Date 12th May 2022

Re: Cholecystectomy for asymptomatic gallstones, 77144

Dear Prof Lian-Sheng Ma

Editorial Office Director, Company Editor-in-Chief, Editorial Office

Many thanks for seeking peer review of our manuscript. We appreciate the time and effort in critical review and suggestions to improve and enhance the manuscript. We have made necessary edits and include point by point responses to reviewer comments.

Reviewer 1

Comment 1: The following points are mentioned to improve the quality of the article for the authors: First, this article is a descriptive-analytical article about the prophylaxis of cholecystectomy in asymptomatic patients. The descriptive aspect of the article is stronger than the analytical aspect. Not strong.

Response 1:

Many thanks for valuable and pertinent assessment of our manuscript. We agree the descriptive nature of our manuscript and it is fit for the theme "Field of Vision" for our journal. The analytical aspect is not strong due to lack of scientific data on "cholecystectomy for asymptomatic gallstones". Where data is available, we have added it. However, this is like a "chicken and egg" situation. Without data, we cannot have critical appraisal and add scientific rigour; while without raising awareness about consideration and offering patients a choice, the current perception and teaching/training on "asymptomatic gallstones should not be offered surgery" will continue to percolate and plague the next generation of trainees and learners. It is with such intent that authors raise the awareness via this manuscript. To add to analytical aspect, we have provided Markov modeling accounting for probabilities based on current evidence or making reasonable assumptions where data is lacking. As this comment is qualitative, no edits are made in the manuscript.

Comment 2: Second, the topic does not seem to be attractive to readers and there is nothing new in the topic.

Response 2: We respect your opinion that the debate of "operate or not to operate asymptomatic gallstone patients" doesn't exist. There is only one way – don't operate. Thus, there is nothing new in this topic. With this manuscript, we intend to convey that this topic should (if not must) be dismissed as "done, dusted or dead"; as there is compelling contrary data. For example if we go back in history, Sir William Halsted, father of modern residency system of training, suffered

from biliary colic for several years and was treated for gastritis/dyspepsia and atypical angina; only to add post cholecystectomy morbidity. There are modern studies to show that morbidity of laparoscopic cholecystectomy for cholecystitis patients is 4 to 8 times compared to morbidity of operating on patients with biliary colic. We argue that asymptomatic patients should be made aware and given a choice. This is also in keeping with principles of patient autonomy regarding information disclosure aspect of informed consent taking process. We simply are making a point that patient should be provided with adequate information so they can exercise their choice. As this comment is qualitative, no edits are made in the manuscript.

Comment 3: Third, this article does not seem to have valid evidence for changing scientific guidelines.

Response 3: We agree that based on non-data related manuscript, guidelines cannot (and should not) be changed. The purpose is not to pursue change in management guidelines; but to persuade surgical community to pause and reflect about many asymptomatic patients out in community who are told "no need surgery, wait for symptoms". Majority are not told that when complications occur, the outcomes could be worse off! It is the fine balance of accepting potential morbidity of surgery for asymptomatic gallstones versus morbidity of surgery for cholecystitis/cholangitis/pancreatitis etc. Patients must be given information and they should have a choice. As this comment is qualitative, no edits are made in the manuscript.

Reviewer 2

Comment 1:

This article discussed the need for surgical treatment in patients with asymptomatic gallstones. The present article recommend that an option of cholecystectomy should be discussed with all asymptomatic gallstone patients and it is up to the patient to decide whether to undergo cholecystectomy. However, current guidelines recommended that people with asymptomatic stones do not need treatment unless they develop symptoms. People with asymptomatic gallstone should be actively involved in the process of therapeutic decision making. For people without a medical background, will they make the best therapeutic decision though there is disclosure of material information? Ultimately, does the medical community need to make a policy? If so, what should the policy be?

Response 1:

Thank you for your pertinent and insightful comments. You ask a deep question "if patient will make best therapeutic decision even after disclosure of material information". Our manuscript cannot answer this question, as in current climate, the majority of patients are deprived of the material information! This is the point of coming out with this partly descriptive-partly opinion piece to stimulate surgical community on this common population burden that seems to frequently taken an easy approach "wait for symptoms". In our opinion, this is one sided facts. Majority of patients ought to be told the implications of "waiting" and potential pitfalls. It is

possible that most patients, even with material information, may still decide to “wait for symptoms”, and that is fine. Any person of adult years and sound mind has a right to determine what ought to happen to his or her body and one cannot be considered incompetent or labelled insane if he or she makes an unwise choice. Afterall, we doctors can only recommend therapy based on medical perspective and it is only patient and none other than a patient who knows economical, social, cultural, value-belief, etc many other dimensions that determine his or her choice.

With regards to the policy, it is our opinion that it should be data-driven (if not must). Currently data for asymptomatic gallstones exist in limited medical indications and we have covered it adequately. However, in light of your comments, we have cited the justifications behind current guidelines to better exemplify our points. We have also included a point on the autonomy of patients in the conclusion to address that patients have the right to decide on their treatment even though it may not be the best in the eyes of the medical community or based on scientific evidence.

Thank you

Best regards,

Brian Lee Juin Hsien

Qai Ven Yap

Jee Keem Low

Yiong Huak Chan

Vishal G Shelat