

Cholelithiasis – Biliary Colic CLIFF Peer Review

1. *Strength of evidence presented in CLIFF in modeling the characteristics and mission impact of this medical condition within the spaceflight environment?*

Score: 3

Grading Scale:

4 - *Confident*

3 - *Somewhat confident*

2 – *Neutral*

1 – *Somewhat unconfident*

0 – *Not confident*

2. How confident are you that these data accurately represent the spaceflight environment?	Tables 1, 2 Composite Incidence and Level of Confidence	Table 3, 4 BC/WC Loss of Crew and probability	Table 4 - Clinical Phase 1, 2 durations Table 5 – CP 2 Loss of Crew	Table 4 – RTDC % Table 6 – RTDC Loss of Crew	Table 4 – Loss of Crew Life % Table 7 – Loss of Crew Life, Loss of Crew	Table 8 – TI
Score	3	3	2	3	3	3

Comments and limitations:

1. General comments. This CLIFF covers two related but separate conditions, acute biliary colic and acute cholecystitis. Acute biliary colic often arises from obstruction of the cystic duct by a stone or sludge and results in pain from contractions of the gallbladder. This can also result from dysfunction of the sphincter of Oddi. Risk factors for acute biliary colic are female gender, obesity, abrupt weight changes, hormonal contraception, hypercholesterolemia, sickle cell disease, and malignancies. Astronauts are well screened for many of the risk factors, including the presence of gall stones, and are at lower risk than the general population. If the cause of biliary colic persists, it can lead to infection and acute cholecystitis. There have been no recorded cases of either biliary colic or cholecystitis during spaceflight. The best case for this CLIFF is a course of uncomplicated biliary colic which resolves spontaneously or causes minimal disturbance requiring only symptomatic pain management. The worst case is defined as acute cholecystitis with likely complications requiring significant pain management, antibiotic administration, and likely definitive surgical management.

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2. Incidence. As there are no reports of cases of biliary colic or cholecystitis during spaceflight data, a predictive model for astronauts developed at the Glenn Research Center was used for the composite incidence. This model was developed using data from LSAH (terrestrial astronaut data as well as spaceflight) and several large terrestrial studies. Information from these sources was combined using a Bayesian update approach to estimate the average rate of “severe gallstone disease.” This was the same model that was used in the IMM CLIFF. However, the model looked at biliary pancreatitis, acute cholecystitis, and cholangitis but did not include biliary colic; the latter is included in the best case definition. The worst case condition definitions do not include biliary pancreatitis and cholangitis which were included in the model. This is a limitation of the analysis. From the output of this model an incidence calculation was made. Because of gender differences in incidence noted in the data, separate male and female distributions were calculated. The best case/worst case percentage is based on terrestrial studies indicating that 20-30% of hospitalized gallstone patients, who were otherwise generally healthy, developed acute cholecystitis. This may overestimate the incidence given that some patients with resolved biliary colic may not seek medical assistance or be hospitalized. The clinical phase durations, RTDC and Loss of crew life probabilities are supported by the BC/WC definitions and terrestrial evidence, and I am in agreement with their calculation. The TBC and UTBC RTDC probabilities are set at 0% while TWC and UTWC RTDC probabilities were considered to be 100%, both based on the case definitions. Since sepsis is a separate condition, this possibility is not considered. The probability density curve that was derived appears to be a reasonable representation of the data presented.

3. Clinical phase data. I am in agreement with the clinical phase 1 duration entered in this CLIFF. This data was compiled by a team of expert clinicians, and I was involved in the discussions leading to the calculation of the clinical phase duration. CP2 was supported by terrestrial evidence.

4. Task impairment. The analysis was performed and reviewed by a separate team of expert clinicians. I am aware of the methods that were used but did not directly participate in the discussions.

5. Dependence on mission phase or duration of mission. This medical condition is not dependent on mission phase. However, once an astronaut forms a stone, the likelihood of having a subsequent event increases.

6. Limitations

- There are no instances of symptomatic gall biliary colic during spaceflight among U.S. astronauts. Therefore, terrestrial general population studies and astronaut terrestrial data were modelled and used for incidence and outcomes.
- A limitation to the incidence calculation is that an assumption was made that gallstone disease occurs at some characteristic constant rate over the period of interest without accounting for physiological and environmental risk factors for disease.
- The model looked at biliary pancreatitis, acute cholecystitis, and cholangitis but did not include biliary colic; the latter is included in the best case definition. The worst case condition definitions do not include biliary pancreatitis and cholangitis which were included in the model.
- It is unknown to what extent spaceflight environmental and physiological factors increase the likelihood of the development of symptomatic gallstones in flight.
- Once an astronaut develops a gallstone, it is likely that his/her risk for future stones and complications increases. Thus, this would increase the conditional probability of acute cholecystitis or biliary colic.

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- The best case/worst case percentage is based on a terrestrial study indicating that 20-30% of hospitalized gallstone patients, who were otherwise generally healthy, developed acute cholecystitis. This may overestimate the incidence given that some patients with resolved biliary colic may not seek medical assistance or be hospitalized.
- For worst case scenarios representing complex pathology, the uncertainties around diagnostic and therapeutic capabilities limit the accuracy of risk assessment. For example, ultrasound diagnostic limitations by the operator to assess anatomic measurements (such as common bile duct diameter) can greatly affect diagnosis and prognosis. Likewise, the ability to perform ultrasound-guided percutaneous drainage is a possible capability for long duration missions, but the uncertainty as to its provision limits the precision in risk assessment.

Reviewed by:

David C. Hilmer