SSC Subcommittee Project/Collaborative Project

NAME OF PROJECT

Management of antiphospholipid antibody-positive patients with ischaemic stroke, transient ischaemic attack or other brain ischaemic injury

Subcommittee on Lupus anticoagulant/ antiphospholipid antibodies

Person responsible (Chair / Principal Investigator): **Hannah Cohen** (Chair, ISTH-SSC Subcommittee on Lupus Anticoagulant / Antiphospholipid Antibodies) / **Hannah Cohen** (Principal Investigator)

Other investigators: Deepa Arachchillage, Sam Schulman, Katrien Devreese, Robert Roubey, Diana Aguiar de Sousa, Doruk Erkan, Steven Levine, David Werring, David Isenberg

Description Abstract:

The optimal strategy for management of antiphospholipid antibody-positive patients with acute ischemic stroke (AIS), transient ischemic attack (TIA), or other brain ischemic injury is poorly defined. The identification of patients with thrombotic APS and their optimal management is of high clinical importance to prevent potentially avoidable recurrent arterial and venous thrombosis. The clinical importance of identifying these clinical manifestations of APS has been recognized in successive ISTH guidance documents [1,2] and the National Clinical Guideline for Stroke for the UK and Ireland [3]. However, an ISTH SSC LA/aPL Subcommittee survey highlighted the diverse approaches to diagnosis and antithrombotic treatment of patients with APS and AIS, TIA, or other brain ischemic injury [4]. While there was generally good agreement on several aspects, including which patients with AIS or TIA to test for aPL, there was less agreement on other aspects, including aPL testing for brain ischemic injury other than AIS/TIA or if an alternative cause for stroke or TIA exists; which aPL tests to perform, their timing and age cut-off; and aPL phenotype to trigger antithrombotic treatment. Only 39% advised aPL testing in patients with vascular cognitive impairment or dementia and there was a general absence of local guidance defining criteria for aPL testing, with the greatest lack (82%) for cognitive impairment/dementia, with cognitive impairment common in patients with aPL, and associated with white matter hyperintensities (WMH), ischemic lesions, and cortical atrophy [4].

The need for patients with APS-associated AIS or TIA to receive antithrombotic treatment is established. In a prospective cohort study of 1000 patients with APS, in which approximately 20% of patients with APS had stroke and 11% of patients with APS had TIA at baseline, 25% of patients on antithrombotic treatment developed thrombosis over 5 to 10 years of follow-up (5.3% AIS and 4.7% TIA) [5]. However, a variety of antithrombotic options exist, due to the lack of definitive data. Two RCTs comparing standard-intensity vs high-intensity warfarin in patients with thrombotic APS concluded that standard-intensity warfarin is appropriate for patients with thrombotic APS. However, in both studies, patients with arterial thrombotic APS were underrepresented: 44 of 109 (34 arterial only) in one [6] and 27 of 114 in the other [7]. A systematic review and meta-analysis

reported that 22% of patients with initial stroke or other arterial occlusion on VKA or DOAC (95% CI, 0.15-0.31), and 21.6% of patients receiving antiplatelet therapy (95% CI, 0.18-0.26), developed recurrent thromboembolism over 2 years follow-up [8].

A further review and meta-analysis reported that combined antithrombotic therapy (VKA plus single antiplatelet treatment) may be more effective than single agents for secondary prophylaxis for APS-associated arterial thrombosis, and that dual antiplatelet treatment may be more effective than single agents [9]. Antithrombotic treatment for a first APS-associated TIA or white matter hyperintensities (WMH) is important to address, a first TIA being associated with a high risk of subsequent TIA/AIS, estimated at up to 20% within 90 days [10] and an opportunity to institute secondary prevention therapy. In the SSC Subcommittee survey, only 50.5% recommended antithrombotic treatment after a first TIA [4].

The proposed document will give clarity and guidance to healthcare professionals based on available evidence. Uncertainty in this field will be addressed. A more uniform multidisciplinary, consensus approach to the management of antiphospholipid antibody-positive patients with AIS, TIA and other brain ischaemic injury, would represent a major advance in the field as it would ultimately lead to improved patient care. This guidance will also serve as a call and focus for research.

Design and methodology:

Recommendations will be based on systematic review of the literature and expert opinion. The guidance will also be informed by the findings of the ISTH SSC Subcommittee on Lupus Anticoagulant/Antiphospholipid Antibodies survey on diagnosis and antithrombotic treatment of APS-associated AIS, TIA, or other brain ischemic injury [4].

The method endorsed by the ISTH Guidance and Guidelines Committee Panel on writing guidance will be applied. Accordingly, the wording “recommend” indicates a strong consensus among the co-authors; “suggest,” a moderate consensus; and “propose” the areas where there is limited knowledge.

Expected timeline:

Project stage/set up: December 2023

Launch: January 2024

Duration 12 months

Finalization/analysis: third quartile 2024

Reporting: end 2024.

Expected outcomes (ie. publications):

Publication of Guidance from the Scientific and Standardization Committee for Lupus Anticoagulant/Antiphospholipid Antibodies Subcommittee of the International Society on Thrombosis and Haemostasis, in the Journal of Thrombosis and Haemostasis:

Title: Management of antiphospholipid antibody-positive patients with ischaemic stroke, transient ischaemic attack or other brain ischaemic injury

Authorship: Hannah Cohen, Deepa Arachchillage, Sam Schulman, Katrien Devreese, Robert Roubey, Diana Aguiar de Sousa, Doruk Erkan, Steven Levine, David Werring, David Isenberg

Description of project set/up and management, needed infrastructure and resources (summary):

Hannah Cohen (Chair, SSC LA/aPL) will lead the project, supported by the current co-chairs of the subcommittee. In addition, experienced recognized authorities in the field will contribute.

No resources needed.

References:

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