The GPSs were then revised based on feedbacks that were redistributed to the panelists for further revisions and finalization.

2 | COMMENT

The Guidelines panel discussed a number of additional considerations to support good clinical care of patients with thrombotic thrombocytopenic purpura (TTP). The "GPSs" are not evidence-based recommendations. Specifically, they are not based on systematic search or formal review of the evidence. These statements are intended to provide a "snapshot" of the care provided to patients with TTP by expert health care providers. They address scenarios in which there is very limited high-certainty evidence, yet there is a body of indirect evidence and/or clinical experience that suggests the net benefit of certain actions. GPSs are intended to guide health care providers who have limited experience in treating TTP. They should be used with caution; the provider's own clinical judgment, in combination with the individual patient's clinical situation, values, and preferences, should all be considered.

3 | SUPPORTIVE CARE

The following statements pertain to initial emergency care and general supportive care of patients with TTP.

3.1 | Statement 1

Clinicians generally consider a diagnosis of TTP in individuals presenting with thrombocytopenia and microangiopathic hemolytic anemia.[1-4] Patients may be critically ill, or may have relatively minor and nonspecific complaints. Importantly, the classic signs of TTP (eg, hemolytic anemia, thrombocytopenia, fever, neurologic abnormalities, and renal abnormalities) also known as "Raynaud's Pentad" are present in only 40% of patients; therefore, the historical pentad only are only seen in the more severe forms of the disease, or in patients left without appropriate treatment resulting from a delayed diagnosis. The prevalence of this catastrophic presentation has decreased in past few decades as the result of better awareness of the disease among practitioners.[4-7] Therefore, the presence of thrombocytopenia and microangiopathic hemolytic anemia without other explanation should prompt a suspicion of TTP in the differential diagnosis.[8]

3.2 | Statement 2

We did not systematically search and review the evidence on different clinical or laboratory approaches for diagnostic workup of a patient with suspected TTP. However, an initial laboratory evaluation of presumptive TTP should include a complete blood count with careful review of a peripheral blood film for lack of platelets and presence of fragmented red blood cells (or schistocytes), serum lactate dehydrogenase, and creatinine, testing to demonstrate hemolysis (eg, low haptoglobin, increased indirect bilirubin), coagulation testing (which is expected to be relatively normal in TTP unless it is a severe form of the disease[5] and there is a concomitant disseminated intravascular coagulation).[9] A direct Coombs test is expected to be negative in TTP, but may be positive in autoimmune hemolytic anemia. Troponin I and electrocardiogram should be systematically performed to identify subclinical cardiac involvement.[5,10,11] Computed tomography/magnetic resonance imaging of the brain may also be included in the initial evaluation for TTP if there are symptoms and signs, suggestive of brain injury.[12-16]

3.3 | Statement 3

If the index of suspicion for TTP is high, clinicians should consider the emergency initiation of therapeutic plasma exchange (TPE) and corticosteroids. Because of the severity and instability of their illness, and the foundational role of TPE in the treatment of TTP, patients experiencing an acute event of TTP are usually urgently transferred to a facility that can perform TPE, ideally overseen by a clinician who has expertise in the management of TTP. Most of these patients (>95%) if plasma ADAMTS13 activity is less than 10 IU/dL (or <10% of normal) are immune-mediated TTP or iTTP.

For a suspected iTTP, a blood sample should be obtained for plasma ADAMTS13 testing (eg, activity and inhibitors or anti-ADAMTS13 IgG, etc.) before the initiation of TPE. Daily TPE is generally initiated as soon as possible with fresh frozen plasma (FFP), or cryopoor plasma, or solvent detergent-treated (SD) plasma as a replacement fluid. The volume of the replacement fluid is usually 1.0 to 1.5 times of patient's plasma volume (ie, 40-60 mL/kg) every 24 hours until normalization of patient's platelet counts and serum lactate dehydrogenase.

Patients with a suspected or confirmed hereditary or congenital TTP (cTTP) are generally treated with plasma infusion (10 to 15 mL/kg) at a frequency of every 1 to 3 weeks for maintenance therapy or daily for a symptomatic patient until the symptoms resolve and normalization of platelet counts.[17-19]

3.4 | Statement 4

Because of the severity and instability of their illness, TTP patients experiencing an acute event are often managed in a setting with critical/intensive care capabilities, including continuous monitoring of neurologic status, cardiac status, and oxygen saturation. Initial management in a critical/intensive care setting is considered appropriate on the grounds that TTP patients may deteriorate quickly, and have a high risk of severe organ dysfunction such as coma, ischemic stroke, seizures, myocardial infarction, congestive heart failure, arrhythmias, mesenteric ischemia, pancreatitis, and acute kidney injury. All