Age-Period-Cohort Analysis of Sex Differences in Peripheral Arterial Disease Prevalence in China, 1990–2019: Postprint

Authors: Liu Linbo, Liao Zhijie, Yang Wenfan, Bai Dandan, Dongmei Wang, Shi Sen, Shi Sen

Date: 2023-07-27T00:00:00+00:00

Abstract

Background Peripheral artery disease (PAD) is a common and serious cardiovascular disease that is prone to complications of limb ischemia and adverse cardiovascular events. The prevalence of PAD exhibits gender differences, yet related research is relatively scarce. A comprehensive understanding of the gender differences in PAD prevalence in China is crucial for the formulation of public health policies.

Objective To analyze the gender differences in PAD prevalence in China and their underlying causes, thereby providing a theoretical basis for targeted screening and preventive measures.

Methods Data on PAD cases, prevalence, age-standardized prevalence, disease burden attributable risk factors, and corresponding 95% uncertainty intervals (UI) for Chinese males and females, as well as for females globally and in Japan, South Korea, and India, were extracted from the 2019 Global Burden of Disease (GBD) database. R language was used for data analysis and visualization in this study. Joinpoint software was employed to analyze the temporal trends of PAD prevalence among Chinese males and females from 1990 to 2019, calculating the annual percent change (APC) and average annual percent change (AAPC) in PAD prevalence along with their 95% confidence intervals (CI). A Bayesian age-period-cohort (BAPC) model was utilized to project PAD cases and prevalence from 2020 to 2035.

Results In 2019, the number of PAD cases in China was 71.74$\times$10^{5}$ for males and 213.15$\times$10^{5}$ for females. Compared with 1990, the number of PAD cases in 2019 increased by 154.22% for males and 181.27% for females. In 2019, the number of PAD cases and prevalence among females in Japan, South Korea, India, and globally all increased compared with 1990, but

the age-standardized prevalence decreased. In 1990, the age-standardized prevalence of PAD among Chinese females was 57.80% and 76.35% of that among Japanese and South Korean females, respectively, whereas in 2019 it was 1.10 times and 1.33 times that of Japanese and South Korean females, respectively. The prevalence of PAD among Chinese males was $462.40/10^5$ in 1990 and $989.79/10^5$ in 2019, representing an increase of 114.05%, with an upward trend observed from 1990-2019. The prevalence of PAD among Chinese females was $1321.44/10^5$ in 1990 and $3055.85/10^5$ in 2019, representing an increase of 131.25%, with an upward trend observed from 1990-2019. In 2019, the prevalence of PAD among Chinese females was 3.09 times that of males. The age-standardized prevalence of PAD among Chinese males was $731.02/10^5$ in 1990 and $744.96/10^5$ in 2019, representing an increase of 1.91%, with upward trends from 1990-1993 and 1993-2005, and a downward trend from 2005-2019. The age-standardized prevalence of PAD among Chinese females was $1839.43/10^5$ in 1990 and $2022.13/10^5$ in 2019, representing an increase of 9.93%, with an upward trend from 1990-2005 and a non-significant trend from 2005-2019 ($P>0.05$). In 2019, the age-standardized prevalence of PAD among Chinese females was 2.71 times that of males. BAPC model projections indicate that the number of PAD cases in China will reach 101.30$\times10^{5}$ for males and 319.24$\times10^{5}$ for females by 2035. The number of PAD cases among Chinese females in 2035 will increase by 49.77% compared with 2019. By age group, in 2019, Chinese females aged 65-69 years had the highest number of PAD cases at 35.15$\times10^{5}$, whereas in 2035, the age group 70–74 years is projected to have the highest number at 55.89$\times10^{5}$. The number of PAD cases among Chinese females aged 40-44, 45-49, 50-54, and 55-59 years in 2035 will be lower than in 2019, while cases among those aged 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, and $ 95 years will be higher than in 2019. The age-standardized prevalence of PAD in China in 2035 is projected to be 712 for males and $1945.97/10^5$ for females, representing decreases of 4.41% and 3.77%, respectively, compared with 2019. By age group, the prevalence of PAD among Chinese females in 2035 will increase with age across all strata, and except for the $ $95 years group, the prevalence in all other age groups will decrease compared with 2019. In 2019, the disease burden of PAD in China was attributable to six risk factors: hypertension, smoking, diabetes, renal insufficiency, high-salt diet, and lead exposure. The most significant risk factor for males was smoking (44.32%), followed by hypertension (18.97%) and diabetes (16.11%). The most significant risk factor for females was hypertension (32.31%), followed by diabetes (24.81%) and renal insufficiency (17.27%).

Conclusion The number of cases, prevalence, and age-standardized prevalence of PAD among Chinese females are all significantly higher than those among males, and the age-standardized prevalence has already exceeded that of Japan and South Korea. In the foreseeable future, the number of PAD cases among Chinese females will continue to increase, with the growth becoming increasingly pronounced among elderly women. Therefore, greater attention should be paid to the gender- and age-related patterns of PAD, the gender differences in risk factors among PAD patients, and necessary screening and preventive measures should be implemented.

Full Text

Age-Period-Cohort Model Analysis of Gender Differences in Peripheral Arterial Disease Prevalence from 1990 to 2019 in China

LIU Linbo[1], LIAO Zhijie[1], YANG Wenfan[2], BAI Dandan[1], WANG Dongmei[1], SHI Sen[2]*

[1]Department of Vascular Surgery, the Third Hospital of Mianyang/Sichuan Mental Health Center, Mianyang 621000, China

[2]Department of Vascular Surgery, the Affiliated Hospital of Southwest Medical University, Luzhou 646099, China

*Corresponding author: SHI Sen, Chief physician; E-mail: 50242042@qq.com

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Abstract

Background: Peripheral artery disease (PAD) is a common and serious cardiovascular disease prone to complications of limb ischemia and adverse cardiovascular events. PAD prevalence exhibits gender differences, yet related research remains relatively scarce. A comprehensive understanding of gender disparities in PAD prevalence in China is essential for public health policy development.

Objective: To analyze gender differences in PAD prevalence in China and their underlying causes, providing a theoretical basis for targeted screening and preventive measures.

Methods: Data on PAD cases, prevalence, age-standardized prevalence, disease burden attributable risk factors, and corresponding 95% uncertainty intervals (UI) were extracted from the 2019 Global Burden of Disease (GBD) database for Chinese males and females, as well as for females globally and in Japan, Korea, and India. R software was used for data analysis and visualization. Joinpoint software analyzed temporal trends in PAD prevalence among Chinese males and females from 1990 to 2019, calculating the annual percentage change (APC) and average annual percentage change (AAPC) with 95% confidence intervals (CI). A Bayesian age-period-cohort (BAPC) model predicted PAD cases and prevalence for 2020–2035.

Results: In 2019, China had an estimated 71.74$×10^{4}$ male PAD cases and 213.15$×10^{4}$ female cases. Compared with 1990, the number of PAD cases increased by 154.22% in males and 181.27% in females. In 2019, female PAD cases and prevalence in Japan, Korea, India, and globally were all higher than in 1990, but age-standardized prevalence decreased. In 1990, Chinese female age-standardized PAD prevalence was 57.80% and 76.35% of that in Japanese and Korean women, respectively, but by 2019 it was 1.10 and

1.33 times higher. Chinese male PAD prevalence was 462.40/100,000 in 1990 and 989.79/100,000 in 2019 (a 114.05% increase), showing an upward trend throughout 1990-2019. Chinese female PAD prevalence was 1,321.44/100,000 in 1990 and 3,055.85/100,000 in 2019 (a 131.25% increase), also showing an upward trend from 1990 to 2019. In 2019, Chinese female PAD prevalence was 3.09 times that of males. Chinese male age-standardized PAD prevalence was 731.02/100,000 in 1990 and 744.96/100,000 in 2019 (a 1.91% increase), with increasing trends during 1990-1993 and 1993-2005, but a decreasing trend from 2005 to 2019. Chinese female age-standardized PAD prevalence was 1,839.43/100,000 in 1990 and 2,022.13/100,000 in 2019 (a 9.93% increase), showing an increasing trend from 1990-2005, with non-significant trends thereafter (P>0.05). In 2019, Chinese female age-standardized PAD prevalence was 2.71 times that of males. BAPC model predictions indicate that by 2035, Chinese male PAD cases will reach 101.30$×10^{4}$ and female cases 319.24$×10^{4}, representinga49.77×10^{4}), whilethoseaged70–74willhavethemostin2035(55.89×10^{4}$). Female cases in age groups 40-44, 45-49, 50-54, and 55-59 will be lower in 2035 than in 2019, while cases in groups 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, and $ $95 will be higher. In 2035, Chinese male and female age-standardized PAD prevalence will be 712.09/100,000 and 1,945.97/100,000, respectively, representing decreases of 4.41% and 3.77% from 2019. By age, female PAD prevalence in 2035 will increase with age, with rates lower than 2019 in all groups except those $ $95 years. In 2019, China' s PAD disease burden was attributable to six risk factors: hypertension, smoking, diabetes, renal insufficiency, high-salt diet, and lead exposure. The leading risk factor for men was smoking (44.32%), followed by hypertension (18.97%) and diabetes (16.11%). For women, the leading risk factor was hypertension (32.31%), followed by diabetes (24.81%) and renal insufficiency (17.27%).

Conclusions: The number of cases, prevalence, and age-standardized prevalence of PAD in Chinese women are significantly higher than in men, with age-standardized prevalence now exceeding that of Japan and Korea. In the foreseeable future, the number of Chinese women with PAD will continue to increase, particularly among elderly women. Greater attention must be paid to gender- and age-related patterns in PAD, as well as gender differences in risk factors, with necessary screening and preventive measures implemented accordingly.

Keywords: Peripheral artery disease; Prevalence; Global Burden of Disease; Bayesian age-period-cohort; Bayesian forecast

Introduction

Peripheral artery disease (PAD) is a highly prevalent condition, ranking as the third most common cardiovascular disease after coronary artery disease and stroke. Most PAD patients are asymptomatic or have atypical symptoms, with only about 10% experiencing classic claudication, posing a major challenge for early diagnosis. However, regardless of symptom presentation—whether intermittent claudication, atypical leg pain, or critical limb ischemia—PAD patients face significantly increased risks of adverse cardiovascular events and mortality. The risk of cardiovascular death increases threefold in PAD patients, with more severe disease correlating with higher likelihood of death from myocardial infarction or stroke.

The 2019 Global Burden of Disease (GBD) study estimated approximately 113 million PAD patients worldwide, with over one-fifth dying from coronary or cerebrovascular disease within 10 years. This represents a substantial public health problem. However, PAD research remains limited compared to coronary artery disease and stroke, with relatively little public attention, and clinical guidelines for PAD risk management often rely on evidence from coronary heart disease patients.

Research has identified gender differences in PAD prevalence, with women accounting for 52.23% of PAD patients globally, particularly in low- and middle-income countries where women face higher risks than men. Compared to men, women with PAD experience greater declines in exercise capacity and quality of life, higher depression risk, and increased acute cardiovascular event risk. Additionally, the burden of PAD-related disability and mortality is more severe in women. Consequently, experts have called for greater attention to gender differences in PAD, with increased focus on female patients.

Few domestic studies have reported gender-specific PAD outcomes. Therefore, a comprehensive understanding of gender disparities in PAD prevalence in China will facilitate more effective prevention, diagnosis, and control strategies.

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1. Methods

1.1 Data Sources PAD prevalence data (1990–2019) were obtained from the 2019 GBD database (http://ghdx.healthdata.org/gbd-results-tool). The GBD database provided relevant data for Chinese males and females and for females globally and in Japan, Korea, and India, including PAD cases, prevalence, age-standardized prevalence, disease burden attributable risk factors, and corresponding 95% uncertainty intervals (UI). R software (version 4.2.1) was used for data analysis and visualization.

1.2.1 Joinpoint Regression Analysis Joinpoint software (version 4.9.1.0) analyzed temporal trends in PAD prevalence among Chinese males and females from 1990 to 2019. The Monte Carlo permutation test, the default optimal model selection method in Joinpoint software, was used with adjusted statistical significance levels ($P<0.05$ considered significant). The number of joinpoints relates to the number of observations (time span), with system defaults of 0 minimum and 5 maximum, though researchers can customize this. This study set the number of joinpoints to 2. The annual percentage change (APC) and average annual percentage change (AAPC) in PAD prevalence were calculated with 95% confidence intervals (CI).

1.2.2 Bayesian Age-Period-Cohort (BAPC) Model Based on PAD cases and prevalence from the GBD database (1990-2019), this study used a BAPC model to predict PAD cases and prevalence for 2020-2035. The GBD dataset provided PAD prevalence data for individuals \$ \$40 years, divided into 5-year age groups: 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, and \$ \$95 years. The BAPC model was fitted using a Poisson model with integrated nested Laplace approximation (INLA) to predict epidemiological trends. This study employed second-order random walk (RW2) modeling to examine age, period, and cohort effects, estimating PAD cases and prevalence. The prediction process was implemented using the BAPC and INLA packages in R.

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2. Results

2.1 PAD Prevalence in 1990 and 2019 In 2019, China had an estimated 71.74\$×10^{4}\$ male PAD cases and 213.15\$×10^{4}\$ female cases. Compared with 1990, the number of PAD cases increased by 154.22% in males and 181.27% in females . In 2019, female PAD cases and prevalence in Japan, Korea, India, and globally were all higher than in 1990, but age-standardized prevalence decreased. Japan showed the largest decrease (41.98%), followed by Korea (36.93%), India (2.59%), and globally (20.45%). However, Chinese female age-standardized prevalence increased by 9.93%. In 1990, Chinese female age-standardized PAD prevalence was 57.80% and 76.35% of that in Japanese and Korean women, respectively, but by 2019 it was 1.10 and 1.33 times higher. In 1990, Chinese female PAD cases accounted for 16.92% of the global total, rising to 28.01% in 2019 [TABLE:1, FIGURE:1].

2.2 Trends in Crude and Age-Standardized Prevalence Chinese male crude PAD prevalence was 462.40/100,000 in 1990 and 989.79/100,000 in 2019 (a 114.05% increase) [TABLE:1, FIGURE:2]. Trends showed increases during 1990-1999 (APC 2.58%), 1999-2007 (APC 3.17%), and 2007-2019 (APC 2.39%), with an AAPC of 2.66% for 1990-2019 . Chinese female crude PAD prevalence was 1,321.44/100,000 in 1990 and 3,055.85/100,000 in 2019 (a 131.25% increase) [TABLE:1, FIGURE:2]. Trends showed increases during 1990-2006 (APC 2.90%), 2006-2009 (APC 2.21%), and 2009-2019 (APC 3.24%), with an AAPC of 2.94% for 1990-2019 .

Chinese male age-standardized PAD prevalence was 731.02/100,000 in 1990 and 744.96/100,000 in 2019 (a 1.91% increase) [TABLE:1, FIGURE:3]. Trends increased during 1990-1993 (APC 0.91%) and 1993-2005 (APC 0.49%), but decreased during 2005-2019 (APC -0.50%), with an AAPC of 0.05% for 1990-2019 .

Chinese female age-standardized PAD prevalence was 1,839.43/100,000 in 1990 and 2,022.13/100,000 in 2019 (a 9.93% increase) [TABLE:1, FIGURE:3]. Trends increased during 1990-2005 (APC 0.73%), with non-significant changes during 2005-2009 and 2009-2019 (P>0.05). The AAPC for 1990-2019 was 0.28% .

2.3 Predictions for 2035 BAPC model predictions indicate that by 2035, Chinese male PAD cases will reach 101.30$\times 10^{4}$ and female cases 319.24$\times 10^{4}$, representing a 49.77$\times 10$ {4}), while those aged 70–74 will have the most in 2035 (55.89$\times 10^{4}$). In 2035, female cases in age groups 40-44, 45-49, 50-54, and 55-59 will be lower than in 2019, while cases in groups 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, and $ $95 will be higher [TABLE:3, FIGURE:4].

In 2035, Chinese male and female age-standardized PAD prevalence will be 712.09/100,000 and 1,945.97/100,000, respectively, representing decreases of 4.41% and 3.77% from 2019. By age, female PAD prevalence in 2035 will increase with age, with rates lower than 2019 in all groups except those $ $95 years [TABLE:3, FIGURE:4].

2.4 Analysis of Attributable Risk Factors In 2019, China' s PAD disease burden was attributable to six risk factors: hypertension, smoking, diabetes, renal insufficiency, high-salt diet, and lead exposure. The leading risk factor for men was smoking (44.32%), followed by hypertension (18.97%) and diabetes (16.11%). For women, the leading risk factor was hypertension (32.31%), followed by diabetes (24.81%) and renal insufficiency (17.27%). Smoking accounted for only 14.91% of female risk factors .

Discussion

This study used GBD 2019 data to evaluate PAD prevalence in China from 1990 to 2019. The findings show that the number of PAD cases, crude prevalence, and age-standardized prevalence all increased during this period. In 2019, China had over 21 million PAD patients. By 2035, female PAD cases are projected to reach nearly 32 million, 3.15 times the male number. Although over 50% of these patients have asymptomatic PAD without obvious impact on lower limb function or quality of life, this condition reflects poor systemic vascular health and predicts future fatal cardiovascular events. Asymptomatic PAD patients have a 20-60% increased risk of myocardial infarction and 40% increased risk of stroke. PAD signifies higher rates of polyvascular disease, representing a massive global medical and economic burden. Understanding PAD epidemiological characteristics can better guide disease prevention, treatment, and public policy.

Previous PAD research, due to gender bias in population screening or clinical sampling and gender differences in healthcare-seeking behavior, identified male sex as an independent risk factor for PAD. However, understanding of PAD gender differences has evolved with recent research. Current data show higher PAD prevalence in women. A cross-sectional study of Beijing's urban population also found higher PAD prevalence in women (13.6%) than men (8.0%). This study similarly found significantly higher PAD prevalence in Chinese women.

Research indicates that asymptomatic and atypical symptoms are more common in female PAD patients, often misdiagnosed as arthritis, spinal stenosis, or neuropathy. However, due to lower leg strength and cardiopulmonary function compared to men, women experience greater impairment in lower limb function and quality of life despite similar PAD severity, warranting increased attention to female PAD.

Few studies have analyzed why female PAD prevalence exceeds male prevalence. The mechanisms remain unclear but likely involve multiple factors related to sociodemographic structure, diagnostic methods, and risk factor differences. First, regarding sociodemographic structure, China' s life expectancy has continuously improved over the past 30 years, with women living longer than men. Women account for 54.39% of the population over 70 and 61.09% over 80. PAD prevalence increases with age, and this study found Chinese female PAD prevalence exceeds 15% in those over 75. With accelerating population aging globally and in China, this study' s 2035 predictions confirm that PAD cases will continue to increase while age-standardized prevalence decreases—a manifestation of population aging. This may contribute to gender differences in PAD prevalence. Additionally, while male PAD mortality increased over the past 30 years in China, female PAD mortality decreased, further extending survival. Some attribute this to women' s potential survival advantage regarding coronary heart disease and stroke, as PAD patients rarely die from PAD itself but from other cardiovascular diseases, with men more likely to die from coronary disease. These factors may contribute to persistently rising female PAD prevalence.

Second, diagnostic methods differ. The ankle-brachial index (ABI) is a noninvasive tool for PAD screening and diagnosis. The 2016 AHA/ACC guidelines recommend ABI as the initial diagnostic method for PAD, with ABI <0.90 establishing the diagnosis. However, ABI differs by gender. A Scottish screening study of adults without cardiovascular disease history showed women' s average ABI was 0.05 lower than men' s (1.01 vs. 1.06). A U.S. epidemiological study found women' s ABI approximately 0.02 lower than men' s. These differences may relate to normal physiological gender differences in height and small vessel diameter. Taller height correlates with higher ankle systolic pressure and higher ABI values. Since men are on average taller than women, their ABI values are higher. Some scholars propose that using ABI <0.90 as a universal diagnostic threshold may not accurately distinguish actual PAD prevalence between genders. In China, gender height differences may be more pronounced, potentially creating larger ABI disparities requiring epidemiological validation. Conversely, male PAD prevalence may be underestimated. Some patients with exertional claudication have normal resting ABI, and exercise ABI testing can help differentiate PAD, but this is often impractical in large epidemiological studies.

Men have higher rates of critical limb ischemia and amputation, and patients with amputation or critical limb ischemia are typically excluded from population studies. Male PAD is more common among those with lower socioeconomic status and education, potentially related to smoking and unhealthy dietary patterns. Most ABI screening in China occurs in major eastern medical centers and urban communities, with less screening in economically underdeveloped central/western regions and rural areas, potentially leading to underestimation of male PAD.

Third, risk factors differ. This study analyzed 2019 Chinese PAD disease burden attributable risk factors. For men, smoking was the leading risk factor (44.32%). For women, hypertension was primary, followed by diabetes, with smoking ranking fourth. Although women have lower smoking rates, their exposure to secondhand smoke is significantly higher. It is estimated that over half of Chinese female non-smokers are exposed to passive smoking, a potential contributor to increased female PAD prevalence. Additionally, diabetes is the second-leading risk factor for female PAD burden, and studies show women with diabetes have higher PAD risk than men with diabetes. Women also have unique risk factors, including estrogen-related changes in postmenopausal status, higher serum oxidative stress marker levels, and oral contraceptive use. Some scholars suggest oral contraceptive use may explain higher PAD prevalence in women under 40 compared to men. Women who experience preeclampsia or gestational hypertension during pregnancy have higher PAD risk.

In summary, due to gender differences in sociodemographic structure, diagnostic methods, and risk factors, Chinese female PAD prevalence significantly exceeds male prevalence. This study also found Chinese female age-standardized PAD prevalence has increased substantially over the past 30 years, now exceeding that of high-income countries like Japan and Korea and far surpassing India, another developing country. Meanwhile, Japan, Korea, India, and global female age-standardized PAD prevalence decreased, and Chinese male age-standardized PAD prevalence declined over the past decade. Notably, in 2019, Chinese female PAD patients accounted for approximately 28.01% of the global female PAD population. This study predicts that by 2035, Chinese female PAD cases will increase by approximately 49.77% compared with 2019. With foreseeable trends of population aging and increasing chronic diseases like hypertension and diabetes, more PAD cases are expected. PAD is a health issue that cannot be ignored. Greater awareness among healthcare workers and the public is needed, particularly more gender-based epidemiological and clinical research to improve prevention, early diagnosis, and treatment of PAD, especially in women, thereby reducing PAD-related economic burden and adverse outcomes.

This study has several limitations. First, GBD data quality and quantity depend heavily on modeling inputs, which vary substantially across countries and regions, potentially biasing PAD burden estimates. Second, PAD often coexists with serious comorbidities like myocardial infarction or stroke, which may mask PAD' s specific burden, leading to underestimation. Third, the GBD database lacks data on other risk factors (e.g., hypercholesterolemia), limiting comprehensive risk factor and burden analysis.

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Funding: Sichuan Provincial Health Commission Research Project (18PJ488); Sichuan Medical Association (Hengrui) Scientific Research Fund Special Project (2021HR65)

Author Contributions: LIU Linbo and SHI Sen designed and reviewed the study. LIU Linbo, LIAO Zhijie, and YANG Wenfan analyzed and interpreted data and conducted literature review. YANG Wenfan, BAI Dandan, and WANG Dongmei created figures, organized materials, and drafted the manuscript. SHI Sen revised and approved the final manuscript. All authors approved the final version.

Conflict of Interest: None declared.

Received: 2023-03-28
Revised: 2023-07-06

Correspondence to: SHI Sen, Chief physician; E-mail: 50242042@qq.com

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