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Wan Chai, Hong Kong, China

### ESPS Peer-review Report

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

**ESPS Manuscript NO:** 3861

**Title:** The surprisingly low prevalence of hepatic steatosis in Cushing' s syndrome

**Reviewer code:** 00628780

**Science editor:** Wang, Jin-Lei

**Date sent for review:** 2013-05-29 19:10

**Date reviewed:** 2013-06-05 01:32

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

Very interesting and insightful manuscript, which deals with an important clinical issue in patients with Cushing's syndrome. Clearly written manuscript from two well-respected researchers in this particular field of research.



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## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 3861

**Title:** The surprisingly low prevalence of hepatic steatosis in Cushing’s syndrome

**Reviewer code:** 02508171

**Science editor:** Wang, Jin-Lei

**Date sent for review:** 2013-05-29 19:10

**Date reviewed:** 2013-06-13 23:50

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"/> Existed	<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"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

This is an interesting overview of the literature related to hepatic steatosis, its prevalence, clinical consequences and, in particular, the pathogenesis of this disorder. The authors focused on the link between hypercortisolism and obesity/metabolic syndrome. The main question of the work relates to the low prevalence of hepatic steatosis (only 20%) described in 50 then newly diagnosed patients with CS based on appropriate CT scans available for retrospective analysis. The authors have tried to explain this finding by the anti-inflammatory effect of high circulating levels of glucocorticoids. I have several considerations: 1) The title of the paper reflects only one paper out of the 98 included in the review. I have found the title quite misleading and that it narrows the actually rather broad subject of the paper. In my view it should be changed into “Pathogenesis of hepatic steatosis. Contradictions of the current view” or “The link between hypercortisolism and non-alcoholic fatty liver disease” or something else appropriate, but not the existing title. It gives the impression of an original study on patients with Cushing’s syndrome, or it might be the title of a “Letter to the editor”. 2) Considering the 50% five-year survival rate of patients with endogenous Cushing’s syndrome (without any treatment) [Plotz D, Knowlton AI, Ragan C.: The Natural History of Cushing’s Disease. Am J Med, 1952, 13:597-614] and the fact that all patients enrolled into the study by Rockall AG, et.al. were all newly diagnosed patients, the author should discuss the question of time exposure as a possible explanation for the relatively low prevalence of hepatic steatosis in patients with endogenous Cushing’s syndrome. 3) At least two diagnostic studies aiming to evaluate patients with Cushing’s syndrome among patients with obesity have found that late-night salivary cortisol (free cortisol) is increased in patients with obesity. Baid, et.al. reported that late night salivary cortisol was frequently above the laboratory-provided reference range in obese and overweight subjects



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(n=369) [SM Baid, et.al.: Specificity of screening tests for Cushing's syndrome in an overweight and obese population. *Journal of Clinical Endocrinology Metabolism*. 94, 3857-3864 (2009)]. In another paper late-night salivary cortisol was statistically significantly increased in patients with obesity and some features of Cushing's syndrome, in whom endogenous Cushing's syndrome was excluded, versus healthy, normal BMI control subjects [ZE Belaya, et.al.: Diagnostic performance of late-night salivary cortisol measured by automated electrochemiluminescence immunoassay in obese and overweight patients referred to exclude Cushing's syndrome. *Endocrine* 41, 494-500 (2012)]. Thus, the relative hypercortisolemia (the increase in free cortisol or circadian disturbance) in patients with metabolic syndrome should not be completely eliminated. The authors should discuss this as well. 4) Maybe the structure should be slightly changed. The paragraph "Hepatic steatosis, visceral fat and 11b-hydroxysteroid dehydrogenase type 1" seems rather unstructured and difficult to read. 5) The last sentence of the summary "This in vivo model (are you referring to Cushing's syndrome?) could also help clarifying the mechanisms of non alcoholic fatty liver disease" seems too speculative and actually does not accurately reflect the content.