Common Conditions Requiring Long-Term Anticoagulation in Neurosurgical Patients

Augustus J. Perez, MD[a], Gerald A. Grant, MD[b,*]

KEYWORDS

• Anticoagulation • Antithrombotic • Thrombophilia • Prothrombotic • Thrombogenic
• Atrial fibrillation • Mechanical heart valve • Bioprosthetic valve

KEY POINTS

- Atrial fibrillation, mechanical heart valves, and thrombophilia represent chronic medical conditions requiring anticoagulation.
- Warfarin has represented the standard treatment of these conditions.
- Although direct oral anticoagulants have shown promise and have antidotes to immediately reverse their activity, studies have not demonstrated universal efficacy.
- Chronic anticoagulation in neurosurgical patients must be approached by taking into account both the scientific literature supporting its use with individual patient profiles.

INTRODUCTION

Long-term anticoagulant therapy serves primarily to arrest the propagation of thrombus, thereby preventing the development of highly morbid conditions related to impairment of vital tissues at the terminus of the vascular bed. Costly sequelae can include cerebral ischemia, pulmonary embolism (PE) and infarct, and compromise or loss of limbs. The use of anticoagulation in neurosurgical patients urges a continued risk analysis by the surgeon given the inherent complexity proffered by this clinicopathologic schema in the setting of thrombophilia. Therefore, management of neurosurgical patients with conditions such as atrial fibrillation (AF), mechanical heart valves, and other prothrombotic states necessitates application of a vetted strategy to mitigate the potential complications of anticoagulation.

With their continued development, the direct oral anticoagulants (DOACs), which include the direct thrombin and factor X inhibitors, have become de rigueur in the management of certain subsets of this patient population. Their use in neurosurgical patients yields new considerations to be had, in particular, the introduction of adequate reversal agents. Previously, idarucizumab (or Praxbind) was the only reversal agent against dabigatran (Pradaxa) approved by the Food and Drug Administration (FDA). At the time of drafting this article, the FDA released its approval of andexanet alfa (AndexXa) for use against apixaban (Eliquis) and rivaroxaban (Xarelto). Further enumeration of these considerations

Disclosure Statement: The authors have nothing to disclose.
[a] Pediatric Neurosurgery, Department of Neurosurgery, Stanford University Medical Center, 300 Pasteur Drive Room R211, MC 5325, Stanford, CA 94305, USA; [b] Department of Neurosurgery, Stanford University Medical Center, 300 Pasteur Drive Room R211, MC 5327, Stanford, CA 94305, USA
* Corresponding author.
E-mail address: ggrant2@stanford.edu

Neurosurg Clin N Am 29 (2018) 529–535
https://doi.org/10.1016/j.nec.2018.06.009

relates to patient management and clinical trajectory regarding secondary hemorrhage potential.

This article serves as a brief exposition of the more common chronic clinical entities that require the use of prolonged anticoagulant therapy with special consideration for neurosurgical patients. This exposition includes a discussion of established treatment strategies across all available treatment options.

THROMBOEMBOLIC RISK ASSESSMENT AND MANAGEMENT IN ATRIAL FIBRILLATION

With evidence that suggests an increasing incidence and prevalence, AF represents a global health concern that portends a higher consequent risk of death, heart failure, and thromboembolic events.[1–3] As the most common sustained cardiac arrhythmia, the number of individuals worldwide with AF has been estimated at approximately 33.5 million in 2010[3] and the total estimated cost is approximately 1% of health care expenditure.[2] In the United States, the prevalence of AF in 2005 was 3.03 million with a projected increase to 7.56 million by 2050.[4] The Framingham Heart Study provided a lifetime risk of the development of AF as 26% for men and 23% for women aged 40 to 95 years.[5] AF has been historically characterized as occupying a spectrum that ranges from paroxysmal, persistent, long-standing persistent to permanent.

Management of patients with AF focuses on the prevention of the primary sequelae of AF, namely, ischemic stroke secondary to thromboembolism. However, thromboembolic events can also occur in the systemic and pulmonary circulations. Moreover, stroke and transient ischemic attack (TIA) events in the setting of AF have an augmented severity and have been shown to relate worse outcomes compared with these events in the absence of AF. A study by Anderson and colleagues[6] demonstrated a markedly increased ratio of hemispheric to retinal events in the setting of AF versus carotid disease (25:1 compared with 2:1). AF-related stroke, when compared with stroke without AF, seems to confer increased disability and a higher mortality.[7] Additionally, TIAs with their cause in AF are typically prolonged and associated with MRI diffusion changes. Therefore, the American Heart Association (AHA) revised the stroke definition attempts to reclassify these TIAs as stroke.[8]

Current Methods in Risk Assessment

Estimating embolic risk becomes crucial for patient management and, in conjunction with annualized rates of hemorrhagic complications, is the pivot point for decisions on prescribing anticoagulation therapy. Tools, including the one outlined later, have long been in development to navigate this scenario; but a foray into the nuances of this judgment pathway is, of course, beyond the scope of this article. **Table 1** outlines the CHA_2DS_2-VASc model, the contemporary risk assessment model. The resultant score ranges from 0 to a maximum of 9 and represents a range of stroke risk with mean rates of stroke starting at 0.2, 0.6, and 2.2 for scores of 0, 1, and 2, respectively. Most

Table 1
CHA_2DS_2-VASc embolic stroke risk stratification for patients with nonvalvular atrial fibrillation

Definition	Score	Cumulative Score	Unadjusted Ischemic Stroke Rate (% Per Year)
—	—	0	0.2%
Congestive heart failure	1	1	0.6
Hypertension	1	2	2.2
Age ≥75 y old	2	3	3.2
Diabetes mellitus	1	4	4.8
Stroke/TIA/TE	2	5	7.2
Vascular disease (prior MI, PAD, or aortic plaque)	1	6	9.7
Age 65–74 y old	1	7	11.2
Sex category (female)	1	8	10.8
Maximum	*9*	*9*	*12.2*

Abbreviations: MI, myocardial infarction; PAD, peripheral artery disease; TE, thromboembolism.

Modified from Lip GYH, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro heart survey on atrial fibrillation. Chest 2010;137(2):266; with permission.