

Acute Coronary Syndrome 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	4	3	3	3	3	3

Comments and limitations:

General comments. Acute coronary syndrome (ACS) refers to a condition in which there is a suspicion or confirmation of acute myocardial ischemia or infarction. Typical symptoms may include chest pain; radiation of the pain to the arms, jaw, neck, back or stomach; shortness of breath; dizziness/lightheadedness; nausea; and sweating. In the past ACS has been categorized as non-ST-elevation myocardial infarction (NSTEMI), ST-elevation MI (STEMI), or unstable angina (UA). It is now possible to classify more patients who would formerly have been diagnosed with UA as having an NSTEMI through the use of high sensitivity troponin blood testing. Troponin testing has not been available during previous spaceflights, and it is unclear whether this will be an onboard diagnostic tool in the near future. Lack of troponin testing makes it more difficult to distinguish between UA and NSTEMI. On board telemetry monitoring may make it possible to determine if a STEMI has occurred. Most patients who have ACS should undergo risk stratification and possible treatment with cardiac catheterization. There have been no documented cases of ACS during spaceflight although there is one report where ACS was suspected. Although “silent ischemia” does occur, most cases of ACS are symptomatic; therefore, it is unlikely that there has been under-reporting of this condition by astronauts. Astronauts are also closely monitored before and after flight, and it is

Acute Coronary Syndrome CLIFF Peer Review

unlikely that this condition would go undiagnosed. The best case is considered to be unstable angina (unable to exercise without symptoms), or myocardial infarction that can be treated successfully with medications, without clinical signs of congestive heart failure (CHF). The worst case is a myocardial infarction resulting in a crewmember suffering signs of symptomatic CHF. Cardiogenic shock is a separate condition.

2. Incidence. Since there is no spaceflight data available, the incidence calculation was based on a tool for analyzing the risk of ACS/CVA in astronauts called the Astro-CHARM score. This tool utilizes cardiac risk factors and coronary artery calcium scores to estimate the overall 10-year risk in this healthy population. The authors were able to obtain the Astro-CHARM scores for all active duty astronauts. The composite risk was then reduced by eliminating the rate of CVA. From this, a probability distribution was derived that estimates the incidence of ACS. This was felt to be a much better predictor of ACS risk in astronauts than using terrestrial studies that survey the general population. The best case/worst case probabilities used data from two fairly large terrestrial studies that examined outcomes (progression to heart failure) in patients with ACS. The clinical phase durations, return to definitive care (RTDC) and Loss of Crew Life probabilities are supported by terrestrial evidence, and I am in agreement with their calculation. RTDC was determined to be 100% in all cases by the clinical science team. 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 although underlying coronary heart disease may become symptomatic or unmasked during heavy exertion.

6. Limitations

- Terrestrial incidence publications were sourced entirely from DynaMed. No other search engines were utilized.
- The maximum duration for the untreated scenarios is informed by an observational study of 158 patients (75% male, average female age 61.4, average male age 59.2) with angina. There was no categorization of stable vs. unstable angina in this study, and it could be assumed that the longer durations represent stable angina (which is not included in the definition of this condition).
- There is a paucity of data regarding the untreated worst-case scenario probability of LOCL as defined by this CLIFF.
- RTDC probability was assigned to be 100% for both minimum and maximum for all scenarios. In the best-case scenarios, although there are cases of UA/NSTEMI that can successfully be treated with medical management only, the standard of care is cardiac catheterization to risk stratify and to seek a reversible cause of ACS. However, it is possible that there may be cases that do not require further intervention (e.g. stenting, etc.) and could therefore survive without RTDC. The minimum probability of 100% may be an overestimation in these cases, but it was felt by the editor that all ACS cases

Acute Coronary Syndrome CLIFF Peer Review

warrant RTDC for a higher level of care including cardiac catheterization. The ExMC Clinical and Science Team pre-determined that the probability of RTDC for the worst-case scenarios is 100%.

Reviewed by:

David C. Hilmer