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**System LI-RADS w małoinwazyjnym leczeniu raka
wątrobowokomórkowego**

**Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu
w dyscyplinie nauki medyczne**

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Streszczenie w języku angielskim

LI-RADS system in the minimally invasive treatment of hepatocellular carcinoma

Introduction

The treatment response algorithm (LR-TR) is part of the LI-RADS system and is used to evaluate imaging studies of patients with hepatocellular carcinoma (HCC) treated with minimally invasive locoregional therapies. The LR-TR uses a number of imaging features to classify treatment response into one of three main categories: 1) LR-viable (residual active tumor tissue), 2) LR-nonviable (desired treatment outcome) and 3) LR-equivocal. Transarterial chemoembolization (TACE) is a type of minimally invasive therapy that is frequently used in patients with unresectable HCC. Despite the widespread use of the LR-TR in clinical practice, it is not clear whether the response categories correlate with the long-term outcomes following minimally invasive transarterial therapies. Moreover, there is a lack of data on the inter-observer agreement using the LR-TR in patients with HCC treated with TACE. This doctoral dissertation aims to broaden current knowledge of the usefulness of the LR-TR in the field of minimally invasive transarterial therapies.

Publication 1 - Performance of initial LI-RADS 2018 treatment response in predicting survival of patients with hepatocellular carcinoma following TACE: a retrospective, single-center cohort study - *Journal of Cancer Research and Clinical Oncology* 2021 Dec;147(12):3673-3683.

In this paper, the initial response to TACE therapy, expressed in terms of the LR-TR categories, was examined as a potential predictor of long-term patient outcomes. In this retrospective cohort study the data of 302 consecutive patients treated with TACE was analyzed. Two independent experienced radiologists assessed the LR-TR categories following the first treatment cycle, while a third radiologist re-assessed divergent results. The final analysis included 99 treatment-naive HCC patients who were treated with TACE. Overall survival (OS) was the primary endpoint of the study and the Cox proportional hazard model was used for multivariate outcome analyses.

Median OS in the initial LR-viable, LR-equivocal and LR-nonviable response groups were 27, 27 and 73 months, respectively ($p < 0.01$). Preliminary analysis showed a significant correlation between initial LR-viable treatment response and shorter OS (HR 3.76, $p < 0.01$).

However, the multivariate analysis that took into account other significant OS predictors (namely HCC stage, best overall LR-TR response, albumin level and presence of systemic treatment) did not confirm such a correlation (HR 0.98, $p = 0.97$). Of note, the group of patients with LR-equivocal initial response was assumed to be too small to draw conclusions. Overall, this analysis indicates that the initial LR-TR response category is not an independent predictor of overall survival in patients treated with TACE, and poor outcomes of HCC patients who did not achieve a LR-nonviable response after the initial treatment cycle may be due to unfavorable baseline characteristics (namely advanced HCC stage and poor liver function status).

Publication 2 - Inter-observer agreement using the LI-RADS version 2018 CT treatment response algorithm in patients with hepatocellular carcinoma treated with conventional transarterial chemoembolization - *Abdominal Radiology* 2022; 47(1): 115–122.

This analysis, for the first time, established inter-observer agreement using the LR-TR in the categorization of computed tomography (CT) examinations of a homogeneous group of HCC patients undergoing minimally invasive trans-arterial therapy. Two radiologists retrospectively assessed 112 CT studies and evaluated LR-TR after TACE therapy. Inter-observer agreement in the categorization of distinct LR-TR features and final response categories was assessed, while inter-observer agreement was assessed using Cohen's kappa coefficient.

Detailed analysis showed that the LR-TR provides a high degree of inter-observer agreement on the categorization of the presence of arterial phase hyperenhancement ($\kappa=0.79$; 95% CI 0.67–0.90) and the washout feature ($\kappa=0.69$; 95% CI 0.56–0.83), resulting in a highly reproducible assessment of the LR-viable and LR-nonviable categories ($\kappa=0.78$; 95%CI 0.67-0.90 and $\kappa=0.80$; 95%CI 0.68-0.92, respectively). Conversely, for the LR-equivocal category, inter-observer agreement was relatively low ($\kappa=0.25$; 95%CI 0.02-0.49), suggesting a need to refine the criteria to improve inter-observer agreement.

Conclusion

In this dissertation, the correlation between the initial LR-TR response following TACE sessions and long-term treatment outcomes was investigated. The analysis showed that the initial LR-TR category is not an independent predictor of patient outcomes, and other predictors, such as baseline tumor burden or overall best radiological response, are more useful in this regard. Furthermore, for the first time, inter-observer agreement was evaluated using the

LR-TR to categorize CT scans of patients undergoing TACE. The study confirmed high agreement in the categorization of LR-viable and LR-non-viable observations. Nevertheless, future studies may benefit from simplifying or clarifying LR-equivocal response criteria and its components in order to improve inter-reader agreement.