INFOLETTER 5

25 April 2022

Peak troponin concentration might be a predictor for weaning from VA-ECMO after MI

Patient selection for an ECMO treatment to avoid futile cannulations is challenging. A retrospective study from Minneapolis Heart Institute evaluated the use of peak troponin I for the prediction of successful weaning from VA-ECMO in patients with refractory CS after acute MI. A total of 62 patients were included, 62% out of which presented with STEMI. Weaning was successful in 45 of them (group I), the rest (group II) either died (n=10) or received a durable LVAD (n=7). In group I, peak troponin I was significantly lower (89 vs. 434ng/mL, P=0.0001), with a ROC analysis showing a cutoff of 400 ng/mL correctly classifying 90 % patients (sensitivity 71%; specificity 98%). Only one patient was able to successfully wean with troponin I greater than 400ng/mL. Each increase of 50 ng/mL decreased the likelihood of weaning by 33%.

Cardiac troponins are a single, ubiquitous biomarker that is directly linked with the underlying pathology and might be used as an estimator of infarct size, the extent of myocyte injury, and residual LVEF. Although lactate was mentioned as a weaning predictor in previous literature, in the present study it was not associated with a decannulation success (AUC 0.567 [0.393, 0.741]). The authors suggested a troponin I cutoff value of 400 ng/mL. The higher concentration should prompt discussions about either advanced weaning strategies with durable LVADs or heart transplantation, or withdrawal of care rather than prolonged ECMO runs. Larger, multicenter studies are needed to validate these findings.

North, M., Eckman, P., Samara, M., Chavez, I., Schmidt, C., Garberich, R., & Hryniewicz, K. (2021). Peak troponin predicts successful weaning from VA ECMO in patients with acute myocardial infarction complicated by Cardiogenic shock. The International Journal of Artificial Organs, 45(1), 68–74. https://doi.org/10.1177/0391398821991155

Prone-positioning during ECMO for ARDS improves survival

Prone-positioning is one of the most effective treatments for severe acute respiratory distress syndrome (ARDS) in mechanically ventilated patients. In those on ECMO, the evidence is more limited. In a retrospective, single-center study from Paris researchers analyzed the data from the past 8 years. They used a propensity score-matched analysis to compare 64 prone-positioned patients on veno-venous ECMO (VV-ECMO) for ARDS with their 234 non-positioned counterparts. After 90 days from cannulation, more patients were weaned and alive in the positioned group (0.75 vs 0.54, p = 0.03; subdistribution hazard ratio [95% CI], 1.54 [1.05–2.58]) and the 90-day mortality was lower (20% vs 42%, p < 0.01). ECMO duration and complications were comparable. Prone-positioning non-responders (an increase of the static compliance lesser than 3 mL/cm H2O after 16 hours of positioning) composed 47% of the group and had higher percentages of nonaerated or poorly aerated

ventral and medial-ventral lung regions (p = 0.047) on a CT scan before positioning. This finding might help identify patients, who will have the greatest benefit from prone-positioning during ECMO.

The authors stressed the fact that prone positioning in this setting was safe and no ECMO-related complications were noted in the positioned group, notably, no accidental extubation or decannulation occurred during positioning. They argued that the strategy combines two advantages - prone-positioning homogenizes the distribution of transpulmonary pressure, thereby mitigating the ventilator-induced lung-injury risk attributable to alveolar overstretching and cyclic atelectasis and VV-ECMO further protects the injured lung by applying “ultraprotective” ventilation. Indeed, the probability of being weaned from ECMO and alive was greater in the prone-positioned group, however, further prospective randomized clinical trials are needed.

Petit, M., Fetita, C., Gaudemer, A., Treluyer, L., Lebreton, G., Franchineau, G., Hekimian, G., Chommeloux, J., Pineton de Chambrun, M., Brechot, N., Luyt, C.-E., Combes, A., & Schmidt, M. (2021). Prone-positioning for severe acute respiratory distress syndrome requiring extracorporeal membrane oxygenation. *Critical Care Medicine*, *50*(2), 264–274. https://doi.org/10.1097/ccm.0000000000005145

ECMO in cancer patients remains controversive

ECMO is generally used in a highly selected population and its use in patients with severe comorbidities is limited. The present study evaluated a total of 297 cancer patients (median age 56, 72% male, 54% had a solid tumor, 47% a hematologic malignancy) who were treated by VV-ECMO for severe respiratory failure. After 60 days, only 26,8% were alive (95% CI 22.1–32.4%). Independent adverse prognostic factors for overall survival included low platelet count (HR 0.997, 95% CI 0.996–0.999; P = 0.0001 per 1000 platelets/µl), elevated lactate levels (HR 1.048, 95% CI 1.012–1.084; P = 0.0077), and disease status (progressive disease [HR 1.871, 95% CI 1.081–3.238; P = 0.0253], newly diagnosed [HR 1.571, 95% CI 1.044–2.364; P = 0.0304]). Overall, based on a propensity score-matched analysis with patients who received mechanical ventilation only, there was no significant survival advantage for the ECMO treatment.

However, even though the retrospective statistical analysis did not show benefit, a minority of patients achieved long-term survival after VV-ECMO. According to the authors, the prognosis of cancer patients in this setting therefore should not generally be regarded as futile. However, prognostic tools for better candidate selection are needed. They also observed a high rate of severe bleeding episodes (38%), which was associated with thrombocytopenia and recent chemotherapy, making thrombocytopenia a factor to seriously consider before cannulation. Since increased bleeding-related complications seem to be an important contributing factor for poor outcomes in thrombocytopenic patients, further improvements in coagulation and bleeding management are needed.

Kochanek, M., Kochanek, J., Böll, B., Eichenauer, D. A., Beutel, G., Bracht, H., Braune, S., Eisner, F., Friesecke, S., Günther, U., Heinz, G., Hallek, M., Karagiannidis, C., Kluge, S., Kogelmann, K., Lebiedz, P., Lepper, P. M., Liebregts, T., Lueck, C., … Shimabukuro-Vornhagen, A. (2022). Veno-venous extracorporeal membrane oxygenation (VV-ECMO) for severe respiratory failure in adult cancer patients: A retrospective multicenter analysis. *Intensive Care Medicine*, *48*(3), 332–342. https://doi.org/10.1007/s00134-022-06635-y

Lactate level predicts survival on VA-ECMO the strongest while taken on the third day

Elevated serum lactate is associated with a worse prognosis while on VA-ECMO for cardiogenic shock. However, according to the present study, the prognostic significance relies on the timing. In this study, lactate was measured before ECMO initiation and on days 1, 3, 5, and 10. Out of a total of 238 patients, 54.2% were successfully weaned and 41.2% were discharged alive. Both weaned and discharged alive subjects had a significantly lower lactic acid level pre-ECMO and at days 1,3 and 5 when compared with unsuccessfully weaned patients or those who died. Absolute lactate concentration on day 3 was a superior predictor of hospital survival than pre-ECMO and day 1 measurements, as well as a reduction from pre-ECMO value to day 1 or day 3. The cut-off value associated with hospital survival was ≤ 1.7 meq/L.

Overall, the magnitude of lactate reduction was a weaker predictor of the outcome than absolute levels. The investigators pointed out that there is so much emphasis, including the attempts to make a clinical prognosis, based on pre-ECMO lactate, while the lactate level well into ECMO support was more meaningful for prognosis. However, the study is limited by its retrospective, single-center design.

Omar, H. R., Handshoe, J. W., Tribble, T., & Guglin, M. (2021). Survival on venoarterial extracorporeal membrane oxygenation in cardiogenic shock. *ASAIO Journal*, *Publish Ahead of Print*. https://doi.org/10.1097/mat.0000000000001413

Whole body CT after ECPR might help to find hidden pathologies and should be protocolized

Hidden pathologies might contribute to the high morbidity and mortality of patients resuscitated with ECPR. The utility of screening for compression-related injuries, cannulation-related complications, etiology of cardiac arrest, incidental findings, and evidence of hypoxic brain injury with the whole-body computed tomography (WBCT) post ECPR was evaluated in a single-center retrospective study. Clinically significant findings were present in all but one out of 38 patients with a mean of 3.3 ± 1.7 findings per patient. Intervention as a direct result of the finding was performed in 54% (20/37). Evidence of a hypoxic brain injury was seen on WBCT of 15 patients and was associated with clinical brain death more often than in a group without such finding (67% vs. 4%).

The investigators pointed out a high frequency of an intervention prompted by a WBCT finding, that could have gone missed without the imaging. They, therefore, advocate for a protocolized use of WBCT in all ECPR patients, ideally as soon as possible after the cannulation to maximize the available window to perform time-sensitive interventions as a result of imaging findings. The most common finding was compression-related injury e.g. rib fracture (79%), although rarely intervened. On the other hand, life-threatening and potentially occult compression-related liver injury was also detected. Acording to the authors, the benefit of early WBCT after ECPR likely outweighs the risks of contrast and radiation exposure and manipulation risks. Additionally, WBCT serves as a prognostic modality for the development of brain death. Further investigation regarding the survival impact that WBCT provides is needed.

Osofsky, R., Owen, B., Elks, W., Das Gupta, J., Clark, R., Kraai, E., Rana, M. U. A. A., Marinaro, J., & Guliani, S. (2021). Protocolized whole-body computed tomography imaging after extracorporeal membrane oxygenation (ECMO) cannulation for cardiac arrest. *ASAIO Journal*, *67*(11), 1196–1203. https://doi.org/10.1097/mat.0000000000001516

Durable Mechanical Circulatory Support in Myocarditis is Feasible with Good Outcomes, but a Full Recovery was Rare

Severe myocarditis may warrant a durable mechanical circulatory support (MCS). The retrospective study analyzed data from the IMACS registry and the myocarditis patients (n=180), who formed 1.3% of the registry population, were compared with nonischemic cardiomyopathy (NICM) cases (n=6 602). Heart failure lasted less than a month in 22% of myocarditis patients, 1-12 months in 22,6%, and more than a year in 55,4%. Myocarditis patients were younger than those with NICM (45 vs. 52 years, $P < 0.001$), were more often implanted with INTERMACS profile 1 (30% vs. 15%, $P < 0.001$) and a biventricular mechanical support (BIVAD) was used more frequently (18% vs. 6.7%, $P < 0.001$). Postimplant survival was comparable to NICM for both LVAD and BIVAD, but the myocarditis patients recovered more often when assessed 1 year after the implantation with no difference by the duration of HF (5% vs. 1.7%, $P = 0.0003$). Adverse events (bleeding, infection, and neurologic dysfunction) were all lower in the myocarditis than NICM.

The authors concluded that while myocarditis patients were initially sicker with an approximately three times higher need for BIVAD, long-term outcomes were generally good, and successful explantation within a year was more common than in NICM, although overall rare. Although right ventricle (RV) impairment is common in myocarditis, there was no difference in overall survival between myocarditis and NICM whether they received isolated LVAD or BIVAD, suggesting that level of RV involvement varies among patients, and that carefully selected patients with myocarditis can do well with isolated LVAD. Further studies are needed to identify the subgroup of patients with myocarditis who do not require RV support. The low recovery rate suggests that once current criteria for advanced HF are met

in patients with myocarditis, they are unlikely to recover. Heart transplantation, therefore, should not be delayed in these patients, especially given the risk of early and late right ventricular failure.

HF.Al-Kindi, S. G., Xie, R., Kirklin, J. K., Cowger, J., Oliveira, G. H., Krabatsch, T., Nakatani, T., Schueler, S., Leet, A., Golstein, D., & Elamm, C. A. (2021). Outcomes of durable mechanical circulatory support in myocarditis. *ASAIO Journal*, *Publish Ahead of Print*. https://doi.org/10.1097/mat.0000000000001430

Partial Flow in Carefully Selected VA-ECMO Patients with Refractory CS Provides the Same Survival and End-Organ Perfusion as Full Flow

Optimal VA-ECMO flow in cardiogenic shock needs to be individually selected, with sufficient perfusion on one side and the risk of an increased left ventricle afterload, distention, and intracardiac stasis on the other. A single-center retrospective propensity score-matched analysis compared outcomes of patients with a full flow (flow index > 2.2 L/min/m2; n=405) with those with a partial flow (flow index < 2.2 L/min/m2; n=83). In-hospital mortality was comparable (51% vs. 55%, p = 0.59) and there was no difference in the change in renal, hepatic function, or lactate level, nor in the rates of continuous venovenous hemofiltration initiation (p = 0.41) at 72 hours post-implant. Regarding hemodynamics, a statistically non-significant trend of less common LV distention requiring LV vent placement was noted in the partial flow group (12% vs. 7%, p = 0.16).

All the data were collected in a single-center, where a partial flow strategy with flow titration is being gradually implemented. The investigators suggest that in patients who can tolerate partial flow VA ECMO from a hemodynamic and tissue perfusion standpoint, partial flow in conjunction with native cardiac output does not compromise the outcome, however, not all patients may be suitable candidates for partial flow VA-ECMO. By reducing the necessity for further LV vent devices, such as IABP or Impella, one would also expect a reduction in the complications associated with using such devices, though this study was not designed to measure such a difference.

Singh, S. K., Ning, Y., Kurlansky, P., Kaku, Y., Naka, Y., Takayama, H., Sayer, G., Uriel, N., Masoumi, A., Fried, J. A., & Takeda, K. (2021). Impact of venoarterial extracorporeal membrane oxygenation flow on outcomes in cardiogenic shock. *ASAIO Journal*, *68*(2), 239–246. https://doi.org/10.1097/mat.0000000000001462

Invasive strategy in OHCA involving intraarrest transport and ECPR. An effect on neurologic outcome of a comprehensive approach. The Prague OHCA Study.

The prognosis of a refractory out-of-hospital cardiac arrest (OHCA) is generally poor but new invasive approaches are being tested. The effect of an intra-arrest transport to a cardiac center, ECPR, and immediate invasive investigation and therapy was evaluated in a clinical

trial from Charles University in Prague. A total of 256 patients with witnessed refractory OHCA were electronicall randomized during an ongoing chest compressions to either invasive or standard approach, i.e. regular advanced cardiac life support on-site. The trial was stopped at the recommendation of the data and safety monitoring board when prespecified criteria for futility were met before reaching the goal of 285 subjects. Survival with neurologically favorable outcome (CPC 1-2) at 180 days occurred in 31.5% of the invasively treated group vs. 22.0% in those with standard resuscitation care (OR 1.63 [95% CI, 0.93 to 2.85]; difference, 9.5% [95% CI, −1.3% to 20.1%]; P = 0.09.) However, considering wide confidence intervals in the between-group difference for the primary outcome, the study may have been underpowered to detect a clinically important difference in favor of the invasive strategy group. Neurologic recovery (CPC 1-2 at any time within the first 30 days) was significantly more common with invasive approach - 30.6% vs 18.2% patients (OR, 1.99 [95% CI, 1.11 to 3.57]; difference, 12.4% [95% CI, 1.9% to 22.7%]; P = 0.02), and cardiac recovery at 30 days (no need for pharmacological or mechanical cardiac support for at least 24 hours) was seen in 43.5% vs 34.1% (OR, 1.49 [95% CI, 0.91 to 2.47]; difference, 9.4% [95% CI, −2.5% to 21%]; P = 0.12). Bleeding was more common with invasive strategy (31% vs 15%).

Patients were randomized after approximately 25 minutes of ongoing cardiac arrest, thus including 15 minutes of advanced cardiac life support. Based on the author's suggestion, this is a reasonable time to consider rescue interventions such as ECPR followed by immediate coronary reperfusion. Patients experienced true refractory OHCAs, with majority being resuscitated for more than 45 minutes in both groups while a still substantial proportion of patients ultimately achieved sustained return of spontaneous circulation. An ongoing question remains as to whether it is possible to identify patients early during CPR who may ultimately benefit from such an approach. Although the trial did not show the significant benefit of the invasive approach compared to standard, a twice higher survival in standard strategy arm was observed. This phenomenon may be attributed to a very high level of bystander and telephone assissted CPR provided and intensive team training for the invasive strategy improving outcome similarly in the standard strategy group. Overall excellent outcome of 27% CPC 1-2 survival in the whole study, 48% in shockable rhythm subgroup of the invasive arm and 22% in ECPR cohort was noted. The obvious benefit of the invasive approach was pronounced most in the subgroup of patients resuscitated more than 45 minutes.

Belohlavek, J., Smalcova, J., Rob, D., Franek, O., Smid, O., Pokorna, M., Horák, J., Mrazek, V., Kovarnik, T., Zemanek, D., Kral, A., Havranek, S., Kavalkova, P., Kompelentova, L., Tomková, H., Mejstrik, A., Valasek, J., Peran, D., Pekara, J. et al. Effect of intra-arrest transport, extracorporeal cardiopulmonary resuscitation, and immediate invasive assessment and treatment on functional neurologic outcome in refractory out-of-hospital cardiac arrest. JAMA, 327(8), 737. https://doi.org/10.1001/jama.2022.1025