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CASE REPORT

From Flow Modulation to Resection: First in Human Combination of Liver Venous Deprivation and Balloon-Occluded Chemoembolization (LVD-B-TACE): A Case Report Demonstrating a Novel Sequential Concept

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Abstract: Curative surgical treatment of hepatocellular carcinoma (HCC) is limited to liver transplantation (LT) and liver resection (LR), but many patients are ineligible due to insufficient future liver remnant (FLR). Liver venous deprivation (LVD) induces more rapid hypertrophy than portal vein embolization (PVE) but may trigger the hepatic arterial buffer response (HABR), leading to increased arterial inflow and potentially stimulating tumor growth, especially for HCC. We report a 75-year-old male with HCC and advanced fibrosis, in whom extended LVD was followed 3 days later by balloon-occluded transarterial chemoembolization (B-TACE) to coincide with HABR, providing more selective tumor control, higher intratumoral drug concentration, and low risk of non-target embolization compared to standard TACE, which is desirable in the field of deprived livers. Within three weeks, FLR increased from 33% to 51% with degree of hypertrophy (DH) 15.8%, kinetic growth rate (KGR) 5.3%/week and relative growth rate (RGR) 47,6% accompanied by near-complete tumor response, enabling curative hepatectomy. Despite postoperative complications, R0 resection was achieved. This case illustrates the technical feasibility of sequential LVD followed by B-TACE in this specific order, suggesting that such an approach may help reduce the hepatic arterial buffer response within the tumor, support rapid hypertrophy, and facilitate resectability in carefully selected patients, including elderly individuals with comorbidities. To the best of our knowledge, and based on a comprehensive literature search, this is the first reported case of LVD-B-TACE.

Keywords: liver cancer, hepatocellular carcinoma, future liver remnant, liver resection, liver venous deprivation, balloon-occluded chemoembolization

Introduction

Liver transplantation (LT) and hepatic resection (LR) remain the only surgical options that offer curative potential for hepatocellular carcinoma (HCC).[1] A key question at the beginning of treatment is whether a patient is eligible for one of these potentially curative approaches. However, in many cases, LR is precluded by an insufficient future liver remnant (FLR). Moreover, patients with advanced fibrosis or cirrhosis are at increased risk of postoperative liver failure when FLR is inadequate.[2,3] Finally, even in the absence of standard contraindications, some patients may decline the proposed surgical treatment for various personal reasons.

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These situations generate a need for seeking options leading to maximally effective treatment – in many cases beyond established guidelines.

Well-established approaches to increase FLR include portal vein embolization (PVE) or ligation, two-stage liver resection, associating liver partition and portal vein ligation for staged hepatectomy (ALPPS). More recently, liver venous deprivation (LVD) has emerged as a technique that simultaneously blocks portal inflow and hepatic venous outflow, thereby accelerating hypertrophy of the contralateral lobe. Compared with PVE alone, LVD achieves faster and more pronounced hypertrophy, potentially reducing the probability of tumor growth during the waiting period before LR.[2,3] Progression during this phase nevertheless remains a significant risk, partly because LVD may trigger hepatic arterial buffer response (HABR), a compensatory mechanism in which reduction of portal venous inflow results in reciprocal augmentation of hepatic arterial perfusion in the embolized segments. This is supported by both clinical and experimental models of portal vein occlusion which have demonstrated measurable increases in arterial flow, leading to relative arterial dominance in these areas.[4–7] Given that hepatocellular carcinoma derives the majority of its blood supply from the hepatic artery, such hemodynamic redistribution may theoretically enhance tumor perfusion and potentially facilitate tumor progression during the hypertrophy interval.[8]

Therefore, balloon-occluded TACE (B-TACE) appears to be a particularly suitable counterstrategy because temporary occlusion of the arterial branch supplying the lesion alters the local pressure gradient, leads to compensatory opening of intersegmental collaterals, and redistribution of flow toward the tumor tissue, which has low vascular resistance due to neovascularization. All this promotes more selective accumulation of the embolization mixture in the lesion, limits off-target embolization due to the antireflux mechanism, and leads to more effective local tumor control compared to standard TACE.[9–12] In the post-LVD setting, when arterial inflow to the embolized segments is accelerated, it can be assumed that this mechanism may act even more significantly, as the higher inflow may further enhance the pressure-controlled flow redistribution toward the tumor tissue.

We present a case report of a patient in whom a multimodal approach combining LVD and B-TACE in short time frame successfully enabled the conversion of an initially unresectable HCC to resectable and subsequently curative surgical procedure.

Case Report

A 75-year-old male was referred to our center with a centrally located liver tumor in terrain of advanced liver fibrosis due to metabolic dysfunction-associated steatohepatitis (MASH). At the time of diagnosis, the patient had early-stage disease (Barcelona Clinic Liver Cancer stage A), preserved liver function (Child–Pugh class A) and excellent functional status (performance status 0). His medical history included ischemic heart disease with preserved ejection fraction, type 2 diabetes mellitus controlled with oral antidiabetic medication, arterial hypertension and a previous urinary bladder cancer in remission.

Initial contrast-enhanced CT revealed a 45 mm lesion located centrally at the junction of segments S5/8 and S4a/S4b (Figure 1). The lesion demonstrated typical hallmarks of HCC: arterial phase hypervascularity, washout in the portal phase, and capsule enhancement in the delayed phase, fulfilling LI-RADS 5 criteria.[13] No extrahepatic spread or vascular invasion was identified. Volumetric analysis calculated the left lobe volume at 672 mL, corresponding to only 33% of the total liver volume. Given the patient's advanced fibrosis and comorbidities, current recommendations suggest a minimum safe FLR of 40%; therefore, immediate surgery was contraindicated.[14]

The case was discussed at a multidisciplinary tumor board (MDT). Liver transplantation was evaluated but deemed relatively contraindicated due to the patient's prior malignancy and the patient declined this option. Other treatments including stereotactic body radiotherapy (SBRT), transarterial radioembolization (TARE) and systemic therapy were considered; however, none offered curative intent.

The hepatic venous pressure gradient measured 7.5 mmHg, excluding clinically significant portal hypertension and allowing consideration of hepatic resection. The main challenge was borderline resectability related to tumor size and the need to achieve sufficient FLR while maintaining effective local tumor control within a limited timeframe.

PVE was considered, but hypertrophy of the contralateral lobe was expected to be slower.[15] ALPPS was rejected due to concerns about increased perioperative risk in elderly patient. In contrast, LVD was favored for its potential to induce faster hypertrophy with a lower risk profile and the possibility of a stepwise approach if needed. Therefore, a combined endovascular strategy consisting of extended LVD followed by B-TACE was proposed to promote FLR growth and

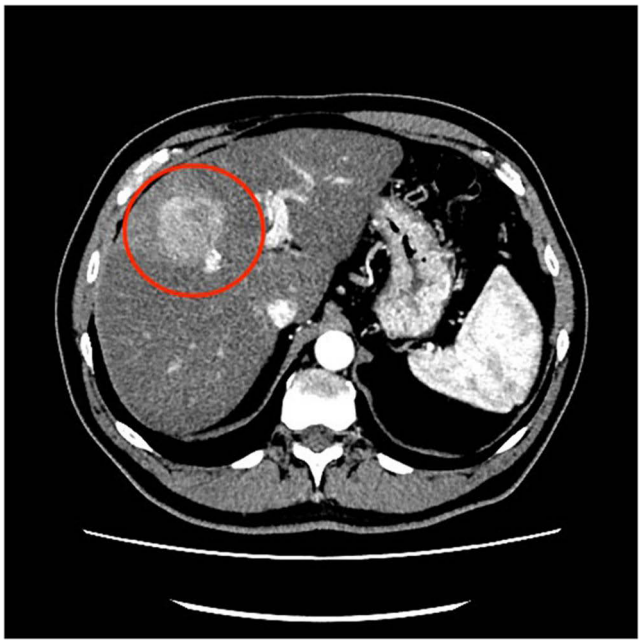

Figure 1 CT, arterial phase, HCC lesion 45 mm (red circle), LI-RADS 5.

reduce the risk of tumor progression during the hypertrophy period. SBRT was defined as a second-line option in case of treatment failure.

At the time of presentation to the MDT, the patient had well-preserved liver function, and therefore no clear limitations to the proposed treatment were identified, as confirmed in consultation with a hepatologist.

Under USG and cone-beam CT (CBCT) guidance, a Chiba needle was used to puncture portal vein. Through guidewires (0.014" and 0.035") and sequential dilatation with sheaths (4–8F) embolization of the right portal vein using SIM1 catheter was performed using a lipiodol–Histoacryl mixture (10 mL, ratio 8:1). Puncture tract in liver were sealed with residual glue. The right and middle hepatic vein were occluded through femoral vein access (7F sheaths) with four vascular plugs Amplatzer II from 14 to 22 mm (Abbott, USA). The size of the plugs was selected after measurement of the vein diameters, with approximately 40% oversizing to prevent migration (Figures 2 and 3). We prefer the transfemoral approach to reduce seeding of tumor cells during repeated transhepatic punctures. The procedure lasted approximately 180 minutes and was uneventful.

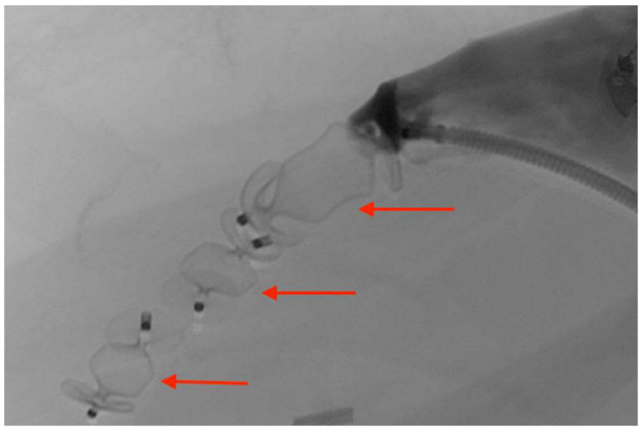

Figure 2 Three vascular occluders (red arrows) in the right hepatic vein inserted through a transfemoral approach.

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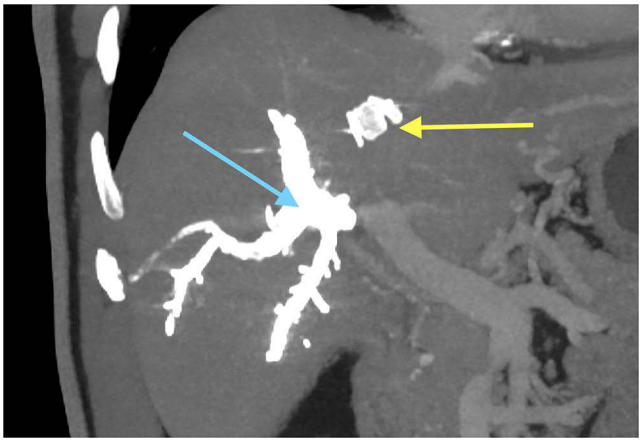

Figure 3 CT, portal phase, glue in the right portal vein (blue arrow), one of the occluders in the middle hepatic vein (yellow arrow).

Three days later, during the period of established hepatic arterial buffer response (HABR), B-TACE was performed to minimize the risk of local progression and maximize therapeutic effect. From right femoral approach via 5F sheath RC1 catheter was placed into the right hepatic artery arising from the superior mesenteric artery. Navigation with angiography and CBCT enabled selective catheterization with a microballoon catheter (Occlusafe, 2.7F, Terumo, Japan). After balloon occlusion, balloon-occluded arterial stump pressure (BOASP) decreased from 97 to 34 mmHg. A total dose of 100 mg doxorubicin was administered in accordance with our institutional protocol, which considers liver functional reserve and does not exceed recognized maximum dose limits. The drug was loaded onto LifePearls microspheres (Terumo, Japan) of 100±25 µm and 200±50 µm diameter. Final angiography of a CBCT confirmed satisfactory intratumoral deposition of the microspheres with minimal off-target embolization (Figure 4).

The procedure lasted 100 minutes and was uncomplicated. Elevation of liver function tests was observed after LVD, with alanine aminotransferase (ALT) increasing from 109 U/L at baseline to 457 U/L on the third day following the procedure. However, no impairment of synthetic or excretory liver function was detected, as evidenced by normal coagulation parameters and bilirubin levels. Liver enzyme values subsequently declined gradually and eventually fell

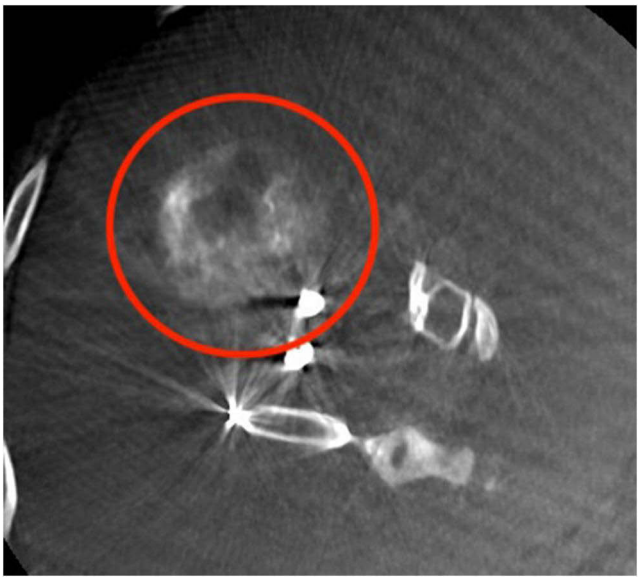

Figure 4 Non-contrast CBCT after B-TACE demonstrates intratumoral retention of dense embolization material (red circle) without evidence of non-target embolization.

below baseline levels. The baseline ALT elevation was long-standing and consistent with metabolic dysfunction-associated steatohepatitis (MASH) as the underlying etiology of cirrhosis.

Restaging CT performed three weeks after LVD demonstrated near-complete radiological response, with only small 6 mm focal residue of viable tumor tissue (Figure 5), corresponding to near-complete tumor debulking.[16] Importantly, volumetry revealed an increase in FLR from 33% (672 mL) to 51% (992 mL). Degree of hypertrophy (DH) was 15.78%, kinetic growth rate (KGR) was 5.26% and relative growth rate (RGR) 47.6% (Figures 6 and 7). These results allowed us to perform a safe LR.

Four weeks after the initial procedure, the patient underwent right hepatectomy. Histology confirmed complete resection (R0) of poorly differentiated HCC which was almost completely necrotic (Figure 8). According to the pathologist, the microspheres were only found in the tumor and very rarely in the nearby surrounding parenchyma (Figure 9). The postoperative course was

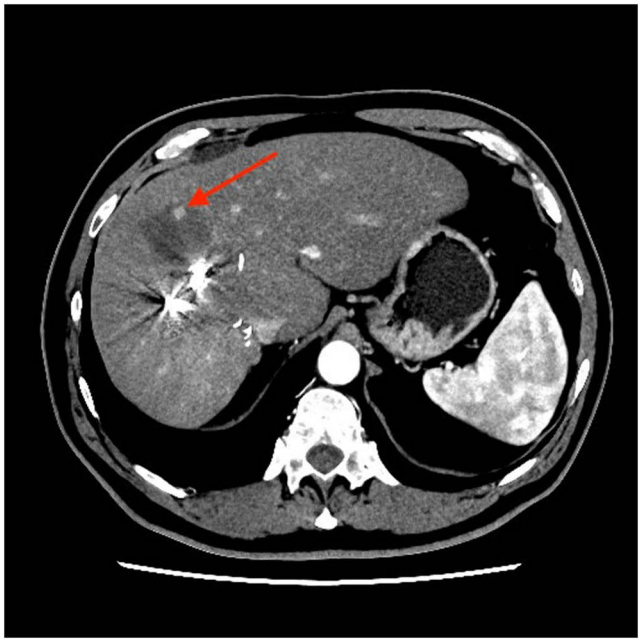

Figure 5 CT, late arterial phase, after B-TACE only a small 6 mm residue of viable tissue (red arrow).

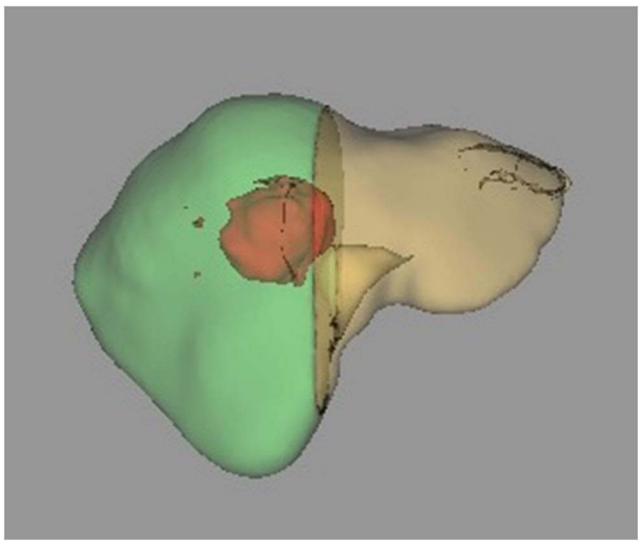

Figure 6 CT volumetry before LVD, FLR 33%.

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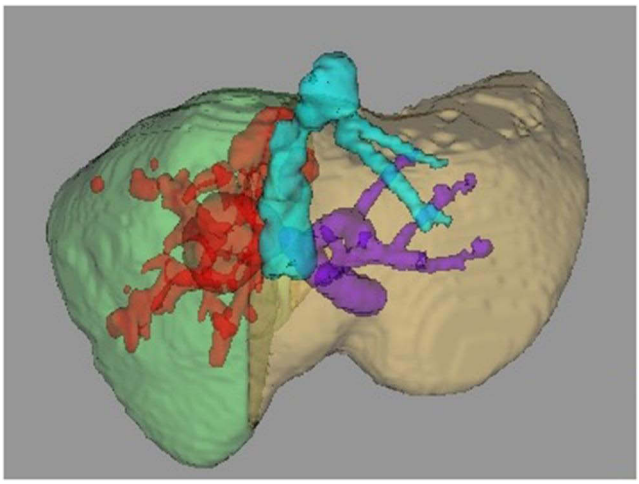

Figure 7 CT volumetry after LVD, FLR 51%.

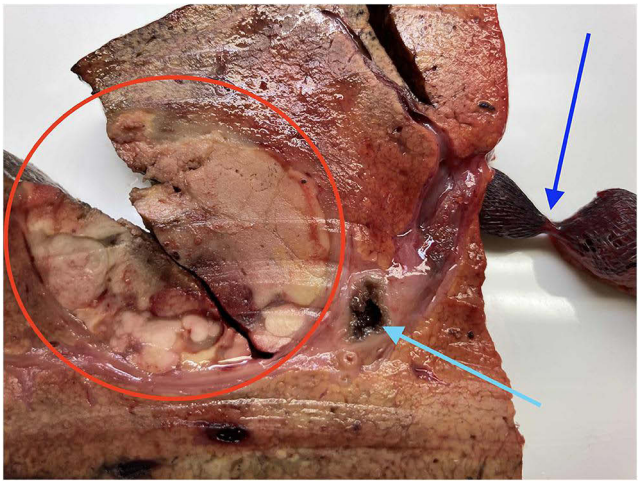

Figure 8 Post-dissection pathological specimen, necrotic tumor (red circle), glue in the portal branch (light blue arrow), occluder in the hepatic vein (dark blue arrow).

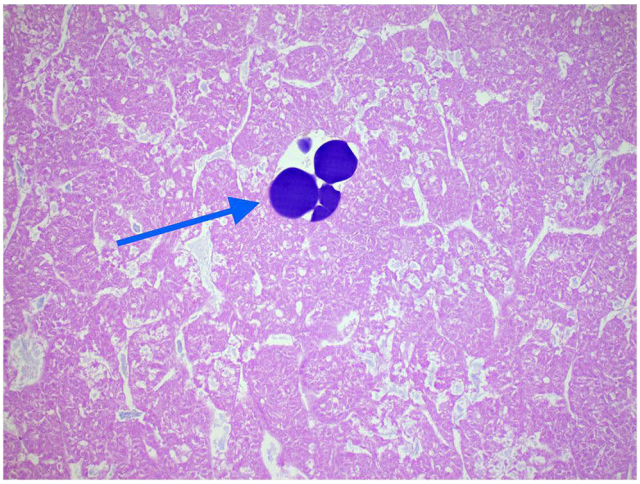

Figure 9 Histological section (hematoxylin-eosin) showing extensive tumor necrosis with microspheres (blue arrow) located almost exclusively intratumorally and only very rarely in the adjacent peritumoral tissue, confirming predominantly intratumoral distribution.

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complicated by bilateral pleural effusion requiring drainage and minor pulmonary embolism treated with anticoagulation. The patient was discharged in good condition on postoperative day 17.

Discussion

This case demonstrates the clinical potential of sequential combination of LVD and B-TACE to achieve curative resection in patients initially ineligible for LR due to insufficient FLR.

According to several studies and CIRSE standards of practice, LVD (also termed double-vein embolization – it depends whether you use plugs or glue to seal the hepatic veins) is a safe and effective method to induce rapid hypertrophy of the contralateral lobe. Reported FLR increases are consistently greater than after PVE alone. In addition, simultaneous portal and hepatic vein embolization accelerates regeneration and reduces the risk of tumor progression compared to sequential approaches.[2,3,14,15]

Our choice to add B-TACE was motivated by the well-recognized risk of HCC progression during the hypertrophy phase. Following LVD, compensatory hemodynamic changes occur with increased arterial inflow to the embolized segments and may accelerate tumor growth during the waiting period.[4–7] It is known that up to 15–20% of patients undergoing PVE or LVD ultimately become non-resectable due to such progression.[8] In our case, B-TACE was performed to counterbalance the HABR, thereby ensuring both effective local tumor control and safe hypertrophy of the FLR.

Importantly, we consider the order of the two procedures to be critical, especially in HCC. Performing LVD first and then B-TACE seems to be more advantageous in our view than the reverse order. If B-TACE is performed first, its antitumoral effect would likely be partially neutralized by the subsequent hemodynamic changes induced by LVD, including the development of arterial collaterals. Such changes could reduce embolization efficiency and allow partial tumor reperfusion. Based on these considerations, it may be preferable to perform B-TACE in the early interval after LVD—ie, within the first week, when the HABR is fully established. Moreover, embolization mixture retention is prolonged in the devascularized lobe, as both portal and hepatic venous outflow are partially restricted. Furthermore, B-TACE after LVD appears from our point of view to be more advantageous than standard TACE because the HABR may potentiate the redistribution of flow through intersegmental collaterals, further enhancing the effect of B-TACE.[9–12]

However, several limitations must be acknowledged. The sequential approach combining LVD and B-TACE is technically demanding, requires multiple punctures and longer procedural time, and may increase the risk of access-related complications such as bleeding or vascular injury. It also increases cumulative radiation exposure, procedural burden, and resource utilization compared to single-modality strategies. Potential complications of liver regeneration techniques and B-TACE include infectious events such as cholangitis, abscess formation or sepsis, as well as bile duct injury, cholestasis and transient liver failure.[14] Close peri- and post-procedural monitoring of liver function tests, bilirubin levels, coagulation parameters and inflammatory markers is therefore essential.

In the present case, none of the above-mentioned complications were observed. Careful patient selection remains crucial, particularly in individuals with impaired baseline liver function or pre-existing biliary abnormalities, including biliary dilatation, prior biliary interventions or bilioenteric anastomosis.[14] In our patient, both procedures were completed safely and resulted in significant hypertrophy within three weeks, closely matching literature outcomes.[15,17]

This concept requires further validation, as the present report is based on a single case and does not allow for generalization. The proposed sequential strategy remains hypothetical and should be confirmed in larger patient cohorts. At our institution, we plan to apply this approach in carefully selected patients, as we anticipate that a subset may benefit from this strategy. In general, it should be considered only in patients with well-preserved liver function and borderline resectable tumors, within a limited therapeutic window for potentially curative intervention, and after thorough assessment of the associated risks. A crucial prerequisite is the confirmed absence of eligibility for liver transplantation for various reasons. The optimal timing of B-TACE after LVD has not been established, and in this case, performing B-TACE three days after LVD was based on pathophysiological rationale. Patient heterogeneity, particularly the degree of fibrosis or cirrhosis may further influence safety and efficacy. While this case confirms the technical feasibility of the sequential approach, this technically complex strategy should be reserved for specialized centers with sufficient interventional expertise and applied only after multidisciplinary consensus that the anticipated oncological benefit justifies the potential risks.

According to our review of PubMed, Scopus, and Google Scholar, no peer-reviewed publication has specifically reported the combination of LVD and B-TACE. Published approaches have mainly focused on performing standard TACE prior to LVD. The innovativeness of our case lies in the opposite sequential arrangement and the use of a microballoon technique, which in our view synergistically utilize the HABR to achieve higher chemoembolization efficacy; such an approach has not been identified in the available literature.

Finally, from a broader perspective, this case highlights the value of multidisciplinary collaboration. The combination of interventional radiology, appropriate hepatological approach, and surgical management allowed us to convert a patient who was initially ineligible for LR into a candidate for potentially curative surgery. Postoperative complications, although significant, were manageable and did not compromise the oncological outcome.

Conclusion

Sequential LVD followed by B-TACE may represent a promising multimodal strategy for selected patients with HCC and insufficient FLR. Performing LVD first may enable rapid contralateral hypertrophy, while subsequent B-TACE could reduce the hepatic arterial buffer response within the tumor more effectively than standard TACE and maintain tumor control during the hypertrophic phase. By synchronizing regenerative and oncological control strategies, this approach may improve the chances of conversion to resectability.

In this case, the strategy proved technically feasible and enabled successful resection in an elderly patient with comorbidities. However, given the single-case nature of this report, these findings should be interpreted with caution. Further experience in a larger number of patients is required to better define the safety and oncological benefit of this approach.

Abbreviations

ALPPS, Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy; B-TACE, Balloon-Occluded Transarterial Chemoembolization; CBCT, Cone-Beam Computed Tomography; DH, Degree of Hypertrophy; FLR, Future Liver Remnant; HABR, Hepatic Arterial Buffer Response; HCC, Hepatocellular Carcinoma; HVPG, Hepatic Venous Pressure Gradient; KGR, Kinetic Growth Rate; LI-RADS, Liver Imaging Reporting and Data System; LR, Liver Resection; LT, Liver Transplantation; LVD, Liver Venous Deprivation; MDT, Multidisciplinary Tumor Board; MASH, Metabolic Dysfunction-Associated Steatohepatitis; PVE, Portal Vein Embolization; RGR, Relative Growth Rate; SBRT, Stereotactic Body Radiotherapy; TARE, Transarterial Radioembolization.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal approval by the Institutional Review Board (IRB) was not required.

Informed Consent

Written informed consent was obtained from the patient for the procedure and for participation in this case report.

Consent for Publication

Written informed consent for publication was obtained from the patient for all individual data included in this case report, including accompanying images.

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Disclosure

The authors declare no conflicts of interest in this work.

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