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Original Article

Comparative morphology of the internal elastic lamina of cerebral and peripheral arteries

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Abstract: Background: Atherosclerosis progresses later and with fewer complicated plaques in cerebral arteries than in peripheral arteries. The internal elastic lamina has been proposed to be important for the migration of smooth muscle cells into the intima during intimal thickening and atherosclerosis. Methods: A total of 280 segments were retrieved from 14 autopsy specimens. Five sites were selected for analysis in each case: the middle cerebral artery, basilar artery, coronary artery, iliac artery and renal artery. We investigated the differences in the internal elastic lamina of cerebral and peripheral arteries. Results: The average thickness of the internal elastic lamina of the cerebral arteries was larger than that of the peripheral arteries in both the early and advanced atherosclerotic plaque groups. Among the cerebral arteries, the basilar arteries had a thicker internal elastic lamina than the middle cerebral arteries. Among the peripheral arteries, the renal arteries had the thickest internal elastic lamina, followed by the iliac arteries and coronary arteries. Atherosclerosis led to a reduction in the thickness of the internal elastic lamina of the basilar, middle cerebral, and renal arteries. The stratification of the internal elastic lamina of iliac arteries significantly affected its measurement. The internal elastic lamina of coronary arteries was not affected by atherosclerosis, but it appeared fragmented. Conclusion: The results suggest that the characteristics of atherosclerotic plaques in cerebral and peripheral arteries may be related to the characteristics of the internal elastic lamina.

Keywords: Atherosclerosis, internal elastic lamina, cerebral arteries, peripheral arteries

Introduction

Atherosclerosis is a systemic disease that is characterized by focal thickening of the intima, most commonly affecting the cerebral and peripheral arteries [1]. It can lead to serious clinical consequences, such as heart attack and cerebrovascular disease [2].

It has been reported that cerebral atherosclerosis develops later in life than atherosclerosis of peripheral arteries [3]. Although atherosclerotic lesions are prevalent in cerebral arteries, they infrequently show features of complicated plaques [4, 5]. The internal elastic lamina forms the barrier between the intima and media in the arterial wall. Increasing evidence indicates that the migration of vascular smooth muscle cells from the media to the intima through the internal elastic lamina represents a key event in the pathogenesis of atherosclerotic plaques [6-8]. It is not clear whether the differences in the characteristics of atherosclerosis between cerebral and peripheral arteries are caused by differences in the characteristics of the internal elastic lamina. Previous studies have shown that the external elastic lamina can maintain the elasticity of the arterial wall, and the disappearance of the external elastic lamina of the internal carotid artery can easily lead to lumen stenosis. Consequently, the present study was set up to investigate and compare the characteristics of the internal elastic lamina and external elastic lamina of cerebral arteries and peripheral arteries and to explore their role in the formation of atherosclerosis.

Materials and methods

All anatomic material was retrieved randomly from 14 autopsy specimens at the Department of Pathology, Captical Medical University, China, from patients who died from unexpected death at ages ranging from 26 to 68 years. The following five sites were selected for analysis, without special labeling of the left or right sides: the middle cerebral artery, basilar artery, coronary artery, iliac artery and renal artery. For every autopsy case, segments with macroscopically visible atherosclerosis were selected. If macroscopic indications of atherosclerosis were absent, a representative artery segment was selected. Samples were fixed in 10% neutral formalin and embedded in paraffin using standard techniques. Histologic sections with thicknesses of 4 μm were cut, stained with hematoxylin-eosin (H&E) and elastic van Gieson (EvG) methods, and examined under a light microscope. The presence of the internal elastic lamina and external elastic lamina in the vessel wall was evaluated. We carefully observed the histologic structure of the internal elastic lamina of each site and compared it between the cerebral and peripheral arteries. The internal elastic lamina was classified as fragmented or continuous. The concentration of elastin fibers in the internal elastic lamina according to EvG staining was classified as high, moderate or low. The external elastic lamina was classified as absent, fragmented, or continuous. To avoid the influence of atherosclerotic plaques on the internal elastic lamina, we divided the experimental cases into two groups: a group without atherosclerotic plaques or with early atherosclerotic plaques and a group with advanced atherosclerotic plaques, and we compared the internal elastic lamina of different arteries. The chi-square test was used to compare the thickness of the internal elastic lamina in different parts, and the Wilcoxon test was used to compare the early atherosclerotic plaques in the same part with the relatively advanced group.

Results

We selected 2 segments from the same site in each case from each group. A total of 280 segments of arteries were evaluated. According to the severity of the atherosclerotic plaque, we divided the samples into two groups: one without atherosclerotic plaques or with early atherosclerotic plaques and the other with advanced atherosclerotic plaques. The characteristics of the internal elastic lamina varied visibly in different sites.

To accurately assess the thickness of the internal elastic lamina, we randomly selected four points for measurement under a high-power field of vision and averaged them. The thickness of the internal elastic lamina in cerebral arteries and peripheral arteries was compared in the early atherosclerotic plaque group and the advanced atherosclerotic plaque group. The results showed that the average thickness of the internal elastic lamina of the cerebral arteries was larger than that of the peripheral arteries in both groups, and the difference was statistically significant. This was especially true for basilar arteries, which had a much thicker internal elastic lamina than the middle cerebral arteries. Among the peripheral arteries, the mean thickness of the internal elastic lamina of renal arteries was the largest. This value was close to the average thickness of the internal elastic lamina of the middle cerebral arteries. The mean thickness of the internal elastic lamina of the iliac and coronary arteries was relatively small. The thickness of the internal elastic lamina was significantly associated with position in all cases (**Figure 1**; **Table 1**).

After comparing the early atherosclerotic plaque group with the advanced atherosclerotic plaque group, it was found that the mean thickness of the internal elastic lamina was larger in the group with early atherosclerotic plaques in basilar arteries, middle cerebral arteries, and renal arteries. However, the internal elastic lamina of the iliac arteries was thinner in the group with early atherosclerotic plaques, which was related to the facile stratification of the internal elastic lamina of the iliac arteries. There was no significant difference in the thickness of the internal elastic lamina of the coronary arteries between the group with early atherosclerotic plaques and the group with advanced atherosclerotic plaques (**Figure 2**; **Table 2**).

EvG staining showed that the elastin fiber density of the internal elastic lamina was high in basilar arteries, moderate in middle cerebral arteries and renal arteries, and low in iliac arteries and coronary arteries. The internal elastic lamina of iliac arteries was denser than that of the coronary arteries.

In addition to the thickness and width, other characteristics of the internal elastic lamina, such as delamination and folding, were also

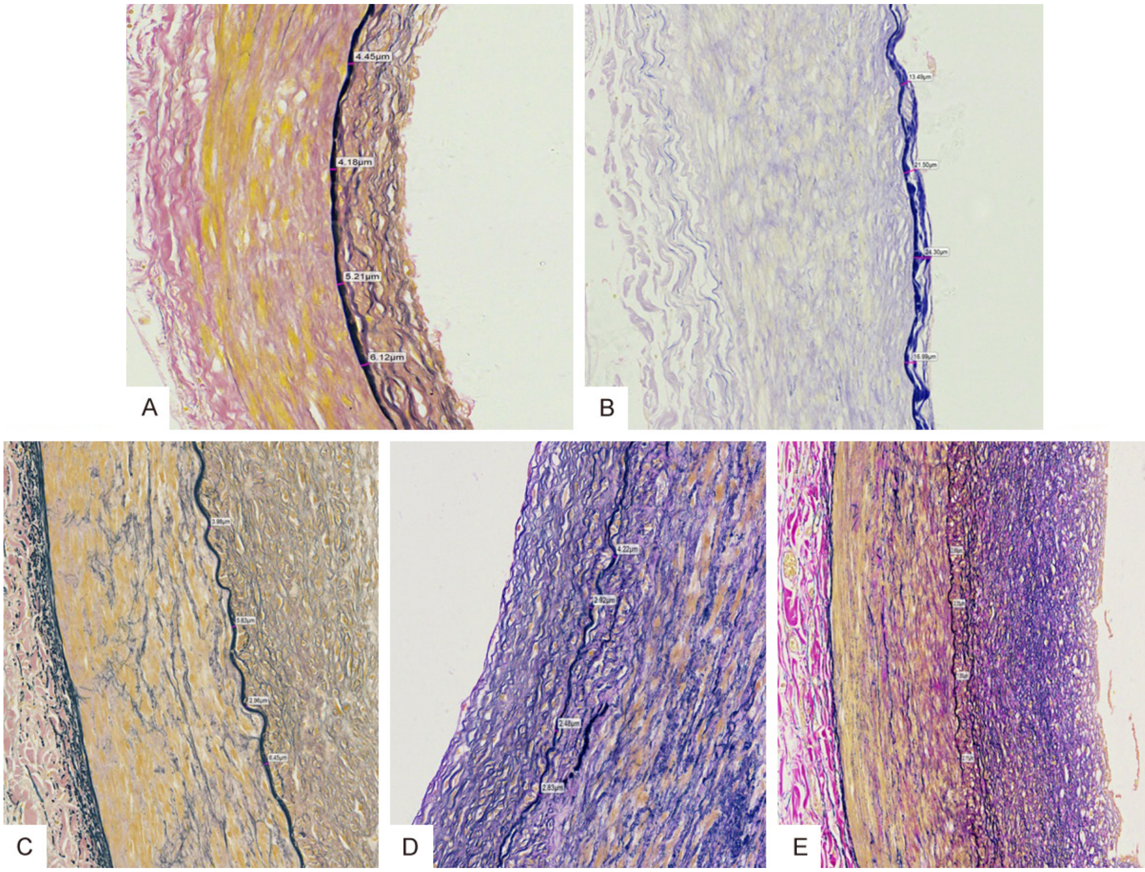

Figure 1. The internal elastic lamina of the early atherosclerotic plaque group (×400 magnification). EvG-stained sections showing the internal elastic lamina in middle cerebral arteries (A), basilar arteries (B), renal arteries (C), iliac arteries (D), and coronary arteries (E).

Table 1. Comparison of the thickness of the internal elastic lamina of cerebral arteries with peripheral arteries

Group	Site	Mean	*t*	*P*
Early atherosclerotic plaque group	Cerebral arteries	11.96	6.43	$P<0.001$
	Peripheral arteries	3.30		
Advanced atherosclerotic plaque group	Cerebral arteries	9.85	6.80	$P<0.001$
	Peripheral arteries	3.12		

The t-test results of two independent samples showed that the internal elastic lamina of the cerebral arteries was thicker than that of the peripheral arteries in the group with early atherosclerotic plaques and the group with advanced atherosclerotic plaques.

taken into account. Delamination was present in the internal elastic lamina of both cerebral and peripheral arteries. The layered internal elastic lamina could be either monolinear or polylinear. In this study, we found that delamination was most often seen in the iliac arteries (**Figure 3A**), followed by the renal and cerebral arteries. In addition, we also observed the separation of the intima and atherosclerotic plaques from the internal elastic lamina. This separation was more visible in the middle cerebral arteries, basilar arteries and iliac arteries. Folding was one of the most common features of the internal elastic lamina, and it could be found in both cerebral and peripheral arteries. It was more obvious around atherosclerotic plaques in iliac arteries and renal arteries (**Figure 3B**), with the appearance of waves and coils [9, 10]. Furthermore, the internal elastic laminas of all the investigated cerebral and

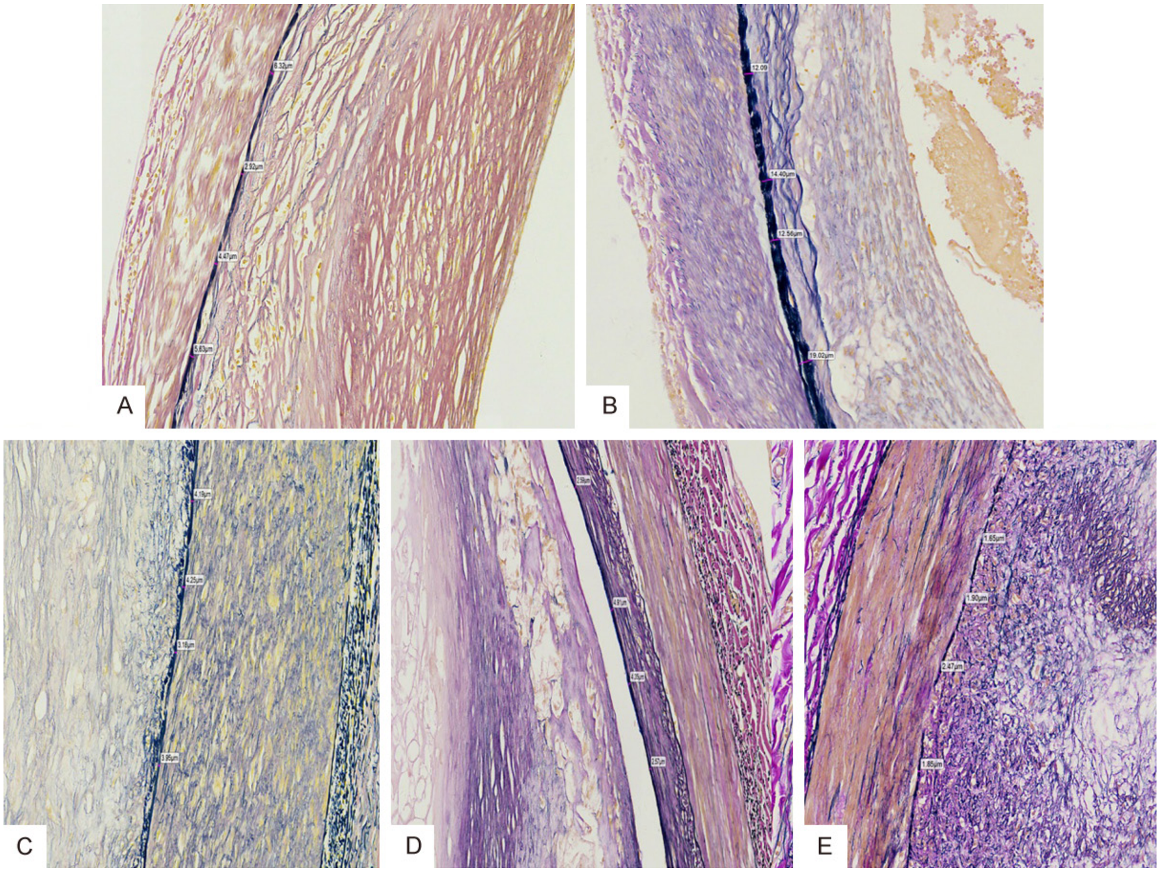

Figure 2. The internal elastic lamina of the advanced atherosclerotic plaque group (*400 magnification). EvG-stained sections showing the internal elastic lamina in the middle cerebral arteries (A), basilar arteries (B), renal arteries (C), iliac arteries (D), and coronary arteries (E).

Table 2. Comparison of the mean thickness of the internal elastic lamina of the basilar artery, middle cerebral artery, renal artery, iliac artery and coronary artery in the early atherosclerotic plaque group and advanced atherosclerotic plaque group

Site	Mean		t	*P*
	Early atherosclerotic plaque group	Advanced atherosclerotic plaque group		
Basilar arteries	18.90	14.94	42.01	*P*<0.001
Middle cerebral arteries	5.03	4.75	6.13	*P*<0.001
Renal arteries	4.71	3.80	14.70	*P*<0.001
Iliac arteries	3.07	3.61	-12.37	*P*<0.001
Coronary arteries	2.12	1.94	1.78	*P*=0.097

The differences in the internal elastic lamina of the basilar artery, middle cerebral artery and renal artery between the group with early atherosclerotic plaques and the group with advanced atherosclerotic plaques were statistically significant. The internal elastic lamina of the iliac artery was thicker than that of the recombination group. There was no difference in the thickness of the internal elastic lamina in the coronary arteries between the two groups.

peripheral arteries were continuous except for the coronary arteries. In the coronary arteries, the internal elastic lamina was fragmented (**Figure 3C**), with visible interruptions, especially in the presence of advanced plaques. We found that in the same patient, atherosclerotic plaques in the coronary arteries were more pronounced and more severe than in other arteries.

The external elastic lamina was frequently observed in the basilar arteries, renal arteries,

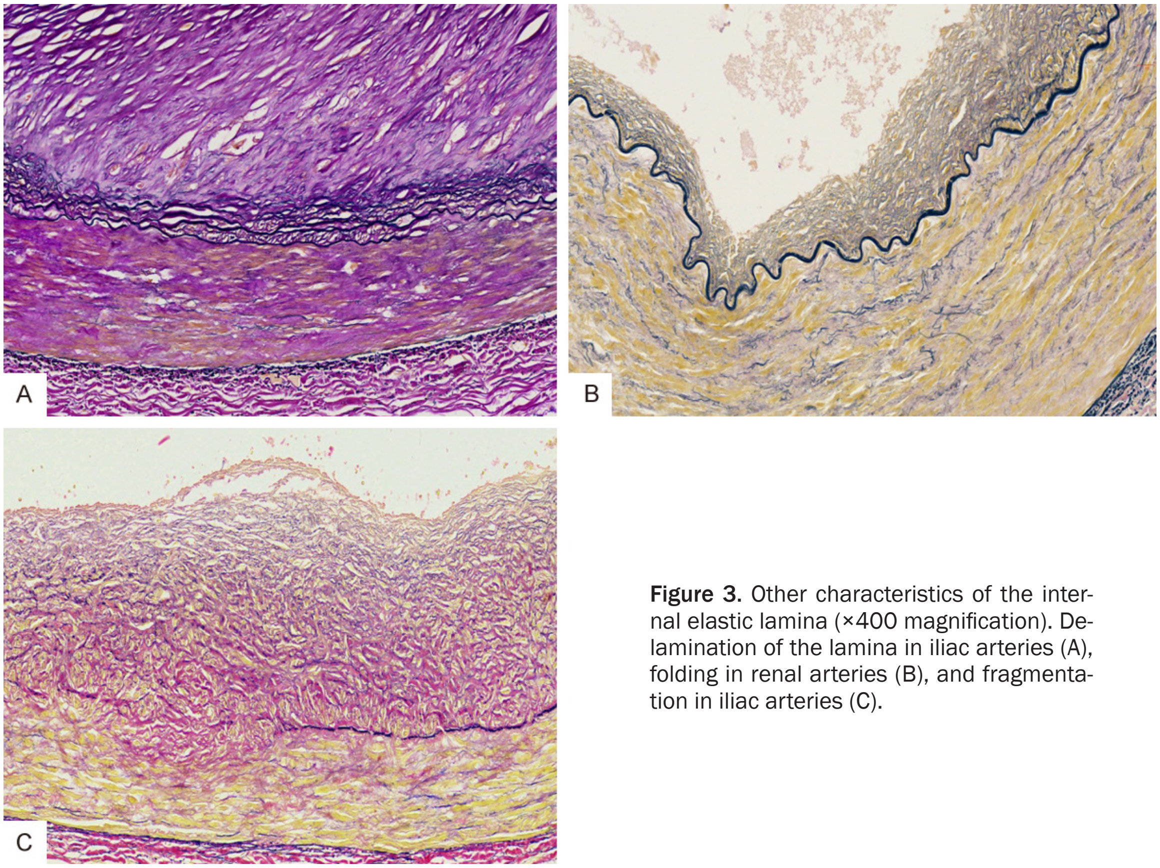

Figure 3. Other characteristics of the internal elastic lamina (×400 magnification). Delamination of the lamina in iliac arteries (A), folding in renal arteries (B), and fragmentation in iliac arteries (C).

iliac arteries and coronary arteries, while it was absent in the middle cerebral arteries. By contrast, the external elastic lamina of the coronary, iliac, and renal arteries was continuous, but it was fragmented in the basilar arteries.

Discussion

Our results suggest that the internal elastic lamina of cerebral arteries was thicker than that of peripheral arteries. EvG staining showed that the concentration of elastic fibers in the internal elastic lamina was high in the basilar arteries and moderately high in the middle cerebral arteries. The wider internal elastic lamina and denser elastic fibers could block the migration of smooth muscle cells so that atherosclerosis of cerebral arteries developed later and was less severe than in peripheral arteries [11]. The internal elastic lamina of the basilar arteries was significantly thicker than that of the middle cerebral arteries, and the internal elastic lamina of the basilar arteries was more able to block the migration of smooth muscle cells, so the incidence of basilar atherosclerosis was lower than that of the middle cerebral arteries [12, 13].

When comparing the early and advanced atherosclerotic plaque groups, the internal elastic lamina was thicker in the group with early atherosclerotic plaques in the basilar arteries, middle cerebral arteries, and renal arteries, and the difference was significant. These results suggest that atherosclerotic plaques exert pressure on the internal elastic lamina. The delamination of the internal elastic lamina in the iliac arteries makes it difficult to measure, which may explain why the internal elastic lamina in the group with advanced atherosclerotic plaques was thicker than that in the group with early atherosclerotic plaques. In our study, delamination was also found to be a common phenomenon in the internal elastic lamina of the iliac arteries, which was not associated with atherosclerotic lesions. However, it easily led to measurement errors. In our experiments, we tried to select two layers instead of multiple layers for measurement. The best way to solve this problem may be to explore a more accurate measurement method, which could better confirm the situation of the internal elastic lamina. There was no significant difference in the thickness of the internal elastic lamina of coronary arteries between the two groups, which indicated that atherosclerotic plaques had no significant effect on the internal elastic lamina of coronary arteries. It was possible that the internal elastic lamina of coronary arteries itself was thin, and the internal elastic lamina caused by the compression of atherosclerotic plaques was not easy to measure.

The internal elastic lamina of the peripheral arteries was relatively thin, but it was complete, except for the coronary arteries. By contrast, the internal elastic lamina of coronary arteries was fragmented [14]. In the same patient, the atherosclerotic plaques of the coronary arteries were more pronounced than those of other arteries. In particular, advanced atherosclerotic plaques were often seen in coronary arteries, even exhibiting intraplaque hemorrhage in some cases. A fragmented internal elastic lamina of coronary arteries might allow smooth muscle cells to migrate into the intima and thus lead to intimal thickening and atherosclerosis [15, 16]. According to this hypothesis, the thickness and continuity of the internal elastic lamina in cerebral arteries might block the migration of smooth muscle cells and thus delay the formation of atherosclerotic plaques. In fact, it has already been reported that atherosclerosis is less severe in human cerebral arteries than in the aorta and coronary arteries [17, 18]. Of course, the formation of cerebral atherosclerotic plaques is also related to the characteristics of cerebral blood flow as well as the age of patients, in addition to factors related to the internal elastic lamina [19].

The external elastic lamina is another important feature of blood vessels. It is different from the internal elastic lamina. Our study showed that the external elastic lamina was present in the basilar arteries and all of the peripheral arteries. However, it was absent from the middle cerebral arteries, which represent the largest branches of the internal carotid artery [12]. An earlier study reported that the external elastic lamina was absent from the internal carotid artery [20]. Moreover, others suggested that the external elastic lamina was mainly associated with the sampled location [11]. Microscopic examination of the arterial wall of the internal carotid artery showed that the external elastic lamina was present in the petrous portion of the internal carotid artery but disappeared within the cavernous portion. The external elastic lamina was not observed in the intradural segments of the internal carotid artery [21].

In conclusion, the internal elastic lamina of cerebral arteries was thicker and denser than that of peripheral arteries. This difference might play a role in the delayed pathogenesis of cerebral atherosclerosis by preventing the migration of smooth muscle cells in cerebral arteries. Because the sample size in our autopsy series was relatively small, the results presented here must be verified using more extensive material. Attention must be paid to the characteristics of delamination and folding of the internal elastic membrane and whether they also play a role in the migration of smooth muscle cells for the formation of atherosclerosis. Whether it is easier for smooth muscle cells to choose areas that are not delaminated and folded or whether these areas are more favorable for smooth muscle cell migration is worth exploring.

Disclosure of conflict of interest

None.

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