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The significance of calcium and magnesium content in drinking water for arterial stiffness among residents of the Slovak Republic

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ABSTRACT

Arterial stiffness (AS) is a significant risk factor for cardiovascular diseases, which are the leading cause of death in developed countries. Based on the measurement of AS among residents supplied with soft drinking water (100 respondents) and hard water (100 respondents), a significant difference was found in the pulse wave velocity (PWVao), arterial age, and the difference between arterial and actual age (delta – Δ age). Among respondents consuming soft drinking water, PWVao was higher by 1.9 m s^{-1}, arterial age was higher by 23 years, and Δ age was higher by 14.5 years. As an intervention, originally soft drinking water was treated to increase calcium (Ca) and magnesium (Mg) content by approximately 10–15 mg l^{-1}. After 18 months of consuming water with elevated Ca and Mg content, PWVao decreased by 0.93 m s^{-1}, arterial age decreased by 10.42 years, and Δ age decreased by 11.79 years among respondents originally consuming soft drinking water. Thus, their risk of developing CVD was significantly reduced.

Key words: arterial age, arterial stiffness, cardiovascular risk, drinking water, intervention study

HIGHLIGHTS

- Soft and hard water residents showed differences in pulse wave velocity (PWVao), arterial age, and Δ age.
- An intervention increased calcium and magnesium in soft water by 10–15 mg l^{-1}.
- After 18 months, treated water reduced PWVao by 0.93 m s^{-1}, arterial age by 10.42 years, and Δ age by 11.79 years.
- Water composition impacts cardiovascular health.
- Water quality interventions can be preventive measures.

INTRODUCTION

Among the primary risk factors for cardiovascular diseases (CVDs) are notably stress, obesity, genetic factors, unhealthy dietary habits, smoking, and excessive alcohol consumption. Environmental factors are also important, particularly air quality and the quality of drinking water (WHO 2011). Regarding drinking water, the most crucial factor is the content of calcium (Ca) and magnesium (Mg), known as water hardness. The impact of drinking water hardness on CVD has been extensively studied in various countries worldwide and confirmed by several meta-analyses: with increasing Ca and especially Mg content the risk of CVD mortality decreases (Catling *et al.* 2005; Jiang *et al.* 2016; Gianfredi *et al.* 2017; Georeli *et al.* 2024). Most authors suggest that the beneficial contents of Ca and Mg for human health, including the vascular system, fall within the ranges of 30–80 mg l^{-1} (Ca) and 10–50 mg l^{-1} (Mg), respectively (Rosborg & Kožíšek 2020). In the Slovak Republic (SR), an optimal content of these elements has been derived, where the mortality from CVD is lowest and life expectancy is highest, with Mg > 25 mg l^{-1} and Ca > 50 mg l^{-1} (Rapant *et al.* 2017, 2021).

A significant risk factor for the development of CVDs is the loss of elasticity in arteries, commonly referred to as arterial stiffness (AS) (e.g., DeLoach & Townsend 2008; Shirwany & Zou 2010; Joris *et al.* 2016; Kakaletsis *et al.* 2024; Tan & Tan 2024). The measurement of AS, as a non-invasive method, has become an important part of the predictive determination of cardiovascular risk in preclinical medicine and diagnostics in the last 30–40 years (e.g., Illyes 2005). Recently, a new study was published examining the impact of AS, demonstrating a relationship between AS and carotid atherosclerosis (Vogiatzi *et al.* 2023).

While the influence of Ca and Mg content in drinking water on the incidence/mortality of CVD has been described in countless epidemiological studies, the relationship between AS and the content of Ca and Mg in drinking water has been studied only to a limited extent (Rapant *et al.* 2019; Cvečková & Rapant 2022). In these studies, it was found that the residents of the SR supplied with soft drinking water with low Ca content ($\leq$30 mg l^{-1}) and Mg ($\leq$10 mg l^{-1}) have significantly reduced arterial elasticity compared with residents supplied with hard drinking water with elevated Ca ($\geq$50 mg l^{-1}) and Mg ($\geq$25 mg l^{-1}) content. On average, they demonstrate a 1.0–1.5 m s^{-1} increase in pulse wave velocity (PWVao) and an arterial age elevated by 5–15 years.

At present, there is a lack of comprehensive global literature and published studies explicitly detailing the relationship between water hardness, specifically the Ca and Mg content, and AS. Nonetheless, it can be hypothesized that insufficient magnesium levels in drinking water may contribute to the development of AS. Magnesium plays a crucial role in vascular health, and its deficiency might lead to decreased arterial compliance, promoting stiffer arteries. Further research is needed to elucidate the specific mechanisms underlying this potential relationship. As mentioned in the introduction, numerous studies in the global literature link increased incidence/mortality of CVD with deficient levels of Ca and Mg in drinking water. Similarly, there is a significant amount of research highlighting the importance of AS in the development of CVD. Therefore, we hypothesized that when people start consuming drinking water with elevated levels of Ca and Mg, their AS parameters would improve. The study deals with measurement of AS of the residents supplied with drinking water of varying and changing hardness. The magnitude of CVD associated with AS has not been yet monitored, neither in the study area nor in the SR. The primary aim of the contribution is to verify that individuals supplied with soft drinking water exhibit impaired vascular elasticity compared with those supplied with hard drinking water. However, the main objective of this intervention study is to determine whether the vascular elasticity of residents, and consequently, the risk of developing CVD, supplied with soft drinking water, improves when they begin consuming water with elevated levels of Ca and Mg.

MATERIAL AND METHODS

Area description

The measurement of AS was conducted in two areas supplied with drinking water from public water supplies of varying hardness. The first area received soft water, while the second area received hard water (Figure 1). The basic characteristics of Ca and Mg content in drinking water and health indicators of CVD are presented in Table 1 (both municipalities), according to Cvečková & Rapant (2022). All water sources used for public supply are regularly monitored in accordance with Slovak legislation. The concentrations of harmful substances, such as nitrates (NO_3), ammonium (NH_4), toxic metals, and organic

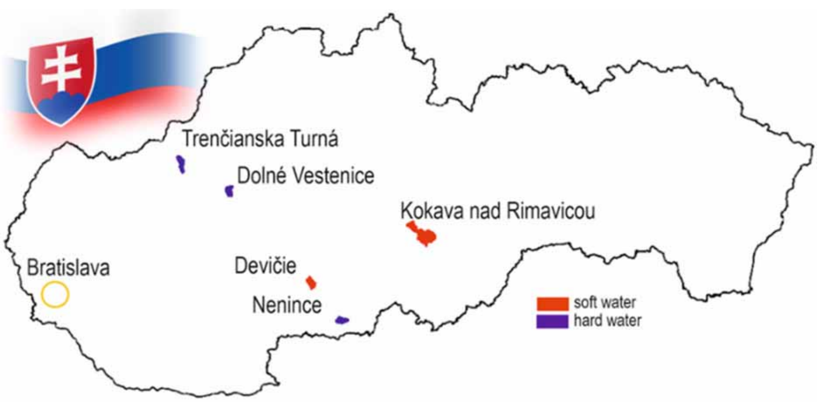

Figure 1 | The location of the studied municipalities in the SR.

pollutants, are significantly below the limit values for drinking water. Therefore, we have not included these parameters in the study. Instead, we focus on the concentrations of Ca and Mg, which are directly relevant to the study's objectives. Conductivity values are included to differentiate between soft water and water with increased hardness. CVD health indicators represent 15-year average values for the years 1994–2008. Values for health indicators for the entire SR are also provided for comparison.

From the data presented in Table 1, it is evident that the Ca and Mg content, as well as water hardness, are significantly higher in the hard water group, while the values of CVD health indicators are notably more adverse in the soft water group.

Enrichment of drinking water with Ca and Mg

In order to reduce the risk of CVD and improve AS, drinking water in communities with soft water (Devičie and Kokava nad Rimavicou) was enriched with Ca and Mg as part of the LIFE – WATER & HEALTH project. Enrichment of drinking water with Ca and Mg, known as recarbonatization, was carried out using recarbonatization reactors, where carbonate rock (half-burnt dolomite) was dissolved under CO_2 saturation to produce a concentrate with high Ca and Mg content. The concentrate was added directly to water sources. A detailed description of the recarbonatization process along with the technical documentation of both reactors is provided in another paper (Dudáš *et al.* 2022; Cvečková & Rapant 2022; Rapant *et al.* 2022). Recarbonatization in both communities began in July 2023 and continues to the present. The Ca and Mg content in drinking water in both communities increased on average by 10 mg l^{-1} (Mg) and 10–15 mg l^{-1} (Ca), which represents a two- to three-fold increase compared with the original content. The level of increase in Ca and Mg content in drinking water was determined based on Health Risk Assessment calculations for deficient essential elements (Rapant *et al.* 2020).

Measurement of AS

The phrase 'arterial stiffness' is a general term that refers to the loss of arterial compliance or changes in vessel wall properties, or both (Shirwany & Zou 2010). The measurement of AS is a simple technique, that was established as a useful non-invasive approach in health prevention in the past 20–25 years (Laurent 2007; DeLoach & Townsend 2008). Markers of AS, such as increased aortic PWVao and increased central aortic pressure, are independent predictors of cardiovascular risk (Illyes 2005). They represent tissue biomarkers of the arteries. These markers have been shown to be better prognosticators than the traditional blood pressure measurement, as well as the biomarkers in the bloodstream. In addition, their significant predictive value specifies the risk assessment provided by the traditional risk factors. The AS measurement gives insights into the actual pathological processes through the evaluation of the loss of elasticity of the aorta. Over time, the endothelial damage progresses and causes damage to the arterial elasticity, resulting in the loss of elasticity of the vessel wall. In susceptible patients, it leads to premature vascular aging, resulting in the early development of cardiovascular complications. Vascular aging can also be measured directly through the non-invasive method of measuring the AS, central pressure, and the wave reflection. In this study, the measurements of AS were performed with an arteriograph developed in Hungary and patented in over 30 countries (Arteriograph, TensioMed Ltd, Budapest, Hungary). The arteriograph can easily measure, without any health risk, such physiological parameters characterizing the state of arteries, which are independent of

Table 1 | Characteristics of the content of Ca and Mg in drinking water before intervention and selected CVD health indicators of the monitored municipalities

Municipalities	Ca (mg l^{-1})	Mg (mg l^{-1})	Conductivity (μS cm^{-1})	ReI	SMRI (%)	LTE (years)
Soft water						
Devičie	30.0	10.1	280	806.64	137.54	68.43
Kokava nad Rimavicou	19.1	3.5	117	822.39	128.20	71.83
Hard water						
Dolné Vestenice	88.1	27.6	598	287.36	94.95	74.63
Nenince	82.6	37.5	996	454.37	77.89	74.33
Trenčianska Turná	62.4	23.7	429	454.91	76.15	77.09
SR	–	–		531.24	100	72.65

RеI, relative mortality for CVD; SMRI, indirect age-standardized mortality rate of CVD; LTE, lifetime expectancy.

further known risk factors (age, sex, blood pressure, cholesterol, and smoking), and can reliably assess the state of the cardiovascular system and predict the risk of complications in asymptomatic, at first sight 'healthy', patients. These parameters are also confirmed by international guidelines for the diagnosis of the target organ damage (Williams *et al.* 2018).

The measurement can determine more than just the actual systolic and diastolic blood pressure. The cuff attached to the arm detects the entire pulse curve, which corresponds to changes in blood pressure (Lenkey *et al.* 2014). These curves are subsequently processed by a computer program. The information obtained characterizes the function of small arteries using pressure ratios in the main artery (aorta) in close proximity to the heart and flexibility of the arteries by measuring the aortic PWVao. Based on PWVao values, the so-called arterial age of the individual can be derived. Based on more than 10,000 measurements provided by the company Arteriograph, the Central European median PWVao values for different age groups of population were derived, which represents a standard against which the measured results are compared. The relationship between the age and PWVao values for the Central European population is shown in Table 2. With increasing age, PWVao values also increase. Calculation of arterial age represents an integrated software output of the arteriograph. More information about the method can be obtained online through educational videos of the producer (TensioMed n.d.).

In this study, the AS was determined through measurements of PWVao and the arterial age of respondents. The measured results were compared with average values established for the Central European population. PWVao of 6–10 $m{\cdot}s^{-1}$ is considered a standard value (The Reference Values for Arterial Stiffness' Collaboration 2010). Average arterial age does not correspond to the actual age of an individual, but it reflects the status (age) of arteries. The arterial age can be higher or lower than the actual age of the respondent. The more flexible the walls of the arteries, the lower the PWVao, indicating healthier arteries with an age lower than the physical, i.e., actual age of the measured respondents. In consideration of the age of the measured respondents, we present the results in terms of Δ age, which represents the difference between arterial and actual age. To measure AS, a meticulously designed methodology has been established, guaranteeing both accuracy and reliability across diverse populations. The process involves the use of a single, highly calibrated instrument operated by a trained technician to minimize variability and ensure consistent results. More information can be found on our website: http://fns.uniba.sk/lifewaterhealth/.

Selection of study participants

The study is based on comparing the level of AS between two groups of residents from areas supplied with soft and hard drinking water. In the first stage of measurement (May–June 2021), according to the LIFE – WATER and HEALTH project, 100 respondents supplied with hard drinking water (D. Vestenice, T. Turná, and Nenince) and 107 respondents supplied with soft drinking water (Devičie and Kokava nad Rimavicou) were measured. The areas were selected based on varying levels of Ca and Mg in drinking water, which are reflected in different health indicators of CVD (Rapant *et al.* 2021). The selection of respondents was random and included both males and females. The basic selection criteria were as follows: (i) at least 5 years of residency, (ii) use of drinking water exclusively from a public supply, and (iii) respondents not treated for CVD and other serious chronic diseases, such as diabetes, kidney disease, and chronic inflammation.

All participants in the project gave their informed consent for the measurement of AS and completed a brief questionnaire on their health status, actual age, height, weight, and smoking and alcohol drinking habits before taking part in the study. The basic statistics of these characteristics are shown in Table 3 for all individuals participating in this study.

The next three stages of measurement were conducted specifically on respondents supplied with soft drinking water (in the municipalities of Devičie and Kokava nad Rimavicou), after the enrichment of drinking water with Ca and Mg. These stages occurred approximately at 6-month intervals following the commencement of recarbonatization. More respondents were supplied with soft drinking water to ensure statistically significant data collection in the case of unexpected absences during the second to fourth stages of measurement. Prior to the COVID-19 pandemic, not all respondents who participated in the first stage of measurement attended the second to fourth stages (due to quarantine or COVID-19). To meet the technical requirements of the LIFE – WATER and HEALTH project (100 respondents), AS was also measured in substitute study subjects from

Table 2 | Median PWVao values and age of the Central European population according to reference (TensioMed, The Arteriograph Company)

Age (years)	**10**	**15**	**20**	**25**	**30**	**35**	**40**	**45**	**50**	**55**	**60**
PWVao ($m\ s^{-1}$)	5.35	6.00	6.60	6.80	7.00	7.30	7.70	8.30	8.60	8.80	9.00

Table 3 | Measurement of AS – the initial stage of measurement (before the intervention, i.e., enrichment of drinking water with Ca and Mg)

	Hard water (100 respondents)					Soft water (107 respondents)				
Parameters	Me	$\bar{x}$	SD	Min	Max	Me	$\bar{x}$	SD	Min	Max
Age	38	39.8	10.5	20	61	50	48.5	13.9	16	80
BMI	25.6	25.6	4.4	17.3	40.3	26.6	27.2	5.3	17.1	53.4
PWVao	7.8	7.9	1.3	6	12.2	9.8	9.8	1.5	6.2	14.9
Arterial age	41.5	42.0	16.9	15	80	68	65.2	15.9	17	92
Δ age	2	2.2	13.9	–32	50	16	16.7	18.2	–27	61
Gender	Men – 38 (38%), Women – 62 (62%)					Men – 39 (36.5%), Women – 68 (63.5%)				
Alcohol	Yes – 27 (27%), No – 73 (73%)					Yes – 57 (53.3%), No – 50 (46.7%)				
Smoking	Yes – 21 (21%), No – 79 (79%)					Yes – 30 (28%), No – 77 (72%)				
PWVao > 10 ($m\ s^{-1}$)	9 respondents					40 respondents				

both municipalities. Substitute study subjects were selected according to the same criteria as the primary respondents. However, the inclusion of substitute study subjects may have introduced potential biases into the study results. To mitigate this issue, we consider the findings derived from the primary respondents, without the inclusion of substitutes, to be the most reliable and valid. This approach ensures the integrity of the study's outcomes by minimizing any potential bias arising from respondent substitution. This circumstance could have potentially influenced the obtained results. Therefore, we present the results twice: first for respondents who participated in the first stage, and second, for all measured respondents, including substitutes who did not participate in the first stage of measurement. Complete results of AS measurements are available at http://fns.uniba.sk/lifewaterhealth/.

Ethical considerations

The study was performed in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the Regional Public Health Authority of Zvolen (approval no. ZV/KA/2014/1/183). Participation in the research was voluntary and fully anonymous, and participants included in the study were informed that the results of this study would only be used for scientific purposes.

Statistical analysis

The results of measurement AS (PWVao, arterial age, and Δ age) were expressed using median (Me), average ($\bar{x}$), standard deviation (SD), and range (Min–Max). We also present the results in the form of box plots. A box plot is a data visualization tool that provides a concise overview of data distribution from central tendencies to potential outliers. Utilizing multiple methods (Kernel density estimation test, Shapiro–Wilk test, Hartigan dip test), we tested the distributional characteristics of the assessed data. Given the non-linear distribution of the data, the relationship between the tested variables was quantified using Spearman's rank correlation. The statistical significance was determined based on the *p*-values. In the case $p < 0.001$, we consider the results very highly statistically significant (***), when $p < 0.01$ – highly statistically significant (**) and when $p < 0.05$, we consider the results statistically significant (*).

RESULTS AND DISCUSSION

The results of the first stage of AS measurement in municipalities supplied with drinking water of various hardness are presented in Table 3, which also includes the basic characteristics of the respondents who participated in the measurement. Differences in PWVao values and Δ age as a function of water hardness are presented in the form of box plots in Figures 2 and 3.

As evident from the achieved results presented in Table 3 and Figures 2 and 3, significant differences in AS parameters were found among residents supplied with drinking water of varying hardness. The PWVao values, arterial age, and Δ age were notably less favourable among residents supplied with soft drinking water, i.e., water with low Ca and Mg content. The

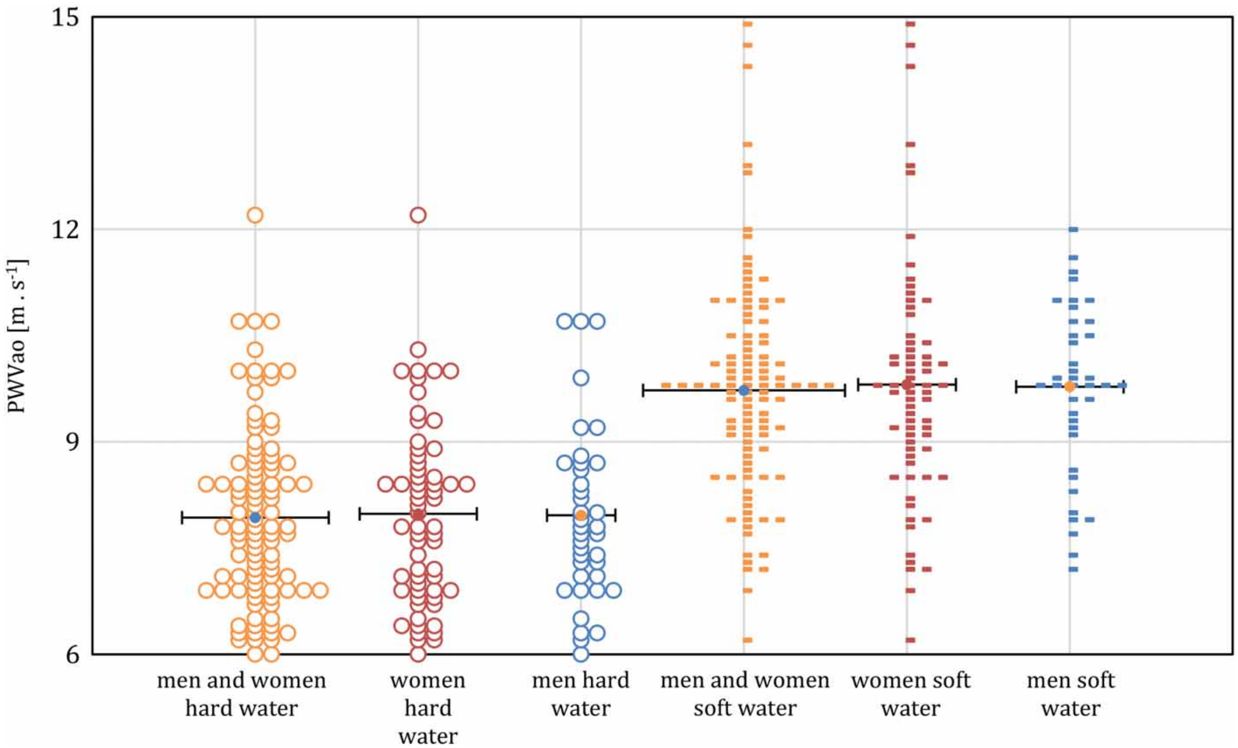

Figure 2 | The distribution of PWVoa among residents living in areas with different concentrations of Ca and Mg in drinking water.

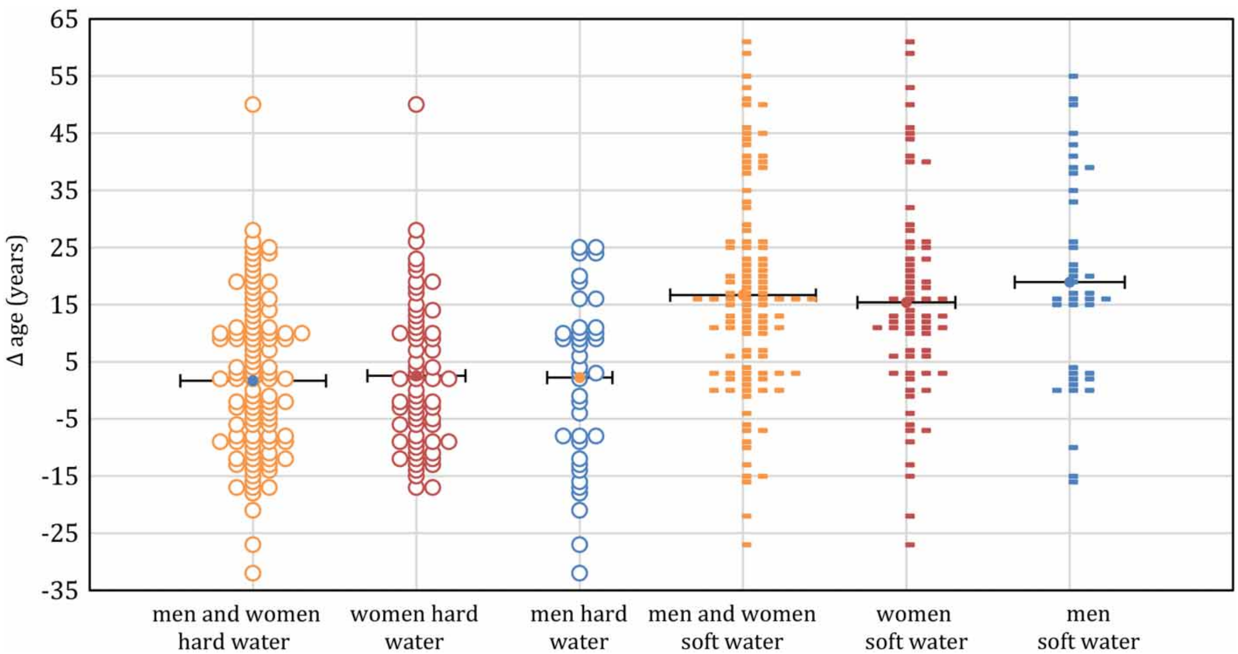

Figure 3 | The distribution of the Δ age of residents living in areas with different concentrations of Ca and Mg in drinking water.

average PWVao values were over 1.8 $m\ s^{-1}$ higher, arterial age was more than 23 years higher, and Δ age was higher by 14.5 years among residents supplied with soft drinking water in comparison with residents drinking water with higher Ca and Mg content.

PWVao and arterial age values also notably depend on the current age, increasing with advancing age. As evident from Table 3, the average current age of respondents supplied with soft drinking water is approximately 10 years higher. For residents of Central Europe (including the SR), a 10-year increase in age on average causes a PWVao increase of 0.7–0.9 m s^{-1} (Table 2). Taking this into consideration, it can be assumed (to eliminate the 10-year age difference between both groups of respondents) that PWVao values for residents supplied with soft drinking water are approximately 1 m s^{-1} higher than those for residents supplied with hard drinking water. This fact is best reflected by Δ age, making its results more objective than arterial age values. We did not observe any significant differences based on gender. Similar results, indicating a less favourable state in AS parameters in the case of population drinking water with low levels of Ca and Mg, were also reported in the study of Rapant *et al.* (2019).

Results of the statistical analysis – Spearman correlation coefficient values (*R*) with indications of statistical dependence (*p*)– are presented in Table 4. Based on statistical analysis (Table 4), the closest relationship ($R = 0.77$ to 0.99, with $p < 0.001$) was observed between AS parameters (PWVao, arterial age, and Δ age) and the content of Ca and Mg in drinking water ($R = 0.99$, $p < 0.001$). Among AS risk factors, besides the content of Ca and Mg in water, body mass index (BMI), alcohol consumption, and smoking were ascertained through the questionnaire. The highest dependency ($R = -0.51$, $p < 0.001$) was observed between the content of Ca and Mg and PWVao. Similarly, a significant negative correlation was observed between the content of Ca and Mg in drinking water and arterial age ($R = -0.52$, $p < 0.001$) and Δ age ($R = -0.28$, $p < 0.001$), indicating a high statistical dependency between the content of Ca and Mg in drinking water and AS parameters. Among other AS risk factors, a dependency of PWVao, arterial age, and Δ age on alcohol consumption was observed ($R = 0.24$ to 0.31, $p < 0.001$). A lower dependency was observed between BMI and arterial age ($R = 0.23$, $p < 0.001$) and BMI and PWVao ($R = 0.23$, $p < 0.05$). No statistically significant dependency between AS and smoking was recorded. From the above, it is evident that PWVao, arterial age, and Δ age are most influenced by the content of Ca and Mg in drinking water. No statistically significant relationship according to gender was demonstrated. Similar results, showing the highest impact of the content of Ca and Mg in drinking water on AS parameters, were found in the study of Rapant *et al.* (2019).

The results of AS measurement across all four measurement stages, solely for residents supplied with soft drinking water (stage I), and after drinking water recarbonatization (stages II–IV), are presented in Table 5. Only the average values of PWVao, Δ age, and arterial age are provided for all respondents (including substitutes) and without substitute study subjects. Detailed characteristics of stages II–IV of AS measurement are provided in Supplementary material S1 and S2. A graphical representation of the distribution of PWVao values and Δ age in the group without substitute study subjects is presented in Figure 4. A graphical representation of the distribution of PWVao and Δ age in the group with substitute study subjects is provided in Supplementary material S3.

As evident from Table 5 and Figure 4 (also from Supplementary material S1, S2, and S3), where the results of AS II, III, and IV stages of measuring AS after enriching drinking water with Ca and Mg compared with stage I (with original low levels of Ca and Mg in drinking water) are presented, in all cases, a gradual and significant improvement in AS parameters was documented after recarbonatization of drinking water. In the group without substitute study subjects, there was a decrease in

Table 4 | The values of Spearman correlation coefficients (*R*) indicating statistical dependence (*p*)

	PWVao	Arterial age	Δ age	BMI	Smoking	Alcohol	Gender	Ca	Mg
PWVao	1	0.99***	0.77***	0.23*	0.03	0.31***	0.00	−0.51***	−0.51***
Arterial age	0.99***	1	0.78***	0.23***	0.03	0.30***	0.00	−0.52***	−0.51***
Δ age	0.77***	0.78***	1	0.06	0.11	0.24***	0.04	−0.28***	−0.28***
BMI	0.23***	0.23***	0.06	1	−0.03	0.09	0.15*	−0.18*	−0.18*
Smoking	0.03	0.03	0.11	−0.03	1	0.33***	−0.02	−0.03	−0.03
Alcohol	0.31	0.03***	0.24***	0.09	0.33***	1	0.02	−0.29***	−0.29***
Gender	0.00	0.00	0.04	0.15	−0.02	0.02	1	0.08	0.08
Ca	−0.51***	−0.52***	−0.28***	−0.18*	−0.03	−0.29***	0.08	1	0.99***
Mg	−0.51***	−0.51***	−0.28***	−0.18*	−0.03	−0.29***	0.08	0.99***	1

Note: * $p < 0.05$ statistically significant, ** $p < 0.01$ highly statistically significant, *** $p < 0.001$ very highly statistically significant.

Table 5 | Results of the measurement of the AS in four stages of measurement (Devičie and Kokava nad Rimavicou)

	Without substitute study subjects				With substitute study subjects			
Stages	***n***	**PWVao**	**Arterial age**	**Δ age**	***n***	**PWVao**	**Arterial age**	**Δ age**
I stage (May 2021)	107	9.78	65.17	16.68	107	9.78	65.17	16.68
II stage (December 2021)	93	9.44	61.69	14.24	100	9.50	62.47	14.60
III stage (June 2022)	88	9.19	58.91	10.48	98	9.23	59.15	11.35
IV stage (December 2022)	100	8.85	54.75	4.89	114	8.94	55.70	5.13

Note: *n* is the number of respondents, data representing arithmetical mean.

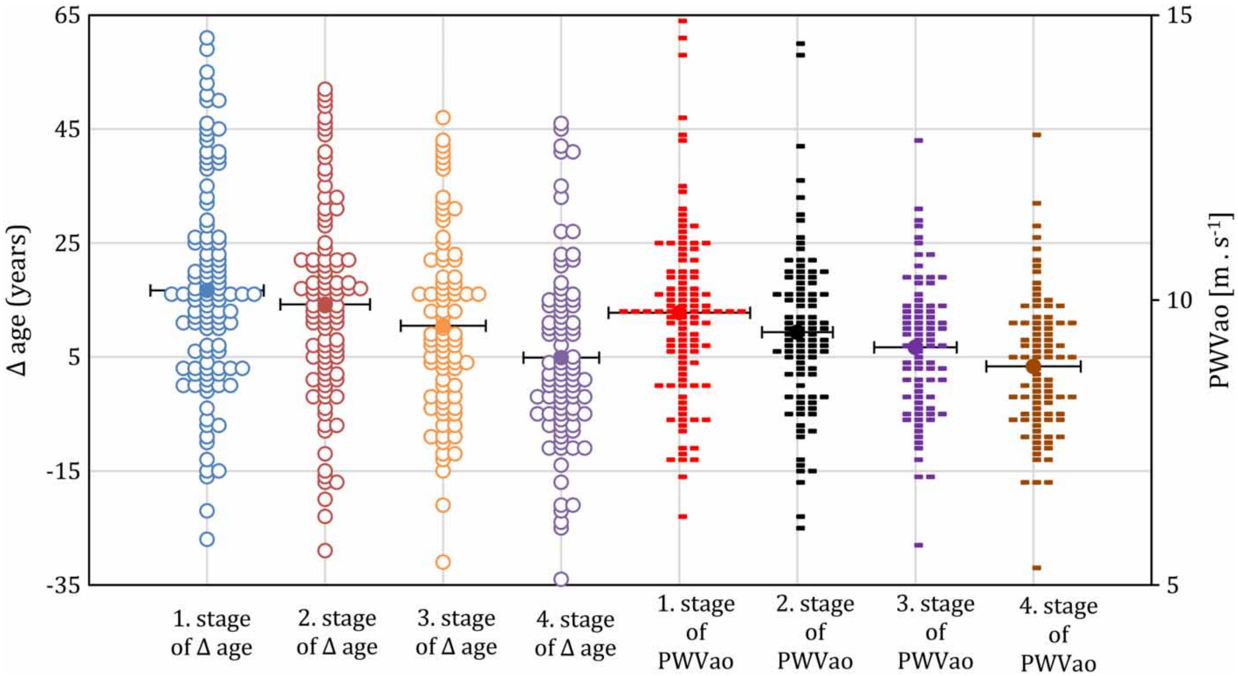

Figure 4 | The distribution of Δ age and PWVao among residents for four stages was measured without substitute study subjects.

PWVao from 9.78 to 8.85 m s^{-1}, arterial age from 65.17 to 54.75, and Δ age from 16.68 to 4.89 years. Practically, the same decrease was observed in the group with substitute study subjects. The measurement of AS, as previously mentioned, was complicated by the COVID-19 pandemic, primarily affecting stages II and III of the measurement. COVID-19 manifests with a reduction in AS (Jannasz *et al.* 2023). Perhaps for this reason, the most significant improvement in PWVao was recorded in the fourth stage of the measurement, when the COVID-19 pandemic in Slovakia was weak. The achieved improvement in AS parameters is very significant. The residents of the Devičie and Kokava nad Rimavicou municipalities are approaching the AS parameters of residents supplied with hard drinking water. However, it should be noted that these residents had their daily intake of Ca and Mg in drinking water increased 2–3 times during 18 months. Currently, no specific confounding variables have been identified that could impact the observed relationship between drinking water hardness, characterized by Ca and Mg content, and cardiovascular health outcomes, particularly AS. CVDs are linked to a multitude of pathophysiological processes and risk factors. It is important to note that if any of the major risk factors for CVD, as outlined in the introduction, are predominant, the incidence of CVD will occur independently of the Ca and Mg levels in drinking water. This suggests that while water hardness may play a role, other significant risk factors must also be considered in the analysis of cardiovascular health outcomes. The observed improvements in AS parameters following the 18-month consumption of drinking water enriched with Ca and Mg are primarily limited by the relatively small number of respondents and the impact of the COVID-19 pandemic. Despite these limitations, our results confirm improvements in AS among the study participants. We acknowledge that the small sample size and pandemic conditions are significant limitations. Additionally, similar dependencies with worse AS with soft drinking water consumption have been documented in other regions of Slovakia (Rapant *et al.* 2019). According to the literature, COVID-19 negatively affects AS parameters. Nevertheless, our results, even amidst the pandemic, confirmed improvements in AS in both groups with and without substitute study subjects.

AS is a critical risk factor for the incidence/mortality of CVD, which is the leading cause of death in developed countries worldwide. In the SR, approximately 47–48% of the deceased die from CVD each year (NCZI 2021). From the achieved results, it is evident that among the monitored risk factors for AS, the most significant impact is exerted by the content of Ca and Mg in drinking water, which seem to be higher than the impact of BMI, alcohol consumption, or smoking. Similar findings were observed in terms of CVD mortality in the territory of Slovakia. In several areas supplied with drinking water deficient in Ca and Mg, CVD mortality rates were higher than in the areas with hard drinking water. For instance, ReI values were higher by 60–70%, SMRI values by 28–35%, and premature CVD mortality rates by 25–35% (Rapant *et al.* 2014, 2021; Cvečková *et al.* 2017). In these areas and the studies cited, besides BMI, alcohol consumption, and smoking, the level and availability of healthcare, dietary habits, lifestyle, physical activities, and socioeconomic conditions were also controlled and assessed as known CVD risk factors. The level of these health determinants was similar in both areas, slightly better in areas supplied with soft drinking water. Consequently, the content of Ca and Mg in drinking water emerges as highly significant, impacting both AS and the incidence/mortality of CVD. Particularly higher values of age-standardized mortality and premature mortality from CVD (approximately 30%) among residents supplied with soft drinking water can thus be associated with deficient Ca and Mg content in drinking water. From the perspective of the pathophysiology of CVD and information obtained from earlier epidemiological studies from abroad (e.g., Catling *et al.* 2005), we consider the influence of Mg to be more significant than that of Ca. However, we cannot objectively assess this, as the content of Ca and Mg in Slovak drinking water almost always occurs together.

This impact of drinking water Ca and Mg on AS surpasses that of BMI, alcohol consumption, or smoking in our study. This is not to question the key influence of these lifestyle factors on CVD development, which has been repeatedly demonstrated in many studies (e.g., Rippe 2018). Even if low drinking water Ca and Mg were a less significant factor with a relative risk of around 20%, with today's huge prevalence of CVD, even a negative impact of 20, 10, or only 5% would have a large societal impact (Calderon & Hunter 2009). In the EU, CVD is the leading cause of death, accounting for over 1.8 million deaths every year, which corresponds to 37% of all deaths (Løgstrup 2020), 5% of this number translates to almost 100 thousand deaths. In absolute terms, this would represent a number of deaths that would be many times higher than all other deaths caused by chemical or microbial contamination of drinking water in Europe. The reported incidence of legionellosis in the EU is about 6,000 cases per year with a fatality rate of 10% (WHO 2017) or about 600 deaths. Even if we add to this number of deaths from bladder cancer caused by disinfection by-products, which would be another order of magnitude of hundreds of cases per year (Evlampidou *et al.* 2020), and sporadic deaths from other drinking water contaminants, we see that we are at a fraction of the minimum numbers of deaths caused by low Mg and Ca in drinking water.

The long-term enhancement of Ca and Mg levels in drinking water for populations with initially soft water is anticipated to significantly reduce the incidence and mortality rates associated with CVDs. Existing literature suggests that deficiencies in Ca and Mg in drinking water are linked to increased incidences of various other diagnoses, particularly oncological diseases, diabetes mellitus or metabolic syndrome, nervous system, and others (Joslyn *et al.* 1990; Yang *et al.* 2000; Naumann *et al.* 2017; Rapant *et al.* 2019; Rosborg & Kožíšek 2020). Thus, it is plausible to expect that improving the Ca and Mg content in drinking water will lead to broader health benefits.

CONCLUSION

The achieved results confirmed the significant impact of the content of Ca and Mg in drinking water on AS, surpassing the influence of BMI, alcohol consumption, or smoking. Residents supplied with drinking water low in Ca and Mg exhibit significantly worsened AS parameters compared with those supplied with drinking water enriched in Ca and Mg. This condition is manifested by an increase in PWVao (by 1.9 m s^{-1}), an increase in arterial age (by 23.2 years), and an increase in Δ age (by 14.5 years). Following the increase in Ca and Mg content in drinking water (on average by 10–15 mg l^{-1}), a substantial improvement in arterial flexibility was observed in residents originally supplied with drinking water low in Ca and Mg after 18 months. This improvement was reflected in a reduction in PWVao (by 0.93 m s^{-1}), a reduction in arterial age (by 10.42 years), and a reduction in Δ age (by 11.79 years). Statistical analysis also confirmed the highest impact of Ca and Mg content in drinking water on AS, which was greater than the impact of BMI, alcohol consumption, and smoking.

The obtained results clearly indicate that AS is significantly influenced by the content of Ca and Mg in drinking water. If our findings are confirmed in other countries, it will provide further justification for including Ca and Mg among the regulated parameters in WHO drinking water standards, at least as supplementary values. Based on these results, it is recommended that AS measurements be incorporated into the indicators of cardiovascular risk/mortality for CVDs, especially in areas where the population is supplied with soft drinking water with low Ca and Mg levels. Administrative authorities should alert residents supplied with drinking water low in Ca and Mg to the high risk of developing CVD. The relevant authorities qualified to inform residents about the increased risk of developing CVD due to low Ca and Mg levels in drinking water are the respective Regional Public Health Authorities. They should recommend increased consumption of nutritional supplements based on Ca and Mg or encourage them to supplement their required daily intake of Ca and Mg by regularly consuming small amounts of mineral water with increased Ca and Mg content.

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AUTHOR CONTRIBUTIONS

S.R. conceptualized the study and prepared the methodology of the experiment supervised by P.Č. who collaborated on processing raw data, created tables and graphs, and assisted in translating and editing the study, V.C. prepared and wrote the original draft. I.H. conducted the measurement of arterial stiffness, F.K. contributed to writing – reviewing, editing, and visualization, and B.S. contributed to formal analysis and data curation. All authors have read and agreed on the article to be published.

ETHICS STATEMENT

Free and informed consent of the participants or their legal representatives was obtained and the study protocol was approved by the appropriate Committee for the Protection of Human Participants, the Ethics Committee of the Regional Public Health Authority of Zvolen, the Regional Public Health Authority of Zvolen, Slovakia, Protocol # ZV/KA/2014/1/183, approval date 05 September 2021.

DATA AVAILABILITY STATEMENT

All relevant data are included in the paper or its Supplementary Information.

CONFLICT OF INTEREST

The authors declare there is no conflict.

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