

Research progress on relationship between wall shear stress and intracranial aneurysm

Da Li¹; Yunxia Jiang¹; An Wu^{2*}

1. The Second School of Clinical Medicine, Zhejiang Chinese Medical University, Hangzhou, People's Republic of China

2. Department of Neurosurgery, The Quzhou Affiliated Hospital of Wenzhou Medical University, Quzhou People's Hospital, Quzhou, 324000, People's Republic of China

*Corresponding author: Mr. An Wu, E-mail: 34887740@qq.com

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Abstract¹

Intracranial aneurysm (IA) is a cerebrovascular disease characterized by abnormal expansion of intracranial arteries caused by pathological weakness of vascular wall. Subarachnoid hemorrhage (SAH) caused by intracranial aneurysm rupture is related to high mortality and morbidity. Hemodynamic is the mechanism of researching the flow of blood in cerebrovascular and cardiovascular system, the relationship between blood flow, blood resistance and blood pressure were studied, the wall shear stress (WSS) generated by blood flow on the vascular wall plays an important role in the formation and rupture of

intracranial aneurysm. This article discusses the research progress of the effect of WSS on intracranial aneurysm and enrich clinical theory.

Keyword

Hemodynamic; intracranial aneurysm; wall shear stress; interventional therapy; antiplatelet treatment

Introduction

The blood flow can be considered to be composed of numerous very small layers, and its ideal motion state is concentric stratification. Theoretically, the blood flow velocity close to the outermost wall of the blood vessel is zero, and the largest at the center. WSS is the tangential friction force generated by the liquid flowing on the surface of the blood vessel per unit area near

Corresponding author: An Wu, M. D. degree
Professional title: Master
Research direction: Cerebral vascular diseases;
Neurosurgery; Neurological intervention
Department of Neurosurgery, The Quzhou Affiliated
Hospital of Wenzhou Medical University, Quzhou
People's Hospital, China

the wall of blood vessel.

Intracranial aneurysm

Currently, WSS is one of the reasons of aneurysm formation and rupture[1], increasing WSS can promote the formation of intracranial aneurysms[2]. At the arterial intersection, the smaller angle, the higher WSS, can form aneurysm easier; however, the smaller WSS will make aneurysm rupture easier after aneurysm formation[3]. For example, some scholars have pointed out that the increase of intravascular WSS caused by internal carotid artery occlusion may be a high risk factor of communicating artery aneurysm growth[2]. The growth of aneurysm width is the most significant factor in the process of aneurysm formation[4], WSS decreases significantly after this process, especially the high incidence area of aneurysm growth and rupture: communicating artery aneurysm and posterior circulation area [5]. If the property of the aneurysm is divided into stable and unstable, the unstable will have a larger low WSS area[6]. The rupture of intracranial aneurysm is significantly correlated with its reduced WSS, the mean, maximum and minimum WSS are significantly lower than unruptured aneurysm[7].

Actually, aneurysm can be classified small, medium, large, giant (< 5mm, 5-10mm or 10-15mm, 15-20mm or 20-25mm, > 25mm). Compared with other types of aneurysms, small aneurysms have a higher risk of rupture, accounting for 69.9% to 71.8% of all ruptured aneurysms[8]. SAH caused by ruptured aneurysms for 7.5% every year, and women have a higher proportion[9]. Variable factors of aneurysm rupture included smoking, hypertension and drinking. Unchangeable factors include gender and age[10], and WSS and Oscillatory shear index(OSI) are independent significant variables to identify the status of intracranial aneurysms[11]. A single-center trial of 1232 cases showed that the risk factors of aneurysm rupture included basic cardiovascular and cerebrovascular diseases, aneurysm size, shape, type of coil during intervention, and location of aneurysm[12]. A prospective randomized trial showed that the risk of growth and rupture of aneurysms with a diameter of less than 3 mm was the lowest[13]. The rupture probability of aneurysms with a diameter of 3-4mm was 0.36%[14]. The overall growth rate and rupture rate of aneurysms with a diameter of less than 5mm were 6.0% and 0.4% respectively[

15]. Consistent with the results of this study, another research also showed that the more spherical the small aneurysms less than 5mm in diameter, have the higher WSS; the more irregular aneurysm larger than 5mm, have the lower WSS[16]. For stable aneurysms, the proportion of growing aneurysms with a diameter greater than the neck is greater[17]. Geng Zhou et al. point out that a low shear magnitude can promote macrophage-related chronic inflammation and atherosclerotic changes. These atherosclerotic inflammatory changes and metalloproteinase production by macrophages can predispose wall to thinning and further rupture[18], endothelial cells produce reactive oxygen species, increase adhesion molecules and cytokines on the surface of the blood vessel wall, reduce the pressure of endothelial cells on physiological hemodynamics, and ultimately promote aneurysm rupture[19]. Recent studies have further confirmed that low WSS can lead to rupture of IAs, Zhang et al. point out 4D-MRI and Black Blood MRI(BB-MRI) were performed on 49 patients with unruptured aneurysms, low WSS can increase the permeability of the aneurysm wall, manifested as Aneurysm Wall Enhancement(AWE)[20], and low WSS may be an independent predictor of AWE[21].

More irregular shape is a character of rupture aneurysms, if exposed to a detrimental hemodynamic environment to the growth aneurysms, it can be manifested as faster blood flow, higher WSS and more unstable and complex blood flow[22]. Lorenzo et al. point out that anterior communicating aneurysms were more likely to rupture than other locations, about 34.8%[23]. Zhang X et al. reported that WSS is an important factor in the formation of anterior communicating aneurysms at the corner of the anterior communicating artery(ACA) A1 and A2[24]. Aneurysms mainly occur in the dominant vascular of the A1 segment[25], and the WSS exceeds 12.3 dyne/cm^3 , the risk of aneurysm rupture is significantly increased[26], this provides a vital clue for early intervention of aneurysm rupture and timing for surgery. Similarly, some scholars believe that low shear area(LSA) may also be a predict indicator of aneurysm rupture[27]. Some studies have shown that the risk of rupture of distal aneurysms will increase when the proximal aneurysms are treated after surgery or vascular interventional therapy[28]. 2014, Xiang proposed the rupture resemblance score(RRS), though cannot predict the rupture of aneurysm, it provided similarity between rupture and unruptured aneurysms by morphology and

hemodynamic , by comparing morphology and hemodynamic , the closer to rupture aneurysms , the higher risk of rupture. In a clinical trial of 47 patients with aneurysm , this score took a great assistant role in managing and making treatment plan of unruptured aneurysms. [29]

Complex aneurysms

Complex aneurysms include cystic , fusiform , blood blister-shaped , and most of the characteristics are wide neck , huge and irregular shape. A comparing trial of wide neck and narrow neck point out that the former has higher risk of rupture and rupture aneurysms have higher pressure and lower WSS , the surgery risk is also high[30]. However , the theory of high risk of narrow neck surgery is also given in the industry . Whether there is a correlation between aneurysm morphology and rupture is still controversial.

Treatment and Prevention

Currently , the treatment of IAs can be divided into vascular intervention and surgery are treatments. Recently , flow device(FD) become an new and developing treatment of vascular intervention for IAs , it changes blood flow to make IAs have a hemodynamic condition with lower blood flow

velocity , reduces the influence of WSS in IAs on endothelial cells , makes an great environment for occlusion of tumor and reconstruction of vessels[31]. The treatment includes single FD, overlay FDs and FDs combine with coil embolization. Comparing with traditional embolization therapy, the postoperative bleeding rate is lower and the operation process is safer cause by advantage of device structure , the mechanism is that the characteristics of not entering aneurysms but choosing to change the direction of blood flow in the aneurysms reduce the risk of rupture , and avoiding aneurysms rupture caused by coils or operating problems. Overlaying FDs can establish a denser gird in the aneurysm neck , and the WSS of the aneurysm is effectively reduced , the blood flow into aneurysm is inhibited thus achieve vascular reconstruction of aneurysm to form embolization and prevent rupture . This is the most effective for large diameter or wide neck aneurysms , if only a single stent is used for treatment into certain condition , 50% coverage of the stent has the same effect as the overlay stents[32].

The effect of FDs treatment is significant, the complete embolization rate of aneurysms is 88.5% close to 90% in the 1 year follow-up. Postoperative complications are mainly concentrated in stent stenosis , but SAH caused by

aneurysm rupture also occurs during the operation, the reason may be that the space required for FD implantation is larger than vessels[33]. For security and validity, a clinical and anatomical trial of 103 patients treated with FD for 1 year showed that, for small unruptured aneurysms less than 10mm, the complete embolization rate reached 73.3% and the postoperative mortality and disability rate did not exceed 3%, and the success rate was 81.8%[34]. At the same time, there is also a study that has reported that when this method is used to treat IAs and vertebral aneurysms with huge thrombosis, due to the morphological changes of the artery in which the stent is placed, the blood flow into the target aneurysm causes a change in intracranial pressure, blood flow and WSS, which further deteriorates the condition of the aneurysm, leading to the pressure around the aneurysm neck increasing and may promote the rupture of the aneurysm[35].

FDs combined with coil embolization is also an optional method for complex aneurysms including wide neck, saccular aneurysms and fusiform aneurysms. A report with 72 patients used this method in 2018, the complete embolization rate was 85%, 96% and 100% at 6, 12 and 24 months after operation, respectively[8]. A case of using FD to treat posterior inferior

cerebral aneurysm in China, a comparative study was performed with overlaid FDs and FDs combined coils, and the result showed that the effect of overlaid FD on reducing WSS was slightly inferior to that of FD combined coil, the degree of reduction was most obvious in FD combined with 10% coil embolization rate[36]. At the same time, by comparing the effect of the number of overlaid stents in the parent artery on WSS, it can be known that when the number of stents reaches 3, the decrease of WSS will significantly [37].

Intraoperative and postoperative complications

Although intervention and craniotomy clipping are the major treatments at currently, there are also have high rate of disability and mortality[38]. Intraoperative aneurysmal rupture is the serious complications of clipping and intervention, once it occurs, it will have a serious adverse effect on the prognosis of patients[39].

Intervention also has risk of aneurysms recurrence, Tsukada et al compared the hemodynamic pressure of healthy blood vessels after parent artery occlusion and FD stent treatment of internal carotid artery(ICA) aneurysms, and conclude that the WSS and blood flow of the C1 segment of the healthy side of the ICA increased significantly after operation,

and the parent artery occlusion was more easier to recurrence the new aneurysms[39]. Yuan J et al reported that the neck of the recurrent middle cerebral artery bifurcation aneurysms have higher WSS after intervention[40]. Interventional coil embolization has the highest recurrence rate of aneurysms , especially large aneurysms and aneurysms in the corpus callosum[41] , it may be related to the characteristics of aneurysm before embolization and the changes after embolization , including the size of aneurysm , less embolization of aneurysm neck and blood flow in aneurysm[42], and the pressure in aneurysm may not change significantly after operation[43].

Antiplatelet treatment(AT) , that is aspirin and /or clopidogrel , is the main method of preventing embolization and re-rupture before and after neurosurgical interventional therapy and the risk of aneurysm growth in patients which using aspirin can be reduced about 80%[44]. However , a study on whether the use of antiplatelet therapy during the treatment of 1163 patients with acute aneurysm rupture increased the risk of external ventricular drainage bleeding , showed that the probability of external ventricular drainage related bleeding in patients treated with dual antiplatelet therapy(DAPT) was 20.9% , while the probability of bleeding with single antiplatelet therapy or without

antiplatelet therapy was 9.0%. Therefore , DAPT has the disadvantage of increasing the risk of bleeding during treatment[45] , and postoperative intractable hemorrhage is still the main factor for patients to change or reduce the dose of DAPT , even if the intracranial aneurysm can be occluded in 6 months after treatment[46]. However , in a safety trail of comparing the use of tirofiban and DAPT in the treatment of aneurysms , the researchers pointed out that there are no effect in 141 patients on platelet and hemoglobin counts , and the addition of heparin did not increase the probability of bleeding in patients[47].

Conclusions

The formation and rupture of IAs has a strong correlation with the WSS of parent arteries , and the prevention of aneurysms rupture is important owing to its caused by it is a disease with high risk of disability and mortality. IAs with low flow(low WSS , low pressure , low velocity) may often rupture and with high flow(high WSS , high pressure , complex shapes)may often growth. However , the growth and rupture of aneurysms is a dynamic process , and it is difficult to dynamically collect the information into aneurysms , such as WSS , velocity and OSI . Therefore , it is important to clarify the range of WSS before aneurysms rupture.

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