The association between kidney function decline and hearing loss: a cross-sectional study

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Abstract

Background The relationship between kidney function and hearing loss has long been recognized, but evidence mostly come from small observational studies. The aim of this study is to explore the association between kidney function decline and hearing loss in a large population-based study.Methods Data collected in the Chinese Health and Retirement Longitudinal Study (CHARLS) in 2015 was used for analysis. A cross-sectional study was conducted among 12508 participants aged 45 years and older. Hearing loss, the outcome of this study, was defined based on interviewees' responses to three survey questions about hearing in the CHARLS study. Estimated glomerular filtration rate (eGFR) was employed to assess kidney function, and participants were classified into three categories based on eGFR: ≥ 90, 60-89 and < 60 mL/min/1.73m2. Multivariable Logistic regression was employed to adjust for potential confounders, including demographics, health related behaviors, and cardiovascular risk factors.Results The overall prevalence of self-reported hearing loss in the study population was 23.55%. Compared with participants having eGFR ≥ 90 mL/min/1.73m2, there was an increased risk of hearing loss among those participants with eGFR of 60-89 mL/min/1.73m2 (odds ratio: 1.11, 95% confidence interval: 1.00-1.22) and eGFR < 60 mL/min/1.73m2 (odds ratio: 1.26, 95% confidence interval: 1.05-1.51) after adjusting for potential confounders.Conclusions Kidney function decline was independently associated with hearing loss. Testing for hearing should be included in the integrated management among patients with chronic kidney disease.

Background

The World Health Organization (WHO) reported that around 432 million adults suffer from disabling hearing loss in 2018, and it is estimated that over 900 million people will have disabling hearing loss by 2050 [1]. Hearing loss in adults not only bring communication difficulties in daily life, but also have negative impacts on cognitive and psychosocial function, lead to social isolation, cause financial strain and finally lower health-related quality of life indirectly [2–4]. As most hearing loss are acquired and hard to get recovered, but could be prevented, exploring the risk factors of hearing loss has great significance.

The effects of aging on the auditory system are considered as the leading cause of adult-onset hearing loss [5]. Meanwhile, the association between hearing loss and genetic mutations [6, 7], noise exposure [8], use of ototoxic drugs in treatment[9, 10], and chronic diseases such as hypertension and diabetes [11, 12] have also been demonstrated in existent studies.

Kidney disease has become a growing public health issue of global concern in recent years. Since the first report on Alport Syndrome revealing that hereditary familial nephritis is related to sensorineural deafness in 1927 [13], a wide variety of congenital syndromes such as Fabry disease, Branchio-oto-renal syndrome, Alstrom syndrome, and Bartter syndrome, have been recognized to have both hearing and kidney manifestations [14–16]. Furthermore, some observational studies assessed auditory function of patients with end stage kidney disease (ESKD) or receiving kidney replacement therapy [17–21]. For example, Meena et at. [20] studied 50 cases of ESKD and 50 healthy volunteers and found that 28% of

the ESKD patients had sensorineural hearing loss, while the prevalence was only 6% in the control group. Zeigelboim et al. [19] found that the patients with ESKD had significantly higher hearing thresholds for high frequencies than the control groups. Here the hearing threshold refers to the minimum level of sound that evokes an auditory sensation [22]. Renda et al. [21] also found a significant association between the duration of hemodialysis and hearing loss in children aged 6–18 years with dialytic chronic kidney disease (CKD).

However, most of those existent studies had small sample sizes and the enrolled patients were with kidney failure, and few studies focused on the association between hearing loss and mild-to-moderate chronic kidney function decline in large population [23, 24]. Vilayur et al. [23] presented the first community-based study and demonstrated an association between moderate CKD and hearing loss in Australian population. Seo et al. [24] found individuals with CKD were more likely to have hearing impairment, based on the Korean National Health and Nutritional Examination Survey. But the sample size of their study was also relatively small, and only the hearing status of two different eGFR groups: ≥ 60 and < 60 mL/min/1.73 m^2 were compared.

In this study, we conducted a cross-sectional population-based study to explore the relationship between kidney function decline and hearing loss, taking advantage of the representative sample of general population aged 45 years or older and the strict quality control process of the Chinese Health and Retirement Longitudinal Study (CHARLS) [25].

Methods

Study population

The CHARLS study is a nationally representative longitudinal survey of China's middle age and elderly population, providing a high-quality public micro-database with social, economic, and health information. Samples were selected using multistage probability sampling, taking into consideration regional and socioeconomic disparities. CHARLS also has a good cross-study comparability of results as it was harmonized with leading international research studies in the Health and Retirement Study (HRS) model. [25]

Data used in our study are from the CHARLS dataset collected in 2015, including a total of 20967 individuals. Information about demographic characteristics, health-related behaviors and lifestyles, and health status were collected through face-to-face computer-assisted personal interview (CAPI). Anthropometric and physical measurements were provided, and fasting blood samples were collected by trained nurses from township hospitals or China Center for Disease Prevention and Control (CDC) according to a standard protocol.

The exclusion criteria of the study were: (1) demographic data not recorded; (2) age < 45 years old; (3) creatinine data or hearing status data not recorded. Finally, a total of 12508 participants were included

for final analysis. The process of selecting participants is shown in Fig. 1.

Hearing loss

In our study, hearing loss was identified through self-reporting. We used hearing related questions in the CHARLS survey to determine if a patient had hearing loss or not. The hearing related CHARLS survey questions are listed in Table 1. A participant would be defined as having hearing loss if he or she met one of the following three criteria: 1) having hearing problem; 2) wearing a hearing aid; 3) hearing status is poor.

Table 1
Hearing related questions in the CHARLS survey

(1) Do you have hearing problem?
1. Yes
2. No
(2) Do you ever wear a hearing aid?
1. Yes
2. No
(3) Would you say your hearing is excellent, very good, good, fair, or poor? (How is your hearing with a hearing aid if you normally use it? How is your hearing without a hearing aid if you normally don't use it?)
1. Excellent
2. Very good
3. Good
4. Fair
5. Poor

Kidney function decline

The estimated glomerular filtration rate (eGFR) is considered as the best overall index of kidney function in health and disease [26]. In this study, we estimated GFR using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [27]. The CKD-EPI equation is as follows:

$$\mathrm{GFR\ (mL/min/1.73m^2)} = \mathbf{141}\times\min(\mathrm{Scr}/\kappa,\mathbf{1})^{\alpha}\times\max(\mathrm{Scr}/\kappa,\mathbf{1})^{-\mathbf{1.209}}\times\mathbf{0.993}^{\mathrm{Age}}\times\mathbf{1.018}\ [\mathit{if\ female}]\times\mathbf{1.159}\ [\mathit{if\ black}] \quad (1)$$

In Eq. (1), "Scr" represents serum creatinine and its measure unit is mg/dL. κ is 0.7 for females and 0.9 for males, α is -0.329 for females and − 0.411 for males, "min" means the minimum value of Scr/κ and 1,

and “max” means the maximum value of Scr/κ and 1.

Participants were stratified into three groups based on eGFR values: ≥ 90, 60–89, and < 60 mL/min/1.73 m^2. The cut points for grouping were set according to the different stages of CKD defined by the Kidney Disease Outcomes Quality Initiative (K/DOQI) CKD guidelines [28].

Other predictor variables

We chose predictor variables by referring to hearing loss risk factors reported in the existent literatures [5, 29] and their availabilities in CHARLS dataset. In addition to eGFR, predictor variables used in the regression model include demographic characteristics (age, gender, education, residence area), health related behaviors (smoking and drinking status) and cardiovascular risk factors (body mass index (BMI), central obesity, hypertension, diabetes, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol). Demographics and health related behavior information were obtained from the questionnaire. BMI was defined as weight (in kilograms) divided by squared height (in meters), was acquired through physical measurements. Participants were categorized as underweight (< 18.5 kg/m^2), normal weight (18.5 to 24.9 kg/m^2), overweight (25.0 to 29.9 kg/m^2), and obesity (≥ 30 kg/m^2) based on BMI. In our study, central obesity was defined as waist circumference ≥ 80 cm for females and ≥ 102 cm for males; hypertension, was defined as mean systolic pressure ≥ 140 mmHg or mean diastolic pressure ≥ 90 mmHg, or a self-report hypertension; diabetes, was defined as fasting plasma glucose ≥ 126 mg/dL or HbA1c concentration ≥ 6.5%, or a self-reported doctor diagnosis. HDL cholesterol, and LDL cholesterol were obtained from the results of laboratory tests directly.

Statistical analysis

Descriptive statistics for continuous variables were presented using means and the standard deviations (SD), while frequencies and percentages were used for categorical variable characteristics description. Student’s t-test was used to compare mean values of continuous variables between participants with and without hearing loss, and the differences of hearing loss prevalence among different categorical variable groups were tested using Pearson

test. The association between reduced eGFR and hearing loss was modeled using logistic regression function, and the odds ratios (ORs) with 95% confidence intervals (CIs) of hearing loss for different eGFR categories were presented. Multivariable Logistic regression models were constructed to adjust for potential confounding variables (age [45–54 years, 55–64 years, ≥ 65 years], gender [male, female], education [illiterate, literate, primary school, middle school, high school and above], residence area [urban or rural], smoking [never, current, past], drinking [never, current, past], BMI [underweight, normal weight, overweight, obesity], central obesity [yes or no], hypertension [yes or no], diabetes [yes or no], HDL cholesterol [continuous value], and LDL cholesterol [continuous value]). The missing values of BMI and central obesity were considered as a separate unknown category in analysis.

All analyses were performed using STATA software (version 14.0). All P values were based on two-sided tests with a significance level of 0.05.

Results

Totally 12508 participants (5889 men and 6619 women) aged 45 years and older were included in the final dataset for analysis. The characteristics of participant data and the distribution of self-reported hearing loss prevalence are presented in Table 2. Overall, the prevalence of self-reported hearing loss in our study was 23.55%. Significant differences in hearing loss prevalence were observed among participants with different age, education background, residence area, smoking status, drinking status, BMI, chronic health status (having hypertension or not, having diabetes or not), and eGFR (all with P values < 0.001). The prevalence of hearing loss showed a significant increasing trend with the decrease of eGFR. 35.83% of the participants with an eGFR < 60 mL/min/1.73 m^2 had self-reported hearing loss, and the prevalence was nearly twice of the prevalence in those participants with eGFR ≥ 90 mL/min/1.73 m^2 (19.42%).

Table 2
Characteristics of participants

Variables	hearing loss (N = 12508)		P value
	NO	YES	
Total	9562 (76.45)	2946 (23.55)	
Age (years)			< 0.001
45 ~ 54	3401 (86.43)	534 (13.57)	
55 ~ 64	3596 (79.95)	902 (20.05)	
≥ 65	2565 (62.94)	1510 (37.06)	
Male	4507 (76.53)	1382 (23.47)	0.832
Education			< 0.001
illiterate	2602 (67.57)	1249 (32.43)	
literate	710 (74.97)	237 (25.03)	
primary	2444 (75.62)	788 (24.38)	
middle	2516 (83.42)	500 (16.58)	
high and above	1277 (88.13)	172 (11.87)	
Rural	7668 (75.24)	2523 (24.76)	< 0.001
Smoking			< 0.001
Never	5686 (76.96)	1702 (23.04)	
Current	2707 (77.90)	768 (22.10)	
Past	1164 (71.06)	474 (28.94)	
Drinking			< 0.001
Never	5106 (76.02)	1611 (23.98)	
Current	3469 (79.18)	912 (20.82)	
Past	973 (69.90)	419 (30.10)	

Note: data are expressed as number (%) or mean ± SD, unless otherwise indicated.

†There are 2.11% of BMI, 3.54% of central obesity were missing.

Abbreviations: BMI body mass index, HDL high-density lipoprotein, LDL low-density lipoprotein, eGFR estimated glomerular filtration rate.

Variables	hearing loss (N = 12508)		P value
	NO	YES	
BMI (kg/m^2)			< 0.001
< 18.5	469 (66.81)	233 (33.19)	
18.5 ~ 24.9	5407 (75.76)	1730 (24.24)	
25.0 ~ 29.9	2959 (79.91)	758 (20.39)	
≥ 30.0	533 (77.47)	155 (22.53)	
Central Obesity	2554 (77.23)	753 (22.77)	0.383
Hypertension	4041(72.37)	1543(27.63)	< 0.001
Diabetes	1912(72.81)	714(27.19)	< 0.001
HDL Cholesterol (mg/dL)	51.17 ± 11.49	51.37 ± 12.05	0.424
LDL Cholesterol (mg/dL)	102.66 ± 28.96	101.78 ± 29.15	0.152
eGFR (mL/min/1.73 m^2)			< 0.001
≥ 90	6042 (80.58)	1456 (19.42)	
60 ~ 89	3074 (71.24)	1241 (28.76)	
< 60	446 (64.17)	249 (35.83)	
Note: data are expressed as number (%) or mean ± SD, unless otherwise indicated.			
†There are 2.11% of BMI, 3.54% of central obesity were missing.			
Abbreviations: BMI body mass index, HDL high-density lipoprotein, LDL low-density lipoprotein, eGFR estimated glomerular filtration rate.			

The results of Logistic regression analysis of the association between eGFR and hearing loss after adjusting for potential confounders are listed in Table 3. Compared with participants with eGFR ≥ 90 mL/min/1.73 m^2, the ORs of participants with eGFR of 60–89 mL/min/1.73 m^2 and eGFR < 60 mL/min/1.73 m^2 were 1.11 (95%CI, 1.00-1.22; p = 0.047) and 1.26 (95%CI, 1.05–1.51; p = 0.012), respectively.

Table 3
Adjusted odds ratios (ORs) and 95% confidence intervals (95%CIs) for hearing loss in relation to the eGFR categories[a]

Variable	OR	95%CI	P value
eGFR (mL/min/1.73 m^2)			
≥ 90	Reference		
60 ~ 89	1.11	1.00-1.22	0.047
60	1.26	1.05–1.51	0.012

[a]Adjusted for age, gender, education, residence area, smoking, drinking, BMI, central obesity, hypertension, diabetes, HDL cholesterol, LDL cholesterol.

Discussion And Conclusions

This study indicated that 23.55% of middle-aged and older Chinese had hearing loss and the prevalence increased with age. In the process of exploring the association between eGFR and hearing loss, we observed that participants with lower eGFR had higher risk to developing hearing loss.

It is a little bit difficult to compare the prevalence of hearing loss in this study with previous studies due to the fact that the included participants in different studies were in different age groups, and the hearing loss was defined and measured using different instruments in different studies. The pure-tone audiometry and self-reporting are two common ways to assess hearing status in hearing related studies [23, 24, 29–34]. Pure tone audiometry is to find the hearing threshold at a specific frequency [22]. Most studies [23, 29] performed pure tone audiometry at 0.5, 1, 2, and 4 kHz. Based on the WHO's recommendations [35], an average threshold > 25 dB hearing level (HL) in the better hearing ear was defined as hearing loss, and an average threshold > 40 dB HL in the better hearing ear was defined as disabling hearing loss. The most recent two large-scale hearing loss studies [29, 36] based on the population of China were nearly a decade apart. In 2006, Sun et al. [36] reported that 11.04% of older adults (≥ 60 years) were diagnosed as hearing disability (> 40 dB HL), and that study was based on the data of the Second China National Sample Survey on Disability. In 2015, Gong et al. [29] also conducted a survey including 6984 older adults (≥ 60 years) in four provinces (Jilin, Guangdong, Gansu, and Shaanxi) of China, and reported that the prevalence of hearing loss (> 25dB HL) and disabling hearing loss (> 40 dB HL) were 58.85% and 24.10% respectively. A study [30] based on the Health Survey for England 2014, a nationally representative cross-sectional survey, reported that 26% of men and 20% of women aged 45 years and over had hearing loss (> 35 dB HL at 3.0 kHz of the better-hearing ear). Amieva et al. [32] used self-perceived hearing loss in their study. A short questionnaire survey was conducted to assess hearing loss of elderly participants (≥ 65 years) randomly selected from the general French population. Their study showed that 4% of the participants reported major hearing loss and 31% reported moderate hearing loss. Besides, the WHO's report [1] showed that approximately one-third of the

population aged over 65 years worldwide suffer from disabling hearing loss. In our study, the prevalence of hearing loss among participants aged 45–54, 55–64, and ≥ 65 years were 13.57%, 20.05%, 37.06%, respectively, which were similar to the reports of England, France and WHO.

The association between kidney function decline and hearing loss found in our study was consistent with some previously published studies [23, 24]. Seo et al. [24] found that an eGFR < 60 mL/min/1.73 m^2 had a significant independent influence on the hearing status of adults, and they reported that the OR of hearing impairment in participants with eGFR < 60 mL/min/1.73 m^2 was 1.25 (95%CI, 1.12–1.64) compared with those having eGFR ≥ 60 mL/min/1.73 m^2, after adjusting for age, sex, smoking, alcohol, BMI, diabetes mellitus, hypertension, dyslipidemia and microalbuminuria. Similarly, Vilayur et al. [23] found an independent association between moderate CKD and hearing loss, and the OR was 1.43 (95%CI, 1.10–1.84). They also reported that participants with eGFR < 45 mL/min/1.73 m^2 had the highest prevalence of hearing loss (73%) compared with those with eGFR ≥ 90 mL/min/1.73 m^2 (19%; adjusted OR = 2.4; 95%CI, 1.3–4.5). Moreover, Lin et al. [37] used data extracted from the Taiwan National Health Insurance Research Database, and found that the incidence of sudden sensorineural hearing loss (SSHL) was 1.57 times higher in the CKD group compared to the non-CKD group. In a prospective study of 1843 individuals, Gupta et al. [38] found that lower eGFR was significantly associated with incident hearing loss at speech frequencies when estimated GFR with an equation that includes both SCr and cystatin C, but no significant association was found when GFR was estimated using SCr-based equation. The result was kind of inconsistent with ours and it may be due to the different study populations, different definition of hearing loss, and different SCr measurement. Our study also provided a valid epidemiological evidence for the association between kidney function decline and hearing loss while we had a quite large sample size and high quality dataset.

The underlying mechanism of the association between kidney function decline and hearing loss is still unclear. There is evidence that many physiological, pathological and pharmacological similarities exist in the cochlea and kidney [39], which may account for the similar effects of some medications and immunological factors on the two organs. Both the stria vascularis of cochlea and glomerulus of kidney are epithelia structures which are intimately associated with the vascular system [39, 40], and a number of ion channels and transporters (involved in K^+ cycling, and endolymphatic K^+, Na^+, Ca^{2+}, and pH homeostasis) are expressed in both the inner ear and kidney [41]. Some studies [42–44] also indicated that abnormalities of nerve conduction in central and peripheral pathways in ESKD patients, probably influence the auditory response. Besides, Yassin et. al. [45] found that the degree of hearing loss was directly related to the degree of hyponatremia irrespective of the level of blood urea, and the cochlear affections were greatly improved by correcting kidney failure and restoring the serum sodium. Govender et. al. [46] reported that cochlear function in patients with CKD could be affected by elevated electrolyte, urea and creatinine levels, concomitant conditions such as hypertension, and ototoxic drugs such as furosemide.

The main strengths of our study include the nationally representative large-scale dataset, high response rate, and strict quality control process. However, there are certain limitations in our study. Firstly, the causal inference could not be drawn based on the current cross-sectional study. Secondly, information bias might exist as hearing loss was defined on the basis of self-reported results. But the reliability of self-reported hearing loss has been demonstrated in existent studies [47, 48]. Ferrite et al. [47] studied the validity of the following two questions: “Do you feel you have a hearing loss?” and “In general, would you say your hearing is ‘excellent,’ ‘very good,’ ‘good,’ ‘fair,’ ‘poor’?”, which are similar to the survey questions used in our study, and their study showed that responses to each of the two questions are accurate enough to be used as evidence of hearing loss in epidemiological studies about adult populations. Thirdly, the information of albuminuria was not available in our study, which is a potential confounder in the association between kidney function decline and hearing loss. Finally, the possibility of residual confounding exists.

Conclusions

This study indicated that kidney function decline was independently associated with hearing loss and patients with kidney function decline had a higher risk of developing hearing loss. We recommend that testing for hearing should be included in the integrated management among patients with chronic kidney disease, and patients with chronic kidney diseases need to pay attention to their hearing conditions so as to make suitable interventions at appropriate time to prevent the development of hearing loss.

Abbreviations

CHARLS: Chinese Health and Retirement Longitudinal Study; eGFR: Estimated Glomerular Filtration Rate; World Health Organization (WHO); End Stage Kidney Disease (ESKD); CKD: Chronic Kidney Disease; HRS: Health and Retirement Study; CAPI: Computer-Assisted Personal Interview; CDC: Center for Disease Prevention and Control; CKD-EPI : Chronic Kidney Disease Epidemiology Collaboration; K/DOQI: Kidney Disease Outcomes Quality Initiative; BMI: Body Mass Index; HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein; SD: Standard Deviations; OR: Odds Ratio; CI: Confidence Intervals; HL: Hearing Level; SSHL: Sudden Sensorineural Hearing Loss.

Declarations

Ethics approval and consent to participate

The Biomedical Ethics Review Committee of Peking University approved this study, and all participants gave written informed consent before participation.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from “http://charls.pku.edu.cn./”.

Competing Interests

Luxia Zhang received research funding from AstraZeneca. The remaining authors declare that they have no competing interests.

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Authors’ Contributions

Conception and design: WL, LZ, GK; data acquisition and pre-processing: QM, YW, YZ; data analysis and interpretation of results: WL, CY, LL, HW, ZS; manuscript drafting: WL. GK, LZ and YZ contributed important intellectual content during manuscript revision. All authors have read and approved the final manuscript.

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Figures

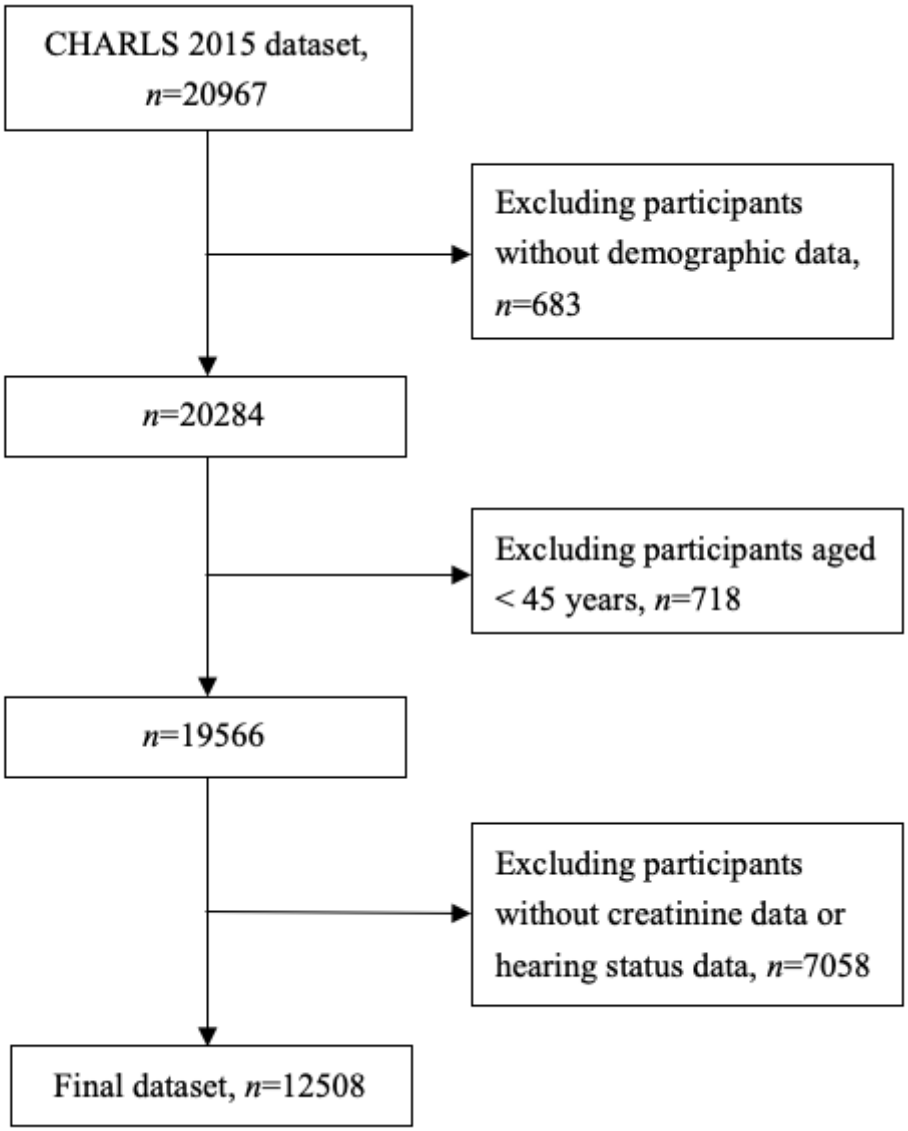

Figure 1

Flow chart of the selection of participants