Application of the Altshock-2 randomized trial enrollment criteria to the Altshock-2 registry population: are we missing someone?

M. Milani1, M. Pagnesi2, G. Tavecchia1, M. Bertaina3, S. Frea4, G.M. De Ferrari4, A. Sacco5, G. Tavazzi6, C. Colombo6, A. Pullara6, L. Villanova1, C. Sorini Dini7, S. Valente5, N. Morici8, F. Pappalardo6

1ASST Great Metropolitan Niguarda, Milan, Italy
2Civil Hospital of Brescia, Brescia, Italy
3Torino North Emergency San Giovanni Bosco, Turin, Italy
4A.O.U. San Giovanni Battista Molinette, Turin, Italy
5I.R.C.C.S. San Matteo Polyclinic, Pavia, Italy
6SS. Antonio E Biagio E Cesare Arrigo Hospital, Alessandria, Italy
7Senese University Hospital, Siena, Italy
8Don Gnocchi Foundation - IRCCS Centro S. Maria Nascente, Milan, Italy

On behalf of Altshock-2 investigators

Funding Acknowledgements: None.

Background: The Altshock-2 randomized trial is currently enrolling patients with acute decompensated heart failure (ADHF)-related cardiogenic shock (CS), randomizing them to early intra-aortic balloon pump (IABP) or standard of care. Concomitantly, the prospective observational Altshock-2 registry is collecting data on consecutive patients with CS. Due to the recent changes in the Society for Cardiovascular Angiography and Interventions (SCAI) shock stages and their value in ADHF scenario, inclusion and exclusion criteria of the trial have been modified in a dedicated protocol amendment (January 31st, 2023). How this change could impact on patients’ enrollment in the trial is unknown.

Purpose: To identify patients enrolled in the Altshock-2 registry who met the inclusion and exclusion criteria of the Altshock-2 trial, applying original and new criteria (i.e. before and after protocol amendment).

Methods: Among the 354 patients with CS enrolled in the Altshock-2 registry up to August 31st, 2022, 121 patients (34.2%) with ADHF-CS were considered for the present analysis and evaluated for potential enrollment in the Altshock-2 trial according to old and new inclusion and exclusion criteria.

Results: Application of the original inclusion criteria of the Altshock-2 trial selected 51 patients (42.1%) potentially eligible for inclusion in the trial (i.e. age ≤75, hypotension or need of vasoactive drugs, pre-existing diagnosis of heart failure with left ventricular ejection fraction ≤35%, at least one criterion of overt hypoperfusion). The subsequent application of the original exclusion criteria resulted in 29 patients (24.0%) who did not meet exclusion criteria and were therefore eligible for enrollment in the trial. Detailed reasons for inclusion and exclusion are reported in Figure 1. Application of new inclusion criteria selected 61 patients (50.4%) potentially eligible for inclusion in the trial (i.e. age ≤75, need of vasoactive drugs, left ventricular ejection fraction ≤35%, SCAI class B-D according to the updated 2022 CS Working Group definition). Subsequent application of the new exclusion criteria resulted in 58 patients (47.9%) who did not meet exclusion criteria and were therefore eligible for enrollment in the trial. Detailed reasons for inclusion and exclusion are reported in Figure 2.

Conclusions: Among 121 patients with ADHF-CS enrolled in the Altshock-2 registry, application of the original inclusion and exclusion criteria of the Altshock-2 trial identified a subset of 29 patients (24%) who could be suitable for enrollment in the trial. Application of the new inclusion and exclusion criteria selected a higher proportion of patients (58 patients, 47.9%) potentially suitable for enrollment in the trial. These data highlight the challenge of performing randomized trials in ADHF-CS as the timely identification of patients is yet a major issue, despite admission to centers who are actively participating in clinical research.
**Old inclusion and exclusion criteria**

- **ADHF:** 121 patients
  - age > 75: 18 patients
  - ADHF + age ≤ 75: 103 patients
    - LVEF > 35: 39 patients
    - ADHF + age ≤ 75 + LVEF ≤ 35%: 64 patients
      - SCAI A-B: 11 patient
        - Missing SCAI class: 2 patients
        - ADHF + age ≤ 75 + LVEF ≤ 35% + SCAI C-D-E: 51 patients

- **ADHF + age ≤ 75 + LVEF ≤ 35% + SCAI C-D-E:** 51 patients
  - CS sympotms > 6 hours: 19 patients
  - ADHF + age ≤ 75 + LVEF ≤ 35% + SCAI C-D-E - symptoms > 6 hours: 32 patients
  - OHCA: 2 patients
  - ADHF + age ≤ 75 + LVEF ≤ 35% + SCAI C-D-E - symptoms > 6 hours - OHCA: 30 patients
    - Severe aortic stenosis: 1 patient

- **ADHF + age ≤ 75 + LVEF ≤ 35% + SCAI C-D-E - symptoms > 6 hours - OHCA - AoS:** 29 patients

**New inclusion and exclusion criteria**

- **ADHF:** 121 patients
  - age > 75: 18 patients
  - ADHF + age ≤ 75: 103 patients
    - LVEF > 35: 39 patients
    - ADHF + age ≤ 75 + LVEF ≤ 35%: 64 patients
      - SCAI A: 1 patient
        - Missing SCAI class: 2 patients
        - ADHF + age ≤ 75 + LVEF ≤ 35% + SCAI B-C-D-E: 61 patients

- **ADHF + age ≤ 75 + LVEF ≤ 35% + SCAI B-C-D-E:** 61 patients
  - OHCA: 2 patients
  - ADHF + age ≤ 75 + LVEF ≤ 35% + SCAI B-C-D-E - OHCA: 59 patients
    - Severe aortic stenosis: 1 patient
  - ADHF + age ≤ 75 + LVEF ≤ 35% + SCAI B-C-D-E - OHCA - AoS: 58 patients