Comparison of Four Blood Pressure Indexes for the Prediction of 10-Year Stroke Risk in Middle-Aged and Older Asians

Katsuyuki Miura, Yoshiyuki Soyama, Yuko Morikawa, Muneko Nishijo, Yumiko Nakanishi, Yuchi Naruse, Katsushi Yoshita, Sadanobu Kagamimori, Hideaki Nakagawa

Abstract—Information has been sparse on the comparison of 4 blood pressure (BP) indexes (systolic BP [SBP], diastolic BP [DBP], pulse pressure [PP], and mean BP [MBP]) in relation to long-term stroke incidence, especially in middle-aged and older Asian people. A prospective cohort study was performed in 4989 Japanese (1523 men and 3466 women) aged 35 to 79 at baseline with 10 years of follow-up. End points included stroke incidence (total, ischemic, and hemorrhagic). Multivariate-adjusted hazard ratios with a 1-SD higher value for each BP index were determined by Cox proportional hazard analyses; Wald χ² tests were used to compare the strength of relationships. Analyses were also done for each of 4 age-gender groups consisting of men and women aged 35 to 64 and 65 to 79 years. During follow-up, 132 participants developed stroke. Adjusted hazard ratios for all strokes were 1.68 for SBP, 1.72 for DBP, and 1.80 for MBP, which were higher than that for PP (1.34). SBP and DBP were related positively to stroke risk after adjustment of each other. PP was not the strongest predictor in any age-gender groups among 4 BP indexes. In men aged 65 to 79 years, SBP showed the strongest relationship to all stroke risk (hazard ratio 1.62) among 4 BP indexes. In women aged 65 to 79 years, hazard ratios for all strokes were 2.48 for MBP, 2.46 for DBP, 2.25 for SBP, and 1.57 for PP. The long-term incident stroke risk of high BP in Asians should be assessed by SBP and DBP together, or by MBP, not by PP.

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Key Words: stroke ■ blood pressure ■ epidemiology

Blood pressure (BP) is an established major risk factor for coronary heart disease and stroke.¹⁻⁴ Risk relationships for systolic BP (SBP) and diastolic BP (DBP) are generally regarded to be continuous, graded, strong, independent of other risk factors, and etiologically significant. Some data indicate that SBP is a stronger predictor of cardiovascular diseases than DBP.⁵⁻⁸ Several epidemiological studies reported that pulse pressure (PP), the difference between SBP and DBP, is a useful predictor for coronary heart disease, especially in older people.⁹⁻¹³ These reports emphasized the importance of PP as a coronary risk factor, especially because PP is often higher after age 50, apparently because of increased arterial stiffness.¹⁴⁻¹⁶ However, recent cohort studies including older people showed that the relationship of PP to mortality from total cardiovascular diseases and coronary heart disease was less strong than those of other BP indexes.¹⁷⁻²⁰ For stroke, 2 recent large-scale cohort study collaborations reported that PP was less useful in predicting long-term stroke risk than SBP.¹⁹,²⁰ Because a large part of the study participants in these studies were white (even in 1 study from the Asia Pacific region), investigations only for Asian people whose stroke occurrence is relatively higher than that in Western countries are sparse. Moreover, because most previous reports were on fatal stroke events and there would be more nonfatal stroke events not investigated, studies on stroke incidence including nonfatal events are desirable. Therefore, it is uncertain whether PP is superior to SBP or DBP in predicting future stroke incidence in various age-sex groups of Asians.

This report compares relationships of 4 BP indices (PP, SBP, DBP, and mean BP [MBP]) with 10-year stroke incidence in a middle-aged and older Japanese cohort (total 4989 men and women aged 35 to 79 years). The specific goals of this research are to assess, in this Asian population sample: (1) whether PP is the best predictor among the 4 indices; (2) whether the relationship of SBP is stronger than that of PP; (3) relationship of MBP; and (4) relationships of SBP and DBP, after adjustment for each other, to stroke incidence.

Methods

Study Population

The methods of the Oyabe study have been described previously.²¹,²² Briefly, the city of Oyabe is located in Toyama Prefecture in the

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participants involved in the present study were observed at 10 years of follow-up. The baseline characteristics of the participants are shown in Table 1. The participants were divided into five groups according to the incidence of stroke during 10 years of follow-up: (1) those who did not develop stroke during the follow-up period, (2) those who developed stroke during the follow-up period, (3) those who recovered from stroke during the follow-up period, (4) those who died from stroke during the follow-up period, and (5) those who were lost to follow-up during the follow-up period.

Baseline Examination
Data collected at baseline included age, sex, height, weight, BP, serum total cholesterol, serum HDL-cholesterol (HDL-C), smoking status, and alcohol consumption. A single BP measurement was obtained by trained staff using a random zero sphygmomanometer (Hawksley and Sons Ltd.) after a 5-minute rest period in the seated position. The staff of BP measurement is composed of physicians and public health nurses who were trained using the manual of operations of the INTERSALT study;21 some of them were certified for BP measurement in INTERSALT and trained other staff. Blood samples were obtained via cubital vein puncture without regard to the time of the previous meal. The questionnaire administered by trained staff included medical history, subjective symptoms, and the status of cigarette smoking and alcohol consumption. The status of alcohol consumption was divided into 3 categories: nondrinkers, occasional drinkers, and everyday drinkers.

End Points
Vital status and the incidence of stroke were ascertained through the end of 1998, with a follow-up of ~10 years. Stroke events were assessed from the population-based stroke registration system of Oyabe. Details of this registration system were described previously.21 In brief, this registration system of stroke has been continuously active for prevention of stroke and rehabilitation since 1967. Information regarding stroke was documented mainly for cases of hospitalization and outpatients by physicians of all general hospitals and general practitioners in Oyabe and general hospitals in neighboring cities. Physicians reported the events in a prescribed format involving items related to neurological deficit, trends of symptom, and past history. The type of stroke was classified according to the criteria of the Stroke Committee established by the Japanese Ministry of Education,24 which modified the diagnostic criteria of the ad hoc committee established by the Advisory Council for the National Institute of Neurological Diseases and Blindness, Public Health Service.25 Registered cases include ischemic stroke, intracranial hemorrhage, and subarachnoid hemorrhage; transient ischemic attacks and those patients presenting with asymptomatic lesions detected by brain imaging were not included. Hospitals equipped with x-ray computed tomography scanners reported ≥85% of registered cases. To complete the registration, stroke information was gathered from death certificates as well. Death events from death certificates were coded by trained doctors according to the International Classification of Diseases, 9th Revision (ICD-9), and mortality caused by stroke was defined as ICD-9 code 430 to 438.

Exclusions
Participants presenting with a history of stroke (n=65) and those lacking baseline examination data (n=20) were excluded from the cohort. Thus, the report was based on a total of 4989 participants (1523 men and 3466 women) with the following age–gender breakdown: 1085 men aged 35 to 64 years; 438 men aged 65 to 79 years; 2816 women aged 35 to 64 years; and 650 women aged 65 to 79 years.

Statistical Analyses
MBP was calculated as SBP/3+2DBP/3,26 and PP was calculated as MBP–DBP. For each BP index considered separately as a continuous variable, Cox proportional hazards regression was used to determine multivariate-adjusted hazard ratios (HRs) for a level greater by 1 (SD). Wald χ² tests were also used to compare strength of relationships. A Cox model included MBP and DBP simultaneously to assess relationships with adjustment for each other. Another Cox model included MBP and PP simultaneously to assess their independent relationships. HRs were adjusted for other major risk factors and for potential confounders (sex, age, body mass index, serum total cholesterol, serum HDL-C, cigarette smoking, and alcohol consumption). These analyses were done for total participants and for each of

### TABLE 1. Baseline Characteristics According to the Incidence of Stroke During 10 Years of Follow-Up

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Stroke</th>
<th>Stroke</th>
<th>No Stroke</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of participants</td>
<td>1460</td>
<td>63</td>
<td>3397</td>
<td>69</td>
</tr>
<tr>
<td>Age (years)</td>
<td>57.8 (10.9)</td>
<td>67.1 (8.0)*</td>
<td>55.4 (10.6)</td>
<td>64.6 (8.2)*</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>22.7 (2.7)</td>
<td>22.8 (2.7)</td>
<td>23.2 (3.0)</td>
<td>23.0 (2.8)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>129.7 (19.7)</td>
<td>143.5 (20.6)*</td>
<td>124.2 (19.3)</td>
<td>141.4 (22.1)*</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>78.6 (11.1)</td>
<td>84.2 (12.2)*</td>
<td>73.9 (10.8)</td>
<td>81.3 (12.4)*</td>
</tr>
<tr>
<td>Pulse pressure (mm Hg)</td>
<td>51.2 (14.6)</td>
<td>59.3 (17.8)*</td>
<td>50.3 (13.9)</td>
<td>60.1 (16.3)*</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>95.6 (12.8)</td>
<td>104.0 (13.1)*</td>
<td>90.7 (12.6)</td>
<td>101.3 (14.4)*</td>
</tr>
<tr>
<td>Serum total cholesterol (mmol/L)</td>
<td>4.70 (0.84)</td>
<td>4.61 (0.99)</td>
<td>5.17 (0.94)</td>
<td>5.21 (0.83)</td>
</tr>
<tr>
<td>Serum HDL cholesterol (mmol/L)</td>
<td>1.17 (0.32)</td>
<td>1.07 (0.32)</td>
<td>1.24 (0.29)</td>
<td>1.20 (0.35)</td>
</tr>
<tr>
<td>Alcohol consumption (%)</td>
<td>55.7</td>
<td>63.5</td>
<td>2.7</td>
<td>4.4</td>
</tr>
</tbody>
</table>

Values are means (SD), except as noted.
*P<0.001; †P<0.05 vs participants who did not develop stroke.
### Results

In univariate analyses (Table 1), men and women who developed stroke during the follow-up period were older and had higher values of all 4 BP indexes ($P<0.001$). Men who developed stroke had lower serum HDL-C at baseline ($P=0.05$). PP was strongly correlated with SBP in each gender group. All indexes were positively and significantly correlated with each other ($P<0.01$). PP was strongly correlated with SBP (0.90 to 0.92) and DBP (0.92 to 0.94) and relatively weakly correlated with PP (0.48 to 0.55). Correlation between SBP and DBP ranged from 0.67 to 0.72.

During follow-up, 63 men and 69 women developed the first stroke event (Table 2). Twenty-five men and 26 women died as a result of stroke, whereas a total of 388 participants died from all causes. Ninety-two participants were withdrawn by geographic relocation during follow-up (follow-up rate 98.2%). Mean age at the first occurrence of stroke in these 4 age–gender groups. HR estimates were determined by SAS for Windows Release 8e (SAS Institute).

### Table 3. Adjusted HRs* for 4 BP Indexes for Stroke in Total Participants

<table>
<thead>
<tr>
<th>BP Index</th>
<th>One SD (mm Hg)</th>
<th>All Stroke Incidence</th>
<th>Ischemic Stroke Incidence</th>
<th>Hemorrhagic Stroke Incidence</th>
<th>All Stroke Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$\chi^2$</td>
<td>HR</td>
<td>95% CI</td>
<td>$\chi^2$</td>
</tr>
<tr>
<td>SBP</td>
<td>19.8</td>
<td>7.4</td>
<td>1.36</td>
<td>1.09–1.70</td>
<td>4.7</td>
</tr>
<tr>
<td>DBP</td>
<td>11.2</td>
<td>7.8</td>
<td>1.39</td>
<td>1.10–1.74</td>
<td>5.3</td>
</tr>
<tr>
<td>PP</td>
<td>14.3</td>
<td>33.6</td>
<td>1.79</td>
<td>1.47–2.17</td>
<td>21.3</td>
</tr>
<tr>
<td>MBP†</td>
<td>13.0</td>
<td>0.0</td>
<td>0.01</td>
<td>0.84–1.22</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Cl indicates confidence interval.

*HRs are calculated for each BP index higher by 1 SD and adjusted for sex, age, body mass index, total cholesterol, HDL-C, smoking, and alcohol consumption using Cox proportional hazard model.

†SBP and DBP are included in the same model.

‡MBP and PP are included in the same model.
indexes in both age groups of women. A Cox model including SBP and DBP showed that the relationship of each BP remained positive. PP did not show significant relationships after adjustment of MBP in both age groups of women. These results in men and women were similar when ischemic stroke incidence was chosen as the end point.

**Discussion**

The main findings from this 10-year follow-up study on stroke incidence in middle-aged and older Japanese men and women are: (1) for total participants, MBP was the strongest predictor for stroke incidence (total, ischemic, and hemorrhagic); (2) for total participants, SBP and DBP were similarly strong predictors for stroke incidence, and the relationships were positive after adjustment of each other; (3) PP was not the strongest predictor for stroke incidence in any age-gender groups, including older people, among 4 BP indexes and was not related to stroke after adjustment of MBP; (4) in older men, the strongest relationship to stroke was observed for SBP; and (5) in older women, SBP and DBP showed the similarly strong relationships to stroke risk.

Several studies have suggested that PP may be a useful predictor of coronary heart disease and total cardiovascular diseases, especially in older people. However, recent cohort studies including older people showed that the relationship of PP to mortality from total cardiovascular diseases and coronary heart disease was less strong than those of other BP indexes. For stroke, the predictive power of PP has not been fully investigated, but 2 recent large-scale cohort study collaborations reported that PP was less useful in predicting long-term stroke risk than SBP. One of those studies, the Asia Pacific Cohort Studies Collaboration, performed analyses similar to our study on BP and fatal stroke events, comparing HRs for a 1-SD difference in each of 4 BP indexes. The study showed that the strongest relationships were observed for SBP in men aged 50 to 69 years (HRs ranged between 1.5 and 2.0) and in women of all age groups (HRs ranged between 1.3 and 1.9). MBP and DBP in men <50 years old (HR 2.5) and PP and SBP in men aged ≥70 years (HR 1.4) showed similarly strong relationships. Major differences of this study from ours were that the study end point was mainly fatal stroke events, not incident stroke, and that, although the study was from the Asia Pacific region, a large part of the study participants seemed to be whites in.

**TABLE 4. Adjusted HRs* for 4 BP Indexes for All Stroke Incidence by 4 Age–Gender Groups†**

<table>
<thead>
<tr>
<th>BP Index</th>
<th>1 SD (mm Hg)</th>
<th>χ²</th>
<th>HR</th>
<th>95% CI</th>
<th>1 SD (mm Hg)</th>
<th>χ²</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Aged 35–64 years at baseline</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>18.6</td>
<td>3.0</td>
<td>1.41</td>
<td>0.96–2.08</td>
<td>19.5</td>
<td>9.2</td>
<td>1.56</td>
<td>1.17–2.08</td>
</tr>
<tr>
<td>DBP</td>
<td>10.7</td>
<td>11.5</td>
<td>1.79</td>
<td>1.28–2.50</td>
<td>10.9</td>
<td>9.0</td>
<td>1.63</td>
<td>1.19–2.25</td>
</tr>
<tr>
<td>PP</td>
<td>14.0</td>
<td>0.0</td>
<td>0.97</td>
<td>0.63–1.48</td>
<td>13.4</td>
<td>3.7</td>
<td>1.32</td>
<td>0.99–1.74</td>
</tr>
<tr>
<td>MBP</td>
<td>12.2</td>
<td>8.3</td>
<td>1.71</td>
<td>1.19–2.46</td>
<td>12.6</td>
<td>10.9</td>
<td>1.66</td>
<td>1.23–2.25</td>
</tr>
<tr>
<td>SBP‡</td>
<td>0.2</td>
<td>0.89</td>
<td>0.50–1.56</td>
<td>1.6</td>
<td>1.30</td>
<td>0.86–1.97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBP</td>
<td>7.0</td>
<td>1.93</td>
<td>1.19–3.14</td>
<td>1.5</td>
<td>1.33</td>
<td>0.84–2.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MBP§</td>
<td>11.7</td>
<td>1.95</td>
<td>1.33–2.87</td>
<td>6.7</td>
<td>1.65</td>
<td>1.13–2.41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PP</td>
<td>2.2</td>
<td>0.71</td>
<td>0.45–1.12</td>
<td>0.0</td>
<td>1.01</td>
<td>0.71–1.44</td>
<td></td>
<td></td>
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<tr>
<td>Aged 65–79 years at baseline</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>20.8</td>
<td>10.0</td>
<td>1.62</td>
<td>1.20–2.19</td>
<td>19.7</td>
<td>20.2</td>
<td>2.25</td>
<td>1.58–3.20</td>
</tr>
<tr>
<td>DBP</td>
<td>11.4</td>
<td>4.6</td>
<td>1.43</td>
<td>1.03–1.98</td>
<td>10.5</td>
<td>23.6</td>
<td>2.46</td>
<td>1.71–3.53</td>
</tr>
<tr>
<td>PP</td>
<td>15.1</td>
<td>6.5</td>
<td>1.44</td>
<td>1.09–1.89</td>
<td>14.8</td>
<td>6.4</td>
<td>1.57</td>
<td>1.11–2.24</td>
</tr>
<tr>
<td>MBP</td>
<td>14.0</td>
<td>8.2</td>
<td>1.60</td>
<td>1.16–2.20</td>
<td>12.4</td>
<td>27.2</td>
<td>2.48</td>
<td>1.77–3.50</td>
</tr>
<tr>
<td>SBP‡</td>
<td>5.3</td>
<td>1.58</td>
<td>1.07–2.34</td>
<td>2.6</td>
<td>1.49</td>
<td>0.91–2.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBP</td>
<td>0.0</td>
<td>1.04</td>
<td>0.69–1.58</td>
<td>5.4</td>
<td>1.82</td>
<td>1.10–3.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MBP§</td>
<td>3.6</td>
<td>1.43</td>
<td>0.99–2.06</td>
<td>19.0</td>
<td>2.61</td>
<td>1.70–4.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PP</td>
<td>1.5</td>
<td>1.23</td>
<td>0.89–1.70</td>
<td>0.1</td>
<td>0.92</td>
<td>0.59–1.44</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI indicates confidence interval.

*HRs are calculated for each BP index higher by 1 SD and adjusted for age, body mass index, total cholesterol, HDL-C, smoking, and alcohol consumption using Cox proportional hazard model.

†Numbers of events are 20 in men aged 35–64 years, 43 in men aged 65–79 years, 39 in women aged 35–64 years, and 30 in women aged 65–79 years.

‡SBP and DBP are included in the same model.

§MBP and PP are included in the same model.
Australia. Thus, our study would be the first investigating the relationships of 4 BP indexes to incident stroke risk in a pure Asian population.

Because some previous studies suggested the importance of PP in older people in predicting the risk of coronary heart disease, the relationship of PP to stroke incidence in older people should be carefully investigated. For participants aged 65 to 79 years (mean age 73 years) in the present study, PP was less important than SBP and MBP in men and than SBP, DBP, and MBP in women. As far as we know, the Cardiovascular Health Study would be the only cohort study comparing BP indexes in relation to incident stroke risk in older people. In the study, 5888 men and women aged ≥65 years (mean age 73 years) participated from 4 US centers, and adjusted HRs for 1 SD difference in each BP were 1.34 for SBP, 1.29 for DBP, and 1.21 for PP. Although it is consistent that SBP was more important than PP also in older populations in the United States and Japan, an interesting finding is that HRs for 1 SD change in SBP were higher in Japan (1.62 in men and 2.25 in women for all stroke incidence) than in the United States. The effect of SBP on stroke incidence would be stronger in Asian populations than in Western populations, although 15% of participants in the Cardiovascular Health Study were black.

Some previous reports on PP included SBP and PP in the same multivariate model. However, we did not use this model and showed results only for 2 models that included SBP and DBP or MBP and PP. As we discussed in our previous article, one cannot by regression assess the association of SBP with morbidity or mortality adjusted for PP because the coefficient for SBP from that model is actually the association of DBP adjusted for PP. Our judgment is that the appropriate regression model with 2 BP indexes is the model including SBP and DBP. In these models for total participants, SBP and DBP showed similarly positive relationships independently from each other. For all age–gender groups, DBP did not show inverse relationships after adjustment of SBP; such a relationship was reported from the Framingham Study for coronary heart disease as the end point.

Recent discussions on diagnosis and treatment of high BP have focused on SBP more than DBP, especially in older people. However, in our study, the relationships of DBP were as strong as those of SBP in total participants and were stronger than those of SBP in middle-aged men and in older women. Moreover, with adjustment for SBP, DBP was also positively and significantly related to stroke risk in total participants. These results also indicate a role for DBP in long-term stroke risk evaluation in men and women. In fact, in middle-aged people, previous epidemiological studies have shown that cardiovascular disease risk generally increased with DBP level in each stratum of SBP level. The importance of DBP should be considered further in Asian men and women in predicting future stroke.

Although MBP showed the strongest association with stroke risk in analyses of total participants, apparently, reflecting modest additive effects of SBP and DBP, χ² tests and HRs were generally similar to those of SBP and DBP. MBP could be a slightly better predictor of long-term stroke risk than SBP and DBP in Asian. However, use of this index may not be practical in daily clinical and public health practice at present because there are no guidelines for hypertension diagnosis and management using MBP.

A limitation of the present study is that results were based on a single measurement of BP, hence they probably underestimate true associations because of regression dilution bias. Nonetheless, as shown here and in many other prospective population studies, a single BP reading is strongly predictive of future cardiovascular events. On the other hand, our highly standardized BP measurement using random zero sphygmomanometers by staff trained in the same way to INTERSALT is strength of our study. Another limitation is lack of information at baseline on antihypertensive medication or hormonal status in women. Existence of some participants whose BP was controlled by medication would underestimate the relationship of BP to stroke risk. Lower response rate to the baseline examination in men would be a limitation. However, the results in men would be able to generalize to the Japanese population because there is high equality in socioeconomic status and in Japanese lifestyle. Moreover, each BP index was included as a continuous variable in our statistical models under an assumption that there is a linear relationship between each BP and stroke risk. Analyses according to the categories of BP to look at the shape of relationship were not available because of the relatively small sample size of our study.

**Perspectives**

As to implications of our results for the primary prevention of stroke in Asian: (1) emphasis on PP should be avoided even in older people for the prediction of future stroke risk; (2) the long-term incident stroke risk of high BP should be assessed by SBP and DBP together. Especially for women and middle-aged men, DBP should be given careful consideration for its strong independent relationship to stroke risk; (3) relationships of MBP to stroke risk were generally stronger than those of SBP or DBP. However, use of this index may not be practical in daily clinical and public health practice at present.

**Acknowledgments**

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**References**


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