Editorial

# Acquired von Willebrand Syndrome (AVWS) as an Important Diagnostic Category of Disease

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In this issue of J Atheroscler Thromb, Kalbhenn J *et al.*[1] presented an interesting report on "Acquired von Willebrand Syndrome (AVWS)" in patients treated with extracorporeal membrane oxygenation (ECMO) therapy. von Willebrad factor (VWF) is a unique plasma protein playing crucial role in thrombus formation by capturing flowing platelet to the damaged vascular wall (**Fig. 1**)[2]. Thus, this protein plays essential roles both for the onset of thrombotic disease and bleeding events[3]. However, not many of the physicians taking care of elderly patients (such as atherosclerotic patients) realize the importance of this protein because measurement of VWF is not included in the regular diagnostic blood tests. Due to its crucial role for hemostasis, congenital deficiency or abnormality of VWF was handled as congenital bleeding disorders mostly by pediatrician[4].

In atherosclerotic patients, however, VWF is an important plasma marker for future thrombotic events. The Atherosclerosis Risk in Communities (ARIC) study demonstrated that the high level of plasma VWF was an independent risk factor for future onset of myocardial infarction[5]. Similar finding was found in patients with atrial fibrillation for the onset of stroke[6]. Of note, detailed analysis of the characteristic of VWF in patients with myocardial infarction and heart failure, revealed the increment of larger multimer of VWF in these patients[7, 8]. Indeed, these larger multimer induce platelet aggregation and thrombus formation in an efficient manner. Thus, the deficiency of larger multimer is recognized as bleeding disorder namely type 2A von Willebrand disease[9].

It is rather complicated but larger multimers are cleaved by ADAMTS-13 under certain flow conditions to decrease multimer size[10]. It is interesting that in specific conditions, such as in patients with severe aortic stenosis[11], larger component of VWF multimer disappear. This is most probably due to increased catalytic activity of ADAMTS-13, induced by modified blood flow condition by aortic stenosis. These patients experience serious gastrointestinal hemorrhage known as Heyde's syndrome which was named due to his old report[12]. But, bleeding complication is not limited to gastrointestinal bleeding. These patients population is now defined as acquired von Willebrand disease in patients with aortic stenosis[11].

In this issue, Kalbhenn J, *et al.* demonstrated that similar acquired von Willebrand Syndrome occurs frequently in patients treated by new technology of extracirculation with extracorporeal membrane oxygenation (ECMO). VWF is known to bind with platelet exposed to high shear stress[13]. In condition where blood interacts with artificial substances[14], it is most likely that the percentage of platelets exposed to high shear stress increase due to transient attachment of platelet on artificial lumen. With the progress of artificial circulation, we need to be careful for bleeding tendency due to acquired von Willebrand syndrome in various clinical settings even including intra-aortic balloon pumping (IABP), percutaneous cardiopulmonary support (PCPS), and so on.

## Conflicts of Interest

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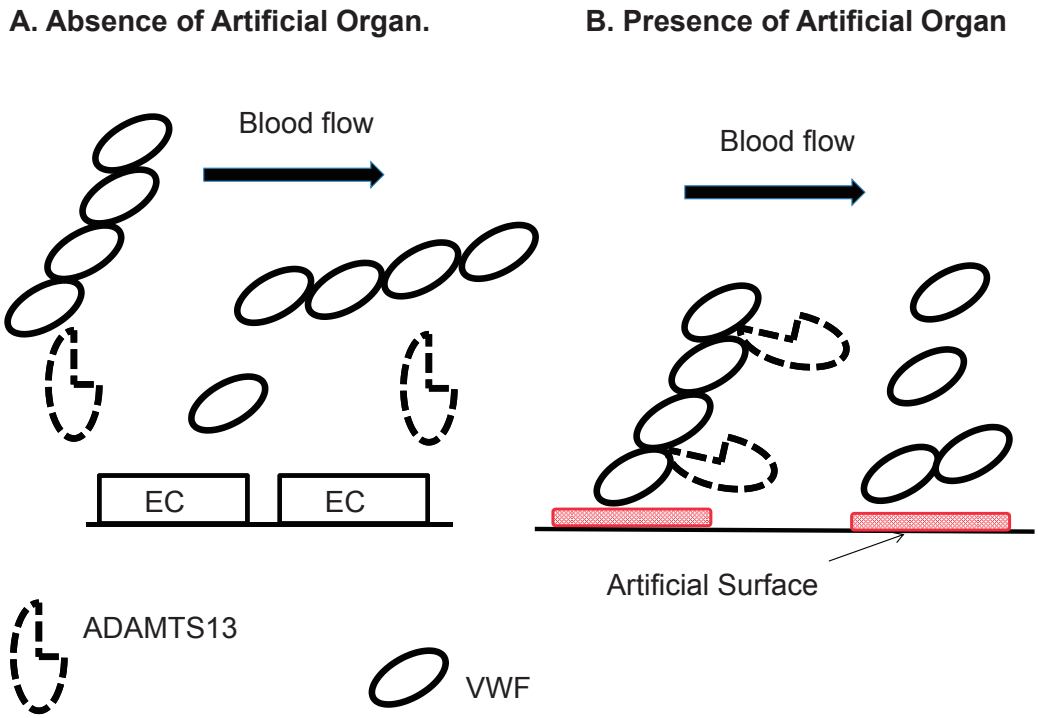


**Fig. 1.** A. In the presence of healthy endothelial cells, larger multimer of VWF released from platelet and endothelial cells are cleave to become normal distribution of multimers. B. In the presence of artificial lumen, VWF multimers were trapped transiently and were exposed to fluid force, which expose cleavage site(s) to ADAMTS13. Then, the concentration of larger multimer in circulation becomes low as compared to healthy human.

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