

The Gulf Journal of Oncology

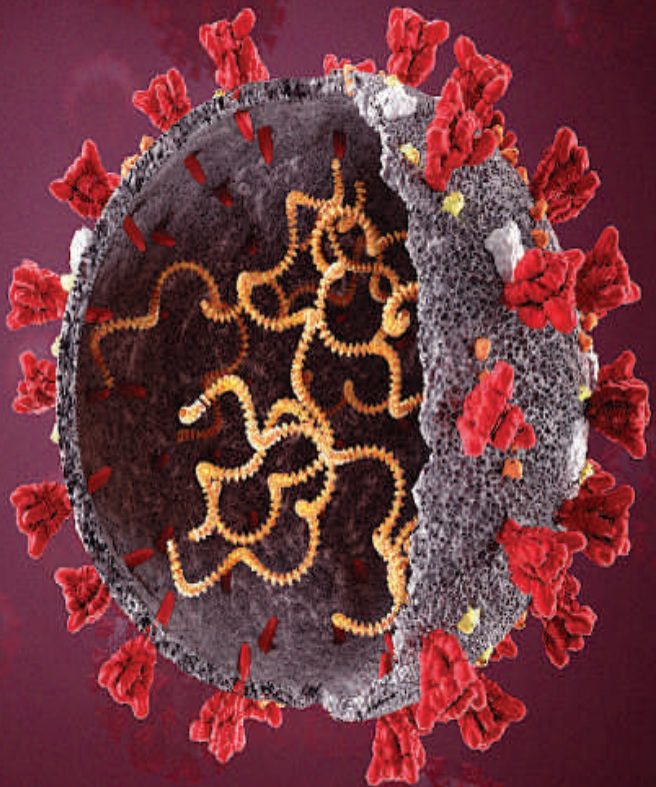


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The Prognostic Value Of The ART Score Before The Second Transarterial Chemoembolization

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Abstract

The transarterial chemoembolization (TACE) is a first–line therapeutic option for advanced hepatocellular carcinoma (HCC). Their indications are clearly defined by learned societies but the challenge is to determine the optimal number of TACE sessions that will benefit patients before switching to other therapies. For this reason, the Assessment for Retreatment with Transarterial chemoembolization (ART) score has been developed. The objective of our work is to show the prognostic value of the ART score before the second TACE.

Methods: This is a retrospective and prospective study of patients with hepatocellular carcinoma on cirrhosis liver who received a TACE between January 2012 to July 2019. The diagnosis of HCC was made according to the non–invasive criteria of EASL with the use of histology for doubtful cases. The ART score was calculated after the first chemoembolization. Patients were divided into 2

groups: group A with an ART score between 0 and 1.5 and group B with a score ≥ 2.5 .

Results: During the study period, 58 patients with HCC on cirrhosis liver received a TACE: 55.17% had an ART score between 0 – 1.5 before the second session and 44.8% had an ART score ≥ 2.5 . Both groups were comparable regarding age, circumstances of discovery and Child's score. The size of the HCC as well as the value of the AFP was further increased in the group B. We observed a significant difference in the radiological response, the Child score and aspartate transaminase rate between the two groups after the first TACE. The overall survival rate at 3 years was 81% in group A versus 19% in group B.

conclusion: The ART score has an independent prognostic value and should be taken into account in the therapeutic strategy before the second TACE.

Keywords: hepatocellular carcinoma, transarterial chemoembolization, ART score.

Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver tumor. It is the second leading cause of cancer in men and the third in women in Africa ^[1]. It usually develops on cirrhosis in 80% of cases. Chronic viral hepatitis infection is the major cause of HCC ^[2]. The diagnostic approach of HCC is different depending on the existence or not of underlying liver cirrhosis. For the early stages of HCC, curative therapies include surgical removal, liver transplantation and percutaneous treatment (radiofrequency ablation, alcohol ablation). Despite all the therapeutic progress, only 30% of the patients can benefit from a curative treatment. In all the other cases the treatment is palliative, HCC is more often diagnosed at the intermediate (BCLC stage B) and advanced (BCLC stage C) stages, when only palliative treatments, such as

transarterial chemoembolization or target therapy, can be considered ^[3]. The indications of TACE are clearly defined by learned societies but the challenge is to determine the optimal number of TACE sessions that will benefit patients before switching to other therapies. For this reason, the Assessment for Retreatment with Transarterial chemoembolization (ART) score has been developed ^[4]. The objective of our work is to show the prognostic value of the ART score before the second TACE.

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Methods:

This is a retrospective and prospective study of patients with hepatocellular carcinoma on cirrhosis liver who received a TACE between January 2012 and July 2019. The diagnosis of HCC was made according to the non-invasive criteria of EASL with the use of histology for doubtful cases. The degree of hepatocellular insufficiency was evaluated by Child–Pugh score.

ART score:

ART score is calculated based on 3 parameters measured just before the second TACE session, including Child–Pugh score increase from base line; aspartate transaminase (AST) increase >25% from baseline and radiologic evidence of tumor response after a previous TACE session. Patients were divided into 2 groups: group A with an ART score between 0 and 1.5 and group B with a score ≥ 2.5 .

Statistical Analysis

The analysis of the results was done with the software Package for Social Science (SPSS version 20) for Windows. Quantitative variables were expressed as average \pm standard deviation. Qualitative variables were expressed in number and percentage (%). We considered a significant p value ≤ 0.05 . The association between ART score and survival at 3 years was studied. Patient survival was assessed using to the Kaplan–Meier method.

Results:

During the study period, we collected 58 patients with HCC on cirrhosis liver who received TACE. The average age was 62 ± 15.42 years with a male predominance. The etiology of cirrhosis was secondary to hepatitis C in 60.34%, hepatitis B in 24.13%, alcohol in 6.89% and secondary to non-alcoholic steatohepatitis in 5.17%. We also report a case of HCC secondary to Alagille Syndrome and another on Budd Chiari syndrome. Screening revealed the tumor in more than half of the cases. All of our patients had CHILD \leq B7: 20.68% were A5, 43% had CHILD A6 and 36% were B7 (table II). Alpha fetoprotein level was normal in 37.9%. The size of HCC nodules exceeded 3 cm in 75.9%. The average number of sessions was 2 [1; 6].

According to RECIST criteria: 74.13% patients presented a partial response; 20.86% presented stabilization and 5.17% patients a complete response. The ART score was between 0 and 1.5 in 55.17% which justified the use of a second TACE and exceeded 2.5 in 44.82%. The follow-up was 18.2 ± 14.5 months. The complications after TACE consisted of the appearance of fever, nausea, anorexia

and pain at the right hypochondrium in almost a half of our patients while 3 others showed signs of liver failure. Survival at 1 year and 3 years was estimated at 81.7% and 48.27% respectively.

Our patients were divided into 2 groups according to ART score (table II): 55.17% had an ART score between 0 – 1.5 before the second session and 44.8% had an ART score ≥ 2.5 . Both groups were comparable in age, circumstances of discovery, and Child–Pugh score. We found a clear male predominance in group A. The size of the HCC as well as the AFP level was increased more in group B. The radiological response after the first TACE was greater in group A 93.7% vs 23.07% while the Child–Pugh score significantly increased in group B 84.61% vs 6.25. The overall survival rate at 3 years was 81% in group A versus 19% in group B (figure I). At multivariate analysis, Child–Pugh score and aspartate transaminase increase

Characteristics	N(%)
Middle age	62 \pm 15.42 ans
Sexe ratio (H/F)	2.2
Etiologies of cirrhosis:	
Hepatitis C	35(60.34%)
Hepatitis B	14(24.13%)
Alcohol	4(6.89%)
Non-alcohol steatohepatitis	3(5.17%)
Alagille syndrome	1(1.72%)
Budd Chiari syndrome	1(1.72%)
Circumstances of discovery	
Screening	44 (75.9%)
Pain of the right hypochondrium	12(20.6%)
Fortuitous	2(3.44%)
Average HCC size	59.45 \pm 27.33 cm
Localisation	
Right lobe	45(77.58%)
Left lobe	12(20.68%)
segment I	1(1.72%)
Portal vein thrombosis	8(13.8%)
Median of AFP rate	23.5 ng/dl [1 ; 22069]
CHILD:	
A5	12(20.68%)
A6	25(43.10%)
B7	21(36.2%)
Sign of portal hypertension	
Presence of swollen veins at the fibroscopy	26 (44.82%)
Presence of porto-systemic collateral veins	9(15.5%)

Table I: characteristics of our patients

	Groupe A: 32 (55,17%)	Groupe II : 26 (44,8%)
Middle age	65.32 years	64.91 years
Sex ratio (H/F)	3	1,4
AFP rate		
≤10 ng/ml	6(18.7%)	3(11.53%)
>10 ng/ml	26(81.25%)	23(88.46%)
Child–Pugh score:		
A5	9(28.125%)	3(11.53%)
A6	12(37.5%)	13(50%)
B7	11(34.37%)	10(38.46%)
The size of HCC ≤ 3cm	6(18.7%)	3(11.53%)
ART score:		
Radiological reponse	30(93.7%)	6(23.07%)
Child–Pugh score increase	2(6.25%)	22(84.61%)
aspartate transaminase increase >25%	1(3.12%)	6(23.07%)
Survival at 3 years	47 (81%)	11(19%)

Table II: comparative table between group A and B

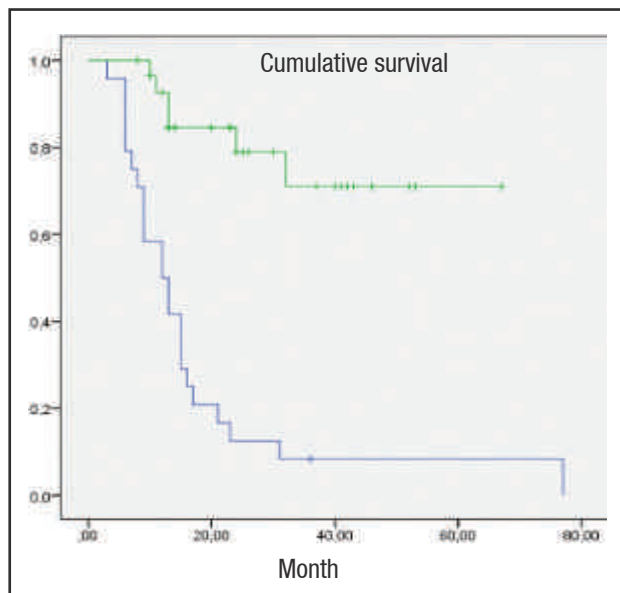


Figure 1: 3–year survival curve of both groups (bleu=group B, green=group A)

are associated with a significant predictor of worse survival with respectively $p = 0.001$ and $p=0,05$ while radiological response is associated with good survival with $p=0,001$.

Discussion:

The presence of portal hypertension and cirrhosis, most often advanced, make hepatocellular carcinoma a complex pathology to be treated. International Bridge study showed that TACE is the most widely used treatment

for HCC worldwide, ahead of both surgical removal and systemic treatments^[5]. Several studies have been interested in studying TACE and, among other things, the contribution of the ART score before the second session.

Our finding of a positive association between survival and an AST increase >25% was similar to the findings of Sieghart et al^[4]. A significant association between radiologic tumor response and survival was also noted in our study, similar to the results of Sieghart et al^[4] and Adhoute et al^[6]. Child–Pugh score increase is associated with a significant predictor of worse survival both in our study and in Sieghart et al^[4], Terzi et al^[7] and Adhoute et al^[6].

Sieghart et al^[4] found that both the lack of a radiologic tumor response and deterioration of liver function (defined as an AST increase >25% and/or an increase of the Child–Pugh score) after the first TACE were associated with a dismal prognosis for patients who were retreated with TACE.

According to Adhoute et al^[6], the ART score was not of major value; using a cut–off value of (0–1.5 vs. ≥ 2.5), there was a statistically significant difference between these two groups but there was no clear relationship between the score and survival. Patients with an ART score of 4, an increase in AST >25%, had a better overall survival than patients with an ART score of 1, not showing a radiologic response, as expected since radiological response is correlated with post–TACE survival times.

Tseng et al^[3] shows that the ART score was not found to be effective in selecting patients for TACE retreatment. Large tumor size, high AST level, high 2nd/1st (pre–TACE) alpha–fetoprotein ratio, AST increase >25%, and lack of radiological response to TACE were independently associated with shorter survival after TACE therapy.

In the same way, Terzi et al^[7] shows the ART score was not found to work as an objective tool to guide TACE retreatment, only the Child–Pugh score increase was an independent predictor of a shorter survival.

Given the limitations of the other therapeutic option, the vast majority of patients with HCC must look to minimally invasive such as transarterial chemoembolization, which has shown efficacy in HCC therapy with palliative therapeutic intent or as a bridge or downstage to liver transplantation^[8].

Conclusion:

The ART score has an independent prognostic value and should be taken into account in the therapeutic strategy before the second TACE. An ART score of 2.5 prior the second TACE identifies patients with a dismal prognosis who may not profit from further TACE sessions.

Conflict of Interests:

All authors agree with the content of the manuscript and there are no conflicts of interests between them.

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