The risk of stroke and associated risk factors in a health examination population

A cross-sectional study

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Abstract

Health examination is an important method for early detection of people with different risk of stroke. This study estimates the risk of stroke and identify risk factors for people who underwent health examinations at the Health Examination Center at West China Hospital, Sichuan University from July 2014 to February 2018. A total of 31,464 people were recruited in this study and divided into 3 groups (low risk, moderate risk, and high risk) according to risk of stroke. We explored possible factors associated with the risk of stroke by using multivariable stepwise logistic regression analysis.

Among the participants, 17,959 were at low risk, 11,825 were at moderate risk, and 1680 were at high risk. Age, smoking, alcohol consumption, body mass index, uric acid, diastolic pressure, systolic pressure, triglycerides, low-density lipoprotein cholesterol, glucose, and brachial-ankle pulse wave velocity (baPWV) were independent significant risk factors for stroke, whereas high-density lipoprotein cholesterol was an independent protective factor for stroke. Interestingly, with increasing age, the percentage of people at moderate or high risk of stroke was increased. The percentages of people at moderate and high risk of stroke were also increased with respect to the stages of baPWV.

This study showed that >40% of the participants were at moderate or high risk of stroke, especially the older participants. Several factors were related to the risk of stroke, especially baPWV. Some preventive action may be adopted early, and more attention can be paid to the health examination population.

Abbreviations: ABI = ankle-brachial index, baPWV = brachial-ankle pulse wave velocity, BMI = body mass index, BP = blood pressure, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, TC = total cholesterol, TGs = triglycerides, UA = uric acid.

Keywords: epidemiology, health examination, risk factor, stroke

1. Introduction

According to the ‘World Health Organization’ criteria, stroke events are defined as “rapidly developing signs of focal (or global) disturbance of cerebral function lasting >24 hours (unless interrupted by surgery or death) with no apparent nonvascular cause.”[1] Stroke is estimated to be the second leading cause of death and a major cause of serious disability for adults worldwide.[2] The proportion of deaths resulting from stroke is approximately 10% to 12% in Western countries, and 12% of these deaths are people <65 years’ old.[3] Stroke can be generally classified into 2 subgroups, ischemic stroke and hemorrhagic stroke, and in China, 43.7% to 78.9% of all stroke cases were ischemic stroke.[4] Furthermore, in China, the annual stroke mortality rate is approximately 115 per 100,000,[5] exceeding heart disease as the leading cause of death. The mortality owing to stroke is about 25% higher than ischemic heart disease in China in 2017. Notably, there are >2 million new stroke cases annually.[6] Currently, Asia, East Europe, and Russia are experiencing the highest rates of mortality and disability-adjusted life years lost as a result of stroke.[4] The consequences of stroke-related disability and death are significant for both society and individuals. Stroke accounts for approximately 2% to 4% of total health care costs in the world, and industrialized countries have shown that >4% of direct health care costs are because of stroke. Because of the burgeoning elderly population in Western societies, stroke-related disability in these societies is estimated to
be ranked as the fourth most important cause of disability-adjusted life years by 2030. Similarly, with an increase in the aging population, the disease burden will increase greatly during the next 20 years, especially in developing countries. The lifestyle in China has changed significantly, along with dramatic transformations in social, economic, and environmental conditions, during the last 30 years. The effect of stroke has now caused serious public health problems in China. Therefore, all measures capable of downregulating the incidence rate of stroke and disability are extremely important.

Currently, the prevalence of stroke in China is similar to that in developed countries; for example, the total age-adjusted incidence of first-ever stroke in China (115.61–219 per 100,000 per year) is not significantly different from that in developed countries (130–410 per 100,000 per year). Therefore, paying more attention to people with a high risk of stroke and searching for possible factors underlying the risk of stroke is very important. Early detection, diagnosis, and treatment are essential for the prevention and control of stroke. Thus, regular health examination is an important method for the early detection of people at risk for stroke. In the present study, we performed a health risk assessment of stroke for people who underwent health examinations at West China Hospital, Chengdu, to reveal the distribution characteristics of risk of stroke among the health examination population. We also discussed the factors that are related to the risk of stroke.

2. Methods

2.1. Study population

This study is a retrospective study. From July 2014 to February 2018, a total of 31,464 cases (17,396 males, 14,068 females) were voluntary, and went to the Health Examination Center at West China Hospital, Sichuan University, for health examination. In the Health Examination Center, the participants did health examination. The following methods were carried out in accordance with the approved guidelines. The corresponding protocol was approved by the Ethics of Research Committee of the West China Hospital of Sichuan University. Written informed consent was obtained from all participants.

2.2. Data collection

All participants completed the questionnaire, physical examination, and laboratory test, and peripheral blood was collected from each subject. Demographic characteristics, including age, sex, marital status, and lifestyle habits (smoking and alcohol consumption) were assessed by trained investigators. Weight was evaluated with a calibrated electronic digital scale, accurate to 100 g, with subjects wearing only light underwear. Height was measured without shoes to the nearest 0.1 cm using a secure portable stadiometer. Body mass index (BMI) was calculated by weight (kilogram)/height\(^2\) (square meter) for each participant. Blood pressure (BP) was recorded twice on the right arm with an electronic sphygmonomanometer with participants in the sitting position after a 10-minute rest. Serum levels of fasting blood glucose, uric acid (UA), total cholesterol (TC), triglycerides (TGs), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) for each individual were determined by an automatic biochemical analyzer (Mindary, BS-820, Shenzhen, China). Brachial-ankle pulse wave velocity (baPWV) was measured by a volume-plethysmographic apparatus (Vasera VS-1000, Fukuda Denshi, Japan). In brief, participants were examined in the supine position after a sufficient sedentary period. A microphone for detecting heart sounds was placed on the left edge of the sternum at the fourth intercostal space. Occlusion and monitoring cuffs were wrapped on both brachial and ankles, and pressure waveforms of the brachial and tibial arteries were collected. Criteria for classification of baPWV were as followings: soft (<1100 cm/s), normal (1100–1400 cm/s), medium hard (1400–1680 cm/s), hard (>1680 cm/s). With respect to ankle-brachial index (ABI), BP was measured in both arms and legs using a manual sphygmononometer (Welch Allyn Tycos 7670–01, Welch Allyn, Skaneateles Falls, NY) and a portable vascular Doppler (Nicolet n800, Natus Medical Inc., San Carlos, CA) with an 8 MHz probe, following a counterclockwise sequence: right arm, right posterior tibialis, right dorsalis pedis, left posterior tibialis, left dorsalis pedis, and left arm. The ABI was computed by dividing the higher of the posterior tibialis or dorsalis pedis BP in each leg by the higher arm systolic BP (right or left). Classification of ABI was defined as: normal (0.9–1.3), hard (0.8–0.9), mild clogging (0.5–0.8), clogging (<0.5).

The risk of stroke for each participant was determined according to the manufacturer’s protocol (Hehe Science And Technology Group Co., Ltd., Hangzhou, China), and there were 3 risk subgroups, including cases with high risk, moderate risk, and low risk. In brief, the calculation of the risk of stroke for each individual included 4 parts: family history, history of present illness, physiological index, and lifestyle. Based on the results of the 4 parts, indices in each part were given with weight/scores. After collecting the total score of all the indices, we divided the risk of stroke for each participant into 3 groups: high risk of stroke (total score >20), moderate risk of stroke (total score between 5 and 20), and low risk of stroke (total score <5). For instance, with respect to family history, there are 8 indices, namely, father with stroke, mother with stroke, (paternal) grandfather with stroke, (paternal) grandmother with stroke, (maternal) grandfather with stroke, (maternal) grandmother with stroke, father with hypertension, and mother with hypertension. If the father of the participant had a stroke, the score was 2.5. Similarly, if the mother of the participant had a stroke, the score was 2.5. Otherwise, the score is 0. In addition, if the grandparents or grandmothers of the participant had a stroke, the score was 0.5, otherwise, the score was 0. Moreover, if the mother or father of the participant had hypertension, the score was 0.1. In contrast, if the mother or father of the participant was not diagnosed with hypertension, the score was 0. Other indices in each part and how to assign the scores are listed in supplementary Table 1, http://links.lww.com/MD/D272.

2.3. Statistical analysis

All statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC). With respect to the results expressed as the mean ± standard deviation, the statistical significance of the data was determined by analysis of variance analysis. When data were expressed as percentages for categorical variables, the \(\chi^2\) test and the Cochran-mantel-haenszel test were used to compare categorical variables. Multivariable logistic regression analysis was used to identify the factors related to risk of stroke (risk of stroke as a dependent variable and sex, age, smoking status, alcohol consumption status, BMI, systolic pressure, diastolic pressure, glucose, UA, TC, TGs, HDL-C, LDL-C, baPWV, and
Table 1
Characteristics of recruited participants.

| Variable                  | Low risk (n = 17995) | Moderate risk (n = 11825) | High risk (n = 1680) | Statistics | P     |
|---------------------------|----------------------|---------------------------|----------------------|------------|-------|
| Age, y                    | 43.18 ± 10.07        | 48.69 ± 9.61              | 50.35 ± 8.79         | L2 = 5582.33 | <.0001 |
| Sex                       |                      |                           |                      |            |       |
| Female, n (%)             | 7607 (43.36)         | 8469 (71.62)              | 1320 (78.57)         | χ² = 2858.92 | <.0001 |
| Male, n (%)               | 10352 (56.64)        | 3356 (28.38)              | 360 (21.43)          |            |       |
| Smoking                   |                      |                           |                      |            |       |
| Yes, n (%)                | 4098 (22.82)         | 7253 (61.34)              | 952 (56.67)          | χ² = 4672.323 | <.0001 |
| No, n (%)                 | 13861 (77.18)        | 4672 (38.66)              | 728 (43.33)          |            |       |
| Alcohol consumption       |                      |                           |                      |            |       |
| Yes, n (%)                | 6707 (37.35)         | 6899 (58.34)              | 1072 (63.61)         | χ² = 1472.96 | <.0001 |
| No, n (%)                 | 11252 (62.65)        | 4026 (41.66)              | 6086 (36.39)         |            |       |
| Body mass index           | 22.51 ± 2.61         | 25.89 ± 3.02              | 27.25 ± 3.35         | F = 5659.61 | <.0001 |
| Uric acid, μmol/L         | 312.08 ± 60.55       | 372.99 ± 80.67            | 398.97 ± 98.87       | F = 2254.78 | <.0001 |
| Diastolic pressure, mmHg  | 73.94 ± 10.87        | 78.51 ± 8.42              | 90.47 ± 12.61        | F = 6457.95 | <.0001 |
| Systolic pressure, mmHg   | 117.94 ± 15.98       | 124.79 ± 14.53            | 142.42 ± 18.19       | F = 6871.31 | <.0001 |
| Triglycerides, mmol/L     | 1.60 ± 1.28          | 1.42 ± 0.40               | 5.22 ± 1.24          |            |       |
| Low-density lipoprotein cholesterol, mmol/L | 2.82 ± 0.77 | 1.42 ± 0.40 | 5.22 ± 1.24 |            |       |
| High-density lipoprotein cholesterol, mmol/L | 1.42 ± 0.40 | 1.42 ± 0.40 | 5.22 ± 1.24 |            |       |
| Glucose, mmol/L           | 5.12 ± 0.39          | 5.12 ± 0.39               | 5.12 ± 0.39          |            |       |
| Total cholesterol, mmol/L | 4.60 ± 0.69          | 5.25 ± 0.97               | 5.75 ± 1.42          |            |       |

ABI = ankle-brachial index, baPWV = brachial-ankle pulse wave velocity.

Age as independent variables. The odds ratio (OR) and its 95% confidence interval (CI) were presented to show the risks. Significance was indicated by a P value <.05.

3. Results

3.1. Characteristics of recruited participants

The general characteristics and possible risk factors for stroke in the study population are presented in Table 1. With respect to baPWV stages, 309 cases were soft, 13,944 were normal, 9201 were medium hard, and 8010 were hard; 30,669 cases were normal with respect to ABI stages, 85 were hard, 238 were mild clogging, and 472 were clogging.

3.2. Comparison of possible risk factors in people at different stages of stroke susceptibility

In the present study, the mean age of people with low risk was 43.18 ± 10.07 years, people with moderate risk was 48.69 ± 9.61 years, and people with high risk was 50.35 ± 8.79 years. The results showed that there was a significant difference in age among the 3 groups (P < .001) (Table 2). To further elucidate the correlation between age and risk of stroke, we divided the participants into 7 groups by age (group 1: 18–20 years, group 2: 21–30 years, group 3: 31–40 years, group 4: 41–50 years, group 5: 51–60 years, group 6: 61–70 years, group 7: 71–80 years). The number (percentage) of people at different stages of stroke susceptibility in different age groups is listed in Table 3 and Figure 1. We found that the percentage of people with moderate or high risk was increased with increasing age. These data suggest that age is related to the risk of stroke and that older age may positively correlate with moderate or high risk. With respect to sex, the percentage of males at low risk was higher than that of females, whereas the percentage of females at moderate or high risk was higher than that of males, suggesting that female sex may positively correlate with moderate or high risk of stroke (Table 2). Similarly, we found that the percentage of people who consumed alcohol at moderate or high risk was higher than that of people who did not consume alcohol (Table 2). The percentage of people who smoked at moderate or high risk was higher than that of people who did not smoke, suggesting that smoking may positively correlate with the risk of stroke. In addition, we
discussed other parameters that may correlate with the risk of stroke, including body mass index (BMI), systolic pressure, diastolic pressure, UA, TC, TGs, LDL-C, HDL-C, and glucose. The results showed that people at high risk had higher BMI, systolic pressure, diastolic pressure, UA, TC, TGs, LDL-C, and glucose compared with people at low risk overall (Table 2). People with high risk had lower HDL-C than people with low risk.

baPWV and ABI have been used as valuable indices of arterial stiffness and as surrogate markers for atherosclerosis. In this study, we discussed the relationship between baPWV and ABI and the risk of stroke. We found that people with a low or moderate risk of stroke showed a higher percentage of soft, normal baPWV compared with that of people with a high risk of stroke (Table 4, Fig. 2). Interestingly, people with a low risk of stroke showed a decreasing percentage of baPWV from soft to hard, whereas people with a moderate risk of stroke showed an increasing percentage of baPWV from soft to hard. With respect to ABI, people with a low risk of stroke showed an increasing percentage of ABI from normal to clogging, whereas people with a moderate risk of stroke showed a decreasing percentage of ABI from normal to clogging overall (Table 5, Fig. 3). These data indicated that people with a higher risk of stroke had a poorer vascular state, including the indices baPWV and ABI.

3.3. Independent risk factors for stroke susceptibility by logistic analysis

To clearly elucidate the association between possible risk factors and stroke risk, multivariable stepwise logistic regression analysis was used to identify the factors related to risk of stroke. Methods to define dummy variables (stages of risk of stroke) and how to assign variables are listed in supplementary Table 2, http://links.lww.com/MD/D272. The results showed that age, smoking,

### Table 3
Comparison of different age groups at different stages of stroke susceptibility.

| Age group, y | Low risk (n = 17959) | Moderate risk (n = 11825) | High risk (n = 1680) | Statistics | P  |
|--------------|----------------------|---------------------------|----------------------|------------|----|
| 18–20, n (%) | 52 (0.29)            | 7 (0.06)                  | 0 (0.00)             | $\chi^2 = 1964.4965$ | <.0001 |
| 21–30, n (%) | 2087 (11.51)         | 406 (3.43)                | 24 (1.43)            | —          | —  |
| 31–40, n (%) | 4750 (26.45)         | 1814 (15.34)              | 186 (11.07)          | —          | —  |
| 41–50, n (%) | 6976 (38.84)         | 4546 (38.44)              | 638 (37.98)          | —          | —  |
| 51–60, n (%) | 3135 (17.46)         | 3590 (30.36)              | 606 (36.07)          | —          | —  |
| 61–70, n (%) | 925 (5.15)           | 1377 (11.64)              | 204 (12.14)          | —          | —  |
| 71–80, n (%) | 54 (0.30)            | 85 (0.73)                 | 22 (1.31)            | —          | —  |

baPWV = brachial-ankle pulse wave velocity.

### Table 4
Comparison of different baPWV statuses at different stages of stroke susceptibility.

| baPWV        | Low risk (n = 17959) | Moderate risk (n = 11825) | High risk (n = 1680) | Statistics | P  |
|--------------|----------------------|---------------------------|----------------------|------------|----|
| Soft, n (%)  | 254 (1.41)           | 53 (0.45)                 | 2 (0.12)             | $\chi^2 = 1915.4123$ | <.0001 |
| Normal, n (%)| 9807 (54.61)         | 3934 (33.27)              | 203 (12.08)          | —          | —  |
| Medium hard, n (%) | 5144 (28.64) | 3661 (30.96)              | 396 (23.57)          | —          | —  |
| Hard, n (%)  | 2754 (15.34)         | 4177 (35.32)              | 1079 (64.23)         | —          | —  |

baPWV = brachial-ankle pulse wave velocity.
alcohol consumption, systolic pressure, diastolic pressure, glucose, BMI, UA, TGs, LDL-C, and baPWV were independent risk factors for stroke, whereas HDL-C was an independent protective factor for stroke risk (Table 6).

4. Discussion
Hypertension is recognized as a risk factor for stroke. In a national hypertension survey in China, a 10% increase in the prevalence of hypertension correlated with a 2.80-fold higher incidence of and 2.68-fold higher mortality from stroke.\textsuperscript{11} In a study from the United Kingdom, an increase of 10 mmHg in systolic pressure showed a relative hazard ratio (HR) of 1.22 for stroke.\textsuperscript{12} Similarly, a study focused on Asian populations reported an increase of 10 mmHg in systolic pressure related to an HR of 3.4 for stroke.\textsuperscript{13} In our study, both diastolic pressure and systolic pressure were significantly correlated with the risk of stroke. People with a higher risk of stroke showed higher diastolic pressure and systolic pressure, suggesting that people who show relatively high blood pressure during a health examination should be aware of stroke. Notably, 2 national hypertension surveys in China revealed that the treatment rates for hypertensive patients were 28.2%,\textsuperscript{14} and 20.3%.\textsuperscript{15} More than 28.8% of treated hypertensive patients had uncontrolled blood pressure.\textsuperscript{16} Moreover, the ratio of controlled to treated individuals was 1:4.2.\textsuperscript{15} Therefore, numerous hypertensive patients in China are either uncontrolled or untreated and are likely to suffer a stroke.

A previous study showed that diabetes mellitus, BMI, hyperlipidemia, smoking, and alcohol consumption are risk factors for stroke. Table 5 shows the comparison of different ABI statuses at different stages of stroke susceptibility.

| ABI       | Low risk (n=17959) | Moderate risk (n=11825) | High risk (n=1680) | Statistics | P    |
|-----------|--------------------|-------------------------|--------------------|------------|------|
| Normal    | 17417              | 11556                   | 1642               | $\chi^2=9.8190$ | <.0017|
| Hard      | 15                 | 50                      | 20                 |            |      |
| Mild clogging | 181            | 34                      | 3                  |            |      |
| Clogging  | 292                | 165                     | 15                 |            |      |

ABI=ankle-brachial index.
Table 6

| Parameters                      | P     | OR    | 95% CI |
|--------------------------------|-------|-------|--------|
| Age                            | <.0001| 1.038 | 1.035–1.041 |
| Smoking                        | <.0001| 1.117 | 1.046–1.192 |
| Alcohol consumption            | <.0001| 1.135 | 1.064–1.211 |
| Body mass index                | <.0001| 1.217 | 1.203–1.230 |
| Uric acid                      | <.0001| 1.001 | 1.001–1.002 |
| Diastolic pressure             | <.0001| 1.025 | 1.021–1.029 |
| Systolic pressure              | <.0001| 1.018 | 1.015–1.021 |
| Triglycerides                  | <.0001| 1.315 | 1.279–1.352 |
| High-density lipoprotein cholestrol | <.0001| 0.504 | 0.459–0.553 |
| Low-density lipoprotein cholestrol | <.0001| 2.600 | 2.409–2.704 |
| Glucose                        | <.0001| 1.078 | 1.053–1.104 |
| baPWV (1)                      | .1061 | 1.169 | 0.832–1.643 |
| baPWV (2)                      | .0104 | 1.426 | 1.013–2.008 |
| baPWV (3)                      | .0002 | 1.519 | 1.076–2.144 |

baPWV = brachial-ankle pulse wave velocity, CI = confidence intervals, OR = odds ratio.

markedly increased all over the world in the years ahead as the global population older than 65 years increases by approximately 9 million people every year. In the present study, people with a higher risk of stroke were older, and the percentage of people with a high risk increased as age increased. Women are suggested to have an increased risk of dying of stroke compared with men. This finding may be related to several reasons. The life expectancy in females is higher than in males, and females were more likely to live alone. Older women were more likely to neglect stroke warning signs and delay emergent management.

In addition, risk factors for stroke, such as diabetes and dyslipidemia, were likely to adversely affect women and women suffered more frequently from atrial fibrillation and hypertension. Furthermore, a lack of protective effects from estrogen may be a probable explanation for stroke death in postmenopausal women. In this study, we found that females showed a higher percentage of moderate and high risk of stroke than males, suggesting that the government should pay increased attention to women, especially older women with a high risk of stroke.

Pulse wave velocity is an index of arterial stiffness and has been used for noninvasive evaluation of subclinical atherosclerotic changes. baPWV, a type of pulse wave velocity, is a promising test method for evaluating the stiffness of both aortic and peripheral arteries. It not only reflects early atherosclerotic changes but also serves as a valuable predictor of mortality due to cardiocerebrovascular events. In a study discussing the potential association between baPWV and metabolic syndrome (MetS) in a Chinese community population, 1271 subjects had MetS out of 5181 study participants; MetS was significantly associated with baPWV (OR: 2.74; 95% CI: 2.28–3.30), and this association strengthened with increasing numbers of MetS components. Similarly, Wang et al discussed the association between baPWV and long-term blood pressure variability (BPV), showing that increased baPWV was accompanied by increased BPV and that baPWV was positively correlated with long-term BPV. In our study, we found that the percentage of people with low risk of stroke was decreased from soft to hard with respect to baPWV, whereas the percentages of people with moderate and high risk were increasing, suggesting that the higher the risk of stroke, the higher the percentage of poor baPWV results. ABL, a simple noninvasive marker of atherosclerosis, is a stroke predictor in addition to the established risk factors that are part of the Framingham risk score. Gronewold et al revealed that 4299 subjects without previous stroke, coronary heart disease, or myocardial infarction were followed up for ischemic and hemorrhagic stroke events during 109.0±23.3 months and found that 104 incident strokes occurred. Subjects suffering stroke had significantly lower ABL values at baseline than the remaining subjects, and ABL predicted stroke in the general population, especially in subjects with classical risk factors, where ABL identified subjects at particularly high stroke risk. This result was similar to our findings, where we found a decreasing percentage of people with moderate or high risk of stroke with respect to ABL from normal to clogging, suggesting that increased risk of stroke was negatively related to ABL.

There were some limitations in this study. First, some data that may correlate with stroke risk were not collected, such as educational level. Second, this study evaluated participants at different stages of stroke risk but did not follow-up the participants, especially participants with a high risk of stroke. Therefore, it is necessary to follow-up the participants in the...
future and possibly take some preventive actions. Although this study had some deficiencies, it had a large sample size, and the results were credible. In addition, the results indicate that participants of different ages and sex may have different stages of stroke risk and that the participants can understand their susceptibility to stroke.

In conclusion, the present study showed that several factors were related to the risk of stroke, especially baPWV. Therefore, surveillance of these factors may be used in health examination populations, especially older people with a high risk of stroke.

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