



Cardiogenic Shock and Adrenal Insufficiency

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A critical illness patient suffering from adrenal insufficiency (AI) can be considered rare. An AI could be associated with several conditions such as septic shock, hemorrhagic shock, and HIV infection¹. Morbidity and mortality outcomes were significantly associated with cardiogenic shock (CS). Patients with adrenal insufficiency have the worst prognosis for CS. On the other hand, AI patients are at risk of serious cardiac complications in the hospital, including heart failure and cardiogenic shock². CS and cardiac arrest are associated with high mortality rates³. AI frequently occurs in a patient with cardiogenic shock^{4,5}. Relative AI was related to low shock-related mortality. Until now, there is little evidence linking AI with cardiogenic shock.

A meta-analysis was conducted to determine if there is an association between AI and cardiogenic shock.⁶ A total of five studies that were observational cohort studies were included in the analysis. According to the Newcastle–Ottawa scale, no study scored well on quality. Furthermore, all studies did not adequately report results like death rates, survival rates, and complications.^{1, 7-10} The Meta-analysis included 285 patients with documented AI in CS. The five eligible studies included in the metanalysis showed the following results. In Bagate et al.2017, adrenal insufficiency was reported at 37% [95% CI; 27%-47%]⁸. According to Miller et al.2008, 12% [95% CI; 5% - 21%] were reported¹⁰. Tol et al.2014 reported 43% [95% CI; 25% - 62%], whereas Kim et al. 2006 reported 43% [95% CI; 25% - 62%]^{1,9}. The Pene et al.2004 report reported 51% [38%-64%]⁷. The pooled random-effects estimate of AI prevalence was 36%, with 95% confidence intervals of 22% - 51%, with significantly high heterogeneity throughout (I² = 83%). A publication bias was detected by Egger's and Begg's correlation tests (p-value = 0.527 and 0.435, respectively). Funnel plots were used to assess publication bias⁶.

The prevalence of primary AI was 36% of CS cases (95 % CI: 23%-51%). This meta-analysis found adequate quality studies on the topic, providing evidence for future AI studies in CS.

However, this meta-analysis also included only a small number of studies, so the value of knowing about outcomes and adverse events related to adrenal function in CS was limited⁶. A meta-analysis examined AI after applying a range of CS types across a broad range of diseases. AI prevalence ranges between 11% and 51%⁶. In a study conducted by Pene et al. in 2005, high AI is associated with a poor prognosis of shock-related mortality⁷. Furthermore, Kim et al. (2006) reported an association between relative AI and a higher mortality rate following cardiac arrest. When analyzed by regression modeling, patients with relative AI have poor outcomes⁹. Additionally, using ROC curves to select the optimal thresholds, Bagate et al.'s 2016 study found that high mortality was significantly predicted by T0 > 798 nmol/L (T0=cortisol level immediately before short corticotropin test) and <Δ max 473 nmol/L (Δ max =differences between highest value 30 or 60 minute after corticotropin stimulation and T0)⁸. Tol et al. (2014) found that adrenal responsiveness does not predict mortality independently¹. The Miller study et al. 2007 found that in most post-cardiac arrest patients, absolute AI was not considered in the vasopressor-dependent shock¹⁰. The meta-analyses indicate that AI is likely associated with high heterogeneity. There was little information available on outcomes⁶. The meta-analysis had certain limitations that need further discussion: Initially, the characteristics of the included studies were inconsistent, including characteristics of patients, etiologies, and methods. In addition, the small number of studies included in the meta-analysis led to a relatively small pooled sample size, which further limited the meta-analysis result. The retrospective cohort study is the major limitation of this meta-analysis.

Based on the available literature, further research is needed to investigate the risk of AI following CS. Future studies should include a prospective design and a sufficient sample size to estimate the prevalence of AI in CS. Additionally, future research should include multicenter studies with randomized controlled settings and outcomes including all possible outcomes.

References

1. Tol MM, Shekar K, Barnett AG, et al. A preliminary investigation into adrenal responsiveness and outcomes in patients with cardiogenic shock after acute myocardial infarction. *J Crit Care*. Jun 2014; 29(3):470 e1-6. doi:10.1016/j.jcrc.2014.01.020
2. Fede G, Spadaro L, Tomaselli T, et al. Adrenocortical dysfunction in liver disease: a systematic review. *Hepatology*. Apr 2012; 55(4):1282-91. doi:10.1002/hep.25573
3. Wang CH, Chen YS, Ma MH. Extracorporeal life support. *Curr Opin Crit Care*. Jun 2013; 19(3):202-7. doi:10.1097/MCC.0b013e32836092a1
4. Rucker G, Schwarzer G, Krahn U, König J, Schwarzer MG. Package 'netmeta'. *Network Meta-Analysis using Frequentist Methods (Version 07-0)*. 2015;
5. Sivukhina EV, Poskrebysheva AS, Smurova Iu V, et al. Altered hypothalamic-pituitary-adrenal axis activity in patients with chronic heart failure. *Horm Metab Res*. Oct 2009; 41(10):778-84. Doi: 10.1055/s-0029-1224182
6. Nso N, Nassar M, Baraka B, Mbome Y, Alfishawy M. Adrenal Insufficiency in patients with cardiogenic shock: A meta-analysis. *Diabetes Metab Syndr*. Nov-Dec 2021; 15(6):102274. doi:10.1016/j.dsx.2021.102274
7. Pene F, Hyvernats H, Mallet V, et al. Prognostic value of relative adrenal insufficiency after out-of-hospital cardiac arrest. *Intensive Care Med*. May 2005; 31(5):627-33. Doi: 10.1007/s00134-005-2603-7
8. Bagate F, Lellouche N, Lim P, et al. Prognostic Value of Relative Adrenal Insufficiency during Cardiogenic Shock: A Prospective Cohort Study with Long-Term Follow-Up. *Shock*. Jan 2017; 47(1):86-92. doi:10.1097/SHK.0000000000000710
9. Kim JJ, Lim YS, Shin JH, et al. Relative adrenal insufficiency after cardiac arrest: impact on postresuscitation disease outcome. *Am J Emerg Med*. Oct 2006; 24(6):684-8. doi:10.1016/j.ajem.2006.02.017
10. Miller JB, Donnino MW, Rogan M, Goyal N. Relative adrenal insufficiency in post-cardiac arrest shock is under-recognized. *Resuscitation*. Feb 2008; 76(2):221-5. doi:10.1016/j.resuscitation.2007.07.034