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RESEARCH

Safety profile of transarterial chemoembolization therapy in elderly patients with hepatocellular carcinoma

Hepatosellüler karsinomlu yaşlı hastalarda transarteriyel kemoembolizasyon tedavisinin güvenlik profili

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Abstract

Purpose: This study explores the safety of ransarterial chemoembolization (TACE) in elderly Hepatocellular carcinoma (HCC) patients, aiming to clarify its suitability and identify risk factors for serious adverse events, ultimately aiding clinical decisions in geriatric oncology.

Materials and Methods: This retrospective study included patients over 18 years of age who were newly diagnosed with HCC based on histopathological confirmation or established non-invasive radiological criteria. All participants received TACE as their initial treatment. Pre- and post-procedural imaging was obtained using either dynamic magnetic resonance imaging (MRI) or triphasic computed tomography (CT).

Results: One hundred twenty-nine patients aged over 18 years with HCC were included in our study. General adverse events were reported in 58.3% of patients in Group A and 66.7% in Group B, while serious adverse events occurred in 33.3% versus 41.7%, respectively. Among patients who experienced at least one serious adverse event after TACE, univariate analysis revealed significant predictive associations with female sex, smoking history, presence of diabetes mellitus, a Child-Pugh classification above A, and BCLC stage B disease. Multivariate analysis revealed that female gender and BCLC stage B were independent risk factors associated with the development of serious adverse events after TACE.

Conclusion: This study revealed that the safety profiles of TACE were comparable between the elderly and younger populations, showing no discernible differences. It was also seen that age had no predictive value for serious adverse events.

Keywords:. Transarterial chemoembolization, hepatocellular carcinoma, safety, eldery, side effects.

Öz

Amaç: Bu çalışma, yaşlı Hepatoselüler karsinomalı (HCC) hastalarda transarteriyel kemoembolizasyonun (TACE) güvenliğini incelemeyi, uygulanabilirliğini netleştirmeyi ve ciddi advers olaylar için risk faktörlerini belirlemeyi hedeflemektedir. Böylelikle bu bulgular, geriatri onkolojisinde klinik karar verme sürecine katkıda bulunacaktır.

Gereç ve Yöntem: Bu retrospektif çalışmaya, histopatolojik doğrulama veya yerleşik non-invaziv radyolojik kriterlere göre yeni tanı almış ve yaşı 18'in üzerinde olan HCC hastaları dahil edilmiştir. Tüm hastalara ilk tedavi olarak TACE uygulanmıştır. İşlem öncesi ve sonrası görüntüleme, dinamik manyetik rezonans görüntüleme (MRG) veya üç fazlı bilgisayarlı tomografi (BT) ile gerçekleştirilmiştir.

Bulgular: Çalışmaya HCC tanısı olan ve yaşı 18'in üzerinde olan toplam 129 hasta dahil edilmiştir. Genel advers olaylar, Grup A'da %58,3 ve Grup B'de %66,7 oranında bildirilirken; ciddi advers olaylar sırasıyla %33,3 ve %41,7 oranında gözlenmiştir. TACE sonrası en az bir ciddi advers olay yaşayan hastalarda yapılan univaryant analizde, kadın cinsiyet, sigara öyküsü, diyabet varlığı, Child-Pugh sınıflamasının A üzerinde olması ve BCLC evresi B olması (ile anlamlı ilişki saptanmıştır. Multivaryant analizde ise, kadın cinsiyet ve BCLC evresi B, TACE sonrası ciddi advers olay gelişimi ile bağımsız risk faktörleri olarak belirlenmiştir.

Sonuç: Bu çalışma, yaşlı ve genç popülasyonlar arasında TACE'nin güvenlik profillerinin karşılaştırılabilir olduğunu ortaya koymuş, yaşın ciddi advers olaylar açısından öngörücü bir değer taşımadığını göstermiştir.

Anahtar kelimeler: Transarteriyel kemoembolizasyon, hepatosellüler karsinom, güvenlik, yaşlılık, yan etkiler

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INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary malignant tumor of the liver, accounting for over 90% of all primary hepatic malignancies. Approximately 85% of HCC cases develop in the context of underlying cirrhosis, with an annual incidence of 2–4% among cirrhotic patients. The major risk factors for HCC include chronic viral hepatitis (hepatitis B and C), alcohol-related liver disease, and non-alcoholic fatty liver disease (NAFLD)[1]. Globally, HCC ranks as the fifth most common cancer and is the second leading cause of cancer-related mortality, particularly among men. The five-year overall survival rate for HCC remains low, at approximately 18%[2,3].

Clinical assessment of patients with HCC is most commonly performed using the Barcelona Clinic Liver Cancer (BCLC) staging system. At the time of diagnosis, nearly 70% of patients are classified as stage B or C according to BCLC criteria. For these stages, locoregional or systemic therapies are considered the primary treatment modalities[4-6].

Transarterial therapies are typically indicated for patients with BCLC stage B (intermediate stage), characterized by multinodular tumors in individuals with preserved liver function and an Eastern Cooperative Oncology Group Performance Status (ECOG-PS) of 0, without evidence of extrahepatic spread or macrovascular invasion[7-9]. A meta-analysis reported an objective response rate of 52.5% and a procedure-related mortality rate below 1%. Most deaths were attributed to the severity of underlying liver disease, underscoring the importance of appropriate patient selection[7,8].

Transarterial chemoembolization (TACE), the most widely used transarterial therapy, is associated with several adverse effects, including nausea, vomiting, fatigue, elevated liver enzymes, bone marrow suppression, exacerbation of pre-existing liver disease, and decompensation of comorbid conditions.[7] The highest response rates to TACE have been observed in patients with intermediate-stage HCC who maintain good performance status and preserved hepatic function[9]. However, patient age and comorbidities play a critical role in determining both the efficacy and safety of TACE. Defining elderly patients remains a subject of debate, with age thresholds ranging from 65 to 80 years. The International Society of Geriatric Oncology currently defines elderly patients as those aged ≥70 years, a criterion widely adopted in HCC-related literature[10].

Although numerous studies have evaluated TACE outcomes in heterogeneous age groups, data specifically focusing on elderly patients and age-related differences in safety profiles remain limited. This study contributes novel insights by comparing general and serious adverse events between patients aged ≥70 years and their younger counterparts, thereby enhancing risk stratification in geriatric oncology. The primary objective is to evaluate the safety of TACE in elderly patients with intermediate-stage HCC and to identify clinical predictors of serious adverse events. By analyzing age-stratified outcomes, this study aims to determine whether chronological age alone should influence treatment decisions. We hypothesize that TACE demonstrates a comparable safety profile in elderly (≥70 years) and non-elderly patients, and that specific clinical parameters rather than age itself serve as independent predictors of adverse outcomes.

MATERIALS AND METHODS

Sample

This retrospective study was conducted at Çukurova University Faculty of Medicine, a tertiary academic medical center in Adana, Turkey, between 2013 and 2024. The institution utilizes a robust electronic health record system that complies with national data protection regulations, enabling reliable data extraction for retrospective research. All patient data were anonymized prior to analysis to ensure confidentiality and reproducibility.

Inclusion criteria were as follows: patients aged ≥18 years; those diagnosed with HCC based on histopathological confirmation or non-invasive radiological criteria; patients undergoing TACE for the first time; and those with dynamic magnetic resonance imaging (MRI) or triphasic computed tomography (CT) scans performed both before and after the procedure. Patients were stratified into two groups: elderly patients (≥70 years) and younger patients (<70 years).

Procedure

All participants provided written informed consent prior to enrollment. The study was conducted in

accordance with the Declaration of Helsinki and was approved by the Çukurova University Faculty of Medicine Clinical Research Ethics Committee (Approval No: 2022/124).

All treatment decisions regarding TACE were made by a multidisciplinary tumor board comprising hepatologists, interventional radiologists, oncologists, and hepatobiliary surgeons. TACE procedures were performed by certified interventional radiologists using standardized techniques in accordance with national and international guidelines.

Data collection

Demographic characteristics, comorbidities, hepatic functional reserve, cirrhotic status, TACE-related parameters, performance status, and post-procedural adverse events were extracted from the institutional electronic medical records.

Definition and timing of adverse events

Adverse events were defined as those occurring immediately post-procedure and up to the radiological evaluation of tumor response at 8–12 weeks following TACE. Serious adverse events were defined as newly developed ascites and/or hepatic encephalopathy, progression to Child-Pugh class C, or TACE-related mortality.

TACE treatment plan

The TACE treatment plan was formulated by a multidisciplinary team including a gastroenterologist, interventional radiologist, oncologist, and hepatobiliary surgeon, guided by the BCLC staging system and individualized patient assessments.

Transfemoral visceral arteriography was performed using standard angiographic techniques. In accordance with current literature, patients who underwent selective/superselective conventional TACE or drug-eluting bead TACE (DEB-TACE) were included. TACE was administered using either lipiodol-based emulsions or doxorubicin-loaded microspheres.[11] C

onventional TACE (cTACE): A triple combination of lipiodol, doxorubicin, and gelfoam was used as the embolic agent. DEB-TACE: Doxorubicin-loaded beads were employed for embolization. Given that HCC is predominantly supplied by branches of the hepatic artery, embolization induces selective tumor hypoxia, ultimately leading to necrosis.

Response assessment and survival definition

Radiologic response was assessed 8–12 weeks after the initial TACE session by comparing post-treatment imaging with baseline scans. Functional status and physiologic reserve were evaluated using the Eastern Cooperative Oncology Group (ECOG) performance scale.[12] Overall survival (OS) was defined as the duration from initial HCC diagnosis to death from any cause.

Statistical analysis

Statistical analyses were performed using SPSS version 25.0. Descriptive statistics were presented as mean ± standard deviation (SD) or median (range), depending on data distribution. Categorical variables (e.g., sex, adverse event occurrence, age group) were compared using the Chi-square test or Fisher's exact test, as appropriate. Continuous variables were analyzed using the independent samples t-test for normally distributed data and the Mann–Whitney U test for non-normally distributed data. Multivariate analysis of predictors for adverse outcomes was conducted using logistic regression. Spearman's rank correlation coefficient was used to assess associations between non-normally distributed variables. A p-value <0.05 was considered statistically significant. To identify predictors of serious adverse events, a stepwise logistic regression model was constructed. Initially, all independent variables were evaluated via univariate analysis. Variables with $p < 0.05$ were included in the multivariate model. Additionally, clinically relevant variables with borderline statistical significance, supported by prior literature, were incorporated. The stepwise forward selection method was used to optimize model performance with minimal variables. Model fit was assessed using the Hosmer–Lemeshow goodness-of-fit test, and explanatory power was reported using the Nagelkerke R^2 statistic.

Post-hoc power analysis was conducted using G*Power 3.1 software, targeting a minimum statistical power of 80% (1-β) at a significance level of 0.05 (α). Assuming adverse event rates of 13% in patients aged ≥70 and 17% in those aged <70, the analysis yielded a power of 84%, supporting the statistical validity of the study's primary findings.

RESULTS

Patients diagnosed with HCC and treated with TACE at Çukurova University between 2013 and 2024 were

retrospectively screened. A total of 129 patients aged ≥18 years who met the inclusion criteria were enrolled in the study. Of these, 45 patients (34.8%) were classified into the elderly group (≥70 years), while 84 patients (65.2%) comprised the younger group (<70 years). Baseline characteristics of the study population are summarized in Table 1. No statistically significant difference in sex distribution was observed between the two groups ($p = 0.502$). The prevalence of NAFLD was significantly higher in the younger group compared to the elderly group ($p < 0.05$). Conversely, the incidence of hypertension was significantly greater among elderly patients ($p < 0.05$). A cirrhotic background was also more frequently observed in the elderly group ($p < 0.05$). Regarding performance status, the majority of patients in the younger group had an ECOG score of 0, whereas ECOG 1 was significantly more common in the elderly group ($p < 0.05$). Smoking rates were notably higher in the younger cohort ($p < 0.05$). When assessed for overall survival, the elderly group demonstrated a significantly shorter life expectancy compared to their younger counterparts ($p < 0.05$).

Table 1. Patients baseline characteristics

Variable	Age <70 years		Age ≥70 years		Overall cohort		P value
	n	%	n	%	n	%	
Male	66	78.6	33	73.3	99	76.7	0.502
Age (years) (Mean±SD, [Min-Max])	56.71±9.64 [26-68]	58.5 [52.25-64]	74.93±4.1 [70-82]	74 [71-79]	63.07±11.92 [26-82]	64 [56-72]	<0.001
Etiology	n, (%)		n,(%)		n,(%)		
HBV	57	67.9	30	66.7	87	67.4	0.002
HCV	12	14.3	6	13.3	18	14.0	
NAFLD	12	14.3*	0	0.0	12	9.3	
Others	3	3.6	9	20.0*	12	9.3	
Comorbidities	n	%	n	%	n	%	
HT	9	10.7	21	46.7	30	23.3	<0.001
DM	18	21.4	12	26.7	30	23.3	0.502
CAD	9	10.7	3	6.7	12	9.3	0.451
Smoking	39	46.4	9	20.0	48	37.2	0.003
Presence of cirrhosis	54	64.3	39	86.7	93	72.1	0.007
ECOG	n	%	n	%	n	%	
0	69	82.1*	24	53.3	93	72.1	0.001
1	15	17.9	18	40.0*	33	25.6	
2	0	0.0	3	6.7*	3	2.3	
CPC	n	%	n	%	n	%	
A	63	75.0	33	73.3	96	74.4	0.836
B	21	25.0	12	26.7	33	25.6	
Ascites (n,%)	78	92.9	39	86.7	117	90.7	0.249
Albumin (g/dL)(Mean±SD, [Min-Max])	3.41±0.53 [2.1-4.6]	3.35 [3.03-3.78]	3.36±0.46 [2.5-4]	3.4 [3-3.8]	3.39±0.5 [2.1-4.6]	3.4 [3-3.8]	0.858
PTT (sn) (Mean±SD, [Min-Max])	13.44±1.65 [10.6-17]	13.35 [12.03-14.3]	13.55±2.13 [11-18.9]	13.1 [12-14]	13.48±1.83 [10.6-18.9]	13.1 [12-14]	0.624
Total bilirubin (mg/dL) (Mean±SD, [Min-Max])	1.16±0.69 [0-3.11]	1.08 [0.71-1.59]	1.11±0.54 [0.44-2.7]	1 [0.78-1.27]	1.14±0.64 [0-3.11]	1.05 [0.74-1.5]	0.593
AFP (ng/mL) (Mean±SD, [Min-Max])	538.19±1932 .46 [2.2-10292]	10.65 [6-115.25]	961.79±3180.9 [1-12700]	8 [3.5-236]	685.96±2437.35 [1-12700]	9.2 [5.2-128]	0.213
Survival time (months) (Mean±SD, [Min-Max])	46.11±34.29 [2-115]	37.5 [15-80.5]	32±25.74 [2-80]	23 [10-60]	41.19±32.18 [2-115]	33 [15-77]	0.031

* significantly higher rate ($p<0.05$); HBV, hepatitis B; HCV, hepatitis C; NAFLD, non-alcoholic fatty liver disease; HT, hypertension; DM, diabetes mellitus, CAD, coronary artery disease; ECOG, the Eastern Cooperative Oncology Group; CPC, Child-Pugh classification; PTT, prothrombin time; AFP, alfa-fetoprotein.

Table 2. HCC characteristics and treatments features

Variables	Age <70 years		Age ≥70 years		Overall cohort		P value
	N	%	N	%	N	%	
Single tumor	42	50.0	27	60.0	69	53.5	0.278
Multiple tumors	42	50.0	18	40.0	60	46.5	
MTD (cm), (Mean±SD)	4.93±4.13 [2-25]	4 [3-4.6]	4.57±1.74 [2.3-7.5]	4 [3-7]	4.8±3.48 [2-25]	4 [3-5.2]	0.786
Portal vein thrombosis (n,%)	6	7.1	9	20.0	15	11.9	0.030
BCLC (n,%)							
A	27	33.3	9	20.0	36	28.6	0.059
B	48	59.3	27	60.0	75	59.5	
C	6	7.4	9	20.0	15	11.9	
TACE characteristics (*n,%*)							
Selective	48	57.1	27	60.0	75	58.1	0.754
Superselective	36	42.9	18	40.0	54	41.9	
Conventional	15	17.9	9	20.0	24	18.6	0.766
Drug-eluting	69	82.1	36	80.0	105	81.4	
Post-TACE treatments (*n,%*)							
Ablation	15	17.9	12	26.7	27	20.9	0.01
TACE	6	7.1	3	6.7	9	7.0	
TARE	9	10.7	3	6.7	12	9.3	
Tx	21	25.0*	0	0.0	21	16.3	
Systemic therapy	21	25.0	12	26.6	33	25.5	

* significantly higher rate (p<0.05)
MTD, maximal tumor diameter; BCLC, Barcelona Clinic of Liver Cancer; Tx, transplantation.

Table 3. Post-TACE adverse events

Adverse events	Age <70 years		Age ≥70 years		Overall cohort		
	N	%	N	%	n	%	p
Ascites	15	17.9	6	13.3	21	16.3	0.507
Encephalopathy	12	14.3	9	20.0	21	16.3	0.402
Death	6	7.1	3	6.7	9	7.0	0.999**
PES	63	75.0	27	60.0	90	69.8	0.077
Abdominal pain	63	75.0	27	60.0	90	69.8	0.077
Fever	39	46.4	15	33.3	54	41.9	0.151
Nausea-vomiting	24	28.6	9	20.0	33	25.6	0.288
Fatigue	54	64.3	21	46.7	75	58.1	0.053
Ischemic cholecystitis	9	11.1	3	6.7	12	9.5	0.415
Hematoma	6	7.1	3	6.7	9	7.0	0.999**
Ischemic gastroduodenal ulcer	9	10.7	6	13.3	15	11.6	0.658
ARF	9	11.1	6	13.3	15	11.9	0.712
DM decompensation	9	10.7	6	13.3	15	11.6	0.658
Post-TACE CPC (*n,%*)							
A	57	67.9	30	66.7	87	67.4	0.723
B	24	28.6	12	26.7	36	27.9	
C	3	3.6	3	6.7	6	4.7	

p: Chi-square test **Fisher's Exact
PES, post embolization syndrome; ARF, acute kidney failure; DM, diabetes mellitus; CPC, child-pugh classification.

Table 4. Predictive factors of serious adverse events (univariate and multivariate analyses)

Variables	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Age (>70) (years)	1.944 (0.856-4.416)	0.112		
Sex (female)	5.417 (2.168-13.536)	**<0.001**	5.123 (1.736-15.117)	**0.003**
HT	1.232 (0.497-3.057)	0.652		
CAD	1.50 (0.595-3.779)	0.390		
DM	10.875 (2,729-43,339)	**0.001**	0.878 (0.257-3.003)	0.835
Smoking	2.40 (1.064-5.413)	**0.035**	2.242 (0.563-8.935)	0.252
Cirrhosis	1.143 (0.470-2.780)	0.768		
Etiology				
HBV	Ref.	0.696		
HCV	-	0.998		
NAFLD	2.111 (0.623-7.156)	0.230		
Others	-	0.999		
CPC	3.333 (1.413-7.862)	**0.006**	2.142 (0.625-7.346)	0.226
ECOG				
0	Ref.	0.217		
1	2.190 (0.910-5.274)	0.080		
2	-	0.999		
Solitary/ Multiple	1.800 (0.805-4.024)	0.152		
PVT	0.650 (0.171-2.466)	0.527		
AFP (>400)	0.889 (0.319-2.476)	0.822		
BCLC				
A	Ref.	0.020	Ref.	0.058
B	5.867 (1.629-21.133)	**0.007**	5.659 (1.361-23.528)	**0.017**
C	2.750 (0.487-15.532)	0.252	4.557 (0.606-34.256)	0.141
Global/selective TACE	0.556 (0.248-1.242)	0.152		
Conventional/Drug-eluting TACE	3.043 (0.843-10.984)	0.089		

HT, hypertension; CAD, coronary artery disease, DM, diabetes mellitus; HBV, hepatitis B; HCV, hepatitis C; NAFLD, non-alcoholic fatty liver disease; CPC, child-pugh classification; ECOG, the Eastern Cooperative Oncology Group; PVT, portal vein thrombosis; AFP, alfa-fetoprotein; BCLC, Barcelona Clinic of Liver Cancer.

Table 2 presents the tumor-related characteristics and treatment details of patients with HCC. Notably, both age groups demonstrated comparable tumor morphology and maximal tumor diameter (MTD), with no statistically significant differences observed ($p > 0.05$). However, the incidence of portal vein thrombosis was significantly higher in the elderly group ($p < 0.05$). Regarding the technical aspects of the TACE procedures, no significant differences were found between the two groups ($p > 0.05$). Post-TACE treatment modalities revealed that liver transplantation was significantly more frequent among younger patients, as expected ($p < 0.05$).

Adverse events observed after TACE are summarized in Table 3. When serious complications were compared between younger and elderly patients, the following rates were noted: ascites (17.9% vs. 13.3%), hepatic encephalopathy (14.3% vs. 20%), mortality (7.1% vs. 6.7%), and post-TACE Child-Pugh class C (CPC-C) shift (3.6% vs. 6.7%).

Regarding general adverse events, the most frequently reported complications in both groups included post-embolization syndrome (PES) (75% in younger vs. 60% in elderly), abdominal pain (75% vs. 60%), fever (46.4% vs. 33.3%), nausea and vomiting (28.6% vs. 33%), and fatigue (64.3% vs. 46.7%). No statistically significant differences were observed between the two age groups in terms of either serious or general adverse events ($p > 0.05$).

Predictive factors associated with serious adverse events were evaluated, and the relevant findings are

presented in Table 4. In patients who experienced at least one serious adverse event, univariate analysis revealed that female sex, smoking status, presence of diabetes mellitus, Child-Pugh class A, and BCLC stage B were significantly associated with increased risk ($p < 0.05$). Multivariate analysis identified female sex and BCLC stage B as independent risk factors for serious adverse events ($p < 0.05$). Among these, female sex and BCLC stage B demonstrated the strongest predictive value, with hazard ratios of 5.123 and 5.659, respectively.

DISCUSSION

The primary aim of this study was to evaluate both the efficacy and safety of TACE in patients aged ≥70 years. A review of the existing literature revealed a paucity of studies specifically addressing this age group. As the global population continues to age, the incidence of HCC like many other malignancies increases with advancing age. However, older adults remain underrepresented in clinical trials, and the safety and efficacy of oncologic treatments in this demographic are not well established. Therefore, it is essential to develop tailored strategies and clinical practices for managing cancer in elderly patients. This study sought to address two key questions: (1) Are there significant risk factors that predict adverse events in older patients? (2) Can TACE be safely and effectively administered in this population?

Our findings demonstrated a statistically significant difference in overall survival (OS) between elderly and younger patients ($p < 0.05$). This disparity may be attributed to the limited use of curative treatments, such as liver transplantation, in older individuals. A recent study similarly reported reduced survival in elderly patients, consistent with our results[13]. Conversely, another study found no significant difference in OS between age groups, although it did not specify post-TACE treatment options.[14] The impact of curative interventions particularly liver transplantation on survival outcomes in younger patients remains unclear.

In a study by Cohen et al., no significant difference in OS was observed between older and younger patients, nor among subgroups within the elderly cohort.[15] In our analysis, adverse events following TACE did not differ significantly between age groups. Literature review revealed that adverse events occurring during the post-procedural period (up to tumor response evaluation) were categorized as early or late, with similar rates observed across age groups[13]. Likewise, a multicenter study reported no significant age-related differences in adverse events; however, it failed to account for procedural heterogeneity and comorbidities critical determinants of treatment outcomes in elderly patients[15]. These omissions represent notable limitations.

A prospective study also found no significant difference in adverse event rates between older and younger patients.[16] In our cohort, predictors of serious adverse events including newly developed ascites, hepatic encephalopathy, progression to Child-Pugh class C, and TACE-related mortality were systematically evaluated. Among patients experiencing at least one serious adverse event, female sex, smoking history, presence of diabetes mellitus, Child-Pugh class ≥B, and BCLC stage B were identified as significant predictors. Notably, age was not an independent risk factor. Neither the type of TACE procedure nor tumor morphology demonstrated predictive value. Interestingly, female sex emerged as an independent risk factor a finding not previously reported in the literature. Additionally, while BCLC stage B was associated with increased risk, stage C was not, warranting further investigation. A recent study identified Child-Pugh class ≥B, tumor multifocality, MELD score ≥9, alcohol use, prior liver decompensation, ECOG performance status ≥1, and doxorubicin-based chemotherapy as predictors of serious adverse events. Among these, Child-Pugh ≥B, tumor multifocality, and MELD ≥9 were confirmed as independent risk factors.[13]

This study has several limitations. First, the retrospective design spanning nearly a decade introduces potential variability in diagnostic and therapeutic protocols, which may affect data consistency. Second, the inherent heterogeneity of patient selection in retrospective analyses poses a risk of selection bias. Third, the evolution of TACE techniques over time contributes to procedural variability. Additionally, as a single-center study, the generalizability of our findings may be limited. Finally, elderly patients with multiple or uncontrolled comorbidities may have been excluded from TACE, potentially skewing the results.

In conclusion, our study found no significant differences in the safety profile of TACE between elderly and younger patients. Furthermore, age was not identified as an independent predictor of serious adverse events. Given the increasing prevalence of HCC in aging populations, future research should

prioritize multicenter, prospective trials incorporating standardized definitions of adverse events and uniform TACE protocols. Comprehensive geriatric assessments including frailty indices, nutritional status, and comorbidity burden should be integrated into clinical decision-making to better evaluate individual treatment risks. Additionally, sex-based biological differences and tumor characteristics warrant further exploration, particularly in light of our finding that female sex was an independent predictor of serious adverse events. The unexpected association of intermediate BCLC stage (B) with increased risk, while advanced stage (C) was not, also merits deeper investigation. Finally, studies incorporating radiomic analysis and molecular profiling may facilitate personalized TACE strategies, enhancing both safety and efficacy in elderly patients with HCC.

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