

January 20, 2023

Seung Ok Lee, MD, PhD.

Medicine, Jeonbuk National University Medical School, Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital.

20 Geonjiro, Dukjingu, Jeonju, Jeonbuk, 54907, South Korea.

Phone: 82-63-250-1289; Fax: 82-63-255-1609; E-mail: solee@jbnu.ac.kr

Manuscript ID:

Dear Executive Managing Editor of *the World Journal of Clinical Cases*

We appreciate your kind review of our manuscript entitled “**Classification of Hepatobiliary Scintigraphy Pattern in Segmented Gallbladder according to the Anatomical Discordance**” and the suggestions raised during its review. These suggestions have been addressed, and the corresponding modifications have been made to the manuscript in response to the reviewers’ comments. A point-by-point response to the reviewers’ comments is enclosed.

We hope that the revised manuscript is satisfactory for publication in *the World Journal of Clinical Cases*.

Thank you very much for your time and consideration.

Sincerely,

Seung Ok Lee, M.D., Ph.D.

Answers to specific comments

Reviewers' comments:

Reviewer #1:

1. The clinical application of this study is limited as HBS is rarely done in clinical practice. Moreover, as mentioned in the study, more than 50% patients had associated gallstones or chronic cholecystitis which itself is an indication for cholecystectomy.

Answer: Thank you for your comments. HBS hasn't been implemented much recently. Also, as you mentioned, gallstones or chronic cholecystitis are indications for cholecystectomy. Patients who underwent HBS are cases with ambiguous symptoms and gallstones, and it is considered to be a test that can help when making decisions about patients and surgery. In addition, in Korea, there are cases in which patients do not want surgery even if they are recommended, so HBS helps to confirm and persuade the contractility of the gallbladder during patient counseling. We wrote the additions in discussion (rows 240-252).

Discussion (page 9)

- *Gallstones are one of the most common biliary tract diseases, and its prevalence is known to be 5.9-21.9% in the West and 3.1-10.7% in Asia.(15) Diagnosis of gallstones are made incidentally in most of the people, and remain asymptomatic throughout their lives. During a follow-up period of 10–15 years, symptoms appear in approximately 15–25% of patients, and the risk of developing biliary pain due to complications is reported to be approximately 2–3% per year.(16-18) Patients with symptomatic gallstones are at high risk of gallstone-related complications, and cholecystectomy is recommended in such cases.(19) In addition, cholecystectomy is recommended if there are risk factors for gallbladder cancer (e.g., anomalous pancreatic ductal drainage, gallbladder adenoma, porcelain gallbladder, or large gallstones (especially larger than 3 cm)).(20-22) However, if a patient with gallstones has ambiguous symptoms, it is often difficult to distinguish gallstone-related symptoms; therefore, blood tests, ultrasound, HBS, and the patient's personal circumstances are considered to determine the need for surgery.*

2. It is important to understand that gallstones themselves can impact HBS findings. So, if we have to study the impact of segmented GB on HBS then we should only include patients of segmented GB without gallstones. The authors can perform a subgroup analysis of such patients. But looking at the presented data, I believe the number would be small.

Answer: Thank you for your comments. As you said, gallstones can affect HBS findings. We have not found clear evidence of the influence of gallstone on HBS interpretation. We believe that while gallstones may affect the contractility of the GB, reduced contractility may also affect gallstone development. And as mentioned earlier, HBS is not routinely performed in gallstone disease and chronic cholecystitis. Unfortunately, the sub-analysis was difficult due to lack of data. The limitations of small-scale studies are mentioned in discussion.

Reviewer #3:

1. The style, language and grammar require major revision.

Answer: Thank you for your comments. We once again requested English proofreading and submitted the manuscript after correction.