Short Leukocyte Telomere Length Is Associated with Aortic Dissection

Jiangtao Yan, Yan Yang, Chen Chen, Jia Peng, Hu Ding and Dao Wen Wang

Abstract

Background  Aortic dissection is an age-related and lethal vascular disease. Aging, which is associated with degeneration, is the major risk factor of aortic dissection. Telomeres are specialized DNA structures located at the end of eukaryotic chromosomes, the telomere length could be considered as an index of vascular aging. The purpose of present study was undertaken to investigate the relationship between the leukocyte telomere length and aortic dissection.

Methods and Results  Seventy-two patients with aortic dissection and seventy-two sex- and age-matched subjects without vascular diseases were collected. Leukocyte telomere length ratio (T/S ratio) was measured using a quantitative PCR method and analyzed. A significantly shorter leukocyte telomere length in the patients with aortic dissection was found compared to the controls, [median 1.02 (interquartile range {IQR}: 0.83-1.37) vs median 1.63 [IQR: 1.18-2.51), p<0.001]. The telomere length in the control group showed a trend of inverse correlation with age (r=-0.226, p=0.056) , however, there was no significant correlation in aortic dissection (r=0.062, p=0.607). The short leukocyte telomere length was associated with aortic dissection, even after adjustment for other risk factor (OR=0.214, 95% CI: 0.085-0.537).

Conclusion  Leukocyte telomere length could be an independent predictor of aortic dissection. Measurement of the leukocyte telomere length may be valuable for patients with a high risk of aortic dissection.

Key words: telomere length, aortic dissection, aging

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Introduction

Aortic dissection is an uncommon and lethal vascular disease with high mortality rates (1). Previous population-based studies showed that the morbidity of aortic dissection is about 3 cases per 100,000 people per year, however, it has exhibited a steady increase in recent years (2-4). This increase might be associated with the development of diagnostic imaging techniques and the increasing age of the population (5).

Aging is a major risk factor for cardiovascular diseases, including aortic dissection (6, 7). Compared with chronological age, biological age is a much better predictor for cardiovascular diseases (8). Telomeres are specialized DNA structures located at the end of eukaryotic chromosomes, which are characterized by tandem repeats of a specific DNA sequence (TTAGGG) (9). The telomeres could cap the chromosome ends and protect them from enzymatic degradation, reconstruction, fusion and loss. Because of the ‘end replication problem’, telomere attrition occurs naturally with each cell division. When telomeres reach a critical short length, they lose their protective function, which results in the cell senescence. Hence, the telomere length could be thought as an index of the biological age of the cell.

There is evidence indicating that telomere shortening occurs in human vessels (10), and recent epidemiological studies have suggested that telomere shortening is related to age-associated vascular diseases, such as hypertension (11), atherosclerosis (12, 13), coronary heart diseases (14), and aortic aneurysm (15). The telomere length in the endothelial cells of the aorta shows a strong inverse correlation with
Subjects

In this study 72 patients with aortic dissection from Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology (Wuhan, China) were collected. All patients were diagnosed with Computed Tomographic Arteriography or aortic angiography. Iatrogenic and traumatic aortic dissections were excluded in this study. Seventy-two sex- and age-matched subjects without vascular diseases were randomly selected through SPSS 13.0 statistical package from the health examination population with a total of 995 subjects as the control group. This study was approved by the ethical committees of Tongji Hospital of Tongji Medical College, and all of the participants provided the informed consent.

All subjects were evaluated for detailed medical history and family history, especially hypertension, diabetes and other cardiovascular risk factors such as cigarette smoking and blood pressure, fasting blood glucose, blood lipid levels were recorded and strict physical examinations were performed and recorded by trained physicians. The blood samples of the subjects were drawn with anticoagulation by ethylenediaminetetraacetic acid-sodium (EDTA-Na). After centrifugation at 3,000 rpm for 15 minutes, the blood was separated into plasma and white cells. The plasma and white cells were stored at -80°C until used.

Measurement of telomere length

DNA was extracted from white cells using the QG-Mini 80 workflow with DB-S kit (Fuji Film Corporation, Tokyo, Japan) as instructed. Telomere length ratio (T/S ratio) was measured using a quantitative PCR method as described previously (11), which compared the ratio of the telomere repeat copy number (T) and single-copy gene copy number (S) in a given sample. Telomere length could play an important role in the aortic dissection. In the present study, the leukocyte telomere length of seventy-two patients with aortic dissection and sex-, age-matched control subjects (without aortic dissection) was measured to investigate the relationship between the telomere length and aortic dissection.

Results

Characteristics of participants

The characteristics of 72 patients with aortic dissection and 72 sex-, age-matched controls at recruitment are shown in Table 1. There was no significant difference in sex distribution, age, total cholesterol and history of diabetes and current or ex-smoker between the group of aortic dissection and the control group. However, there were more patients with a history of hypertension in the group of aortic dissection compared to the control group (64% vs. 27.8%, p=0.001). The telomere length of patients with aortic dissection was significantly shorter than that of the control group, [median 1.02 (interquartile range {IQR}: 0.83-1.37) vs median 1.63 (IQR: 1.18-2.51), p<0.001], which suggested that short telomere length might be associated with aortic dissection.
Table 1. Characteristics of Participants

<table>
<thead>
<tr>
<th></th>
<th>Aortic dissection (n=72)</th>
<th>Control (n=72)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, year</td>
<td>55.11±10.41</td>
<td>55.50±10.15</td>
<td>0.821</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>57 (79%)</td>
<td>57 (79%)</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>46 (64%)</td>
<td>20 (27.8%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>5 (6.9%)</td>
<td>6 (8.3%)</td>
<td>0.763</td>
</tr>
<tr>
<td>Current or ex-smoker, n (%)</td>
<td>44 (61%)</td>
<td>38 (52.7%)</td>
<td>0.508</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>4.30±1.01</td>
<td>4.02±1.03</td>
<td>0.108</td>
</tr>
</tbody>
</table>

The correlation between telomere length and age in cases and controls.

The correlation between telomere length and age in aortic dissection group and control group is shown in Fig. 1. The correlation between telomere length and age in the control group showed a trend of inverse correlation with age (r=-0.226, p=0.056), however, there was no significant correlation in aortic dissection (r=0.062, p=0.607).

The telomere length distribution within each age category in cases and controls

Because telomere length is age-related, we stratified the samples into 3 categories of age at recruitment (<50 years, n=25; 50 to 59 years, n=22; and ≥60 years, n=25). The telomere length distribution was determined independently within each category in cases and controls, respectively, as shown in Fig. 2. A significant shorter mean telomere length could be found in the aortic dissection group within each age category compared to the control group, (median 1.02 [IQR: 0.85-1.37] vs median 2.01 [IQR: 1.28-2.90], p=0.001; median 1.09 [IQR: 0.82-1.45] vs median 1.64 [IQR: 1.28-3.25], p=0.001; median 0.97 [IQR: 0.81-1.30] vs median 1.42 [IQR: 0.89-1.96], p=0.033).

The relationship between telomere length and aortic dissection

Conditional logistic regression analysis was used to assess the relationship between telomere length and aortic dissection, adjusted for other individual risk factors such as history of hypertension, diabetes, smoking, total cholesterol level as shown in Table 2, which indicated an inverse relationship between telomere length and aortic dissection independent of other risk factors (OR=0.214, 95% CI: 0.085-0.537).

Discussion

In the present study, a significantly shorter leukocyte telomere length was found in the patients with aortic dissection compared to the controls. The telomere length in the control group showed a trend of inverse correlation with age, however, there was no significant correlation in aortic dissection. There was a significantly shorter telomere length in aortic dissection within each age category compared to the controls. The short leukocyte telomere length was associated with aortic dissection, even after adjustment for other risk factors.

Aortic dissection is an age-dependent life-threatening vascular disease. The major risk factors of aortic dissection include old age, history of hypertension, atherosclerosis, previous cardiovascular surgery, and hereditary vascular diseases (5). Aging, which is associated with degeneration, is the most common risk factor of aortic dissection. Recently, vascular aging, which is characterized by age-related medial degeneration and sclerosis as a pathological description (7) has aroused the interest of many medical researchers. The vascular aging occurs in large arteries, which could result in aortic aneurysm or dissection. This process could occasionally start early in young, which suggests that a biological age could influence the vascular aging process except for chronological age. Epidemiological evidence has shown that telomere length, as an index of biological age, could be a better predictor of aging-related vascular aging rather than chronological age (8). In present study, a short mean leukocyte telomere length in patients with aortic dissection was found compared to controls, which indicated that leukocyte telomere length could be an important predictor.

Further, the correlation between telomere length and chronological age was analyzed in patients with aortic dissection and controls, respectively. The telomere length in the control group showed a trend of inverse correlation with age, in agreement with previous reports (11), however, there was no significant correlation in aortic dissection, furthermore, the mean telomere length in aortic dissection was significantly shorter than that in the controls within each age.
category. Atturu and colleagues (15) have found a similar result in patients with aortic aneurysm. Those results suggest that the vascular aging could have occurred early life in patients with aortic dissection, which could cause the onset of aortic dissection in young patients. Thus, telomere length could be an early predictor of aortic dissection.

There are many known risk factors for non-iatrogenic and non-traumatic aortic dissections. In this study, the conditional logistic regression analysis was used to assess the relationship between telomere length and aortic dissection, adjusted for other individual risk factors such as history of hypertension, diabetes, smoking, total cholesterol level, which indicated an inverse relationship between telomere length and aortic dissection independent of other risk factors. This result demonstrates that short leukocyte telomere length is an independent predictor of aortic dissection.

Previous studies have shown that a history of hypertension is an important predisposing factor for aortic dissection in elderly people, and it is present in more than 70% of patients (17), which is similar to the results of our study. The present study showed that the history of hypertension was an independent risk factor of aortic dissection. Yang and colleagues (11) have found a short telomere length in Chinese patients with hypertension; in addition, subjects with a shorter telomere length were at a higher risk of development of coronary artery diseases than individuals with a longer telomere length. Those results suggest that telomere length could be a good marker of vascular aging caused by different risk factors, such as hypertension, older age, etc.

In summary, this study found a short leukocyte telomere length in patients with aortic dissection, which was associated with aortic dissection independent of other risk factors. These results indicated that leukocyte telomere length could be an independent predictor of aortic dissection. It may be valuable to measure the leukocyte telomere length for patients with a high risk of aortic dissection.

The authors state that they have no Conflict of Interest (COI).

References

![Figure 2. Telomere length of aortic dissection and control within different age categories. Median and Interquartile range (box) of telomere length are shown. A significantly short telomere length in aortic dissection could be found within each age category compared with control.](image)