Assessing Imaging Response to Therapy

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KEYWORDS

• World Health Organization (WHO) • Response evaluation criteria in solid tumors (RECIST)
• European Association for the Study of the Liver (EASL) • Modified RECIST (mRECIST)
• Response assessment • Computed tomography (CT) • MR imaging

KEY POINTS

- Accurate assessment of response to locoregional therapies (LRTs) is crucial because objective response can be a surrogate of improved survival.
- Tumor size and necrosis guidelines are the gold standard for assessing imaging response to LRTs.
- Newer imaging modalities (eg, functional MR imaging, PET with fluorodeoxyglucose [FDG-PET]) and biomarkers of response (eg, serum tumor markers) show promise as ancillary tools in assessing response to therapy.

INTRODUCTION

LRTs, such as radiofrequency ablation (RFA), transarterial chemoembolization (TACE), and radioembolization, have proved valuable in the treatment of patients with cancer, most commonly in the liver.[1] Accurate assessment of response to these therapies is crucial because objective response can be a surrogate of improved survival.[2] Imaging plays an essential role in the objective evaluation of tumor response to most cancer therapies, including LRTs. Because imaging response following LRTs has been shown to predict patient survival times,[3] one of the goals of LRTs should be to achieve a radiologic response. Assessing imaging response to LRTs, however, can be challenging and is evolving.

There are several radiologic criteria that are commonly used to assess imaging response to treatment after LRTs, including World Health Organization (WHO),[4] Response Evaluation Criteria in Solid Tumors (RECIST),[5] and European Association for the Study of the Liver (EASL)[6] guidelines. Volumetric techniques and functional imaging (eg, PET) have also been described.[7–10] No universally accepted criteria exist.

This article reviews the different criteria used to assess radiologic response to LRTs, with special attention to imaging assessment following treatment of hepatocellular carcinoma (HCC).

IMAGING TECHNIQUES

Imaging evaluation of patients treated with LRTs is usually performed with cross-sectional imaging, most commonly computed tomography (CT) or MR imaging . Although there has been considerable interest in other imaging modalities, including PET[8,11] and contrast-enhanced ultrasonography (CEUS),[12,13] these are less commonly used. Accurate imaging assessment of response to therapy requires the following:

- Evaluation of tumor size
- Evaluation of tumor margins
- Evaluation of tumor necrosis

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- Detection of residual or recurrent tumor
- Detection of new tumor

The evaluation of treatment success is essential for future treatment decisions and prognosis.[14]

Computed Tomography

CT has been the mainstay of cancer imaging for both initial evaluation and response assessment after treatment. Modern multidetector CT scanners allow thin-section images to be obtained in a single breath-hold with greatly improved speed and resolution, resulting in high-resolution multiplanar reformations.[14] In patients with HCC, multiphase scanning is typically used.[15] The United Network for Organ Sharing currently recommends a multiphasic CT protocol for HCC that includes nonenhanced, late arterial phase, portal venous phase, and delayed phase imaging.[16]

Dual-energy CT (DECT) has become available, and its utility in imaging hypervascular liver masses such as HCC is being evaluated.[17] DECT provides additional information about how tissues of differing densities behave at differing tube voltages. DECT may have utility in evaluating response of HCC to LRTs with higher lesion-to-liver contrast-to-noise ratios on an iodine map, which can be helpful for detecting residual tumor.[18]

MR Imaging

MR imaging provides high-quality soft-tissue contrast and spatial resolution, allowing for multiplanar 3-dimensional reconstructions and maximum intensity projections. The use of functional parameters in MR imaging, such as flow, temperature, tissue oxygenation, dynamic perfusion, and diffusion, further assist in guiding therapy and assessing treatment response.[14]

MR imaging plays a particularly important role in patients with HCC. Contrast-enhanced dynamic T1-weighted imaging with diffusion-weighted imaging can be helpful in assessing treatment-related changes in HCC.[19] MR imaging may be superior to CT in evaluating patients treated with conventional TACE (cTACE) because the beam-hardening effects of the high-density ethiodized oil used in cTACE may obscure small enhancing tumors on CT. However, ethiodized oil does not adversely affect MR signal-intensity characteristics, so residual enhancement can be detected, especially when image subtraction is used.[9,20] Image subtraction can also be helpful in other situations. For example, lesions treated with RFA typically undergo coagulative hemorrhagic necrosis that can appear hyperintense on unenhanced T1-weighted imaging, making contrast-enhanced evaluation challenging.[21] Using image subtraction techniques, MR imaging has been shown to be beneficial in depicting residual enhancement, with excellent correlation with histopathologic degree of tumor necrosis.[22]

Positron Emission Tomography

FDG-PET has become an indispensable tool for evaluating many types of cancer. PET has been incorporated into the response assessment criteria for Hodgkin and non-Hodgkin lymphoma,[23] and it has proven utility in detecting early response and predicting long-term response to imatinib in gastrointestinal stromal tumors (GISTs).[24] For cancers commonly treated with LRTs, such as metastatic colorectal cancer, FDG-PET may be more reliable than CT in the detection of liver metastasis or recurrence in the liver.[25] Gulec and colleagues[26] found that FDG-PET response in patients with colorectal cancer liver metastases treated with radioembolization was strongly associated with survival. On the other hand, FDG-PET has limited sensitivity in the detection of HCC, and its role in assessing response to therapy in this disease has not been validated.[14] At present, lack of widespread availability and lack of sufficient standardization prevent FDG-PET from being widely incorporated into many response criteria. However, it can be used as an adjunct to other imaging modalities following LRTs.

Contrast-Enhanced Ultrasonography

CEUS has been studied to assess response to LRTs including RFA,[13] TACE,[12] and combined techniques.[27] On postablation CEUS, nodules showing no contrast enhancement in the arterial phase correlate with complete necrosis on CT and nodules with persistent arterial vascularization are considered residual tumor.[27] Potential benefits of CEUS include the following: (1) it is easy to use and (2) the high-density ethiodized oil used in cTACE does not limit CEUS interpretation, as can be the case with CT.[12] However, to date, microbubble contrast agents are not approved by the US Food and Drug Administration (FDA) for the evaluation of liver lesions, and this technique is rarely performed in the United States.

DIAGNOSTIC CRITERIA

Early attempts to define objective response of a tumor to an anticancer therapy date back to the 1960s.[28] Shortly thereafter, following a rapid increase in cancer-related research, it became apparent that a common language would be