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Development of the analytical method for the quantification of 3-nitrotirosin and 3-chlorothyrosin in human plasma as potential biomarkers to evaluate minimal liver encephalopathy (MHE)

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Background and aim: Minimal hepatic encephalopathy (MHE) is the earliest form of hepatic encephalopathy (HE) and can affect up to 80% of patients with liver cirrhosis. It is characterized by impaired cognitive function; mainly in the domains of attention, memory, speed of response, surveillance and integrative function. Patients with MHE show reduced performance in selective and which has a negative impact on the patients' health-related quality of life. Currently, there is no gold standard for diagnosis of EHM. Reports Montoluiu et al. evaluated the serum levels of different nitro-oxidative stress metabolites, cyclic guanosine monophosphate (cGMP), nitrites + nitrates and 3-nitrotyrosine (3-NO-Tyr); For each metabolite, its diagnostic precision was evaluated as an indicator of MHE, correlating it with the level of performance in psychometric tests for the diagnosis of HE as a comparison, finding high sensitivity and specificity for 3-nitrotyrosine. Despite the fact that 3-NO-Tyr has been evaluated in EHM, there is a wide variation of results that support its clinical utility, mainly due to the quantification methods used. AIM. To develop an analytical method to quantify the products of nitro-oxidative stress 3-NO-Tyr and 3-chloro-Tyrosine (3-Cl-Tyr) of high sensitivity and specificity to quantify the levels of these metabolites in samples from participating subjects with liver damage and MHE and comparing against the levels of subjects with liver damage without MHE, as well as the baseline level in healthy control subjects.

Material and methods: This study was approved by the Institute's Ethics and Research Committee. An analytical method was developed for the quantification of 3-NO-Tyr as 3-Cl-Tyr by means of triple quadrupole mass spectrometry coupled to an ultra high efficiency liquid chromatography system (UPLC-MS / MS XEVO TqD Waters). The spectrometer was programmed using the molecular transitions of NO-Tyr (227.2> 181.1), Cl-Tyr (216.2> 170.1) and the internal standard (EI) (132.2 > 86.2) for the internal standard respectively. The samples were hydrolyzed prior to processing and analysis to quantify free and protein-derived metabolites.

Results: The method was linear in the range of 0.5 - 2500 nM for both metabolites, it met the validation tests of the analytical methods. The results show that, by means of the developed method, it is possible to perform the simultaneous quantification of free 3-NO-Tyr and Cl-Tyr and protein derivatives, so it can be used to quantify them in samples of MHE, non-MHE and control subjects.

Conclusions: With the developed method, it is possible to accurately and precisely quantify the concentrations of both metabolites in the proposed biological matrix, so if they show differences between study groups, they could be used to determine them in the early diagnosis of MHE.

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Experience of Yttrium-90 radioembolization in patients with hepatocellular carcinoma

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Background and aim: Nowadays there are several treatments for hepatocellular carcinoma BCLC B, among them is radioembolization with Itrio-90 (RE-Y90) which is a form of locoregional intra-arterial brachytherapy towards HCC, among its advantages is prolonging the HCC progression time and improve the quality of life of patients. Adverse effects could be extrahepatic (radiation pneumonitis) and intrahepatic (radiation-induced liver disease), among others. Objective of our work is to assess the time free of progression, response to treatment and adverse effects that occur with the administration of RE-Y90.

Material and methods: All HCC BCLC B patients who were candidates for RE-Y90 were analyzed.

Inclusion criteria: cirrhotic patients of any etiology, with a diagnosis of HCC stage B, Child Pugh A and B with 7 points, who had previously undergone a morphological study (CT / MRI) and arteriography to characterize the lesion, to know the irrigation of the tumor and rule out extrahepatic shunts that contraindicate the application of RE-Y90. Subsequently, the procedure was simulated with MAA-Tc99m in order to record its distribution, perform dosimetry, and on the day of RE-Y90, an image study was performed with PET / CT in order to verify the distribution. Exclusion criteria. Patients with liver cirrhosis of any etiology with BCLC Stage B of the Child Pugh B plus 7 points or those with Child Pugh A or B 7 points with extrahepatic shunts. Do not accept this type of therapy. Patients who were not candidates for this therapy were sessioned at the Gastrointestinal and Liver Tumor Meeting to decide their treatment. Response to treatment at 3 and 6 months was analyzed using the mRECIST criteria, progression-free time at 6 months, and adverse effects were recorded.

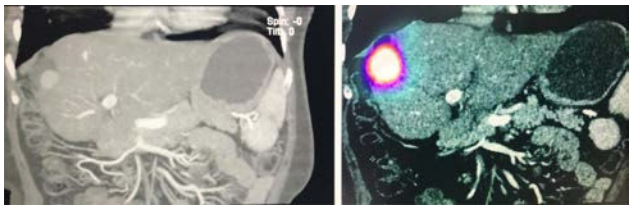
Results: Two patients with HCC BCLC B, a 70-year-old woman with HCC from AIH and a 67-year-old man with HCC of alcohol etiology, both Child Pugh at 6 points, with no data on arterial thrombosis, were performed.

After RE-Y90, there were no complications and the patients were discharged after 24 hours.

Control Computed Axial Tomography was performed with good response, without disease progression at 3 and 6 months, asymptomatic.

Conclusions: RE-Y90 for the treatment of BCLC stage B HCC is a good therapeutic option in well selected patient.

Conflicts of interest: The authors have no conflicts of interest to declare.



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Aspartate aminotransferase as predictor of severity in SARSCoV-2 infection: linear regression model

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Background and aim: Some patients with SARSCov-2 infection develop severe disease (SARS); however, the factors associated with severity are not yet fully understood. Some reports indicate that liver injury may be a poor prognostic factor. AIM**:** To identify the biochemical factors related to the development of SARS with mechanical ventilation (MV) requirement in patients with SARSCov-2 and COVID-19.

Methods. Type of study: Observational. Cohort study. Procedure: Data from COVID-19 patients were collected at admission time to a tertiary care center. Differential factors were identified between seriously ill SARS + MV patients versus stable patients without MV. Transformation to the natural logarithm of significant variables was performed and multiple linear regression was applied, then a predictive model of severity called AAD (*Age-AST-D dimer*) was constructed.

Results: 166 patients were included, 114(68.7%) men, mean age 50.6 ± 13.3 years-old, 27(16.3%) developed SARS + MV. In the comparative analysis between those with SARS + MV versus stable patients without MV we found significant raises of ALT (225.4 ± 341.2 vs. 41.3 ± 41.1; $P = 0.003$), AST 325.3 ± 382.4 vs. 52.8 ± 47.1; $P = 0.001$), LDH (764.6 ± 401.9 vs. 461.0 ± 185.6; $P = 0.001$), D dimer (7765 ± 9109 vs. 1871 ± 4146; $P = 0.003$), age (58.6 ± 12.7 vs. 49.1 ± 12.8; $P = 0$-001). The results of the regression are shown in the Table, where model 3 was the one that best explained the development of SARS + MV; with these variables was constructed the model called AAD, where: [AAD = 3.896 + ln(age)x-0.218 + ln(AST)x-0.185 + ln(DD)x0.070], where a value ≤ 2.75 had sensitivity = 0.797 and 1-specificity = 0.391, AUROC = 0.74 (95%CI: 0.62-0.86; $P < 0.0001$), to predict the risk of developing SARS + MV (OR = 5.8, 95%CI: 2.2-15.4; $P = 0.001$).

Conclusions: Elevation of AST (probable marker of liver damage) is an important predictor of progression to SARS, together with elevation of D-dimer and age early (at admission) and efficiently predict which patients will potentially require MV.

Conflicts of interest: The authors have no conflicts of interest to declare.

Multiple linear regression models predictive of SARS development in patients with COVID-19 and requirement for intubation

Model		Non-standarized Coeficients	Standarized Coeficients		P	95% Confidence Interval for B		Colinearity statistics	
	B	Error Desv.	Beta			Inferior limit	Superior limit	Tolerance	VIF
1	C	2.721	.131		.000	2.462	2.980		
	AST	−.229	.033	−.512	.000	−.293	−.164	1.000	1.000
2	C	3.161	.198		.000	2.770	3.551		
	AST	−.194	.034	−.435	.000	−.261	−.127	.878	1.139
	DD	−.081	.028	−.221	.004	−.135	−.026	.878	1.139
3	C	3.896	.414		.000	3.077	4.714		
	AST	−.185	.034	−.413	.000	−.252	−.118	.860	1.163
	DD	−.070	.028	−.190	.014	−.125	−.014	.844	1.185
	Age	−.218	.108	−.148	.046	−.433	−.004	.915	1.093

AST, aspartate aminotransferase; C, constant; DD, D dimer; VIF, variance inflation factors.

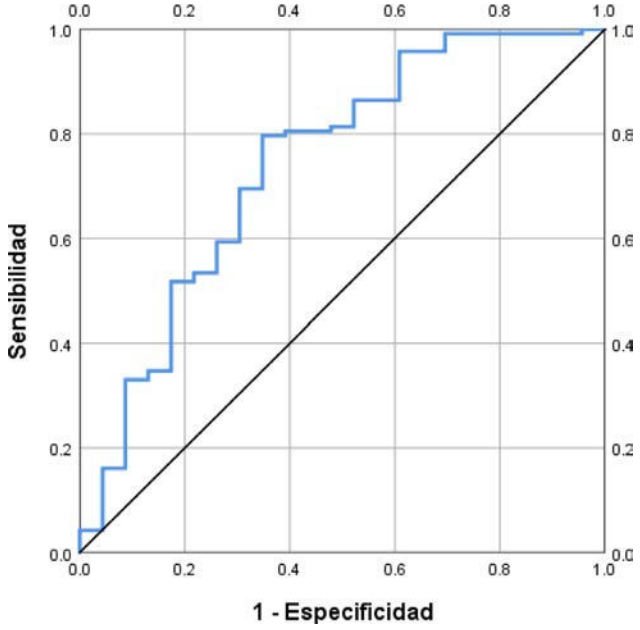
Resume of the model:

R = 0.512, r^2 = 0.262, r^2 adjusted = 0.256, standard error = 0.331.

R = 0.552, r^2 = 0.305, r^2 adjusted = 0.294, standard error = 0.322.

R = 0.570, r^2 = 0.325, r^2 adjusted = 0.310, standard error = 0.318. Durbin-Watson = 1.53.

AAD MODEL TO PREDICT SEVERE FORM (SARS) + INTUBATION



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Classification of alcohol consumption pattern in the Mexican population

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Background and aim: The evaluation of alcohol consumption is estimate by the evaluation of frequency and the concentration of