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## FEATURE ANALYSIS OF COMPUTED TOMOGRAPHIC SIGNS OF HEPATOCELLULAR CARCINOMA IN MULTIPHASE STUDIES

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#### ABSTRACT

Hepatocellular carcinoma is one of the actual problems in the structure of oncological pathology in the world and in Kazakhstan. In the diagnosis of hepatocellular carcinoma, the use of multiphase computed tomography is generally accepted. The article describes the analysis of the results of multiphase computer tomography with the correlation of cytological and histological studies in the diagnosis of hepatocellular carcinoma.

Present study aimed to conduct a retrospective analysis of the results of multiphase computer tomography in patients with hepatocellular carcinoma

Analyzed the archival data of 50 patients with malignant liver tumors, who received specialized treatment at the A.N. Syzganov National scientific center of surgery and Kazakh Scientific Research Institute of Oncology and Radiology in the period 2014 - 2017. All patients underwent multiphase computed tomography. The examination was carried out in 4 phases: native, arterial, port-venous and delayed. The scan was performed on the 30th, 60th and 120 second (respectively) after the administration of contrast agent.

The nodular form was detected in 76% of cases. If in 60% of cases the tumor was localized in the right lobe of the liver, and in 18% of cases - in the left, the lesion of both lobes was observed in 22% of cases. The sizes of the tumors were from 1 cm to 21.1 cm, and the average size of all nodes was 10.6 cm. The outlines of the tumors were uneven, but clearly defined in 92% of cases. In 94% of cases, the density of the formations was hypodense, the structure was heterogeneous with areas of increased and decreased density. The presence of central necrosis in the form of an "asterisk" was visualized in 8% of cases. The non-intensive inhomogeneous hyperenhancement in the arterial phase, with complete "washout" into the porto-venous phase, as well as in the porto-venous and delayed phases, was observed in 6% and 12% cases, respectively. In 80% of cases, hyperenhancement was observed in the arterial and venous phases. At the same time, complete erosion in the delayed phase was observed in 60% of cases, and incomplete leaching - 20%. In cytological studies, hepatocellular carcinoma was confirmed in 69.7% of cases. In 93.1% of cases, hepatocellular carcinoma was confirmed in histological studies.

The nodes of hepatocellular carcinoma in most cases were characterized by clear, uneven contours, hypodense density, heterogeneous structure due to foci of necrosis and cystic component. When the tumor was bolus contrasted, hyperenhancement was in the arterial and port-venous phases, with "washout" in the delayed phase in most cases. According to the received data it can be said that multiphase computed tomography has high information value in the diagnosis of hepatocellular carcinoma.

**KEYWORDS:** liver, hepatocellular carcinoma, multiphase computed tomography

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## Introduction

Hepatocellular carcinoma (HCC) - a malignant liver tumor derived from hepatocytes is the most common type of primary liver cancer (95%) [Bray F, Jemal A, Khazanov A, 2011].

Hepatocellular carcinoma occupies the 5<sup>th</sup> place in the structure of malignant neoplasms and is the 2<sup>nd</sup> most frequent cause of cancer death worldwide (about 800 thousand patients died in 2012) [GLO-BOCAN 2012; Lamarca A et al., 2016].

Although the incidence rate of most cancers declines, the incidence of hepatocellular carcinoma increases, and more than 600,000 new cases of HCC are reported annually in the world [Siegel R et al., 2013, Omata M et al., 2017].

Hepatocellular carcinoma represents a serious medical and social problem in many countries of the world, including in Kazakhstan. In recent years (2013 - 2017) in Kazakhstan, there has been an increase in the incidence of HCC to 5.9 cases per 100,000 populations, and the death rate remains high (about 1,000 people annually). In 2019, 38.6% of the observed patients with HCC died at the end of the year. Five-year survival was 22.9% [Kaydarova D, 2011-2019].

Hepatocellular carcinoma is characterized by aggressive course, in most cases with unfavorable prognosis, the five-year survival rate does not exceed 18%. Postoperative relapse is about 50% of cases [Trefylov A et al., 2014, Kulik LM et al., 2015,].

In the development of hepatocellular carcinoma, persistent infection of the hepatitis B virus and hepatitis C virus, leading to cirrhosis of the liver, with subsequent transformation into cancer,

is generally recognized. And also, aflatoxin B1 and chronic alcohol abuse are risk factors for the development of HCC [Bosetti C et al., 2014].

The development of HCC in the cirrhotic liver is described as a multistage progressive process: a low-differentiated dysplastic node, a highly differentiated dysplastic node, a dysplastic node with a mi-

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

croscopic manifestation of HCC, small foci of HCC, carcinoma. The average time for doubling the mass of the HCC is 93.5 days, which reflects the slow growth of the tumor, and therefore, on average 3 years pass from the onset of HCC to the time of its first manifestation and diagnosis [Kubota K, 2003; Jemal A, Bray F, 2011].

The wide introduction of modern highly informative radiotherapy methods (ultrasound, computed tomography (CT), magnetic resonance imaging) [Gaddikeri S, et al 2014] into clinical practice, as well as their improvement, helped to improve the detection of liver formations, becoming the main methods of non-invasive diagnosis and, accordingly, determination type of subsequent treatment and prognosis of HCC [Albiin N, 2012., Ternovoy S et al., 2015].

According to the recommendations of American and European associations for the study of liver pathology, in the last decade in the diagnosis of liver formations, a multiphase study is widely used in computed tomography. The main goal of CT with the use of contrast agent is to maximize the difference in density between the normal liver parenchyma and neoplasms. The active use of bolus contrast in the study of the liver is very informative and allows not only to make a preliminary diagnosis, but also to conduct differential diagnosis. According to the guidelines, with typical radiation characteristics of the HCC, trephine-biopsy verification is not required. Due to the presence of a developed own pathological vascular network in the HCC structure, intravenous (bolus) contrasting with nonionic iodine-containing contrast preparations is used for differential diagnostics. HCC can be presented depending on the blood supply of both hypo and hypervascular tumor. The hypovascular variant is usually found in the early stages of tumor development and, with contrasting, is insignificant or does not increase at all in the arterial phase. The hypervascular variant has a rapid contrasting in the arterial phase and rapid "washout" in the porto-venous phase or the accumulation of contrast agent by the pseudocapsule. The arterial phase is used to detect anomalies of arterial perfusion of the liver. Thus, the normal hepatic parenchyma surrounding the tumor may be hyperdense in the late arterial phase, which is formed due to the effect of the "draw-well", due to

the fact that the neoplasm promotes a greater influx of arterial blood into the segment or the proportion of the liver to feed both itself and normal hepatic parenchyma. A typical type of arterial blood flow in a tumor is described in the literature as "threads and strips" [Bruix J et al., 2011; Llovet J et al., 2012].

HCC in the background of cirrhosis of the liver is usually surrounded by a capsule, represented by fibrous tissue and a layer of tightened liver tissue [Yu S, 2004]. In CT, the capsule (or pseudocapsule) is defined as a thin hyperdense (hyperintense) rim around the node into the venous or delayed phase [American College of Radiology, 2014]. In the liver, affected by cirrhosis, the appearance of a capsule around the tumor is considered a sign of the progression of the disease [Lim J et al., 2006; Ishigami K et al., 2009; Khan A et al., 2010; Rimola J et al., 2012].

Due to the late diagnosis of hepatocellular carcinoma, the presence of changes at the level of the micro-and macroorganism, not all patients can undergo surgery, despite the development of surgical treatment of HCC in recent years [Ahn SM et al., 2014].

In connection with the progressive slow growth, asymptomatic course and late clinical manifestation, aggressive course and unfavorable prognosis of HCC, the value of early and refining diagnostics increases dramatically.

The study aimed to Conduct a retrospective analysis of the features of computed tomographic signs of hepatocellular carcinoma in multiphase studies

#### MATERIALS AND METHODS

Analyzed of archival data (medical history, outpatient maps, CT studies, cytological and histological research) of 50 patients with malignant liver tumors, whose received specialized treatment (transarterial chemoembolization, radical surgery) in the A.N. Syzganov National scientific center of surgery and Kazakh Scientific Research Institute of Oncology and Radiology in period 2014 - 2017.

The total number of men was 33 (66%) and women 17 (34%) patients, aged 36 to 79 years, with the average age of men being  $61.3 \pm 0.2$  years, women -  $59.7 \pm 0.3$  years. All patients underwent multiphase CT. Multiphase examination of the abdominal cavity was performed on 64-

slice computer tomographs "Light Speed CT" (GE) and "Aquilion 64" (Toshiba) with the following parameters: 130 mA, 120 kV, collimation 0.75, pitch 0.9, the thickness of the cut is 1.0 mm. CT examination was carried out in 4 phases: native, arterial, port-venous and delayed. After the native scan, patients were injected intravenously (bolus) with a non-ionic contrast agent at a rate of 1 ml per 1 kg of body weight with an injector at a rate of 3.5 ml/s. The scan was performed on the 30th, 60th and 120 second (respectively) after the administration of CA.

To verify the diagnosis of malignant liver formation, 66% (33) of patients underwent a fine needle aspiration biopsy under the supervision of ultrasound. Trepan - a biopsy under the supervision of ultrasound was performed by 8% (4) patients. Patients underwent specialized treatment (transarterial chemoembolization from 3 to 5 courses). The next stage of treatment was surgical intervention. Extended combined hemihepatectomy was performed in 42% (21) patients, and partial liver resection (segmentectomy) 14% (7) in patients. Postoperative macro preparations were studied by a histological method.

#### RESULTS

In 84% (42) cases, the liver in size was enlarged, with uneven finely contoured contours in 10% (5) patients with cirrhosis. Of all liver formations, the nodular form was detected in 76% (38) cases, and the multinodular form in 24% (12). If in 60% of cases the tumor was localized in the right lobe of the liver, and in 18% of cases - in the left, the lesion of both lobes was observed in 22% of cases. At the same time, the largest number of nodes were located in the 4, 6 and 7 segments of the liver (Figure).

The sizes of the tumors were from 1 cm to 21.1 cm, and the average size of all nodes was 10.6 cm. The contours of the formations were uneven, but distinct in 92% (46) cases. In 94% (47) cases, the formation density was hypodense, the structure was heterogeneous with areas of increased and decreased density. The presence of central necrosis in the form of an "asterisk" was visualized in 8% (4) cases. In 4% (2) cases, the nodes were represented as a cystic-solid structure. The non-intensive inhomogeneous hyperenhancement in arterial phase,



**FIGURE.** Case of patient A.57 y.o. man with HCC on the multiphase CT **Notes:** (A) Native- In S7 segment of the right lobe of the liver, is determined the density decrease focus. 2.1x2.0x1.8 cm. with smooth, well-defined contours, a homogeneous structure. (B)- arterial and (C) - venous phase- hyperenhancement of contrast agent with a focus. (D) - delay phase- "washout" of contrast agent.

with complete "washout" into the porto-venous phase, as well as in the porto-venous and delayed phases, was observed in 6% (3) and 12% (6) cases, respectively. In 80% (40) cases, the hyperenhancement was observed in the arterial and venous phases. At the same time, complete erosion in the delayed phase was observed in 60% (30) cases, and incomplete leaching - 20% (10) (Table).

*TABLE.* Computed-tomographic semiotics of HCC

Characteristics of formation	N =50(100%)	
	Absolute	Percent
Uneven, clear contours	46	92
Hypodensic, with a heterogeneous structure	47	94
Hyperenhancement in arterial and venous phase	40	80
"Washout" in delayed phase	30	60

In 4% (2) cases, a paradoxical accumulation of contrast agent - the effect of incomplete leaching into the delayed phase with subsequent progressive accumulation was observed. In several cases, the accumulation of contrast agent by the pseudocapsule and along the periphery of formation (16%, 8), solid component and capsule of the cystic component (4%; 2), in the form of nodes and zones (4%; 2). In 14% (7) cases, the patient's own pathological vascular network of education in the arterial phase was visualized. Depending on the localization of the formation, involvement of hepatic vessels (central vein (14%; 7), right (10%; 5) and left (8%, 4) hepatic vessels) was observed in the process. In 24% (12) cases, intra-organ metastases in the liver were detected

In 92% (46) cases hepatocellular carcinoma was diagnosed with multiphase CT. Of the 33 cytological studies performed, hepatocellular carci-

noma was confirmed in 69.7% (23) cases. In 93.1% (27) of cases, HCC was confirmed from 29 histological studies.

In the detection of hepatocellular carcinoma, the correlation of the multiphase CT and the cytological study was 69.7%, multiphase CT and histological examination - 93.1%.

When analyzing the results of the study, it was found that in most cases, the dimensions of the liver were enlarged. The nodular form of hepatocellular carcinoma prevailed in most cases. The largest number of tumors were located in the right lobe of the liver, namely in the 6th and 7th segments. In general, the dimensions of the nodes were more than 2 cm. The nodes of hepatocellular carcinoma in most cases were characterized by clear, uneven contours, hypodense density, heterogeneous structure due to foci of necrosis and cystic component. In bolus contrasted, nodes of HCC characterized hyperenhancement in the arterial and port-venous phases, with "washout" in the delayed phase in most cases. In several cases, there was a pronounced intrinsic vasculature of the tumor. Of all the vessels of the liver, the greatest damage was seen in the central vein. Bolus contrasting of the liver, in several cases, allowed differentiation between the main node of hepatocellular carcinoma and intra-organic secondary metastases nodes, according to the nature of the accumulation of contrast agent.

#### **CONCLUSION**

Thus, with the help of multi-phase computed tomography, it is possible to obtain morphological characteristics of the node of hepatocellular carcinoma, such as dimensions, contours, density, structure, the presence of an intrinsic vasculature of the tumor, involvement in the process of large vessels, etc. The nature of accumulation of contrast medium in bolus contrast is of great importance in differential diagnosis between hepatocellular carcinoma and other liver tumors. According to the received data it can be said that multiphase computed tomography has high information value in the diagnosis of hepatocellular carcinoma. In some cases, the accumulation of contrast material by formation may not be typical of hepatocellular carcinoma. As a consequence, further study of the characteristics of liver tumors is necessary for multiphase computed tomography.

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