

Cervical Spine Fracture 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	2	2	3	3	3

Comments and limitations:

1. **General comments.** Hemorrhoids, with their associated discomfort, are a very common cause of patient complaints. Hemorrhoids can be internal or external to the anal verge and are often found incidentally on physical exam. Grading of internal hemorrhoids is based on the presence of prolapse and reducibility. In this CLIFF, best case is defined as a hemorrhoid that can be treated symptomatically with topical agents or, in the case of internal hemorrhoids, is grade 1-2. Worst case hemorrhoids can not be treated without surgery or hospitalization, have significant complications such as bleeding or thrombosis, or are internal hemorrhoids grades 3-4. There have been 4 reports of hemorrhoids in space, all of which have been best case. Just as on earth, it is possible that many asymptomatic hemorrhoids have occurred in astronauts, but there is no data to determine the number.

2. **Incidence.** A decision was needed to rely on spaceflight data or terrestrial data to determine the composite incidence. Because of the statistical methods that are used to determine the incidence, terrestrial data, with its large sample size, would negate the spaceflight data. For this reason, and the fact that the microgravity environment causes fluid shifts, relative dehydration, and

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frequent constipation, we concluded that the spaceflight data may best reflect the true incidence. Comparing spaceflight and terrestrial studies, it appears that hemorrhoids are 8-15 times more common in microgravity. This is not thought to be unreasonable given the unique microgravity environment. In addition, the wide variance in the spaceflight data better reflects the uncertainty that exists in the estimated incidence value. The best case/worst case probability was based on an average between terrestrial incidence of hospitalization and incidence of grade 3-4 hemorrhoids. Clinical phase durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence, and I am in agreement with their calculation. The probability density curve that was derived appears to be a reasonable representation of the spaceflight 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 should not be dependent on mission phase.

6. Limitations

- Because only 4 cases have occurred in spaceflight, there is considerable uncertainty in the estimated incidence level. Unfortunately, with the statistical methods being used, this data could not be combined with terrestrial and analog studies without unduly influencing the estimated incidence. However, the value that was derived from spaceflight data predicts one case of hemorrhoids approximately every 11.4 person-years which seems reasonable. The spaceflight incidence is notable for being about 8-15 times that of the terrestrial and analog studies which could be a result of the unique physiologic aspects of the spaceflight environment.
- The range of severity of the worst case definition makes calculations of the CP2 duration, RTDC, and Loss of crew life difficult. The WC can range from bleeding or thrombosis from an external hemorrhoid that fails conservative measures but can ultimately be treated to a grade 4 hemorrhoid that cannot be managed in spaceflight and continues to cause morbidity. Despite these limitations, the terrestrial data used was robust; there were good analog studies available; and spaceflight data could be utilized.
- Just as it is likely to be in terrestrial studies, under-reporting for this condition could have been significant during past space missions due to asymptomatic hemorrhoids that may not have been apparent to the crew. This may result in underestimation of the incidence.

Reviewed by:

David C. Hilmers