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Review Article

Role of triphasic computed tomography in prediction of response to transcatheter arterial chemoembolization in unresectable hepatocellular carcinoma patients

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Abstract

Background

The initial approach in the management of hepatocellular carcinoma (HCC) is to determine if either surgical resection or liver transplantation is feasible. Unfortunately, more than three-quarters of the patients are diagnosed during the intermediate or advanced stages of the disease and are considered ineligible for curative resection. Transarterial chemoembolization (TACE) is the current standard of therapy for patients with intermediate-stage HCC according to the Barcelona Clinic Liver Cancer classification.

Aim

This study aims to evaluate the role of triphasic computed tomography (CT) in the prediction of the prognosis of irresectable HCC patients, who had been locally treated with TACE by studying the enhancement (vascularity) pattern and the volume changes of the HCC after TACE.

Patients and methods

Our study included 25 HCC patients as diagnosed by triphasic CT study and serum alpha fetoprotein (AFP) level. The patients were recruited from the National Liver Institute Menoufia HCC Clinic and Radiology Department for assessment of the target lesion after doing TACE as a locoregional therapy for HCC from September 2017 to July 2018.

Results

Prediction model of response in our study depends on all of these variables along with the maximum initial diameter of the target lesion, the baseline serum AFP level, serum level of total bilirubin, INR, splenic size and sex of the patient with an overall accuracy of 88%, sensitivity of 93.3%, specificity of 80%, PPV: 87.5%, and NPV: 88.88%.

Conclusion

Triphasic CT is the most commonly used as the standard imaging technique for predicting and evaluating the therapeutic response in patients with HCC after TACE. It is a more accurate prognostic factor than the AFP serum level estimation.

Keywords: AFP, chemoembolization, hepatocellular carcinoma, transarterial chemoembolization

Introduction

Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver. The global burden of cancer in 2012 was an all-time high of 14 million cases and is predicted to grow to 22 million over the next two decades. Liver cancers have the seventh highest age-adjusted incidence rate in the world, with 0.8 million cases diagnosed for the year 2012. This is the third most common cause of cancer-related death in the world [1].

Liver cancer burden varies markedly by sex and geographic region due to risk factor exposure. The major risk factors include infections (hepatitis B virus, hepatitis C virus, liver

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flukes in endemic areas), behavioral factors (alcohol, tobacco), metabolic factors (excess body fatness), and aflatoxins [2].

Unlike other forms of cancer, the diagnosis of HCC is mostly based on imaging studies and laboratory tests as well. The imaging studies used in diagnosis, treatment planning, and management and follow-up of HCC are ultrasonography, computed tomography (CT) scanning, and MRI [3].

CT scanning is the primary method for HCC detection and diagnosis, in particular, multislice spiral CT, which plays an important role in HCC diagnosis, differential diagnosis, and even HCC staging [4].

Transarterial chemoembolization (TACE) is the current standard of therapy for patients with intermediate-stage HCC according to the Barcelona Clinic Liver Cancer classification. The concept of conventional TACE is the selective obstruction of a tumor-feeding artery by injection of chemotherapeutic agents, leading to ischemic necrosis of the target tumor via cytotoxic and ischemic effects [5].

Patients and methods

This study was carried out on 25 patients presented with irresectable HCC which will be treated locally with TACE.

Patients with chronic renal disease and patients with a history of allergic reactions to contrast media are excluded from our study.

All patients in this study were subjected to the following:

(1) Thorough history taking including age, sex, complaints, history of jaundice, schistosomal infestation, previous surgery, or blood transfusion. History of intake of hepatotoxic drugs or systemic chemotherapy, previous local alcohol injection, or any other local ablation for focal hepatic lesions.
(2) Clinical examination including:

General examination and local abdominal examination.

(3) Laboratory investigations including complete blood count (CBC), liver enzymes, serum bilirubin, albumin and prothrombin activity, serum α-fetoprotein, serum creatinine.
(4) Radiological examination including:
    (a) Real-time ultrasound using an ultrasound machine.
    (b) A retrospective study of the previous CT scans will be done for the patient before TACE to assess the target lesion size.
    (c) Triphasic CT examination of the liver, 4–6 weeks after TACE.

Imaging technique

A 20-G plastic intravenous catheter was placed in the antecubital vein. The line was then connected to a power injector through which 150 ml of Ultravist 300 (Ultravist Bayer Health Care Pharmaceuticals; Berlin, Germany) was injected intravenous at a rate of 4 ml/s. Arterial phase was performed with a scanning delay of 20–40 s from initiation of contrast material injection. The entire liver was scanned in a cephalad-to-caudad direction. After a brief period of quiet breathing, portal venous phase imaging of the entire abdomen will be performed in a cephalad-to-caudad direction during a single breath-hold, using a scanning delay of 60 s.

Results

Our study included 25 HCC patients as diagnosed by triphasic CT study & serum AFP level. Patients were recruited from the national liver institute HCC clinic & radiology department for assessment of the target lesion after doing TACE as a locoregional therapy for HCC.

In our study there were 18 males (72%) and 7 females (28%) with their age ranged between 45-67 years with the mean age 56.48 ± 5.5 years this goes with the results of Demographic health survey 2008 the incidence in males were more than females it's likely due to higher exposure to HCV between males [Tables 1 and 2].

In our study, concerning the hepatic function tests total bilirubin was (1.14 mg/dl±0.41 mg/dl) AST level was (74.84±44.59), ALT level was (68.28±35.16), serum albumin was (3.29 ±0.35g/dl) prothrombin concentration was (79.10%±9.87%), and INR was (1.21±0.21).

Concerning other lab findings, serum creatinine was (0.95mg /dl ±0.19), serum HB was (12.46g/dl ± 0.98), platelets were (135200±47050), and AFP before TACE was 349.58±808.41 and AFP after TACE was 227.91±342.52 ng/ml.

In aim to simplify the response evaluation, we classify the patients into responders (Fig1) (CR & PR) & non responders (Fig 2) (SD & PD) according to the RECIST & m RECIST & we find that: by RECIST, 20 patient over 25 (80%) had SD while 5 patients (20%) had PR while by the mRECIST 10 patients (40%) had SD, 7 patients (28%) had PR while 8 patients (32%) had CR.

Comparing the change in the AFP level to the response in CT by mRECIST we find that:

Ten cases were SD in the CT, 8 of them (80%) lower serum AFP level after TACE while two patients (20%) had a higher level.

Seven cases were PR in the CT, 4 of them had decreased AFP & 3 cases had increased level.

Eight patients showed CR, 7 of them (87.5%) had decreased AFP level while only 1 case had increased AFP level.

A significant negative correlation is found between the AFP level & the tumour response by the RECIST as the response is decreased while the serum AFP level is increased.

When the initial AFP level is high the maximum enhancement area after TACE is increased. Also a significant correlation between the AFP level after TACE & the maximum diameter of the viable tumour tissue [Tables 3-6].

We also find that, no significant relationship between the alteration in the serum level of AFP & the tumour response to TACE.

Discussion

TACE, according to the Barcelona Clinic Liver Cancer algorithm, is recommended for unresectable, single or multinodular, HCC in patients with preserved liver function and no evidence of vascular invasion or extrahepatic spread of disease. Conventional TACE is the most widespread technique and allows both to increase intratumoral retention of a chemotherapy agent and to induce ischemic tumor necrosis through a transient occlusion of tumor-feeding arteries [6].

Evaluation of response to treatment is a key aspect in cancer therapy, because the objective response may become a surrogate marker of improved survival [7].

Compared with another study by Forner *et al.* [8], concerning the hepatic function tests total bilirubin was 1 ± 0.41 mg/dl, AST level was 81.3 ± 53.9, ALT level was 95.4 ± 94.7, serum albumin was 40.4 ± 4 g/dl, prothrombin concentration was 84.1 ± 7.5%, and basal AFP before TACE was 26.5 (1 ± 78 487) ng/ml, while in the study by Ahsun *et al.* [9] the median pre-AFP and post-AFP was 1122 and 601 ng/ml, respectively.

In a study by Ahsun *et al.* [9] on AFP as a marker of radiologic response, progression, and survival and published in the *Journal of Clinical Oncology* on 125 patients, 47 (38%) of them were treated with TACE and 78 (62%) patients with ^{90}Y, 26 (55%) patients who were treated by TACE are AFP responders (>50% reduction of the baseline level), 16 of them had decreased AFP of more than 90% of the baseline level and three (6%) patients had normal AFP level after TACE. The median time to AFP response for all patients was 3.3 months. AFP response was correlated to imaging response in 42 patients, 16 of them showed WHO response (PR) based on RECIST criteria, 10 (62.5%) patients are AFP responders while six (37.5%) were non-AFP responders, 18 patients had SD, 11 (61%) of them are AFP responders, while eight had only progressive disease two of them are AFP responders.

The data presented support the use of AFP response seen after locoregional therapy as an ancillary method of assessing tumor response and survival, as well as an early objective screening tool for progression by imaging[10] (*Clin Oncol* 2009 by *American Society of Clinical Oncology*).

In this study, there is a highly significant relationship between the maximum initial diameter of the target lesion before TACE and the maximum diameter of the lesion after TACE as the

Table 1: Characteristics (age) of the studied population

	Mean	SD	Minimum	Maximum	*n*
Age (years)	56.48	5.524	45	67	25

Table 2: Sex distribution among the studied group

	n (%)
Males	18 (72.0)
Females	7 (28.0)
Total	25 (100)

Table 3: The maximum diameter of the lesion before transarterial chemoembolization in responders and nonresponders

	Response	Mean	SD	*P*
Max1	Nonresponder	5.9	2.99	0.1
	Responder	4.1	1.71	

Table 4: The relation between AFP and response among the studied group

	Response	Mean	SD	*P*
AFP1	Nonresponder	484.70	1239.46	0.68
	Responder	259.51	333.19	
AFP2	Nonresponder	156.45	302.59	0.6
	Responder	275.56	369.03	

Table 5: The maximum diameter of the lesion after transarterial chemoembolization in responders and nonresponders

	Response	Mean	SD	*P*
Max2	Nonresponder	5.73	3.23	0.03
	Responder	3.42	1.79	

Table 6: The maximum enhancing area of the lesion after transarterial chemoembolization in responders and nonresponders

	Response	Mean	SD	*P*
Maximum enhancement	Nonresponder	5.1	2.70	0.00
	Responder	0.97	1.46	

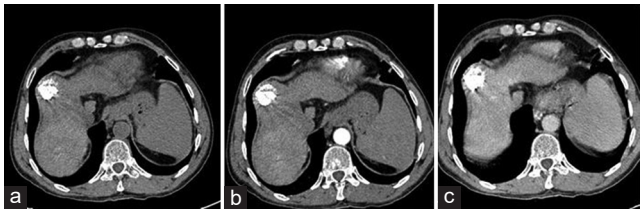

Figure 1: The images show a scan done 6 weeks after the transarterial chemoembolization in (a) precontrast, (b) arterial, (c) portovenous phases showing no residual enhancement.

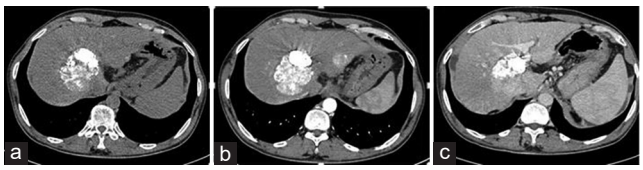

Figure 2: The images show the scan done 6 weeks after the transarterial chemoembolization in (a) precontrast, (b) arterial, and (c) portovenous phases showing no residual enhancement.

initial maximum diameter of the target lesion is increased, the maximum diameter of the lesion after TACE is also increased.

This is also found in the study by Osama *et al.* [11] as the smaller tumors were significantly more likely to respond to TACE than larger tumors.

Shen *et al.* [12] observed that increased tumor size was associated with an increased risk of death, with every centimeter increase in tumor size increasing mortality risk by 37%.

Prediction model of response in this study depends on all of these variables together with the maximum initial diameter of the target lesion, the baseline serum AFP level, serum level of total bilirubin, INR, and sex of the patient with an overall accuracy of 88%, sensitivity of 93.3%, specificity of 80%, positive predictive value (PPV) of 87.5%, and negative predictive value (NPV) of 88.88%

The study by Ha *et al.* [13] states that: prognostic factors that can help us in the prediction of survival rates are: liver function status (Child–Pugh class), tumor burden (size and number of lesions), tumor vascularity, tumor stage, extrahepatic spread of tumor, portal vein involvement, and the use of CTA.

Evaluation of the therapeutic effect of HCC after TACE and radiofrequency ablation is primarily based on the findings of imaging studies. CT is the standard imaging.

CT is commonly used as the standard imaging technique for evaluating therapeutic response in patients with HCC after TACE [14].

Conclusion

Triphasic CT is the most commonly used as the standard imaging technique for predicting and evaluating the therapeutic response in patients with HCC after TACE. It is a more accurate prognostic factor than the AFP serum level estimation.

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Conflicts of interest

There are no conflicts of interest.

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