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Palliative Treatment of Hepatocellular Carcinoma with Percutaneous Ethanol Injection Using Tumor's Feeding Artery Occlusion Under the Ultrasonic Color Doppler Guidance

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ABSTRACT

We evaluate the efficacy of PEIT in patients with HCC using duplex color Doppler US. The study included 27 HCC patients admitted to the University Hospital Centre Zagreb, between 1993 and 1997. PEIT was performed for ablation of tumor supplying vessels in HCCs of < 5 cm in diameter, and as a palliative measure for tumor feeding vessel obliteration in larger tumors. The efficacy of PEIT was evaluated with duplex color Doppler US, and controlled by dynamic CT scan (16 patients) or selective angiography of hepatic artery (11 patients). All patients had well vascularized tumors before PEIT, and after therapy 25 of them showed absent or minimal tumor vascularization. Recanalization of the tumor feeding vessel was detected with Doppler US within 9 months after therapy. Study results suggested that duplex color Doppler US should be the method of choice in the evaluation of PEIT as well as in the follow-up of HCC patients after PEIT.

Keywords: *hepatocellular carcinoma; percutaneous ethanol injection therapy; duplex color Doppler ultrasonography*

Introduction

In all parts of the world, hepatocellular carcinoma frequently coexists with cirrhosis[1]. In ethnic Chinese and black African populations, the cirrhosis is attri-

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buted mostly to chronic HBV infection, whereas in countries with frequent alcohol consumption like Croatia[2] it results mostly from alcohol abuse, as well as with chronic HCV infection, or both[3].

Hepatocellular carcinoma (HCC) ranks as the fifth most common cancer in the world. The incidence of HCC varies widely according to geographic location. The distribution of HCC also differs among ethnic groups within the same country. Marked increase has been shown in the USA over the last two decades, possibly due to expanding pool of patients with chronic hepatitis C. However, the incidence of HCC in eastern Asia and middle Africa is more than five times that of North America and Europe (Table 1). From 1981 to 1985 the peak incidence of HCC occurred in patients 80 to 84 years of age, whereas from 1991 to 1995 the peak was noted in persons 74 to 79 years of age. This shift in incidence toward younger population seen over last 20 years coincides also with the prevalence of the hepatitis C infection, according to various authors[1,2]. The cancer is associated with multiple genetic mutations in the chromosomes of affected hepatocytes. These aberrations can be detected by comparative hybridization. Cellular pathways are regulated by the p53 tumor-suppressor gene which initiates apoptosis. p53 is acivated in response to DNA damage and is frequently mutated in HCC[4,5]. In more than 90% of patients, HCC occurs in association with liver cirrhosis[6,7]. Therefore, many cirrhotic patients currently undergo screening procedures for an early detection of HCC, such as alpha-fetoprotein[8,9] and sonography[10–12]. This practice has resulted in an increased rate of detection of small and unifocal HCC lesions[6,7]. However, many patients with HCC are not eligible for surgical resection of the liver for a variety of reasons, e.g., hepatic dysfunction due to cirrhosis, associated with a high risk of postoperative hepatic failure; advanced age; or extension or multifocal nature of the tumor[6,13]. Thus, for a majority of HCC patients the best methods of treatment are those that result in minimal damage to the uninvolved hepatic tissue. That is why an increasing number of HCC patients are now treated with conservative therapies[14,15].

TABLE 1
INCIDENCE OF HEPATOCELLULAR CARCINOMA IN VARIOUS COUNTRIES AND ETHNIC GROUPS (PER 100.000/ YEAR)*

Country	Males	Females
Mozambique	112.9	30,8
Zimbabwe	64,6	25,4
South Africa		
Black	26,3	8,4
Caucasian	1,2	0,6
United States		
Chinese	19,1	3,6
Black	3,9	1,8
Japanese	3,0	0,4
Caucasian	2,9	1,1
Switzerland	10,2	1,5
Italy	8,6	3,3
Spain	7,2	5,5
France	3,7	1,0
Former Republics of Yugoslavia	2,9	1,2
China	34,4	11,6
New Zealand		
Maori	11,2	4,2
Non-Maori	2,4	1,1
Japan		
Miyigi	11,2	4,0
Nagasaki	25,8	7,9

* According to 1. Parkin, D. M., Muir, C. S., Whelan, S. L., Cancer Incidence in Five Continents, Vol. 5. IARC Publication No. 120. Lyon, International Agency for Research on Cancer, 1997. and 2. Bosch, F. X., Ribes, J, Borras, J., Semin. Liver Dis., 13 (1999) 271.

Percutaneous ethanol injection therapy (PEIT) has been recognized as an effective nonsurgical treatment for HCC[16,17], because it can achieve complete necrosis of

the tumor with minimal damage to the noncancerous hepatic parenchyma[18]. It has proved to be a safe, effective and inexpensive treatment option for patients with cirrhosis and HCC[19], especially for the majority of HCCs with a diameter of <5 cm. However, in daily routine, patients with larger tumors are frequently encountered. In this case, Doppler ultrasonography (US) is used to identify the tumor supplying vessel, followed by US-guided PEIT for tumor hypoperfusion by obliteration of its feeding vessel. Diagnostic imaging is then important to help determine whether complete necrosis of the treated tumor has been achieved, or additional treatment is needed[20,21].

In addition, hepatocellular carcinoma has a characteristic appearance on color Doppler flow imaging[22]. We hypothesized that duplex color Doppler US might be highly useful in evaluating the effects of PEIT on large HCC as well as for demonstrating tumor recurrence during the follow-up period, which we tried to prove in the present study.

Patients and methods

The study included 27 HCC patients (mean age 68, range 35–80 years) admitted between 1993 and 1997 to the Interventional Gastroenterology Unit, Division of Gastroenterology, Department of Internal Medicine, University Hospital Centre in Zagreb, Croatia. There were 23 (85%) men (mean age 65, range 35–80 years) and four (15%) women (mean age 72, range 70–74 years). The patients were classified according to Child liver classification[20], tumor size, and flow rate in the tumor supplying vessel as measured by Doppler US. Two (7%) patients were classified as Child A, three (11%) as Child B, and 22 (82%) as Child C.

B-mode US and duplex color Doppler echography were performed on an Aloka SSD 660 device with a 3.5 MHz convex probe. Tumor size was assessed from the largest tumor diameter (in centimeters) measured by US. Focal lesions were examined by real-time B-mode color Doppler yielding qualitative findings for well vascularized regions of the tumor. The qualitative signals thus obtained were quantitatively analyzed. Blood flow was calculated from three measurements of peak systolic flow rate that was digitally converted to cm/s. The angle of measurement was 45 degrees and was not corrected, as in most cases only a small section of the blood vessel was visualized.

PEIT was performed under US guidance using standard criteria and a Chiba needle for ethanol application. The shortest and optimal route from the skin to the focal lesion, i.e. to the tumor feeding blood vessel, was always used.

Therapy with percutaneous tumor sclerozation was performed with 96% sterile ethanol until a negative Doppler signal was obtained over the tumor supplying blood vessel, which was achieved in 24 patients. In three patients, the procedure had to be discontinued for technical reasons at a point of substantial blood flow reduction. The mean amount of ethanol applied into the liver tumor was 18 (range 6–40) ml. A mean of 3 (range 1–8) sessions *per* patient with a mean of 5 (range 3–10) ml of ethanol *per* procedure were performed.

Study patients were randomly (i.e. according to availability of the method) allocated to control examination by dynamic computed tomography (CT) scan and selective angiography of hepatic artery before and after PEIT. Dynamic CT scan was performed on a Somatom DRH, a third-generation CT device. Stratified images were obtained at 8 mm within 20–30 seconds from administration of triiodide water-soluble contrast medium as a 60–100 ml bolus.

Angiography was performed on a Digitron 2 device for digital subtraction angiography (DSA). Diagnostic evaluation was done according to the following algorithm: 1) abdominal angiography; 2) selective imaging of celiac artery along with visualization of the splenoportal venous axis and intrahepatic portal arborization; 3) selective or supraselective imaging of the common and left or right hepatic artery, depending on the tumorous lesion localization; and 4) control angiography in 14 days from the last PEIT session.

Tumor perfusion was divided into the arterial and venous type, each of them being subdivided into the peripheral (peritumoral) and intratumoral type. The criteria of good, moderate and poor tumor perfusion were established by consensus of three radiologists who either observed or performed all the radiologic studies described. The categories of good, moderate and poor tumor perfusion referred to >50%, <50% and <10% intratumoral contrast medium uptake, respectively[24].

Biochemical parameters (alpha-fetoprotein, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma glutamyltransferase) were determined by standard methods at the Clinical Institute of Laboratory Diagnosis, Laboratory of Biochemistry, University Hospital Centre Zagreb.

Statistical analysis

Distribution of the numerical parameter measurements is presented as median, and 10^{th} and 90^{th} percentile (10%–90% of measurements). Nonparametric Mann-Whitney test was used for between-group comparison of measurements, and nonparametric Wilcoxon pair test for comparison between pre- and posttherapeutic measurements. Correlation between the parameters was determined by calculating Pearson's coefficient of correlation, and correlation between the parameters and dynamics of tumor recanalization by multiple regression analysis. Results of the regression analysis are presented by regression coefficients (b) for the parameters, their standard error (SE (b)), and coefficient of multiple correlation (R^2). Distribution of nominal parameters is shown in contingency tables. Distribution of binarized parameters was compared by use of Fisher's exact test. The level of significance was set at $p<0.05$.

Results

Tumor size median in study patients as measured by classic B-mode US was 9 cm, with 10^{th} and 90^{th} percentile of 2.8 and 18 cm, respectively. There was no statistically significant difference in tumor size between Child A/B and Child C groups (p=0.617). Median flow rate in tumor supplying blood vessel as measured by color Doppler was 9.98 cm/s, with 10^{th} and 90^{th} percentile of 3.76 and 44.24 cm/s, respectively. There was no statistically significant difference in flow rate between Child A/B and Child C groups either (p=0.950). No correlation was found between flow rate through the tumor supplying vessel and tumor size (correlation coefficient $r = -0.021$; $p>0.05$). There was no statistically significant difference between Child A/B and Child C groups in the volume of ethanol applied (p=0.151), number of sessions (p=0.318), or volume of ethanol used *per* session (p=0.803). There was no statistically significant correlation of tumor size and flow rate through tumor supplying vessel with the volume of ethanol applied and number of sessions performed (data not shown).

The efficacy of PEIT was assessed by dynamic CT scan or angiography. The patients were divided into groups according to the method used on control examination (Table 2). Dynamic CT scan and angiography were employed for therapeutic success evaluation in 16 (59%) and 11 (41%) patients, respectively. The 16 pa-

TABLE 2.
CLINICAL, THERAPEUTIC AND BIOCHEMICAL PARAMETERS ACCORDING TO METHOD OF THERAPEUTIC EFFICACY EVALUATION (CT SCAN OR ANGIOGRAPHY)*

Parameter	CT scan	Angiography	p
Number of patients	16 (59%)	11 (41%)	–
Child A/B–C	2/14	3/8	0.316
Age (years)	71 (52–75)	65 (42–75)	0.236
Number of sessions	3 (2–5)	4 (3–4)	0.132
Volume of ethanol (ml)	15.5 (6–25)	25 (13–25)	0.062
Pretherapeutic values:			
Tumor size (cm)	9.5 (3–15)	7.1 (4–18)	0.921
Doppler signal (cm/s)	9.01 (4.02–24.23)	12.02 (5.50–21.58)	0.374
Alpha-fetoprotein (ng/ml)	76.22 (1.98–1314.4)	45 (1.9–1050)	0.632
Apartate aminotransferase (U/L)	34 (11–60)	34 (9–60)	0.694
Alanine aminotransferase (U/L)	25 (11–45)	25 (9.5–77)	0.675
Alkaline phosphatase (U/L)	47.5 (34–222)	70 (34–180)	0.632
Gamma glutamyltransferase (U/L)	62 (19–280)	79 (34–445)	0.459

* Data show number of patients according to groups or median and 10–90th percentile of the measurements.

tients submitted to control examination by dynamic CT scan included 14 Child C and 2 Child A/B patients, whereas control angiography was used in 8 Child C and 3 Child A/B patients. In the group of patients with posttherapeutic CT scan control, the mean number of sessions was 3 (10th and 90th percentile, 2 and 5), with the administration of a mean of 15.5 ml ethanol *per* patient (10th and 90th percentile, 6 and 25 ml). The group of patients with angiography control had a mean of 4 sessions (10th and 90th percentile, 3 and 4), with the application of a mean of 25 ml ethanol *per* patient (10th and 90th percentile, 13 and 25 ml); there was no statistically significant difference between the two groups (p=0.132 and p=0.062, respectively). Neither did the mean pretherapeutic tumor size differ between the two patient groups; it was 9.5 (10th and 90th percentile, 13 and 15) cm and 7.1 (10th and 90th percentile, 4 and 18) cm in the groups controlled by CT scan and angiography, respectively. The mean flow rate through the tumor supplying vessel was 9.01 (10th and 90th percentile, 4.02–24.23) cm/s in the group controlled by CT scan, and 12.02 (10th and 90th percentile, 5.50–21.58) cm/s in the group controlled by

TABLE 3.
PROPORTION AND DISTRIBUTION OF PATIENTS ACCORDING TO TYPE OF TUMOR PERFUSION

Type of perfusion	Type of blood vessel		Total, n (%)
	Vein, n (%)	Artery, n (%)	
Intratumoral	4 (15)	0 (0)	4 (15)
Peripheral	10 (37)	13 (48)	23 (85)
Total	14 (52)	13 (48)	27 (100)

Fisher's exact test = 0.057

angiography; the difference did not reach statistical significance (p=0.374). Accordingly, there was no statistically significant difference in any of the relevant parameters between the two patient groups (Table 2).

Patient distribution according to type of tumor perfusion is illustrated in Table 3.

All the four (15%) patients with intratumoral blood flow had a venous type of tumor perfusion. Peripheral type of tumor perfusion was observed in 23 patients, i.e. venous in 10 (37%) and arterial in 13 (48%) patients. There was no statistically significant difference according to type of tumor perfusion (p=0.057). Results obtained by the two methods of tumor perfusion assessment after PEIT are shown in Figure 1.

Before therapeutic intervention, all 27 patients had well perfused tumors according to the dynamic CT scan or angiography standard criteria. After PEIT, good tumor perfusion considered as a poor therapeutic response persisted in two patients only. In all the remaining 25 patients, moderate to poor tumor perfusion considered as a good therapeutic response was recorded after PEIT. Moderate tumor perfusion was observed in 10 (37%), and poor tumor perfusion considered as an excellent therapeutic response in 15 (56%) patients. The test of proportions yielded a statistically significant proportion change.

Relationship between tumor size and flow rate through tumor feeding vessel before and after PEIT, and dependence of PEIT efficacy on tumor perfusion and method of control evaluation are presented in Table 4.

The mean tumor size reduction of 0.4 cm, achieved in all tumors under study, was statistically significant (p<0.001) (Table 4). Tumor size reduction did not depend on the type of tumor perfusion (p=0.937), and there was no statistically significant difference according to the method of therapeutic success evaluation, i.e. dynamic CT scan or angiography. The mean overall difference in intratumoral flow rate measured before and after PEIT was 9.8 cm/s, with a statistically significant posttherapeutic flow rate decrease (p<0.001). The intratumoral flow rate measured by Doppler showed a comparable reduction irrespective of the CT- or angiography-determined perfusion category, method of perfusion assessment, and type of perfusion (intratumoral or peripheral/peritumoral). In contrast to these parameters, arterial flow rate was statistically more significantly reduced than venous flow rate (p<0.05) (Table 4).

Upon therapy completion, recanalization of the obliterated blood vessel or neovascularization occurred. The median time to the recurrence of Doppler signal over the site of ethanol application was 6 months after PEIT, and 9 months (10th

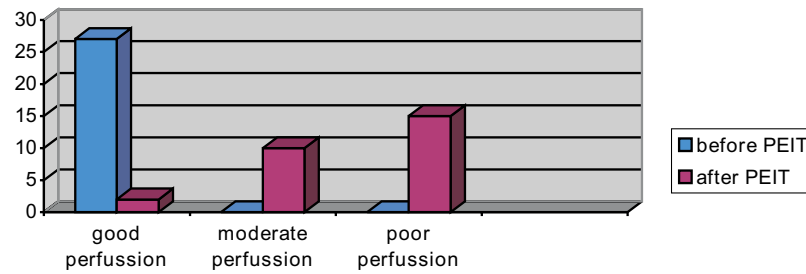

Fig 1. Assessment of tumor perfusion (CT scan/angiography) before and after PEIT.

and 90th percentile, 0 and 9 months) in the study population as a whole.

Results of the analysis of the factors that may play a role in the process of vascularization are presented in Table 5. A statistically significant correlation was found between flow rate through tumor supplying vessel before PEIT and dynamics of vascular recanalization (r = –0.386; p=0.046). Parameter analysis showed the supplying vessel recanalization to occur earlier in patients with higher initial flow

TABLE 4.
TUMOR SIZE AND FLOW RATE THROUGH TUMOR SUPPLYING VESSEL BEFORE AND AFTER PEIT, AND DEPENDENCE OF PEIT EFFICACY ON TUMOR PERFUSION AND METHOD OF CONTROL

	Tumor size (cm)			Flow rate (cm/s)		
	Median	10–90%	p	Median	10–90%	p
Before PEIT	9.1	3–16		9.98	4.23–24.23	
After PEIT	8.7	2.7–15		0	0–8,32	
Difference	0.4	0–1.1	p<0.001	9.80	4.23–21.58	p<0.001
Posttherapeutic difference according to tumor perfusion*						
Moderate perfusion (n=10)	0.25	0–1.7		11.0	3.89–24.32	
Poor perfusion (n=15)	0.1	0–1.1	p=0.937	8.32	5.23–21.34	p=0.437
Posttherapeutic difference according to method of control						
CT scan (n=16)	0	0–2.4		8.32	4.02–20.34	
Angiography (n=11)	0.3	0–1.0	p=0.805	10.11	5.51–21.58	p=0.278
Artery Doppler (n=13)	–	–	–	15.72	8.32–24.23	
Vein Doppler (n=14)	–	–	–	7.79	4.02–10.82	p=0.002
Intratumoral Doppler (n=4)	–	–	–	8.27	7.38–12.02	
Peripheral Doppler (n=23)	–	–	–	9.86	4.23–21.58	p=0.633

*Two patients with unchanged well perfused tumor after PEIT were not included in this analysis, as they could not be compared to any other category.

TABLE 5.
CORRELATION OF TUMOR RECANALIZATION DYNAMICS (MEASURED IN MONTHS FROM THE BEGINNING OF TREATMENT) WITH TUMOR PARAMETERS AND THERAPY USED

	Correlation		Multiple regression analysis			
	r	p	β	SE (β)	p	RHR (95% CIL)
Tumor before therapy (cm)	–0.312	0.102	–0.167	0.087	0.068	0.85 (0.71–1.01)
Difference (cm)	0.074	0.612	–	–	0.450	–
Flow rate (cm/s)	–0.386	0.046	–0.288	0.077	0.001	0.75 (0.64–0.87)
Difference (cm/s)	–0.049	0.807	0.303	0.108	0.010	1.35 (1.10–1.67)
Ethanol volume (ml)	–0.157	0.434	–	–	0.575	–
No. of sessions	0.109	0.588	–	–	0.453	–
Model	–	–	–	–	0.003	–

rate through tumor supplying vessels. The analysis also indicated the pretherapeutic tumor size and flow rate through tumor supplying blood vessel, and pre- to posttherapeutic flow rate difference to be highly useful in the monitoring of recanalization dynamics (Table 5), as they proved to be statistically significant and mutually independent ($p<0.05$ for all parameters except for pretherapeutic size, where $p<0.07$). During the study, the following routine biochemistry parameters were determined before and immediately after PEIT: alkaline phosphatase (AP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma glutamyltransferase (GGT). The values of these parameters showed no statistically significant changes during the procedure ($p>0.05$ for all parameters).

Discussion

In clinical routine, a great number of patients with advanced HCC of >5 cm in diameter and poor hepatic functional reserve, who require optimal and most rational mode of treatment are encountered. Besides the large primary tumor, these patients often have satellite lesions, massive blood vessel infiltration, and poor functional parameters accompanying Child C stage liver cirrhosis. Because of their condition, these patients are noneligible for liver transplantation or resection, as well as for transarterial embolization and chemoembolization due to frequent portal vein thrombosis. Thereapeutic choice is thus limited to systemic chemotherapy, its beneficial effects being quite unconvincing[25], and PEIT[26]. PEIT has been well established in the management of small solitary HCCs, whereas in many centers it is used with much caution for large HCCs. The basic concept of PEIT is to achieve tumor mass reduction by tumor coagulation necrosis induced by intratumoral alcohol instillation. In large tumors, this may be associated with a high risk of complications such as abscesse or rupture into the abdominal cavity with bleeding[27,28].

PEIT is performed under standard US guidance, because the real-time control allows for rapid therapeutic procedure, precise Chiba needle intralesional direction, and continuous monitoring throughout the procedure. The latter is of paramount importance, since it allows for appropriate control of the injected ethanol distribution and prompt identification of possible ethanol escape into a large blood vessel or peritoneal cavity, which may lead to complications such as biliary duct lesions or undesired vascular thrombosis in the healthy tissue adjacent to the tumor[29,30].

Standard US is limited by the fact that the method cannot be used to follow up the PEIT therapeutic success. The criteria of standard US cannot differentiate between complete necrosis and possible persistence of viable tumor cells in the treated area. Therefore, dynamic CT scan, magnetic resonance (MR) or angiography should be used on pre-, peri- and posttherapeutic control, which implies both ethical and financial problems. Without appropriate control, however, some untreated areals may quite easily be left in the tumor, or an unnecessary high amount of ethanol may be instilled into the already completely necrotic areal, thus exposing the patient to the risk of life-threatening complications.

In the present study, the role of duplex color Doppler US as a valuable adjuvant method in the monitoring of PEIT for malignant liver carcinoma was inaugurated. In our approach, color Doppler US is used to identify the tumor supplying vessel, to repeatedly inject a small amount of ethanol paravasally to obliterate the vessel and to cause its thrombosis. Such an approach imitates transarterial embolization with consequential ischemia of the

tumor, and gradual tumor mass reduction without abrupt necrosis and large tumor mass colliquation.

In 24 of 27 patients, ablation of the tumor supplying vessel was achieved after a mean of three therapeutic PEIT sessions with a total of 5 ml ethanol *per* session. In three patients, flow reduction was achieved, however, the procedure had to be discontinued for technical reasons.

Before PEIT, control examination by dynamic CT scan was performed in 16 (59%), and by angiography in 11 (41%) patients. According to standard criteria of tumor perfusion, all tumors belonged to the category of well perfused tumors, as also indicated by color Doppler US[23,31]. After PEIT, poor tumor perfusion was recorded in 15 (56%) and moderate perfusion in 10 (37%) patients, indicating a good therapeutic response in the group of patients with a mean tumor size of 9 cm, most of them classified as Child C with poor hepatic functional reserve. In all these patients, posttherapeutic Doppler signal was negative. In three patients, PEIT procedure had to be discontinued before complete obliteration of the supplying vessel had been achieved, because of the underlying liver disease exacerbation. Even then, a positive Doppler signal was recorded over the respective areal. Persistence of good tumor perfusion was confirmed by comparative methods, pointing to the high reliability of the nonaggressive US method in evaluation of liver tumor perfusion during therapeutic procedures. There was no statistically significant difference in the amount of ethanol and number of PEIT sessions between patient groups classified either according to Child or tumor size, also pointing to high precision of the therapeutic agent dosage under color Doppler US guidance.

An interesting distribution of the tumor perfusion types as recorded by color Doppler US was observed. So, the venous and arterial type of tumor perfusion predominated in 14 (52%) and 13 (48%) patients, respectively. On color Doppler signal analysis, the intratumoral and peripheral types of liver tumor arterial perfusion are usually considered[32]. It is of utmost importance, as the patients with a predominant venous tumor perfusion who are not eligible for interventional procedures such as transarterial embolization can thus be identified. In our patients, peripheral tumor perfusion, either arterial (48%) or venous (37%), prevailed, which is consistent with literature data[33].

The overall mean difference in flow rate through the tumor supplying vessel of 9.8 cm/s was recorded in study patients, indicating an excellent therapeutic response to PEIT and statistically expressed as a significant difference. It should be emphasized that a significantly greater reduction was recorded for arterial compared with venous flow rate ($p=0.02$). This statistical significance resulted from the fact that arterial flow rate is by definition almost twofold venous flow rate, and treatment was performed until the blood flow, arterial or venous, was stopped, i.e. until Doppler signal over the respective vessel disappeared.

It should be emphasized, however, that such a therapeutic approach is of palliative nature, as most patients included in the study had HCCs sized >5 cm and Child C liver cirrhosis. In these patients, the natural course of the underlying disease leads to the feeding vessel recanalization or neovascularization at another site. Color Doppler has a very important role in timely detection of the new signal over the tumor, thus enabling the procedure to be repeated as needed. In all our patients, Doppler signal over the tumor was recorded again within 9 months, or at a mean of 6 months. Analysis of the factors relevant for the time needed for Doppler signal recurrence over the tumor identified flow rate through tumor supplying vessel, difference between

pre- and posttherapeutic flow rate, and tumor size as the variables directly determining the dynamics of repeat PEIT.

Our results showed the classic Doppler US to be the method of choice in the follow-up of the effect of PEIT on HCC. Sophisticated examinations such as spiral CT scan or dynamic MR should be used in strictly selected patient population in whom tumor viability cannot be assessed by Doppler US[20,24,26,34–37]. Color Doppler US should be done just before PEIT. Positive intratumoral Doppler signals persisting after intratumoral ethanol instillation confirm the presence of viable tumor cells, indicating an additional ethanol application. Doppler US is very useful in this step of the procedure, allowing for target intratumoral or peritumoral application of ethanol at the site of blood vessel thus detected. If no intratumoral circulation is recorded by classic Doppler US, the examination should be repeated with the use of a contrast signal amplifier, whereby additional injection therapy can be administered if necessary. The next step to rule out false-negative results includes the use of conventional radiologic methods or recent methods of spiral CT scan and dynamic MR[38].

The presented protocol of the follow-up of the therapeutic success achieved by PEIT has a number of advantages. Firstly, allowing for multiple target ethanol injection into the viable portions of HCC, repeat ethanol injections into the HCC portions where the tumor has already been destroyed are avoided, thus reducing the length of treatment and number of interventions. Secondly, such a follow-up allows for controlled ethanol administration and prevents ethanol overdosage, which may be potentially hazardous in case of its systemic distribution[31]. Thirdly, a high proportion of patients are identified who do not need expensive and invasive follow-up methods such as angiography, CT scan and MR[39,40].

In conclusion, assessment of the value of percutaneous ethanol injection therapy for malignant tumors of the liver by duplex color Doppler US was found to be a highly reliable method. At the same time, the method is open for the wide and rapid implementation of the latest digital techniques. Development of devices characterized by improved sensitivity in the detection of slow flow rates through small intratumoral vessels, presenting a major limitation of the classic Doppler US, is expected in the future[26].

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PALIJATIVNO LIJEČENJE HEPATOCELULARNOG KARCINOMA POMOĆU PERKUTANE INJEKCIJE ETANOLA U HRANIDBENU ARTERIJU TUMORA POD VODSTVOM ULTRAZVUKA

S A Ž E T A K

Proučavali smo efikasnost perkutane injekcije etanola (PEIT) pod vodstvom ultrazvuka kod pacijanata s hepatocelularnim karcinomom. (HCC). Studija je provedena na 27 pacijenata s HCC-om primljenih u Klinički bolnički centar Zagreb, od 1993. do 1997. godine. PEIT je provođen za ablaciju hranidbene arterije kod HCC promjera manjeg od 5 cm i kao palijativna metoda kod većih tumora. Efikasnost PEIT-a mjerena je s Duplex color Dopplerom, te je kontrolirana dinamičkim CT-om (16 pacijanata) ili selektivnom angiografijom hepatičke arterije (11 pacijenata). Svi pacijenti imali su dobro vaskularizirani tumor prije PEIT-a, a nakon terapije 25 pacijanata pokazivalo je odsutnost ili minimalnu vaskularizaciju tumora. Rekanalizacija hranidbene arterije ustanovljena je pomoću UZV-a 9 mjeseci nakon terapije. Ovaj rad pokazuje da je Doppler UZV metoda izbora za evaluaciju PEIT-a, kao i za praćenje pacijenata s HCC nakon PEIT-a.