Traumatic Hypovolemic Shock 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: 2

   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	*2*	*2*	*3*	*3*	*2*	*3*

Comments and limitations:

1. **General comments.** This CLiFF characterizes the risk of traumatic hypovolemic shock during spaceflight. Shock is defined as cellular and tissue hypoxia caused by lack of circulatory perfusion. Most commonly in traumatic events this occurs due to blood loss (hypovolemic shock), but other etiologies include cardiogenic shock (congestive heart failure), distributive shock (anaphylaxis), obstructive shock (cardiac tamponade, pulmonary embolism), septic shock (infections), and neurogenic shock could occur. There have been no reports of traumatic hypovolemic shock during spaceflight. Since this CLiFF considers shock due to trauma, there will be overlap with other trauma CLiFFs (trauma to the head, chest, and abdomen). It is felt that during Artemis missions in which the vehicles are of much smaller size than ISS, the risk of significant trauma that would lead to hypovolemia in microgravity is extremely small. Ideally, this condition would only be applied to non-EVA surface operations since the helmet and hard upper torso of the suit protect the astronaut from severe trauma to the head, chest, abdomen, and, to a lesser extent, to the extremities. However, the current version of IMPACT prevents us segmenting the mission into surface EVA or non-EVA operations. For now, the incidence of this CLiFF will only apply to all surface operations. For purposes of this CLIFF the best case scenario is defined as traumatic hypovolemic shock resulting in

signs of end organ compromise that resolves with fluid resuscitation. The worst case scenario is traumatic hypovolemic shock resulting in signs of end organ compromise that fails to resolve with fluid resuscitation or requires blood transfusion.

2. **Incidence.** There is little spaceflight data that can be utilized to calculate the incidence of traumatic hypovolemic shock as there have only been relatively minor traumatic injuries during spaceflight, and none of them has resulted in hypovolemic shock. In order to calculate the incidence, a study by Johnston in 2019 looked at LSAH astronauts and found 14 hospitalizations due to trauma during that period, none of which occurred during spaceflight. Some of these injuries were likely caused by falls, especially in retired, older astronauts and thus are best applied to spaceflight operations during partial G operations. There are several limitations to using this cohort since it includes an older, population that is frailer than active astronauts. It also is unknown how many of these hospitalizations were for hypovolemic shock, and whether the mechanism of the injury is applicable to spaceflight (auto accident, for example). However, it is felt to be the most representative group to use for incidence. As mentioned in the section above, the risk of trauma severe enough to cause hypovolemic shock is considered to be extremely low in microgravity onboard small vehicles that will be used on Artemis missions, and as compared to a partial gravity environment, such as on the lunar or Martian surface. Since MPRAT currently only has the capability to segment the missions between EVA and non-EVA operations, this incidence will be applied to all surface operations, both on EVA and inside the habitat. This will likely lead to a slight overestimate as the EVA suit will provide protection against blunt chest trauma. The best case/worst case probability split is based on terrestrial studies, including a meta-analysis, that reported organ failure meeting the worst case definition, of between 14.4% and 24% in hemorrhagic shock patients presenting after trauma. The midpoint of these studies is 20% and was chosen as the WC probability. This could be an overestimate given the healthier astronaut population, but this is offset by the relatively hypovolemic state of astronauts in low gravity environments. The clinical phase durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence and case definitions. RTDC used the need for surgery or blood transfusion as a surrogate per the case definitions. There is a paucity of data in the untreated cases, and expert opinion was relied upon to estimate the Loss of crew life in these instances.

3. **Clinical phase data**. I am in agreement with the clinical phase durations 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 durations.

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 is dependent on mission phase as it is only applicable to surface operations under partial G conditions.

6. **Limitations**

- There is currently no documented incident of traumatic hypovolemic shock during spaceflight. There is also no suitable analog population as etiologies of trauma in spaceflight are dissimilar to those in military or terrestrial environments. However, the Johnston paper, which reports trauma of astronauts outside of their spaceflight duties, has been used as a surrogate. This may include injuries from elderly astronaut falls, may

include hospitalizations that did not result in traumatic hypovolemic shock and may also include injuries that are only possible terrestrially (e.g. gunshot wounds). Therefore, this is likely overestimating the incidence, and therefore should only be applied for surface-based operations (partial G) as the incidence of trauma will be markedly lower in microgravity.

- This medical condition is constrained by mission segment. The incidence is assumed to be zero during microgravity operations and is only applied during surface operations.
- During Artemis missions in which the vehicles are of much smaller size than ISS, the risk of significant trauma that would lead to hypovolemia in microgravity is extremely small. Ideally, this condition would only be applied to non-EVA surface operations since the helmet and hard upper torso of the suit protect the astronaut from severe trauma to the head, chest, abdomen, and, to a lesser extent, to the extremities. However, the current version of IMPACT prevents us from segmenting the mission into surface EVA or non-EVA operations. For now, the incidence of this CLiFF will only apply to all surface operations.
- Since this CLiFF considers shock due to trauma, there will be overlap with other trauma CLiFFs (trauma to the head, chest, and abdomen).
- For WC/BC scenarios, due to the fundamental differences between the terrestrial and space environments, probability data is most likely not transferable. The BC/WC could be an overestimate given the healthier astronaut population, but this is offset by the relatively hypovolemic state of astronauts in low gravity environments.
- According to current ATLS guideline, those with Class II hemorrhage or above would most likely require blood transfusion. Current treatment guidelines also recommend repleting intravascular volume with blood products as soon as possible following all cases of traumatic hypovolemic shock. However, in space, blood products are unlikely to be readily available, and therefore crews would rely heavily on IVF for hypovolemia treatment. Consequently, treatment data from terrestrial literature are not ideal representations of scenarios that could happen during spaceflight. It is also difficult to assign treatment durations, RTDC, and Loss of crew life for untreated scenarios as the presence of continued blood loss would greatly alter the outcomes.
- There is a paucity of data in the untreated cases, and expert opinion was relied upon to estimate the Loss of crew life in these instances.

Reviewed by:

David C. Hilmers