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## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 15689

**Title:** Cholecystectomy is Independently Associated with Nonalcoholic Fatty Liver Disease in Asian Population

**Reviewer's code:** 03022396

**Reviewer's country:** Iran

**Science editor:** Jing Yu

**Date sent for review:** 2014-12-05 12:06

**Date reviewed:** 2014-12-27 16:52

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

### COMMENTS TO AUTHORS

no comment



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

**ESPS manuscript NO:** 15689

**Title:** Cholecystectomy is Independently Associated with Nonalcoholic Fatty Liver Disease in Asian Population

**Reviewer's code:** 00071689

**Reviewer's country:** Turkey

**Science editor:** Jing Yu

**Date sent for review:** 2014-12-05 12:06

**Date reviewed:** 2015-01-03 09:40

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

?The introduction section was written in detail. There are 17 references cited in this section and the total number of references is 38. Some sentences may be moved/added to the discussion section and shortened. ?I think more clear information about the health system must be given in the material and method section. What is the way to give the chance of collecting this large number of subjects in one year period? For example how is obtaining ultrasonography for each subject available? Is this a routine examination for periodic check-up?



**ESPS PEER-REVIEW REPORT**

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

**ESPS manuscript NO:** 15689

**Title:** Cholecystectomy is Independently Associated with Nonalcoholic Fatty Liver Disease in Asian Population

**Reviewer’s code:** 00058082

**Reviewer’s country:** Italy

**Science editor:** Jing Yu

**Date sent for review:** 2014-12-05 12:06

**Date reviewed:** 2015-01-06 20:35

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

**COMMENTS TO AUTHORS**

This is an interesting paper on the association of gallstone disease with nonalcoholic fatty liver disease (NAFLD), two frequent conditions sharing similar risk factors. The authors examined a wide sample of Asian population (17,612 people), showing that over 30% of the subjects had NAFLD and over 6% presented gallstone disease, with the prevalence of gallstone disease significantly increasing in the presence of NAFLD and vice-versa. Multivariate regression analysis showed that cholecystectomy, but not gallstones, was associated with NAFLD, even after adjustment for insulin resistance. The authors conclude that cholecystectomy, but not gallstones, is independently associated with NAFLD after adjustment for metabolic risk factors, data suggesting that cholecystectomy may be an independent risk factor for NAFLD. The methodology is sound. The paper is clearly written and the results and their interpretation are convincing. I only have minor suggestions for manuscript improvement, as follows: - An important aspect of cholelithiasis is the frequent occurrence of biliary colics/associated cholecystitis and referred tenderness in the upper right abdominal quadrant. Pain/acute inflammation is normally the main reason for deciding to



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proceed with cholecystectomy. Although the authors explain the association between cholecystectomy and NAFLD mainly in terms of alterations of bile acid metabolism subsequent to cholecystectomy and/or gallbladder-related hormonal effects, it cannot be excluded a relationship between pain/inflammatory symptoms preceding/motivating cholecystectomy and the occurrence of NAFLD. Was there any attempt in the examined patients to assess previous occurrence of biliary pain/number of colics? This aspect should be discussed by the authors and a relevant paper quoted in this regard, i.e., -Giamberardino et al, Relationship between pain symptoms and referred sensory and trophic changes in patients with gallbladder pathology. *Pain*. 2005 Mar;114(1-2):239-49. -Which type of cholecystectomy was performed in the patients? Open or laparoscopic? In such a large sample, I suppose that both interventions were represented. Was there any difference in the prevalence of NAFLD among patients undergoing open cholecystectomy and those undergoing laparoscopy? These two procedures differ greatly regarding invasiveness and postoperative outcome in the patients, also with respect to postoperative pain. It would be interesting to know if there is any correlation of NAFLD with the type of intervention and also with the percentage of conversion (if any), especially as conversion shares some of the risk factors of NAFLD (e.g., diabetes) [see Costantini et al, Risk factors for conversion of laparoscopic cholecystectomy, *Ann Ital Chir*. 2012 May-Jun;83(3):245-52; and Controlling pain in the post-operative setting, *Int J Clin Pharmacol Ther*. 2011 Feb;49(2):116-27].