Age-Related Changes in Thrombosis and Hemostasis

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The global share of older people, aged 60 years or older increased from 9.2% in 1990 to 11.7% in 2013 and will continue to grow as a proportion of the world population, reaching 21.1% by 2050.1

Approximately, one in four deaths worldwide is attributable to stroke or ischemic heart disease. Stroke is the leading cause of disability. Venous thromboembolic disease, pulmonary embolism and deep venous thrombosis, contributes substantially to the global burden of disease. The incidence of arterial and venous thrombosis increases with age.2 Given the aging of the population, the impact of thrombotic disorders worldwide is expected to increase dramatically. Likewise, the risk of bleeding in the older population is also higher.

This issue of Seminars in Thrombosis & Hemostasis is devoted to aging and the perturbations that occur with aging that may account for the increased risk for both thrombosis and hemorrhage. To begin with, Favaloro et al3 reviewed the hemostatic markers that are measurable in most clinical hemostasis laboratories, with age-related changes in both the procoagulant and anticoagulant factors, with additional discussions on the need for potential age-adjusted normal ranges. This is well illustrated in D-dimer testing as a means for predicting the recurrence of venous thrombosis, and is extensively reviewed in the next article by Lippi et al.4 Among those hemostasis factors affected most by age-related changes is the increase in von Willebrand factor. The implications of such changes on the risk of thrombosis and in the treatment of von Willebrand disease are therefore discussed by Konkle.5

One of the often underrecognized modulators of hemostasis and an important pathogenic factor in vascular diseases is plasminogen activator inhibitor 1 (PAI-1). Recently, PAI-1 was found to have a role in senescence. Eren et al provide both the background and genetic basis of the association between PAI-1 and senescence and further demonstrate how PAI-1 knockout can restore the shortened life span of the Klotho (kl/kl) mice.5 The changes in PAI-1 expression with aging and elevated PAI-1 in several age-related pathologies including malignancies, insulin resistance, inflammation, and stress are then reviewed by Yamamoto et al.7 These authors also provided findings showing how increased PAI-1 contributes to the progression of aging by promoting fibrosis and thrombosis.

Platelets, likewise, undergo changes with aging. Among these changes is the decreased antiaggregation response to nitric oxide, a phenomenon described by Procter et al.8 Their article is followed by a discussion by Schlauedecker and Becker of the increased inflammatory responses in aging contributing to the elevated thrombophilia.9

The remaining part of this issue is devoted to situations seen in the clinical practice in the aging population, starting with a review by Cunningham et al of the role of thrombogenic microparticles in autoimmune diseases, including rheumatoid arthritis, systemic sclerosis, and systemic lupus erythematosus affecting older individuals.10 Next is the discussion by McMahon and Kwaan on the increased hazards in the older patients with immune thrombocytopenic purpura. Older adults are also more often taking multiple drugs and are at higher risk for drug-induced thrombocytopenia.11 Anticoagulants are more often used in older than in younger individuals and their administration poses a greater risk as well, as pointed out by Ko and Hylek.12

Advances in our basic understanding of these age-related changes will help to improve interventions for this increased vulnerability as we age. Elucidating clinical patterns and environmental triggers that compound these risks will augment efforts to translate discovery to the bedside. We trust that our readers will be as excited as we are in exploring these efforts.
References