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## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 13915

**Title:** Factors predicting aggressiveness of non-hypervascular hepatic nodules detected on the hepatobiliary phase of gadolinium ethoxybenzyl diethylene-triamine-pentaacetic-acid enhanced MRI studies in cirrhotic patients

**Reviewer code:** 02941360

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-09-07 19:11

**Date reviewed:** 2014-09-22 17:34

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

Very good job. I am personally waiting a future paper of yours evaluating the prognostic value of your formula in a larger group of patients. Keep up the good work.

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**ESPS manuscript NO:** 13915

**Title:** Factors predicting aggressiveness of non-hypervascular hepatic nodules detected on the hepatobiliary phase of gadolinium ethoxybenzyl diethylene-triamine-pentaacetic-acid enhanced MRI studies in cirrhotic patients

**Reviewer code:** 00002232

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-09-07 19:11

**Date reviewed:** 2014-10-16 17:28

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair		BPG Search:	
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Existing	<input type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

### COMMENTS TO AUTHORS

In this study, Kanefuji et al. examined whether it is possible to establish a prognostic formula for non-hypervascular hepatic nodules (NHNs). This question is an important question to ask in order to be able to stratify patients with high risk of developing HCC. This is a retrospective study that considered 236 patients who underwent Gd-EOB-DTPA-MRI screening between May 2008 and January 2010. Seventy-three NHNs were identified in 29 patients. The authors generated a multivariate logistic regression model with six independent predictive factors that was further validated in a test group obtained from the same population. The authors reported for the test group positive and negative predictive values of 90% and 75%, respectively. Therefore, the authors conclude that the model, together with Gd-EOB-DTPA-MRI, has clinical utility in predicting aggressiveness of NHNs. MAJOR COMMENTS 1.- One of the main limitations of the study is that multivariate logistic regression was used to model pseudoreplicate data (73 NHNs in 29 patients). This fact, contravenes one of the fundamental assumptions of logistic regression, which is the independence of errors. Therefore, I would recommend the use of other statistical strategies such as mixed-effects models to overcome this limitation. 2.- The relatively small number of cases and the retrospective experimental design are major weakness of this study. These methodological shortcomings compromise the robustness of the conclusions. A prospective study or a large number



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of cases would support more robustly the author's conclusion. **MINOR COMMENTS** 1. In Table 2, can the authors provide confidence intervals? This would help the readers assess the precision of the model and evaluate for any overlap. 2. Could the authors provide more information on goodness-of-fit summary statistic for the model (e.g.: Lemeshow-Hosmer) and the goodness-of-fit statistics for the independent variables? In addition, and due to the small number of cases, I would recommend performing ten-fold cross validation to assess how well the model predicts based on new information. The authors assessed the accuracy of the model by dividing the 73 NHNs cases in one training and one test group. This fit measure may be insufficient and biased by over-fitting, considering the proportion of cases and variables. 3. The author should consider asking a native English speaker and writer to edit the manuscript for grammar and readability.



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## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 13915

**Title:** Factors predicting aggressiveness of non-hypervascular hepatic nodules detected on the hepatobiliary phase of gadolinium ethoxybenzyl diethylene-triamine-pentaacetic-acid enhanced MRI studies in cirrhotic patients

**Reviewer code:** 00504791

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-09-07 19:11

**Date reviewed:** 2014-10-13 01:15

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

This was an interesting article. It studies a derived formula for the efficient prediction of fate for non-hypervascular hepatic nodules, which appears to be frequently detected after the introduction of gadolinium ethoxybenzyl diethylene-triamine-pentaacetic-acid in a magnetic resonance imaging study. This appears to be significant on a regression analyze but has limited applicability as well as no formal pathologic confirmation as of yet. This is a novel and interesting article and worthy of further study. This is well written very complex and well studied. Obviously pathologic confirmation would be desirable.

## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 13915

**Title:** Factors predicting aggressiveness of non-hypervascular hepatic nodules detected on the hepatobiliary phase of gadolinium ethoxybenzyl diethylene-triamine-pentaacetic-acid enhanced MRI studies in cirrhotic patients

**Reviewer code:** 02098942

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-09-07 19:11

**Date reviewed:** 2014-09-08 10:41

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Existing	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

### COMMENTS TO AUTHORS

Kanefuji et al performed this study to establish a prognostic formula that distinguishes non-hypervascular hepatic nodules with higher aggressiveness from less hazardous one. While the topic is of interest, the manuscript has a few problems to be revised. 1. Basically, is this really a randomized controlled study? There is no description about calculation of sample size. Moreover, the authors stated in the paragraph of Patients and nodules that this study was a retrospective study. Which is true? The authors should clearly state calculation of sample size in case of a randomized controlled study. 2. As the authors mentioned in the Discussion, these findings obtained from such small number of cases cannot draw definite conclusions, except for a randomized controlled study with a definite study design. 3. There seems to be no clear description of sample number in each group in Materials and Methods section or Results section. Moreover, supplement Tables show that all nodules from case 21 to 29 belong to validation group. It seems funny, if this study is a randomized controlled study.