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Efficacy of Intra-Arterial Ethanol Embolization as A Treatment for Patients with Hepatocellular Carcinoma with Malignant Portal Vein Thrombosis

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ABSTRACT

Background: With rising rates of hepatocellular carcinoma, Egypt has the highest global prevalence of hepatocellular carcinoma (HCC). It has been demonstrated that intra-arterial lipiodol ethanol combination embolization is efficient in the treatment of HCC.

Objective: To highlight the efficacy of the intra-arterial ethanol embolization in treatment of hepatocellular carcinoma with malignant portal vein thrombosis (PVT).

Patients and Methods: This follow up study was conducted on 46 patients with hepatocellular carcinoma and malignant portal vein thrombosis done in National Liver Institute, Menoufiya University from March 2020 to March 2022.

Results: Status and reaction at the conclusion of the research both substantially correlated with PVT (P<0.001). Complete responses were more frequently found in grade II patients (4 patients) than in grade III patients (12 patients), according to data (50.00%). In this trial, 46 patients were involved; 8 patients (17.4%) died, and 38 patients (82.6%) survived; 26.1% of these patients declined follow-up or lost touch, and 17.4% had a full response. Status at the conclusion of the program was revealed to be significantly negatively correlated with PVT grade. However, there was no discernible relationship between study status at the conclusion and gender, ascites, Child score, or number of sessions.

Conclusion: Trans arterial ethanol embolization (TAELE) can be used for early-stage HCC, as well as for intermediate-stage disease if other curative modalities are not feasible and can be considered when treating selected patients with segmental portal vein tumor thrombosis (PVTT) (grade I) and preserved liver function.

Keywords: Ethanol embolization, hepatocellular carcinoma, malignant, portal vein, thrombosis.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the seventh most common malignancy worldwide in terms of cancer diagnosis rates. It is currently the third most common cause of cancer-related mortality and its incidence is rising. Due to late-stage presentation, co-morbidities, and a lack of donors, only 10% of patients can receive curative therapy [(1)]. HCC has a wide range of causes, including alcohol use, chemical exposure, cirrhosis, nonalcoholic steatohepatitis, nonalcoholic fatty liver disease, and hepatitis B and C infection. In addition to the diverse etiological reasons of HCC, patients with the condition have varying liver function, which has an effect on treatment planning [(2)].

The cornerstone of treatment for intermediate BCLC B illness, according to the Barcelona Clinic Liver Cancer (BCLC) staging classification, is conventional trans arterial chemoembolization (cTACE). With the development of drug-eluting beads and TACE, chemotherapy can now be administered in a more regulated manner (DEB-TACE). For HCC patients with BCLC B illness, radioembolization, which is also an intra-arterial therapy, represents an alternative route of care [(3)]. By inflicting endothelial injury and thrombus on the arteriolar lumen of tumor feeder arteries and tumor vasculature, ethanol can have an embolization effect, resulting in tumor infarction. It has been demonstrated that intra-arterial lipiodol ethanol combination embolization is efficient in the treatment of HCC. Portal vein tumor thrombosis (PVTT) feeding channels are intricate. However, in most of PVTT had the same blood supply characteristics as intrahepatic lesions, indicating that most nutrient vessels of PVTT correspond to liver arteries [(4)].

Slowly infusing an insoluble substance, such as the lipiodol ethanol mixture, which manifests as tiny droplets travelling through the hepatic sinusoids and to the portal vein, may cause dual embolization. By doing so, the tumor's supply arteries and its nearby parenchymal portal veins are completely embolized. The entire tumor, including the tumor border, which is frequently supplied by portal venules, can be infarcted very effectively by long-term embolization of both the arterioles and portal venules [(5)].

In contrast to a gelatin sponge, the treatment group diffuses within tumor cells in addition to inducing tumor ischemia and hypoxia. Hypoxia and ischemia may act as powerful angiogenesis and carcinogenesis stimulators, promoting collateral circulation and reestablishing tumor blood supply; and these may eventually lead to tumor proliferation and recurrence [(6)]. For cTACE, lipiodol is injected directly into the target vasculature while being combined with one or more chemotherapeutics. The drugs are transported by lipiodol, which then settles close to the tumor. Doxorubicin is loaded into drug-eluting microspheres in DEB-TACE, an evolution of cTACE. Once injected close to the tumor, the medication is released slowly and deliberately, producing anti-tumoral effects. In the end, radioembolization involves injecting 30-micron-sized particles that eventually lodge inside the tumor. While

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the radioactive material is decaying, the tumor receives a modest dose rate of brachytherapy [7].

Aim of the study: It is to highlight the efficacy of the intra-arterial ethanol embolization in treatment of hepatocellular carcinoma with malignant portal vein thrombosis.

PATIENTS AND METHODS

A total of 46 patients with hepatocellular carcinoma and malignant portal vein thrombosis were included in this study and enrolled from National Liver Institute, Menoufiya University from March 2020 to March 2022.

Ethical consent:

The study received the approval of The Ethical Committee of National Liver Institute, Menoufiya University. A written informed consent was taken from the all included patients after explaining the aim of study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

All subjects included in this study were divided into two groups as follows: **Group I:** included 8 patients of portal vein tumor thrombosis grade II and **Group II:** included 38 patients of portal vein tumor thrombosis grade III.

Inclusion criteria: patients with HCC, confirmed histologically or diagnosed by significantly elevated αfetoprotein levels (>250 ng/mL) and imaging by CT, MRI, ultrasound, or angiography, there was no age limit.

Exclusion criteria: second malignancy, any local, or systemic pretreatment, extrahepatic metastases, Child-Pugh C score, complete portal vein thrombosis, serum creatinine >1.5 mg/dl, severe- and therapy-resistant hepatic encephalopathy, contraindications for peripheral artery catheterization.

All participants included in our study were subjected to the following:

Full history taking: included personal, present, past and family history, **Clinical examination**. **Laboratory investigations:** as creatinine level, coagulation profile, liver function tests and alpha feto protein level. **Radiological investigations:** as Triphasic CT or dynamic MRI of the abdomen and pelvis before and after the procedure for follow up.

Therapeutic procedures of intra-arterial ethanol embolization:

In each patient, a diagnostic angiography was done. The left or right hepatic artery was the location of the catheter tip for TACE. The artery supplying the lesion was injected with 5–10 mL of a solution containing 10 mg of mitomycin C (Medac, Hamburg, Germany) in 10 mL of iodized oil under fluoroscopic guidance(s). Immediately prior to injection, the mitomycin/oil mixture was created by vigorously mixing for a short period of time. Gelatin-sponge particles were used to embolize (Gelfoam; Upjohn, Kalamazoo, MI, USA). If there was a contralateral HCC and a unilateral portal vein thrombosis, the corresponding lobe underwent chemoperfusion without embolization (TAC). The extent of the vascular blockage was angiographically shown at the conclusion of the surgery.

For observation, patients typically spent one day in the hospital. CT scan was done two weeks after TACE. The findings were explained as follows: In the early vascular phase, tumor necrosis manifests as hypo attenuated and contrast medium-non-enhanced lesion(s); remaining tumor manifests as contrast medium-enhanced lesion(s). Every 6–10 weeks, the operation was repeated until one of the following end goals was reached: (1) no viable tumor cells could be seen by CT or biopsy; (2) procedure contraindications developed; or (3) patient death. Only in cases with compensated cirrhosis Child-Pugh was TACE conducted on patients who experienced thrombosis of the major portal trunk. Appropriate collateral circulation and a score surrounding the thrombosis (cavernous transformation with prograde intrahepatic portal perfusion on ultrasound Doppler flow examination).

Statistical Analysis:

Using Microsoft Excel software, data from historical records, routine clinical examinations, and outcome measures were coded, inputted, and analyzed. The Statistical Package for the Social Sciences (SPSS version 25.0) was used to import the data (Armonk, NY: IBM Corp, 2018). Analytical statistics included the Chi-square test (χ^2), one-way ANOVA (F test), Spearman's correlation (r), and correlation coefficient test. Descriptive statistics comprised percentages (%), means (x), and standard deviations (SD) (Person test). Statistical significance was defined as a P value 0.05 or lower.

RESULTS

A CONSORT flow chart of the study population is shown in **Figure 1**. Of 52 patients with hepatocellular carcinoma and malignant portal vein thrombosis included in this study, they attended to National Liver Institute, Menoufiya University from March 2020 to March 2022, 6 patients excluded from our study, (4 of them did not meet the inclusion criteria and 2 declined consent), 46 patients were willing to participate and consented for participation in the study and were analyzed statistically (8 patients had PVTT grade (II) and remind 38 patients had PVTT grade (III).

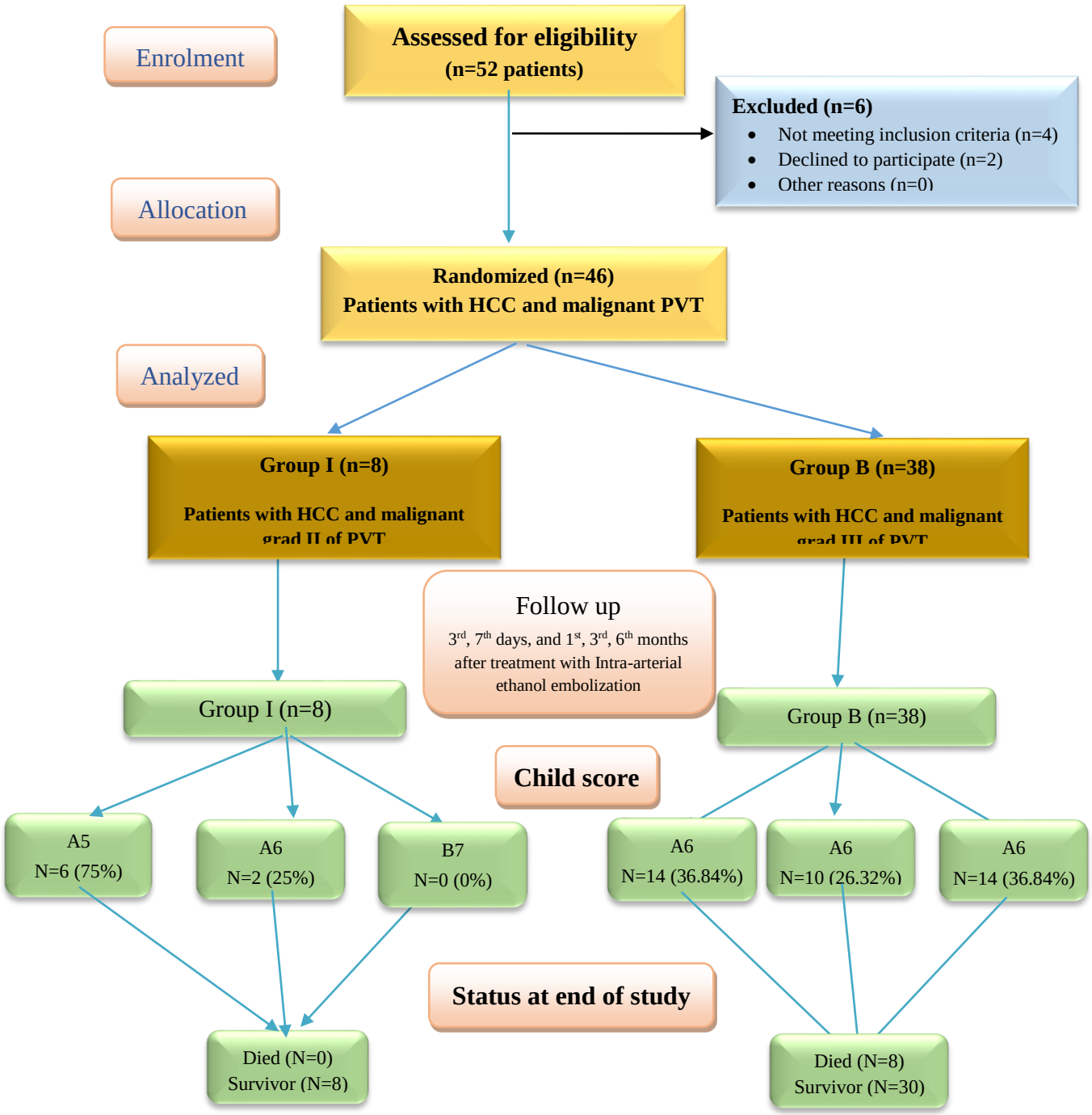

Figure (1): Flowchart of the studied patients with HCC and malignant PVT.

From March 2020 to March 2022, a total of 46 patients with hepatocellular carcinoma and malignant portal vein thrombosis were enrolled at the National Liver Institute, Menoufia University, for this study. Patients' ages ranged from (53.00-75.00 years) in this study, with a mean of (61.22±6.88 years). While the majority of the study's patients (91.3%) were men. The age difference between PVT grades II and III was statistically significant (p<0.001). However, there was no correlation between the grade of the portal vein tumor thrombus and the gender, amount of ethanol, or number of sessions (P>0.05) **(Table 1)**.

Table (1): Portal vein tumor thrombus grades in relation to demographic data, number of sessions and ethanol amounts**.**

Variables	PVT grades				U	p value	95%CI	
	II (N=8)		I (N=38)				Lower	Upper
Age/year (Mean±SD)	55.75±2.87		62.37±6.95		4.368	**<0.001***	-9.73	-3.51
Gender: N (%)								
Male	6	75.00	36	94.74	3.242	0.072	---	---
Female	2	25.00	2	5.26				
Number of sessions (Mean±SD)	1.50±0. 31		1.26±0.24		1.170	0.271	-0.22	0.69
Ethanol amount (ml)- (Mean±SD)	19.25±2.76		17.42±3.45		1.623	0.130	-0.62	4.28

PVT: Portal vein tumor thrombus, U: Mann-Whitney test, *significant

Also, AST, ALT, total and direct bilirubin, total bilirubin and direct bilirubin (1 and 3 months ago), ALT (3 and 6 months ago) and direct bilirubin (6 months ago) did not significantly correlate with the grades of portal vein tumor thrombus (P>0.05). However, grade III of PVT was substantially associated with higher levels of AST (1, 3, and 6 months ago), ALT (1 month ago), and total bilirubin (6 months ago), (P<0.05) **(Table 2)**.

Table (2): Portal vein tumor thrombus grades in relation to laboratory investigations at 1,3 and 6 months

Variables	PVT grades		U	P value	95%CI	
	II (N=8)	III (N=38)			Lower	Upper
	Mean±SD	Mean±SD				
Total bilirubin (1 month)	1.08±0.27	0.99±0.11	0.741	0.470	-0.16	0.33
Direct bilirubin (1 month)	0.35±0.09	0.36±0.05	0.160	0.874	-0.14	0.12
AST (1 month)	27.00±1.85	44.11±10.50	4.423	**<0.001***	-24.93	-9.28
ALT (1 month)	11.25±2.31	32.37±7.86	5.337	**<0.001***	-29.12	-13.12
Total bilirubin (3 months)	1.00±0.23	0.98±0.21	0.153	0.881	-0.28	0.32
Direct bilirubin (3 months)	0.28±0.04	0.35±0.04	1.105	0.281	-0.22	0.07
AST (3 months)	30.25±7.87	48.16±11.83	3.208	**0.003***	-29.18	-6.64
ALT (3 months)	21.75±5.76	34.37±8.84	1.415	0.182	-31.99	6.75
Total bilirubin (6 months)	0.78±0.04	0.96±0.04	2.277	**0.029***	-0.36	-0.02
Direct bilirubin (6 months)	0.33±0.05	0.29±0.06	0.586	0.561	-0.08	0.15
AST (6 months)	34.25±8.21	53.63±12.31	2.325	**0.025***	-36.18	-2.58
ALT (6 months)	24.75±4.29	35.53±8.71	1.543	0.137	-25.25	3.70

PVT: Portal vein tumor thrombus, U: Mann-Whitney test, *significant

In the current study, the grades of the portal vein tumor thrombus did not significantly correlate with ascites (P>0.05). While there was a substantial correlation between PVT and the tumor's characteristics and locations (P>0.05), in 8 grade II patients (100%) and 24 grade III patients (63.16%), distinct tumors were detected. Four patients in grades II and III were more likely to have tumor VIII sites (50.0% and 10.53%), respectively **(Table 3)**.

Table (3): Portal vein tumor thrombus grades in relation to diagnostic data and characters and sites of the tumor.

Variables	PVT grades				X^2	p-value
	II (N=8)		III (N=38)			
	N	%	N	%		
Ascites:						
No	6	75.00	30	78.95	0.061	0.806
Mild	2	25.00	8	21.05		
Virus C:						
No	0	0.00	0	0.00	NA	---
Yes	8	100.00	38	100.00		
Tumor characters (1 vs 2):						
Distinct	8	100.00	24	63.16	4.237	**0.040***
Ill-defined	0	0.00	14	36.84		
Site of the tumor:						
VI, VII	0	0.00	4	10.53		
II	0	0.00	4	10.53		
III	0	0.00	4	10.53		
IV	0	0.00	2	5.26		
V	2	25.00	0	0.00		
VI	0	0.00	4	10.53		
VII	0	0.00	2	5.26		
VIII	4	50.00	4	10.53	32.079	**0.006***
II, VI	0	0.00	2	5.26		
II, IV	0	0.00	2	5.26		
III, VII	0	0.00	2	5.26		
V, VII	0	0.00	2	5.26		
V, VI	2	25.00	0	0.00		
V, VIII	0	0.00	2	5.26		
IV, VI	0	0.00	2	5.26		
VI, VII, VIII	0	0.00	2	5.26		

PVT: Portal vein tumor thrombus

Additionally, PVT and portal thrombus were substantially correlated (P>0.001). Six grade II patients (75%) had more right anterior portal thrombi, while 16 grade III patients (84.22%) had more right and left portal thrombi. As for the relationship between mRECIST after the second session and PVT graduates, P>0.001. Four patients with grade II showed a complete response (100%) while eight patients with grade III showed a partial response (80%). However, there was no correlation between Child score and portal vein tumor thrombus grades using mRECIST after a single session (P>0.05) **(Table 4)**.

Table (4): Portal vein tumor thrombus grades in relation to portal thrombus, mRECIST and Child score.

Variables	PVT grades				X^2	p-value
	II (N=8)		III (N=38)			
	N	%	N	%		
Portal thrombus:					46.000	**<0.001***
Right	0	0.00	16	42.11		
Right anterior	6	75.00	0	0.00		
Main right PV	0	0.00	6	15.79		
Right posterior	2	25.00	0	0.00		
Left	0	0.00	16	42.11		
mRECIST after single session:					3.541	0.316
Progression	0	0.00	10	26.32		
Partial response	6	75.00	18	47.37		
Complete response	2	25.00	8	21.05		
Stable disease	0	0.00	2	5.26		
mRECIST after 2nd session:	N=4		N=10		21.63	**<0.001***
Progression	0	0.00	2	20.00		
Partial response	0	0.00	8	80.00		
Complete response	4	100.00	0	0.00		
Child score:					5.165	0.076
A5	6	75.00	14	36.84		
A6	2	25.00	10	26.32		
B7	0	0.00	14	36.84		

PVT: Portal vein tumor thrombus, *: Statistically significant

Concerning, status at the end of study and response were significantly relation with PVT, (P<0.001). Complete response more found in 4 grade II patients (50.00%) while, refused follow up more found in 12 grade III patients (31.58%) **(Table 5)**.

Table (5): Portal vein tumor thrombus grades in relation to status at end of study and response.

Variables	PVT grades				X^2	p-value
	II (N=8)		III (N=38)			
	N	%	N	%		
Status at end of study:					13.518	**0.019***
Died:	**0**	**0.00**	**8**	**21.05**		
Survivor:	**8**	**100.00**	**30**	**78.95**		
Lost contact	2	25.00	10	26.32		
Refused follow up	0	0.00	12	31.58		
Complete response	4	50.00	4	10.53		
Nexavar after 2nd session	2	25.00	2	5.26		
Patient choose chemo	0	0.00	2	5.26		

PVT: Portal vein tumor thrombus, *: Statistically significant

Also, AST, ALT and direct bilirubin were significantly increased after 3 days of treatment than baseline, 7 days and (1, 3 and 6 months) of treatment. However, there were no significant differences between the studied patients pre and post treatment regarding total bilirubin (p>0.05) **(Table 6)**.

Table (6): Laboratory investigation before and after procedure among the studied patients.

Variables	Before procedure	After procedure					F	p value
	Baseline	3 days	7 days	1 month	3 months	6 months		
Total Bilirubin (µmol/L) Mean ±SD	0.97±0.03	1.11±0.31	1.09±0.20	1.00±0.19	0.98±0.01	0.93±0.01	1.405	0.223
Post hoc	P1=0.101, P2=0.175, P3=0.719, P4=0.918, P5=0.607, P6=0.773, P7=0.199, P8=0.124, P9=0.**031***, P10=0.319, P11=0.210, P12=0.062, P13=0.797, P14=0.382, P15=0.537							
Direct Bilirub. (µmol/L) Mean±SD	0.30±0.06	0.54±0.04	0.39±0.01	0.36±0.01	0.34±0.02	0.30±0.02	4.469	**<0.001***
Post hoc	**P1<0.001*,** P2=0.118, P3=0.305, P4=0.504, P5=0.983, P6=0.015, P7=0.003, P8=0.001, **P9<0.001*,** P10=0.590, P11=0.370, P12=0.123, P13=0.720, P14=0.315, P15=0.518							
AST (U/L) Mean±SD	38.57±9.20	81.74±13.04	52.43±11.03	41.13±9.30	45.04±11.08	50.26±13.69	9.563	**<0.001***
Post hoc	**P1<0.001*,** P2=0.055, P3=0.721, P4=0.368, P5=0.105, **P6<0.001*, P7<0.001*, P8<0.001*, P9<0.001*,** P10=0.117, P11=0.304, P12=0.762, P13=0.586, P14=0.205, P15=0.468							
ALT (U/L) (3days) Mean±SD	35.74±8.73	70.52±15.97	46.00±11.77	28.70±6.12	32.17±7.10	33.65±5.83	10.349	**<0.001***
Post hoc	**P1<0.001*,** P2=0.134, P3=0.303, P4=0.602, P5=0.760, **P6<0.001*, P7<0.001*, P8<0.001*, P9<0.001*,** P10=0.012, P11=0.044, P12=0.072, P13=0.611, P14=0.469, P15=0.829							

AST: Aspartate aminotransferase, **ALT**: Alanine transaminase, *: Statistically significant

Furthermore, there was no significant relation ethanol amounts (ml) with status at end of study (p=0.072) **(Table 7)**.

Table (7): Relation between ethanol amount (ml) with status at end of study among the studied patients

Variable	Ethanol amount (ml)		
	Mean ±SD	Range	Median (IQR)
Status at end of study			
Died	17.50±2.67	15.00-20.00	17.50(5.00)
Lost contact	18.00±3.30	15.00-23.00	17.50(5.00)
Refused follow up	19.00±3.13	15.00-23.00	20.00(6.00)
Complete response	18.50±4.11	12.00-22.00	20.00(7.50)
Nexavar after 2nd session	13.50±1.73	12.00-15.00	13.50(3.00)
KW	2.210		
P Value	0.072		

Finally, age and PVT grade were found to be the most significant predictors of the identification of hepatocellular carcinoma in patients with malignant portal vein thrombosis, according to the results of multiple logistic regression analysis. While the Child score, the location of the tumor, and the discovery of hepatocellular carcinoma did not correlate with malignant portal vein thrombosis (P> 0.05) **(Table 8)**.

Table (8): Multinomial logistic regression analysis using as the studied variable as detection of hepatocellular carcinoma with malignant portal vein thrombosis.

Variables	β	Std. Error	Wald	Sig.	Exp (β)	95% CI for Exp (B)	
						Lower	Upper
Age (years)	-0.964	0.400	5.793	**0.016***	0.381	0.174	0.836
Child score	-0.296	0.503	0.347	0.556	0.744	0.278	1.992
Site of the tumor	0.138	0.135	1.050	0.305	1.148	0.881	1.496
Grade PVT	-1.901	0.959	3.932	**0.047***	0.149	0.023	.978

DISCUSSION

This study showed that, a total of 46 patients their ages ranged from (53.00-75.00 years) with mean (61.22±6.88 years). While, (91.3%) of the studied patients were male. This result is similar to that reported in Egyptian literature by **Abdelkader *et al.*** [8] who found that men were more likely than females to present with HCC (32 males, 67%) compared to 16 females, 33%). In addition, **Abdelaziz *et al.*** [9] discovered that 71% of the HCC patients they evaluated were men and 29% were women. This outcome is comparable to that observed by **El-Zayadi *et al.*** [10]**,** who discovered that 77.7% of the patients with HCC who were evaluated were men and 22.3% were women. They also discovered that men had an estimated risk of developing HCC that was about three times higher than that of women.

Hepatitis C Virus (HCV) is responsible for 10% to 20% of virus- associated HCC**.** In this regard, this present study showed that, (21.7%) of the studied patients had mild ascites, all of them had virus C. In the study conducted by **Abdelmaksoud *et al.*** [11] found all cases developed HCC on top of cirrhosis that was mainly due to HCV (85%). Also, **Ibrahim *et al.*** [12] found HCV marker was higher in both groups with 18 (72%) and 20 (80%) respectively. **Cheng *et al.*** [13] divided PVT into four types based on tumor site and extent: the segmental or sectoral portal vein branches (type I), the right or left portal vein (type II), the main portal vein trunk (type III), or the superior mesenteric vein (type IV).

In the present study 82.6% of patients had II grade PVTT. **Abdelmaksoud *et al.*** [11] found to be clear, the majority of their patients (76.4%) had type II PVT (main stem PVT), and it was completely occluded in (81.6%) of the patients, although the type of PVTT was one of the independent predictors of survival in the study carried out by **Liu *et al.*** [14]**,** the kind of PVT, the quantity of tumor lesions, the liver function, and the metastasis can all be used by physicians to anticipate these patients' prognoses and assist them choose the right candidates.

This study showed that, 47.8% of the studied patients had portal thrombus in main right branch. In the same line, **Abdelmaksoud *et al.*** [11] found the right branch (17.9%, n=25), the left branch (5.7%, n=8), and the main PV (76.45%, n=107) were all thrombosed. The extent of the thrombus was partial in 18.4% of the cases (n=19) and total in 81.6% of the cases (n=84).

Additionally, this study revealed that, according to mRECIST criteria, 52.2% of the investigated patients experienced a partial response. According to **Duran *et al.*** [15]**,** 52.4% of patients had an objective response as measured by mRECIST. This study verified the combination therapy's safety profile when it used an interrupted sorafenib strategy.

In the current study, a total of 46 patients included in this study, 8 patients (17.4%) died and 38 patients were survivor (82.6%), 26.1% of them refused follow up or lost contact, followed by 17.4% had complete response. HCC patients with PVTT who were treated with TACE had a 28.6% 1-year survival rate, according to **Yamada *et al.*** [16]. A 30% 1-year survival rate and a 28.2% PVTT response rate were then reported by **Chung *et al.*** [17]. The 1-year survival rates reported by **Georgiades *et al.*** [18] **and Takayasu *et al.*** [19] were 25% and 35%, respectively. According to **Peng *et al.*** [20], the 1-year survival rate for PVTT was 36.1%. According to a different study by **Salem *et al.*** [21], objective response rates of 42% for Y90 radioembolization for the overall patient group were 7.9 months, and survival rates varied by Child-Pugh stage. Patient survival was much longer for those with Child-Pugh A disease than for those with Child-Pugh B disease (17.2 vs. 7.7 months). According to numerous studies, patients who receive TACE, particularly those who receive less selective or repeated TACE, have reduced liver function. Repeated TACE in patients with refractory illness may worsen liver function, obstructing the effectiveness of other systemic medications and reducing overall survival [22].

Additionally, in the current investigation, grade III PVT patients had significantly higher total and direct bilirubin levels 3 days after the surgery than did grade II PVT patients. However, there are no links between the severity of the portal vein tumor thrombus and the AST and ALT levels three days after the procedure or the direct bilirubin, AST, and ALT levels seven days after the procedure, (P>0.05). This result was congruence with **Somma *et al.*** [23] who found that, no discernible difference was found between the trans arterial ethanol embolization (TAELE) group and the conventional trans arterial chemoembolization (cTACE) group in the number of patients with abnormal AST, ALT, or total bilirubin values between the time periods T0 (the day before the procedure) and T1 (within the first week after the procedure). For the TAELE group, a significant decline in the proportion of patients with aberrant AST, ALT, and total bilirubin readings was seen in the time window T1–T2.

This study showed that, AST, ALT and total bilirubin were significantly increased among grade III than grade II of PVT. However, no significant relations between portal vein tumor thrombus grades with total bilirubin and direct bilirubin, ALT and direct bilirubin. In this regard, **Somma *et al.*** [23] showed that, in the time-range T0-T2, a significant decrease in the number of patients with abnormal values of total bilirubin was diagnosed for TAELE group. Also, in our study, no significant relations between portal vein tumor thrombus grades with ascites.

Chung *et al.* [24] found no discernible difference was found between the trans arterial ethanol embolization group and the conventional trans arterial chemoembolization (cTACE) group in the number of patients with abnormal AST, ALT, or total bilirubin

values between the time periods T0 and T1. For the TAELE group, a significant decline in the proportion of patients with aberrant AST, ALT, and total bilirubin readings was seen in the time window T1–T2 in the study done by **Liu *et al.* [14]**.

Also, in our study, characters and sites of the tumor were significantly related with PVT, (P>0.05). Distinct tumor more found in 8 grade II patients (100.0%) and 24 grade III patients (63.16%). Segment VIII tumor site more found in 4 grade II patients (50.0%) and 4 grade III patients (10.53%). According to **Liu *et al.* [14]**, patients with 1-2 tumor lesions had considerably higher median overall survival than patients with 3 or more malignancies (8.1 months versus 4.5 months). According to **Somma *et al.* [23]**, patients receiving TAELE treatment had a considerably higher rate of tumor size reduction than those receiving cTACE treatment. The increased level of devascularization attained in lesions treated with TAELE was likely the cause of this. It has been proposed that embolization-related ischemia may be the primary reason causing tumor size decrease after trans-arterial treatments and that cTACE may exhibit less significant embolizing activity than other embolizing techniques, such as TAELE. Anyway, the question of whether this finding means a better prognosis should be investigated in prospective studies on larger series of patients.

CONCLUSIONS

Additionally, ethanol can cause a condition known as persistent microcirculatory embolization, which stops the growth of malignancies by drying vascular endothelial cells, denaturing proteins, and coagulating platelets. TEA stands for transarterial lipiodol-ethanol combination injection. Compared to Gelfoam embolization, ethanol embolization is effective, safe, and may lengthen patients' lives in those with HCC and malignant portal thrombus.

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