CANCER DIAGNOSIS & PROGNOSIS
4: 808-813 (2024) doi: 10.21873/cdp.10400

# Effectiveness of Steerable Microcatheters During Transarterial Chemoembolization for Hepatocellular Carcinoma

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**Abstract.** *Background/Aim: Although transarterial chemoembolization (TACE) is a key treatment for hepatocellular carcinoma (HCC), its effectiveness depends on the cannulation of the microcatheter tip into the feeding artery. Steerable microcatheters allow remote operation of the tip, enabling its insertion into feeding arteries otherwise difficult to reach. This study investigated the indications and effectiveness of steerable microcatheters in TACE for HCC. Patients and Methods: We retrospectively examined 22 patients with HCC who underwent TACE using steerable microcatheters at our Department between December 2014 and July 2024. Previous TACE administration, number of TACE sessions, and feeding artery disruption affecting TACE were examined. Results: Among the first TACE cases requiring steerable catheters, three demonstrated steep bifurcation of the celiac artery or superior mesenteric artery from the parent artery, two had sharp bends in the posterior segment, and four had the left hepatic artery bifurcating from the left gastric artery. All three procedures performed in the inferior phrenic artery required second TACE sessions. Steerable microcatheters were used in two patients during their eighth TACE session; both procedures involved selective cannulation of neovessels feeding from a new anastomotic branch to segment 4, following damage to the main feeding artery from repeated treatments. Conclusion: Steerable microcatheters were effective in reaching steep or strongly bending branches of the parent or feeding artery in the first TACE cases or neovessels and anastomotic branches in previous TACE cases. Studies with larger sample sizes are warranted to validate the use of steerable microcatheters for effective TACE.*

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*Key Words:* Hepatocellular carcinoma, transarterial chemoembolization, steerable microcatheters, selective catheterization, neovessels, steep bifurcation.



Hepatocellular carcinoma (HCC), which represents approximately 90% of primary liver cancers, is the sixth most common carcinoma worldwide, with a dismal prognosis (1). Transarterial chemoembolization (TACE) plays a major role in the treatment of HCC, particularly in patients with intermediate stage (Barcelona Clinic Liver Cancer stage B) HCC (2), where it is considered a standard treatment. However, TACE may be ineffective for conditions that may i) lead to TACE refractoriness; ii) shift liver reserve to Child-Pugh B following TACE; and iii) not be expected to benefit from TACE (3).

The ultimate goal of TACE is to induce total tumor necrosis (4). However, the effectiveness of TACE is based on cannulation of the microcatheter tip into the feeding artery, making the vessel choice and device used essential factors for clinical success. Currently, specific devices for patients who do not respond to TACE are limited. Recent advances in device development have improved their performance during normal use. Moreover, selective catheterization can now address procedural challenges attributed to sharp bifurcations, feeding artery tortuosity, and small artery diameter. One such device, the LEONIS Mova® steerable microcatheter, is the world's first microcatheter to allow the tip of the catheter to be bent by up to 180˚ through a handle for changing the direction of the catheter tip during insertion into the feeding artery (5, 6). This design allows the rapid selection of difficult vessel openings.

In this study, we examined the indications and effectiveness of steerable microcatheters in patients with HCC.

## Patients and Methods

*Study participants.* We retrospectively collected the data of patients who underwent abdominal angiography at the Saiseikai Niigata Hospital between December 2014 and July 2024. The exclusion criteria were i) TACE for liver metastatic tumor and ii) use of steerable microcatheters for portal hypertension. Patients were

eligible for the use of the microcatheter if they fulfilled the following criteria: i) previously attempted insertion into the target feeding artery was unsuccessful using conventional microcatheters and microwires; and ii) preoperative examinations, such as contrast studies, indicated that the target vessel was technically difficult to reach using conventional techniques due to anatomical reasons, such as a series of steep bends, multiple feeding arteries with different branching angles, multiple target and non-target arteries branching close together, or a thin target feeding artery branching from a large parent feeding artery.

Overall, we included 22 patients who underwent TACE using a steerable microcatheter for HCC when selective cannulation was not possible with conventional guidewire operation or triple-angle catheters.

*Principle of operation (Steerable microcatheter, Figure 1).* The steerable LEONIS Mova® (Sumitomo Bakelite Co., Ltd., Tokyo, Japan) microcatheter allows the direction of the catheter tip to be manipulated by rotating a dial on a handheld control unit and applying tension to the operating wires. The catheter's moving tip and dial are connected by two control wires in the catheter wall. Tip displacement can be controlled by using the dial stopper. This microcatheter has a steering dial at the proximal grip, which provides the operator with optimal control of the direction of the steerable tip. The steering dial can be locked with the dial stopper to maintain the intended direction. The steering dial mechanism allows up to 180˚ articulation in opposing directions.

*TACE procedure.* TACE was performed by puncturing the femoral artery using the Selsinger technique, inserting a 5F introducer and a 5F catheter, and advancing the steerable microcatheter to a subregional or further peripheral feeding vessel using the coaxial technique. After embolization, angiography was performed to confirm lipiodol accumulation in the tumor and absence of tumor staining.

*Ethics approval and informed consent.* This study was approved by the Institutional Review Board of Saiseikai Niigata Hospital and conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all the patients.

*Statistical analysis.* Categorical variables are expressed as numbers, and continuous variables are expressed as mean and standard deviations. All the statistical analyses were performed using EZR (Saitama Medical Centre, Jichi Medical University, Shimotsuke, Japan), a graphical user interface for R version 3.2.2 (The R Foundation for Statistical Computing, Vienna, Austria) (7).

## Results

*Patient characteristics.* Of the 22 patients, 13 were male and nine were female; the mean patient age was 70.31±7.08 years. The clinical background of all the patients is summarized in Table I. The ratio of background liver factors for hepatitis B virus: hepatitis C virus: Non-B Non-C was 5:6:11. The average number of TACE sessions was 2.59.

*Use of steerable microcatheters (Table II).* The use of steerable microcatheters was required for the first TACE session in three patients due to steep bifurcation of the celiac artery or superior mesenteric artery (SMA) from the parent artery, two patients due to sharp bends in the posterior region, and four patients due to bifurcation of the left hepatic artery from the left gastric artery (LGA) with steep sharp angles (selective cannulation). All three patients in which the inferior phrenic artery (IPA) was used for TACE underwent TACE for the second time.

In two patients, a steerable microcatheter was used in the eighth TACE session for selective cannulation of neovessels feeding from a new anastomotic branch into the segment 4 region after severe damage to the main feeder by repeated treatment. In addition, all patients had previously undergone TACE with triple-angled microcatheters with a triple-tip geometry prior to the use of steerable microcatheters. No complications were observed in any of the patients.

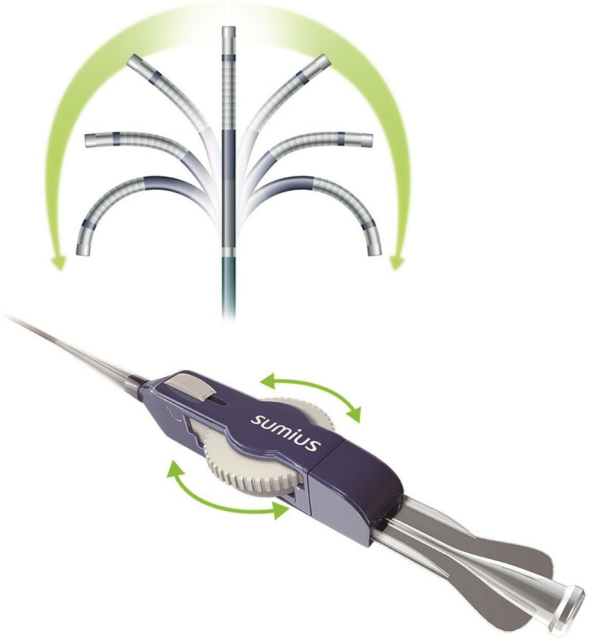


Figure 1. *Appearance and operability of the steerable microcatheter. The tip is rotated 180 in both directions by turning the dial on the catheter handle to the left and right.*

Table I. *Demographic and clinical characteristics of 22 patients with unresectable hepatocellular carcinoma using steerable microcatheter for transarterial chemoembolization (TACE).*

| Demographic variables | Mean±SD | Range |
|---|---|---|
| Age (years) | 70.31±7.08 | 56-81 |
| Sex (Male:Female) | 13:9 | |
| Etiology (HBV/HCV/NonHBVNonHCV) | 5:6:11 | |
| TACE procedure ($1^{st}/2^{nd}/3^{rd}/4^{th}/5^{th}/6^{th}/7^{th}/8^{th}$) | 9/7/1/1/1/1/0/2 | 1-8 |

SD: Standard deviation; HBV: Hepatitis B virus; HCV: hepatitis C virus.

Table II. *Details of transarterial chemoembolization (TACE) procedures with a steerable microcatheter.*

| Case | Age | Sex | Etiology | TACE session | Target artery |
|---|---|---|---|---|---|
| Case 1 | 60 | M | Alc | 6 | LHA from LGA with steep sharp angles |
| Case 2 | 67 | M | Alc | 1 | Steep bifurcation from celiac artery |
| Case 3 | 75 | M | HCV | 1 | LHA from LGA with steep sharp angles |
| Case 4 | 69 | F | HCV | 1 | LHA from LGA with steep sharp angles |
| Case 5 | 71 | M | Alc | 5 | Steep bifurcation from celiac artery |
| Case 6 | 77 | M | Alc | 1 | Steep bifurcation from celiac artery |
| Case 7 | 81 | F | HCV | 2 | Inferior phrenic artery |
| Case 8 | 81 | M | HCV | 2 | Inferior phrenic artery |
| Case 9 | 71 | M | NASH | 1 | Sharp bends in the posterior A6 |
| Case 10 | 68 | M | HCV | 2 | RHA of steep displacement from superior mesenteric artery A8 from A4 anastomosis (LHA) |
| Case 11 | 70 | F | HCV | 2 | Inferior phrenic artery |
| Case 12 | 73 | M | HBV | 8 | RHA of steep displacement from superior mesenteric artery |
| Case 13 | 56 | M | HBV | 1 | Sharp bends in the posterior A6 |
| Case 14 | 56 | M | HBV | 2 | Sharp bends in the posterior A6 |
| Case 15 | 74 | F | NASH | 1 | RHA of steep displacement from superior mesenteric artery |
| Case 16 | 69 | F | HBV | 1 | LHA from LGA with steep sharp angles |
| Case 17 | 74 | F | NASH | 2 | RHA of steep displacement from superior mesenteric artery |
| Case 18 | 75 | F | NASH | 3 | RHA of steep displacement from superior mesenteric artery |
| Case 19 | 72 | M | HBV | 8 | Anastomotic branch into the segment 4 after repeated TACE |
| Case 20 | 59 | F | Alc | 1 | LHA (A2) with steep sharp angles |
| Case 21 | 75 | F | NASH | 4 | RHA of steep displacement from superior mesenteric artery |
| Case 22 | 74 | M | Alc | 2 | LHA (A3) with steep sharp angles |

M: Male; F: Female; Alc: alcoholic; HBV: hepatitis B virus; HCV: hepatitis C virus; NASH: non-alcoholic steatohepatitis; LHA: left hepatic artery; LGA: left gastric artery; RHA: right hepatic artery.

*Representative case*. The patient was an 81-year-old female with HCV-related HCC. TACE/radiofrequency ablation was performed for segment 4-8 HCC beginning in the early 2000s. During follow-up, local recurrence was detected at the same site. Computed tomography (CT) hepatic arteriography confirmed that the site was not a feeder from the initial A8. The recurrence was fed from the right diaphragmatic artery, which also appeared to be narrow on angiography; however, the catheter could not be selectively inserted into this artery using various guidewires (Figure 2A). Therefore, the patient underwent TACE with the steerable catheter (Figure 2B). No recurrence was observed after the use of TACE with a steerable microcatheter.

## Discussion

TACE has advanced with the development of TACE devices (8). However, few reports have analyzed the effectiveness of steerable microcatheter in TACE for HCC. This study investigated the effectiveness and indications of steerable microcatheters for selective TACE to achieve complete necrosis in HCC.

The steerable microcatheter, LEONIS Mova®, is an advanced device that allows the tip to be bent by 180˚ with a hand-held dial, making it ideal for catheter insertion into feeding arteries with smaller diameters, tangentially bifurcating inferior transverse arteries, and steeply branching hepatic arteries. The main feature of the steerable microcatheter is that the shape of the tip can be changed to fit the shape of the vessel once advanced to the desired arterial origin (5, 6).

The effectiveness of steerable microcatheter was validated in animal experiments and developed as a commercial medical device (5, 6). The maneuvers allowed by the steerable microcatheter were very useful in this study. Thus, the steerable microcatheter can quickly and reliably reach deep localized diseased feeding arteries without a microwire to adapt to complex branches and tortuous feeding arteries. This enables accurate contrast and drug administration. It also shortens the treatment time, reducing the burden on healthcare professionals and patients.

TACE procedures should consider hepatic artery transection and extrahepatic collateral channels. Thus, it may be necessary to insert a catheter into the LGA or the SMA. HCC can also result in extrahepatic collateral channels, depending on the site of the channel and surrounding extension (9). Selecting small branches diverging at a steep angle from the parent artery is often challenging with conventional microcatheters. In the present study, the steerable microcatheter was useful in cases of steep bifurcation from the celiac artery and steep displacement from the SMA. The steerable microcatheter is expected to

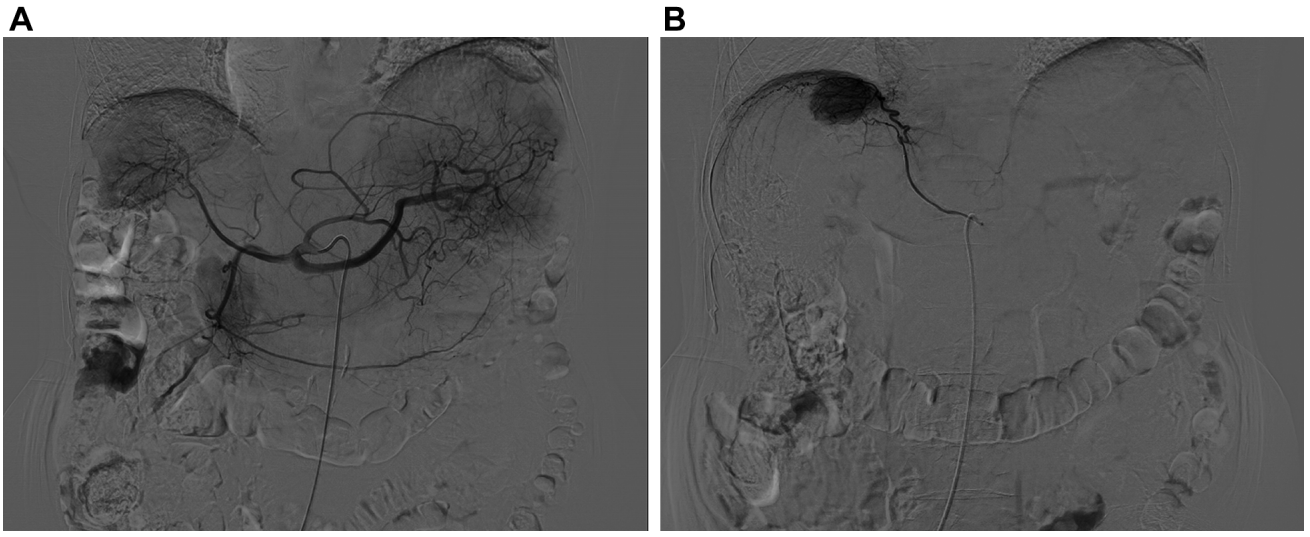


Figure 2. *Representative case. The patient was an 81-year-old female with HCV-related recurrent hepatocellular carcinoma. A) Celiac angiograms did not show hypervascular staining due to thin inferior phrenic artery and insufficient contrast. B) Right inferior phrenic angiogram shows hypervascular staining by steerable microcatheter. Transcatheter arterial chemoembolization (TACE) via the right inferior phrenic artery was performed.*

facilitate microguidewire insertion by directing the tip angle toward the target vessel. However, after microguidewire insertion, attempts to follow the microcatheter sometimes result in deflection of the microcatheter in the parent artery, making catheter insertion impossible. In addition, hemodynamic difficulties with reinsertion are often experienced during repeat interventional radiology treatment for HCC. In the present study, the average number of TACE sessions per patient was 2.59, suggesting the usefulness of the steerable microcatheter in selective TACE to neovessels, including anastomotic branches.

Although the IPA is known for its high potential as an extrahepatic branch trophic artery, its smaller diameter compared to the celiac artery diameter and its branching from the proximal cephalic or dorsal aspect of the celiac artery sometimes make cannulation challenging. The IPA accounts for 83% of the TACE collateral vessels, with a reported success rate of 96% (10). The angulation of the vessel after bifurcation can be easily assessed on 3D images (11). However, successful cannulation of the IPA also depends on the technical skill of the clinician, and the success rate varies between centers. One reason is that the IPA branches from the proximal celiac artery. Hence, the origin of the inferior transverse artery is first identified with the parent catheter hanging lightly over the proximal celiac artery, but the parent catheter is often unstable and easily dislodged, making the origin difficult to identify. In such cases, the microcatheter or microguidewire tip is inverted into a hairpin shape to carefully explore the origin of the inferior transverse artery; however, the parent catheter is still unstable, the torque of the microguidewire is not transmitted, and cannulation from the medium-diameter artery to the small-diameter artery is generally not performed. To resolve this, the catheter is inserted in the middle of the arterial wall. In some cases, strategies such as creating a side hole on the tip of the parent catheter to allow passage of the microcatheter are successful. Nonetheless, the establishment of a technique for the stable and superselective insertion of a microcatheter into the IPA is necessary.

When the steerable microcatheter is used for cannulation of inverted target vessels, the angle of the microcatheter tip can be locked to prevent kickback when inserting the guidewire and then unlocked when guiding the microcatheter along the guidewire, releasing the shape of the microcatheter tip as presented in the representative case. The ability to adjust and fix the angle of the tip while the microcatheter is inserted into the vessel and to unlock it at any time is a major advantage of steerable microcatheters. With the introduction of better software to identify target vessels, the difficulty in identifying target vessels is also reduced. Moreover, reliable cannulation of target vessels is becoming increasingly important. The steerable microcatheter will be useful in cases where cannulation is difficult to perform using conventional devices and may provide important advances against TACE failure.

Utilization of a steerable microcatheter, with or without a guidewire, leads to easier and faster target vessel selection in complex vessel anatomy (12). In TACE for HCC, superselective treatment is required not only to increase the therapeutic effect but also to prevent deterioration of liver function following treatment.

After TACE, the artery is narrowed by vasculitis, leading to poor filling of the embolized material during repeated

TACE. If the hepatic arterial branches are occluded, the tumor is fed by extrahepatic vessels, some of which may be difficult to select, and if the extrahepatic blood supply is not developed, the tumor is also nourished by the portal vein. Such tumors are usually refractory to treatment and additional TACE is unlikely to be effective. Therefore, the therapeutic efficacy of TACE decreases with tumor recurrence or progression and additional TACE sessions. Furthermore, repeated TACE can damage the hepatic artery, liver parenchyma, and bile ducts, leading to a vicious cycle of reduced hepatic reserve. (13). Recently, the superselective administration using drug eluting bead (DEB) TACE (DEBTACE) with microspheres <150 μm was shown to have impact on the reduction of hepatobiliary toxicity and the loss of systemic adverse events (14). Selective TACE is also necessary to increase the effectiveness of DEBTACE, thus steerable catheters are useful in DEBTACE. Therefore, TACE should aim at complete remission.

When collateral pathways are present, drug administration to the hepatic artery alone is insufficient for achieving a therapeutic effect. Preoperative CT and intraoperative angiography, CT angiography, and CT arterial portography can estimate the hepatic artery transection and collateral pathways from extrahepatic sources, reducing intraoperative radiation exposure and contrast agent use and enabling highly effective treatment. The addition of TACE was found to improve survival in multimodal treatment alongside ablation for advanced HCC with portal vein tumor thrombus (15). Moreover, the successful use of a steerable catheter in a well-executed TACE procedure is crucial for the future role of TACE.

*Study limitations*. First, the sample size was relatively small. Second, the study did not compare patients at different disease stages. Third, the retrospective design may have introduced bias in the selection of the patients. Lastly, the study only considered data from a single center. Future prospective clinical trials with larger sample sizes and varied multicenter patient populations are warranted to verify our findings.

## Conclusion

Steerable catheters have a tip shape that can be changed according to the vessel morphology and were found to improve the quality of TACE and reduce the incidence of TACE refractoriness. Therefore, steerable microcatheters can be useful for the treatment of various other clinical conditions for all TACE procedures.

## Conflicts of Interest

The Authors have no conflicts of interest to declare in relation to this study.

## Authors' Contributions

Conceptualization: Toru Ishikawa; Data Curation: Toru Ishikawa; Formal Analysis: Toru Ishikawa; Investigation: Toru Ishikawa, Ryo Sato, Hiroki Natsui, Takahiro Iwasawa, Masahiro Ogawa, Yuji Kobayashi, Toshifumi Sato, Junji Yokoyama, and Terasu Honma; Methodology: Toru Ishikawa; Project Administration: Toru Ishikawa; Resources: Toru Ishikawa; Software: Toru Ishikawa; Visualization: Toru Ishikawa; Writing – Original Draft: Toru Ishikawa; Writing – Review & Editing: Toru Ishikawa, Ryo Sato, Hiroki Natsui, Takahiro Iwasawa, Masahiro Ogawa, Yuji Kobayashi, Toshifumi Sato, Junji Yokoyama, and Terasu Honma.

## Acknowledgements

The original images in Figure 1 were provided by SUMITOMO BAKELITE CO., LTD. (Tokyo, Japan). We declare that we have no financial relationship to the company. The Authors thank Editage (www.editage.com) for English language editing.

## Funding

None.

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*Received September 12, 2024*
*Revised September 26, 2024*
*Accepted September 30, 2024*