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ORIGINAL ARTICLE

Hypertension and mortality in the Golestan Cohort Study: A prospective study of 50 000 adults in Iran

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High blood pressure has been the second most important determinant of disease burden in Iran since the 1990s. Despite well-recognized evidence on the association of high blood pressure and mortality in other countries, this relationship has not been fully investigated in the demographic setting of Iran. The current study is the first large-scale longitudinal study of this association in Iran. Briefly, 50 045 subjects between 40 and 75 years of age have been recruited and followed. Blood pressure measurements were carried out at baseline. Causes of death were reported and verified by verbal autopsy throughout the follow-up period. The outcomes of interest were all-cause deaths and deaths due to ischemic heart disease (IHD) or stroke. Cox proportional hazards regression models were used to estimate hazard ratios (HRs). A total of 46 674 subjects free from cardiovascular disease at baseline were analyzed. Absolute mortality rates increased along with increasing systolic or diastolic blood pressure above 120 and 80 mm Hg, respectively. Adjusted HRs (95% confidence intervals) for each 20 mm Hg increase in systolic blood pressure in all age groups were 1.18 (1.13–1.23) for all-cause mortality, 1.21 (1.13–1.31) for deaths due to IHD and 1.50 (1.39–1.63) for deaths due to stroke. Unadjusted and adjusted HRs were higher in younger subjects and decreased with increasing age of the participants. High blood pressure is a serious threat to the health of Iranians. The entire health-care system of Iran should be involved in a comprehensive action plan for controlling blood pressure.

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INTRODUCTION

High blood pressure is a well-recognized risk factor for several causes of morbidity and mortality,[1–4] chiefly ischemic heart disease (IHD) and stroke. The Global Burden of Disease (GBD) study 2010 reported high blood pressure as the second most important contributor to the burden of disease in the world.[5] On the basis of GBD 2010, Disability-Adjusted Life Years (DALYs) lost attributable to hypertension surpasses several other important risk factors such as alcohol use, cigarette smoking and high body mass index in most countries.[5]

In Iran, high blood pressure has remained the second most important determinant of disease burden in Iran from 1990 to 2010.[5–7] During this period, the percentage of total DALYs attributed to high blood pressure increased from 6% of DALYs in 1990 to 10% of DALYs in 2010, suggesting an increase in importance.[7] However, these estimates are based on assumptions about the prevalence and relative risk of various outcomes associated with hypertension in Iran. Many of these estimates are obtained from studies conducted in other countries, mostly Western countries, and they may not be accurate reflections of the comparable numbers in Iran or other Middle-Eastern countries. For example, although evidence shows that the prevalence of high blood pressure is declining in Western countries,[8,9] there seems to be a rise in mean blood pressure in developing countries.[10] Considering the higher number and rates of deaths and morbidities in developing countries, high blood pressure may exert a higher burden in middle and low-income countries than in the high-income world.[10,11]

There are indeed some data on the prevalence of hypertension in Iran. A nationwide study of adults aged 18 years and older, using data from the Third National Surveillance of Risk Factors for Non-Communicable Diseases (2007), showed the prevalence of hypertension was 26.6%.[12] This is comparable with what has been found in studies from other countries, such as the 28.5% prevalence reported from the National Health and Nutrition Examination Survey (NHANES) in the United States.[8] Studies of older populations in Iran have, as expected, shown higher prevalences of hypertension. For example, a recent report on the prevalence of hypertension from a cohort of individuals aged 40 or higher showed a prevalence of 42%.[13]

As for relative risks, there are only two studies from Iran on the association of blood pressure with cardiovascular event mortality. In a study by Hadaegh *et al.*[14] in 2012, each one standard deviation increase in systolic blood pressure (SBP) was associated with a 35% increased risk of cardiovascular disease mortality. Farzadfar *et al.*[15] showed that in 2005, 41 000 deaths were attributable to high blood pressure in men and 39 000 deaths in women, and if blood pressure had been optimal, life expectancy would have increased significantly. However, large prospective studies are the best research designs to accurately calculate the

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hazard ratios (HRs) of high blood pressure at the population level. In the current study, we aimed to estimate the association between high SBP and diastolic blood pressure (DBP) and all-cause mortality, mortality due to IHD and stroke among the adult general population, using data from the Golestan Cohort Study, the largest prospective cohort study in Middle East and North Africa. Additional blood pressure indices were also evaluated, including hypertension, the difference between SBP and DBP, and the difference in blood pressure between right and left arms, recently suggested as a determinant of mortality.[16] The ultimate aim of the study was to investigate the association within the demographic and ethnic setting of Iran, and to test the consistency of these results with those previously reported from other countries.

MATERIALS AND METHODS

Study population

The Golestan Cohort Study (GCS) was launched in 2004 in eastern Golestan Province, in northeastern Iran. A total number of 50 045 participants aged 40–75 years were recruited from 2004 to 2008 and have been followed up for a median of 7.1 years. The participation rate was 81% in women and 66% in men. The primary objective of this cohort was to detect risk factors of esophageal cancer in Golestan Province. Sample size was calculated such that in 10 years, there will be enough cases of esophageal cancer to detect odds ratios between 1.5 and 2.0, depending on the prevalence of the exposure, with a power of 90%. This sample size ($n = 50\ 045$) provides ample power to detect the association between high blood pressure and total mortality, cardiovascular diseases, and stroke, as these outcomes are far more common than esophageal cancer. The only exclusion criteria were being either unwilling to take part in any stage of the study or being a temporary resident in Golestan Province. The details of the Golestan Cohort Study are available elsewhere.[17]

Data collection methods

Study participants were recruited from Gonbad city (20%) and 326 villages (80%) in eastern Golestan Province. Questionnaires were filled out by trained interviewers, and questions were asked about the following characteristics: residence area (urban or rural), marital status (married or not), ethnicity (Turkmen or non-Turkmen), education (five categories: illiterate, less than or equal to 5 years of education, 6–8 years of education, high school education or university education), wealth score (see below), smoking (pack years), opium use (ever used), physical activity (see below), and history of any heart disease (including rheumatic heart disease), stroke, chronic obstructive pulmonary disease, renal failure, liver disease, jaundice and tuberculosis.[17]

The wealth score was calculated using multiple correspondence analyses. A composite score was built on personal car, motorbike, black and white TV, color TV, refrigerator, freezer, vacuum cleaner and washing machine ownership variables, as well as house ownership, house structure, house size (tertiles), having a bath in the residence and occupation. The details are described elsewhere.[18] Physical activity was defined in terms of metabolic equivalent task.

Height and weight were measured at baseline, and body mass index was calculated for all participants. Also at baseline, blood pressure was measured twice, with a 10-min interval, from both arms in the sitting position using Richter auscultatory sphygmomanometers.

Follow-up

Participants were followed up by annual phone calls from their recruitment (2004–2008) through 30 October 2013. The follow-up was successful for over 99% of study participants. In case a death was identified by these phone calls, by local health workers or through monthly death registration reports, a general practitioner visited the home of the deceased. Causes of death were ascertained through verbal autopsy and the investigation of available medical documents. Using the collected documents, two independent internists determined the cause of death with ICD-10 codes. If the two were concordant, a diagnosis was made. Otherwise, the final diagnosis was made by a third more senior internist. Death due to IHDs was coded as I20–I25, and stroke was coded as I60–I69. Circulatory diseases, cancers, respiratory diseases, digestive diseases and injuries were the most prevalent other causes of death. The details of participant follow-up and cause of death determination procedures are described elsewhere.[19]

Definition of hypertension and study outcomes

The exposures of interest in this study included the levels of SBP and DBP as well as the prevalence of hypertension and prehypertension. The definitions of hypertension and prehypertension were adopted from the seventh report of the U.S. Joint National Committee on the prevention and control of hypertension (JNC7)[20] unchanged in eighth report and comparable with the 2013 practice guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC).[21] Hypertension was defined as having baseline SBP higher than or equal to 140 mm Hg, having baseline DBP higher than or equal to 90 mm Hg, or being under treatment with anti-hypertensive medications at any time during the preceding 6 months at baseline. Prehypertension was defined as having SBP higher than or equal to 120 mm Hg but less than 140 mm Hg, or having DBP higher than or equal to 80 mm Hg but lower than 90 mm Hg. This definition matches the definition of ESH/ESC of normal and high normal blood pressure. Optimal blood pressure was defined as having SBP less than 120 mm Hg and DBP less than 80 mm Hg.[20,21]

The outcomes of interest in this study included all-cause mortality, IHD mortality and stroke mortality. Individuals diagnosed as having heart disease or stroke at baseline were excluded from the analyses.

Statistical analyses

We used Cox proportional hazards models to estimate the relation between levels of SBP and DBP and all-cause and cause-specific mortality. Unadjusted and adjusted HRs and their 95% confidence intervals were calculated for each 20 mm Hg increase in SBP or 10 mm Hg increase in DBP. Adjustments were carried out for sex, ethnicity, residence area (urban or rural), marital status, wealth score, education, smoking, opium use, physical activity, body mass index, a history of diabetes, chronic respiratory or renal diseases, cancer, or tuberculosis, and being under hypertension treatment at baseline. Diabetes was diagnosed based on self-report or a history of medical treatment. These potential confounders were chosen based on reports of previous studies on GCS data which showed their association with all-cause or cause-specific mortality.

We performed similar analyses for hypertension and prehypertension, as defined above. The reference group for hypertension included subjects with SBP lower than 140 mm Hg and DBP lower than 90 mm Hg. The reference group for prehypertension included subjects with SBP lower than 120 mm Hg and DBP lower than 80 mm Hg. We also performed analyses of pulse pressure (defined as SBP-DBP), mean arterial pressure (2/3 DBP+1/3 SBP) and mid blood pressure (1/2 SBP+1/2 DBP).[2] A number of studies have reported an association of pulse pressure with incidence of myocardial infarction.[22,23] Inter-arm comparisons were measured based on other significant results in previous studies.[16,24] HRs for the above mentioned alternative indices of blood pressure were calculated for each 20 mm Hg increase in pulse pressure, mean arterial pressure or mid blood pressure, or each 20 mm Hg difference in SBP or DBP between the two arms.

Code availability

Age-standardized mortality rates were calculated based on the 2006 census in Iran. All analyses were carried out in Stata software version 11 (StataCorp., College Station, TX, USA). Codes are available upon request from the corresponding author.

The study was approved by the ethics committee of Tehran University of Medical Sciences, and a written informed consent was signed by all participants in the study. Illiterate invitees were asked to visit the study center and to observe the procedures before signing the written informed consent.

RESULTS

A total number of 50 045 participants were recruited and followed up through 30 October 2013. A total of 3371 participants who were diagnosed as having heart disease or stroke before enrollment into the cohort were excluded. Thus, analyses were performed on the remaining 46 674 subjects. Participants were followed up for 328 441 person-years. About 58% of subjects were women, 76% were Turkmen, 81% were rural dwellers, 88% were married and 70% were illiterate.

The mean age of participants at baseline was 51.6 years (s.d.: 8.8): 49% were between 40 and 49 years, 31% between 50 and 59 years, 15% between 60 and 69 years and 5% were 70 years of age or more. The mean SBP was 127.0 ± 23.9 mm Hg and the mean DBP was 77.0 ± 13.7 mm Hg. The mean ± s.d. for SBP and DBP by sex and age are shown in Table 1. Both mean SBP and mean DBP were significantly higher in women compared wiht men ($P < 0.001$) and both mean SBP and mean DBP were also significantly higher in older than younger groups, in both men and women ($P < 0.001$). The difference in mean SBP was significant between categories of ethnicity, marital status, education, smoking, opium use and hypertension treatment. The difference in mean DBP was significant between categories of area of residence, marital status, education, smoking, opium use and hypertension treatment (Table 1).

A total of 3018 participants died during the follow-up, among whom 829 subjects have died because of IHD and 483 subjects died because of stroke. Among women, 1295 subjects died because of all causes, 359 because of IHD and 241 because of stroke. Among men, 1723, 470 and 242 subjects died because of all causes, IHD and stroke, respectively. The crude all-cause mortality rate (95% confidence interval), IHD mortality rate (95% confidence interval) and stroke mortality rate (95% confidence interval) were 918.9 (855.9–951.4), 252.4 (235.2–269.9) and 147.1 (133.9–160.1) per 1 00 000 person-years, respectively.

The lowess plots of age-standardized mortality rates are shown in Figure 1, in which SBP has been categorized into 10-mm Hg intervals and DBP into 5-mm Hg intervals. The mortality rates have been reported for all-cause and cause-specific mortality due to

Table 1. Means and standard deviations of baseline systolic and diastolic blood pressure among women and men and four age categories, area of residence, ethnicity, marital status, education, smoking, opium use and hypertension treatment status at baseline

	Number	*SBP (mm Hg) Mean ± s.d.*	*P-value*	*DBP (mm Hg) Mean ± s.d.*	*P-value*
All	46 674	127.0 ± 23.9		77.0 ± 13.7	
Females					
All	26 823	128.0 ± 24.6		77.7 ± 13.8	
40–49	13 522	122.2 ± 21.9	< 0.001	76.2 ± 13.6	< 0.001
50–59	8740	131.4 ± 25.2		78.9 ± 14.0	
60–69	3522	137.9 ± 26.0		79.9 ± 13.6	
70+	1039	142.2 ± 26.2		79.7 ± 13.5	
Males					
All	19 803	125.5 ± 22.8		76.2 ± 13.5	
40–49	9417	119.4 ± 19.3	< 0.001	74.9 ± 13.2	< 0.001
50–59	5924	127.3 ± 23.0		77.1 ± 13.8	
60–69	3077	134.5 ± 25.0		78.0 ± 13.6	
70+	1385	139.1 ± 24.4		77.8 ± 13.0	
Area of residence					
Urban	8934	126.8 ± 23.4	0.530	77.7 ± 12.2	< 0.001
Rural	37 682	127.0 ± 24.0		76.9 ± 14.0	
Etnicity					
Turkmen	34 939	127.3 ± 24.2	< 0.001	77.0 ± 14.1	0.553
Non-Turkmen	11 678	126.1 ± 23.0		77.1 ± 12.3	
Marital status					
Married	41 126	126.2 ± 23.5	< 0.001	76.9 ± 13.6	< 0.001
Non-married	5491	132.3 ± 26.1		78.1 ± 14.0	
Education					
Illiterate	32 543	128.6 ± 24.9	< 0.001	77.2 ± 14.1	< 0.001
⩽5 years	7983	124.2 ± 21.6		77.0 ± 12.9	
6-8 years	2083	122.3 ± 20.2		76.1 ± 12.2	
High school	3001	121.6 ± 19.6		76.1 ± 12.2	
University	1007	122.0 ± 19.2		77.2 ± 11.6	
Smoking					
Ever smoker	7939	121.9 ± 22.5	< 0.001	74.1 ± 13.5	< 0.001
Never smoker	38 678	128.0 ± 24.0		77.7 ± 13.6	
Opium use					
Ever	7709	123.1 ± 24.5	< 0.001	73.8 ± 14.2	0.001
Never	38 908	127.7 ± 23.7		77.7 ± 13.5	
Hypertension treatment					
No	27 960	114.0 ± 13.5	< 0.001	70.9 ± 10.3	< 0.001
Yes	18 694	146.5 ± 22.7		86.2 ± 13.0	

Abbreviations: DBP, diastolic blood pressure; SBP, systolic blood pressure.

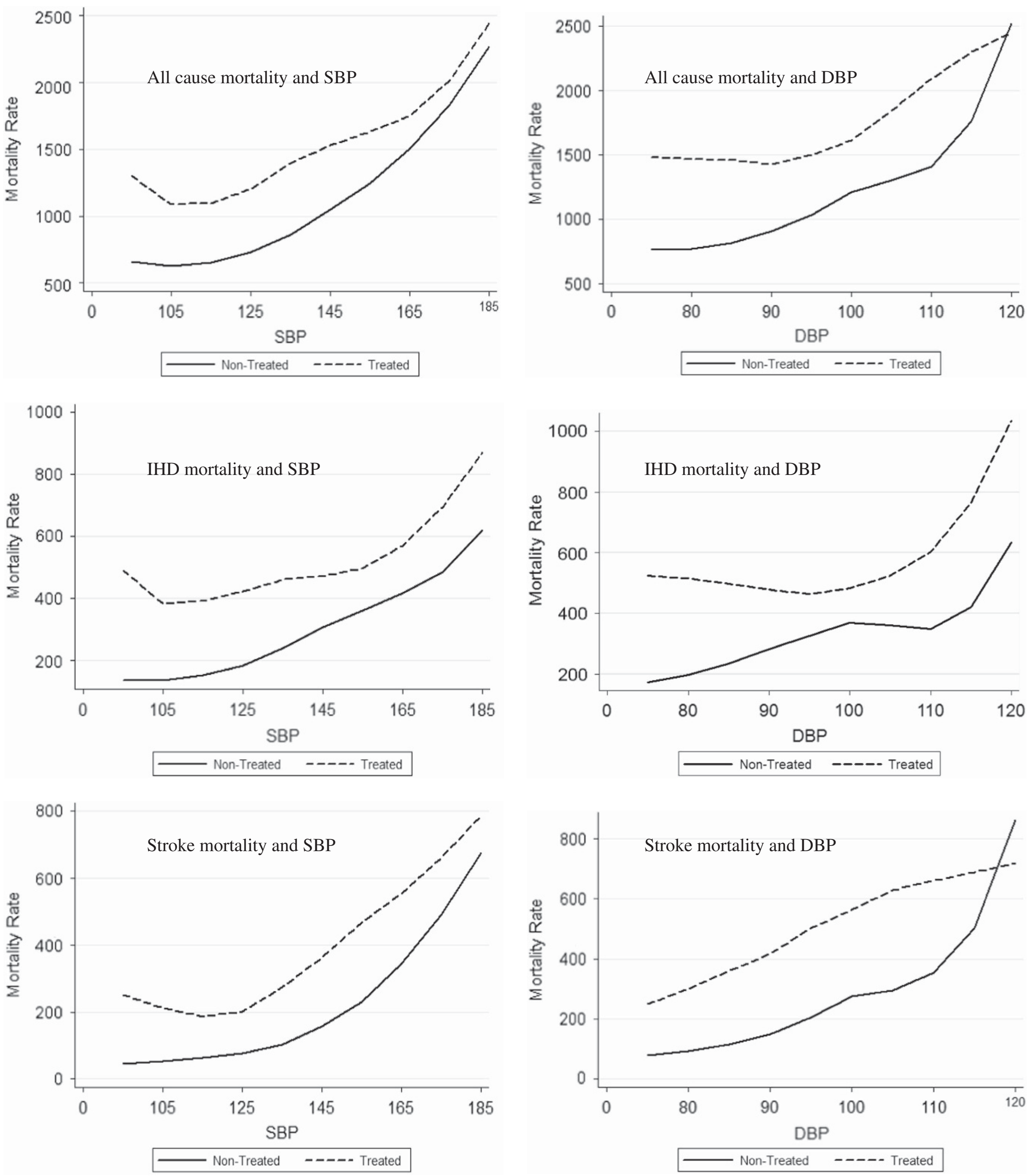

Figure 1. Age-standardized mortality rates by SBP and DBP levels.

IHD and stroke, stratified by hypertension treatment groups. For both SBP and DBP, the mortality rates decline with decreasing blood pressure until a point where a further decline in blood pressure is associated with a steady state or increase in the mortality rate. For SBP, the lines of the mortality rates level off at 115 mm Hg, above which no evidence of any threshold in rate can be seen and below which, the HR is insignificant. The same happens for DBP at 75 mm Hg. Another important point to note is that along the entire range of SBP and DBP, mortality rates are higher in the treated group compared with the non-treated group of subjects.

The age-specific HRs for association of mortality with each 20 mm Hg increase in SBP higher than 120 mm Hg and each 10 mm Hg increase in DBP higher than 80 mm Hg are shown in Figure 2. These thresholds were chosen because they were defined in the JNC7 report as the upper limits for optimal SBP and DBP. They also roughly correspond to where the age-standardized mortality rate curves become flat in our study. This figure shows that with increasing age, the HRs of mortality associated with SBP and DBP declined, especially in the case of stroke. The highest HR for stroke (2.07) was observed in the 40–49-year-old group.

Finally, the unadjusted and adjusted HRs for the association of mortality and hypertension, prehypertension, pulse pressure, mean arterial pressure, mid blood pressure and the difference in SBP and DBP between the left and right arms are shown in Table 2. These results show that hypertension, pulse pressure,

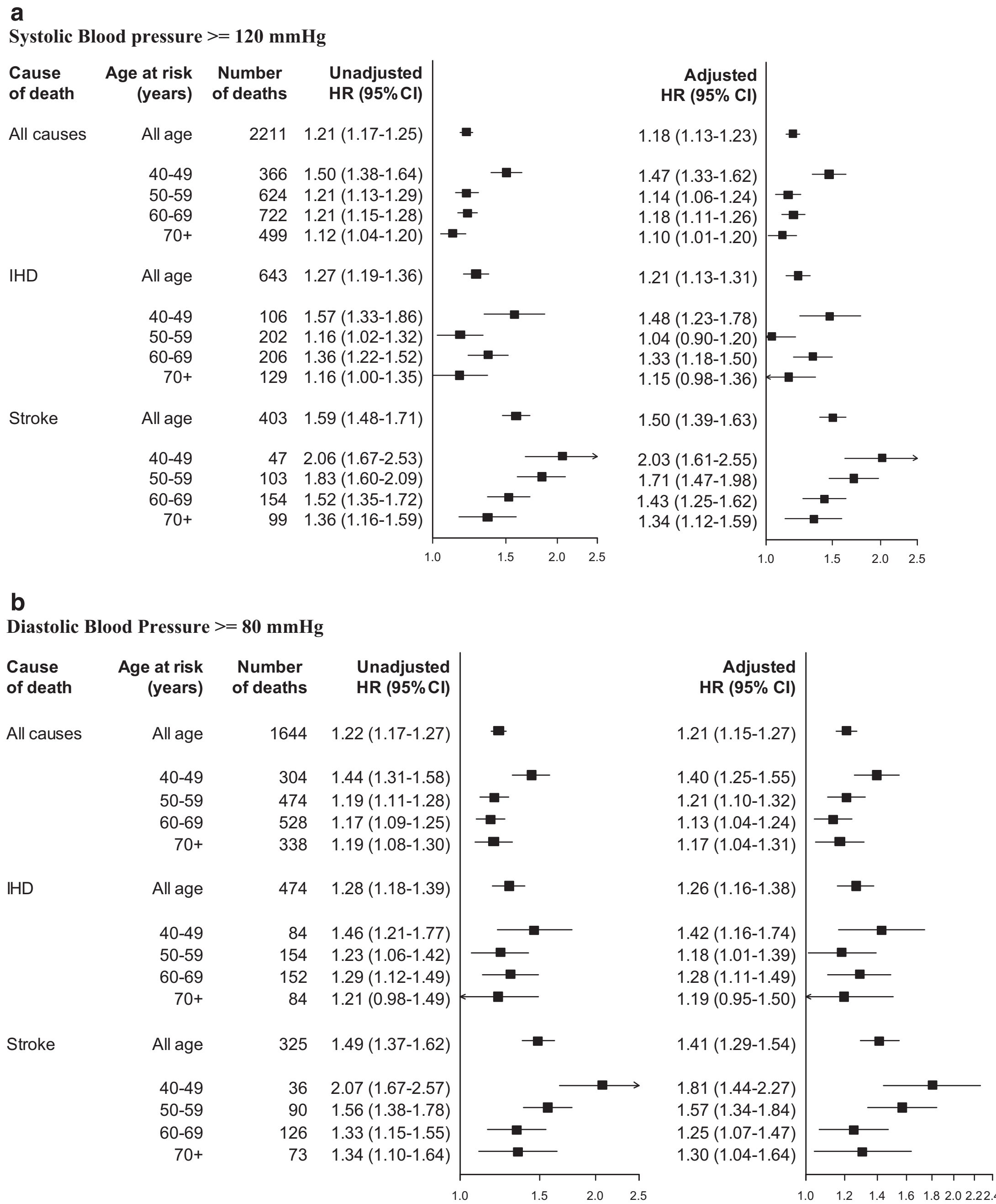

Figure 2. Unadjusted and adjusted HRs for the association between mortality and each 20-mm Hg increase in SBP and each 10-mm Hg increase in DBP.

mean arterial pressure and mid blood pressure were all positively associated with all-cause mortality, IHD mortality and stroke mortality.

DISCUSSION

The results of the current study show a strong association between high blood pressure and overall and cause-specific mortality. The association has been confirmed in numerous studies, leading to clinical guidelines for the treatment of high blood pressure to prevent these outcomes. Still, considering the differences between ethnicities, cultures and countries, it is important to investigate such associations between risk factors and outcomes in specific populations, to make better policy decisions.

The results of our study show a high prevalence of hypertension in Golestan Province, in Northeastern Iran. The results also show that demographic characteristics may have differential associations with the level of blood pressure. For example, in our study, men had lower blood pressures than women at all ages, which is consistent with previous reports.[13] Turkmen, non-married and illiterate subjects, non-smokers and those subjects who do not consume opium also had higher mean SBP. Similarly, urban dwellers, non-married and illiterate subjects, non-smokers and those subjects who do not consume opium had higher mean DBP. Interestingly, although these results related to smoking and opium use may not seem plausible, their effect sizes became greater

Table 2. Hazard ratios for the association of blood pressure indices with all-cause and cause-specific deaths.

Blood pressure index	*All-cause mortality*		*IHD mortality*		*Stroke mortality*	
	Unadjusted hazard ratio	*Adjusted[a] hazard ratio*	*Unadjusted hazard ratio*	*Adjusted[a] hazard ratio*	*Unadjusted hazard ratio*	*Adjusted[a] hazard ratio*
Hypertension[b]	1.35 (1.26–1.46)	1.49 (1.38–1.61)	1.85 (1.60–2.14)	1.90 (1.63–2.22)	2.78 (2.25–3.41)	2.90 (2.33–3.60)
Prehypertension[c]	0.92 (0.83–1.03)	1.03 (0.92–1.16)	1.11 (0.88–1.40)	1.24 (0.98–1.58)	1.06 (0.74–1.51)	1.06 (0.74–1.53)
Pulse pressure (SBP–DBP)[d]	1.20 (1.15–1.24)	1.16 (1.12–1.21)	1.34 (1.24–1.44)	1.24 (1.15–1.34)	1.61 (1.48–1.75)	1.46 (1.34–1.59)
Mean arterial pressure (2/3DBP+1/3SBP)[d]	1.16 (1.11–1.22)	1.21 (1.16–1.27)	1.34 (1.23–1.45)	1.29 (1.18–1.41)	1.87 (1.69–2.06)	1.74 (1.57–1.94)
Mid blood pressure (1/2SBP+1/2DBP)[d]	1.16 (1.12–1.21)	1.20 (1.15–1.25)	1.32 (1.23–1.42)	1.27 (1.18–1.38)	1.78 (1.63–1.94)	1.67 (1.52–1.83)
Difference in SBP between two arms[d]	1.10 (1.02–1.19)	1.05 (0.98–1.14)	1.24 (1.08–1.43)	1.19 (1.03–1.37)	1.20 (1.00–1.45)	1.12 (0.94–1.35)
Difference in DBP between two arms[d]	1.03 (0.92–1.15)	1.00 (0.89–1.12)	1.13 (0.91–1.41)	1.13 (0.91–1.40)	1.19 (0.90–1.57)	1.13 (0.86–1.49)

Abbreviations: DBP, diastolic blood pressure; IHD, ischemic heart disease; SBP, systolic blood pressure. [a]Adjustment has been carried out for sex, ethnicity, residence area (urban or rural), marital status, wealth score, education, smoking, opium use, physical activity, body mass index, and history of diabetes, chronic respiratory or renal diseases, cancers or tuberculosis at baseline. For indices other than hypertension and prehypertension, treatment of hypertension was also included in the adjusted model. [b]High blood pressure (SBP or DBP ⩾ 140/90 mm Hg) versus normal blood pressure (SBP and DBP < 140/90 mm Hg). [c]Prehypertension (defined as SBP and DBP < 140/90 mm Hg and SBP ⩾ 120 mm Hg or DBP ⩾ 80 mm Hg) versus optimal blood pressure (SBP and DBP < 120/80 mm Hg). [d]Hazard ratios have been calculated for the association of mortality rates with each 20 mm Hg increase or difference in or between SBP or DBP.

when HRs were adjusted for other confounders such as sex and education (data not shown).

Figure 1 shows a J-shaped curve of all-cause and cause-specific mortality rates versus 10-mm Hg intervals for SBP and 5-mm Hg intervals for DBP. The declining SBP curve levels off around 115 mm Hg and the DBP curve around 75 mm Hg. These are quite consistent with previous studies, including the Framingham Study, the Western Collaborating Group Study, the Whitehall study and the reports of the Prospective Studies Collaboration.[1–4] In fact, these results confirm the evidence that was used by the Global Burden of Disease 2010 to define the theoretical minimum for calculating the population attributable fraction of mortality attributable to high blood pressure.[5,10]

Another important point worth noting in our study is the higher mortality rates in the treated group compared with the non-treated. These results make perfect sense, as treated subjects with levels of SBP and DBP equivalent to the non-treated group have been exposed to higher blood pressures before they were treated, and thus they are at a greater risk of mortality attributable to the effects of long-term non-optimal blood pressure.

Our results show that in this population, each 20-mm Hg increase in SBP or each 10-mmHg increase in DBP is associated with an approximately 20% increased risk of all-cause mortality. Generally, the HRs were higher in younger groups compared with older people. In other words, treating high blood pressure may have a more protective effect in younger age groups. However, as the total number of deaths is higher in older age groups, the net number of deaths that can be prevented by treating hypertension among the elderly is higher than the number of deaths that can be prevented by treating young people.

Our results also show that there is a strong association in our population between classically defined hypertension and both overall and cause-specific mortality, and similar associations are seen with pulse pressure, mean arterial pressure and mid blood pressure (Table 2). The significant associations of pulse pressure, mean arterial pressure and mid blood pressure with mortality are consistent with previous reports,[2,22,23,25] and they support the hypothesis regarding the association of rigidity in arteries, as measured by any kind of difference between SBP and DBP, with mortality due to cardiovascular events. We found no significant association between prehypertension and mortality, however, which is consistent with the result of a previous study in Iran[26] but contrary to reports from other countries.[27] Neither could we find any association of mortality with the differences in SBP or DBP between right left arm measurements.

Our study has a number of limitations. All of the analyses were carried out based on a single set of measurements at the beginning of the study, which makes it prone to regression dilution bias, and we have not been able to adjust the results accordingly. Another limitation was the probable imprecision in self-reported or unreported clinical conditions at baseline. This imprecision is highest for diabetes as previous studies in Iran have demonstrated that nearly half of diabetics are unaware and thus, the prevalence of diabetes is highly underestimated.[12] A third limitation is the classification of causes of death, which may include errors despite measures such as verbal autopsies that were taken to ensure the quality of these data. And finally, our study had a potential bias in categorization of subjects into treated and non-treated groups, because some subjects may have reported being under treatment, although they were not actually adhering to their prescribed treatment, and a number of other subjects, especially in the illiterate group, may have been under treatment advised by their physicians but were not aware of it or may not have known the name of the medication they were using.

In light of the results of this study, the necessity of investigating the underlying determinants of hypertension in Iran becomes clear. Many factors have been demonstrated to be associated with high blood pressure in other countries, including urbanization, a Western diet, high salt intake, physical inactivity and smoking, collectively considered as demographic and epidemiologic characteristics of societies in transition. Numerous randomized controlled trials have also demonstrated the effectiveness of various interventions in preventing hypertension through controlling these determinants.[28] Studies in Iran show that the diet in a very high proportion of urban dwellers does not meet the World Health Organization (WHO) nutritional goals. Almost half of the population over-consume grains and 20% over-consume dairy products and meat. Intake of poly-unsaturated fatty acids, sodium, fruits and vegetables shows the largest deviation from WHO goals in urban dewellers.[29] Meanwhile in rural dwellers, intake of vitamins is also much less than recommended values.[30] The high sodium intake is partly due to its high values hidden in processed food, rice and bread, and partly due to high consumption of salt at table. Apart from diet, certain unhealthy life style behaviors are prevalent among Iranians including high consumption of tobacco and especially opium, and low levels of physical activity due to inappropriate urban environment. These determinants may have significant contribution to high incidence and prevalence of risk factors for hypertension.

New guidelines have been released in the United States regarding treatment plans for lowering blood pressure. In the general population aged 60 years or older, pharmacologic treatment should be initiated to lower SBP to less than 150 mm Hg and DBP to less than 90 mm Hg, while in the general population <60 years of age, pharmacologic treatment should be initiated to lower SBP to less than 140 mm Hg and DBP to less than 90 mm Hg.[31–34]

Controlling hypertension through the above-mentioned primary and secondary prevention requires a comprehensive action plan that involves the entire health-care system and all collaborators in relevant sectors. After the Islamic revolution in 1979 in Iran, an extensive primary health-care network was established. Through this stratified network, free primary care is provided to disadvantaged communities.[35] Currently 33 000 community health workers (known as 'Behvarz') provide care in 17 600 health houses, which are the most peripheral facilities in the network. Behvarz' are trained personnel recruited from the community covered by the health house. Behvarz' were originally responsible to deliver maternal and child health care, family planning, vaccination, symptomatic treatment of common symptoms and early case detection for diseases like malaria and tuberculosis. Significant decrease in incidence and prevalence of maternal and child mortality, infectious and nutritional diseases, as well as decline in fertility rate were the foremost accomplishments of this system. However, the current system does not possess the necessary capacity for provision of care for non-communicable diseases. New service packages are required to integrate primary care for non-communicable diseases into the network. Further research is also needed to determine the cost effectiveness of each of these service packages at a national scale.

Apart from the health system by itself, the overall economic and social determinants also affect the health of populations. Economic challenges have been vast after the 1979 revolution of Iran, due to domestic strife, an 8-year war and economic sanctions. After the revolution, Iran's gross domestic product (per capita) was halved by 1988 but returned to its original value in 2006. The high inflation rate has been a continuous challenge. The proportion of total health expenditure out of gross domestic product ranged between 1.5 and 2.7% from 1996 till 2006 and the out-of-pocket payment has been over 55%.

Despite all these negative economic indicators, the indicators of access to care (either primary care mentioned above or secondary care) have improved since 1979. The population coverage by primary care in rural areas is over 90%. There are 51 medical schools in Iran. Along with the establishment of medical schools in all provinces, the number of trained physicians, nurses, midwives and other health-care personnel (including Behvraz') has increased, which by themselves have improved access to care. There were 5 physicians per 10 000 in 1976, which increased to 13 in 2007. In 2011, there were 100 000 physicians (14 per 10 000) and 170 000 nurses (22.5 per 10 000) in Iran. In 2007, there were 13 active hospital beds per 10 000 while in 2011, there were about 17 per 10 000, with 82% of hospital beds being in public hospitals. Along with the current plans of the new government in Iran, it is expected that universal health coverage be available for all Iranians, covering up to 90% of costs for patients' medical bills at public hospitals and provision of extra care to remote areas and those suffering from rare diseases. Ultimately, it is the vision and mission of the government in general and the Ministry of Health in particular to establish evidence-based cost-effective policies at national scale, especially regarding the control of major non-communicable diseases and their risk factors, most important of which is high blood pressure.

What is known about topic

- The association of high blood pressure with higher all-cause and cardiovascular disease-specific mortality: Global estimates and national estimates in numerous developed countries have shown this association.
- The controversial association of alternative blood pressure indices (including pulse pressure, mid arterial and mean blood pressure, and difference between two arms) with mortality. Results of studies have been inconsistent in both developed and developing countries.

What this study adds

- The levels of systolic and diastolic blood pressure in a large representative sample of rural and urban areas in Iran as a developing country with scant epidemiological data on blood pressure.
- The association of high blood pressure and mortality in Iran: Global burden of disease studies and studies in developed countries have estimated the contribution of high blood pressure to mortality. The results of our study, however, showed the association adjusted for demographic, anthropometric and lifestyle determinants in a large cohort study for the first time in Iran, which showed the significant burden of high blood pressure in our developing country and its similarity to developed countries.
- The differential association of high blood pressure with mortality among treated versus non-treated participants. The results of our study showed that mortality rates were higher among treated compared with non-treated participants with similar levels of systolic and diastolic blood pressure.
- The association of alternative indices of high blood pressure with mortality. In our study, pulse pressure, mid arterial and mean blood pressure had significant association with mortality while prehypertension had no significant association.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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