Distribution of C-reactive protein and its association with cardiovascular risk factors in a population-based sample of Chinese

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Abstract. C-reactive protein (CRP) levels vary remarkably with ethnic status. Its distribution and correlates should be investigated across diverse populations, and these were limited in a representative Chinese population. We investigated 3133 participants aged 18–80 years in Shanghai, which were sampled using a randomized, stratified, multi-stage sampling method. The distribution of CRP was highly skewed toward a lower level. The median CRP was 0.55 mg/L (0.61 mg/L in males, 0.51 mg/L in females). Participants living in urban region had higher CRP levels than those in rural region (0.67 vs. 0.46 mg/L). CRP levels showed significant correlation with traditional cardiovascular risk factors, and it was most strongly correlated with body mass index. Multivariate logistic regression analyses indicated that elevated CRP (being in the top 15 percentile of CRP; CRP $\geq$ 2.09 mg/L) was significantly associated with obesity, hypertension, diabetes, low high-density lipoprotein cholesterol, high low-density lipoprotein cholesterol, high triglycerides and cardiovascular disease history. In conclusion, the distribution of CRP in adult Chinese was comparable with that of many other Asian populations but different from that of Western populations. Metabolic impairment was associated with elevated CRP, and CRP levels should be interpreted in conjunction with the lipid profile.

Keywords: C-reactive protein, cardiovascular, risk factors, Chinese

1. Introduction

It was reported that only 50% of coronary heart disease was accounted for by traditional risk factors such as smoking, hypertension, diabetes and high blood cholesterol level [1]. In fact, up to half of those having their first coronary event didn’t have traditional cardiovascular risk factors [2]. These in turn led to many investigations to find other potentially important risk factors which influence cardiovascular disease (CVD) risk. Inflammation is thought to play a very important role in atherogenesis [3]. C-reactive protein (CRP), an acute-phase reactant and sensitive marker of subclinical inflammation, is the most extensively studied biomarker.

Previous studies have shown that high CRP is strongly associated with various risk factors of CVD [4,5], and it was advocated to measure CRP to assess CVD risk [6]. The guidelines on CRP testing from American Heart Association/Centers for Disease Control and Prevention (AHA/CDC) suggested that measurement of CRP to improve assessment of people at intermediate coronary heart disease risk, and the CRP levels were proposed to be $> 3.0$ mg/L as high vascular risk [7]. However, this cutoff was based mainly on data from Western populations. It is well known that CRP levels...
vary remarkably with ethnic status [8,9]. The distribution of CRP in Asian populations seemed different from that of Western populations [10]. Therefore, using uniform CRP cutoff points to define vascular risk is likely not appropriate across diverse populations. So, before its use in risk screening in different populations, the distribution and correlates of CRP in the general population should be investigated. However, such information was limited in Chinese. In this study, we aimed to evaluate the distribution of CRP and its association with cardiovascular risk factors in a representative Chinese population, including young, middle-aged and older adults.

2. Methods

2.1. Sample

A representative sample of the Shanghai population of both genders aged 18-80 years was selected, using a randomized, stratified, multiple-stage sampling method. Eligibility criteria were based on age, and mental and physical ability to participate in the survey. In the first stage, we randomly sampled one rural region (Baoshan District) and one urban region (Hongkou District) from 18 districts in Shanghai. In the second stage, we randomly sampled two villages from Baoshan District and two street offices from Hongkou District. In the third stage, several residential areas were sampled. Then, 3600 people (1800 from Baoshan and Hongkou Districts, respectively) were randomly sampled, stratified by gender and age in proportion to the number of inhabitants recorded by the 2000 Shanghai Population Census.

The study was approved by the committee for medical ethics of the Second Military Medical University (SMMU), and an informed written consent was obtained from every participant. From April 2007 to February 2008, a total of 3153 participants (1402 males and 1751 females) completed the survey, and the overall response rate was 87.6%. Participants (N=20) with missing records of the CRP values were deleted from the analyses, and 3133 participants were included in the analyses.

2.2. Data collection

Every participant was asked to complete a comprehensive health and lifestyle questionnaire and to provide a collection of fasting blood samples. General information was collected on age, gender, residential region, marital status, education level, current job, family monthly income, height, weight, smoking status, alcohol consumption, frequency of recreational exercise and medical history (current and previous medical problems and related treatment). Body mass index (BMI) was calculated as weight (kg)/height (m)^2. In order to analyze the reliability of the self-reported values of BMI, 20% of the sample was randomly selected for height and weight measurement. Height was measured using a stadiometer, and weight was measured with participants in light underclothes.

Questionnaires were self-administered, and explanation and supervision were provided by trained interviewers where necessary. The interviewers were social workers at the survey sites, who were trained by supervisors who were professionals from the Department of Health Statistics (DoHS) of the SMMU. Supervisors supervised the work of the interviewers and examined questionnaires for any errors to ensure the quality of the survey. A valid questionnaire was the one that had been audited and signed by a supervisor.

An informed written consent for blood sampling was also obtained from every participant before blood sampling. Participants were required to fast for at least 10 hours. Venous blood samples were collected from each participant, and the samples were refrigerated immediately in an ice box and the box was shipped to Changhai hospital which belongs to the SMMU after blood collections. All samples were tested immediately after they were transferred to the hospital clinical laboratory without storing. Total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides and glucose were measured enzymatically using an automatic chemical analyzer (Hitachi 7600-20, Japan), and plasma CRP were measured with immunonephelometry on a special protein analyzer (Beckman, US). The lower limit of detection was 0.151 mg/L. Undetectable CRP values were recorded as < 0.151 mg/L. The intra-assay and inter-assay coefficients of variation were 3.6% and 4.3%, respectively.

2.3. Definition of cardiovascular risk factors

We used cutoff values from the third National Health and Nutrition Examination Survey (NHANES III) for defining normal, borderline, or abnormal cardiovascular risk factors [5]. They included diabetes mellitus (normal, < 5.55 mmol/L [< 100 mg/dL]; pre-diabetes mellitus, fasting glucose 5.56 to 6.94 mmol/L [100 to
125 mg/dL); and diabetes mellitus, $\geq 6.99$ mmol/L ($\geq 126$ mg/dL) or previously diagnosed diabetes; blood pressure (normal, having no hypertension history; hypertension, having hypertension diagnosed by physicians); total cholesterol levels (normal, $< 5.18$ mmol/L [$< 200$ mg/dL]; borderline high, 5.18 to 6.19 mmol/L [200 to 239 mg/dL]; and high, $\geq 6.22$ mmol/L [$\geq 240$ mg/dL]); triglyceride levels (normal, $< 1.70$ mmol/L [$< 150$ mg/dL]; borderline high, 1.70 to 2.25 mmol/L [150 to 199 mg/dL]; and high, $\geq 2.26$ mmol/L [$\geq 200$ mg/dL]); and HDL-C values (normal, $\geq 1.04$ mmol/L [$\geq 40$ mg/dL] in males and $\geq 1.30$ mmol/L [$\geq 50$ mg/dL] in females; low, $< 1.04$ mmol/L [$< 40$ mg/dL] in males and $< 1.30$ mmol/L [$< 50$ mg/dL] in females); LDL-C (normal, $< 3.37$ mmol/L [130 mg/dL]; borderline high, 3.37 to 4.12 mmol/L [130 to 159 mg/dL]; and high, $\geq 4.14$ mmol/L [$\geq 160$ mg/dL]) [11]. BMI was defined according to the Chinese criterion (normal, $< 24$ kg/m$^2$; overweight, 24 to 28 kg/m$^2$; and obese, $\geq 28$ kg/m$^2$) [12].

Smoking status was classified as never, former and current. Alcohol consumption was grouped into never, $< 4$ times/month, at least one time/week and daily. Physical activity was graded according to frequency into 4 categories as sedentary (never), light activity (less than 4 times per month), moderate activity (at least 1 time per week) and vigorous activity (at least 1 time per day). Marital status was categorized into 4 groups (married, unmarried, divorced or separated, widowed). Family monthly income was defined as “manual worker” and “office worker”. A current job was defined as “manual worker” and “office worker”. A history of CVD was defined as diagnosis with coronary heart disease, myocardial infarction, angina pectoris, cerebrovascular disorder, and so on by physicians.

### 2.4. Statistical analysis

Data were double entered by two independent professional data processors in the DoHS using software Epidata 3.1. Both manual checking and computer checking were conducted to find discrepancies. Student $t$ test for continuous variables and Chi-square test or Cochran-Mantel-Haenszel statistics for categorical variables were applied for the comparison between males and females. The reliability of BMI was assessed by the differences between self-reported and measured values using a paired-sample $t$ test. The median level of CRP was tested with Wilcoxon rank sum test when comparing between strata. Categorical forms of the values were performed in age- and multivariate-adjusted logistic regression analyses. CRP as the dependent variable was dichotomized at the top 15th percentile (2.09 mg/L), and CRP values more than the top 15th percentile values were defined as elevated CRP. The odds ratios (ORs) and 95% confidence interval (CI) for elevated CRP were calculated. Data management and statistical analysis were performed with the SAS statistical package version 9.1.3 (SAS Institute, Cary, North Carolina). Statistical tests were 2-sided, and a $p$ value $< 0.05$ was considered statistically significant.

### 3. Results

Characteristics of the 3133 participants (1393 males and 1740 females) are shown in Table 1. The mean age was 47.8 years (47.8 for males and 47.8 for females). Compared with the females, the males had higher BMI and triglycerides, lower HDL-C and higher prevalence of hypertension and diabetes (all $p < 0.05$). More males smoked and drank. About 5.0% of the participants (158/3133) reported having history of CVD, and 136 participants with history of CVD reported that they had received treatments. A total of 244 participants reported that they had diabetes or were diagnosed as diabetes. Among them, 128 participants received treatments. A total of 650 had hypertension, and 597 of them received treatments. In total, 696 were treated as someone may receive one or more treatments. The absolute differences between the self-reported and measured values of BMI ranged from 0.0 to 4.5 kg/m$^2$. The paired-sample $t$ test indicated that the difference was not statistically significant ($p = 0.6364$).

Table 2 presents the distribution of CRP by gender, age, region, BMI, blood pressure, glucose, total cholesterol, HDL-C, LDL-C, triglycerides, smoking and alcohol consumption categories. Median CRP was 0.55 mg/L for all the participants (0.61 mg/L in males and 0.51 mg/L in females). The distribution of CRP for both males and females were highly skewed toward a lower level. Among the participants, 165 (5.3%) had a CRP level $< 0.15$ mg/L, and more than 65% of the participants ($N = 2108$) had a CRP level $< 1$ mg/L. The percentages of those with CRP levels $> 3$ mg/L based on AHA/CDC defined risk categories were 10.2% ($N = 318$) in the whole population (11.1% in males, 9.4% in females). Only 1.3% of the participants ($N = 42$) had CRP $> 10$ mg/L. CRP levels increased with age, though the CRP levels were a little lower in age of 30–39 years than those of younger
Table 1

Characteristics of the participants by gender

| Characteristic                  | Total (N = 3133) | Male (N = 1393) | Female (N = 1740) | P value† |
|--------------------------------|------------------|-----------------|-------------------|---------|
| Mean age (years)               | 47.8 ± 14.1      | 47.8 ± 14.1     | 47.8 ± 14.1       | 0.9615  |
| BMI (kg/m²)                    | 23.2 ± 3.3       | 23.7 ± 3.3      | 22.8 ± 3.3        | < 0.0001|
| Total cholesterol (mmol/L)     | 4.9 ± 1.2        | 4.9 ± 1.5       | 5.0 ± 1.0         | 0.0886  |
| LDL-C (mmol/L)                 | 3.2 ± 0.9        | 3.2 ± 0.8       | 3.2 ± 0.9         | 0.5337  |
| HDL-C (mmol/L)                 | 1.4 ± 0.3        | 1.3 ± 0.3       | 1.5 ± 0.3         | < 0.0001|
| Triglycerides (mmol/L)         | 1.5 ± 1.2        | 1.7 ± 1.4       | 1.3 ± 1.0         | < 0.0001|
| Serum glucose (mmol/L)         | 5.3 ± 1.4        | 5.3 ± 1.5       | 5.3 ± 1.3         | 0.6937  |
| Hypertension (%)               | 650 (20.8)       | 313 (22.5)      | 337 (19.4)        | 0.0334  |
| Marital status (%)             |                 |                 | < 0.0001          |         |
| Married                        | 2678 (85.5)      | 1187 (85.3)     | 1492 (85.8)       |         |
| Unmarried                      | 288 (9.2)        | 166 (11.9)      | 122 (7.0)         |         |
| Divorced or separated          | 46 (1.5)         | 18 (1.3)        | 28 (1.6)          |         |
| Widowed                        | 119 (3.8)        | 21 (1.5)        | 98 (5.6)          |         |
| Family monthly income (%)      |                 |                 | 0.3234            |         |
| Less than 1999 Yuan            | 1247 (39.8)      | 541 (38.8)      | 706 (40.6)        |         |
| More than 1999 Yuan            | 1886 (60.2)      | 852 (61.2)      | 1034 (59.4)       |         |
| Current job                    | 0.0002           |                 |                   |         |
| Manual worker                  | 2311 (73.8)      | 982 (70.5)      | 1329 (76.4)       |         |
| Office worker                  | 822 (26.2)       | 411 (29.5)      | 411 (23.6)        |         |
| Glucose category (%)           |                 |                 | 0.0024            |         |
| Normal                         | 2304 (73.5)      | 1025 (73.6)     | 1279 (73.5)       |         |
| Prediabetes                    | 585 (18.7)       | 237 (17.0)      | 348 (20.0)        |         |
| Diabetes                       | 244 (7.8)        | 131 (9.4)       | 113 (6.5)         |         |
| Smoking status (%)             |                 |                 | < 0.0001          |         |
| Never                          | 2132 (68.1)      | 434 (31.2)      | 1698 (97.6)       |         |
| Former                         | 81 (2.6)         | 79 (5.7)        | 2 (0.1)           |         |
| Current                        | 920 (29.4)       | 880 (63.2)      | 40 (2.3)          |         |
| Alcohol consumption (%)        |                 |                 | < 0.0001          |         |
| Never                          | 2560 (80.0)      | 800 (57.4)      | 1760 (98.1)       |         |
| < 4 times/month                | 127 (4.1)        | 122 (8.8)       | 5 (8.8)           |         |
| One time/week                  | 170 (5.4)        | 156 (11.2)      | 14 (0.8)          |         |
| Daily                          | 330 (10.5)       | 315 (22.6)      | 15 (0.9)          |         |
| Physical activity (%)          |                 |                 | 0.7381            |         |
| Sedentary                      | 577 (18.4)       | 261 (18.8)      | 316 (18.2)        |         |
| Light activity                 | 144 (4.6)        | 68 (4.9)        | 76 (4.4)          |         |
| Moderate activity              | 327 (10.4)       | 138 (9.9)       | 189 (10.9)        |         |
| Vigorous activity              | 2083 (66.5)      | 925 (66.5)      | 1158 (66.6)       |         |
| CVD history (%)                |                 |                 | 0.3448            |         |
| No                             | 2975 (95.0)      | 1317 (94.5)     | 1658 (95.3)       |         |
| Yes                            | 158 (5.0)        | 76 (5.5)        | 82 (4.7)          |         |

BMI = body mass index; CVD = Cardiovascular disease; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol.

*Values are arithmetic means ± SD unless indicated otherwise. †P value was calculated by comparing men with women.

The median CRP of participants in urban and rural areas was 0.67 mg/L and 0.46 mg/L, respectively. Those who had higher BMI, hypertension, higher glucose, higher total cholesterol, higher LDL-C, higher triglycerides and lower HDL-C had significantly higher CRP levels (all p < 0.05). There was significant difference of CRP levels among the categories of smoking (p = 0.0066). However, the difference was not significant (p = 0.1392) when females were excluded from the analysis. We didn’t find a difference in CRP levels among the different alcohol consumption categories (p = 0.2397), even only in males (p = 0.1048).

When the 696 participants with treatments for CVD or hypertension or diabetes were excluded, the median CRP was 0.49 mg/L which was not increased. Furthermore, when the participants with history of CVD, hypertension, diabetes or with CRP > 10 mg/L were all excluded from the analyses (n = 2288), the CRP levels became lower with median CRP was 0.47 mg/L. The median levels of CRP decreased slightly in females (0.43 mg/L) and males (0.52 mg/L). Medians of CRP for age groups 18 to 29, 30 to 39, 40 to 49, 50 to 59, 60 to 69, 70 to 80 years were 0.41, 0.37, 0.45, 0.55, 0.65 and 0.88 mg/L.
Table 2
Distribution of C-reactive protein levels (mg/L) among the participants aged 18–80 years in Shanghai, China (N = 3133)

| Variable     | Percentile | 5th | 10th | 25th | 33.3th | 50th | 66.7th | 75th | 90th | 95th |
|--------------|------------|-----|------|------|--------|------|--------|------|------|------|
| Total        | N=3133     | 3133| 0.15 | 0.16 | 0.26   | 0.34 | 0.55   | 0.95 | 1.34 | 3.04 |
| Gender       | Female     | 1740| 0.15 | 0.16 | 0.22   | 0.31 | 0.51   | 0.84 | 1.22 | 2.81 |
|              | Male       | 1393| 0.16 | 0.16 | 0.30   | 0.38 | 0.61   | 1.09 | 1.50 | 3.21 |
| Age          | 18–29      | 347 | 0.15 | 0.16 | 0.17   | 0.23 | 0.42   | 0.72 | 1.03 | 2.77 |
|              | 30–39      | 493 | 0.15 | 0.16 | 0.18   | 0.24 | 0.40   | 0.68 | 1.02 | 2.23 |
|              | 40–49      | 1061| 0.15 | 0.16 | 0.25   | 0.32 | 0.49   | 0.82 | 1.13 | 2.39 |
|              | 50–59      | 593 | 0.16 | 0.17 | 0.31   | 0.42 | 0.64   | 1.14 | 1.50 | 3.07 |
|              | 60–69      | 378 | 0.16 | 0.19 | 0.35   | 0.50 | 0.82   | 1.32 | 1.88 | 4.20 |
|              | 70–80      | 261 | 0.16 | 0.22 | 0.45   | 0.57 | 0.98   | 1.55 | 1.98 | 4.31 |
| Region       | Urban      | 1568| 0.16 | 0.16 | 0.32   | 0.42 | 0.67   | 1.14 | 1.53 | 3.56 |
|              | Rural      | 1565| 0.15 | 0.16 | 0.21   | 0.28 | 0.46   | 0.74 | 1.11 | 2.40 |
| BMI          | Normal     | 1906| 0.15 | 0.16 | 0.19   | 0.26 | 0.43   | 0.67 | 0.93 | 2.22 |
|              | Overweight | 970 | 0.16 | 0.21 | 0.36   | 0.47 | 0.75   | 1.30 | 1.64 | 3.42 |
|              | Obese      | 253 | 0.25 | 0.34 | 0.65   | 0.91 | 1.49   | 2.10 | 2.73 | 4.62 |
| Blood pressure | Normal   | 2483| 0.15 | 0.16 | 0.23   | 0.31 | 0.49   | 0.81 | 1.14 | 2.45 |
|              | Hypertension | 650 | 0.16 | 0.21 | 0.42   | 0.55 | 0.92   | 1.56 | 2.12 | 3.95 |
| Glucose      | Normal     | 2304| 0.15 | 0.16 | 0.24   | 0.31 | 0.50   | 0.84 | 1.19 | 2.58 |
|              | Pre-diabetes | 585 | 0.15 | 0.16 | 0.30   | 0.42  | 0.69   | 1.16 | 1.57 | 3.31 |
|              | Diabetes   | 244 | 0.16 | 0.18 | 0.41   | 0.59  | 0.99   | 1.70 | 2.65 | 5.08 |
| Total cholesterol | Normal | 1998| 0.15 | 0.16 | 0.21   | 0.29 | 0.47   | 0.79 | 1.11 | 2.75 |
|              | Borderline | 860 | 0.16 | 0.17 | 0.31   | 0.40 | 0.68   | 1.17 | 1.57 | 3.30 |
|              | High       | 275 | 0.16 | 0.26 | 0.50   | 0.61 | 0.91   | 1.52 | 1.82 | 3.50 |
| HDL-C        | Normal     | 2268| 0.15 | 0.16 | 0.24   | 0.32 | 0.52   | 0.89 | 1.23 | 2.87 |
|              | Low        | 865 | 0.16 | 0.16 | 0.31   | 0.39 | 0.65   | 1.19 | 1.56 | 3.57 |
| LDL-C        | Normal     | 1907| 0.15 | 0.16 | 0.21   | 0.28 | 0.47   | 0.77 | 1.09 | 2.69 |
|              | Borderline | 853 | 0.16 | 0.17 | 0.31   | 0.40 | 0.66   | 1.15 | 1.54 | 3.16 |
|              | High       | 373 | 0.16 | 0.24 | 0.48   | 0.60 | 0.87   | 1.49 | 1.92 | 3.71 |
| Triglycerides | Normal    | 2319| 0.15 | 0.16 | 0.21   | 0.28 | 0.46   | 0.74 | 1.07 | 2.51 |
|              | Borderline | 381 | 0.18 | 0.23 | 0.43   | 0.55 | 0.88   | 1.36 | 1.64 | 3.75 |
|              | High       | 433 | 0.17 | 0.28 | 0.52   | 0.68 | 1.10   | 1.74 | 2.22 | 3.58 |
| Smoking      | Never      | 2132| 0.15 | 0.16 | 0.24   | 0.32 | 0.54   | 0.90 | 1.31 | 2.96 |
|              | Former     | 81  | 0.16 | 0.18 | 0.37   | 0.45 | 0.69   | 1.07 | 1.36 | 2.73 |
|              | Current    | 920 | 0.16 | 0.16 | 0.29   | 0.36 | 0.57   | 1.04 | 1.49 | 3.11 |
| Alcohol consumption | Never | 2505| 0.15 | 0.16 | 0.25   | 0.34 | 0.55   | 0.94 | 1.33 | 3.01 |
|              | < 4 times/month | 127 | 0.15 | 0.15 | 0.24   | 0.34 | 0.56   | 0.93 | 1.22 | 3.10 |
|              | One time/week | 170 | 0.16 | 0.16 | 0.24   | 0.33 | 0.51   | 0.92 | 1.33 | 3.33 |
|              | Daily      | 330 | 0.16 | 0.17 | 0.29   | 0.38 | 0.63   | 1.05 | 1.57 | 3.20 |

BMI = body mass index; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol.

Prevalence of elevated CRP (CRP $\geq 2.09$ mg/L) in the participants based on potential risk factors is shown in Table 3. The prevalence was higher in males than in females (16.8% vs. 13.7%); however, this association was not significant in the multivariate analysis (OR: 1.2 [95%CI: 0.9–1.7]). Participants who lived in rural region had a lower prevalence of elevated CRP than those in urban region (12.2% vs. 18.0%), and the difference was confirmed in multivariate-adjusted logistic regression analysis (OR: 0.7 [95%CI: 0.5–0.9]).
Table 3
Age- and multivariate-adjusted odds ratios (ORs) for elevated CRP∗

| Variable            | Prevalence of elevated CRP N (%) | Age- adjusted OR (95% CI) | Multivariate- adjusted† OR (95% CI) |
|---------------------|----------------------------------|--------------------------|-------------------------------------|
| Gender              |                                  |                          |                                     |
| Female (N = 1740)   | 13.7                             | 1.0                      | 1.0                                 |
| Male (N = 1393)     | 16.8                             | 1.3 (1.1–1.6)            | 1.2 (0.9–1.7)                       |
| Region              |                                  |                          |                                     |
| Urban (N = 1568)    | 18.0                             | 1.0                      | 1.0                                 |
| Rural (N = 1565)    | 12.2                             | 0.7 (0.5–0.8)            | 0.7 (0.5–0.9)                       |
| BMI                 |                                  |                          |                                     |
| Normal (N = 1906)   | 10.8                             | 1.0                      | 1.0                                 |
| Overweight (N = 970)| 18.7                             | 1.8 (1.5–2.3)            | 1.1 (1.2–1.9)                       |
| Obese (N = 253)     | 34.0                             | 4.3 (3.2–5.8)            | 3.2 (2.3–4.5)                       |
| Hypertension        |                                  |                          |                                     |
| No (N = 2483)       | 12.5                             | 1.0                      | 1.0                                 |
| Yes (N = 650)       | 25.1                             | 2.0 (1.6–2.5)            | 1.4 (1.1–1.8)                       |
| Glucose             |                                  |                          |                                     |
| Normal (N = 2304)   | 12.9                             | 1.0                      | 1.0                                 |
| Pre-diabetes (N = 585)| 18.1                          | 1.4 (1.3–1.8)            | 1.3 (1.0–1.6)                       |
| Diabetes (N = 244)  | 28.7                             | 2.2 (1.6–3.1)            | 1.7 (1.2–2.4)                       |
| Total cholesterol   |                                  |                          |                                     |
| Normal (N = 1998)   | 13.0                             | 1.0                      | 1.0                                 |
| Borderline (N = 860)| 18.3                             | 1.3 (1.8–1.7)            | 0.9 (0.6–1.2)                       |
| High (N = 275)      | 20.7                             | 1.4 (1.0–2.0)            | 0.6 (0.4–1.1)                       |
| HDL-C               |                                  |                          |                                     |
| Normal (N = 2268)   | 13.6                             | 1.0                      | 1.0                                 |
| Low (N = 865)       | 19.2                             | 1.5 (1.2–1.8)            | 1.4 (1.1–1.8)                       |
| LDL-C               |                                  |                          |                                     |
| Normal (N = 1907)   | 12.7                             | 1.0                      | 1.0                                 |
| Borderline (N = 853)| 16.8                             | 1.3 (1.0–1.6)            | 1.2 (0.9–1.7)                       |
| High (N = 373)      | 23.6                             | 1.8 (1.4–2.4)            | 2.0 (1.3–3.6)                       |
| Triglycerides       |                                  |                          |                                     |
| Normal (N = 2319)   | 12.3                             | 1.0                      | 1.0                                 |
| Borderline (N = 381)| 19.2                             | 1.6 (1.2–2.2)            | 1.1 (0.8–1.5)                       |
| High (N = 433)      | 26.8                             | 2.5 (1.9–3.2)            | 1.7 (1.3–2.2)                       |
| Smoking             |                                  |                          |                                     |
| Never (N = 2132)    | 14.6                             | 1.0                      | 1.0                                 |
| Former (N = 81)     | 16.1                             | 0.9 (0.5–1.7)            | 0.6 (0.3–1.2)                       |
| Current (N = 920)   | 16.2                             | 1.2 (0.9–1.5)            | 1.1 (0.8–1.5)                       |
| Alcohol consumption |                                  |                          |                                     |
| Never (N = 2505)    | 15.0                             | 1.0                      | 1.0                                 |
| < 4 times/month (N = 127)| 13.4                      | 0.9 (0.6–1.6)            | 0.7 (0.4–1.3)                       |
| One time/week (N = 170)| 15.9                        | 1.1 (0.7–1.7)            | 0.9 (0.6–1.5)                       |
| Daily (N = 330)     | 16.1                             | 1.0 (0.7–1.4)            | 0.9 (0.6–1.3)                       |
| CVD history         |                                  |                          |                                     |
| No (n = 2975)       | 14.4                             | 1.0                      | 1.0                                 |
| Yes (n = 158)       | 29.1                             | 1.8 (1.3–2.7)            | 1.5 (1.0–2.3)                       |

BMI = body mass index; CRP = C-reactive protein; CVD = Cardiovascular disease; CI = confidence interval; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol.
∗Elevated CRP was defined as being in the top 15 percentile of CRP (CRP ≥ 2.09 mg/L).
†Adjusted for presented variables plus age (continuous), region, education, marital status, alcohol consumption, family monthly income and physical activity multivariate-adjusted logistic regression analyses.

The prevalence of elevated CRP increased with increasing BMI, and BMI was also positively associated with CRP in the multivariate analysis (Table 3). Participants with hypertension had a higher prevalence of elevated CRP than those without (multivariate OR: 1.4 [95%CI: 1.1–1.8]). Participants with diabetes were more likely to have elevated CRP than those with normal glucose (multivariate OR: 1.7 [95%CI: 1.2–2.4]). People with higher total cholesterol showed an increased likelihood of reporting elevated CRP, but after multivariate ad-
4. Discussion

Recently, a prospective study comprising about 28,000 females reported that CRP is a better predictor of the risk of cardiovascular events than LDL-C [13]. The implication of this and many other supporting studies is profound, and CRP may be used to screen patients with atherosclerosis and its associated clinical syndromes. It has been advocated to measure CRP for CVD risk assessment [6]. However, the current “reference intervals” of CRP have been derived almost exclusively from European or European American reference populations, and its applicability to other populations is unclear, so before advocating the widespread use of CRP as a screening test for individuals who are at risk for CVD, the AHA/CDC in their scientific statement called for information on population-based CRP generated from blacks, Hispanics, Native Americans, and people of Asian and South Asian heritage [14]. There were few studies on distribution of CRP in a representative Chinese population. Table 4 presents the medians of the CRP levels among Chinese reported in different studies [15–21]. However, among these studies, only X. Ye et al and we reported CRP levels in a random sample. And X. Ye et al investigated the distribution of CRP levels only in middle-aged and older Chinese people, and they didn’t provide the data of young adults and the detailed distribution of CRP [17]. The differences were not substantial among these reports and most of the studies reported that the median of CRP levels was lower than 1 mg/L except for Y. Bao’s report [19]. Here, we investigated the distribution of CRP in a representative Chinese population including young, middle-aged and older people, and provided data for a wide range of CRP values and the precise relationship between elevated CRP and the traditional cardiovascular risk factors.

The distribution of CRP in adult Chinese was comparable with that of many other Asian populations but different from that of Western populations. The median of CRP reported here was near to that reported in previous studies in other Asian countries. Median CRP values were 0.60 mg/L for males and 0.40 mg/L for females in Koreans aged 16–64 years [22], and 0.6 mg/L for males and 0.45 mg/L for females in Japanese aged more than 40 years [23]. These levels of CRP are quite low and are approximately one third to half of the median values in Caucasians [24,25]. In multiethnic population studies, the CRP levels of Chinese were significantly lower than those of Caucasian populations [10,26]. The reason why most Asians have significantly lower CRP levels than Western populations is unclear. Relatively low BMI, genetic diversity and other factors such as diet and lifestyle may influence the CRP levels [27,28].

Our study reported that CRP levels were higher in males than in females, just as many but not all studies in Asian reported [22,23]. One plausible explanation for higher CRP levels in males may be that traditional risk factors of CVD levels were higher in males than in females just as mentioned above. However, the impacts of genders attenuated remarkably after adjusting for other potential factors. It was also reported that no significant difference in the CRP levels between males and females in Chinese [17]. In Western countries, however, conflicting reports existed which reported that

| First author | Gender | Age (years) | N   | CRP (mg/L) |
|--------------|--------|------------|-----|------------|
| Our study    | Male   | 47.8       | 1740| 0.61       |
| B. Yuan      | Female | 47.8       | 1393| 0.51       |
| Q. Dong      | Male   | 21.0–66.0  | 365 | 0.70       |
| X. Ye        | Male   | 58.8       | 1458| 0.67       |
| J. Sun       | Male   | 45.0–74.0  | 702 | 1.00       |
| Y. Bao       | Male   | 53.2       | 2379| 1.28       |
| H. Sun       | Male   | < 50.0     | 70  | 0.72       |
| S. He        | Both   | > 50.0     | 170 | 1.09       |
|              | Both   | 20.0–70.0  | 506 | 0.45       |

Table 4 Differences in medians of CRP levels among different studies of Chinese

CRP = C-reactive protein.
higher CRP levels were in females than in males [24, 29]. Many factors, such as BMI, lifestyle factors, blood pressure, hormone replacement therapy use, and so on, may influence the relationship between gender [4,24]. More studies are needed to investigate the gender difference of CRP levels.

In line with the results from other populations, there was a linear increase in CRP levels as age increased [24, 30]. These results were consistent with those reported for apparently healthy adult populations in Western countries and Asian countries. The median CRP of the participants aged 70–80 years was 2.3-fold higher compared with those in the group of 18–30 years. We also found that CRP levels were higher in individuals living in urban than in rural regions just as that reported in Asians [17,23]. The reason for the difference in CRP levels based on location is not entirely clear in our investigation. It may be attributed to the higher prevalence of the metabolic syndrome and overweight in urban than in rural residents in Chinese [31].

Only 1 in 8 participants showed CRP > 3.0 mg/L in this study population. The proportion of CRP > 3.0 mg/L was very low, just as a report in Japanese [23]. However, in Western countries, about 1 in 4 males and 3.0 mg/L was very low, just as a report in Japanese [23]. The median CRP of the participants aged 70–80 years was 2.3-fold higher compared with those in the group of 18–30 years. We also found that CRP levels were higher in individuals living in urban than in rural regions just as that reported in Asians [17,23]. The reason for the difference in CRP levels based on location is not entirely clear in our investigation. It may be attributed to the higher prevalence of the metabolic syndrome and overweight in urban than in rural residents in Chinese [31].

CRP was positively associated with age, BMI, total cholesterol, LDL-C, triglycerides, and glucose, and negatively with HDL-C, which in line with other studies [23,32]. Elevated CRP was also positively associated with obesity, hypertension, diabetes, high triglycerides, and low HDL-C. These factors are features of metabolic syndrome. Increasing evidence indicated that metabolic syndrome was an important risk factor for CVD incidence [33,34], while CRP levels were associated with the individual metabolic syndrome features and metabolic syndrome itself [35,36]. Our results reconfirmed the fact that CRP was a good marker representing an elevated risk of metabolic impairment.

Whether high LDL-C was related to elevated CRP is controversial. It was reported that CRP related to LDL-C neither in males nor in females [23]. Arena R et al reported that CRP correlated with LDL-C only in females [37], while Lao XQ et al reported that the association between LDL-C and CRP was of borderline significant in males and not significant in females [30]. However, in the current study, we found borderline and abnormal LDL-C increased the prevalence of elevated CRP, which was consistent with other studies [4,35].

We didn’t find alcohol consumption was associated with elevated CRP, just as many studies reported [36, 37]. It was reported that smoking was related to higher CRP [29,40], and there were also studies that reported the association was only in males [23,24]. In our study, more males smoked; however, we didn’t find the relationship in the current study. The reason for the discrepancy between our study and others is not entirely clear, and it may be due to the differences in population characteristics.

Admittedly, with the cross-sectional nature, it is impossible to establish a cause-effect relationship between CRP levels and CVD risk factors. Hence, the ORs should be viewed as measures of association under the appropriate inference. Another potential concern is that CRP, HDL-C, LDL-C, triglyceride and blood glucose levels were measured only once, which might have led to random errors and may not reflect fluctuation over time. CVD history and hypertension were self-reported and what medicine the participants had taken, was not investigated, which are also potential limitations. Besides, we didn’t assess female hormone use in the present study. Though it was reported that females with hormone replacement therapy had higher CRP levels than those without [18], we found the levels of CRP were higher in males than in females in this study, so we believe the effect of hormone replacement therapy could be ignored in Chinese adults just as a report in Japanese population [23].

In conclusion, the study is a large-scale, population-based study to investigate the distribution of CRP and associated traditional cardiovascular risk factors in a Chinese population which represents a wide range of young, middle-aged and older people. So the findings can be generalized to the general population of Chinese adults and the data can be used by Asian public officials for the development of risk CRP definition. The overall CRP levels in both genders were low, and the distribution of CRP was comparable with that of
many other Asian populations but different from that of Western populations. There was a positive association between elevated CRP levels and feathers of metabolic syndrome including obesity, hypertension, diabetes, low HDL-C and high triglycerides, as well as high LDL-C. These findings suggest that metabolic impairment is associated with a systemic inflammatory response, and CRP levels should be interpreted in conjunction with the lipid profile. Prospective studies on the association of CVD risk factors with CRP levels are needed in China so that a Chinese-specific CRP cutoff point for CVD risk assessment can be identified.

Acknowledgments

The study was supported by grants from AstraZeneca R&D, Möln达尔, Sweden, and we declare that we have no any conflicts of interests. We gratefully acknowledge Shanghai CDC, Hongkou CDC and Baoshan CDC for their assistance in designing the study, selecting participants and field work. We also thank the respondents who gave their time and effort to participate in the study.

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