Multiparameteric Response Assessment of Hepatocellular Carcinoma Treated with Transarterial Chemoembolization Predicts Patient Survival Times

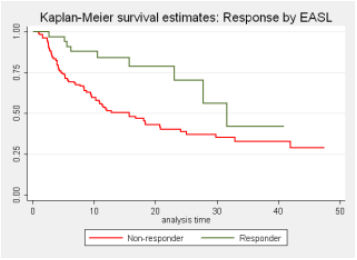
Susanne Bonekamp[1], Zhen Li[2], Vivek Gowdra Halappa[1], Celia Pamela Corona-Villalobos[1], Jean-Francois H. Geschwind[1], and Ihab R Kamel[1]
[1]Radiology, Johns Hopkins University, Baltimore, Maryland, United States, [2]Radiology, Tongji Medical College, Wuhan, China, People's Republic of

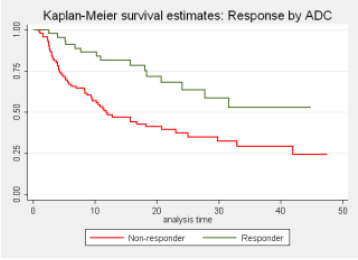
Background: It is not clear whether survival times of patients with hepatocellular carcinoma (HCC) are associated with their response to therapy or which measurement of response to therapy may be optimal. The purpose of this study was to test the hypothesis that contrast-enhanced MRI and diffusion weighted MRI together had a higher discriminating accuracy than a single measurement or current criteria developed to assess response to treatment and predict patient survival.

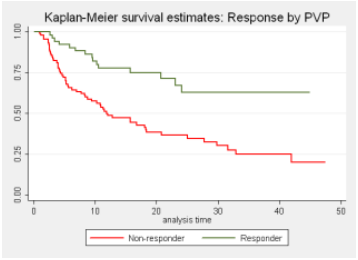
Methods: The clinical and MR imaging data of 141 patients (115 male, mean age 63 years) was retrospectively analyzed. All patients included in this study underwent a standardized imaging protocol before and 3-4 weeks after transarterial chemoembolization (TACE). MR imaging was performed on a 1.5-T MRI scanner (Siemens Magnetom Avanto) using a phased array torso coil. The protocol included breath-hold diffusion-weighted echoplanar images (matrix, 128 x 128; slice thickness, 8 mm; interslice gap, 2 mm; b value, 0 & 750 s/mm^2; TR 3000 ms; TE 69 ms; received bandwidth, 64 kHz) and breath-hold contrast-enhanced (0.1 mmol/kg intravenous gadopentetate; Magnevist; Bayer, Wayne, NJ) T1-weighted 3D fat suppressed spoiled gradient-echo images (field of view, 320–400 mm; matrix, 192 x 160; slice thickness, 2.5 mm; TR 5.77 ms; TE 2.77 ms; received bandwidth, 64 kHz; flip angle, 10°) in the hepatic arterial phase (HAP) (20 s), and portal venous phase (PVP) (70 s) phase. For each patient we evaluated Response Evaluation Criteria in Solid Tumors (RECIST) and the European Association for the Study of Liver Disease (EASL) (3) criteria. HCC index lesions were analyzed using proprietary software, MROncotreat (Siemens Medical Solutions, USA). Tumors were segmented using and interactive, seed-based technique. For each study the software automatically generated tumor diameter, volumetric ADC, HAP and PVP enhancement. The primary end point was overall survival (OS).

Statistical analysis included univariate and multivariate analyses using the Cox proportional hazards model. The discriminating ability of the prognostic models was assessed with Harrel's c –index (4). A *c*-index value of 0.5 represents no discriminating ability and a value of 1.0 represents perfect discrimination. *P* values less than .05 was considered statistically significant. STATA version 10.1 (StataCorp, College Station, TX) was used for all statistical analyses.

Results: Overall median survival of the 141 patients with HCC was 20.7 months (95%-CI = 12.8 – 31.6 month). Survival by response criteria is shown in table 1 and figures 1 to 4.







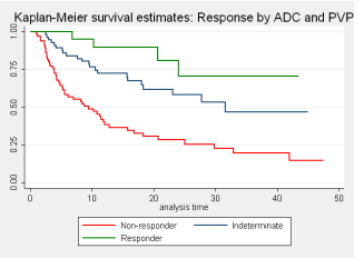


Figure 1: Response groups by EASL **Figure 2:** Response groups by ADC **Figure 3:** Response groups by PVP **Figure 4:** Response groups by ADC and PVP

Table 1: Survival Analysis by Response Status at 3-4 weeks after TACE

Characteristic	Category	N	25% Survival	Hazard Ratio (95%- Confidence Interval)	P	c-index (95%- Confidence Interval)
RECIST	Responder	4	10.6 month	0.54 (0.07 – 3.92)	0.545	0.50 (0.49 – 0.50)
	Non-responder	137	5.6 month			
EASL	Responder	33	31.6 month	0.39 (0.19 - 0.78)	0.008	0.54 (0.50 – 0.57)
	Non-responder	108	4.6 month			
25% ADC increase	Responder	45	23.1 month	0.39 (0.22 – 0.69)	0.001	0.57 (0.53 – 0.62)
	Non-responder	96	4.3 month			
75% HAP decrease	Responder	32	9.6 month	0.65 (0.36 – 1.19)	0.165	0.52 (0.48 – 0.56)
	Non-responder	109	5.3 month			
50% PVP decrease	Responder	90	15.7 month	0.35 (0.20 – 0.62)	<0.001	0.56 (0.52 – 0.61)
	Non-responder	51	4.3 month			
25% ADC + 50% PVP	Responder	20	23.1 month	0.39 (0.27 – 0.58)	<0.001	0.61 (0.56 – 0.65)
	Indeterminate	56	10.6 month			
	Non-responder	65	3.9 month			

Conclusion: The results suggest that volumetric functional response criteria discriminate substantially better than size measurements. Furthermore, the combination of decrease in PVP by 50% and increase in ADC by 25% was found to improve discrimination substantially in the patients with HCC who were treated with TACE.

References: 1. Therasse P et al. J Natl Cancer Inst. 2000 Feb 2;92(3):205-16. 2. Eisenhauer EA et al. Eur J Cancer. 2009 Jan;45(2):228-47. 3. Bruix J, et al. J Hepatol. 2001 Sep;35(3):421-30. 4. Harrell FE,Jr, et al. Stat Med. 1984 Apr-Jun;3(2):143-52.