ELSEVIER

Canadian Association of Radiologists Journal xx (2016) 1−15

CANADIAN ASSOCIATION OF RADIOLOGISTS JOURNAL

www.carjonline.org

Abdominal Imaging / Imagerie abdominale

Hepatocellular Carcinoma Post Embolotherapy: Imaging Appearances and Pitfalls on Computed Tomography and Magnetic Resonance Imaging

Rita Y. W. Chiu, MD*, Wan W. Yap, MBChB, Roshni Patel, MBBS, David Liu, MD, Darren Klass, MD, PhD, Alison C. Harris, MBChB

Department of Radiology, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada

Abstract

Embolotherapies used in the treatment of hepatocellular carcinoma (HCC) include bland embolization, conventional transarterial chemoembolization (cTACE) using ethiodol as a carrier, TACE with drug-eluting beads and super absorbent polymer microspheres (DEB-TACE), and selective internal radiation therapy (SIRT). Successfully treated HCC lesions undergo coagulation necrosis, and appear as nonenhancing hypoattenuating or hypointense lesions in the embolized region on computed tomography (CT) and magnetic resonance. Residual or recurrent tumours demonstrate arterial enhancement with portal venous phase wash-out of contrast, features characteristic of HCC, in and/or around the embolized area. Certain imaging features that result from the procedure itself may limit assessment of response. In conventional TACE, the high-attenuating retained ethiodized oil may obscure arterially-enhancing tumours and limit detection of residual tumours; thus a noncontrast CT on follow-up imaging is important post-cTACE. Hyperenhancement within or around the treated zone can be seen after cTACE, DEB-TACE, or SIRT due to physiologic inflammatory response and may mimic residual tumour. Recognition of these pitfalls is important in the evaluation embolotherapy response.

Résumé

Les thérapies par embolisation visant à traiter le carcinome hépatocellulaire englobent l'embolisation seule, la chimio-embolisation transartérielle classique avec émulsion d'éthiodol (cTACE), la chimio-embolisation transartérielle avec billes à élution de médicaments et microsphères de polymère superabsorbant (DEB-TACE) et la radiothérapie interne sélective (SIRT). Quand le traitement fonctionne, il induit une nécrose de coagulation. On observe alors des lésions hypo-atténuées sans contraste ou hypointenses dans la région embolisée à l'examen de tomodensitométrie (TDM) et d'imagerie par résonance magnétique (IRM). En cas de tumeurs résiduelles ou récurrentes, on constate des prises de contraste artérielles avec élimination du produit de contraste à la phase veineuse portale, des caractéristiques propres au carcinome hépatocellulaire, à l'intérieur ou à proximité de la région embolisée. L'intervention produit certaines caractéristiques d'imagerie qui restreignent l'évaluation de la réponse au traitement. L'huile d'éthiode hautement atténuante utilisée pour la chimio-embolisation transartérielle peut en effet obscurcir les tumeurs et limiter la capacité à détecter les tumeurs résiduelles. Il est donc important de réaliser une TDM de suivi sans produit de contraste à la suite d'une cTACE. On remarque aussi une grande prise de contraste à l'intérieur ou à proximité de la région traitée à la suite d'une cTACE, d'une DEB-TACE ou d'une SIRT en raison d'une réaction inflammatoire physiologique. Celle-ci peut donner l'impression qu'il s'agit d'une tumeur résiduelle. Il est donc essentiel de reconnaître ces pièges lorsqu'on évalue la réponse à la thérapie par embolisation.

Key Words: Drug-eluting beads and super absorbent polymer microspheres; Embolotherapy; Hepatocellular carcinoma; Selective internal radiation therapy; Transarterial chemoembolization

Hepatocellular carcinoma (HCC) develops predominantly as a result of irreparable damage to background liver, either as a result of viral infection, toxins, or autoimmune disease. The worldwide incidence of HCC is increasing, and is the third leading cause of cancer-related death [1]. In Canada, the incidence rate of liver cancer increased by an average of 3.6% per year between 1997−2007 in men, and 2.6% per year between 1986−2007 in women, with an estimated 2100

* Address for correspondence: Rita Y. W. Chiu, MD, Department of Radiology, Faculty of Medicine, University of British Columbia, 3350-950 West 10th Ave, Vancouver, British Columbia V5Z1M9, Canada.

E-mail address: rywchiu@gmail.com (R. Y. W. Chiu).

0846-5371/$ - see front matter
http://dx.doi.org/10.1016/j.carj.2015.09.006

new cases in 2013 [2]. Definitive treatment of HCC includes surgical resection or liver transplantation. However, several minimally invasive locoregional therapies have proven to successfully treat HCC, including radiofrequency ablation, transarterial chemoembolization (TACE), and selective internal radiation therapy (SIRT). Treatment decisions depend on many factors and can be variable between institutions, and the Barcelona Clinic Liver Cancer staging classification and treatment algorithm is frequently used to direct therapy based on tumour stage, liver functional status, physical status, and cancer-related symptoms [3].

Follow-up imaging is essential in assessing treatment response after locoregional therapies and determining if further therapy is required. Response to treatment has classically been measured by change in tumour size and number, according to the World Health Organization (WHO) and Response Evaluation Criteria in Solid Tumours (RECIST) guidelines. The WHO criteria published in 1979 measures tumours in 2 dimensions—the longest diameter is multiplied by the greatest perpendicular diameter [4]. The RECIST guideline published in 2000 (version 1.0) includes unidimensional measurement of tumours by their longest diameter in the axial plane [5], and was initially adopted by regulatory agencies such as the U.S. Food and Drug Administration for drug approval. Disease progression was defined as greater than 20% increase in the sum of diameters of target lesions. The RECIST guideline was revised in 2009 (version 1.1) to include a greater than 5 mm absolute increase, in addition to 20% increase, in the sum of all diameters of target lesions [6].

The major pitfall of the WHO and RECIST criteria with regards to assessing tumour response are that they do not account for tumour necrosis induced by locoregional embolotherapies such as TACE and SIRT. Since tumour necrosis does not always correlate with corresponding change in tumour size, the effectiveness in locoregional therapies are not properly reflected in the WHO and RECIST guidelines. The European Association for the Study of the Liver recommended measuring the reduction in viable tumour (ie, areas of contrast uptake on the arterial phase) rather than overall tumour size [7]. The modified RECIST (mRECIST) criteria was developed by the American Association of Liver Disease for evaluation of HCC specifically, where only the viable portion of the tumour is included as the target lesion [8]. Table 1 compares the differences in response definitions between WHO, RECIST, RECIST 1.1, and mRECIST.

Multiple imaging modalities may be used to determine HCC tumour viability after locoregional embolotherapies, particularly computed tomography (CT) and magnetic resonance imaging (MRI). The aim of this article is to discuss the imaging appearances and pitfalls of HCCs following embolotherapies on CT and MRI.

Imaging Protocols

Computed Tomography

Multidetector CT (MDCT) is a widely utilised imaging modality following locoregional embolotherapy, allowing for acquisition of contiguous slices in multiple phases following intravenous contrast administration [8]. At our institution, MDCT is performed either on a 64-slice scanner (Siemens SOMATOM Sensation Cardiac, Siemens Healthcare, Erlangen, Germany), 320-slice scanner (Toshiba Aquilion 1, Toshiba Medical Systems, Tochigi, Japan), or dual-source 128-slice scanner (Siemens SOMATOM Definition FLASH, Siemens Healthcare, Erlangen,

Table 1
Comparison of tumour response criteria among WHO guidelines [2], RECIST 1.0 [3], RECIST 1.1 [4], and mRECIST for HCC [8]

Tumour response	WHO	RECIST 1.0	RECIST 1.1	mRECIST for HCC
Complete response	Disappearance of all known disease, determined by 2 observations not less than 4 weeks apart	Disappearance of all target lesions	Disappearance of all target lesions	Disappearance of any intratumoural arterial enhancement in all target lesions
Partial response	50% or more decrease in total tumour size of the lesions which have been measured to determine the effect of therapy by 2 observations not less than 4 weeks apart	At least 30% decrease in sum of diameters of target lesions	At least 30% decrease in sum of diameters of target lesions	At least 30% decrease in sum of diameters of viable (intratumoural arterial enhancement) target lesions, taking as reference the baseline sum of diameters of target lesions
Stable disease	50% decrease in total tumour size cannot be established nor has a 25% increase in size in 1 or more measurable lesions been demonstrated	Any case that does not qualify for partial response or progressive disease	Any case that does not qualify for partial response or progressive disease	Any case that does not qualify for partial response or progressive disease
Progressive disease	25% or more increase in size of 1 or more measurable lesions, or appearance of new lesions	At least 20% increase in sum of all diameters of target lesions	At least 20% increase and 5 mm absolute increase in sum of all diameters of target lesions	At least 20% increase in sum of diameters of viable target lesions, taking as reference the smallest sum of diameters of viable target lesions recorded since treatment started

HCC = hepatocellular carcinoma; mRECIST = Modified Response Evaluation Criteria in Solid Tumours; RECIST = Response Evaluation Criteria in Solid Tumours; WHO = World Health Organization.