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The effect of using different embolic agents on survival in transarterial chemoembolization of hepatocellular carcinoma: gelfoam versus polyvinyl alcohol

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PURPOSE
We aimed to compare the effect of using different embolic agents such as gelfoam and polyvinyl alcohol (PVA) on survival, tumor response, and complications in transarterial chemoembolization (TACE) of hepatocellular carcinoma (HCC) patients.

MATERIALS AND METHODS
We retrospectively reviewed the medical records of 38 inoperable HCC patients who underwent TACE between August 1998 and April 2007. A total of 50 TACE sessions were performed using PVA (n=18) or gelfoam particles (n=20), following the application of 60 mg doxorubicin with 10–20 mL lipiodol emulsion. The PVA and gelfoam groups were compared based on clinical, laboratory, and demographic variables. Survival rates were calculated starting from the first TACE session using the Kaplan-Meier analysis.

RESULTS
There was no significant difference between the survival rates of PVA and gelfoam groups (P = 0.235). Overall survival rates at 12, 24, 36, 48, and 60 months were 55%, 36%, 15%, 7%, and 5%, respectively. Tumor response, age, lipiodol accumulation type, number of HCC foci, complications, and serum alpha-fetoprotein level were significant factors for survival in all patients.

CONCLUSION
Use of gelfoam or PVA as the embolic agent did not have a significant impact on survival. Complete tumor response, intensive lipiodol accumulation in tumor, older age (>60 years), fewer (≤3) HCC foci, and low serum alpha-fetoprotein level (≤400 ng/mL) were found to improve cumulative survival significantly.

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Hepatocellular carcinoma (HCC) is the most common primary malignant tumor of the liver and the third leading cause of cancer death worldwide. More than 90% of HCC occurs following liver cirrhosis (1). Transplantation, ablative treatments, and surgical resection are considered as curative treatments (2). Unfortunately, only 30% of HCC cases are eligible for these curative treatments at the time of diagnosis, while the majority is diagnosed in advanced stage, beyond the criteria for surgical therapy (3, 4). Transarterial chemoembolization (TACE) remains the most widely used and established palliative treatment in the management of patients with advanced HCC, with proven survival benefits over the best supportive care (5–8). Despite the worldwide acceptance of TACE in the treatment of surgically unresectable HCC, there is still no standard protocol for its use (9). Various TACE techniques which comprise selective or superselective catheterization, different chemotherapeutic regimens (doxorubicin, 5-fluorouracil, cisplatin, mytomycin-c, epirubicin, neocarzinostatin), and different embolization agents can influence the patient outcome (10, 11). Furthermore a previous review stated that polyvinyl alcohol (PVA) particles may be better than gelatin sponge in TACE treatment (12). Thus, the primary aim of our study was to compare the effect of different embolic agents such as PVA and gelfoam on survival and patient outcome in the treatment of surgically unresectable HCC. The secondary aim was to investigate the effect of TACE on survival.

Materials and methods

Patient selection

We retrospectively reviewed 38 HCC patients (28 men, 10 women; mean age, 62.8±12.4 years) who underwent TACE between August 1998 and April 2007 in our institution. The study protocol was approved by the local ethics committee, and all patients gave a written informed consent before the procedure. Patients with surgically unresectable HCC were evaluated by an oncology board and underwent TACE procedure upon the decision of this board. Patients with surgically unresectable HCC, with or without portal branch thrombosis, and without previous TACE treatment were included in the study. Patients with main portal vein thrombosis, hepatic failure, or extrahepatic metastasis were excluded. History of concomittant radiofrequency ablation (RFA) or percutaneous ethanol injection (PEI) was not a criterion for exclusion. Doxorubicin (60 mg) with lipiodol emulsion (10–20 mL) was administered to all patients before embolization. Twenty patients underwent embolization with gelfoam and 18 patients underwent embolization with PVA. Two patients in gelfoam group had previous PEI and RFA treatments. Two pa-

tients in the gelfoam group underwent additional PEI, and two patients in the PVA group underwent additional RFA. Medical records were obtained from the hospital information system, and radiological data were retrieved using the picture archiving and communication system.

Chemoembolization procedure and technique

All patients underwent triple phase multidetector CT (unenhanced, arterial and venous phases) within a month before the TACE session. CT examinations were performed using a 16-detector CT (Brilliance 16, Philips Medical Systems, Best, the Netherlands) in supine position. Axial scanning parameters were as follows: tube voltage, 120 kV; mAs, 300; collimation, 16×1.5 mm; matrix, 512×512; rotation time, 0.75 s; pitch, 0.93; FOV, 40 cm; slice thickness, 5 mm.

All patients were preprocedurally starved at least eight hours and hydrated with 150–200 mL/h of normal saline solution. TACE was performed by interventional radiologists (O.D. and A.Y.G.) who had similar experience and expertise in the management of HCC. Superior mesenteric angiography was performed to determine the portal venous patency and possible right hepatic arterial variations. Then, right and left hepatic angiography was performed to determine the tumor-bearing artery for drug administration. After selective or superselective catheterization of the distal feeding artery with a microcatheter (Progreat, Terumo, Tokyo, Japan), doxorubicin (Adriblastine, Pfizer, Nerviano, Italy) (1 mg/kg of weight, maximum 60 mg) mixed with 10–20 mL of iodized oil emulsion (Lipiodol, Guerbet, Aulnay-sous-Bois, France) and 10 mL of contrast agent (Ultravist 300/100 mL Bayer Schering Pharma, Berlin, Germany) was administered in all patients before the embolization step. After the administration of lipiodol chemotherapy, embolization was performed using 1–2 mm diameter gelfoam particles (Gelitaspon, Gelita Medical BV, Amsterdam, the Netherlands) or 150–250 μm PVA particles. Injection of lipiodol chemotherapy and embolization were performed under realtime floroscopy to avoid the reflux of the injected material. When the flow slowed down significantly with stagnation, embolization was stopped for a while to allow flow restoration. Then embolization was reinstated until complete occlusion of the feeding artery was achieved.

Tumor response assessment

Tumor response was assessed on multiphase contrast-enhanced CT, one month after the TACE session. In one patient follow-up imaging was performed by magnetic resonance imaging (MRI) due to renal functional disorder. An abdominal radiologist with a six-year experience, who was blinded to TACE technique, reviewed the CT and MRI data. We used the modified RECIST criteria (13, 14) to assess the tumor response as follows: complete response, elimination of any intratumor arterial enhancement in all target lesions; partial response, at least 30% decrease in the sum of the largest diameters of viable target lesions; stable disease, any cases which do not qualify for either partial response or progressive disease; and progressive disease, at least 20% increment in the sum of the largest diameters of viable target lesions. Progressive disease was also noted when one or more new lesions were detected. Viable lesions were defined by the presence of an enhanced area inside the tumor at arterial phase.

Lipiodol deposition was also semiquantitatively assessed by opacification on unenhanced CT. Four types of lipiodol deposition were defined as follows: type 1, diffuse homogeneous opacification of the tumor focus; type 2, mostly homogeneous opacification; type 3, weak heterogeneous opacification; type 4, very weak or no opacification of the tumor focus (15).

Additional TACE session was performed if tumor enhancement was determined on follow-up CT. TACE session was performed twice in 10 patients (26.3%), and three times in six patients (15.8%). If there was no enhancement of the tumor, patients underwent screening with repeat CT imaging performed every three months.

Assessment parameters

Potential prognostic factors of tumor response and survival were analyzed, including patient characteristics such as age and gender, cirrhosis etiology, serum alanine and aspartate aminotransferases, total serum bilirubin, albumin, prothrombin time, Child-Pugh class, Okuda class; tumor characteristics such as tumor size and number, portal vein thrombosis, serum alpha-fetoprotein (AFP); procedure-related factors such as TACE technique, type of embolization agent; short-term post-therapeutic evaluation such as postembolization syndrome, tumor response, tumor lipiodol fixation, liver failure, and long-term evaluation such as the number of TACE sessions, and the date of death.

Statistical analysis

Overall survival was evaluated by Kaplan-Meier curves and compared between groups using the log rank test. The univariate analysis for overall survival was performed using the log-rank test on Kaplan-Meier curves for categorical variables and the univariate Cox Model for continuous variables. Results were expressed as mean±standard deviation. Chi-square and Mann-Whitney U tests were used in comparison of categorical and continuous variables, respectively.

To determine factors affecting survival, continuous variables and some multinomial categorical variables were dichotomized as follows: percentage of hepatic involvement ≤50% vs. >50%, tumor diameter ≤5 cm vs. >5 cm, number of HCC foci ≤3 vs. >3, aspartate aminotransferase level ≤63 U/L vs. >63 U/L, AFP level ≤400 ng/mL vs. >400 ng/mL, age ≤60 years vs. >60 years (16), number of TACE sessions ≤1 and >1, type of lipiodol accumulation (type 1 vs. the other types), type of tumor response (type 4 vs. the other types).

A P value less than 0.05 was considered as statistically significant. The statistical software used was Statistical Package for Social Sciences, version 17 (SPSS Inc., Chicago, Illinois, USA).

Results

Thirty-eight patients underwent TACE treatment in the study period; all subjects died in the course of the study. One patient underwent liver transplantation in the follow-up period, but he died right after the trans-

plantation surgery. Overall survival rates for the whole study group was 55%, 36%, 15%, 7%, and 5% at 12, 24, 36, 48, and 60 months respectively. Mean survival of the whole group was 18.7±18.2 months (range, 1–72 months).

The gelfoam and PVA groups were similar in all factors except in Child-Pugh and Okuda classification (Table 1). The PVA group had significantly more patients in Child-Pugh A (P = 0.01) and Okuda class I (P = 0.04). However this result did not effect the duration of follow-up (P = 0.79) or the survival rates of the two groups (P = 0.235). Survival rates at 12, 24, 36, 48 and 60 months were 66%, 44%, 16%, 11%, and 5% for PVA the group and 45%, 30%, 15%, 5%, and 5% for the gelfoam group (Figure).

A total of 60 TACE sessions (mean, 1.5) were performed in 38 patients. Twenty patients in the gelfoam group underwent 29 sessions (mean, 1.4) and 18 patients in the PVA group underwent 31 sessions (mean, 1.7) (P = 0.18).

Prognostic factor analysis for survival is shown in Table 2. Patients with ≤3 HCC nodules (n=29) had significantly better survival than patients with >3 HCC nodules (n=9); survival rates at 12, 24, 36, 48 and 60 months were 58%, 44%, 20%, 10%, and 6% for patients with ≤3 HCC nodules and 44%, 11%, 0%, 0%, and 0% for patients with >3 HCC nodules (P = 0.023); mean survival was 21 months and nine months, respectively.

Patients with AFP levels ≤400 ng/mL (n=31) had significantly better survival than patients with AFP levels >400 ng/mL (n=7); survival at 12, 24, 36, 48 and 60 months were 64%, 45%, 19%, 9%, and 6% for patients with AFP ≤400 ng/mL and 14%, 0%, 0%, 0%, and 0%, for patients with AFP >400 ng/mL (P < 0.001); mean survival was 31 months and 17 months, respectively.

Ten patients developed complications other than postembolectomy syndrome after the TACE session. Of these, four patients died due to hepatic failure within 30 days, and one patient died due to gastrointestinal bleeding within three days after the TACE, leading to an overall mortality rate of 13%. Two of these five patients were in the gelfoam group (10% of that group); both had Child-Pugh B disease with massive ascites and large tumor sizes exceeding 10 cm in diameter. The remaining three patients were in the PVA group (16% of that group); two patients had Child-Pugh C and one patient had Child A disease. One patient developed an intrahepatic abscess, which healed after insertion of a drainage catheter. We also observed peritonitis (n=1), pleural effusion (n=1), ascites and encephalopathy (n=1), and transient increase in liver enzymes (n=1) in the TACE study group. Patients with (n=10) and without (n=28) complications had significantly different survival rates at 12, 24, 36, 48 and 60 months (20%, 10%, 0%, 0%, and 0% vs. 67%, 42%, 17%, 7%, and 3%; P < 0.001). Mean survival was 11 months in patients with complications and 20 months in patients without complications.

Survival was also analyzed in terms of lipiodol accumulation type. Five patients who did not have follow-up CT due to early mortality within one

Table 1. Characteristics of patients undergoing the TACE procedure

	Total	PVA	Gelfoam	*P*
Patients, *n*	38	18	20	
Age (years), *mean±SD*	62.8±12.4	61±15	63±9.2	0.83
Male gender, %	73.7	77.8	70	0.35
Etiology, %				0.36
HBV	47.4	55.6	40	
HCV	39.5	33.3	45	
Other	13.2	11.1	15	
Child-Pugh class, %				0.01
A	52.6	77.8	30	
B	39.5	11.1	65	
C	7.9	11.1	5	
Okuda class, %				0.04
I	44.7	66.7	25	
II	47.4	22.2	70	
III	7.9	11.1	5	
Maximum HCC size (mm), *mean±SD*	63.3±45.5	64±53.8	62.8±38	0.48
Number of HCC foci, *mean±SD*	2.1±1.2	1.9±1.2	2.3±1.2	0.37
Bilirubin (mg/dL), *mean±SD*	2.4±2.1	2.5±3	2.3±0.7	0.18
Albumin (g/dL), *mean±SD*	3.2±0.7	3.4±0.7	3.0±0.7	0.07
AST (U/L), *mean±SD*	101.9±145.1	105.7±173.9	98.5±118	0.35
ALT (U/L), *mean±SD*	100.3±200.5	126.4±282.5	76.9±75.3	0.69
AFP (ng/mL), *mean±SD*	794±3269	210.2±331.3	1319±4483	0.95
PT (s), *mean±SD*	15.9±4.9	14.7±3.8	16.9±5.7	0.38
Number of TACE sessions, *mean±SD*	1.5±0.7	1.7±0.7	1.4±0.7	0.18
Technique, *n*				0.64
Selective	12	6	6	
Superselective	26	12	14	
PES, %	50	44.4	55	0.52
Complication, %	26.3	16.7	35	0.20
Follow-up (months), *mean±SD*	15.1±14	14.7±11.3	15.4±16.3	0.79

PVA, polyvinyl alcohol; n, number of patients; SD, standard deviation; HBV, Hepatitis B virus; HCV, Hepatitis C virus; HCC, hepatocellular carcinoma; AST, aspartate aminotransferase; ALT, alanine aminotransferase; AFP, alpha-fetoprotein; PT, prothrombin time; TACE, transarterial chemoembolization; PES, postembolectomy syndrome.

Table 2. Effect of variables on survival

Variables	n	*P*
Liver involvement (%), *≤50/>50*	33/5	0.820
Tumor diameter (cm), *≤5/>5*	23/15	0.946
HCC foci, *≤3/>3*	29/9	0.023[a]
Child-Pugh class, *A/B/C*	20/15/3	0.096
Okuda class, *I/II/III*	17/18/3	0.122
AST (U/L), *≤63/>63*	18/20	0.376
AFP (ng/mL), *≤400/>400*	31/7	<0.001[a]
Portal vein thrombosis, *yes/no*	3/35	0.450
Embolic agent, *PVA/gelfoam*	18/20	0.235
Technique, *selective/superselective*	12/26	0.579
PES, *yes/no*	20/18	0.139
Complication, *yes/no*	10/28	<0.001[a]
Etiology, *HBV/HCV/other*	18/15/5	0.316
Lipiodol accumulation type, *type 1/other types*	9/23	0.026[a]
Tumor response type, *type 4/other types*	10/23	0.009[a]
Gender, *female/male*	10/28	0.762
Systemic disease, *yes/no*	14/24	0.731
Age (years), *≤ 60/>60*	12/26	0.014[a]
Number of TACE sessions, *1/>1*	22/16	0.512
RFA, *yes/no*	4/34	0.400
PEI, *yes/no*	4/34	0.169

n, number of patients; HCC, hepatocellular carcinoma; AST, aspartate aminotransferase; AFP, alpha-fetoprotein; PVA, polyvinyl alcohol; PES, postembolectomy syndrome; HBV, Hepatitis B virus; HCV, Hepatitis C virus; TACE, transarterial chemoembolization; RFA, radiofrequency ablation; PEI, percutaneous ethanol injection.
[a]$P < 0.05$.

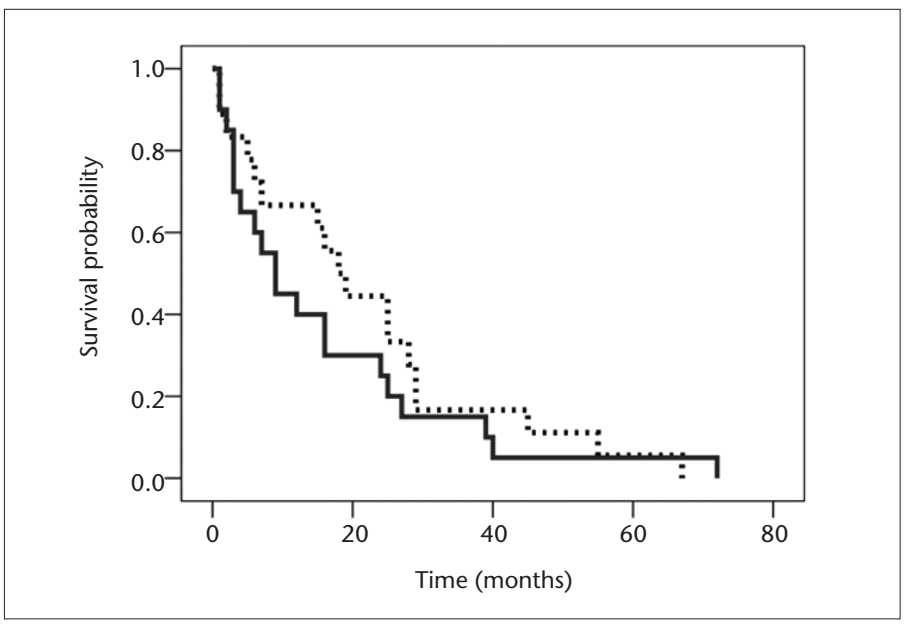

Figure. Kaplan-Meier survival curve of patients who underwent transarterial chemoembolization with polyvinyl alcohol (PVA) or gelfoam. Dashed line indicates the PVA group; solid line represents the gelfoam group. Mean survival was 21.8±18.7 months (95% confidence interval [CI], 13–30 months) for the PVA group and 15.9±17.9 months (95% CI, 8–23 months) for the gelfoam group.

month and one patient who had follow-up MRI instead of CT were excluded from this analysis. Survival of patients with type 1 accumulation (n=9) was significantly better than patients with type 2, 3 or 4 accumulation (n=23); survival rates at 12, 24, 36, 48 and 60 months were 88%, 77%, 55%, 22%, and 22% for type 1 lipiodol accumulation and 52%, 26%, 4%, 4%, and 4% for other types of lipiodol accumulation ($P = 0.026$); mean survival was 35 months and 15 months, respectively. The relationship between lipiodol accumulation type and selectivity of the TACE was significant, such that superselective embolization improved type 1 lipiodol accumulation. A similar relationship was also present between type 1 lipiodol acumulation and complete tumor response.

Tumor response is an important factor of TACE success and complete response is the main goal of the treatment. Patients with complete response (n=10) had significantly better survival compared with other types of response (n=23). Again five patients with early mortality were excluded from this analysis. Survival rates at 12, 24, 36, 48 and 60 months were 70%, 60%, 50%, 30%, and 20% in patients with complete response and 60%, 34%, 4%, 0%, and 0% for patients with other response ($P = 0.009$).

Older patients (>60 years, n=26) had better survival than younger patients (≤60 years, n=12); survival rates at 12, 24, 36, 48 and 60 months were 65%, 46%, 23%, 11%, and 7% for patients >60 years and 33%, 16%, 0%, 0%, and 0% for patients ≤60 years ($P = 0.014$); mean survival was 22 months vs. 10 months, respectively.

Discussion

Our results showed no significant difference in survival of HCC patients treated with TACE using PVA or gelfoam. Furthermore there was no significant difference between PVA and gelfoam groups in terms of complication, postembolectomy syndrome, and the number of TACE sessions. Complete tumor response to treatment, type 1 lipiodol accumulation, older age (>60 years), low number of tumor foci (≤3), and low levels of serum AFP (≤400 ng/mL) were prognostic factors signifi-

cantly associated with higher survival rates. Although superselectivity of embolization was not a significant factor on survival, it was a significant indicator of type 1 lipiodol accumulation, and it can be speculated that selectivity indirectly improves survival.

The benefits reported in two prospective randomized controlled pilot trials secured the role of TACE in the treatment of HCC (5, 17). Lo et al. (17) compared TACE (using cisplatin, lipiodol, and gelfoam) with symptomatic treatment, and determined the survival rates at 12, 24, and 36 months as 57%, 31%, and 26%, vs. 32%, 11%, and 3%, respectively. Llovet et al. (5) compared TACE (using doxorubicin, lipiodol, and gelfoam), transarterial embolization (TAE) (using gelfoam), and symptomatic treatment groups; TACE group had the best survival rates at 12, 24, and 36 months (82%, 63%, and 29%) compared with TAE (75%, 50%, and 29%), and symptomatic treatment groups (63%, 27%, and 17%). In our study the survival rates at 12, 24, and 36 months were 55%, 36% and 15%. Our results were similar with those of Lo et al. (17), but lower than those reported by Llovet et al. (5). This difference can be attributed to better overall condition of the patients in Llovet et al., with the majority of the patients having Child-Pugh A score, small tumor size and good clinical condition.

Previous studies investigated the effect of different chemoterapeutic agents used in TACE on survival. Lo et al. (17) used 30 mg of cisplatin, Llovet et al. (5) administered doxorubicin at varying doses based on serum bilirubin levels, and Barone et al. (18) used a mixture of 20–30 mg of doxorubicin and 6–10 mg of mitomycin C with gelfoam. There is no clear answer for the optimal agents or doses applied in TACE (9). In our study, doxorubicin and lipiodol emulsion was used in both PVA and gelfoam groups.

Embolization is an important aspect of transarterial treatment, especially in HCC patients, since it leads to damage and necrosis in the tumor through arterial occlusion (19). Various embolic agents can be used in TACE such as coils, degradable starch microspheres, autologous blood clot, gelfoam, PVA, and powderized herbs (12). Autologous blood clot and gelfoam could be used as embolizing agents with a temporary occlusion capability on the arteries. Since the blood clot lyses immediately after the embolization, the chance of arterial thrombosis after several sessions of TACE is small (20). In a randomized trial (21), the hepatic artery remained patent for a longer time with blood clot than with gelatin sponge, but there was no difference in survival. On the other hand, a permanent or semipermanent arterial occlusion with more distal obstruction can be achieved with PVA particles, due to their smaller size ranging from 50 to 250 μm in diameter (22) . Brown et al. (10) defined no significant difference in survival between gelfoam powder group and PVA group. Furthermore the number of TACE sessions was significantly greater in the gelatin sponge group than in the PVA group (mean 2.2 vs. 1.6; $P = 0.01$). We also found no difference in survival between the PVA and gelfoam groups. Furthermore no difference was found between the gelfoam and PVA groups regarding the number of TACE sessions (mean 1.7 vs. 1.4; $P = 0.18$). Brown et al. (10) used gelfoam powder (<1 mm diameter), while we used gelfoam particles (1–2 mm diameter) as the embolic agent in TACE. Hence, size difference can be the reason of low number of TACE sessions needed in the gelfoam group in our study. Gelfoam occludes the artery temporarily with recanalization taking place within two weeks (23). On the other hand, PVA is generally considered to be a permanent or semipermanent embolic agent, which is used not only in TACE but also in other procedures such as uterine artery embolization. However, occlusion of the feeding artery for a shorter period of time can be sufficient to achieve satisfactory ischemia to overcome cell pumps that normally expel the chemotherapeutic agents, and result in sufficiently high level of chemotherapeutics to cause tumor necrosis (12). The duration of vascular occlusion needed to induce tumor necrosis is not well known. In pathological analysis of tumors resected approximately 55 days after TACE, gelfoam sponge led to a six-fold increase in cisplatin retention in the tumor compared with the surrounding noncancerous liver tissue; 15 of the 20 index HCCs were completely necrotic and the remaining five demonstrated 70%–90% necrosis (24). Moreover, not all arteries occluded with gelfoam recanalize, and a permanent occlusion rate is about 19% (25). This can explain the insignificant difference between gelfoam and PVA groups in the current study.

Stuart et al. (26) used gelfoam powder as an embolic agent and reported an overall survival time of 16 months in 52 patients. Early (30-day) mortality rate was 17% in that trial. Brown et al. (10) reported an overall survival period of 17 months for both gelfoam and PVA groups with an early mortality rate of 2% and 5%, respectively. In our study overall survival period was 15 months for the gelfoam group and 14 months for the PVA group, with an early mortality rate of 10% and 16%, respectively. Early mortality rates were similar between the gelfoam group and the PVA group. High mortality rates observed by Stuart et al. (26) and our study group can be explained by the inclusion of patients with Child-Pugh C and segmental portal vein thrombosis in the TACE procedure. Additionally, patients with bilobar disease were treated in two lobar infusions separated by a few days in their study. However, most operators performing TACE in bilobar disease separate treatment sessions by a minimum of four weeks (27).

Survival rates were significantly better in patients who experienced no complications compared with patients who had complications. This can be explained by the duration of TACE session, tumor size and Child-Pugh class, since high number of TACE sessions, big tumor size and low Child-Pugh class can increase the complication rates. To our knowledge, no previous study in the literature investigated the effect of complications on survival rates, and further studies are required to shed more light on this issue.

In terms of the number of HCC foci, patients with ≤3 HCC nodules had significantly better survival rates than patients with >3 HCC nodules. There was also a significant relationship between the number of HCC foci and AFP levels, since more tumor foci induce higher AFP levels, which depicts

higher tumoral activity. Furthermore high number of HCC foci means more TACE sessions or selective embolization, thus the tumor response and patient outcome can be affected negatively. Llad et al. (28) defined a significant relationship between the AFP level (cutoff level, 400 ng/mL) and survival in 143 HCC patients; a similar relationship was also observed in our study, where patients with AFP ≤400 ng/mL had better survival than those with AFP >400 ng/mL. Llovet et al. (5) stated that tumor response affects the survival. Llad et al. (28) reported a positive relationship between the reduced tumor size and survival. We also determined a significant effect of tumor response on survival; thus, complete response should be the main goal in TACE for an effective treatment and better survival. Complete tumor response had a significant positive relationship with type 1 lipiodol accumulation and both of them influenced survival significantly. It can be speculated that if a type 1 lipiodol accumulation is seen on unenhanced follow-up CT after the TACE, one can expect a better tumor response and survival. Although superselective embolization indicated type 1 lipiodol accumulation, it had no significant effect on survival in our study. Bouvier et al. (11) reported similar results in their retrospective study. On the other hand, several studies revealed significant improvement on survival with more selective techniques, and recommended the use of these techniques in TACE for better tumor response and patient outcome (11, 15, 29). Age of the patient is an important factor on tumoral invasion, recurrence risk, metastatic potential, survival and prognosis of disease (30). Several studies defined better survival rates at older ages, since younger patients have more agressive disease with a higher grade of HCC at the time of diagnosis (31). In our study we also observed better survival rates in patients over 60 years of age.

This retrospective study has several major limitations. Our study population is relatively small. Retrospective assesment of the subjects limited the scientific impact of the results and did not allow the randomization of patients. Thus, our results need to be validated with further prospective randomized control trials on larger series.

In conclusion, using different embolic agents for TACE had no significant effect on survival. Although PVA group had slightly better survival rates than gelfoam group, this can be attributed to the greater number of Child-Pugh A patients in PVA group than in gelfoam group. Further trials should be focused on the effect of different embolic agents on survival following TACE. Superselective technique should be preferred in TACE for better tumor response and improved patient outcome. Tumor response, number of HCC foci, patient age, serum AFP level, lipiodol accumulation type, and complications due to TACE had a significant effect on survival in HCC treated with TACE.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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