, Richardson H, van Gulik TM, Bennink RJ. Practical guidelines for the use of technetium-99m mebrofenin hepatobiliary scintigraphy in the quantitative assessment of liver function. *Nucl Med Commun.* 2019;40(4):297-307. doi:10.1097/MNM.0000000000000973.

8. Guglielmi A, Ruzzenente A, Conci S, Valdegamberi A, Iacono C. How much remnant is enough in liver resection? *Dig Surg.* 2012;29(1):6-17. Epub 2012 Mar 15. doi:10.1159/000335713

9. Jarnagin WR, Gonen M, Fong Y, et al. Improvement in perioperative outcome after hepatic resection. *Ann Surg.* 2002;236(4):397-407. doi:10.1097/01.SLA.0000029003.66466.B3

10. Cucchetti A, Sposito C, Pinna AD, et al. Competing risk analysis on outcome after hepatic resection of hepatocellular carcinoma in cirrhotic patients. *World J Gastroenterol*. 2017;23(8):1469-1476. doi:10.3748/wjg.v23.i8.1469

11. May BJ, Madoff DC. Portal vein embolization: rationale, technique, and current application. *Semin Intervent Radiol*. 2012;29(2):81-89. doi:10.1055/s-0032-1312568

12. van Lienden KP, van den Esschert JW, de Graaf W, et al. Portal vein embolization before liver resection: a systematic review. *Cardiovasc Intervent Radiol.* 2013;36(1):25-34. Epub 2012 Jul 18. doi:10.1007/s00270-012-0440-y

13. Abulkhir A, Limongelli P, Healey AJ, et al. Preoperative portal vein embolization for major liver resection: a meta-analysis. *Ann Surg.* 2008;247(1):49-57. doi:10.1097/SLA.0b013e31815f6e5b

14. Huiskens J, Olthof PB, van der Stok EP, et al. Does portal vein embolization prior to liver resection influence the oncological outcomes – a propensity score matched comparison. *Eur J Surg Onc*. 2018;44(1):108-114. doi:10.1016/j.ejso.2017.09.017

15. Hirai I, Kimura W, Fuse A, Suto K, Urayama M. Evaluation of preoperative portal embolization for safe hepatectomy, with special reference to assessment of nonembolized lobe function with 99mTc-GSA SPECT scintigraphy. *Surgery*. 2003;133(5):495-506. doi:10.1067/msy.2003.138

16. Uesaka K, Nimura Y, Nagino M. Changes in hepatic lobar function after right portal vein embolization. An appraisal by biliary indocyanine green excretion. *Ann Surg*. 1996;223(1):77-83. doi:10.1097/00000658-199601000-00011

17. Kodama Y, Shimizu T, Endo H, Miyamoto N, Miyasaka K. Complications of percutaneous transhepatic portal vein embolization. *J Vasc Interv Radiol*. 2002;13(12):1233-1237. doi:10.1016/s1051-0443(07)61970-8

18. Di Stefano DR, de Baere T, Denys A, et al. Preoperative percutaneous portal vein embolization: evaluation of adverse events in 188 patients. *Radiology*. 2005;234(2):625-630. doi:10.1148/radiol.2342031996

19. May BJ, Talenfeld AD, Madoff DC. Update on portal vein embolization: evidence-based outcomes, controversies, and novel strategies. *J Vasc Intervent Radiol*. 2013;24(2):241-254. Epub 2013 Jan 28. doi:10.1016/j.jvir.2012.10.017

20. Geschwind J-FH. Locoregional therapy for patients with hepatocellular carcinoma. *Gastroenterol Hepatol (N Y).* 2015;11(10):698-700.

21. Yoo H, Kim JH, Ko G-Y, et al. Sequential transcatheter arterial chemoembolization and portal vein embolization versus portal vein embolization only before major hepatectomy for patients with hepatocellular carcinoma. *Ann Surg Oncol.* 2011;18(5):1251-1257. Epub 2010 Nov 11. doi:10.1245/s10434-010-1423-3

22. Vauthey J-N, Baer HU, Guastella T, Blumgart LH. Comparison of outcome between extended and nonextended liver resections for neoplasms. *Surgery*. 1993;114(5):968-975.

23. Simmonds PC, Primrose JN, Colquitt JL, Garden OJ, Poston GJ, Rees M. Surgical resection of hepatic metastases from colorectal cancer: a systematic review of published studies. *Br J Cancer.* 2006;94(7):982-999. doi:10.1038/sj.bjc.6603033

24. Schroeder RA, Marroquin CE, Bute BP, Khuri S, Henderson WG, Kuo PC. Predictive indices of morbidity and mortality after liver resection. *Ann Surg.* 2006;243(3):373-379. doi:10.1097/01.sla.0000201483.95911.08

25. Alizai PH, Haelsig A, Bruners P, et al. Impact of liver volume and liver function on posthepatectomy liver failure after portal vein embolization—a multivariable cohort analysis. *Ann Med Surg (Lond).* 2018;25:6-11. doi:10.1016/j.amsu.2017.12.003 eCollection 2018 Jan.

26. Guo W-C, He X-F, Li Y-H, Li Z-H, Mei Q-L, Chen Y. The effect of sequential transcatheter arterial chemoembolization (TACE) and portal venous embolizations (PVE) vs. TACE or PVE alone on rabbit VX2 liver carcinoma and on liver regeneration. *Eur Rev Med Pharmacol Sci.* 2016;20(15):3186-3193.

From the [1]Department of Radiology, Johns Hopkins Hospital, Baltimore, Maryland; [2]Department of Surgery, Johns Hopkins Hospital, Baltimore, Maryland; and [3]Johns Hopkins School of Medicine, Baltimore, Maryland.

Disclosure: The authors have completed and returned the ICMJE Form for Disclosure of Potential Conflicts of Interest. The authors report no conflicts of interest regarding the content herein.

Address for correspondence: Andrew R. Kolarich, MD, Johns Hopkins School of Medicine, 1800 Orleans Street, Baltimore, MD 21287. Email: akolari1@jhmi.edu