

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Chinese Journal of Traumatology

journal homepage: <http://www.elsevier.com/locate/CJTEE>

Review Article

What's new in trauma 2020

Wen-Jun Zhao, Gui-E Liu, Yuan Tian, Shuang-Ming Song, Lei Li*

State Key Laboratory of Trauma, Burns and Combined Injury, Research Institute of Surgery, Daping Hospital, Army Medical University, Chongqing, 400042, China

ARTICLE INFO

Article history:

Received 27 January 2021

Received in revised form

27 January 2021

Accepted 27 January 2021

Available online 1 February 2021

Keywords:

Trauma

COVID-19

Trauma-induced coagulopathy

Sepsis

Geriatric trauma

ABSTRACT

Throughout the past 2020, the pandemic COVID-19 has caused a big global shock, meanwhile it brought a great impact on the public health network. Trauma emergency system faced a giant challenge and how to manage trauma under the pandemic of COVID-19 was widely discussed. However, the trauma treatment of special population (geriatric patients and patients taking anticoagulant drugs) has received inadequate attention. Due to the high mortality following severe traumatic hemorrhage, hemostasis and trauma-induced coagulopathy are the important concerns in trauma treatment. Sepsis is another topic should not be ignored when we talking about trauma. COVID-19 itself is a special kind of sepsis, and it may even be called as serious systemic infection syndrome. Sepsis has been become a serious problem waiting to be solved urgently no matter in the fields of trauma, or in intensive care and infection, etc. This article reviewed the research progress in areas including trauma emergency care, trauma bleeding and coagulation, geriatric trauma and basic research of trauma within 2020.

© 2021 Production and hosting by Elsevier B.V. on behalf of Chinese Medical Association. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

2020 was a year filled with roses and thorns. The COVID-19 pandemic has caused an unprecedented disruption to the provision of healthcare worldwide. In this year, the incidence of trauma has been relatively reduced. However, the techniques and procedures of trauma treatment have changed to adapt to the global pandemic situation. This article aims to summarize the progresses or events that have occurred in the international trauma field in the past year.

COVID-19 and traumatic emergency system

In the early days of the outbreak of COVID-19, every single patient presented to traumatic emergency department was suspected COVID-19 infection due to the defects of nucleic acid testing. Therefore, traumatic emergency system or program should be modified in order to adopt to the emergency situation. In early February 2020, the Chinese Journal of Trauma¹ first published an expert consensus on trauma emergency procedures under COVID-19 pandemic. This consensus was organized by the Trauma Medicine Branch of the Chinese Medical Doctor Association, and written

by the first-line trauma surgeons from Wuhan and other senior trauma experts. The timely publication of this consensus played an active role in guiding the treatment of trauma cases in mainland of China during the epidemic. And then, the spinal surgeons from Wuhan, Neural Regeneration and Repair Committee, Chinese Research Hospital Association, Spinal Cord Basic Research Group, Spinal Cord Committee of Chinese Society of Rehabilitation Medicine, Spinal Cord Injury and Rehabilitation Group, Chinese Association of Rehabilitation Medicine jointly issued Guideline for diagnosis and treatment of spine trauma in the epidemic of COVID-19.²

Generally, under the pandemic of novel coronavirus, the epidemiological data showed that the number of traffic crash has dramatically reduced, but the incidence of home injuries, such as fall, has increased significantly. It is irrefutable that the outbreak of COVID-19 did pose a great challenge to the basic concepts of trauma emergency care, such as the golden hour and platinum 10 min. During the pandemic period, doctors and nurses in emergency department have to give first aid only when adequate isolation condition is already. During the treatment, medical staff should be carefully protected and the cross-infection between patients should be strictly prevented. If conditions permit, emergency treatment for suspected and confirmed COVID-19 infected patients should be performed in negative pressure operating room, which can effectively reduce the risk of cross-infection between patient and medical staff, and between patients.

* Corresponding author.

E-mail address: leili@cjtrauma.com (L. Li).

Peer review under responsibility of Chinese Medical Association.

It is worth noting that there were some links between COVID-19 and sepsis. A study of Lin³ reported that the patients who died of COVID-19 infected have different degrees of inflammatory response and damage on their heart, liver, kidney and other organs. And their spleen and lymphatic tissue revealed serious atrophy. There may be disseminated intravascular, etc. The above symptoms are similar to sepsis caused by bacterial infections. It is reasonable to speculate that the essence of severe COVID-19 is a sepsis induced by viral infection, which has the all hallmarks of sepsis including specific pathogen (2019-nCoV), severe systemic inflammatory response (so-called inflammatory storm), deep immunosuppression (lymphocyte depletion and lymphatic tissue atrophy) and multiple organs failure, even persistent inflammation, immunosuppression, and catabolism syndrome in some patients. Therefore, special attention should be paid on low immune function and necessary procedures should be made during anti-inflammatory therapy. In addition, coagulation disorders after infected novel coronavirus is also a problem worthy to be noted. Besides the reported indicator of D-dimer level, the increase of prothrombin time and fibrinogen degradation products often relates to the decrease of lymphocytes count, low immune function and multiple organ dysfunction, even indicate a poor prognosis of the patients.⁴

Hemostasis and trauma-induced coagulopathy

Severe traumatic hemorrhage is the leading cause of death. Therefore, adequate hemostasis is the critical step during emergency care. However, the disturbed balance between coagulation and fibrinolysis induced by trauma shock and subsequent resuscitation and hemostasis medicine, such as transfusion, tranexamic acid (TXA), and so on, provokes another pathophysiological issue, that is trauma-induced coagulopathy (TIC).

In the past year, four major points have drawn our attention on.

Can we prevent the TIC at prehospital environment?

Stansfield et al.⁵ in their review paper suggested that TXA exerts its action on the coagulation process by competitively inhibiting plasminogen activation, thereby reducing conversion of plasminogen into plasmin. This ultimately prevents fibrinolysis and reduces hemorrhage. A loading dose of 1 g of TXA, followed by 1 g infusion over 8 h, given by intravenous administration within a 3 h window period of traumatic injury might achieve the best possible outcomes. Ditillo et al.⁶ collected a total of 19,643 severe trauma adult patients who received 4 or more packed red blood cells per 4 h. Among them, 4945 patients received cryoprecipitate within the first 24 h. The role of cryoprecipitate as an adjunct to transfusion in trauma patients was assessed. The results indicated that the adjunctive use of cryoprecipitate in hemorrhaging trauma patients may reduce mortality without affecting in-hospital complications and transfusion requirements. In addition, another multicenter randomized controlled trial (RCT)⁷ found that a total of 53 adult trauma patients with major haemorrhage received respectively fibrinogen concentrate (28 cases), and placebo (25 cases) pre-hospital at the scene or during transportation to the hospital. The blood clot stability (maximum clot firmness) of patients was assessed. The authors suggested that early fibrinogen concentrate administration is feasible in the complex and time-sensitive environment of prehospital trauma care. After the Trauma Induced Coagulopathy Clinical Score was firstly introduced in 2014 by Tonglet et al.,⁸ they re-introduced a modified Trauma Induced Coagulopathy Clinical Score (mTICCS) in 2017 in a population of 33,385 trauma patients.⁹ The two scoring systems might be very useful tools for early detection of the need for a massive transfusion. In order to further validate the mTICCS in preclinical start of

damage control resuscitation, Horst et al.¹⁰ compared the mTICCS with other popular scoring systems, including trauma-associated severe hemorrhage score, Prince of Wales hospital score, Larson score, assessment of blood consumption score, emergency transfusion score and suggested that the newly developed mTICCS presents a useful tool to predict the need for an mass transfusion in a prehospital situation. Also, one research paper from US Army Institute of Surgical Research indicated that 5% human albumin solutions are isotonic, iso-oncotic, ready-to-use, stable, and compatible with all blood types and should be considered for prehospital resuscitation where blood products are not available or not accepted.¹¹

TIC prevention remains to be a challenge for trauma surgeons, and starting the program before entering a hospital might be a considerable option. Unfortunately, early diagnosis of TIC is an urgent task waiting to be resolved. A research from Italy reported that among 83 adult severe trauma patients without anticoagulant therapy before trauma, 88.8% presented pathological thromboelastography (TEG) on the trauma scene and 92.5% presented TEG at hospital arrival.¹² In addition, hypercoagulation was present in 71.3% patients at scene, and in 82.5% at hospital arrival. However, only 11.3% patients had hyperfibrinolysis at scene, and 8.8% patients at hospital arrival.

Viscoelastic hemostatic assays are believed as a useful tool to standard coagulation test nowadays in clinical lab,^{13,14} such as thromboelastometry and TEG, however, as a kind of point-of-care device, TEG or thromboelastometry is often placed in the clinical laboratory to detect blood coagulation in a general hospital.

Severe TIC has a high incidence and is directly related to the patient's prognosis. It is not only the main cause of multiple organ failure, but also an important cause of death. A twenty-month-long prospective cohort study from Tunisia indicated that among the total 365 admitted trauma patients 27 developed a pulmonary embolism within 72 h of trauma.¹⁵ The risk factors associated with early pulmonary embolism were older, obesity (body mass index >30), sequential organ failure assessment score on admission and lower extremity long-bone fracture.

The study of Spasiano et al.¹² further proved that a patient may have coagulation disorders at extreme early stage of trauma. Therefore, TIC prevention should be performed at early stage of trauma treatment, even be focused at emergency rescue on the scene. Blood visco elasticity test may help to detect whether there is TIC in a patient quickly. Moreover, trauma surgeons should be alert to TIC, and TEG or thromboelastometry should be equipped in the emergency room, intensive care unit and even in ambulance as a point-of-care device, in order to determine the patient's coagulation function status as soon as possible. It is necessary to stop bleeding by using some drugs (such as TXA, fibrinogen concentrate) at the prehospital period, even massive transfusion, etc. However, the application timing and principles of these drugs still need to be further discussed.

TIC in a special population

As aging society is coming, more and more people are suffering from chronic diseases. Among them, people who have to take anti-coagulants for a long time due to cardiovascular and cerebrovascular diseases or genetic diseases are also gradually increasing. When severe trauma occurs on these people, especially traumatic brain injury (TBI) or traumatic intracerebral hemorrhage (tICH) accompany TIC, how to deal with the situation becomes another challenge for trauma surgeons.

Lee et al.¹⁶ in their meta-analysis research reported that a total of 1,365,446 trauma patients were divided into two groups: pre-injury anticoagulation and no preinjury anticoagulation. Compared

with the latter group, the preinjury anticoagulation patients were associated with higher risks of overall mortality, in-hospital mortality, intracerebral hemorrhage, and shorter length of hospital stay. This study aroused our vigilance again that more attention should be paid to these populations who received anticoagulants before injury. The history of antiplatelet drugs (aspirin, clopidogrel, etc.) intake may lead to increased progression of tICH, higher need for neurosurgical intervention, poorer neurologic outcomes, and increased mortality in about one fifth of trauma patients. Therefore, for such patients, platelet transfusion may improve their prognosis once they suffer trauma and blood loss. Meanwhile, the use of antithrombotic drugs is increasing with the aging population. Intake of antithrombotic drugs in these patients is controversial. Some physicians believed that antithrombotic drugs should be discontinued because this may lead to an increased risk of hemorrhagic, but research of Matsuoka et al.¹⁷ suggested that antithrombotic drugs have no significant effect on the volume of intraoperative blood loss in emergency gastrointestinal surgery after adjustment for confounding factors by propensity score matching.

In addition, blunt cerebrovascular injury is often associated with cerebrovascular accidents, Hanna et al.¹⁸ reported that prophylaxis of antiplatelet agents were associated with a lower rate of cerebrovascular accident in the first 6 months after discharge. However, another systemic meta-analysis review suggested that current evidence does not support the use of platelet transfusion in patients with tICH on prehospital antiplatelets, highlighting the need for a prospective evaluation of this practice.⁷ It's necessary to pointed out that the pathogenic mechanism of TIC remains unclear until now, and increased tissue factor, activation of protein C pathway, and platelet dysfunction may play important roles in it. Special attention should be paid on qualitative platelet defects. The past clinical laboratory only detect platelet counts, but for trauma patients, especially for patients with TBI, the platelet counts may be in the normal range, but its activation is significantly enhanced, which is more likely to cause thrombosis. With gradually promotion of viscoelastic assays and wide use of TEG, the kinetics and stability in clot formation can be monitored, specifically, platelet mapping (TEG–platelet mapping) can assess clot strength and platelet response to different agonists (ex vivo). Dynamic analysis of platelet function status is an index for assessing the possibility of TIC in trauma patients.

Coagulation function test

As we already know, in order to figure out trauma patients' coagulation function, routine coagulation function test (such as coagulation routine examination: the activated partial thromboplastin time, prothrombin time, thrombin time and quantitatively determine fibrinogen) should be conducted on trauma patients with oral anticoagulants when they presenting to emergency department. In recent years, TEG and thromboelastometry as gradually popularize techniques provide good methods to detect coagulation function of trauma patients or severe patients. However, different anticoagulant drugs have different anticoagulant targets, so searching a method to detect the concentration of anticoagulant drugs in patients is meaningful for guiding clinical TIC treatment. A report from Virginia Commonwealth University showed liquid chromatography–mass spectrum etry can accurately, sensitively and specifically test the concentration of several common oral anticoagulants (such as apixaban, rivaroxaban, and dabigatran) in the blood of emergency trauma patients.¹⁹ Although liquid chromatography–mass spectrum has a good detection effect, it is expensive and time-consuming. At present, it can only be used in level I trauma centers or large-scale comprehensive teaching

hospitals. There is still a long way to go for the wider application of liquid chromatography–mass spectrum in level III trauma centers in remote areas.

Venous thromboembolism (VTE) following trauma

VTE, including deep vein thrombosis and pulmonary embolus, is often associated with trauma patients or surgical patients, which has been closed attention because it has obtained the major causes of hospital-related morbidity and mortality. Among them, the obese trauma victims are a particular group of population who may have more incidence of VTE than others. VTE prophylaxis might have some benefits in trauma patients. Controversy exists regarding the optimal thromboprophylaxis regimen following orthopaedic trauma: low-molecular-weight heparin or aspirin, which one is more effective on fracture trauma patients? A RCT research from Maryland, the US²⁰ reported that no evidence of superiority between low-molecular-weight heparin and aspirin for VTE prevention after 329 fracture cases investigation (enoxaparin 30 mg twice daily, $n = 164$ and aspirin 81 mg twice daily, $n = 165$).

Geriatric trauma

With improvements in healthcare, human's life has been gradually extended, and the proportion of the elderly population has gradually increased, which led to an increasing incidence of trauma in this population. Geriatric trauma has become a serious problem in trauma care. In 2020, a report from British Orthopaedic Association Trauma Committee pointed out that the average age of trauma patients in the UK has soared from 36 years in 1990 to 59 years in 2017.²¹

A study from Pennsylvania, the US, retrospectively analyzed all trauma patients aged over 65 years and injury severe score (ISS) > 9 from 2003 to 2015, and found that the geriatric trauma patients received by non-traumatic centers with a higher undertriage rate than that in trauma centers. That is to say, geriatric patients were less likely to have trauma team activation than younger patients despite a similar percentage of severe injuries.²² Undertriage is often the main reason for the low success rate of trauma treatment.

For young people, isolated chest trauma injury is mostly resulted from a high energy mechanism. Young patients who suffered blunt chest trauma can achieve a satisfactory outcome by early surgical stabilization of rib fractures. But for the elderly patients, most of their injuries were caused by falls. It seems that the rate of early surgical stabilization of rib fracture is not high. Zhu et al.²³ repeatedly conducted stratified and propensity score-matched analysis, and found that for the geriatric isolated rib fracture patients, early surgical stabilization of rib fracture can not only improve the survival rate, but also reduce the incidence of ventilator associated pneumonia, as well as shorten ICU lengths of stay and hospital lengths of stay.

In a 7-year-observation study conducted in Switzerland, one-to-one pairing was performed by the statistical software program based on gender, exact ISS, mechanism of injury (penetrating/blunt), exact Glasgow coma scale at admission, base excess, and the presence of coagulopathy. It was found that although the incidence of complications in elderly patients is higher, there was no significant difference in mortality and length of hospital stay between elderly trauma patients (>70 years old), and non-elderly trauma patients. The most common complications of elderly trauma patients were anemia, coronary heart disease, and lung infections. According to the authors' analysis, it may be because the medical staff concerned more about these diseases than others when the elderly trauma patients were admitted to the hospital. Furthermore, from the data presented by the authors, at the time of admission, the

elderly patients have higher systolic blood pressure (133/125) and lower base excess ($-4.1/-3.6$), but the presence of coagulopathy (INR > 1.4) seems with a higher rate (30.2%/20.3%).²⁴ Unfortunately, the authors did not follow up the elderly trauma patients for the final outcomes of 1 year or 3 years after being discharged from the hospital. Previous studies have found that patients with sepsis, especially the elderly patients, have a third peak in mortality within one year after discharge.^{25,26} Obviously, further researches were needed to investigate the quality of life and outcomes within 1 year after discharge of elderly trauma patients.

Interestingly, single-nucleotide polymorphism is generally considered to be related to the incidence of post-traumatic sepsis. A study from the University of Pittsburgh found that the phenotype AA of rs2075650 in TOMM40 is not only related to longevity, but also seems to be related to the prognosis of elderly trauma patients (65–90 years old).²⁷ The elderly trauma patients with phenotype AA have significantly lower requirement for ventilation and fewer days on mechanical ventilation. But this difference is not significant in young trauma patients. In addition, the authors further screened the expressions of 31 inflammation-related mediators in the serum of trauma patients. Compared AA phenotype of elderly trauma patients with the AG/GG phenotype, there was only 1 up-regulated expression of inflammatory mediators, but 2 expressions are suppressed (IL-25 and IL-33). In the AA phenotype of young trauma patients (18–30 years old), there is only one inflammatory mediator whose expression was suppressed, but there were 8 inflammatory mediators whose expression is up-regulated. Obviously, the rs2075650 gene polymorphism gradually appears to be more protective for elderly trauma patients with age.

Clearly, as the aging society is coming, emergency trauma treatment and care of elderly trauma patients is one of the most important issues in our society. The current trauma care system did not pay much attention on this special population and trauma in them is often under-triaged, which deserves more attention.

Sepsis

In recent years, there are numerous studies on sepsis treatment strategies, however, the mortality rate of sepsis has not decreased significantly, and it has become a nightmare for microbiological immunologists and clinical physicians. The proposal of activated protein C and polymyxin B hemoperfusion (PMX-HP) once made people see the silver linings a while, but subsequent RCTs made the hope dashed. In early 2020, a multi-center RCT research report from Japan has renewed the hope for the treatment strategy of PMX-HP.²⁸ This study found that for patients with all-over septic shock, PMX-HP does not show benefit in all-cause in-hospital mortality among all of them. But for young patients, especially young patients with non-septic shock, PMX-HP therapy can bring a greater benefit than its side effect. However, for elderly patients, especially those over 80 years and with a high disease severity simultaneously, it can significantly improve their prognosis and increase the survival rate of hospitalized patients.

Complement has always been regarded as an important trigger for initiating inflammation and blood coagulation. Usually, C3 has received more attention due to its high content. However, the link between complementary split products (especially membrane attacking complex, soluble C5b-9 complex) and trauma (especially sepsis) has been less studied. Red blood cells are the most abundant cells in the human blood circulatory system. People often paid more attention to the oxygen-carrying function of red blood cells. Whether there is a certain reaction between complementary split products and red blood cells after trauma, and what is the impact on prognosis of trauma patients? were rarely discussed. A study of Satyam et al.²⁹ showed complement split products, C4d, C3d, and

C5b-9 could deposited on the membrane of red blood cells after trauma, which enhances the phosphorylation of band 3 and increases the production of NO in various types of trauma for at least 72 h when ISS < 9 , but C4d may remain a higher level after 72 h when ISS > 9 . Therefore, the decoration of complement components on red blood cells may be associated with the outcome of trauma patients. In addition, another research article by Abe et al.³⁰ from Japan found that sepsis patients were divided into four groups according to their plasma levels of soluble C5b-9 (ng/mL: low: < 260 , moderate: 260–342, high: 343–501, highest: > 501), the Sequential Organ Failure Assessment score of patients varied across these groups in a significant positive correlation.

Generally speaking, the treatment of sepsis, especially the clinical treatment of post-traumatic sepsis, did not make any significant progress in the past 2020. Hereon, it should be pointed out that the treatment of sepsis is still limited to the 3 W+1H strategy (What are the types of the infection? Where is the infection source occurring? When should we administrate the antibiotics? How do we handle hemodynamic management for early stage of septic shock?).³¹ In future, what we need are developing new ways to quickly determine infection type, definite the infection source and choose targeting antibiotics as early as we could. Most of all, it is noteworthy that immunological paralysis is often associated with the onset and development of sepsis.³² Enhance host immune defense is not a panacea, but it is absolutely impossible to ignore the improvement of immune function.

Basic research on trauma

The establishment of emergency trauma care system can improve the success rate of trauma treatment significantly. Unfortunately, there was little progress in researches on post-traumatic sepsis treatment. The progress of clinical disciplines often depends on the important findings of related basic research. In 2020, there were several interesting reports on pathogenesis of traumatic complications have drawn our attention.

A study of Zhou et al.³³ found that macroautophagy/autophagy is a lysosome-dependent degradation pathway that plays a dual role in inflammation, immunity and disease. Autophagy not only eliminates invading foreign organisms or inhibits the activation of the inflammasome, but also mediates the release of cytokines. The process of autophagy is controlled by a family of autophagy-related proteins and autophagy receptors. Extracellular SQSTM1 mediates septic death in mice by activating insulin receptor signaling in macrophage or monocyte. Extracellular SQSTM1 could bind to insulin receptor which in turn activate a NF- κ B metabolic pathway, and lead to aerobic glycolysis and polarization of macrophage. Intraperitoneal injection of anti-SQSTM1-neutralizing monoclonal antibodies or conditional depletion of Insulin receptor in myeloid cells using the Cre-*loxP* system protects mice from lethal sepsis. Interestingly, this finding has been verified in 40 sepsis patients since their severity was associated with the levels of SQSTM1 and insulin receptor expressed in peripheral blood mononuclear cells.

Meanwhile another extracellular substance, cold-inducible RAN-binding protein (CIRP) is believed as a damage-associated molecular pattern, which might be another therapeutic adjunct in management of hemorrhagic shock. Denning et al.³⁴ reported that as a stress responsive RNA chaperon, CIRP can translocate from nucleus to the cytoplasm and release into the circulation becoming extracellular CIRP during hemorrhagic shock. The extracellular CIRP can increase the production of proinflammatory cytokines after binding to the toll-like receptor 4. In this investigation, Gurien et al.³⁵ suggested that extracellular CIRP strongly binds to TREM-1 (triggering receptor expressed on myeloid cells-1, another independent trigger to inflammatory response), after that, this research

group following research to develop a unique human extracellular CIRP-derived ligand dependent 7-amino acid peptide (RGFFRGG) to serve as an antagonist of TREM-1 this peptide might decrease inflammatory insult of the lung in murine hemorrhagic shock model.

While tissue injury occur, cellular death causes release of structural proteins, including actin and myosin, which could induce a serial secondary inflammatory insult, however whether these damage associated related patterns may interact with clot formation and structure remains unclear. Coleman et al.³⁶ reported that high circulating levels of actin are present in trauma patients with severe tissue injury, which may contribute to fibrinolysis shutdown in the setting of tissue injury.

These articles presented a new opinion that extracellular substance in circulation after trauma, shock or sepsis should not be ignored. For years, what we pay more attention is the translocation of bacteria in gut or gut microbiome no matter in trauma or other fields. Recently Walter et al.³⁷ posited that the exceedingly high rate of inter-species transferable pathologies is implausible and overstates the role of the gut microbiome in human disease. Yes, we should pay attention not only to bacterial translocation, but also to the secondary inflammatory damage induced by non-microbial harmful factors, such as necrotic tissue and/or cells debris following trauma, and shock, which has been named as damage associated molecular patterns in the circulating blood.

Trauma sepsis is a kind of excessive inflammatory response against pathogenic microbes, and theoretically glucocorticoid may have some benefits for management of acute inflammatory response, such as major operation or severe trauma. However, whether the administration of glucocorticoid would bring beneficial or potentially harmful effects on and the detail immune modulating properties of glucocorticoid in trauma patient remain controversial. Recently, Ganio et al.³⁸ applied a high-dimensional mass cytometry assay to characterize the immune-modulating effects of a single dose of 125 mg methylprednisolone in a RCT of patients undergoing total hip arthroplasty surgery (NCT02542592). A total of 47 parameters covering 26 cell phenotype cell markers and 11 intracellular proteins were estimated at 1 h, 6 h, 24 h, 48 h, and 2 weeks after total hip arthroplasty surgery. The results indicated a single dose of methylprednisolone alterations of immune cell signaling trajectories, particularly in the adaptive compartments, but the innate signaling responses seems unaffected. In addition, methylprednisolone does not alter these clinical recovery parameters.

The reduced host immune defense is currently considered an indisputable fact. Previous studies usually focused on the number of cells and related immunological indicators. However, cell-specific pathways behind the pathogenic inflammation and immunosuppression following trauma remains unclear. Chen et al.³⁹ from University of Pittsburgh applied single-cell RNA sequencing to circulating and bone marrow mononuclear cells in injured mice and circulating mononuclear cells in trauma patients. In this investigation, authors tried to provide the dynamic changes in transcriptomic patterns in peripheral blood mononuclear cells from severe trauma patients or hemorrhagic shock mice. The Ly6C⁺/CD14⁺ monocytes in circulation have been found profoundly changed after severe injury, including burn, sepsis, etc. Furthermore, the authors discovered that the gene expression pattern of monocytes deviated from steady state in a continuous manner after injury and the changes of monocyte can be generalized into six signatures with distinct and biologically. With these six signatures the trauma patients were defined as two subtypes with different prognosis after severe injury.

Weiss et al.⁴⁰ found that cellular metabolism plays a critical role in the immune response to infection or sepsis. Aerobic glycolysis enables broad metabolic reprogramming of the immune system

that supports innate immune activation and lymphocyte proliferation. Therefore, mitochondrial respiration in PBMCs might be a useful marker of immune function. In their study mitochondrial respiration was lower in children with immunoparalysis compared with those without immunoparalysis, indicating that mitochondrial dysfunction may be associated with measures of immunoparalysis and systemic inflammation in children with sepsis.

Conclusion

In 2020, the sudden COVID-19 pandemic has not only changed our way of life, but also brought great challenge to modern healthcare system. The field of trauma is also facing a great dilemma. In the past year, the emergency trauma care system has made some adaptive adjustments based on the shifted trauma epidemiology characteristics. In this article, we only selected reviews on traumatic emergency system, TIC, geriatric trauma, traumatic sepsis and some basic research related to trauma. We know where we are and we have to start getting a better sense of the darkness.

Funding

Nil.

Ethical statement

Not applicable.

Declaration of competing interest

The authors have no conflicts of interest to declare.

References

- Li Y, Li ZF, Mao QX, et al. Consensus on emergency surgery and infection prevention and control for severe trauma patients during epidemic of corona virus disease 2019. *Chin J Trauma*. 2020;36:97–103. <https://doi.org/10.3760/cma.j.issn.1001-8050.2020.02.001>.
- Wang YL, Zhu FZ, Zeng L, et al. Guideline for diagnosis and treatment of spine trauma in the epidemic of COVID-19. *Chin J Traumatol*. 2020;23:196–201. <https://doi.org/10.1016/j.cjtee.2020.06.003>.
- Lin HY. The severe COVID-19: a sepsis induced by viral infection? And its immunomodulatory therapy. *Chin J Traumatol*. 2020;23:190–195. <https://doi.org/10.1016/j.cjtee.2020.06.002>.
- Liu Y, Gao W, Guo W, et al. Prominent coagulation disorder is closely related to inflammatory response and could be as a prognostic indicator for ICU patients with COVID-19. *J Thromb Thrombolysis*. 2020;50:825–832. <https://doi.org/10.1007/s11239-020-02174-9>.
- Stansfield R, Morris D, Jesulola E. The use of tranexamic acid (TXA) for the management of hemorrhage in trauma patients in the prehospital environment: literature review and descriptive analysis of principal themes. *Shock*. 2020;53:277–283. <https://doi.org/10.1097/SHK.0000000000001389>.
- Ditillo M, Hanna K, Castanon L, et al. The role of cryoprecipitate in massively transfused patients: results from the Trauma Quality Improvement Program database may change your mind. *J Trauma Acute Care Surg*. 2020;89:336–343. <https://doi.org/10.1097/TA.0000000000002764>.
- Alvikas J, Myers SP, Wessel CB, et al. A systematic review and meta-analysis of traumatic intracranial hemorrhage in patients taking prehospital antiplatelet therapy: is there a role for platelet transfusions? *J Trauma Acute Care Surg*. 2020;88:847–854. <https://doi.org/10.1097/TA.0000000000002640>.
- Tonglet ML, Minon JM, Seidel L, et al. Prehospital identification of trauma patients with early acute coagulopathy and massive bleeding: results of a prospective non-interventional clinical trial evaluating the Trauma Induced Coagulopathy Clinical Score (TICCS). *Crit Care*. 2014;18:648. <https://doi.org/10.1186/s13054-014-0648-0>.
- Tonglet M, Lefering R, Minon JM, et al. Prehospital identification of trauma patients requiring transfusion: results of a retrospective study evaluating the use of the trauma induced coagulopathy clinical score (TICCS) in 33,385 patients from the TraumaRegister DGU. *Acta Chir Belg*. 2017;117:385–390. <https://doi.org/10.1080/00015458.2017.1341148>.
- Horst K, Lentzen R, Tonglet M, et al. Validation of the mTICCS score as a useful tool for the early prediction of a massive transfusion in patients with a

- traumatic hemorrhage. *J Clin Med.* 2020;9:945. <https://doi.org/10.3390/jcm9040945>.
11. Kheirabadi BS, Miranda N, Terrazas IB, et al. Should Albumin be considered for prehospital resuscitation in austere environments? A prospective randomized survival study in rabbits. *Shock.* 2020;54:358–367. <https://doi.org/10.1097/SHK.0000000000001480>.
 12. Spasiano A, Barbarino C, Marangone A, et al. Early thromboelastography in acute traumatic coagulopathy: an observational study focusing on pre-hospital trauma care. *Eur J Trauma Emerg Surg.* 2020. <https://doi.org/10.1007/s00068-020-01493-z>.
 13. Pressly MA, Parker RS, Neal MD, et al. Accelerating availability of clinically-relevant parameter estimates from thromboelastogram point-of-care device. *J Trauma Acute Care Surg.* 2020;88:654–660. <https://doi.org/10.1097/TA.0000000000002608>.
 14. Francis RCE, Theurl I, Maegele M, et al. Point-of-Care diagnostics of coagulation in the management of bleeding and transfusion in trauma patients. *Curr Opin Anaesthesiol.* 2020;33:246–252. <https://doi.org/10.1097/ACO.0000000000000836>.
 15. Bahloul M, Dlela M, Bouchaala K, et al. Early post-traumatic pulmonary embolism in intensive care unit: incidence, risks factors, and impact outcome. *Am J Cardiovasc Dis.* 2020;10:207–218.
 16. Lee ZX, Lim XT, Ang E, et al. The effect of preinjury anticoagulation on mortality in trauma patients: a systematic review and meta-analysis. *Injury.* 2020;51:1705–1713. <https://doi.org/10.1016/j.injury.2020.06.010>.
 17. Matsuoka T, Kobayashi K, Lefor AK, et al. Antithrombotic drugs do not increase intraoperative blood loss in emergency gastrointestinal surgery: a single-institution propensity score analysis. *World J Emerg Surg.* 2019;14:63. <https://doi.org/10.1186/s13017-019-0284-8>.
 18. Hanna K, Douglas M, Asmar S, et al. Treatment of blunt cerebrovascular injuries: anticoagulants or antiplatelet agents? *J Trauma Acute Care Surg.* 2020;89:74–79. <https://doi.org/10.1097/TA.0000000000002704>.
 19. Jayaraman S, DeAntonio JH, Leichte SW, et al. Detecting direct oral anticoagulants in trauma patients using liquid chromatography–mass spectrometry: a novel approach to medication reconciliation. *J Trauma Acute Care Surg.* 2020;88:508–514. <https://doi.org/10.1097/TA.0000000000002527>.
 20. Haac BE, O'Hara NN, Manson TT, et al. Aspirin versus low-molecular-weight heparin for venous thromboembolism prophylaxis in orthopaedic trauma patients: a patient-centered randomized controlled trial. *PLoS One.* 2020;15:e0235628. <https://doi.org/10.1371/journal.pone.0235628>. PMID: 32745092; PMCID: PMC7398524.
 21. British Orthopaedic Association Trauma Committee. British Orthopaedic Association's Standards for Trauma (BOAST): care of the older or frail patient with orthopaedic injuries. *Injury.* 2020;51:1419–1421. <https://doi.org/10.1016/j.injury.2020.06.005>.
 22. Horst MA, Morgan ME, Tawnya M, Vernon TM, et al. The geriatric trauma patient: a neglected individual in a mature trauma system. *J Trauma Acute Care Surg.* 2020;89:192–198. <https://doi.org/10.1097/TA.0000000000002646>.
 23. Zhu RC, Roulet AD, Ogami T, et al. Rib fixation in geriatric trauma: mortality benefits for the most vulnerable patients. *J Trauma Acute Care Surg.* 2020;89:103–110. <https://doi.org/10.1097/TA.0000000000002666>.
 24. Jensen KO, Lempert M, Sprengel K, et al. Is there any difference in the outcome of geriatric and non-geriatric severely injured patients?—a seven-year, retrospective, observational cohort study with matched-pair analysis. *J Clin Med.* 2020;9:3544. <https://doi.org/10.3390/jcm9113544>.
 25. Mankowski RT, Anton SD, Ghita GL, et al. Older sepsis survivors suffer persistent disability burden and poor long-term survival. *J Am Geriatr Soc.* 2020;68:1962–1969. <https://doi.org/10.1111/jgs.16435>.
 26. Gardner AK, Ghita GL, Wang Z, et al. The development of chronic critical illness determines physical function, quality of life, and long-term survival among early survivors of sepsis in surgical ICUs. *Crit Care Med.* 2019;47:566–573. <https://doi.org/10.1097/CCM.0000000000003655>.
 27. Lamparello AJ, Namas RA, Schimunek L, et al. An aging-related single-nucleotide polymorphism is associated with altered clinical outcome and distinct inflammatory profiles in aged blunt trauma patients. *Shock.* 2020;53:146–155. <https://doi.org/10.1097/SHK.0000000000001411>.
 28. Nakata H, Yamakawa K, Kabata D, et al. Identifying septic shock populations benefitting from polymyxin B hemoperfusion: a prospective cohort study incorporating a restricted cubic spline regression model. *Shock.* 2020;54:667–674. <https://doi.org/10.1097/SHK.0000000000001533>.
 29. Satyam A, Andreo K, Lapchak PH, et al. Complement deposition on the surface of RBC after trauma serves as a biomarker of moderate trauma severity: a prospective study. *Shock.* 2020;53:16–23. <https://doi.org/10.1097/SHK.0000000000001348>.
 30. Abe T, Kubo K, Izumoto S, et al. Complement activation in human sepsis is related to sepsis-induced disseminated intravascular coagulation. *Shock.* 2020;54:198–204. <https://doi.org/10.1097/SHK.0000000000001504>.
 31. Ospina-Tascón GA, Hernandez G, Alvarez I, et al. Effects of very early start of norepinephrine in patients with septic shock: a propensity score-based analysis. *Crit Care.* 2020;24:52. <https://doi.org/10.1186/s13054-020-2756-3>.
 32. Hotchkiss RS, Opal SM. Activating immunity to fight a foe - a new path. *N Engl J Med.* 2020;382:1270–1272. <https://doi.org/10.1056/NEJMcibr1917242>.
 33. Zhou B, Liu J, Zeng L, et al. Extracellular SQSTM1 mediates bacterial septic death in mice through insulin receptor signalling. *Nat Microbiol.* 2020;5:1576–1587. <https://doi.org/10.1038/s41564-020-00795-7>.
 34. Denning NL, Aziz M, Murao A, et al. Extracellular CIRP as an endogenous TREM-1 ligand to fuel inflammation in sepsis. *JCI Insight.* 2020;5, e134172. <https://doi.org/10.1172/jci.insight.134172>.
 35. Gurien SD, Aziz M, Cagliani J, et al. An extracellular cold-inducible RNA-binding protein-derived small peptide targeting triggering receptor expressed on myeloid cells-1 attenuates hemorrhagic shock. *J Trauma Acute Care Surg.* 2020;88:809–815. <https://doi.org/10.1097/TA.0000000000002664>.
 36. Coleman JR, Moore EE, Freeman K, et al. Actin is associated with tissue injury in trauma patients and produces a hypercoagulable profile in vitro. *J Trauma Acute Care Surg.* 2020;89:87–95. <https://doi.org/10.1097/TA.0000000000002739>.
 37. Walter J, Armet AM, Finlay BB, et al. Establishing or exaggerating causality for the gut microbiome: lessons from human microbiota-associated rodents. *Cell.* 2020;180:221–232. <https://doi.org/10.1016/j.cell.2019.12.025>.
 38. Ganio EA, Stanley N, Lindberg-Larsen V, et al. Preferential inhibition of adaptive immune system dynamics by glucocorticoids in patients after acute surgical trauma. *Nat Commun.* 2020;11:3737. <https://doi.org/10.1038/s41467-020-17565-y>.
 39. Chen T, Delano MJ, Chen K, et al. A roadmap from single-cell transcriptome to patient classification for the immune response to trauma. *JCI Insight.* 2021;6:145108. <https://doi.org/10.1172/jci.insight.145108>.
 40. Weiss SL, Zhang D, Bush J, et al. Mitochondrial dysfunction is associated with an immune paralysis phenotype in pediatric sepsis. *Shock.* 2020;54:285–293. <https://doi.org/10.1097/SHK.0000000000001486>.