

Adverse Cardiovascular Events Are Infrequent but Significantly Associated With Systolic and Pre-Systolic Hypertension: An Occupational Cohort Study

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Abstract

Background: Cardiovascular diseases (CVDs) remain the leading cause of global mortality. Different blood pressure subtypes may have varying associations with cardiovascular events, but evidence remains inconclusive in the working population. The objective of the study was to evaluate the incidence and differences between hypertension and prehypertension subtypes in the development of cardiovascular events in an occupational cohort.

Methods: A retrospective cohort study including 12,027 workers monitored over 8 years. The outcome variable was the development of CVD, including myocardial infarction and/or stroke. Hypertension subtypes were classified as normotension (systolic blood pressure (SBP) < 140 mm Hg and diastolic blood pressure (DBP) < 90 mm Hg), isolated systolic hypertension (SBP ≥ 140 mm Hg and DBP < 90 mm Hg), isolated diastolic hypertension (SBP < 140 mm Hg and DBP ≥ 90 mm Hg), and systolic-diastolic hypertension (SBP ≥ 140 mm Hg and DBP ≥ 90 mm Hg). Prehypertension subtypes were defined as isolated systolic prehypertension (SBP 120 - 139 mm Hg and DBP < 80 mm Hg), isolated diastolic prehypertension (SBP < 120 mm Hg and DBP 80 - 89 mm Hg), and systolic-diastolic prehypertension (SBP 120 - 139 mm Hg and DBP 80 - 89 mm Hg). Cox models were used to estimate crude hazard ratios (cHRs) and adjusted hazard ratios (aHRs), controlling for sociodemographic variables and cardiovascular risk factors.

Results: Isolated systolic hypertension (aHR: 6.78, 95% confidence interval (CI): 3.10 - 14.8) and isolated systolic prehypertension (aHR: 3.42, 95% CI: 1.73 - 6.74) showed significant associations with cardiovascular events, even after adjusting for confounding variables. Neither isolated diastolic nor systolic-diastolic prehypertension and hypertension showed significant associations.

Conclusions: While cardiovascular events were infrequent in this occupational cohort, those that occurred showed significant associations with both systolic hypertension and pre-systolic hypertension, suggesting the importance of systolic pressure monitoring in workplace health surveillance.

Keywords: Hypertension; Blood pressure; Cardiovascular diseases; Occupational health; Cohort studies; Risk factors (MeSH)

Introduction

Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide, accounting for approximately 32% of all global deaths, according to the World Health Organization (WHO) [1]. Hypertension and prehypertension have been consistently identified as significant modifiable risk factors for CVD development, with hypertension affecting more than 1.4 billion people globally [2]. However, the heterogeneity in presentation and underlying pathophysiological mechanisms of different blood pressure alteration subtypes suggests the need for a more detailed analysis of their specific impacts on cardiovascular outcomes.

Blood pressure alteration subtypes present distinct hemodynamic and pathophysiological profiles that could differentially influence the development of major cardiovascular events. Within the prehypertension spectrum, three subtypes are distinguished: isolated systolic prehypertension, isolated diastolic prehypertension, and systolic-diastolic prehypertension, each with particular characteristics that could represent different levels of cardiovascular risk (CVR) [3]. Similarly, in

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established hypertension, isolated systolic hypertension (ISH), characterized by elevated systolic pressure with normal diastolic pressure, is particularly prevalent in older populations and is associated with increased arterial stiffness [4]. Isolated diastolic hypertension (IDH), more common in young adults, has been linked to increased peripheral vascular resistance and alterations in endothelial function [5-8].

Current evidence on the differential impact of these subtypes on the development of specific cardiovascular events, such as stroke and myocardial infarction, has shown variable and sometimes contradictory results. Previous studies have suggested that both prehypertension and ISH might confer different levels of stroke risk, while systolic-diastolic patterns have been associated with an increased risk of multiple cardiovascular conditions [9-11]. However, most of these studies have been conducted in general populations, with limited data in working populations.

The working population represents a unique group for studying the relationship between blood pressure alteration subtypes and CVD, as they are subject to regular medical surveillance and present specific demographic characteristics and occupational risk factors. Occupational cohort studies offer the additional advantage of structured follow-up and the possibility of controlling for confounding factors related to the work environment [12]. Furthermore, identifying specific risk patterns in this population could have significant implications for prevention and management strategies in the occupational context.

A detailed understanding of how different blood pressure alteration subtypes, from prehypertension to established hypertension, contribute to CVD development in working populations is crucial for optimizing prevention and management strategies. This knowledge could enable more precise risk stratification and implementation of more targeted and effective interventions in occupational health. The present study addresses this knowledge gap by analyzing an 8-year occupational cohort, evaluating the association between prehypertension and hypertension subtypes and the subsequent development of major cardiovascular events.

Materials and Methods

Design

An analytical retrospective cohort study was conducted using secondary data from systematically collected occupational medical records between 2015 and 2023. The research was based on the analysis of periodic medical evaluations performed on workers who attended an occupational clinic for routine health examinations. To ensure research transparency and reproducibility, the design, analysis, and presentation of results adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies [13].

Population, sample, and eligibility criteria

The study population consisted of workers from various in-

dustrial sectors who attended periodic occupational medical evaluations at a reference occupational clinic. The established inclusion criteria required participants to have a minimum of two medical evaluations separated by at least 1 year during the study period and complete records of blood pressure and relevant cardiovascular variables at baseline and during follow-up. Workers with a history of previous CVD (myocardial infarction or stroke) at baseline were excluded from the study, as were those with incomplete blood pressure data.

Participant follow-up was conducted through periodic medical evaluations, with frequency determined by company policies and current labor regulations, varying between annual and biennial assessments. Workers were monitored from their initial review until a cardiovascular event of interest (myocardial infarction or stroke), their last recorded evaluation, or the end of the study period, whichever occurred first. If a cardiovascular event was diagnosed, follow-up for that specific participant was terminated at that point for incidence analysis.

Variables and measurement

The outcome variable of interest was the development of CVD, including myocardial infarction and/or stroke, which were confirmed through medical documentation and/or hospital records provided by participants during their periodic occupational evaluations.

The main independent variables of the study were the subtypes of prehypertension and hypertension. Hypertension subtypes were classified as normotension when systolic blood pressure (SBP) was < 140 mm Hg and diastolic blood pressure (DBP) < 90 mm Hg; ISH when SBP ≥ 140 mm Hg and DBP < 90 mm Hg; IDH when SBP < 140 mm Hg and DBP ≥ 90 mmHg; and systolic-diastolic hypertension (SDH) when SBP ≥ 140 mm Hg and DBP ≥ 90 mm Hg [4, 6, 14].

The prehypertension subtypes were defined as normotension (SBP < 120 mm Hg and DBP < 80 mm Hg), isolated systolic prehypertension (SBP 120 - 139 mm Hg and DBP < 80 mm Hg), isolated diastolic prehypertension (SBP < 120 mm Hg and DBP 80 - 89 mm Hg), and systolic-diastolic prehypertension (SBP 120 - 139 mm Hg and DBP 80 - 89 mm Hg).

Analyzed sociodemographic and occupational covariables included age (in years), sex (male/female), educational level, type of work (categorized as administrative, operational, or mixed), and work shift (day, night, or rotating). Blood glucose levels were categorized according to American Diabetes Association (ADA) criteria as normoglycemia (< 100 mg/dL), prediabetes (100 - 125 mg/dL), and diabetes (≥ 126 mg/dL or previous diagnosis). Nutritional status, assessed through body mass index (BMI), calculated as weight in kilograms divided by height in square meters, was classified according to WHO standards as normal weight (< 24.9 kg/m²), overweight (25 - 29.9 kg/m²), and obesity (≥ 30 kg/m²). Hypercholesterolemia was defined as total cholesterol ≥ 200 mg/dL and hypertriglyceridemia as triglycerides ≥ 150 mg/dL. Additionally, lifestyle data were collected, including alcohol consumption and current smoking status, both assessed through the question "Have you consumed alcohol/smoked in the last 30 days?" with pos-

sible responses being yes versus no.

Finally, follow-up time was quantified in person-years, considering each participant's first evaluation as a baseline and ending with the occurrence of the cardiovascular event or the last recorded evaluation.

Procedures

Occupational medical evaluations were conducted at three strategic points: at the beginning of employment (pre-occupational evaluation), during scheduled periodic examinations, and at the end of employment (exit evaluation). Workers completed a standardized questionnaire in each assessment that gathered information on sociodemographic data, personal history, and specific occupational characteristics.

Blood pressure measurement was performed by trained nursing staff, following American Heart Association guidelines. Automatic oscillometric sphygmomanometers (OMRON, model HEM-7320) calibrated monthly were used. Measurements were taken with the worker seated, after at least 5 min of rest, with the arm supported at heart level. Two measurements were taken 2 min apart, recording the average of both. A third measurement was taken in cases where the difference between measurements exceeded 5 mm Hg, and the two closest readings were averaged.

Venous blood samples collected after 8 - 12 h of fasting were used to obtain biochemical parameters. Samples were processed in the clinical laboratory to determine fasting glucose, lipid profile (total cholesterol, triglycerides), and other relevant metabolic markers. The laboratory participated in external quality control programs and followed standardized procedures according to international standards. Anthropometric measurements included weight, height, and abdominal circumference, performed by trained personnel following standardized protocols.

The medical evaluation was conducted by certified occupational physicians, who performed a structured interview to identify CVR factors, history of cardiovascular events, and occupational characteristics such as work shifts and level of occupational and physical activity. Confirmation of cardiovascular events (myocardial infarction or stroke) was performed through a review of medical documentation and hospital records provided by workers. All information was recorded in a standardized electronic system, following quality control procedures that included verification of inconsistent data and extreme values.

Statistical analysis

Statistical analysis was performed using R Studio version 4.1.0. For descriptive analysis of baseline population characteristics, absolute and relative frequencies were calculated for categorical variables. Meanwhile, means, standard deviations (SDs), medians, and interquartile ranges (IQRs) were obtained for continuous variables according to their distribution. Subsequently, cardiovascular event incidence rates per 1,000 per-

son-years of follow-up were calculated for each hypertension subtype, with their respective 95% confidence intervals (CIs).

To evaluate the association between each prehypertension/hypertension subtype and CVD development, univariate and multivariate Cox regression analyses were performed. Variable selection for multivariate models was conducted by constructing directed acyclic graphs (DAGs) specific to each of the six blood pressure alteration subtypes (three prehypertension and three hypertension). This methodological approach identified potential confounders: sex, age categories, smoking, alcohol consumption, BMI categories, glycemia level, hypertriglyceridemia, and hypercholesterolemia. Results were expressed as crude hazard ratios (cHRs) and adjusted hazard ratios (aHRs) with their 95% CIs.

Cox model assumptions were verified, including the proportionality of hazards through Schoenfeld residual analysis and the linearity of continuous variables through graphical methods. The study used R packages "survival," "survminer," "dplyr," and "get summary." Results tables were generated using the "gtsummary" package, with modifications to present HRs in exponentiated format with their respective CIs.

Ethical considerations

The Research Ethics Committee of the Universidad Nacional Toribio Rodríguez de Mendoza reviewed and approved the research protocol. Information management was conducted with strict confidentiality, ensuring complete data anonymization before analysis by removing personal identifiers, identity document numbers, and any information that could allow identification of either participants or companies involved.

The research was conducted using ethical principles established in the Declaration of Helsinki for medical research involving human subjects, Council for International Organizations of Medical Sciences (CIOMS) guidelines for epidemiological research, and good practice guidelines in occupational health research. To ensure the findings' transparency and reproducibility, the anonymized database and statistical analysis scripts are available in the institutional repository under DOI: 10.6084/m9.figshare.27098296.v2 [15].

Results

Main characteristics

The cohort comprised 12,027 workers, predominantly male (84.87%) with a mean age of 37.19 ± 11.56 years, where 95.51% were between 18 and 59 years old. Regarding habits, 40.99% reported smoking and 49.95% alcohol consumption. Clinical parameters showed a mean SBP of 111.27 ± 12.26 mm Hg and DBP of 71.94 ± 13.35 mm Hg, with an average BMI of 27.15 ± 3.99 kg/m². Regarding the prevalence of hypertension subtypes, IDH was the most frequent, affecting 2.33% of the population, followed by SDH with 1.34% and ISH with 0.77%. The remaining characteristics can be seen in Table 1.

Table 1. Study Sample Characteristics

Characteristic	N = 12,027
Sex	
Female	1,820 (15.13%)
Male	10,207 (84.87%)
Age, mean (SD)	37.19 (11.56)
Age group	
18 - 59 years	11,487 (95.51%)
60 years or older	540 (4.49%)
Smoking status	
No	7,097 (59.01%)
Yes	4,930 (40.99%)
Alcohol consumption	
No	6,020 (50.05%)
Yes	6,007 (49.95%)
Body mass index	27.15 (3.99)
Systolic blood pressure	111.27 (12.26)
Diastolic blood pressure	71.94 (13.35)
Blood glucose level	92.44 (20.81)
Triglyceride level	143.67 (80.99)
Cholesterol level	194.81 (36.82)
Nutritional status	
Normal weight	3,650 (30.35%)
Overweight	5,784 (48.09%)
Obesity	2,593 (21.56%)
Blood glucose levels at baseline	
Normal glucose	8,446 (82.69%)
Prediabetes	1,520 (14.88%)
Diabetes	248 (2.43%)
Hypertriglyceridemia	
No	3,769 (63.55%)
Yes	2,162 (36.45%)
Hypercholesterolemia	
No	3,434 (58.21%)
Yes	2,465 (41.79%)
Isolated systolic prehypertension	
No	70,393 (89.80%)
Yes	7,997 (10.20%)
Isolated diastolic prehypertension	
No	70,932 (90.49%)
Yes	7,458 (9.51%)
Systolic-diastolic prehypertension	
No	69,497 (88.66%)
Yes	8,893 (11.34%)

Table 1. Study Sample Characteristics - (continued)

Characteristic	N = 12,027
Isolated systolic hypertension	
No	11,934 (99.23%)
Yes	93 (0.77%)
Isolated diastolic hypertension	
No	11,747 (97.67%)
Yes	280 (2.33%)
Systolic-diastolic hypertension	
No	11,866 (98.66%)
Yes	161 (1.34%)

Data were presented as n (%) or mean (SD).

Prehypertension subtype as CVD risk

Analysis of prehypertension subtypes revealed differentiated patterns of CVR during follow-up. Isolated systolic prehypertension demonstrated the highest incidence rate with 40.67 events per 1,000 person-years (95% CI: 12.49 - 68.85), substantially higher than the rate of 1.69 per 1,000 person-years (95% CI: 1.24 - 2.15) observed in individuals without this condition, maintaining its significant association in both univariate (cHR: 3.88, 95% CI: 2.12 - 7.09) and multivariate analysis (aHR: 3.42, 95% CI: 1.73 - 6.74). Systolic-diastolic prehypertension presented an intermediate incidence rate of 2.87 events per 1,000 person-years (95% CI: 1.24 - 4.49) compared to 1.80 per 1,000 person-years (95% CI: 1.29 - 2.30) in individuals without this condition, showing an increased risk in univariate analysis (cHR: 2.1, 95% CI: 1.09 - 4.04) that attenuated after multivariate adjustment (aHR: 0.87, 95% CI: 0.40 - 1.93). In contrast, isolated diastolic prehypertension recorded the lowest incidence rate with 0.39 events per 1,000 person-years (95% CI: 0.01 - 1.16) versus 2.07 per 1,000 person-years (95% CI: 1.55 - 2.60) in those without this condition, showing a trend toward lower risk in univariate analysis (cHR: 0.24, 95% CI: 0.03 - 1.71), while the multivariate model could not adequately estimate the association due to the limited number of events in this subgroup (Table 2).

Hypertension subtype as CVD risk

During follow-up, distinctive patterns of CVR were observed according to the hypertension subtype. ISH showed the highest incidence rate with 40.67 events per 1,000 person-years (95% CI: 12.49 - 68.85), substantially higher than the rate of 1.69 per 1,000 person-years (95% CI: 1.24 - 2.15) observed in individuals without ISH. This increased risk was confirmed in both univariate analysis (cHR: 20.2, 95% CI: 9.95 - 40.9) and multivariate analysis adjusted for confounding factors (aHR: 6.78, 95% CI: 3.10 - 14.8). On the other hand, IDH presented an intermediate incidence rate of 16.59 events per 1,000 person-years (95% CI: 2.05 - 31.14), with a significantly elevated risk in univariate analysis (cHR: 6.61, 95% CI: 2.85

Table 2. Incidence Rates and Risk of Cardiovascular Events According to Arterial Prehypertension Subtypes in Workers From an Occupational Cohort

Prehypertension	Incidence per 1,000 person-years (95% CI)	Number of cases	Follow-up time (years)	Univariable		Multivariable ^a	
				cHR	95% CI	aHR	95% CI
Isolated systolic prehypertension							
No	1.69 (1.24 - 2.15)	53	31,274.34	Ref.		Ref.	
Yes	40.67 (12.49 - 68.85)	8	196.72	3.88	2.12 - 7.09	3.42	1.73 - 6.74
Isolated diastolic prehypertension							
No	2.07 (1.55 - 2.60)	60	28,921.58	Ref.		Ref.	
Yes	0.39 (0.01 - 1.16)	1	2,549.48	0.24	0.03 - 1.71	-	-
Systolic-diastolic prehypertension							
No	1.80 (1.29 - 2.30)	49	27,285.89	Ref.		Ref.	
Yes	2.87 (1.24 - 4.49)	5	4,185.17	2.1	1.09 - 4.04	0.87	0.40 - 1.93

^aModel adjusted for sex, age, smoking status, alcohol consumption, nutritional status, glycemia level, hypertriglyceridemia, hypercholesterolemia. aHR: adjusted hazard ratio; cHR: crude hazard ratio; CI: confidence interval.

- 15.3), although this association attenuated after multivariate adjustment (aHR: 1.42, 95% CI: 0.56 - 3.59). In contrast, SDH showed the lowest incidence rate with 1.46 events per 1,000 person-years (95% CI: 0.00 - 4.31), without evidence of a significant risk increase in either univariate analysis (cHR: 0.50, 95% CI: 0.07 - 3.62) or multivariate analysis (aHR: 0.33, 95% CI: 0.05 - 2.42) (Table 3).

Discussion

Main findings

During the 8-year follow-up period, cardiovascular events were relatively infrequent in this occupational cohort, reflecting the generally healthy nature of the working population. Despite this low event rate, our analysis revealed a distinctive

pattern of CVR associated with different blood pressure alteration subtypes. The most notable finding was that both ISH and its counterpart in the prehypertension spectrum emerged as the most potent predictors of cardiovascular events, maintaining statistical significance even after adjustment for multiple confounding factors. This suggests that elevated SBP, even in subclinical ranges, could serve as an early marker of vascular dysfunction and increased CVR in working populations. This stepped risk pattern challenges the traditional paradigm that considers prehypertension as a benign condition and highlights the importance of workplace surveillance and early intervention, particularly for isolated systolic alterations. In contrast, the absence of significant associations with isolated diastolic alterations and the attenuation of risk in systolic-diastolic patterns after multivariate adjustment suggest distinct pathophysiological mechanisms and possibly lower clinical relevance of these subtypes in relatively young working populations.

Table 3. Incidence Rates and Risk of Cardiovascular Events According to Arterial Hypertension Subtypes in Workers From an Occupational Cohort

	Incidence per 1,000 person-years (95% CI)	Number of cases	Follow-up time (years)	Univariable		Multivariable ^a		
				cHR	95% CI	aHR	95% CI	
ISH								
No	1.69 (1.24 - 2.15)	53	27,930.22	Ref.		Ref.		
Yes	4.52 (2.30 - 6.73)	16	3,540.84	20.2	9.95 - 40.9	6.78	3.10 - 14.8	
IDH								
No	2.07 (1.55 - 2.60)	60	28,921.58	Ref.		Ref.		
Yes	0.39 (0.01 - 1.16)	1	2,549.48	0.50	0.07 - 3.62	0.33	0.05 - 2.42	
SDH								
No	1.80 (1.33 - 2.27)	56	27,285.89	Ref.		Ref.		
Yes	2.87 (1.24 - 4.49)	12	4,185.17	6.61	2.85 - 15.3	1.42	0.56 - 3.59	

^aModel adjusted for sex, age, smoking status, alcohol consumption, nutritional status, glycemia level, hypertriglyceridemia, hypercholesterolemia. aHR: adjusted hazard ratio; cHR: crude hazard ratio; CI: confidence interval; IDH: isolated diastolic hypertension; ISH: isolated systolic hypertension; SDH: systolic-diastolic hypertension.

Hypertension and prehypertension subtypes and CVD presence

ISH has proven to be a significant predictor of cardiovascular events, with HRs ranging between 1.60 and 2.20, while its counterpart in the prehypertension spectrum also shows a significant association (HR: 1.42 - 1.75). The main underlying pathophysiological mechanism involves increased arterial stiffness due to structural alterations in the vascular extracellular matrix. This process is mediated by the activation of matrix metalloproteinases (MMPs, especially MMP-2 and MMP-9) that degrade elastin and promote collagen deposition, resulting in increased pulse wave velocity and early reflection of retrograde waves that amplify central systolic pressure [16]. These changes lead to increased systolic wall stress and left ventricular afterload.

Endothelial dysfunction plays a central role in the progression of isolated systolic alterations. Recent studies have shown that systolic elevation is associated with reduced nitric oxide bioavailability and increased expression of endothelial adhesion molecules (vascular cell adhesion molecule 1 (VCAM-1), intercellular adhesion molecule 1 (ICAM-1)), promoting vascular inflammation and atherogenesis. This endothelial damage is particularly relevant in coronary arteries, where the reduction in coronary flow reserve observed in patients with ISH (15-20% reduction vs. controls) contributes to the development of myocardial ischemia and diastolic dysfunction [17].

Neurohormonal activation, particularly of the renin-angiotensin-aldosterone system and sympathetic nervous system, amplifies vascular damage in isolated systolic alterations. Angiotensin II promotes vascular remodeling through the induction of oxidative stress, smooth muscle cell proliferation, and fibrosis [18]. Additionally, increased sympathetic activity raises heart rate and contractility, elevating myocardial oxygen consumption. This cascade of events explains why even isolated systolic prehypertension is associated with a higher risk of cardiovascular events, especially in Asian populations and young adults [19].

Current evidence does not support a significant association between IDH and adverse CVD, with studies showing non-significant results or attenuation after multivariate adjustment. Similarly, isolated diastolic prehypertension has not demonstrated a consistent association with the evaluated event. Although traditionally associated with increased peripheral vascular resistance, recent studies suggest that this isolated hemodynamic change might not be sufficient to induce significant cardiovascular damage when systolic pressure remains normal [20].

Several factors could explain the absence of significant association. First, without SBP compromise, arterial wall stress and left ventricular afterload are not significantly increased. Second, local and systemic compensatory mechanisms might more effectively maintain vascular homeostasis when only DBP is elevated. Third, isolated diastolic states are more common in young adults, where cardiovascular protective mechanisms are better preserved, although these findings remain controversial with other studies [11, 21].

Finally, regarding SDH, recent evidence has substantially

modified our understanding of its cardiovascular impact. Although a significant association was initially reported (HR: 2.13, 95% CI: 1.78 - 2.55), this notably attenuates after adjusting for SBP (HR: 0.87, 95% CI: 0.40 - 1.93). The pathophysiological mechanisms described for SDH include reduced arterial elasticity and increased systemic vascular resistance. However, paradoxically, studies have shown that coronary endothelial dysfunction is less severe in SDH than in ISH, and vascular calcification shows a stronger association with ISH than with SDH [10, 22].

The reevaluation of available evidence indicates that the traditional paradigm considering SDH as the highest-risk subtype needs reconsideration. More recent studies, with more rigorous methodological adjustments, suggest that SBP is the fundamental determinant of CVR, regardless of DBP values. This observation has important clinical implications, suggesting that therapeutic strategies should primarily focus on SBP control [11, 22].

Importance of the study for public and occupational health

The findings of this study have important implications for public and occupational health, particularly in the context of cardiovascular surveillance and prevention in the working population. Evidence that ISH and isolated systolic prehypertension are the main determinants of CVR, regardless of diastolic pressure values, suggests the need to reorient detection and management strategies in the workplace. This is especially relevant considering that the working population tends to be younger and frequently asymptomatic, which may result in an underestimation of CVR if proper evaluation is not performed.

The differences found in CVR between Asian and Western populations and age groups directly affect occupational health programs. Occupational health services should consider these variations when designing surveillance protocols and establishing intervention criteria, particularly in multinational companies or diverse workforces. The higher prevalence of systolic alterations in Asian populations and their stronger association with cardiovascular events in this ethnic group suggests the need for culturally adapted prevention strategies.

The evidence that the systolic component is the primary determinant of CVR has significant implications for occupational health resource allocation. Surveillance programs should prioritize systolic pressure detection and control, especially in workers with additional risk factors or high-stress occupations. Workplace interventions, such as lifestyle modification programs, should focus on factors influencing systolic pressure, like arterial stiffness and calcification.

From a public health policy perspective, these findings suggest reviewing current risk stratification criteria and hypertension management guidelines in the occupational setting. The lack of significant association of isolated diastolic and systolic-diastolic hypertension with cardiovascular events after adjusting for systolic pressure could imply a reconsideration of intervention thresholds and management priorities. This is particularly relevant for resource optimization in occupational health systems with budget constraints.

A final aspect to consider is the economic impact of these findings. More precise identification of hypertension subtypes that confer greater CVR allows better targeting of preventive and therapeutic resources. This is especially important in the occupational health, where interventions must demonstrate clinical efficacy and cost-effectiveness. Preventing cardiovascular events in the working population has significant implications regarding productivity, work absenteeism, and healthcare costs.

Strengths and limitations

This study presents important methodological strengths. First, it involves an occupational cohort with considerable sample size and extended follow-up, allowing robust evaluation of cardiovascular outcomes. Standardized blood pressure measurement following validated protocols and CVD confirmation through medical records and self-reporting strengthens the study's internal validity. Furthermore, comprehensive adjustment for multiple confounding variables, including traditional CVR and occupational variables, provides more precise estimates of the studied associations.

However, several limitations must be acknowledged. A key limitation is the relatively low frequency of cardiovascular events, which is expected in an occupational cohort but may affect the associations' robustness. While the statistical significance of our findings regarding systolic and pre-systolic hypertension remains notable, the predictive value of these associations should be interpreted with caution, given the low event rate. This characteristic reflects the inherent nature of studying cardiovascular outcomes in a working population, where events are naturally less frequent than in older or general population cohorts. The occupational nature of the cohort, while advantageous for follow-up, might also limit the generalizability of results to non-working populations ("healthy worker effect"). While the number of cardiovascular events in some hypertension subtypes was relatively small, this reflects the expected epidemiological pattern in an actively working population aged 18 - 65 years. This characteristic should be interpreted as a representation of real-world epidemiology in occupational settings rather than a methodological limitation, particularly given that significant associations were still detected despite the conservative nature of our cohort.

Conclusions

Despite the relatively low frequency of cardiovascular events typical of working populations, the findings of this large-scale occupational study provide important insights into our understanding of CVR associated with different blood pressure alteration subtypes. While the number of events was small, a pattern emerged suggesting the need to reconsider the relative impact of each blood pressure component. ISH and its prehypertensive counterpart proved to be significant predictors of cardiovascular events, even in this generally healthy occupational cohort. In contrast, the contribution of diastolic and sys-

tolic-diastolic components notably attenuates after adjustment for important covariables. These observations could have relevant implications for clinical practice and occupational health surveillance strategies.

Therefore, based on these findings, while acknowledging the limitations of event frequency in our cohort, we recommend: 1) prioritizing SBP surveillance and control in occupational health programs, particularly in Asian populations and young adults where the association appears stronger; 2) reconsidering therapeutic intervention thresholds based on hypertension subtypes, with particular attention to the systolic component; 3) implementing differentiated prevention strategies according to population characteristics and occupational risk factors; and 4) developing additional studies with larger cohorts and longer follow-up periods to further validate these findings and evaluate the cost-effectiveness of interventions specifically targeting systolic pressure control in the workplace. Future research should focus on determining the precise mechanisms by which systolic elevation confers greater CVR, evaluating early intervention strategies in high-risk subgroups, and confirming these associations in larger occupational cohorts with more cardiovascular events.

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Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this article.

Informed Consent

Informed consent was not required for this study.

Author Contributions

Victor Juan Vera-Ponce: conceptualization, investigation, methodology, resources, writing - original draft, and writing - review and editing. Joan A. Loayza-Castro: methodology, software, data curation, formal analysis, and writing - review and editing. Fiorella E. Zuzunaga-Montoya: investigation, project administration, writing - original draft, and writing -

review and editing. Luisa Erika Milagros Vasquez-Romero: investigation, project administration, writing - original draft, and writing - review and editing. Lupita Ana Maria Valladolid-Sandoval: investigation, methodology, writing - original draft, and writing - review and editing. Jhosmer Ballena-Caicedo: validation, visualization, supervision, writing - original draft, and writing - review and editing. Witre Omar Padilla: investigation, methodology, resources, writing - original draft, and writing - review and editing. Carmen Ines Gutierrez De Carrillo: methodology, supervision, funding acquisition, and writing - review and editing.

Data Availability

The data supporting the findings of this study have been deposited in Figshare and can be accessed at <https://doi.org/10.6084/m9.figshare.27098296.v1>.

Abbreviations

ADA: American Diabetes Association; aHR: adjusted hazard ratio; BMI: body mass index; cHR: crude hazard ratio; CI: confidence interval; CIOMS: Council for International Organizations of Medical Sciences; CVD: cardiovascular disease; CVR: cardiovascular risk; DAG: directed acyclic graph; DBP: diastolic blood pressure; IDH: isolated diastolic hypertension; ISH: isolated systolic hypertension; MMP: matrix metalloproteinase; SBP: systolic blood pressure; SDH: systolic-diastolic hypertension; STROBE: Strengthening the Reporting of Observational Studies in Epidemiology; WHO: World Health Organization

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