Journal of Blood Disorders

Open Access

Austin Publishing Group

Editorial

Aging and Thrombosis: The Role of Genetic Factors

Kazachkova N*
Department of Biology, University of the Azores, Portugal

***Corresponding author:** Kazachkova N, Department of Biology, University of the Azores, Rua Mae de Deus – Apartado 1422, 9501-801 Ponta Delgada, Azores, Portugal

Received: November 30, 2016; **Accepted:** December 02, 2016; **Published:** December 05, 2016

Editorial

Deep-Vein Thrombosis (DVT) is a formation of a blood clot in the deep veins, commonly in the legs, it is a serious condition that can cause pain, swelling and tenderness in the leg, and have such a complication as pulmonary embolism, leading to a significant morbidity and mortality. DVT affects approximately 0.1% of persons per year, with overall average age- and sex-adjusted annual incidence of 48 per 100,000 and higher age-adjusted rates among males than females (130 *vs.* 110 per 100,000, respectively) [1]. DVT predominantly affects the elderly, with 1 per 10,000 events in the young (< 40 years old) and 1 per 1000 in the elderly (> 75 years old) [2], making aging one of the strongest risk factors.

Aging is associated with increased level of coagulation system proteins, such as fibrinogen, factors VIII and IX, without a proportional increase in anticoagulant proteins (e.g., proteins C and S, tissue factor pathway inhibitor), it is also associated with increased levels of prothrombotic markers (e.g., thrombin), and significant alterations in the fibrinolytic system resulting in a decrease in fibrinolytic activity [2,3].

Genetic risk factors are estimated to contribute to 7–22% of thrombosis incidence in the elderly [4]. They include variations in a number of genes related to haemostatic factors, such as plasminogen activator inhibitor-1 gene (*PAI-1*), glycoprotein IIIa (*ITGB3*) gene, factor IX (*F9*) and protein C (*PROC*) genes, among others. The prevalence of the most common genetic risk factors for DVT, such as the Leiden mutation in the Factor V *F5* gene (FVL, p. R506Q, rs6025), and genetic variant G20210A in the prothrombin *F2* gene (PT 20210, c.*97G>A, rs1799963), as well as the variant c.677C>T (rs1801133) in the methylenetetrahydrofolate reductase (*MTHFR*) gene, is similar in the young and elderly [3,4], pointing out that genetic risk factors clearly related to venous thrombosis in younger populations are also risk factors in the elderly [5].

Several studies demonstrated that the 4G/5G variant (rs1799768) in the *PAI-1* gene was associated with high plasma PAI-1 levels and an impaired fibrinolysis with age [3,6,7], moreover, the expression of PAI-1 was also significantly induced in a variety of pathologies associated with aging, such as obesity, insulin resistance, emotional stress, immune responses, and vascular sclerosis/remodeling [8]. Glycoprotein IIIa (*ITGB3*) gene represents the genetic variant (PLA1/A2) that can influence both platelet activation and aggregation, PLA2 allele (rs5918) of this gene was found to be statistically less prevalent among older healthy individuals [9]. Certain genetic influence of age-dependent regulation of coagulation factors expression has been demonstrated by several studies [3]. For example, two essential age-regulatory elements, AE5' and AE3', have been identified in the factor IX gene (*F9*), which were demonstrated to be associated with the age-related increase of factor IX levels [10]. Elements controlling the age-related gene expression have also been discovered in the anticoagulant protein C [3,11].

Molecular and anatomic changes in the vessel wall can also predispose to DVT. Endothelial dysfunction, or the loss of the endothelium physiological properties expressed as reduced vasodilatation, impaired fibrinolysis and impaired anti-aggregation, is an important age-associated cardiovascular phenomenon [4]. Endothelial nitric oxide synthase is responsible for the generation of nitric oxide that plays crucial roles in platelet aggregation. It has been demonstrated that SNPs in the endothelial nitric oxide synthase gene (*NOS3*) were associated with the presence of disability in older individuals [12].

Although there are many studies on genetic risk factors for DVT in the general population, the number of studies on genetic risk factors for DVT in the elderly is still scarce, and they are mostly based on small or medium study groups.

In conclusion, further studies in different cohorts and large study groups are necessary to shed a clearer light on the role of genetic risk factors in the development of DVT during aging. It can help to identify high-risk groups, to find therapeutic targets and elaborate preventive measures.

References

1. Kesieme E, Kesieme C, Jebbin N, Irekpita E, Dongo A. Deep vein thrombosis: a clinical review. Journal of blood medicine. 2011; 2: 59-69.
2. Wilkerson WR, Sane DC. Aging and thrombosis. Seminars in thrombosis and hemostasis. 2002; 28: 555-568.
3. Franchini M. Hemostasis and aging. Critical reviews in oncology/hematology. 2006; 60: 144-151.
4. Engbers MJ, van Hylckama Vlieg A, Rosendaal FR. Venous thrombosis in the elderly: incidence, risk factors and risk groups. Journal of thrombosis and haemostasis: JTH. 2010; 8: 2105-2012.
5. Karasu A, Engbers MJ, Cushman M, Rosendaal FR, van Hylckama Vlieg A. Genetic risk factors for venous thrombosis in the elderly in a case-control study. Journal of thrombosis and haemostasis: JTH. 2016; 14: 1759-1764.
6. Eren M, Boe AE, Klyachko EA, Vaughan DE. Role of plasminogen activator inhibitor-1 in senescence and aging. Seminars in thrombosis and hemostasis. 2014; 40: 645-651.
7. Bonfigli AR, Sirolla C, Cenerelli S, Marra M, Boemi M, Franceschi C, et al. Plasminogen activator inhibitor-1 plasma level increases with age in subjects with the 4G allele at position -675 in the promoter region. Thrombosis and haemostasis. 2004; 92: 1164-1165.
8. Yamamoto K, Takeshita K, Kojima T, Takamatsu J, Saito H. Aging and plasminogen activator inhibitor-1 (PAI-1) regulation: implication in the pathogenesis of thrombotic disorders in the elderly. Cardiovascular research. 2005; 66: 276-285.
9. Hessner MJ, Dinauer DM, Kwiatkowski R, Neri B, Raife TJ. Age-dependent

Citation: Kazachkova N. Aging and Thrombosis: The Role of Genetic Factors. J Blood Disord. 2016; 3(1): 1040.

prevalence of vascular disease-associated polymorphisms among 2689 volunteer blood donors. Clinical chemistry. 2001; 47: 1879-1884.

10. Kurachi S, Deyashiki Y, Takeshita J, Kurachi K. Genetic mechanisms of age regulation of human blood coagulation factor IX. Science. 1999; 285: 739-743.

11. Zhang K, Kurachi S, Kurachi K. Genetic mechanisms of age regulation of protein C and blood coagulation. The Journal of biological chemistry. 2002; 277: 4532-4540.

12. Montesanto A, Crocco P, Tallaro F, Pisani F, Mazzei B, Mari V, et al. Common polymorphisms in nitric oxide synthase (NOS) genes influence quality of aging and longevity in humans. Biogerontology. 2013; 14: 177-186.

Citation: Kazachkova N. Aging and Thrombosis: The Role of Genetic Factors. J Blood Disord. 2016; 3(1): 1040.