A Synopsis of Emerging Blood Biomarkers in Trauma, Injury Critical Care, and Recovery: General Overview

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Abstract

In the field of biomarkers nowadays, it is possible to have valid, unbiased detection of novel biomarkers in wide range of clinical research, and from plasma. Researches dealing with biomarkers are mostly focused on detailed

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exploration of plasma proteome at novel depth and identify the detailed biological insights for emerging biomarker discovery. The emerging biomarkers should provide unbiased analysis with novel depth of many relevant proteins, they should have unmatched specificity and quantitative precision, high capacity, and be easily accessible. Further, they should provide characteristic biological indicators that are used to identify (indirect changes) physical damage or disorders of physiological processes in humans or animals. The enhanced and empowered potentials should be therefore provided in the field of detection, diagnostics, prognostics, and intervention direction should be crucial in the field of trauma, injury critical care, and recovery. Lately, researchers and clinicians have intensively worked on identifying novel biomarkers and consequently testing them for everyday clinical practice use. This chapter presents various definition, classifications, and utilization of emerging biomarkers in trauma, injury critical care, and recovery. The chapter provides an overview of the key features and benefits of next-generation biomarkers discovery solutions in the field of cardiovascular critical care, COVID-19, and biomarkers of infection in critical care. The chapter elaborates on deep level the clinical application possibilities quantification and analysis that can be performed by the emerging biomarkers. Further, the chapter presents how we identify the most promising and actionable biomarkers for research and clinical decision-making. Finally, different types of emerging biomarkers in trauma, injury critical care, and recovery are presented. Clearly, as our knowledge in evidence-based medicine is growing, it is necessary for biomarker research to grow along. Hence, the search for novel biomarkers will continue and intensify and provide new information.

Keywords

Emerging · Biomarkers · Novel biomarkers · Trauma · Injury critical care · Recovery · Clinical application

Abbreviations

ACE2	Angiotensin-converting enzyme 2
AMI	Acute myocardial infarction
cfDNA	Cell-free DNA
COVID-19	Coronavirus disease
cTnI	Cardiac troponin I
DNA	Deoxyribonucleic acid
GDF-15	Growth differentiation factor
H3Cit	Citrullinated histone 3
H-FABP	Heart-type fatty acid binding protein
HMGB1	High-mobility group box protein 1
miRNAs	MicroRNAs
MPO	DNA complexes
MT	Metallothioneins
MXR	Multixenobiotic resistance

NETs	Neutrophil extracellular traps
PD	Pharmacodynamic
RNA	Ribonucleic acid
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SIRS	Systemic inflammatory response syndrome
sST2	Soluble suppression of tumorigenicity 2
suPAR	Soluble urokinase-type plasminogen activator receptor
TREM-1	Soluble triggering receptor expressed on myeloid cells 1

Introduction

Recent research has been targeted to identify novel sensitive and specific biomarkers for the improvement in the process of diagnosing, optimizing treatment, and bettering outcomes of diseases. Here we provide an overview of the newer classification, of emerging biomarkers in the field of cardiovascular critical care, COVID-19, and biomarkers of infection in the critical care. As the future studies have the need to develop more accurate diagnostic, prognostic, and predict the clinical outcome, the novel biomarkers that could be more clinically applicable and offer greater patient acceptability than conventional biomarkers need to be classified in several different types to be better understood for future exploration purposes. In the field of biomarkers nowadays, it is possible to have valid, unbiased detection of emerging biomarkers in wide range of clinical research, and from plasma. Researches dealing with biomarkers are mostly focused on detailed exploration of plasma proteome at novel depth and identify the detailed biological insights for emerging biomarker discovery. However, we can distinguish more than one different type of emerging biomarkers and we present the overview in the upcoming subchapter.

Different Types of Emerging Biomarkers in Trauma, Injury Critical Care, and Recovery

There are many types of emerging biomarkers, but commonly used one in trauma, injury critical care, and recovery is identifying molecular biomarkers, organic biomarkers, and population biomarkers, whereas molecular biomarkers include: 1. inhibition/induction of enzymes; 2. change in DNA/RNA; 3. inhibition/induction of MXR (Fig. 1). The mechanism of multixenobiotic resistance (MXR) is present in many organisms as an important cellular detoxification mechanism. It is mediated by the activity of ABC transporters that bind and actively expel various toxic substances from cell; 4. induction of metallothionein. Metallothioneins (MT) present a family of proteins that are rich in cysteine and known for their low molecular weight that ranges between 500 and 14,000 Da. Golgi apparatus is the localization point of metallothioneins. They are highly important for many metabolic reasons but firstly for the ability to bind physiological (such as zinc, copper, and selenium) and

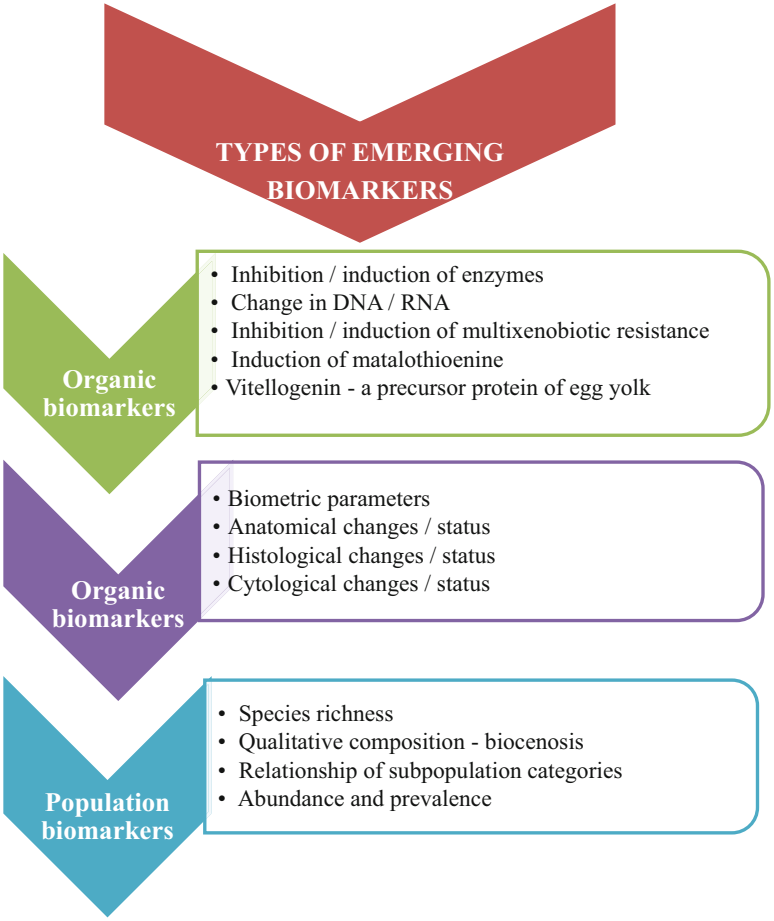

Fig. 1 Types of emerging biomarkers in trauma, injury critical care, and recovery

xenobiotic (e.g., cadmium, mercury, silver, and arsenic) heavy metals. Metallothioneins were revealed in 1957 by scientist Vali and Margoš from a purified Cd-binding protein from the equine renal cortex (Felizola et al. 2013). Metallothionein play an important role in protection against metal toxicity and oxidative stress, and participate in the regulation of zinc and copper concentrations (Wang et al. 2014); and 5. vitellogenin is a precursor protein of egg yolk. It can only be detected in females and it is used as a biomarker in vertebrates. On the other hand, the organic biomarkers are: 1. biometric parameters; 2. anatomical changes/status; 3. histological changes/status; and 4. cytological changes/status. Finally, we can go through population biomarkers, where so far identified ones are: 1. species richness; 2. qualitative composition – biocenosis; 3. relationship of subpopulation categories; and 4. abundance and prevalence. In ecology, local abundance is the relative representation of a species in a particular ecosystem. It is usually measured as the

number of individuals found per sample. The ratio of abundance of one species to one or multiple other species living in an ecosystem is referred to as relative species abundances (Preston 1948). Both indicators are relevant for computing biodiversity. A variety of sampling methods are used to measure abundance. For larger animals, these may include spotlight counts, track counts, and roadkill counts, as well as presence at monitoring stations (Wright 1991). In many plant communities the abundances of plant species are measured by plant cover, i.e., the relative area covered by different plant species in a small plot (Damgaard 2009). Abundance is in the simplest terms usually measured by identifying and counting every individual of every species in a given sector. It is common for the distribution of species to be skewed so that a few species take up the bulk of individuals collected (Verberk 2011). Relative species abundance is calculated by dividing the number of species from one group by the total number of species from all groups.

Classification of Emerging Biomarkers According to Their Main Clinical Application in Trauma, Injury Critical Care, and Recovery

According to their main clinical application, we can divide emerging biomarkers in trauma, injury critical care, and recovery in the following groups (Fig. 2): 1. diagnostic biomarkers. Biomarkers of this category are used to confirm the existence of a disease or medical condition. In this context, diagnostic biomarkers may play an important role to reach a precise diagnosis, identifying patient with a disease and facilitating the classification of patients with the same type of diagnosis to personalize drug treatments, therefore increasing the efficiency of the therapeutic response; 2. monitoring biomarkers. This category includes biomarkers measured at different time points for assessing the presence, status, or extent of a disease or medical condition. Besides this, they can be used to evaluate the effects of medical products or environmental agent exposures; 3. pharmacodynamic/response biomarkers. Pharmacodynamic/response (PD) biomarkers present a vast spectrum of applications from the early phases of the discovery research to the clinical trials and later during the clinical practice. This type of biomarker may be defined as "a biomarker used to show, that a biological response occurred in an individual exposed to a medical product and environmental agent." These biomarkers provide information about proof of mechanism, proof of concept, selection of optimal biological dosing, and understanding response/resistance mechanism; 4. predictive biomarkers. This category includes markers that identify patients more likely to experience an effect (positive or negative) after the exposure to a medical product or an environmental agent. These biomarkers are commonly used in randomized control clinical trials of new therapies as selection criteria for including patients in the study or to stratify them into intervention group; 5. prognostic biomarkers. According to its definitions, theses biomarkers identify the likelihood of a clinical event, disease recurrence, or progression in patients diagnosed with a disease or having a medical condition. In clinical trials, prognostic biomarkers allow to predict the occurrence of a clinical event in the future, such as death, disease

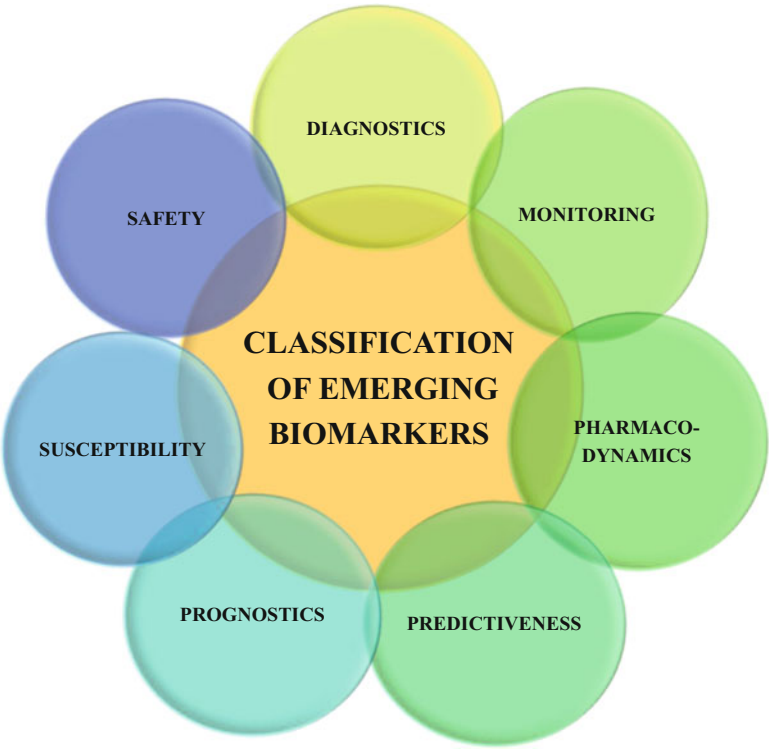

Fig. 2 Classification of emerging biomarkers according to their main clinical application in trauma, injury critical care, and recovery

progression, disease recurrence, or development of a new medical condition; 6. susceptibility or risk biomarkers. Susceptibility/risk biomarkers indicate the potential for developing a disease or medical condition in an individual not currently presenting a clinically apparent disease or medical condition. The major difference between this category of biomarkers and prognostic biomarkers lies in the fact that susceptibility/risk biomarkers are measured in individuals not presenting the disease. Thus, these biomarkers can be detected long before the appearance of a disease and are not useful to describe the response to any specific treatment; and 7. safety biomarkers (Fig. 3). The relevance of this biomarker is to predict toxic adverse events induced by drugs, medical interventions, or environmental agents' exposure. Toxicity can be reflected by the detection of the biomarker or changes in biomarker level, facilitating the necessary actions to prevent irreversible damage, such as those adjustment, treatment interaction, or initiation of a specific treatment (Davis 2017).

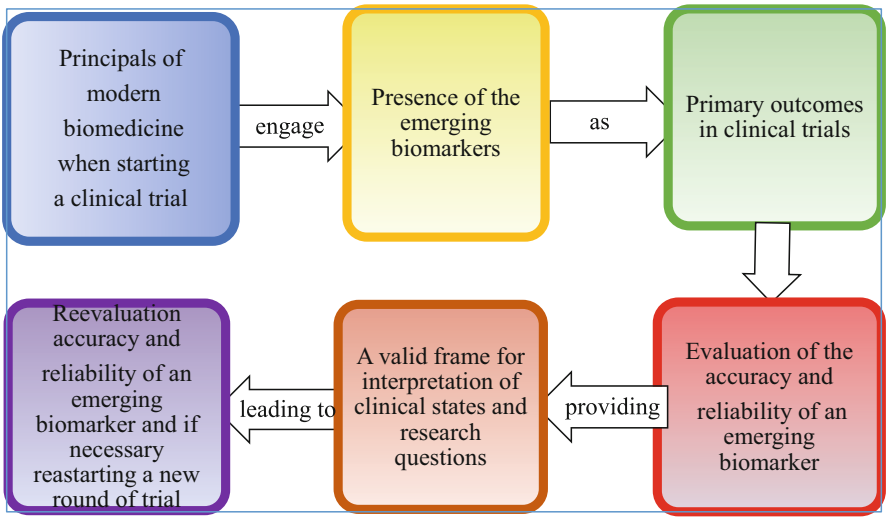

Fig. 3 Role of biomedicine and emerging biomarkers in modern medicine's trauma, injury critical care, and recovery

Fig. 4 Best treatment for all diseases

Role of Biomedicine and Emerging Biomarkers in Modern Medicine's Trauma, Injury Critical Care, and Recovery

Modern medicine and its basic and clinical research and clinical practice in trauma, injury critical care, and recovery rely on biomedicine and biomedical assessments of biomarkers more and more (Flier and Loscalzo 2017) and this applies dominantly on emerging biomarkers (Fig. 4). Biomedicine uses emerging biomarkers and their presence as primary outcomes in clinical trials and practice and this is now a widely

accepted and highly appreciated practice (Strimbu and Tavel 2010). The more one biomarker is specific the more the same biomarker is well characterized and confirmed to correctly predict relevant clinical or research outcomes across a different methodology or type of treatments and different subpopulations (Ray et al. 2010), and this applies even more to emerging biomarkers. Therefore, this kind of approach to assessment is entirely justified and appropriate. However, in many cases, the actual accuracy and reliability of a biomarker is presumed where, in fact, it needs to be further evaluated and reevaluated (Burke 2016) and that is most of all valid for the emerging biomarkers in the field of application in trauma, injury critical care, and recovery. The current conceptual status of biomarkers both in the field of clinical and diagnostic assessment, more specifically in trauma, injury critical care, and recovery, is presented through the roll of both assessment tools (biomarkers) and outcomes in clinical practice and research with the final aim of providing a valid frame for interpretation of clinical states and research questions that rely significantly on such biomedical measures. Biomedical measures derive from biomedicine. Thus, biomedicine is the branch of medicine concerned with the application of the principles of biology and biochemistry to medical research or practice focused mostly on constant identification of emerging biomarkers and other diagnostic and prognostic possibilities.

Modern Medical Diagnostics in Trauma, Injury Critical Care, and Recovery

In medical practice, laboratory diagnostics in the form of emerging biomarker testing are most often used for diagnosing and prognostics as well as monitoring of diseases. All these are used dominantly in the field of trauma, injury critical care, and recovery. This diagnostic strategy is often somewhat uncertain because it can be dishonorable due to the specificity of the emerging biomarker itself or the inaccuracy of the patient's clinical perception or interpretation of the emerging biomarker diagnostic test. The uncertainty caused by the first mentioned phenomenon is today largely reduced by the development of new, more suitable analytical procedures and by paying more attention to quality control in laboratories in regard to development and application of emerging biomarkers. Analytical laboratory methods and procedures that are mostly being developed today are emerging biomarkers of diseases targeted to certain organs that must have specific characteristics in order to meet the condition to be used as biochemical markers for detecting and differentiating certain diseases of a given organ. By applying this definition, we approach the so-called organ specificity of the human biochemical parameter, which changes in clinical enzymology, although to a limited extent. In following subchapters, an overview of some of the emerging biomarkers is presented (Fig. 5).

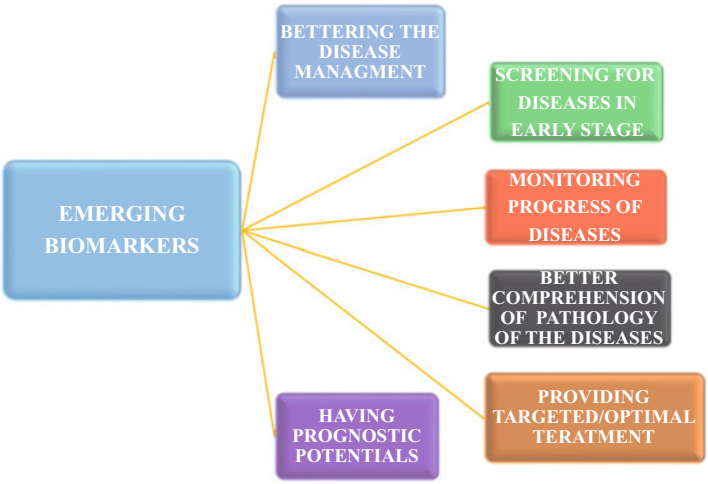

Fig. 5 The potentials of emerging biomarkers in bettering the disease management

An Overview on Emerging Biomarkers in Cardiovascular Events in Trauma, Injury Critical Care, and Recovery

The rapid assessment of patients who are in need of critical care due to cardiovascular symptoms that often are suggestive of an acute coronary syndrome is of great clinical importance. Emerging biomarkers progress toward being progressively significant in this critical care setting to help (Table 1) along with the standard diagnostics comprising electrocardiographic findings and patient history, especially since both mentioned nights sometimes be misleading. Today, cardiac troponin is still the only marker used routinely in this setting due to its myocardial tissue specificity and sensitivity, as well as its established usefulness for therapeutic decision-making. However, even current-generation troponin assays have certain limitations such as insufficient sensitivity for diagnosing unstable angina. Emerging biomarkers for cardiac state have the potential to overcome these limitations. It is inevitable to mention that further studies are needed to elucidate existing dilemmas regarding the optimal cutoffs for diagnosis and risk assessment and to provide as accurate as possible framework in which we can exclude the diagnosis of an acute myocardial infarction. It is also important to mention that some other nonmyocardial tissue-specific markers can help in regard to this diagnostic. Further studies are necessary before these emerging biomarkers can be adopted routinely in clinical practice.

Table 1 Emerging biomarkers in cardiovascular in trauma, injury critical care, and recovery

Blood biomarkers	Clinical use	Clinical use potential	References
Soluble suppression of tumorigenicity 2 (sST2)	Yes	Chronic heart failure and acute coronary syndrome have a prognostic value, while being unaffected by possible confounders such as renal failure, age, sex, and anemia. Serum soluble ST2 is a novel biomarker for neurohormonal activation in patients with heart failure. In patients with severe chronic NYHA class III to IV heart failure, the change in ST2 levels is an independent predictor of subsequent mortality or transplantation	Schernthaner et al. 2017; Li et al. 2021
Heart-type fatty acid binding protein (H-FABP)	Yes	It is found in striated muscle cells and is released to the systemic circulation as a consequence of myocardial damage, also an early indicator of myocardial infarction	Liebetrau et al. 2014
Growth differentiation factor (GDF-15)	Yes	Very useful biomarker in inflammatory processes, cardiovascular disease, and also cancer and kidney injury	Nair et al. 2017
Soluble urokinase-type plasminogen activator receptor (suPAR)	Yes	It is an inflammatory marker and is also useful for risk stratification concerning development of cardiovascular disease. Elevated levels reflect subclinical inflammation and are observed in individuals with increased alcohol consumption or smokers	Backes et al. 2012
Cystatin C	Yes	Background elevated plasma cystatin C levels reflect reduced renal function and increased cardiovascular risk	West et al. 2022
Cardiac troponin I (cTnI)	Yes	Noncausal biomarker for acute myocardial infarction – AMI	Moksnes et al. 2021
High monocyte to high-density lipoprotein cholesterol ratio (MHR)	Yes	High MHR at the time of initiation of dialysis may represent a useful predictor of cardiovascular complications	Kim et al. 2021

Emerging Biomarkers in COVID-19 Critical Care and Recovery

A pandemic of coronavirus disease 2019 (COVID-19), that is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported from Wuhan, China, on 31 December 2019. It is still present and ongoing worldwide. Up to date, best to our knowledge, there is no efficient novel biomarker that would be able to

timely predict the disease progression uninfected. Therefore, all the emerging biomarkers or preexisting biomarkers now in the novel roll of having been used in last two and a half years as relevant in order to analyze the inflammatory profiles of COVID-19 patients indicate their implications in regard to the progression of COVID-19 disease and are of high importance (Table 2). Among the emerging COVID-19 biomarkers one related to coagulopathy process might be one of the most important. Coronavirus disease 2019 (COVID-19) makes patients highly vulnerable to thrombotic and thromboembolic events, provoking excessive inflammation, initiate the endothelial cell activation and injury, as well as inducing the platelet activation and hypercoagulability. Therefore, very often the patients with COVID-19 suffer a prothrombotic or thrombophilia state, with markable elevations in the levels of several emerging biomarkers of thrombosis, which are associated with disease severity and prognosis. Previously known D-dimers were mostly used as indicative early during the onset of the pandemic, but in the last year many novel biomarkers of thrombotic risk in COVID-19 have emerged. We can also notice that emerging biomarkers are found that indicate inflammation at early stage and ones that have prognostic value via respiratory function of patient. Up to date, there is still lack of strict protocol of monitoring defined set of emerging biomarkers in COVID-19. However, a thorough understanding of sensitivity and specificity of these emerging biomarkers might help risk stratification and prognostics, guide interventions, and provide a damage control intervention in future treatments. Further studies of this biomarkers are necessary.

Emerging Biomarkers of Infection in the Critical Care

Previously published evidence confirms that a share over 25% of all annual deaths in the world are due to infection (Dellinger et al. 2013). And sepsis is considered to be an infection (ongoing or threatening to happen) with consequences on the whole organism, on the systemic level, such as systemic inflammatory response syndrome (SIRS) (Dellinger et al. 2013). There is classification within the severity, and the severe sepsis is common; it occupies a significant share of critical care health unit resources, and even more importantly, this state is associated with high mortality (Angus et al. 2001). Good management of the disease and mortality prevention via timely response to infection and sepsis relay on timely diagnosis. The responses in sepsis are happening consecutive steps comprising inflammatory, humoral, cellular, and circulatory invalidities. Timely diagnosis and high-quality risk management of the disease enables quick response and targeted treatment, but are additionally demanding due to the fact that the signs and symptoms of sepsis are nonspecific and highly variable. Emerging biomarkers can be of great help and they can bring an added value to the process of valid decision-making by ruling in or out the presence of sepsis, identifying the severity of infection, and eventually in some cases determining an etiology (e.g., bacterial versus viral infection). Also, biomarkers can help differentiating systemic sepsis from local infection. In the past, a significant number of biomarkers have been already identified in infection and sepsis. However, the established biomarkers lack reliability, validity, and clinical utility confirmation and

Table 2 Emerging biomarkers in COVID-19 critical care and recovery

Blood biomarkers	Clinical use	Clinical use potential	References
Neutrophil extracellular traps (NETs)	Yes	A prothrombotic scaffold consists of neutrophil-derived chromatin associated with pro-coagulant proteins and antimicrobial proteins, such as myeloperoxidase (MPO) or neutrophil elastase. Studies have shown that NET components are present abundantly in plasma, serum, and post.mortem specimens from patients with COVID-19. Autopsy specimens from patients who died from COVID-19 have revealed NET-containing microthrombi in many cases	Zuo et al. 2020; Veras et al. 2020
Cell-free DNA	Yes	Showed a rather weak negative correlation with oxygenation parameters, but its decrease over time predicted the number of ventilator-free days	Huckriede et al. 2021
Myeloperoxidase-DNA complexes (MPO–DNA complexes)	Yes	Correlated strongly with COVID-19 severity and were also associated with thrombotic events in most studies	Guéant et al. 2020
Citrullinated histone 3 (H3Cit)	Yes	Correlated strongly with COVID-19 severity and was also associated with thrombotic events in most studies, also with requirement for respiratory support and mortality	Nicolai et al. 2020
Complement factor (C3, C5, C5a, C5b-9)	Yes	Were associated with disease severity, also studies showed increased activation of the complement system (higher levels of C5a and soluble C5b-9) in critically ill patients, suggesting prognostic utility	Ma et al. 2021
MicroRNAs	Yes	Were correlated with disease severity, and specific circulating microRNA profiles (such as miR-148a-3p, miR-451a, and miR-486-5p) seemed to have prognostic predictive utility	de Gonzalo-Calvo et al. 2021
Angiotensin-converting enzyme 2 (ACE2)	Yes	A case report found increased serum ACE2 levels in a patient with COVID-19 acute respiratory distress syndrome	Nagy et al. 2021
High-mobility group box protein 1 (HMGB1)	Yes	Elevated in the serum and plasma of patients with severe COVID-19 and is associated with an adverse prognosis	Chen et al. 2020
Progranulin	Yes	Expressed in epithelial cells, neurons, and macrophages and promotes inflammation and cell proliferation; progranulin levels were upregulated in patients with COVID-19 and were associated with adverse outcomes, suggesting prognostic utility	Rieder et al. 2020

(continued)

Table 2 (continued)

Blood biomarkers	Clinical use	Clinical use potential	References
Calprotectin	Yes	Was found to be elevated in the serum and plasma from patients with COVID-19 compared with the levels in healthy individuals, also was associated with disease severity and thrombotic risk	Bauer et al. 2021

still await further confirmations. In this subchapter, we provide an overview (Table 3) of the emerging biomarkers that are promising in diagnostics and prognostics. However, these emerging biomarkers also require further validation through more research and practice.

Clinical Outcomes and Emerging Biomarkers: Overlaps and Differences

Contrary to biomarkers, we have clinical outcomes that present type of parameters that do correlate to the health status of person who participates in a clinical trial. Namely, we observe how that participant feels, functions, or survives. Clinical outcomes are the variables that present self-perceived health-related aspects participating in the clinical trial (Fleming and Powers 2012) or objectively measured health-related aspects participating in the clinical trial. Lately with increasing number of clinical trials and both increasing number of emerging biomarkers, there is a noticeable shared approach to monitoring both emerging biomarkers and clinical outcomes when trying to understand the dynamic of the diseases and compose the optimal retreatment protocol. While some of the clinicians and researchers are prone to more trusting that clinical outcomes are the dominant and more applicable in practice, the other researchers rely on emerging biomarkers as well. Eventually, the most likely optimal approach would comprise parallel follow-up. In favor to this approach, we can encounter the situation in which after several repeated clinical trials outcome appears to be a solid indicator for certain health-related aspect, and therefore promoted to a novel biomarker. While this ability to indicate a certain aspect of health presents an overlap between an emerging biomarker and a clinical outcome, on the contra-side the aim of clinical practice is to decrease morbidity and mortality through observing clinical outcomes, while not having in focus the measurable aspects of patients' native biochemistry that are observed through biomarkers activity. Notwithstanding, we are all trying to identify optimal prevention, early detection, and best treatment for all diseases, not exclusively from the point in which we need quantifiable biomarkers that often but not always correlate with the disease but to have good direction in which we parallelly observe the somatic and mental indicators parallel to most likely outcome and through joint action set the final pathway. Thus, both emerging biomarkers and clinical outcome matter (Burke 2017). Some clinical

Table 3 Emerging biomarkers of infection in the critical care

Blood biomarkers	Clinical use	Clinical use potential	References
Soluble triggering receptor expressed on myeloid cells 1 (TREM-1)	Yes	It is a member of the immunoglobulin superfamily, and is greatly upregulated in infections, but not in noninfectious inflammatory conditions; also as an indicator of sepsis it is superior to those of CRP and PCT	Jiyong et al. 2008
Presepsin	Yes	It has a higher sensitivity and specificity in the diagnosis of sepsis as a new biomarker, and is a predictor for the prognosis of sepsis, also it seems that presepsin plays a crucial role as a supplemental method in the early diagnosis of sepsis	Zou et al. 2014
CD64	Yes	Neutrophil CD64 level was found to be an effective diagnostic biomarker for infection in patients with septic syndrome based on sepsis 2 criteria, also some studies showed that neutrophil CD64 outperformed CRP and PCT	Yeh et al. 2019
IL-27	Yes	A sepsis diagnostic biomarker in critically ill children. When used in combination with PCT, IL-27 may improve classification of critically ill adults with sepsis secondary to a non-lung source of infection	Wong et al. 2013
Cell-free DNA (cfDNA)	Yes	It can be considered a good prognostic marker of clinical outcome in septic patients. Its levels increase in case of acute kidney injury complicating sepsis, in particular if CRRT is needed, and are associated with poor outcome	Rhodes and Cecconi 2012
suPAR	Yes	A feasible biomarker for timely diagnosis and prognosis of sepsis. Compared with effective value of PCT, suPAR has similar clinical guiding value, whereas suPAR exhibits higher specificity, which can facilitate the deficiencies of PCT. It can be increased in various infectious diseases, in the blood and also in other tissues	Donadello et al. 2012
MicroRNAs (miRNAs)	Yes	It is associated with the presence and severity of sepsis. Dysregulation of several miRNAs, such as miR-146a, miR-223, miR-15a, miR-16, and miR-150, was found in the peripheral blood of sepsis patients	Wang et al. 2012

outcomes are superior than others. Outcomes that are unreliable or quantifiable give less insight; these include mitigation of not well-defined or unclear symptoms (e.g., severity of pain).

Conclusion

Emerging biomarkers can be of great aide in bettering disease management. The possibilities for these are manifold, especially in the fields of trauma, injury critical care, and recovery. The following instances in which biomarkers can be used effectively are mentioned by Jain: for a better comprehension of the path mechanics of diseases; when screening for diseases in an early stage while patients are still asymptomatic; in unambiguously diagnosing a disease; when writing up a precise description of a disease; in identifying prognoses; in laying a fundament for the development of therapeutics as well as monitoring of the disease with regard to the therapeutics being given, and by predicting which patients have a heightened probability of unwanted side effects of a treatment (Jain 2017). When monitoring patients in post-treatment period, with detection of recurrence or secondary progression of disease or complications, it is higly important to conclude that selecting the tailor-targeted therapies and drugs most likely results in favorable outcomes with a specific patient (personalized medicine).

Limitations of Biomarkers

Although the biomarkers present objective, measurable characteristic of biological activity and even supposing that the information obtained through biomarkers may be in accordance with a patient's own impression of his or her state of health and level of well-being, it is surely probable that this is incorrect. Furthermore, if no fluctuation can be detected or if the identified fluctuation has no relevant measurable effect on a patient's health, this specific aspect has no benefit of being defined as biomarker (Mayeux 2004). The exact same principle applies to many biological lineaments with markedly wide range of possible different modifications between people that minor evidence about health risks can be collected out of them.

To conclude, different types of emerging biomarkers in trauma, injury critical care, and recovery are presented. Clearly, as our knowledge in evidence-based medicine is growing, it is necessary for biomarker research to grow along. Hence, the search for novel biomarkers will continue and intensify and provide new information.

Mini-Dictionary of Terms

- Acute coronary syndrome – a term used to describe a range of conditions associated with sudden, reduced blood flow to the heart. One such condition is a heart attack (myocardial infarction) – when cell death results in damaged or destroyed heart tissue.
- Biocenosis – an association of different organisms forming a closely integrated community.
- Evidence-based medicine – medical practice or care that emphasizes the practical application of the findings of the best available current research.
- Organ specificity – characteristic restricted to a particular organ of the body, such as a cell type, metabolic response, or expression of a particular protein or antigen.
- SIRS – systemic inflammatory response syndrome (SIRS) is an exaggerated defense response of the body to a noxious stressor (infection, trauma, surgery, acute inflammation, ischemia or reperfusion, or malignancy, to name a few) to localize and then eliminate the endogenous or exogenous source of the insult.
- Sensitivity – the ability of a test to correctly identify patients with a disease.
- Sepsis – a potentially life-threatening condition that occurs when the body's response to an infection damages its own tissues.
- Specificity – the ability of a test to correctly identify people without the disease.

Key Facts on Emerging Blood Biomarkers in Trauma, Injury Critical Care, and Recovery

- Recent research has been targeted to identify novel sensitive and specific biomarkers for the improvement in the process of diagnosing, optimizing treatment, and bettering outcomes of diseases.
- Good management of the disease and mortality prevention via timely response to infection and sepsis relay on timely diagnosis.
- Although the biomarkers present objective, measurable characteristic of biological activity and even supposing that the information obtained through biomarkers may be in accordance with a patient's own impression of his or her state of health and level of well-being, it is surely probable that this is incorrect.
- We are all trying to identify optimal prevention, early detection, and best treatment for all diseases, not exclusively from the point in which we need quantifiable biomarkers that often but not always correlate with the disease but to have good direction in which we parallelly observe the somatic and mental indicators parallel to most likely outcome and through joint action set the final pathway.

Summary Points

- The emerging biomarkers should provide unbiased analysis with novel depth of many relevant proteins, they should have unmatched specificity and quantitative precision, high capacity, and easily accessibility.
- Emerging biomarkers can be of great aide in bettering disease management.
- Different types of emerging biomarkers in trauma, injury critical care, and recovery are presented day by day.
- Emerging biomarkers for cardiac state have the potential to overcome troponin's limitations.
- Very often the patients with COVID-19 suffer a prothrombotic or thrombophilia state, with markable elevations in the levels of several novel biomarkers of thrombosis, which are associated with disease severity and prognosis.
- Biomarkers can help differentiating systemic sepsis from local infection.

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