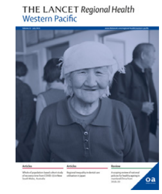
The Lancet Regional Health - Western Pacific 17 (2021) 100280

Contents lists available at ScienceDirect

The Lancet Regional Health - Western Pacific

journal homepage: www.elsevier.com/locate/lanwpc



Incidence and Survival of Aortic Dissection in Urban China: Results from the National Insurance Claims for Epidemiological Research (NICER) Study

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A R T I C L E I N F O

Article history:
Received 10 June 2021
Revised 19 August 2021
Accepted 1 September 2021

Keywords:
Aortic dissection
Incidence
Mortality
Claims data
Chinese

A B S T R A C T

Background: Aortic dissection (AD) represents a significant mortality; however, there is rare epidemiologic information about the demography of AD in Chinese, especially its incidence rate.

Methods: A retrospective cohort study was established using the Urban Employee Basic Medical Insurance claims data covering 346.7 million residents from 23 provinces in China, 2015-2016. AD cases were then linked to database of the Urban Employee Basic Endowment Insurance for death information. Incidence rate was age- and sex-standardized to the 2010 China census population. The associations between AD and related factors were evaluated with Poisson regression models. Moreover, mortality and sex- and age-adjusted survival rate was estimated by Cox models.

Findings: 6084 adult AD cases were included in incidence analysis. Totally 4692(77.1%) were men and 5641(92.7%) were Han Chinese. The overall age- and sex-adjusted incidence rate of AD was 2.78(95%CI:2.59-2.98) per 100,000 person-years. In terms of geographic disparities, the crude incidence rate was significantly higher in Northwest China than South China (4.96[95%CI:4.17-5.75] *vs.* 2.04[95%CI:0.38-3.71] per 100,000 person-years; risk ratio: 2.67[95%CI: 2.34-3.04]). Moreover, survival analysis of 4518 AD patients with 683 recorded deaths during follow-up (median 2.2 years) showed that overall 3-year survival was 83.7%(95%CI:82.4-84.8).

Interpretation: This contemporary population-based cohort study provides a first comprehensive assessment of incidence of AD in urban Chinese adults. The distinct signatures of different incidence with respect to geographic variations may have important implications for clinical management of AD.

Funding: Chinese Ministry of Science and Technology (2020YFC2003503, 2016YFC0903000), and National Natural Science Foundation of China (91846112, 81973132, 81961128006).

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https://doi.org/10.1016/j.lanwpc.2021.100280
2666-6065/

Research in context

Evidence before this study

We searched PubMed for studies published before August 18th, 2021, without language restrictions for full papers, using the terms ("aortic dissection" OR "acute aortic syndrome") AND (prevalence OR incidence OR epidemiology) AND (China OR Chinese). Of the 514 articles identified, there were only two articles reported the estimation of incidence for aortic dissection (AD) in China. According to the results, the estimated incidence of AD was 4.3/100,000 in Taiwan province during 1996-2001, and 2.8/100,000 in 25 cities of mainland China in 2011. The two studies on AD incidence for Chinese were limited by the regional level with few patients included. In short, there is rare epidemiologic information about the demography of AD in Chinese, especially its incidence rate.

Added value of this study

The updated age- and sex-adjusted incidence rate of AD was 2.78 (95%CI, 2.59-2.98) per 100,000 person-years in urban China, and the geographic disparities of incidence of AD were consistent with prevalence of hypertension in China.

Implications of all the available evidence

Our study fills the gaps in epidemiologic information in China and enriches the global map of AD incidence. Moreover, measures that could help promote primary prevention of hypertension are needed to avoid future AD incidence increase and reduce regional disparities in cardiovascular health.

Introduction

Acute aortic dissection (AD) is one of the most severe life-threatening cardiovascular emergencies [1]. Despite its importance, reliable estimation of AD incidence and survival is challenging [2]. As a rare disease, it is impractical to attempt to obtain national epidemiologic estimates prospectively, and data from a limited population or clinical registries may be inaccurate, making national administrative data an essential tool for such investigations in rare diseases [3]. Moreover, little is known about incidence rates of AD in China. The AD incidence rate in 25 cities of China was reported as 2.8/100,000 in 2011, according to sampled inpatient records from health insurance claims [4]; however, the convenience sampling design, calculation using the presumed hospital admission rate, and the fact that merely sixty-five AD patients were identified from the samples in that study, limited accurate estimation of the incidence rate of AD.

In addition, the incidence rates of AD vary substantially among regions. Regional variations in the AD rates are commonly considered to reflect differences in control of its risk factors, e.g., hypertension [5,6]. Current epidemiological knowledge of AD incidence and survival is paramount not only to the disease management of AD but also to improve prioritization of resources and medical management of its risk factors. Thus, accurate data on AD is essential for research and planning of health services to allocate emergency medical resources such as the implementation of chest pain centers accreditation, especially for developing areas [7].

In this paper, we undertook a study using insurance data from 2015 to 2016 with the follow-up till 2018 to provide a broad characterization of AD, epidemiologic estimates, as well as to identify specific groups with an altered propensity for AD. The objective of this study was to estimate the incidence and survival of AD in urban China, with specific examination of demographic and geographic difference.

Methods

Study Design, Data Sources, and Population

This study is a cohort design, using data from the National Insurance Claims for Epidemiological Research (NICER). Details of the data sources and population have been reported previously [8–11]. The overall study design was shown in **Figure 1**. Briefly, there are three basic health insurance schemes in China: the Urban Employee Basic Medical Insurance (UEBMI) for the urban employed, the Urban Resident Basic Medical Insurance (URBMI) for urban residents without formal employment and the New Rural Cooperative Medical Scheme (NRCMS) for rural residents. These three schemes covered more than 92% of the population by 2011 [12]. In this study, we only used the UEBMI database because of its completeness of inpatient, outpatient and emergency records. It is used for working and retired employees in cities (i.e., employers and employees from government agencies and institutions, state-owned enterprises, private businesses, social organizations, and other private entities).

Provinces/cities without detailed information on diagnosis were excluded. Data about 346.7 million residents in 23 provinces (about 52.1% of overall urban population in China) were included in this study. (**eTable 1-2** in the Supplement) The inclusion criteria of the population were residents who (1) had UEMBI insurance during 2015 to 2016; (2) enrolled in the 23 provinces included; and (3) aged 18 years and older in each year during the study period. Subjects with the following conditions were excluded: (1) without a valid national insurance identifier; and (2) had conflicting information recorded, i.e., records of the medical treatment reimbursement time being earlier than the individual's first enrollment time.

After patients with AD during the study period were identified, we then linked them to the database of the Urban Employee Basic Endowment Insurance (UEBEI) which recorded the information of death (all-cause mortality). Insurance data were anonymized for research purposes. This study was approved by the Peking University Institutional Review Board (IRB00001052-18012-Exemption), which granted a consent waiver because of the use of deidentified administrative databases.

Data collection

Specific data resources essential to the current study from UEBMI included: (1) Basic demographic characteristics of enrollees including sex, ethnicity, and date of birth; (2) Information related to the diagnosis, i.e., visiting date, International Classification of Diseases (ICD) code of the primary and secondary diagnosis (ICD-9 or ICD-10), name of primary and secondary diagnosis (free text), and type of the medical service (emergency, outpatient, or inpatient service). In addition, the concomitant diseases including hypertension, diabetes, coronary artery diseases, aortic aneurysm and Marfan syndrome were also extracted by the linked insurance records before their first AD records. Death information from UEBEI was recorded as yes or no with exact date of death. Information on death was collected until June 30th, 2018. Not all patients were followed up, 1566 patients who failed to link to the UEBEI database were excluded in survival analysis. (**Figure 1**)

AD identification

AD case was identified by the presence of any of the following ICD codes: "441.0" (ICD-9) or "I71.0" (ICD-10), or medical

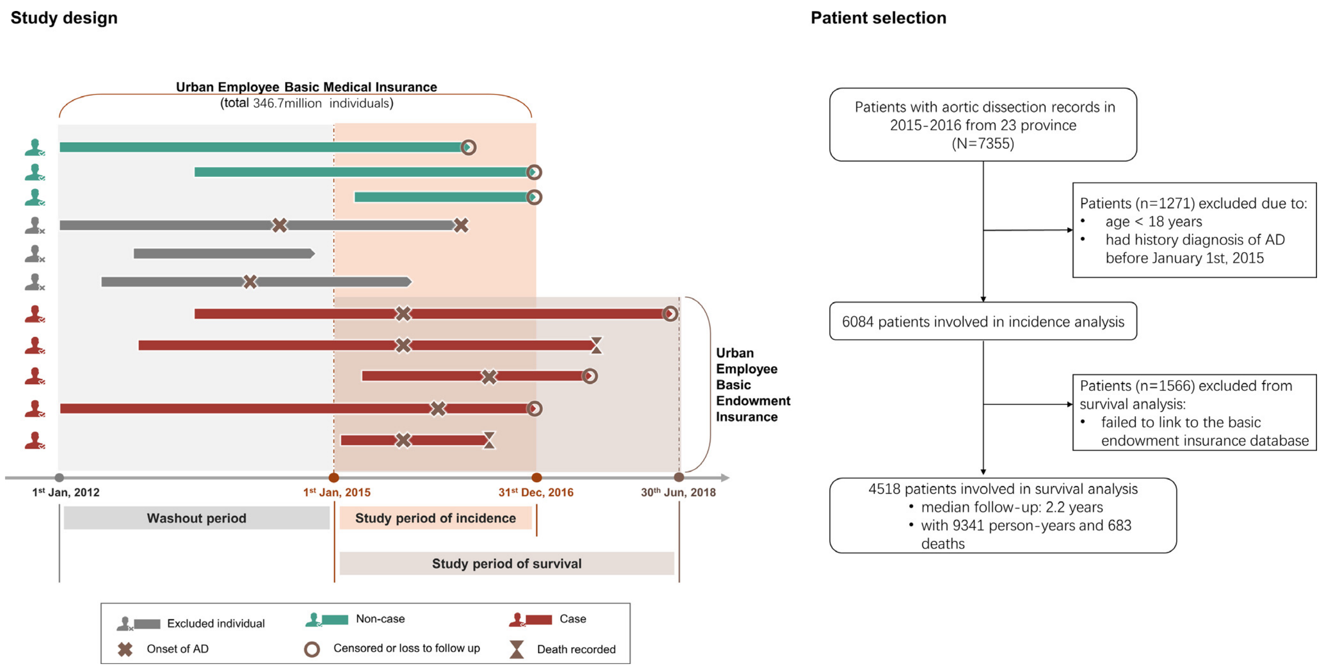

Figure 1. Study design and flowchart of study patients in the study.

terms in Chinese including aortic dissection (or rupture). To minimize the possibility of missing patients, we firstly constructed a relatively loose algorithm to extract potential patients from the database with fuzzy string matching technique, using “dissection”, “aorta”, “rupture”, “TEVAR”, “WHEAT”, “BENTALL”, “SUN”, “DAVID” and “AAS” as key words. There were 35,452 diagnostic items extracted at this stage.

Secondly, to confirm the diagnosis, two investigators (KL and DJ) independently reviewed all the diagnostic terms among these firstly filtered subjects. The keywords used after manual confirmation according to ICD-9 code, ICD-10 codes and medical terms in Chinese was shown in the **eTable 3**. Total 18,841 subjects were identified as the potential pool of AD cases from January 1st, 2012 to December 31st, 2016 at this stage.

Then, these two investigators reviewed the diagnostic information for each potential case. Patients who were diagnosed as intramural hematoma, penetrating aortic ulcer, traumatic or syphilitic AD were excluded. Patients with diagnostic items containing words like “undetermined”, “uncertainty”, “?”, “possible”, or “suspicious” were considered as suspected AD case. These suspected AD cases were used only in the sensitivity analysis. Patients with onset of AD during January 1st 2015 and December 31st 2016 were included in our study to calculate the incidence of AD. Correspondingly, total 7355 AD cases were considered as confirmed AD cases and 461 subjects were suspected AD cases between 2015 and 2016 (**Figure 1**).

Finally, shown in **Figure 1**, patients with previous diagnosis of AD before 2015 were further excluded in the primary analysis. Data between 2012 to 2014 was considered as the wash-out period to minimize the impacts of prevalent AD cases. There were 6084 cases with 2686 distinct AD related diagnosis in the incidence analysis. For patients who had multiple AD diagnoses, we only consider the earliest record related to AD in the incidence analysis. Subtypes of diseases were available in subset of the patients. AD case was classified according to the Stanford system (type A or type B).

Statistical Analysis

We calculated incidence rate using a two-stage approach [8,9]. In the first stage, the method for estimating the incidence rate in each province was as follows: the denominator used to calculate the incidence of AD was the total person-years in each province in the UEBMI database. The numerator was the number of patients with AD estimated from the denominator population in each province, considering the missing data. This method was described previously in detail [8] and included in the **Appendix** for convenience. In the second stage, the national or regional average estimates were calculated by pooling the estimates from each province using a random effects meta-analysis. We calculated the standardized rates based on the population distribution in the China’s 2010 national population census. Incidence rates were also estimated by sex, age groups and geographical region in China (East, Northeast, Northwest, Central, South, and Southwest). Several sensitivity analyses were conducted to assess the robustness of the results: (1) including all suspected AD cases, (2) including only observed cases to assess the lower bounds of the rates, and (3) applying negative binomial regression models alternatively for overdispersion in the Poisson regression model.

Kaplan-Meier survival curves were generated for overall patients and subtypes of patients. Moreover, age- and sex-adjusted survival curves were also plotted with age adjusted to 65 years. Survival time was calculated from the date of first diagnosis in UEBMI to date of death or June 30th 2018, whichever earlier. In addition, we performed a multivariable Cox model to evaluate the association between mortality and risk factors including age, sex, ethnicity, concomitant diseases, or visiting time of the medical service, adjusted for province. Hazard ratios during follow-up were calculated. Analyses were performed using Stata (version 15.0) software (Stata Corp, College Station, Texas, USA). All *P*-values were two-tailed and have not been adjusted for multiple testing. A *P*-value <0.05 was considered statistically significant. Two-sided *P*-values and 95% confidence intervals (95%CI) were used.

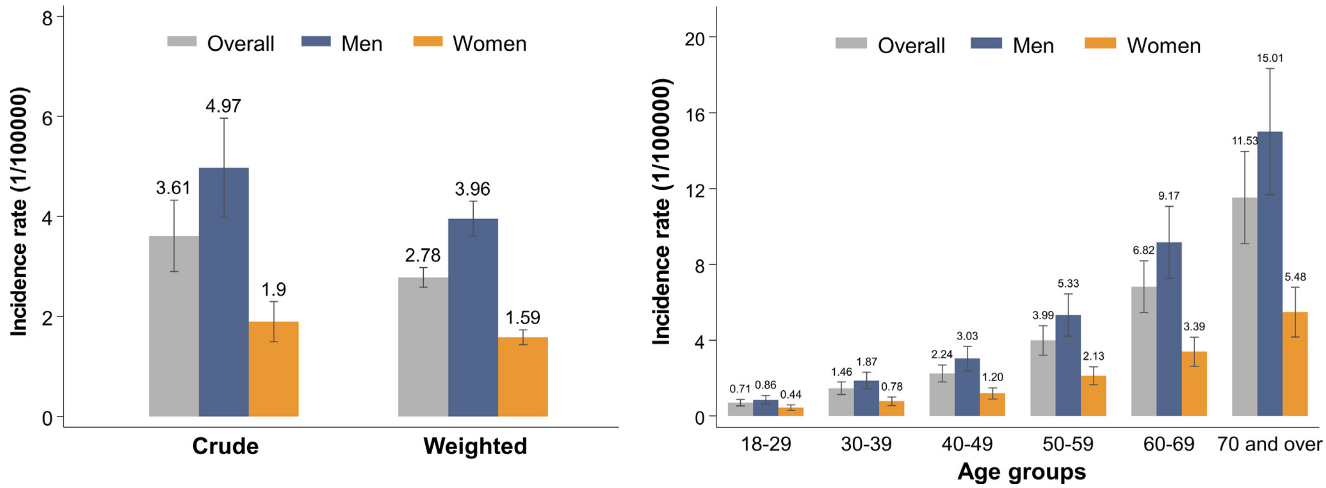

Figure 2. Incidence rate of aortic dissection in China by sex and age groups
Overall Crude incidence: 3.61 (95% CI: 2.90, 4.33); Weighted incidence: 2.78 (95% CI: 2.59, 2.98). Detailed estimations were shown in **eTable 4**.

Table 1
General characteristics of aortic dissection patients in China by sex

	Total (n=6084)	Men (n=4692)	Women (n=1392)	P value
Age in years, mean (SD)	58.81 (14.61)	58.28 (14.22)	60.61 (15.76)	<0.0001
Ethnic groups				0.3214
Han	5641 (92.7%)	4343 (92.6%)	1298 (93.2%)	
Mongolia	18 (0.3%)	11 (0.2%)	7 (0.5%)	
Muslim	41 (0.7%)	28 (0.6%)	13 (0.9%)	
Uyghur	15 (0.2%)	12 (0.3%)	3 (0.2%)	
Zhuang	20 (0.3%)	17 (0.4%)	3 (0.2%)	
Man	37 (0.6%)	30 (0.6%)	7 (0.5%)	
Others	132 (2.2%)	109 (2.3%)	23 (1.7%)	
Unknown	180 (3.0%)	142 (3.0%)	38 (2.7%)	
Type of dissection				0.0187
Stanford A	375 (6.2%)	285 (6.1%)	90 (6.5%)	
Stanford B	983 (16.2%)	792 (16.9%)	191 (13.7%)	
Unknown	4726 (77.7%)	3615 (77.0%)	1111 (79.8%)	
Concomitant diseases				
Aortic aneurysm	1084 (17.8%)	839 (17.9%)	245 (17.6%)	0.8099
Hypertension	1812 (29.8%)	1363 (29.0%)	449 (32.3%)	0.0216
Coronary heart disease	846 (13.9%)	616 (13.1%)	230 (16.5%)	0.0013
Diabetes	426 (7.0%)	304 (6.5%)	122 (8.8%)	0.0033
Marfan syndrome	30 (0.5%)	19 (0.4%)	11 (0.8%)	0.0715

Role of the funding source

The funding sources of this study did not influence nor participate in study design, data collection, data analysis, data interpretation, or drafting of the paper. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Incidence of AD

A total of 7355 AD cases were identified in the insurance database during 2015-2016. After exclusion for those younger than 18 years or who had history diagnosis of AD before January 1st, 2015 (n=1271), we identified 6084 AD patients in incidence analysis and 4518 AD patients in survival analysis with eligibility criteria (**Figure 1**). General characteristics of all 6084 patients with AD were presented in the **Table 1**. Overall, patients with AD had a mean (SD) age of 58.81 (14.61) years, 4692 were men (77.1%) and 5641 were Han Chinese (92.7%). Compared with men, women with AD cases had greater proportions of common concomitant diseases, such as hypertension (449[32.3%] *vs.* 1363[29.0%], $P<0.05$), coronary heart disease (230[16.5%] *vs.* 616[13.1%], $P<0.05$), or diabetes (122[8.8%] *vs.* 304[6.5%], $P<0.05$). Among 6084 AD patients, 375 (6.2%) were reported as Stanford type A, with a higher proportion of type A subtype among women (90[6.5%]) than counterpart among men (285[6.1%]) ($P<0.05$).

As illustrated in **Figure 2**, crude incidence rate of AD among men was 4.97(95%CI, 3.98-5.97) per 100,000 person-years, compared with 1.90(95%CI, 1.50-2.30) per 100,000 person-years among women. The age- and sex-adjusted incidence rate of AD was 2.78(95%CI, 2.59-2.98) per 100,000 person-years. In different age groups, incidence rates of AD ranged from 0.71(95%CI, 0.54-0.89) per 100,000 person-years for 18-29 years to 11.53(95%CI, 9.10-13.97) per 100,000 person-years for 70 years and above. Gender gap was pronounced among each group: the incidence rates were more than double the rates for men than counterparts for women (**eTable 4**).

Incidence rates according to ethnic groups or regions in China are provided in **Table 2**. Compared with Han Chinese (3.71 [95%CI, 3.00-4.42] per 100,000 person-years), it seems that Muslim has highest crude rate (6.79 [95%CI, 4.59-9.00] per 100,000 person-years, risk ratio: 1.75 [95%CI, 1.38-2.23]) in each ethnic group, followed by Mongolia (6.26 [95%CI, 0.19-12.32] per 100,000 person-years), while Uyghur has lowest crude incidence rate (3.38 [95%CI, 2.34-4.43] per 100,000 person-years). Meanwhile, crude incidence

Table 2
Incidence rate of aortic dissection patients by ethnic groups and regions in China

	No. of participants	Crude incidence rate (1/100,000, 95% CI)	Risk ratio (95% CI)#
Ethnic groups	323,051,701		
Han	307,871,540 (95.3%)	3.71 (3.00, 4.42)	reference
Mongolia	1,540,737 (0.5%)	6.26 (0.19, 12.32)	1.08(0.76,1.55)
Muslim	1,348,395 (0.4%)	6.79 (4.59, 9.00)	1.75(1.38,2.23)
Uyghur	1,697,836 (0.5%)	3.38 (2.34, 4.43)	0.82(0.57,1.16)
Zhuang	2,929,802 (0.9%)	3.68 (1.60, 5.77)	1.29(0.91,1.82)
Man	2,036,618 (0.6%)	4.49 (1.89, 7.10)	0.98(0.75,1.27)
Others	5,626,773 (1.7%)	4.16 (2.65, 5.66)	1.12(0.95,1.33)
Regions	346,731,265		
Northwest China	17,853,679 (5.1%)	4.96 (4.17, 5.75)	2.67(2.34,3.04)
Northeast China	54,935,490 (15.8%)	3.93 (2.58, 5.28)	2.24(2.01,2.49)
East China	119,509,294 (34.5%)	3.78 (2.49, 5.08)	2.08(1.88,2.31)
Central China	52,533,725 (15.2%)	3.19 (1.03, 5.35)	2.53(2.25,2.83)
Southwest China	26,421,373 (7.6%)	3.69 (0.68, 6.70)	2.47(2.19,2.78)
South China	75,477,704 (21.8%)	2.04 (0.38, 3.71)	reference

Risk ratios for ethnic groups were estimated adjusting for province, incident year, age group (10 years) and sex. Risk ratios for regions were estimated adjusting for incident year, age group (10 years), sex and ethnic groups.

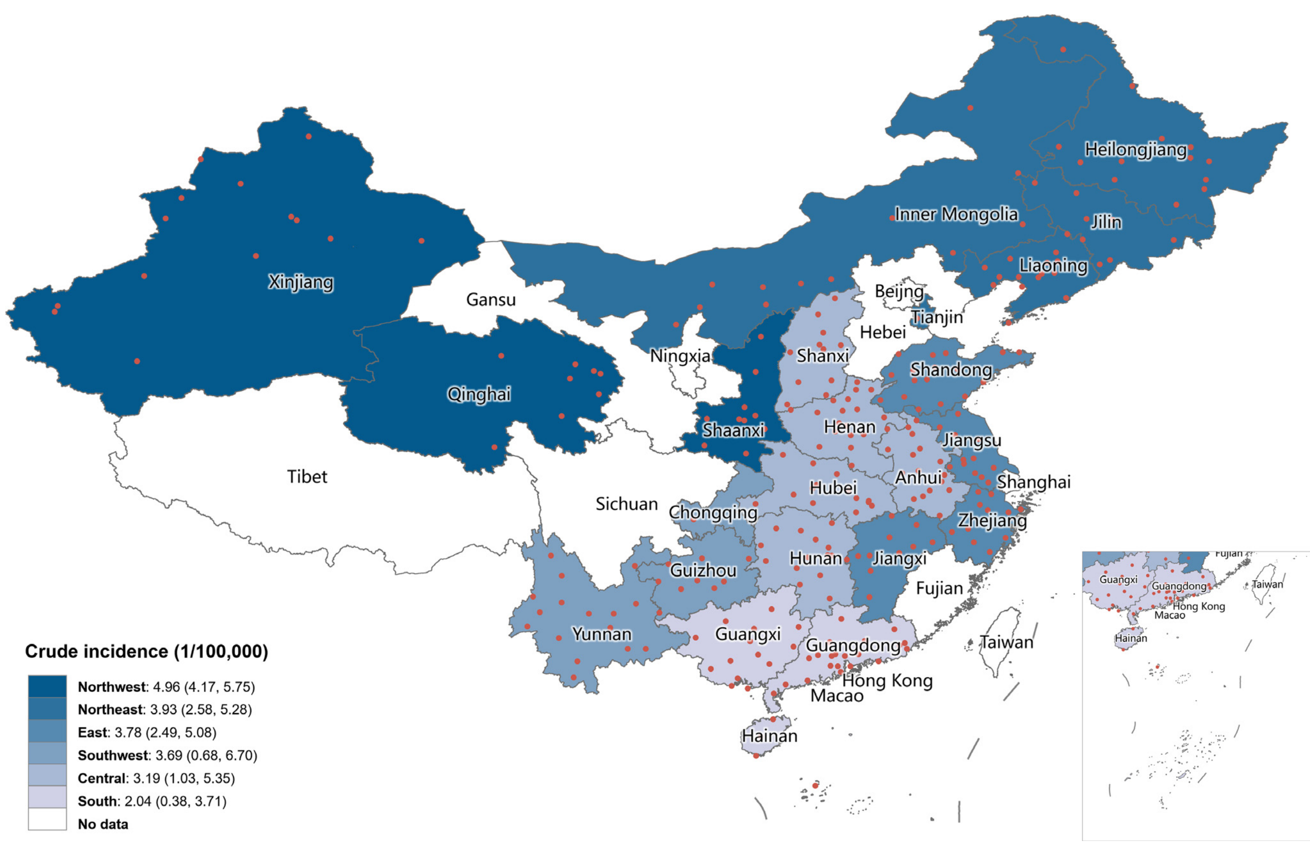

Figure 3. Map for incidence rate in different regions of China (Caption: The red spots on the map represent cities covered in our study).

rate was significantly higher in Northwest China (4.96 [95%CI, 4.17-5.75] per 100,000 person-years) than in South China (2.04 [95%CI, 0.38-3.71] per 100,000 person-years) based on geographic regions (**Figure 3**). After adjustment for incident year, age group, sex, and ethnic groups in the Poisson regression model, the risk ratio for Northwest remained statistically significant (risk ratio: 2.67 [95%CI, 2.34-3.04]). As the variance in each region is still high, the incidence rates in each province were presented in the forest plot for comparisons (**Figure 4**).

In regard to the sensitivity analysis, the weighted incidence rate of AD ranged from 2.03(95%CI, 1.95-2.10) per 100,000 person-years for the lower bound without any imputation methods to 2.81(95%CI, 2.62-3.00) per 100,000 person-years for including suspected AD cases in analysis. Moreover, the estimated weighted incidence rate by the negative binomial regression model was 2.79 (95%CI, 2.59-2.98) per 100,000 person-years, suggested that our results were robust. (**eTable 5**)

Survival analysis

During 9341 person-years of observation (median 2.2 years), totally 683 deaths were recorded. Among these deaths, 353(51.7%)

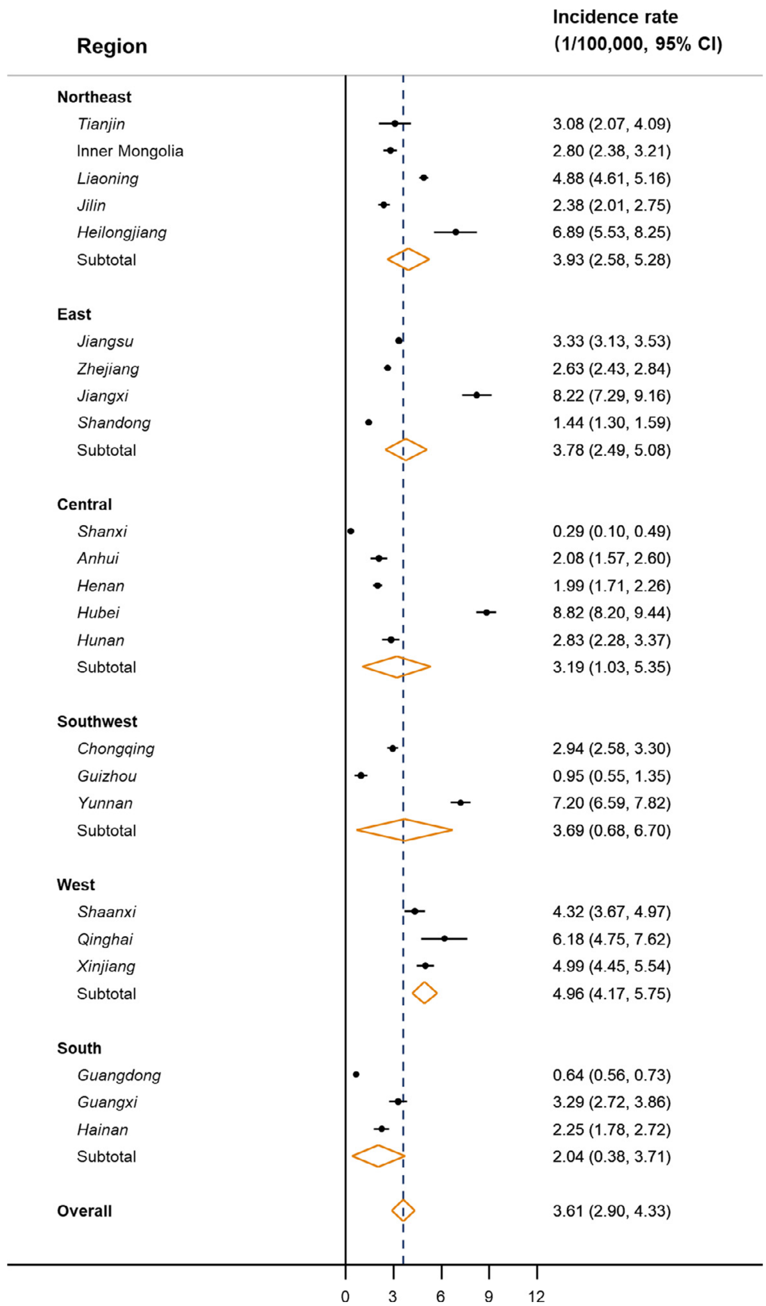

Figure 4. Crude incidence rate of aortic dissection in different regions of China

occurred within the first 30 days and 557(81.6%) were within one year. The overall crude mortality rate for AD cases during follow-up was 73.1(95%CI: 67.7-78.8) per 1,000 person-years. The average age at death was 67.8 (SD:14.3) years. (**eTable 6**).

Kaplan-Meier survival curves of patients with AD were displayed in **Figure 5**. The crude 3-year survival for these patients were 83.7%(95%CI: 82.4%-84.8%) for all AD patients, respectively (**eTable 6**). Moreover, the age and sex-specific mortality rate of AD cases during follow-up were showed in **eFigure 1**. Mortality increased with age in both sexes. Substantial increment was observed after 70 years, especially for women. AD mortality increased from 26.32(95%CI: 11.36-51.86) in age less than 40 years to 304.19(95%CI: 230.39-394.12) per 1000 person-years in age over 80 for women, and from 29.37(95%CI: 19.01-43.36) to 254.56(95%CI: 204.96-312.55) for men, respectively (**eTable 7**). Compared with men, mortality in women went up faster with age.

Discussion

Our study using large-scale claims demonstrated a comparative incidence rate and survival of AD as earlier studies. For example, recent studies have reported AD incidence rates in Minnesota, United States (4.4/100,000) [13], Ontario, Canada (4.6/100,000) [14], Oxfordshire, United Kingdom (6/100,000) [15], New South Wales, Australia (3.47/100,000) [16], Iceland (2.53/100,000) [3], and Korea (3.76/100,000) [17]. The incidence rate of AD in Taiwan province increased from 4.3/100,000 during 1996-2001 to 5.6/100,000 during 2005-2011, based on data from health insurance database [18,19]. The International Registry of Acute Aortic Dissections (IRAD) study reported that 16% patients with type A acute AD died during 5-year follow-up [20]. The 3-year survival for discharged patients ranged from 69% to 90% among the acute type

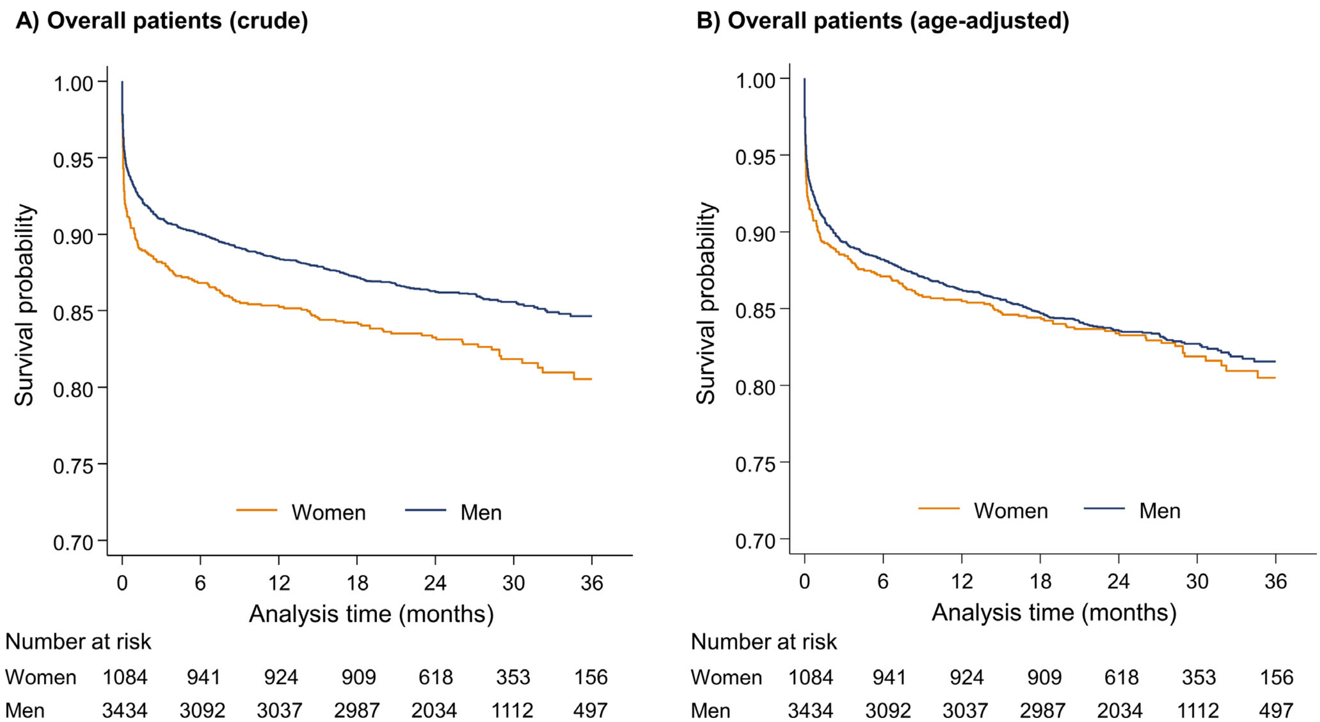

Figure 5. Survival curve of aortic dissection patients in China.
Total 4518 aortic dissection patients were included. During a median follow-up of 2.2 years, 683 deaths were recorded.
A) Kaplan-meier survival curve was plotted among overall aortic dissection patients by sex. The 3-year survival rates for overall, women and men patients were 83.7% (95%CI: 82.4, 84.8), 84.7% (95%CI: 83.3, 86.0) and 80.5% (95%CI: 77.7, 83.1), respectively; B) the survival probability of patients in men and women was estimated adjusting for age (65 years). The 3-year survival rates for overall, women and men patients were 80.9% (95%CI: 73.2, 86.6), 80.2% (95%CI: 72.6, 85.8) and 81.6% (95%CI: 74.5, 86.9), respectively. Detailed estimations were shown in **eTable 6**.

A AD patients and 76% to 83% among the acute type B AD patients [21].

It is noted that, especially for the estimation of incidence, some published information may not be representative of the population because many regional studies on population-based cohorts or electronic health records-based registries do not have sufficient patients as numerator or accurate source population as denominator estimation when calculating the rate. Although reliable age-specific population-based incidence figures of AD are available for Western countries, such data as well as the survival are not previously available in China [22]. The incidence in our urban Chinese population is higher in men than in women and increases with age, which is consistent with population-based study from other European countries, while the mean age of our urban Chinese population is notably younger than western populations (e.g., 58.2 in China *vs.* 66.9 in Iceland [3] and 70 in Sweden [23]). This finding is of relevance in the likely trajectory of the incidence of AD as the recent trend of population aging in China.

Besides age, the incidence of AD is related to the prevalence of risk factors, the most important being untreated hypertension [2,15]. Compared with Western nations, higher prevalence of hypertension, as well as lower awareness and control rates in China, could account for regional variations in the rates of AD incidence. Moreover, our study indicated higher AD incidence rates in North than South, which is consistent with the fact that prevalence of hypertension was significantly higher in northern than southern China [24]. The geographic disparities in both our study and another population-based study [25], suggested that increased attention should be paid to these specific regions with different strategies in hypertension and other risk factor management. Recent data from the China PEACE Million Persons Project showed that even among Chinese adults aged 35-75 years with health insurance (albeit with copayments), nearly half have hypertension, while fewer than one third are being treated, and fewer than one in twelve are in control of their blood pressure [26]. Our study only estimated the incidence of AD in urban China. Of note, compared with urban populations, rural Chinese had higher hypertension prevalence while lower awareness, treatment, and control rates [26], thus rural residents might have higher incidence and mortality of AD which requires further investigations. This situation should inform measures that could help promote primary prevention of hypertension to avoid future AD incidence increase in China.

Strengths and limitations of this study

The main strengths of this study include a well-defined subset of urban Chinese population and a large quantity of AD cases included in the analysis, which permitted evaluation of geographic variations, as well as sensitivity analyses that allowed a comprehensive approach to assessment of the robustness of incidence rate. Because the total population is drawn from administrative claims across China census regions, our study overcomes selection biases associated with tertiary single or multicenter investigations. Given the size and demographic heterogeneity of the cohort, these results may be at least generalized to the insured urban Chinese population. Nevertheless, this retrospective analysis also has limitations that warrant consideration when interpreting the results. Firstly, our analysis is subject to the limitations inherent to research based on the claims database. As other epidemiological studies [27], we could not capture patients with AD who were excluded out of hospital deaths that did not get clinically diagnosed. From this perspective, similar to other relevant studies [14,17], this may cause the underestimation of AD incidence rate and overestimation of AD survival. But the seriousness of AD along with stable and reproducible diagnostic definitions gives reason to believe that there were few false-positive cases; hence, our results provided a reasonably conservative underestimation of AD incidence rate. Secondly, our study was only based on the insurance database in urban China without nationwide representative sampling used in traditional epidemiological survey, regardless of the relatively large sample size. However, traditional survey may not be feasible for rare diseases such as AD. Thirdly, we could not differentiate between type A and B for numerous AD cases. This might affect the survival estimations for subtypes of AD shown in the supplementary documents. Many important clinical features for AD patients were not included in analysis, since this information is not made available in the database. However, the focus of the present study was the incidence with respect to demographic characteristics. Finally, the data reported here was from two years only (i.e. 2015-2016) and presentations might not reflect secular trends.

Conclusions

This contemporary population-based study provides, to our knowledge, a first comprehensive assessment of the incidence and survival of AD in urban China. The distinct signatures of the different incidence with respect to age and geographic variations may have important implications for clinical management of risk factors and planning of health services.

Contributors

Dr Xun Tang and Ke Lu contributed equally as first authors, and Drs Pei Gao, Yuan Wang and Jie Du contributed equally as corresponding authors. Dr Pei Gao had full access to all of the data in the study, and Drs Pei Gao, Yuan Wang and Jie Du take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Xun Tang, Ke Lu, Pei Gao, and Jie Du drafted the manuscript. All authors contributed to the study design and implementation, interpretation of results, and critical review of the manuscript for important intellectual content. All authors approved the final version of the manuscript.

Data sharing statement

No additional data available.

Editor note

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Declaration of Competing Interest

There are no conflicts of interest to declare.

Acknowledgements

This study was supported by the Chinese Ministry of Science and Technology (2020YFC2003503, 2016YFC0903000), and the National Natural Science Foundation of China (91846112, 81973132, and 81961128006).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.lanwpc.2021.100280.

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