

Organ injury scaling 2018 update: Spleen, liver, and kidney

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Dear Editor,

The AAST patient assessment committee has recently published “Organ injury scaling 2018 update: spleen, liver and kidney.” We appreciate the continual efforts of the committee to refine and improve the grading system, and we are excited to check a lot of anticipated changes to the nephritic trauma grading once in nearly three decades, addressing a variety of challenges that had become apparent over the years.

Initially outlined in 1989, the Organ Injury Scaling was basically and primarily based on the anatomic findings encountered mostly at the time of open exploration of the eviscerate organ; however, currently, with advances in CT technology and its widespread use, incorporating key radiologic findings within the grading system was logical. Incorporating the vascular supply is additionally a vital addition to the grading system. A depth of parenchymal laceration of 1 cm is used to separate grade 2 and 3 injuries. However, the principle behind selecting this cut for this purpose is unclear, and it should be capricious. Laceration depth offers very little information in predicting the requirement for interventions once further information like hematoma size and vascular distinction extravasation are obtainable. Another ambiguity is the use of segmental vein or artery injury within the organization, it is unclear if segmental injury is the description of vascular anatomy, one among the 5 segmental nephritic arteries supplying the kidneys.

Taken along, these updates within the nephritic injury grading replicate a number of this evidence in management of renal trauma. Anyone is required to know the implications of these changes and learn whether or not this updates grading system can improve the prediction of outcomes. Prophetic tools like normograms and a lot of objective criteria ought to be used in clinical follow-up to pick out patients who would have the benefit of interventions from trauma management after nephritic trauma.

DISCLOSURE

The author declares no funding or conflicts of interest.

J Trauma Acute Care Surg
Volume 89, Number 6

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Fibrinolytic therapy in patients with COVID-19 and acute respiratory distress syndrome: Is this a feasible approach?

To the Editor:

In late December 2019, several local health facilities reported clusters of patients with pneumonia of unknown cause that were epidemiologically linked to a seafood and wet animal wholesale market in Wuhan, Hubei Province, China.¹

Deep sequencing analysis from lower respiratory tract samples indicated a novel coronavirus, which was named coronavirus disease 2019 (COVID-19).² In severe cases, patients with COVID-19 develop a type of acute respiratory distress syndrome (ARDS), sepsis, and multiorgan failure. Moreover, older age and comorbidities are associated with higher mortality.³

The fibrinolytic system is often suppressed during ARDS where fibrin accumulation can promote hyaline membrane formation and alveolar fibrosis. Depressed pulmonary fibrinolysis is largely due to increased levels of plasminogen activator inhibitor 1 in both plasma and bronchoalveolar lavage fluid.⁴ Furthermore, it is observed that an endothelial damage that disrupts pulmonary regulation promotes ventilation-perfusion mismatch (the primary cause of initial hypoxemia) and develops

thrombogenesis.⁵ Fibrin deposition is the result of an imbalance of the coagulation and fibrinolytic pathways, and several therapeutic strategies have been explored to target the dysfunction of these systems in ARDS.⁶ In particular, the use of fibrinolytic therapy (including plasminogen activators) to limit ARDS progression and reduce ARDS-induced death has received strong support from animal models.⁷ Human studies are limited, although in a phase 1 clinical trial, Hardaway et al.⁸ showed that the administration of urokinase or streptokinase resulted in a significant improvement of PaO₂ level in patients with severe ARDS secondary to trauma or sepsis. In this study, these patients had a PaO₂ level of less than 60 mm Hg, which increased to 231.5 mm Hg following thrombolytic therapy with an overall 30% survival rate and no incidence of bleeding.^{6,8}

Previous data on fibrinolytic therapy in ARDS associated to the prothrombotic state and clinical findings with pulmonary vascular thromboocclusive disease in COVID-19 suggest that the use of tissue plasminogen activator (tPA) may have an impact in the treatment of severe COVID-19 induced ARDS, when all medical efforts and treatment options were exhausted.⁹

The rationale for fibrinolytic therapy is due to the pathologic fibrin deposition that reflects a dysfunctional clotting system, with enhanced clot formation and fibrinolysis suppression, related to tissue factor produced by alveolar epithelial cells and macrophages, and high levels of plasminogen activator inhibitor 1 produced by endothelial cells or activated platelets.¹⁰

In COVID-19 pneumonia, the thrombi play a direct and significant role in gas exchange abnormalities and in multisystem organ dysfunction. The preserved lung compliance noted early in the course of COVID-19 patients with bilateral airspace opacities suggests that the observed pulmonary infiltrates could represent areas of pulmonary infarct and hemorrhage.

Therefore, thrombolysis could improve alveolar ventilation by restoring blood flow to previously occluded regions. This redistribution would reduce blood flow to vasodilated vessels, decreasing the shunt fraction and improving oxygenation.¹¹

Currently, there are only case reports and case series showing efficacy of tPA in COVID-19 patients with severe ARDS, demonstrating improvement of PaO₂/FiO₂ ratio with no bleeding complications. In a recent case series of five COVID-19 patients with severe hypoxemia (PaO₂, <80 mmHg) and D-dimer greater than 1.5 µg/mL, all subjects received a protocol including 25 mg of tPA intravenous bolus given for 2 hours, followed by 25 mg continuous infusion for the next 22 hours. Each patient was placed on a weight-based

continuous heparin infusion after thrombolytic therapy. The administration of tPA was followed by an improvement of oxygen requirement in all patients, and three of them avoided mechanical ventilation after tPA infusion.¹² In another case report from three cases with COVID-19 and severe ARDS, Wang et al.¹³ observed a transient improvement in the PaO₂/FiO₂ ratio among two cases and sustained 50% improvement in one case following administration of 25 mg bolus of intravenous tPA followed by a further 25 mg infusion for 22 hours.

Presently, there is an ongoing phase 2 clinical trial,¹⁴ open label, assessing the use of intravenous fibrinolytic therapy with tPA versus standard of care for patients infected with COVID-19 resulting in severe respiratory failure. Patients will be randomized in three groups. A control group will be standard of care according to the institution's protocol for ARDS. In the first experimental group, patients will receive 50 mg of tPA intravenous bolus for 2 hours, given as a 10-mg push followed by the remaining 40 mg over a total time of 2 hours. After tPA infusion, unfractionated heparin will be delivered intravenously, and the heparin drip will be continued to maintain the activated partial thromboplastin time at 60 to 80 seconds. In the second experimental group, patients will receive 100 mg of tPA intravenous bolus for 2 hours, given as a 10-mg push followed by the remaining 90 mg over a total time of 2 hours. Unfractionated heparin will be delivered in the same way as in the other experimental group. Primary outcome will be the PaO₂/FiO₂ ratio improvement from pre-to-post intervention in all groups. The results from the phase 2a clinical trial conducted by Moore et al.¹⁵ will be useful to develop a phase 3 clinical trial to assess the role of fibrinolytic therapy in COVID-19-induced ARDS and will be helpful for the medical community facing this challenge.

Because of the lack of effective therapies for refractory COVID-19 hypoxemic respiratory failure, where health care providers have used all available treatment options and where extracorporeal membrane oxygenation (ECMO) is not available (mainly in low-middle income countries), fibrinolytic therapy might be an option for a desperate clinical setting. However, even with a pathophysiologic rationale, the lack of clinical studies turns clinicians uncomfortable regarding the management of fibrinolytic therapy to improve PaO₂ level in COVID-19 patients with refractory ARDS. Therefore, clinical trials with fibrinolytic therapy in COVID-19 patients with severe and refractory ARDS are urgently needed to elucidate this question.

DISCLOSURE

The authors declare no conflicts of interest.

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Multidisciplinary prehospital critical care

Dear Editor:

We read with interest the discussion by Carroll et al.¹ of prehospital critical care in “Early and prehospital trauma deaths: Who might benefit from advanced resuscitative care?” Their article adds substance to the growing body of evidence in support of prehospital critical care. The military experience for the last 20 years has shown the benefit to selected patient populations of critical care response teams (e.g., UK Medical Emergency Response Team, US Critical Care Air Transport).^{2,3} Clearly, patients suffering from minor injuries, as well as those with devastating and nonsurvivable injuries, do not benefit from field critical care. Those patients burdened with serious and survivable injuries, however, do benefit from such an approach.

The US National Academies of Sciences, Engineering, and Medicine have called for integration of civilian and military trauma systems to achieve zero preventable deaths.⁴ The civilian practice of emergency medical service (EMS) outside of the United States often features prehospital physicians. The program at the Greater Sydney Area Helicopter EMS, for example, has a rigorous application and selection process, followed by intensive in situ simulation training. A dedicated aeromedical syllabus includes life-, limb-, and sight-saving procedures with pig and human cadaveric laboratory time, consolidated by proctored field shifts for new crew members. In contrast, EMS physicians in the United States typically provide administrative oversight rather than field care.

As physicians with backgrounds in emergency medicine, anesthesia, and critical care, as well as prehospital retrieval experience, we are excited to see the concept of prehospital critical care gain attention. Carroll et al.¹ have added important data to the literature, which provide additional support for the concept of physician-based prehospital critical care. As they point out, however, “operationalizing of this type of care will be challenging.” In Australia, not unlike the rural United States, distance to a major trauma center can be a challenge that has demanded innovation. Prehospital blood products improve hemodynamics in hemorrhagic shock, and in New South Wales, Australia, prehospital massive transfusion protocols have been developed to allow more patients