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"No-Touch" Left Approach for Recipient Hepatectomy: A Promising Strategy to Minimize Hepatocellular Carcinoma Recurrence in Liver Transplantation

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Background. Managing hepatocellular carcinoma (HCC) presents significant clinical challenges, often necessitating orthotopic liver transplantation (OLT). To mitigate the risk of iatrogenic metastasis during OLT and reduce posttransplantation recurrence (PTR), we introduced the "no-touch" left (NTL) approach for recipient hepatectomy in OLT. **Methods.** In this retrospective cohort study, our aim was to compare the safety and PTR rates in patients undergoing OLT via either the NTL technique or the conventional approach for recipient hepatectomy. We included 106 patients who met the Hangzhou criteria and exhibited a high tumor burden in the right lobe, with 50 patients assigned to the NTL group and 56 to the conventional group. The primary endpoint was the 1-y PTR rate, whereas secondary endpoints encompassed the safety of the NTL approach, PTR rates at 2 and 5 y, and overall survival. **Results.** Baseline demographics and clinical characteristics showed no significant differences between the groups. The NTL approach exhibited major surgical outcomes similar to those of the conventional approach. The cumulative PTR rates at 1, 2, and 5 y were 14.0% in the NTL group, compared with 24.5%, 35.8%, and 35.8% in the conventional group ($P = 0.013$). Cumulative overall survival rates at 1, 2, and 5 y were 94.0%, 91.9%, and 89.7% in the NTL group and 88.7%, 75.5%, and 72.5% in the conventional group ($P = 0.03$). **Conclusions.** This innovative surgical technique enhances safety and significantly reduces the risk of PTR, leading to improved long-term survival. Further prospective studies with larger cohorts and longer follow-up periods are needed to validate our findings and establish the NTL approach as a standard practice in OLT.

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Hepatocellular carcinoma (HCC) presents significant challenges in clinical management, often necessitating orthotopic liver transplantation (OLT) as a treatment option. The conventional approach to recipient hepatectomy in OLT involves the complete division of the right hepatic lobe and the subsequent mobilization of the liver from the hepatic fossa before clamping the vena cava.[1,2] However, manipulation of the native liver during these surgical procedures carries a considerable risk of iatrogenic metastasis, as tumor cells can potentially disseminate into the systemic circulation through the vena cava, leading to distant metastasis, and this risk is particularly pronounced in patients with a high tumor burden of HCC in the right hepatic lobe and where such high tumor burden may increase the likelihood of tumor cell spread.[3,4]

To address these concerns and mitigate the risk of iatrogenic metastasis, we adopted the "no-touch" left (NTL) approach for recipient hepatectomy in HCC patients with high tumor burden in the right hepatic lobe undergoing OLT. The NTL approach is based on 2 fundamental principles. First, it emphasizes avoiding any direct contact with the tumor until the inflow and outflow of blood in the liver are completely blocked. Second, to ensure adherence to the first principle, the approach involves dividing the blood vessels

and mobilizing the native liver in a direction from left to right.

Since 2015, the NTL approach has been applied in our center to patients presenting with high tumor burden in the right lobe (HTBRL) and receiving OLT. HTBRL was defined as follows: (1) having a total tumor number of ≤5, (2) having a total tumor diameter between 5 and 15 cm, and (3) tumor occurrence limited to segments 5–8 without affecting segments 1–4 of the liver. In this study, we aim to report the safety and long-term outcomes of the NTL approach, specifically focusing on its impact on reducing posttransplantation recurrence (PTR). Our results demonstrated a significant reduction in recurrence rates with the NTL approach compared with the conventional approach. Additionally, we present important findings related to the safety profile and long-term outcomes associated with this novel surgical technique.

MATERIALS AND METHODS

Study Design

This retrospective cohort study with prospectively collected data aimed to compare the safety and PTR in patients with HTBRL who received either the NTL approach or the conventional approach for recipient hepatectomy. The study adhered to the principles outlined in the Declaration of Helsinki, and the study protocol received approval from the institutional review board of the China-Japan Friendship Hospital, Beijing, China. Written informed consent was obtained from all patients included in the study. The flowchart of the study is shown in Figure 1.

The criteria for the NTL approach in this study were as follows: (1) patients must first meet the Hangzhou criteria, which means having a total tumor diameter of ≤8 cm or >8 cm with grade I or II tumors and an alpha-fetoprotein

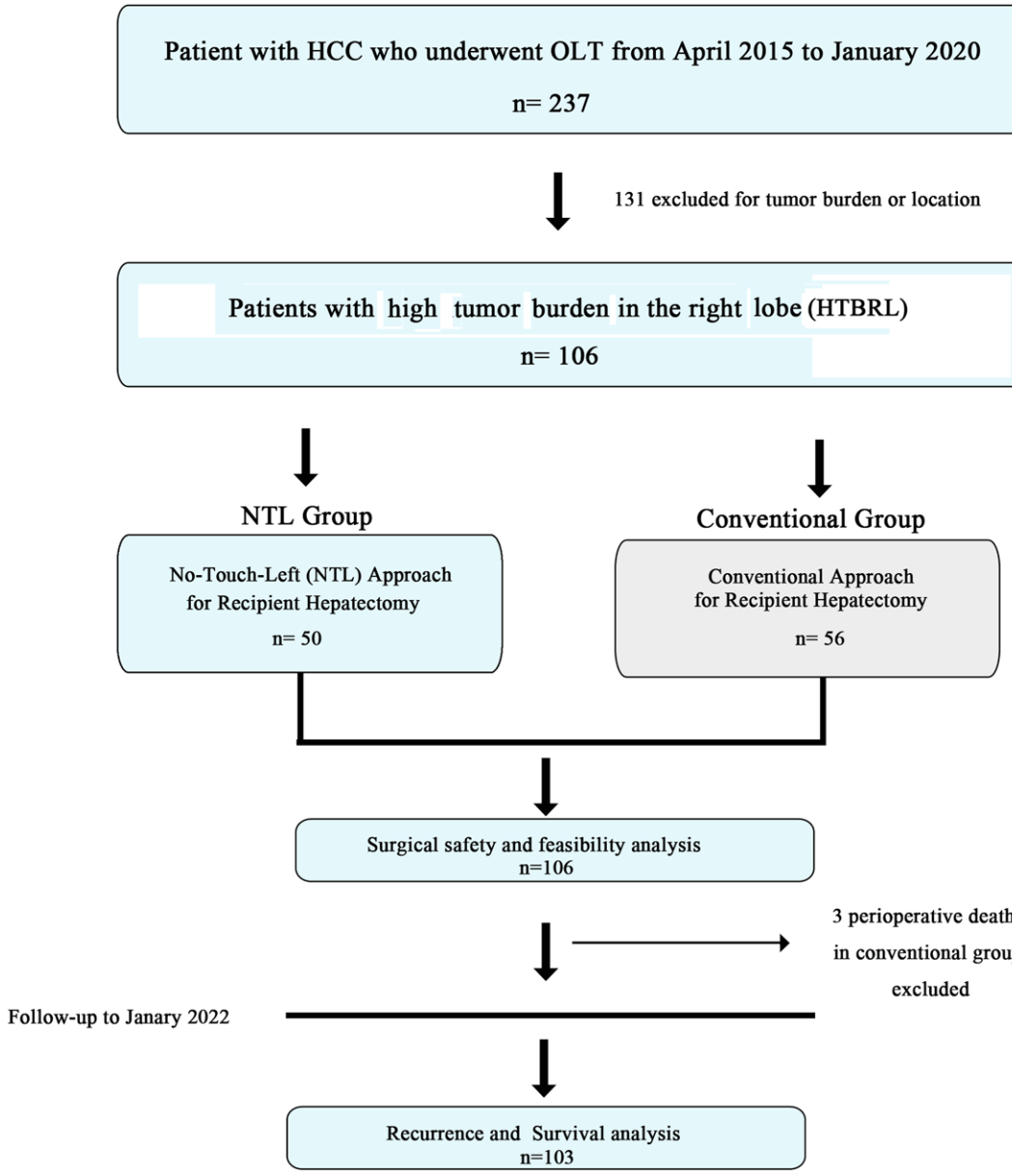

FIGURE 1. Flowchart of the study. HCC, hepatocellular carcinoma; OLT, orthotopic liver transplantation.

(AFP) level of ≤400 ng/mL.[5] Meeting the Hangzhou criteria is essential for becoming eligible for OLT at our center. (2) In addition to the Hangzhou criteria, patients must also meet the criteria for HTBRL to be considered for the NTL approach.

The primary endpoint of this study was the 1-y recurrence rate in the studied patients. The other endpoints were the safety of the NTL approach, the 2-y and 5-y recurrence rates, and the overall survival (OS).

Patients

Between April 2015 and January 2020, a total of 237 consecutive patients with HCC who met the Hangzhou criteria underwent OLT at our center. Among them, 106 patients who exhibited HTBRL were included in this study. Of the 106 patients, 50 received the NTL approach and 56 received the conventional approach for their recipient hepatectomy.

Two groups of experienced surgeons were qualified to perform OLT in our center. In one group, which included the authors, the NTL approach has been exclusively performed. In the other group, the conventional approach was exclusively used. Importantly, aside from differences in the recipient hepatectomy approach, both groups adhered to the same standard procedures for OLT. This standardization encompassed patient eligibility criteria, donor and graft management, perioperative patient care, follow-up protocols, etc. As a result, whether a patient underwent NTL or the conventional approach depended on which group they were initially referred to. The transplanted liver was obtained either from donation after cardiac death or donation after brain death.

Surgical Procedures of Recipient Hepatectomy

All patients underwent the Benz incision technique. The liver vessels were isolated and sequentially clamped starting from the hepatic artery, followed by the portal vein, and, finally, the hepatic vein.

Conventional Approach

In the conventional approach, the dissection of the liver hilum was performed first. After the dissection of the eighth lymph node, the common hepatic artery was exposed. Subsequently, the proper hepatic artery, gastroduodenal artery, right gastric artery, left hepatic artery, and right hepatic artery were exposed along the course of the common hepatic artery. Once the positions of these arteries were confirmed, the gastroduodenal artery, right gastric artery, left hepatic artery, and right hepatic artery were ligated. After ligating the cystic duct, the bile duct was dissected and ligated near the common hepatic duct close to the liver. The connective tissue anterior to the portal vein was dissected, and the portal vein was isolated as far as possible toward the upper edge of the pancreas to ensure sufficient length for anastomosis. The 12th lymph node and the connective tissue surrounding the portal vein were removed. The left and right ligaments of the liver were divided to expose the left and right sides of the inferior vena cava. The short hepatic veins were ligated and disconnected. Finally, the portal and hepatic veins were disconnected to completely remove the native liver.

NTL Approach

As illustrated in Figures 2 and 3, the NTL approach begins with the dissection of the liver hilum, including the dissection of the 8th and 12th lymph nodes, and the exposure of the portal vein, hepatic artery, and common bile duct. Subsequently, the left coronary and triangular ligaments of the liver were divided, allowing the left hepatic lobe to be rotated counterclockwise toward the right. After dissecting the hepatogastric ligament, the short hepatic veins were ligated sequentially between the caudate lobe and the inferior vena cava until the common trunk of the left and middle hepatic veins was exposed. Once the common trunk of the left and middle hepatic veins was clamped, the right hepatic vein was exposed from the left side (as shown in Figure 2). Finally, after clamping the portal vein and right hepatic veins, the right hepatic ligament was dissected to completely remove the diseased liver.

Subsequent Procedures

After the completion of the recipient hepatectomy, regardless of the approach used, the donor liver was meticulously implanted with all subsequent procedures conducted in accordance with the standardized conventional OLT protocol.

Posttransplant Immunosuppression

In this study, all patients adhered to a standardized posttransplant immunosuppression protocol, reflecting well-established practices in our center. This protocol involved a sequential regimen starting with a combination of tacrolimus and mycophenolate mofetil as the initial antirejection drugs. Specifically, tacrolimus blood concentration was carefully managed to achieve a target level of 6.0–8.0 μg/L. After the initial 4 wk posttransplantation, the regimen was adjusted by transitioning from mycophenolate mofetil to sirolimus, aiming for a target level of 3.0–5.0 μg/L, while simultaneously reducing the tacrolimus target level to 3.0–5.0 μg/L. These adjustments marked a transition to a maintenance phase, where tacrolimus and sirolimus, at these targeted levels, were consistently used as the immunosuppressive therapy regimen.

PostTransplantation Follow-up

All patients received standardized postoperative care and follow-up according to a predefined protocol. Intraoperative and postoperative complications were documented for all patients. Follow-up evaluations included regular monitoring of serum AFP levels, chest computed tomography scans, and contrast-enhanced abdominal MRI scans every 3 mo posttransplantation to detect any signs of tumor recurrence. Additional radiological examinations of other sites were conducted when recurrence was suspected, after negative results from chest computed tomography and abdominal MRI scans. HCC recurrence was defined as the detection of the newly formed lesion(s) in any metastatic site through imaging studies, with or without an increase in serum AFP levels. All suspected recurrences were confirmed by a team consisting of 2 independent radiologists and 2 surgeons. OS was calculated from the date of liver transplantation to the date of the last follow-up or death. In cases of recurrence, the treatment was decided by a multidisciplinary team and

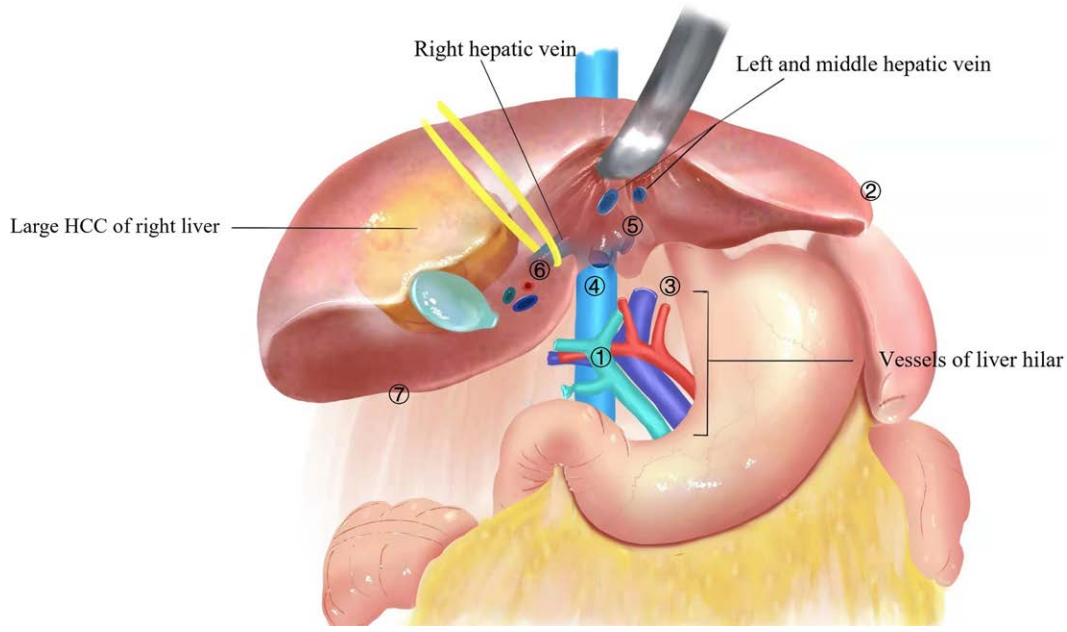

FIGURE 2. Schematic diagram of the NTL approach. Steps: (1) dissect the first liver hilar, (2) divide the left coronary and triangular ligaments of the liver and dissect the hepatogastric ligament, (3) ligate the short hepatic veins between the caudate lobe and inferior vena cava, (4) expose and cut off the left and middle hepatic vein, (5) expose and cut off the right hepatic vein, and (6) dissect the right hepatic ligament. A comparison of the NTL approach and the conventional approach is shown as below: HCC, hepatocellular carcinoma; NTL, no-touch left.

Approach	Sequence of steps					
NTL	1	2	3	4	5	6
Conventional	1	2	6	3	4	5

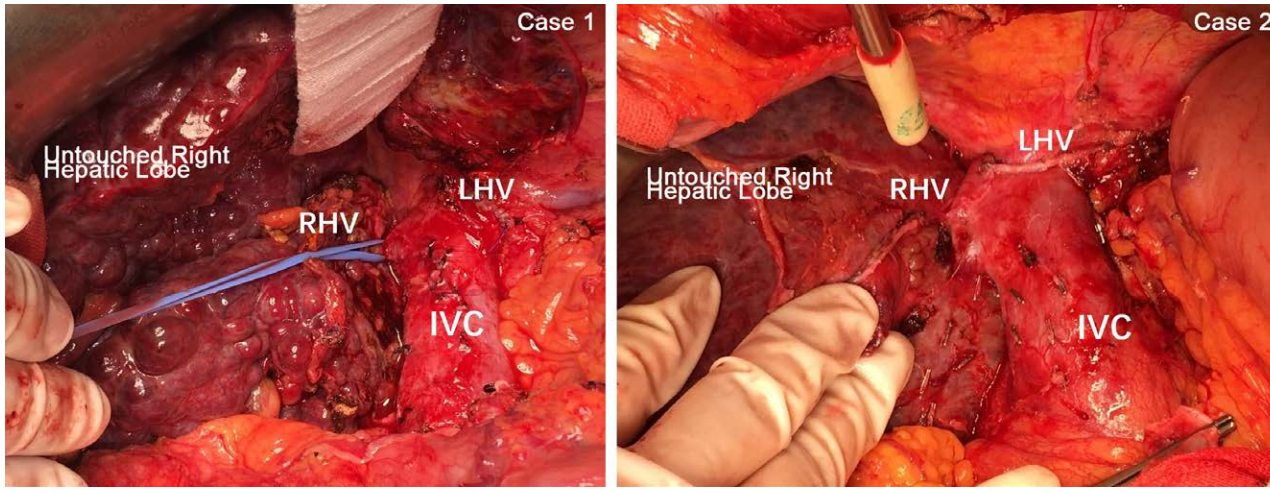

FIGURE 3. Intraoperative images showcasing 2 representative cases from the NTL approach group. The left hepatic lobe was rotated counterclockwise toward the right, and the short hepatic veins were meticulously ligated in sequence between the caudate lobe and the IVC. Simultaneously, the right hepatic vein was carefully exposed from the left side, all while leaving the right hepatic lobe untouched. IVC, inferior vena cava; LHV, left hepatic vein; NTL, no-touch left; RHV, right hepatic vein.

therapies were included but were not limited to molecular targeted therapy, local ablation, surgical reception, and radiotherapy.

Statistical Analysis

Statistical analysis was conducted using SPSS version 20.0 statistical software (IBM Corp., Armonk, NY). The chi-square test or Fisher exact test was used to compare discrete variables, whereas the Mann-Whitney *U* test was used for comparing continuous variables. Survival analysis, including cumulative survival and recurrence-free survival, was estimated using the Kaplan-Meier survival method. The log-rank test was used for statistical comparisons of survival distributions. Multivariate analysis using the Cox proportional hazard regression model was performed to identify independent prognostic factors for overall cumulative survival.

A significance level of P value of <0.05 was considered statistically significant.

RESULTS

Demographics and Clinical Characteristics of the Study Patients

Out of the 106 patients enrolled in the study, 50 (47.2%) underwent the NTL approach, whereas 56 (52.8%) underwent the conventional approach for recipient hepatectomy. By the end of follow-up, the mean follow-up time was 46.2 mo (range, 5–80 mo) in the NTL group and 38.1 mo (range, 4–81 mo) in the conventional group. As presented in Table 1, the baseline demographics and clinical characteristics of the 2 groups showed no significant differences. Graft liver information is presented in Table S1 (**SDC,** http://links.lww.com/TXD/A658). Furthermore, postoperative pathological characteristics, including microvascular invasion (38.0% in the NTL group versus 39.3% in the conventional group, $P = 0.893$); TNM staging (stage I/II/III [14/26/10] in the NTL group versus stage I/II/III [13/33/10] in the conventional group, $P = 0.767$); and tumor differentiation grade (well/moderate/poor [4/39/7] in the NTL group versus well/moderate/poor [13/33/10] in the conventional group, $P = 0.481$), also exhibited no statistically significant differences. The postoperative pathology also confirmed the HTBRL in all patients.

Pretransplantation HCC Treatment

Among the patients in the NTL group, 29 (58.0%) underwent pretransplantation HCC treatments, whereas in the conventional group, 31 patients (55.4%) received such treatments. Specifically, 13 patients (26.0%) in the NTL group and 19 patients (21.4%) in the conventional group received transarterial chemoembolization (TACE) only ($P = 0.591$). Meanwhile, 16 patients (32.0%) in the NTL group and 19 patients (33.9%) in the conventional group received both TACE and oral tyrosine kinase inhibitor (TKI) treatments ($P = 0.676$). The oral TKI treatments administered were either sorafenib or lenvatinib at the recommended dosages. None of the patients received TKI alone as their pretransplantation treatment in this study.

TABLE 1.

Demographics and clinical characteristics

Parameters	NTL group (N = 50)	Conventional group (N = 56)	*P*
Sex, male/female	40/10	45/11	0.964
Age, y, median (range)	54.8 (34–72)	52.9 (29–67)	0.251
Chronic HBV infection, n (%)	40 (80.0)	49 (87.5)	0.298
AFP, ng/mL, n (%)			0.604
<100	35 (70.0)	34 (60.7)	
100–400	7 (14.0)	10 (17.9)	
≥400	8 (16.0)	12 (21.4)	
ALB, g/L, median (range)	36 (26–47)	36 (23–50)	0.667
HBG, g/L, median (range)	117.2 (66–168)	116.6 (61–167)	0.896
Preoperative TACE, n (%)	13 (26.0)	12 (21.4)	0.591
Preoperative TKI and TACE, n (%)	16 (32.0)	19 (33.9)	0.676
Total tumor number			0.730
1	26	30	
2	13	15	
3	8	10	
4 or 5	3	1	
Year of transplantation, mean ± SD	3.9 ± 1.9	3.0 ± 2.7	0.358
Total tumor diameter, cm, mean ± SD	8.3 ± 3.4	7.8 ± 2.6	0.369
Microvascular invasion, n (%)	19 (38.0)	22 (39.3)	0.893
TNM staging, n (%)			0.767
Stage I	14 (28.0)	13 (23.2)	
Stage II	26 (52.0)	33 (58.9)	
Stage III	10 (20.0)	10 (17.9)	
Tumor differentiation grade, n (%)			0.481
Well	4 (8.0)	4 (7.1)	
Moderate	39 (78.0)	39 (69.6)	
Poor	7 (14.0)	13 (23.3)	
MELD score, n			0.554
<10	7	11	
10–19	35	35	
20–29	5	6	
≥30	3	4	

AFP, alpha-fetoprotein; HBV, hepatitis B virus; ALB, albumin; HGB, hemoglobin; MELD, Model for End-Stage Liver Disease; TACE, transarterial chemoembolization; TKI, tyrosine kinase inhibitor, namely sorafenib or lenvatinib in this study.

Safety and Feasibility of the NTL Approach

Next, we compared the major surgical parameters between the NTL and conventional approaches, as presented in Table 2. The median operation time was 518 min in the NTL group and 525 min in the conventional group ($P = 0.732$). The median intraoperative blood loss was 900 mL in the NTL group and 1040 mL in the conventional group ($P = 0.381$). Similarly, the intraoperative blood transfusion was 1140 mL in the NTL approach group and 1400 mL in the conventional approach group ($P = 0.279$). The mean cold ischemic time was 452 min in the NTL group and 458 min in the conventional group ($P = 0.724$). The incidence of surgery-related complications in the NTL group was 4.0% (2 cases), whereas the same in the conventional group was 7.1% (4 cases; $P = 0.489$).

Of the 2 surgery-related complications cases in the NTL group, one was related to ischemic-type biliary lesions and the other one involved postoperative ascites. Both patients in the NTL group fully recovered after appropriate treatment. In contrast, the 4 surgery-related complications cases in the conventional group included biliary leakage, acute kidney impairment, delayed recovery of liver function, and intracerebral hemorrhage. Three patients in the conventional group succumbed to these complications within 30 d after surgery, leading to perioperative death. No perioperative deaths occurred in the NTL group ($P = 0.099$).

The NTL approach demonstrated comparability to the conventional approach in major surgical parameters, such as operation time, intraoperative blood loss, and transfusion. However, the NTL approach showed a potential advantage in safety profiles concerning the incidence of surgery-related complications and perioperative death.

Posttransplantation HCC Recurrence

To compare the impact of the NTL approach with the conventional approach on posttransplantation HCC recurrence, we excluded 3 cases of perioperative death, leaving 103 cases for further analysis. During the follow-up period, 26 (25.2%) patients experienced HCC recurrence, with 7 cases in the NTL group and 19 cases in the conventional group. In the NTL group, all 7 recurrences occurred within the first year (median: 7 mo; range, 3–11 mo), whereas in the conventional group, 13 recurrences occurred in the first year and 6 in the second year (median: 7 mo; range, 3–21 mo). No recurrences occurred 2 y after the OLT in any patients.

As shown in Figure 4, the NTL group exhibited significantly reduced recurrence compared with the conventional group ($P = 0.013$). The cumulative recurrence rates at 1, 2, and 5 y were 14.0% (95% CI, 4.4%-23.6%), 14.0% (95% CI, 4.4%-23.6%), and 14.0% (95% CI, 4.4%-23.6%), respectively, in the NTL group, whereas they were 24.5% (95% CI, 12.9%-36.1%), 35.8% (95% CI, 22.9%-48.7%), and 35.8% (95% CI, 22.9%-48.7%), respectively, in the conventional group.

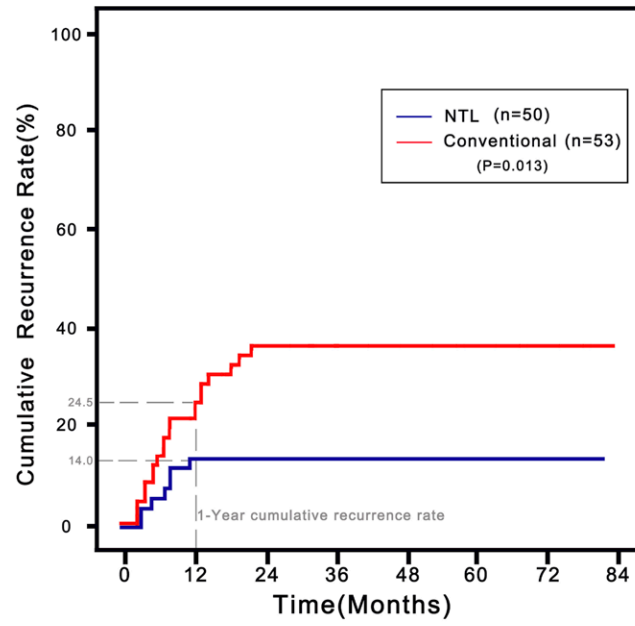

FIGURE 4. Cumulative recurrence rate of patients who underwent OLT with either the NTL approach or the conventional approach for recipient hepatectomy. NTL, no-touch left; OLT, orthotopic liver transplantation.

A Cox hazard model was applied to determine the risk factors associated with PTR. Table 3 presents the results of univariate and multivariate analyses, indicating that baseline AFP of ≥400 ng/mL (HR = 3.85; 95% CI, 1.66-8.96; $P = 0.022$) and the application of the conventional approach for recipient hepatectomy (HR = 2.64; 95% CI, 1.11-6.30; $P = 0.029$) were the only 2 independent risk factors for PTR.

Posttransplantation Survival

At the end of the follow-up, 84 patients (81.5%) survived and 19 (19.5%) patients died (5 in the NTL group and 14 in the conventional group). All 19 patients succumbed to HCC recurrence and progression. There were no patients lost in the follow-up. For the dead cases, the median time from transplantation to death was 12 mo (range, 4–33 mo) in the NTL group and 14.5 mo (range, 6–38 mo) in the conventional group.

TABLE 2.

Comparison of major surgical parameters between NTL and conventional approach

Parameters	NTL group (N = 50)	Conventional group (N = 56)	*P*
Intraoperative blood loss, mL, median (range)	900 (200–3000)	1040 (200–6000)	0.381
Intraoperative blood transfusion, mL, median (range)	1140 (0–4000)	1400 (0–6400)	0.279
Operating time, min, median (range)	518 (300–780)	525 (360–810)	0.732
Cold ischemic time, min, median (range)	452 (360–540)	458 (360–540)	0.724
Surgery-related complications, n (%)	2 (4.0)	4 (7.1)	0.489
Perioperative death, n, (%)	0 (0.0)	3 (5.4)	0.099

NTL, no-touch left.

TABLE 3.

Univariate and multivariate analyses of the risk factors for post-LT HCC recurrence

	Univariate analysis			Multivariate analysis		
Variables	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
AFP, ng/mL						
<100[a]	1					
100–400	1.54	0.50-4.79	0.452			
≥400	4.06	1.75-9.42	**0.010**	3.85	1.66-8.96	**0.022**
Total tumor diameter, cm						
<10[a]	1					
≥10	1.07	0.40-2.84	0.889			
Total tumor number						
1[a]	1					
2	1.27	0.52-3.11	0.600			
≥3	1.28	0.48-3.41	0.622			
Microvascular invasion						
No[a]	1					
Yes	2.06	0.95-4.46	0.066			
TNM stage						
Stage I[a]	1					
Stage II	1.21	0.22-12.40	0.629			
Stage IIII	1.25	0.57-35.63	0.153			
Differentiation						
Well[a]	1					
Moderate	1.65	0.49-3.23	0.642			
Poor	4.51	0.38-4.11	0.709			
HBV infection						
No[a]	1					
Yes	1.33	0.50-3.52	0.570			
Preoperative TACE						
No[a]	1					
Yes	0.87	0.53-2.48	0.728			
Preoperative TKI and TACE						
No[a]	1					
Yes	0.64	0.29-1.39	0.257			
RH approach						
NTL[a]	1					
Conventional	2.78	1.17-6.62	**0.021**	2.64	1.11-6.30	**0.029**

Total tumor burden is the sum of the diameter of all tumors. Variables were analyzed by a univariate model of the Cox proportional hazard test; those with a *P* value of <0.05 are shown here and were forwarded to the multivariate analysis.Bold values indicate statistical significance ($P \leq 0.05$).

[a]Reference values.

AFP, alpha-fetoprotein; CI, confidence interval; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HR, hazard ratio; LT, liver transplant; NTL, no-touch left; RH, recipient hepatectomy; TACE, transarterial chemoembolization; TKI, tyrosine kinase inhibitor, specifically sorafenib or lenvatinib in this study.

The posttransplantation OS in patients who received the NTL or conventional approach for recipient hepatectomy was compared using the Kaplan-Meier survival method. As shown in Figure 5, patients in the NTL group exhibited a significantly higher OS rate ($P = 0.03$). The cumulative OS rates at 1, 2, and 5 y were 94.0% (95% CI, 88.5%-99.5%), 91.9% (95% CI, 84.1%-99.2%), and 89.7% (95% CI, 80.9%-98.5%), respectively, in the NTL group, whereas they were 88.7% (95% CI, 80.1%-97.3%), 75.5% (95% CI, 22.9%-48.7%), and 72.5% (69.7%-84.9%), respectively, in the conventional group.

We then analyzed the risk factors associated with posttransplantation survival. Table 4 presents the results of univariate and multivariate analyses, indicating that baseline AFP of ≥400 ng/mL (HR = 3.51; 95% CI, 1.35-9.15; $P = 0.016$) and the application of the conventional approach for recipient hepatectomy (HR = 3.22; 95% CI, 1.18-8.76; $P = 0.022$) were the only 2 independent risk factors for posttransplantation survival.

DISCUSSION

Currently, OLT remains the most critical therapeutic measure and the sole potential curative option for treating HCC.[6,7] Despite notable advancements in patient selection criteria,[8-13] immunosuppressive regimens, and system treatments of HCC, the risk of PTR persists, posing a substantial threat to the overall success and long-term outcomes of liver transplantation.[14,15] To our knowledge, the present study is the first study that demonstrates that new surgical techniques for recipient hepatectomy may reduce the PTR for patients undergoing OLT. Our NTL approach was safe and feasible, showing a comparable efficacy to the conventional approach. More importantly, the implementation of the NTL approach has led to a substantial reduction in PTR and significantly improved OS in patients with HCC. These encouraging outcomes highlight the potential of the NTL approach as a valuable surgical strategy to enhance the long-term outcomes and prognosis of patients with HCC undergoing transplantation.

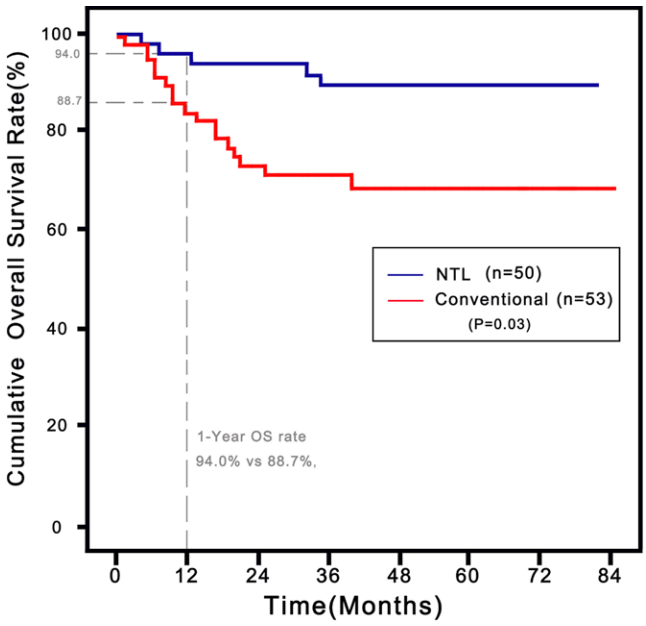

FIGURE 5. Cumulative overall survival rate of patients who underwent OLT with either the NTL approach or the conventional approach for recipient hepatectomy. NTL, no-touch left; OLT, orthotopic liver transplantation.

Recipient hepatectomy is the first and critical part of the whole OLT procedure. In the conventional approach of recipient hepatectomy, to dissect the right perihepatic ligament, the right hepatic lobe must be rotated clockwise to the left side to expose the inferior vena cava. Force and pressure to the tumor-harboring liver tissue were almost unavoidable in this procedure, particularly in patients who underwent bridging TACE and presented severe adhesions of parahepatic tissue. The NTL approach refrains from touching the right hepatic lobe until all vascular connections to the liver and systemic circulation are fully severed. This meticulous approach effectively prevented the inadvertent release of tumor cells into the systemic circulation because of surgical compression of the liver tissue, and it significantly reduced the PTR, as demonstrated by our study.

In the tumor tissue, loose cell connections and an abundant blood supply make tumor cells highly susceptible to detachment under external forces such as rotation or mobilization during operation. These features may cause the entry of tumor cells into the bloodstream, consequently leading to metastasis.[16,17] Studies[18,19] have revealed that surgical resection of HCC can increase circulating tumor cell counts, especially in patients with microvascular tumor thrombus. Minimizing tumor movement and compression before cutting off its blood supply during surgery may help reduce the risk of iatrogenic metastasis. In the study by Liu et al,[3] a comparison was made between liver resection through the anterior approach, similar to the NTL and conventional approaches for very large right liver tumors. The findings showed that anterior hepatectomy involved less compression and manipulation of the liver tumor, resulting in lower intraoperative bleeding and reduced postoperative recurrence and mortality rates. Additionally, Yoon et al[20,21] outlined their recipient hepatectomy technique in living donor liver transplantation, closely adhering to the fundamental principle of the NTL approach, which emphasizes refraining from tumor manipulation until hepatic vascular structures are fully excluded.

For the present study, we selected patients with HTBRL to apply the NTL approach. However, this does not mean that it will exclusively benefit these patients. HCC distribution has been reported as follows: 47.3% in both the left and right hepatic lobes, 34.8% in the right hepatic lobe, and 17.9% in the left hepatic lobe.[16] Therefore, in theory, the NTL approach may reduce the risk of PTR in all patients with HCC affecting the right hepatic lobe, encompassing at least 80% of all OLT recipients. Moreover, considering that (1) the NTL approach has demonstrated safety and comparability to the conventional approach in all surgical parameters and that (2) the NTL technique is easy to learn, with experienced transplant surgeons being able to transition from the conventional approach to the NTL approach within 4–8 wk based on our own training experience, we believe that the NTL approach has broader applications in the field of OLT and may potentially replace the conventional approach in the future.

The recurrence rate observed in the conventional group in our study appears to be notably higher than the figures reported for patients meeting other widely recognized criteria, which typically show rates <20%.[8-14] In our investigation, we used the Hangzhou criteria, which are extensively used in China for patient selection eligibility. Notably, the reported 1-y, 3-y, and 5-y PTR rates for patients meeting the Hangzhou criteria were 16.3%, 34.4%, and 37.6%, respectively.[5] These rates are comparable with the PTR rate observed in the conventional group in our study, which were 24.5% at 1 y, 35.8% at 3 y, and 35.8% at 5 y.

A high AFP level before transplantation significantly elevates the risk of HCC recurrence after LT. This association is widely recognized by several leading criteria for LT, including the Hangzhou,[5] UCSF,[9] Asan,[12] and Tokyo[13] criteria. Our study reveals that despite using the NTL approach, pretransplant AFP levels of 400 ng/mL or higher remain an independent risk factor for post-LT HCC recurrence. This finding underscores the importance of meticulous patient selection, particularly for those with high pretransplant AFP levels. Moreover, in conjunction with NTL approach, comprehensive pretransplant bridging and downstaging treatments may significantly reduce HCC recurrence posttransplantation.

Although our study adds valuable evidence supporting the efficacy and safety of the NTL approach, we acknowledge the limitations inherent in retrospective cohort studies. Additional prospective investigations with larger sample sizes and longer follow-up periods are warranted to further validate the benefits of the NTL approach in reducing PTR and enhancing OS in HTBRL patients undergoing OLT.

In conclusion, the "no-touch" left approach for recipient hepatectomy in HTBRL patients undergoing OLT represents a promising advancement in the management of HCC. By emphasizing the avoidance of direct tumor contact during surgical procedures, the NTL approach demonstrates a significant reduction in PTR and improved OS. Therefore, adopting the NTL approach in clinical practice has the potential to enhance the outcomes of OLT for HCC and merits further research to establish its role as a standard surgical technique.

TABLE 4.

Univariate and multivariate analyses of the risk factors for post-LT overall survival

	Univariate analysis			Multivariate analysis		
Variables	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
AFP, ng/mL						
<100	1					
100–400	2.43	0.81-7.26	0.112			
≥400	3.85	1.48-9.98	**0.010**	3.51	1.35-9.15	**0.016**
Total tumor diameter, cm						
<10	1					
≥10	1.14	0.42-3.10	0.791			
Total tumor number						
1	1					
2	1.33	0.36-4.91	0.671			
≥3	1.94	0.50-7.50	0.338			
Microvascular invasion						
No[a]	1					
Yes	1.37	0.59-3.12	0.459			
TNM						
Stage I[a]	1					
Stage II	1.08	0.46-3.60	0.904			
Stage IIII	1.28	0.29-4.04	0.643			
Differentiation						
Well[a]	1					
Moderate	1.30	0.17-9.89	0.804			
Poor	3.59	0.45-28.74	0.228			
HBV infection						
No[a]	1					
Yes	1.20	0.36-4.06	0.769			
Preoperative TACE						
No[a]	1					
Yes	0.72	0.30-1.71	0.456			
Preoperative TKI and TACE						
No[a]	1					
Yes	0.57	0.25-1.32	0.192			
RH approach						
NTL[a]	1					
Conventional	3.49	1.29-9.46	**0.014**	3.22	1.18-8.76	**0.022**

Total tumor burden is the sum of the diameter of all tumors. Variables were analyzed by a univariate model of the Cox proportional hazard test; those with a *P* value of <0.05 are shown here and were forwarded to the multivariate analysis.Bold values indicate statistical significance ($P \leq 0.05$).

[a]Reference values.

AFP, alpha-fetoprotein; CI, confidence interval; HBV, hepatitis B virus; HR, hazard ratio; LT, liver transplant; NTL, no-touch left; RH, recipient hepatectomy; TACE, transarterial chemoembolization; TKI, tyrosine kinase inhibitor, specifically sorafenib or lenvatinib in this study.

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