Transradial versus transfemoral approach for TACE: a retrospective study

Ke You[1], Tao Guo[2,3], Da Sun[4], Hao Song[4]* and Zuojin Liu[1]*

Abstract

Objective Transcatheter arterial chemoembolization (TACE) has been widely applied in the treatment of hepatocellular carcinoma (HCC). Our study aimed to investigate the feasibility and efficacy of transradial access as an alternative to transfemoral access for TACE.

Methods Patients undergoing TACE were divided into the radial artery (RA) route group or the femoral artery (FA) route group according to the operation approach, namely, transradial or transfemoral access. We retrospectively analysed the clinical characteristics, technical outcomes, clinical efficacy and incidence of adverse events to compare the two technologies for intervention for HCC.

Results Transradial access was found to achieve superior technical outcomes and clinical efficacy, as the patients in the RA group had a lower rate of hepatic arterial spasm, a higher partial response rate and a lower progression rate than the patients in the FA group according to the mRECIST evaluations. In contrast, the liver function indices and VAS (visual analogue scale) pain scores were consistent across the two groups. Moreover, patients in the RA group had a shorter length of stay than those in the FA group, despite similar hospitalization expenses. The total adverse events were significantly reduced by transradial access for TACE (72.5% vs. 84.1%, $P = 0.027$).

Conclusion Our study suggested that transradial access is an effective and feasible alternative to transfemoral access for TACE. Large-scale prospective randomized controlled studies are expected.

Keywords Transradial access, Transfemoral access, TACE

*Correspondence:
Hao Song
songhaoshanghai@126.com
Zuojin Liu
300376@hospital.cqmu.edu.cn
[1] Department of Hepatobiliary Surgery, The Second Affiliated Hospital of Chongqing Medical University, Linjiang Road 74, Chongqing 400010, China
[2] Liuzhou Key Laboratory of Infection Disease and ImmunologyGuangxi Health Commission Key Laboratory of Clinical Biotechnology, Liuzhou People's Hospital affiliated to Guangxi Medical University, Liuzhou 545006, China
[3] Department of Pathophysiology, School of Basic Medical Sciences, Weifang Medical University, Weifang 261053, China
[4] Department of Organ Transplantation, Third Affiliated Hospital of Naval Military Medical University, North Moyu Road 700, Shanghai 201805, China

Introduction

Primary hepatocellular carcinoma (HCC) is often diagnosed at advanced stages as a result of insidious onset; thus, it is imperative to develop nonsurgical therapies for unresectable tumours. Transcatheter arterial chemoembolization (TACE) is an extensive and effective approach for HCC and is recommended in most clinical guidelines as a superior treatment for unresectable hepatocellular carcinoma [1–4].

Traditional TACE is based on the percutaneous catheterization technique developed in 1953 [5] and is performed through femoral arterial access, which has been extensively applied in many catheterization interventions [6, 7]. Progress has been made in the development of technologies and materials, and angiography and intervention via transradial access to the upper limbs have

You *et al. BMC Gastroenterology*   (2023) 23:11

Page 2 of 10

been recently developed for coronary disease therapy [8]. Clinicians have reported that transradial access for cardiac catheterization significantly reduces the risk of local vascular complications and the incidence of postoperative adverse events [9, 10]. Additionally, patients preferred transradial to transfemoral access, as transradial access produces less discomfort and is associated with lower hospital costs [11, 12]. Considering that TACE via the femoral approach requires restrictive immobilization of the lower limb after the operation and results in delayed ambulation with a longer monitoring duration, transradial access technology is increasingly applied as an alternative to transfemoral access for angiography and intervention of other visceral organs and vessels, such as hepatic, uterine artery and peripheral interventions [13–15].

Several clinical studies have compared transfemoral and transradial access approaches for TACE [16–20], although reliable evidence for the extensive application of transradial access for TACE for the treatment of hepatic carcinoma is still lacking. Indeed, catheterization via a radial approach was reported to require higher technical skills with a decreased success rate [10], and patients could be exposed to a higher dose of radiation than with transfemoral access [21], which might make clinicians reluctant to use a radial approach for TACE. Thus, the application of transradial access remains controversial. The present research focused on the intraoperative technical outcomes and postoperative clinical parametric data of transradial access as an alternative to traditional transfemoral access for TACE in HCC patients and is intended to provide a reference for its clinical application.

Methods
Study population
Patients with primary HCC from the Second Affiliated Hospital of Chongqing Medical University were retrospectively assessed from 2018 to 2021. TACE treatments, including transradial or transfemoral access, were performed on the patients in this study. The TACE intervention approach was decided by the patients after they deliberated with the attending physician, and written informed consent was obtained from all patients prior to TACE treatment. The present study was designed and conducted in accordance with the principles of the Helsinki Declaration and was approved by the ethics committees of the involved hospital.

Inclusion and exclusion criteria
The inclusion criteria were as follows: (1) age ≥ 18 years; (2) diagnosed primary HCC; (3) patients with unresectable HCC with no plan for further resection within one month [22, 23]; (4) liver function graded as Child–Pugh class A or B; (5) normal preoperative blood pressure; (6) successful TACE; and (7) complete intraoperative and postoperative follow-up records.

The exclusion criteria were as follows: (1) age < 18 years; (2) severe liver dysfunction and inability to tolerate TACE operation; (3) allergy to lipiodol or chemotherapeutic agents; (4) severe arterial disease; (5) systemic infection or complications with other severe diseases; (6) failed operation or death; and (7) absence of required parametric data or drop-out cases; (8) transferred patients or patients with combined hepatic procedures.

Procedures and treatments
The modified Allen's test was performed prior to transradial access to determine the patients' suitability for vascular access [24]. Transradial access was performed by puncturing the radial artery with a 21-G needle after topical anesthesia with 1% lidocaine, and ultrasound guidance was used when necessary. Following successful arterial puncture, a 4F Glidesheath Slender (Merit Medical®, USA) vascular introducer sheath was placed over a 0.021-inch microwire at the puncture site, thus allowing the use of a catheter. After insertion, a mix of 2.5 mg of verapamil, 2 mL of 2% lidocaine, and 2000 IU of heparin was injected via the introducer sheath to prevent vasospasm and avoid clot formation. A 4F × 125 cm Ultimate 1 Performa catheter was advanced into the abdominal aorta over a 0.038-inch × 180 cm Glidewire with a 1.5 mm J-tip. The inserted 4F catheter was then advanced to the celiac and/or superior mesenteric artery, depending on the target vessel to be embolized. Superselective catheterization was performed with a 2.7-F microcatheter advanced into the hepatic artery that was feeding the tumours. Embolization was performed with an emulsion consisting of pirarubicin, lobaplatin, and lipiodol injection. The doses of chemotherapeutic agents used for embolization depended on the conditions of the tumour and patients. In addition, microspheres (HENGRUI Medical®, China) were injected to enhance the embolization efficacy according to the sizes of the tumour vessels.

Transfemoral access was performed with a 4F introducer sheath (COOK Medical®, USA) advanced into the right common femoral artery. A 4F × 80 cm catheter was utilized to select the celiac and/or superior mesenteric artery for catheterization. In addition, superselective catheterization and chemoembolization were performed by placing a 2.7-F microcatheter into the target vessels feeding the tumours.

Haemostatic devices were used after TACE. For patients who underwent the RA route approach, a manual haemostasis device (Radiquick®, China) was utilized on the access site for 2 ~ 4 h without bed rest restriction. In the FA route group, the included subjects were

administered an electronic haemostasis device (Efinger®, China) for 6 ~ 8 h with bedrest. Patients in both groups received routine preoperative and postoperative treatments in addition to RA- or FA-route TACE. Symptomatic treatments were routinely carried out for postoperative syndromes.

Data collection

General patient information and basic parameters, including age, sex, HBV infection, liver function and tumour conditions, were collected prior to the TACE procedure. Intraoperative technical outcomes, such as operation duration, superselection, hepatic arterial spasm, and dose of chemotherapeutic agent, were quantitatively compared. Hepatic arterial spasm was recorded when significant visible segmental stenosis of the hepatic artery under DSA occurred during TACE. The efficacy and safety of the 2 approaches were compared based on the tumour response according to the modified Response Evaluation Criteria in Solid Tumours (mRECIST) for HCC [25] and adverse events. The evaluation of mRECIST was performed by 2 investigators independently. For the enrolled subjects with inconsistent mRECIST assessment, the results were decided through group discussion to reach a final consensus. Moreover, other parametric data, such as postoperative liver function, length of stay (LOS), visual analogue scale (VAS) score of abdominal pain, and cost of hospitalization (Chinese Yuan, CNY), were also quantitatively analysed. Liver function was indexed to the peak values within 7 postoperative days. The LOS was calculated based on inpatients receiving TACE treatment only and patients were discharged until the absence of postoperative adverse events. All included subjects would be stratified and compared.

Statistical analysis

The analysis for continuous variables was performed with Student's *t test*, and the results are presented as the means with standard error of the mean (SEM). Categorical variables were compared by employing χ^2 or Fisher's exact test. A *P* value < 0.05 was considered a statistically significant difference between the two groups. All data manipulation and statistical analysis were accomplished with IBM SPSS Statistics for Windows Version 22.0.

Results

Patient characteristics

In total, 373 patients were retrospectively assessed. Three patients were excluded for failed TACE, and 20 patients were excluded on account of incomplete parametric data. In addition, another 34 deaths or drop-out cases and 18 cholangiocarcinoma or metastatic carcinoma cases were excluded. We also excluded the 22 transferred patients and the subjects with combined hepatic procedures. Finally, 276 subjects were included in the present study, with 131 patients in the RA route group and 145 in the FA route group (Fig. 1). The demographic and baseline characteristics are summarized in Table 1. The baselines of the two groups were consistent, including the patients' general information (age and sex), preoperative liver function indices, and tumour-associated parameters.

Technical outcomes

To compare the technical outcomes between the two routes, we investigated the intraoperative parametric data, including operation time, rate of superselection, hepatic arterial spasm and puncture site haematoma, and consumption of chemo-dose. All parameters were intraoperatively recorded, and representative images for the RA and FA route groups are presented in Fig. 2. The operation duration of the RA group was 84.86 ± 2.09 min, similar to that of the FA group (80.1 ± 2.37 min). Additionally, the doses of chemotherapeutic agents and rates of superselection and puncture site haematoma were also similar (Table 2). Interestingly, no hepatic arterial spasm was observed in the RA group, but 10 subjects were observed in the FA route group, indicating that the rate of hepatic arterial spasm was significantly higher in the FA route group (*P* = 0.002) (Table 2).

Efficacy

We evaluated the efficacy of TACE according to the mRECIST guidelines for primary HCC. The partial response rate in the RA route group was significantly higher than that in the FA route group (30.5% vs. 18.6%, *P* = 0.024). Conversely, more patients in the progression stage were observed in the FA route group after TACE than in the RA route group (12.2% vs. 27.6%, *P* = 0.002) (Fig. 3). These data suggest that RA-route TACE is more efficient than FA-route TACE. Postoperative liver functions indicated by the peak values of related indices TBIL (21.03 ± 1.13 vs. 22.45 ± 1.00 μmol/L, *P* = 0.344), ALT (72.21 ± 6.93 vs. 82.43 ± 6.99 U/L, *P* = 0.301), and AST (127.5 ± 17.25 vs. 131.9 ± 12.43 U/L, *P* = 0.832) were also compared between the two groups, and no significant intragroup differences were revealed (Fig. 4). However, an obviously shorter LOS (8.42 ± 0.36 vs. 9.63 ± 0.35 days, *P* = 0.018) was observed in patients who received RA-route TACE, while the VAS score (3.84 ± 0.14 vs. 4.10 ± 0.13, *P* = 0.162) and hospitalization expenses (45,072 ± 1506 vs. 46,890 ± 1472 CNY, *P* = 0.389) were similar to those of patients receiving FA route TACE (Fig. 5).
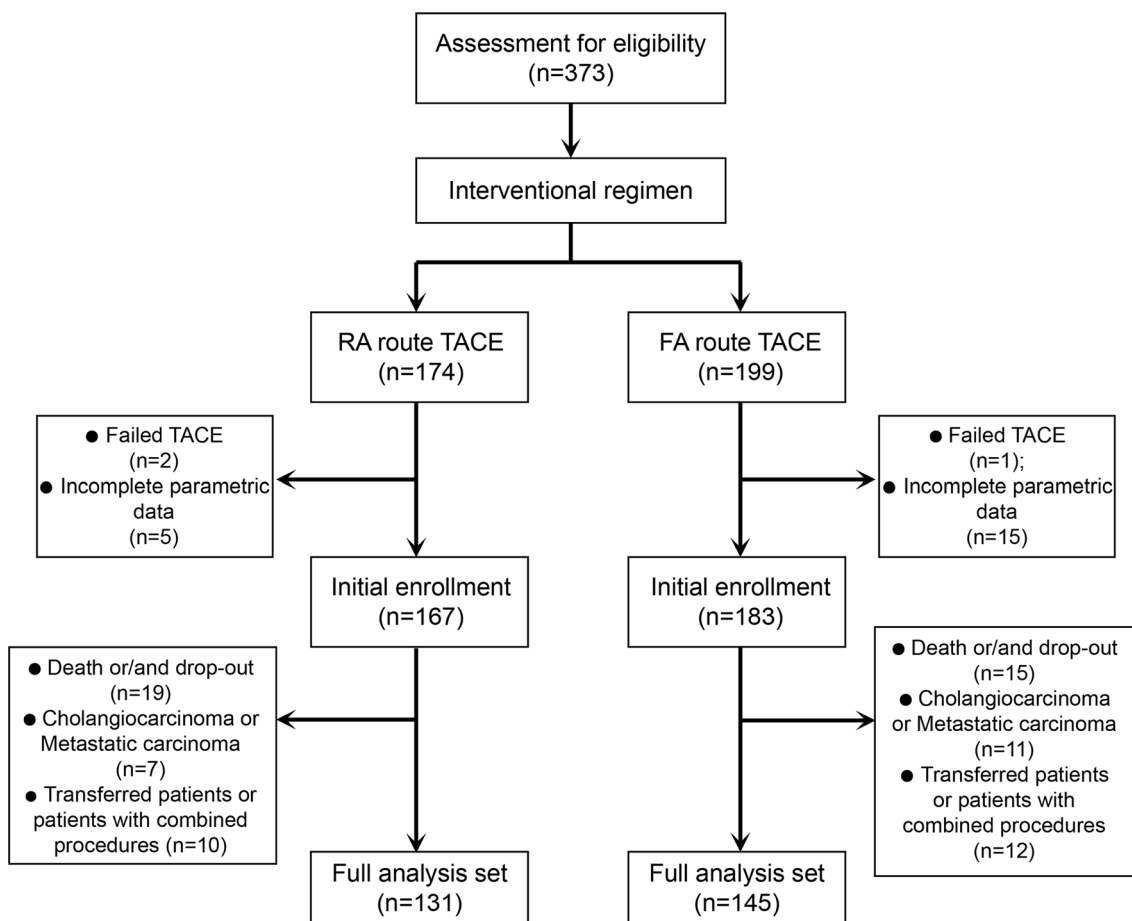
Fig. 1 Patient flow chart. TACE, transarterial chemoembolization

Safety

The incidence rates of adverse events (AEs) commonly seen in the postoperative period are listed in Table 3. For general AEs, the occurrence of fever was significantly reduced in the RA route group (33.6% vs. 52.4%, $P = 0.002$). In addition, fewer patients suffered nausea (30.5% vs. 53.1%) and vomiting (13.7% vs. 24.8%) in the RA route group than in the FA route group. In summary, the total proportion of patients with adverse events in the RA group was 72.5% versus 84.1% in the FA group, with a *p* value of 0.027. Thus, transradial access is a safe and practical choice for hepatic intervention.

Stratified analysis

To further investigate the potential impacts of the differences mentioned above, including hepatic arterial spasm, the rate of partial response and progression, and adverse events, we conducted stratified analysis regarding tumour size and AFP. The results indicated that the RA route presented a lower rate of arterial spasm ($P = 0.013$)

and tumour progression ($P = 0.007$) in tumours < 5 cm and a higher rate of partial response ($P = 0.019$) in tumours > 5 cm. Meanwhile, the RA route revealed superiorities in patients with lower AFP and subjects in the TACE only stratified group but not in subjects with high AFP (Table 4). On the other hand, according to the results of stratified intergroups, patients with tumours < 5 cm and lower AFP more or less presented superiorities in the LOS, tumour response and AEs (Table 4).

Discussion

The intraoperative technical outcomes implied a lower rate of hepatic arterial spasm in the RA route group. Kiemeneij et al. [26] reported that radial artery spasm manifested when patients felt forearm pain or when there was resistance to the advancement of the intra-arterial equipment. In other words, arterial spasm may be attributed to the stimulation of catheterization and friction of the sheath against the vessel, leading to patient discomfort and obstruction of the embolization procedure. Similarly, for the hepatic artery, considering vascular anatomy,

You *et al. BMC Gastroenterology*   (2023) 23:11

Page 5 of 10

Table 1 Baseline characteristics of included patients

Item	RA route	FA route	*P*
Number of patients	131	145	
Gender [n]			
Male	117	132	0.687
Female	14	13	
Age			
HBV [n]			
Absent	14	17	0.849
Present	117	128	
HCV [n]			
Absent	129	140	0.451
Present	2	5	
Alcohol abuse [n]			
Absent	129	140	0.451
Present	2	5	
Nodule number [n]			
1	58	62	0.809
≥ 2	73	83	
Maximum tumor size (cm)			
≤ 5	74	72	0.278
> 5	57	73	
Tumor locations			
Left lobe	15	17	0.713
Right lobe	87	90	
Mixed or diffused	29	38	
Child–Pugh [n]			
A	114	130	0.573
B	17	15	
AFP			
≤ 400 ng/dL	94	88	0.057
> 400 ng/dL	37	57	
Pre-operative liver function			
TBIL (μmol/L)	15.26 ± 0.78	27.34 ± 11.63	0.325
ALT (U/L)	40.29 ± 2.23	48.14 ± 4.26	0.115
AST (U/L)	54.72 ± 5.19	73.41 ± 12.71	0.191

long-range catheterization and sheath movement, TACE could provoke visible hepatic artery spasm, as previously reported [27]. On the other hand, transfemoral access is the conventional approach for angiography and is a relatively easy operating procedure. Comparatively, transradial access technology is more challenging and calls for longer surgery duration, a greater level of proficiency [10, 21] and inevitably demands more advanced catheterization devices for its extensive application. The sheath, which is utilized for the transradial approach, is designed to be more applicable to the anatomy of liver vessels in terms of shape and length and requires gentler and more discreet operation when catheterizing compared with the catheters used for the transfemoral approach. These factors may reduce the incidence of hepatic arterial spasm in the RA route. The reduced proclivity to hepatic arterial spasm with the RA approach might contribute to tumour angiography and improve the subsequent chemoembolization of the vessels feeding the tumours, thus yielding superior efficacy after treatment. According to our results, the grades assessed in accordance with mRECIST determined that transradial access yielded preferable effectiveness to transfemoral access.

Transradial access was confirmed to be a reliable alternative to transfemoral access chemoembolization and to be relatively safe. We revealed that the overall incidence of adverse events was significantly lower in the RA group than in the FA group. Fever, nausea and vomiting, the typical symptoms of postembolization syndrome [28], were less common in patients undergoing transradial access chemoembolization. This result may also be related to the abovementioned gentle procedure associated with transradial access and the design of the vascular devices used. A large randomized comparative study also reported that transradial access for coronary intervention achieved a lower incidence rate of entry site complications [29]. In our research, puncture site haematoma occurred in 2 patients in the FA route group, but
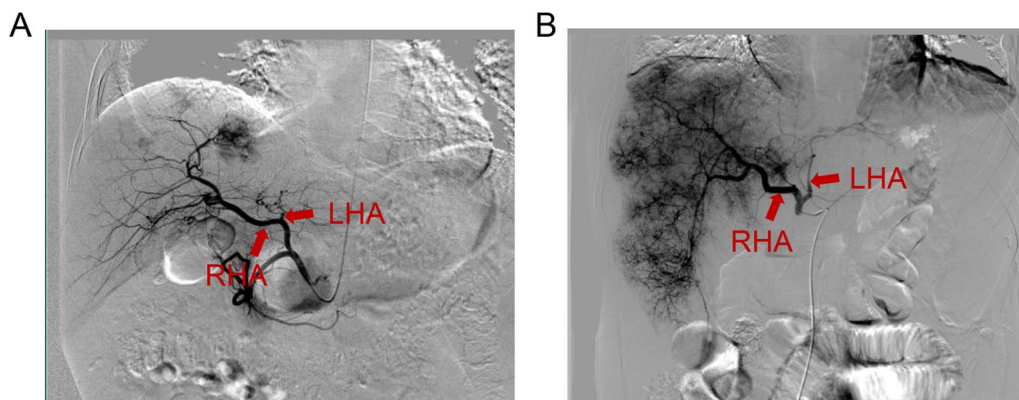

Fig. 2 Representative pictures under DSA during TACE regarding the **A** RA route and **B** FA route. RHA, right hepatic artery; LHA, left hepatic artery

You *et al. BMC Gastroenterology*   (2023) 23:11

Page 6 of 10

Table 2 Intraoperative technical outcomes of TACE patients

Item	RA-route	FA-route	P
Number of patients	131	145	
Operation time (min)	84.86 ± 2.09	80.61 ± 2.37	0.184
Superselection			
Yes	131	143	0.499
No	0	2	
Rate of arterial spasm (%)			
Yes	0	10	**0.002**
No	131	135	
Rate of puncture site hematoma (%)			
Yes	0	2	0.499
No	131	143	
Consumption of chemo-dose (ml)			
Lipiodol	9.83 ± 0.28	10.30 ± 0.37	0.336
Microsphere	2.60 ± 0.39	3.69 ± 0.46	0.075
Pirarubicin	36.87 ± 2.04	33.97 ± 1.55	0.253
Lobaplatin	18.02 ± 1.71	21.94 ± 1.71	0.107

The bold numbers of *P*-value represent statistical differences

no significant intragroup differences were found. Obvious abdominal pain was also equally frequent in the RA and FA groups, consistent with the approximated VAS scores. Other common complications, such as intrahepatic infection, hypertension and coagulation, were not different between the two groups.

Previous research describing the feasibility and efficacy of transradial access in TACE indicated that the procedure time was similar to that of transfemoral access [18–20], in accordance with our results. However, a systematic review that statistically pooled the results suggested that the overall procedure time was significantly longer in the transradial access group [30]. On the other hand, previous studies reported a risk of procedure failure despite no difference in results between the two access approaches [17, 18]. The present study omitted cases of incomplete or failed procedures to consider the efficacy and safety of the different access methods, eliminating the influence of procedural proficiency and heterogeneous circumstances. In addition, the high success rate of TACE
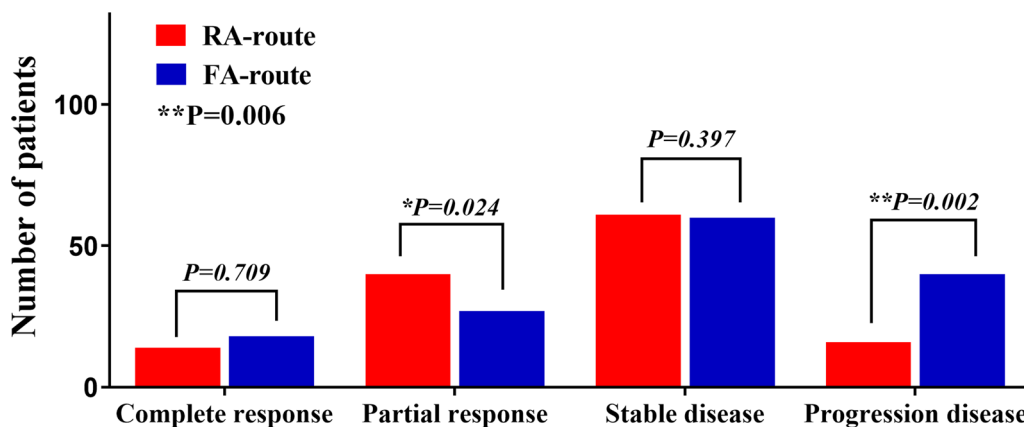

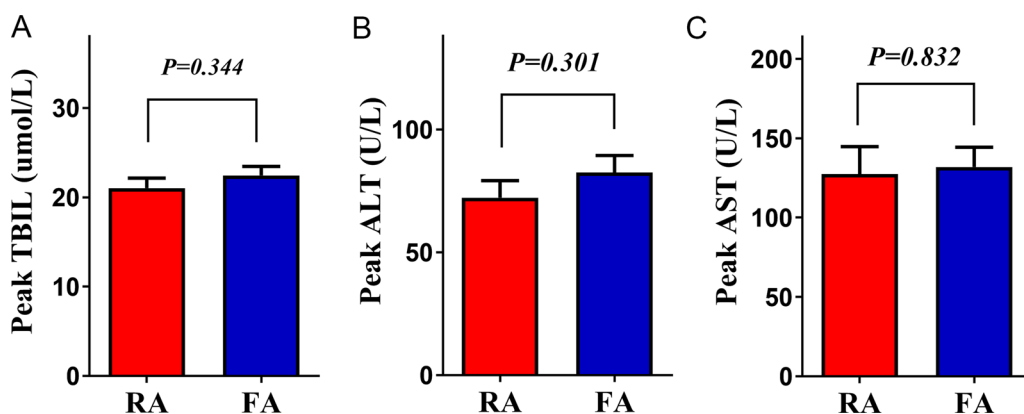**Fig. 3** Assessment of the tumour response after TACE based on mRECIST guidelines for each group

Fig. 4 The peak values of liver function indices, including **A** TBIL, **B** ALT and **C** AST, within 7 days following the operation for patients in each group. TBIL, total bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase
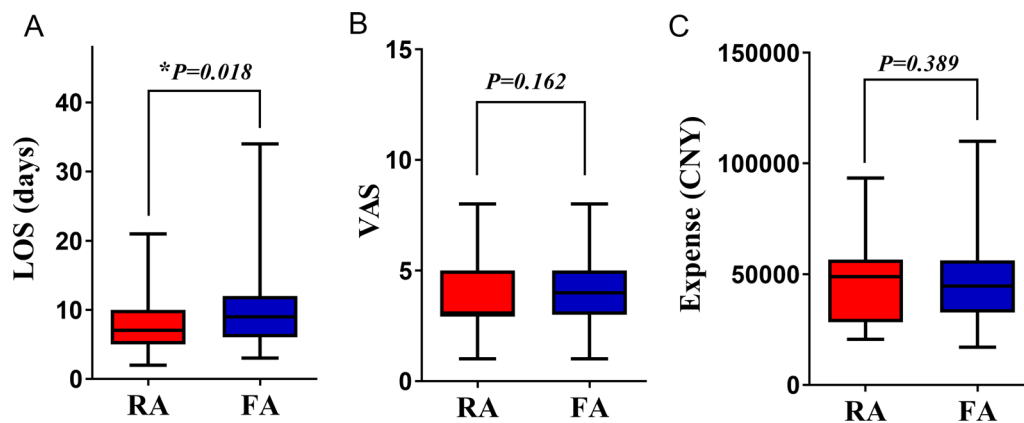
You *et al. BMC Gastroenterology*   (2023) 23:11

Page 7 of 10

Fig. 5 Hospitalization evaluation of the RA route and FA route groups compared by **A** LOS, **B** VAS pain scores, and **C** hospitalization expense for each group. LOS, length of stay; VAS, visual analogue scale

Table 3 Postoperative adverse events of included TACE patients

Item	RA-route (131)	FA-route (145)	P
General events [n (%)]			
Fever	44 (33.6)	76 (52.4)	**0.002**
Fatigue	17 (13.0)	29 (20.0)	0.145
Gastrointestinal events [n (%)]			
Nausea	40 (30.5)	77 (53.1)	**< 0.001**
Vomiting	18 (13.7)	36 (24.8)	**0.022**
Constipation	9 (6.9)	9 (6.2)	0.999
Obvious abdominal pain	61 (46.6)	79 (54.5)	0.147
Ascites	6 (4.6)	4 (3.0)	0.525
Diarrhea	2 (1.5)	0 (0)	0.224
Others [n (%)]			
Wound infection	0 (0)	0 (0)	–
Intrahepatic infections	0 (0)	3 (2.1)	0.249
Hypertension	10 (7.6)	7 (4.8)	0.453
Urine retention	1 (0.8)	2 (1.4)	0.999
Coagulation	0 (0)	2 (1.4)	0.499
Vasovagal reaction	0 (0)	0 (0)	–
Pancreatitis	0 (0)	0 (0)	–
Total cases with AE [n (%)]	95 (72.5)	122 (84.1)	**0.027**

The bold numbers of *P*-value represent statistical differences

via a radial approach is expected along with the technical progress of materials and increased procedural experience of clinicians. Moreover, the stratified analysis determined the superiority of the RA approach in different subgroups, especially for patients with tumours < 5 cm or lower AFP, indicating that the RA route may provide more potential benefits at certain stratifications. The results of stratified analysis also demonstrated that, to some extent, the subjects with tumours < 5 cm or lower AFP revealed better clinical outcomes after TACE, consistent with previous reports [31, 32]. Notably, the conclusions based on stratified analysis still need to be further verified, mainly because there are many relevant influencing factors, and the sample size of some subgroups was significantly smaller after stratification.

Patients who underwent TACE via a femoral arterial approach were required to remain immobilized in the supine position for at least 6 h after the operation to prevent bleeding and haematoma. Pressure haemostatic devices were applied in both TACE groups, but no bedrest was needed for subjects with the RA route, which caused delayed ambulation in the FA route group. Delayed ambulation necessitated a longer monitoring time and, thus, increased patient discomfort [16]. The results of a patient questionnaire also indicated that patients preferred transradial access to transfemoral access [19]. Both delayed ambulation and discomfort may contribute to gastrointestinal peristalsis disorder, which may also potentially increase the incidence of gastrointestinal AEs. On the other hand, for the LOS of clinical outcomes, patients in the RA route group had a significantly shorter LOS than those in the FA route group. The gentler procedure, earlier ambulation and fewer AEs may result in a shorter LOS, which was also confirmed in a previous study [16]. Nevertheless, TACE patients were generally discharged until the absence of AEs in our institution. Therefore, the overall LOS in our study seemed to be longer than usual. However, the main conclusion was that the shorter LOS in the RA route group did not fluctuate. Moreover, the hospitalization expenses were similar in both groups in the present study, in contrast with results reported in other studies [16, 17]. Costs likely differ across different institutions, causing discrepancies in hospitalization expense data. In addition, patients receiving TACE treatment are mainly charged in terms of operation-related costs, and the consumable materials and medicines are approximately accordant in both operation

Table 4 Stratified analysis based on the results with differences

Stratified items	Rate of hepatic arterial spasm			LOS			mRECIST (PR)			mRECIST (progression)			Total subjects with AEs		
	RA route	FA route	P	RA route	FA route	P	RA route	FA route	P	RA route	FA route	P	RA route	FA route	P
Tumor size (cm)															
≤ 5	0	6	**0.013**	7.64±0.47	8.61±0.38	0.111	17	12	0.408	4	15	**0.007**	48	55	0.148
> 5	0	4	0.131	9.42±0.54	10.64±0.57	0.134	23	15	**0.019**	12	25	0.119	47	67	0.177
P	0.999	0.532		**0.015**	**0.004**		**0.037**	0.670		**0.013**	0.094		**0.030**	**0.013**	
AFP															
≤ 400 ng/dL	0	7	**0.005**	8.26±0.46	9.17±0.47	0.168	31	16	**0.028**	8	19	**0.021**	62	72	**0.019**
> 400 ng/dL	0	3	0.276	8.81±0.52	10.35±0.53	0.051	9	11	0.611	8	21	0.170	33	50	0.999
P	0.999	0.740		0.503	0.108		0.402	0.999		0.071	0.057		**0.009**	0.485	

The bold numbers of *P*-value represent statistical differences

You *et al. BMC Gastroenterology*   (2023) 23:11

Page 9 of 10

approaches, although the AE treatments were significantly more common in the FA route group. Perioperative management for patients was performed routinely according to the protocols at a predictable cost. Thus, TACE with transradial access is a practical alternative to traditional transfemoral access and does not increase the hospitalization cost.

This retrospective clinical study compared transradial and transfemoral access technology in hepatic carcinoma following the technical and clinical outcomes. However, the study has some limitations. Previous studies reported the fluoroscopy time during the procedure, which is an underlying factor associated with radiation dose and contrast volume [19, 33], and this parameter was absent in our evaluation. While we assessed the VAS score and postoperative complications, we did not assess patient preference for the access approach used for TACE treatment [34]. We hypothesized that hepatic arterial spasm might influence the tumour response after TACE, but due to the low incidence of hepatic arterial spasm, this speculation could not be addressed in the current study. However, this may be an interesting direction in future clinical research. Therefore, a large-scale randomized controlled trial with rigorous design is warranted to determine the feasibility and reliability of transradial access to replace transfemoral access for future hepatic interventions.

In conclusion, transradial access is a feasible alternative to transfemoral access which has less hepatic arterial spam with the help of advanced catheterization and has shorter hospitalization stays while reducing postoperative complications.

Availability of data and materials
The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Human Subjects Committee of The Second Affiliated Hospital of Chongqing Medical University, and all the participants signed written informed consent forms. The present study was designed and conducted in accordance with the principles of the Helsinki Declaration.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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You *et al. BMC Gastroenterology*   (2023) 23:11

Page 10 of 10

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