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Wan Chai, Hong Kong, China

## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 7161

**Title:** Association of Metabolic Syndromes and Risk Factors with Ampullary Tumors Development

**Reviewer code:** 02543775

**Science editor:** Ma, Ya-Juan

**Date sent for review:** 2013-11-06 19:27

**Date reviewed:** 2013-12-29 02:47

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	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

The manuscript "Association of Metabolic Syndromes and Risk Factors with Ampullary Tumors Development" is a well-written paper and the originality of the paper is very good. Comments: Comment 1: Page 4, line 4-7: "Ampullary cancer is less aggressive and has a better prognosis after curative resection than cancer of the distal bile duct or the pancreas. The favorable prognosis is thought to be due to its early clinical presentation with obstructive jaundice and its high resectability rate." Page 6, line 19-21: "All specimens were classified following an examination at the Department of Pathology, Peking Union Medical College Hospital." The precise origin of a periampullary adenocarcinoma (ampulla, distal bile duct, pancreas, papilla Vater (duodenum)) is often difficult to determine even with standardized histopathologic evaluation. Inaccurate and inconsistent distinction between pancreatic, ampullary and distal bile duct cancer may result in obfuscation of key clinicopathological data (C. S. Verbeke1, I. P. Gladhaug, Resection margin involvement and tumour origin in pancreatic head cancer, Br J Surg. 2012 Aug;99(8):1036-49). Please include in Methods how the specimens were examined at the Department of Pathology, Peking Union Medical College Hospital. In addition to tumor origin, the histologic type of differentiation has been shown to have biologic and prognostic relevance for ampullary adenocarcinoma. Kimura et al were the first to demonstrate that adenocarcinomas originating in the ampulla of Vater may be classified as having either "intestinal" or "pancreatobiliary" type of histologic differentiation (Kimura W, Futakawa N, Yamagata S, Wada Y, Kuroda A, Muto T, Esaki Y: Different clinicopathologic findings in two histologic types of carcinoma of papilla of Vater. Jpn J Cancer Res 1994, 85:161-166). This can be attributed to the fact that bile and pancreatic duct epithelia meet at the duodenal mucosa. Long-term survival for patients with ampullary carcinomas equals pancreatic, biliary, and duodenal



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carcinomas when the same histologic type is compared (Westgaard A, Pomianowska E, Clausen OP, Gladhaug IP. Intestinal-type and pancreatobiliary-type adenocarcinomas: how does ampullary carcinoma differ from other periampullary malignancies?, *Ann Surg Oncol.* 2013 Feb;20(2):430-9). The authors should consider to classify the 124 ampullary cancers into intestinal or pancreatobiliary type of differentiation. The authors focus on malignant transformation via the adenoma-carcinoma sequence. Intestinal or pancreatobiliary type are likely to have very different molecular pathogeneses. Putatively, intestinal type follow the adenoma-carcinoma sequence as colorectal cancer, and pancreatobiliary type as pancreatobiliary cancer. In addition, the significant relation of chronic pancreatitis to ampullary cancer found in the current study may be related to this point. Comment 2: Page 10, line 3: "To our knowledge, this is the first and the largest population-based case-control study to evaluate metabolic syndromes as risk factors for ampullary tumors." Page 13, line 4 and 5: "First, it is a hospital-based study in a single institution, not a population-based study". The authors must make corrections and define type of study. Is it a population based study or not? Comment 3: Page 8, line 2-5: "The ampullary tumor patients and the control group had the same mean age (61.8±11.2 years, 61.7±11.2 years,  $p = 0.934$ ) and there were no differences in sex between two groups ( $p = 1.000$ ).". Please add in Statistical analysis how age (parametric/non-parametric) and sex were analyzed. Comment 4: Page 13, line 1 and 2: "...in the carcinogenesis of ampullary tumors, whereas cigarette smoking, alcohol abuse, cholecystectomy, and obesity are risk factors." If cigarette smoking, alcohol abuse, cholecystectomy, and obesity are risk factors in the carcinogenesis of ampullary tumors, is this based on the