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Adjustment of lipiodol dose according to tumor blood supply during transcatheter arterial chemoembolization for large hepatocellular carcinoma by multidetector helical CT

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Abstract

AIM: To work out an individualized lipiodol dose in transcatheter arterial chemoembolization (TACE) for large hepatocellular carcinoma (HCC) according to its blood supply evaluated by CT.

METHODS: One hundred patients with large HCC (more than 8 cm in diameter) were studied by multidetector helical CT. Patterns of blood supply of HCC were divided into sufficient blood supply, poor blood supply, mixed blood supply and arteriovenous (A-V) shunt. The dose of ultra-fluid lipiodol was determined by diameter and blood supply type of HCC. Patients were divided into two groups (50 cases each): lipiodol perfusion group and iodized oil perfusion group according to tumor diameter and the blood supply type of tumor.

RESULTS: The confirmation and effective rates were 82%, 84% in the first group and 36%, 46% in the second group ($P < 0.01$).

CONCLUSION: A relatively individualized lipiodol dose may be determined according to the blood supply pattern and the tumor diameter by CT imaging.

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INTRODUCTION

A critical issue in treating large hepatocellular carcinoma (HCC) is determining the optimum lipiodol and antitumor drug dose before transcatheter arterial chemoembolization (TACE). Over-dose will damage hepatic function and inadequate dose will lead to poor treatment effect. Tumor blood supply is the crucial factor for determining lipiodol dose. Lipiodol dose was worked out according to the HCC blood supply check by CT scan, then the actual perfusion dose and curative effect were compared in order to assess the therapeutic efficacy.

MATERIALS AND METHODS

Patients

One hundred patients (91 male and 9 female, age range 20-72 years,

mean age 48 years) with large HCC (diameter larger than 8 cm) were prepared for TACE. All HCC cases were confirmed by clinic, laboratory and image examinations.

Methods

CT scan CT scan patterns were as follows: multi-slice helical CT (Lightspeed QX/I, GE Corporation); 5 mm-thick-section; Pitch 3:1; non-enhanced scanning performed along with arterial phase, portal-venous phase and delayed-phase at 20-25 s, 45-50 s and 2-3 min, respectively; at 120 kV; 270-300 mA; high pressure injector as well as nonionic-contrast media injected at a rate of 3 mL/s (standard 1.2-1.5 mL/kg). The images were obtained by picture archiving and communication system (PACS) and relevant diagnostic reports writing workstation (DELL 21 in monitor, resolving power 1 920 × 1 920). Radiologists analyzed the CT images by using analysis software on Radworks 5.1 to determine the tumor contrast features and confirm the blood supply patterns and further work out the lipiodol dose.

DSA examination DSA (Advantx TC, GE Corporation) was selected and the hepatic artery, coeliac artery and mesenteric artery were detected; the contrast media was injected to reveal the tumor blood supply; the correlation between CT and DSA images was analyzed. Catheter was put into nourishing artery with super-selection skill and anti-carcinoma drug and iodine oil were perfused.

Perfusion dose All cases were randomly divided into two groups. In testing group, dose was determined based on maximum tumor diameter along with the pattern of blood supply. When the sufficient blood supply was concerned, lipiodol dose would be 2-3 times tumor's diameter (If tumor diameter of sufficient blood supply was about 10 cm, the lipiodol dose would be about 20-30 mL). As for the poor blood supply, the dose would be equal to its diameter; lipiodol was perfused till tumor volume was filled completely. To mixed blood supply, the dose was adjusted according to its sufficient blood supply area. When A-V shunt existed, lipiodol amount was determined according to actual condition during TACE. In control group dose was determined based on tumor size (If tumor was about 10 cm, lipiodol dose would be 10 mL accordingly).

Reference standard of lipiodol congregration In CT film, we took the area which lipiodol actually occupied within tumor as a criterion after first TACE: over 75% area as complete filling, area between 50-74% as relatively complete filling, below 49% area as partial filling. Through CT scanning, complete filling and relatively complete filling accorded with pre-operation criterion and partial filling did not.

Evaluation criterion for curative effect With short term follow-up of 6 mo, according to evaluation criterion established by WHO, curative effect could be divided into: complete response (CR), partial response (PR), no change (NC), and progressive deterioration (PD). The three former items were regarded as effective and PD ineffective.

Statistics Confirmation rate and effective rate were assessed by χ^2 test.

RESULTS

Four types of blood supply patterns of large HCC

Type I, abundant blood supply, which could be further divided into Ia and Ib subtype. Ia subtype: Tumor displayed obviously homogeneous or non-homogeneous hyper-dense contrast in arterial phase after enhancement in which broadened nourishing vessels were like radiated, piebald, petal or tuberous shape, and were still in enhancement at portal-venous phase and tailed off at delayed-phase. In DSA, tumor's nourishing arteries broadened and small vessel was hyperplasia in radiated and clasp shape. Ib subtype: Compared with surroundings of hepatic parenchyma in CT, tumor presented slight enhancement and were still in relative hypodense in arterial and portal-venous phases where slightly broadened or nodular arteries at arterial phase could be seen. And palisade shape enhancement could be found at portal-venous phase. Many small vessels showed in DSA film.

Type II, poor blood supply, tumor showed no or mild enhancement during arterial phase, portal-venous phase or delayed phase. In DSA, the nourishing arteries presented no or slight widening and small vessels were in absence; during parenchyma phase, the tumor showed slightly staining.

Type III, mixed blood supply, tumor consisted of sufficient blood supply areas and poor blood supply areas, some areas took on apparent contrast while others did slightly. In DSA, sufficient blood supply areas and poor supply areas co-existed in a tumor.

Type IV, A-V shunt portal vein showed at arterial phase in advance while tumor rarely contrasted at arterial or portal venous phase. In DSA, the normal hepatic artery evidently enlarged rather than tumor arteries. A great amount of contrast media could flow into fistula existed in tumor through portal vein or hepatic vein so that involved veins visualized.

From Tables 1, 2, types I-III in CT scan accorded to that in DSA, and the type of A-V shunt in CT scan is very different from that in DSA. The confirmation rate of lipiodol perfusion was 82% in testing group and 36% in control group. In terms of the effective rate, the difference was significant between testing group (84%) and control group (46%).

Table 1 Blood supply of 100 cases large HCC classified in CT and DSA

Item	Case	Sufficient blood supply		Poor blood supply		Mixed blood supply		A-V shunt	
		Case	%	Case	%	Case	%	Case	%
CT	100	75	75	14	14	7	7	4	4
DSA	100	72	72	12	12	6	6	10	10

Table 2 Curative effects in two groups

Group	Case	PR	NC	PD	Effective rate (%)
Testing group	50	24	18	8	84.0
Control group	50	7	16	27	46.0

CP: Complete response; PR: Partial response; NC: No change; PD: Progressive deterioration.

DISCUSSION

Lipiodol dose is determined by tumor blood supply, patients' general conditions, tolerance to operation, catheter position, etc., of which tumor blood supply plays a crucial role. CT and DSA can display the tumor blood supply well. With sufficient blood supply, tumors in CT scan show apparent enhancement and in DSA display a large amount of inordinately dilated vessels, even "blood lake". With poor blood supply, tumors

reveal little enhancement as well as a small number of vessels. The display rate and staining extent of the vessels were different when the catheter ends reached coeliac trunk, common hepatic artery or proper hepatic artery. Tumor staining extent was significantly higher in latter two because most of blood stream could flow back to splenic artery when catheter was in coeliac trunk. In addition, display rate and staining extent of small vessels were in direct proportion to contrast media amount and injection rate. Two cases revealing no classical trabecula and roundish contrast features in CT were misdiagnosed as poor blood supply type, but the nourishing arteries were presented in arterial phase and a large amount of small vessels appeared in portal venous phase and in DSA lipiodol filled in the tumor completely.

It is of great significance to work out a set of individualized therapy before TACE. Previously, lipiodol dose was determined by tumor's size^[1]. In another word, lipiodol dose should correspond to tumor size and if lipiodol dose is equal to tumor diameter or 1.5 times the diameter, it will produce good curative effect, and if dose is beyond twice the diameter, it will have fewer effects and even damage the hepatic function, leading to cirrhosis. Matsuo^[2] believed that in conventional TACE, lipiodol should be over 5 mL if tumor diameter is less than 5 cm, and the maximum dose will be 10 mL when the tumor develops to more than 5 cm in diameter. With the improvement of the catheter quality and the development of the superselective skills, the catheter can be superselected directly into tumor supply arteries with ease, and lipiodol dose can rise up to 20 mL to fill the tumor less than 10 cm in diameter and 30 mL or more to the tumor more than 10 cm. But in poor blood supply cases, the lipiodol dose should not be over its necessity because lipiodol can flow back and disperse into the normal liver parenchyma. As for mixed blood supply, the dose will rely on the sufficient blood supply area in tumor. Tumor has its shape and volume, supposing to make the lipiodol fill in the tumor as much as possible, it is not enough to inject lipiodol dose into tumor just as its maximum diameter, especially in sufficient blood supply tumor. The tumor will survive if lipiodol dose is not sufficient. Theoretically, tumor cell can be killed only when lipiodol has obstructed all supply vessels and drug flows completely into the tumor. Over dose of drug and lipiodol will make hepatic function get worse in the case of the liver cirrhosis. For these reasons above, to make the drug and lipiodol fill as completely in the tumor as possible, lipiodol dose ought to be based not only on tumor diameter but also on individual blood supply.

CT film can reflect tumor's position, shape, size, quantity as well as blood supply, thus providing guidance for therapy. Patterns of tumor blood supply can be divided into 3 types at arterial phase in CT scan: sufficient blood supply, poor blood supply and mixed blood supply. The survival rate of sufficient blood supply is obviously higher than that of poor blood supply^[3,4]. Vogl^[5] held that lipiodol filling over 75% area of tumor was complete filling and 50-70% area was comparatively complete filling, and the survival rate was encouraging in these two circumstances.

Chung suggested that over-dose lipiodol injection could lead to pulmonary artery embolism when obvious artery-vein shunt exists, especially in hepatic arterial-venous fistula of large HCC. CT can illustrate obvious A-V shunt and provide guidance for therapy. In such cases, lipiodol dose should be decreased and fistula embolized by gelfoam, then correct dose of lipiodol injected to perfuse tumors.

In the first time of therapy, lipiodol dose should be relatively excessive to completely fill in the tumor, because tumor cells can produce the drug resistance with the increase of TACE operation, the artery will be impaired more or less by lipiodol even produce stenosis or obstruction, and finally, the sufficient blood supply of tumor may turn into poor blood supply, meanwhile, the normal hepatic parenchyma may gradually

become cirrhosis, or deteriorated from intrinsic cirrhosis, which would bring side effects and even interrupt the treatment.

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