Recommendations for Minimal Laboratory Testing Panels in Patients with COVID-19: Potential for Prognostic Monitoring

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A new infective outbreak, which has been finally defined as coronavirus disease 2019 (COVID-19), has now taken hold all around the world.[1] Although this is recognized as a viral respiratory illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pathophysiology of the disease is far wider than respiratory, including long-term risk for adverse cardiovascular disease, thromboembolic disorders, and multiple organ failure (MOF).[2] The initial clinical course of the respiratory disease can be complicated by the development of interstitial pneumonia in a considerable number of patients, evolving toward acute respiratory distress syndrome in up to 10 to 15% of these, who will then require mechanical ventilation or intensive care.[3] Increasingly recognized, however, is the potential for the development of some forms of thrombotic coagulopathies including intravascular disseminated coagulation (DIC) in a subset of patients and indeed also being prognostic for poor morbidity and mortality.[4,5]

Based on our understanding of the emerging literature, we aim to provide in this short commentary a simple list (►**Table 1**) of laboratory tests, as may be recommended for patients with COVID-19 and to potentially assist in prognostic monitoring of such patients. The rationale for the listing is also provided and based on recent reports around clinical and laboratory features of COVID-19 affected patients.[4–11] However, we recognize that such a list is time-relevant and potentially time-limited and may quickly change as new information emerges. Thus, at all times, local experts should be consulted as available and testing modified accordingly. As an example, antithrombin is noted as lower in COVID-19 cases than in controls[11]; however, there is no current evidence that antithrombin is differentially lower in severe cases and thus may not have clear prognostic value. As another example, the extent of thrombocytopenia does seem to be associated with the severity of disease[12] and thus has been included in ►**Table 1**. On the other hand, there is considerable interaction between platelets and viruses,[13] and therefore an assessment of other platelet indices may also become relevant in the future.

Thus, currently, we recommend a *minimum* test panel for hematology comprising (1) a complete or full blood count (CBC/FBC, representing the United States, European, United Kingdom, Australian nomenclature), (2) routine coagulation tests (prothrombin time [PT] and activated partial thromboplastin time [APTT]), (3) fibrinogen, and (4) D-dimer (optional: other associated tests such as fibrin/fibrinogen degradation products and fibrin monomers as locally available or supported). We also recommend a series of biochemistry and other tests (►**Table 1**), including markers for inflammation, electrolyte disturbance, liver dysfunction, and renal and cardiac damage, which would reflect the development of viral sepsis, systemic inflammatory response syndrome, and/or MOF, which are all conditions associated with an extraordinarily enhanced risk of thrombotic coagulopathies.

Our recommendations in part relate to emerging evidence that intravascular coagulation, inclusive of DIC, is a feature of poor prognosis in seriously affected patients.[4–11] Also widely recognized is worsening organ damage, even death. Our recommendations are tempered by our expertise in the area of hemostasis and biochemistry, and therefore some gaps are unavoidable.

Nevertheless, several lines of evidence now attest that elevation of thrombotic biomarkers, especially D-dimer, is commonplace in patients with COVID-19,[4–11] especially in those with more severe disease.[4] Therefore, routine monitoring of D-dimer and other useful tests such as PT, APTT, fibrinogen,

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Table 1 Recommendations for laboratory tests in patients with COVID-19[a]

Test	Abbreviation	Rationale for inclusion	Considerations
Hematology (including hemostasis/coagulation)			
Complete/full blood count	CBC/FBC	Identification of lymphopenia, neutrophilia, and thrombocytopenia	Include platelet count, differential for lymphocyte count
Prothrombin Time	PT	Identification of ongoing coagulopathy	
Activated partial thromboplastin time	APTT		
Fibrinogen	Fbg or Fib	Identification of ongoing (consumption) coagulopathy	
D-dimer		Identification of ongoing (consumption or thrombotic) coagulopathy	[b]
Biochemistry and other tests			
Electrolytes		Identification of metabolic derangement	
Glucose			
C-reactive protein	CRP	Monitoring of infection/ inflammatory response	[b]
Lactate dehydrogenase	LDH	Identification of lung injury and/or multiple organ failure	
Aspartate aminotransferase	AST	Identification of liver injury	
Alanine aminotransferase	ALT		
Bilirubin			
Albumin		Identification of liver failure	
Creatine kinase (also known as creatine phosphokinase or phosphocreatine kinase)	CK	Identification of muscle injury	
Lipase		Identification of pancreatic injury	
blood urea nitrogen	BUN	Identification of kidney injury and/or failure	
Creatinine			
Cardiac biomarkers (troponin I or T)		Identification of cardiac injury	[b]
Brain natriuretic peptide	BNP	Identification of cardiac failure	[c]
Ferritin		Monitoring of infection/inflammatory response	[b]
Procalcitonin	PCT	Identification of bacterial coinfections	[b]
Presepsin		Monitoring of severity of viral infection	[d]

Abbreviation: COVID-19, coronavirus disease 2019.

[a]These tests may have some prognostic value in COVID-19 patients. However, we recognize that such a list is time-relevant and potentially time-limited and may quickly change as new information emerges. Thus, at all times, local experts should be consulted as available and testing modified accordingly.

[b]"Gating rule": unless clinically justified, testing should not generally be reordered within 24 hours of an existing test.

[c]For selected patients with signs of MOF/SIRS; discuss with an expert (laboratory) clinician/senior or clinical scientist.

[d]For patients under intensive care.

and platelet count would help to rapidly and accurately detect patients at a higher risk or those who have already developed DIC as well as venous thromboembolism, and whereby different clinical management may be required according to clinical settings.

This is, for example, supported by evidence published by Tang et al, showing that most hospitalized patients with COVID-19 who died match criteria for a diagnosis of DIC (i.e., $\sim$ 71 vs. $<$ 1% in survivors),[5] a finding that was also later confirmed in a subsequent study of Han et al.[11] To some extent, the situation with COVID-19 reflects a similar, albeit seemingly worse, coagulopathic risk than other viruses.[14–16]

Whether an early establishment of antithrombotic treatment in patients with severe COVID-19 would be beneficial to prevent (at least) thrombotic coagulopathies remains largely unexplored and indeed should be the subject of urgent studies. Although glycosaminoglycans (thus including heparins) also have some antiviral activities[17] and would thus seem promising therapeutic agents in COVID-19, the identification of the most appropriate antithrombotic treatment, maximizing

benefits and possessing the best balance between bleeding and thrombotic risk in such patients, reflects another compelling need at this time.

Caveats

The recommendations are not intended for implementation in all patients who have tested positive for COVID-19, for example, people with mild disease who have self-isolated at home, but rather for hospitalized patients with potentially severe disease. The information provided here is for guidance only and is based on our understanding of the emerging literature at the time of writing. As the information is time-relevant and potentially time-limited, such guidance may quickly change as new information emerges. Thus, at all times, local experts should be consulted as available and testing modified accordingly. The opinions in this commentary are those of the authors and not necessarily those of the University of Verona or NSW Health Pathology.

Conflicts of Interest
None.

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