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Mineral composition and ratios in aortic valves, serum, and epicardial fat among patients with aortic stenosis undergoing aortic valve replacement

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Aortic stenosis (AS) is a leading cause of surgical intervention in adults with acquired heart disease, driven by an aging population and advancements in diagnostic and treatment approaches. This study aimed to investigate levels of macroelements (Ca, K, Na, Mg, and P) in aortic valve tissues, serum, and epicardial fat in patients undergoing aortic valve replacement due to degenerative disease. Elemental composition was determined using inductively coupled plasma mass spectrometry. Analyses revealed a distinct accumulation of Ca and P in aortic valve tissues, not correlated to and exceeding that in epicardial adipose tissue, suggesting localized mineralization. Significant relationships between serum and aortic valve element concentrations were found, with serum K and Mg levels inversely correlated with Ca and P deposition and Ca/P ratio in the valve, highlighting their potential role as calcification inhibitors. Moreover, serum and valvular Na/K ratios were positively correlated. Furthermore, patient age was associated with increased Ca, Mg, Na, P levels, and Ca/P ratio in valve tissues, reinforcing age as a risk factor for valvular calcification. Creatinine and lipoprotein (a) levels correlated positively with valvular K content and Ca/P ratio, respectively, while high-density lipoprotein cholesterol concentration was positively associated with Ca, Mg, and P content in epicardial fat. Patients with increased transvalvular systolic pressure gradient revealed higher valvular Na content. Future longitudinal research should address mineralization across earlier disease stages, exploring additional trace elements and molecular contributors to advance understanding of calcification mechanisms, ultimately aiding in developing biomarkers or therapeutic strategies for postponing or preventing AS onset.

Keywords Macroelements, Cardiovascular system, Epicardial adipose tissue, Aortic valve stenosis, Analytical study

Aortic stenosis (AS) is currently the leading indication for surgery in adults with acquired heart disease[1,2], with over 400,000 aortic valve prostheses implanted globally each year[3]. Additionally, projections suggest that until 2050, the number of individuals with aortic valve disease requiring intervention - whether through surgical aortic valve replacement (SAVR) or transcatheter aortic valve implantation (TAVI) - could double[4]. This anticipated rise in demand is attributed to several factors. First, the aging global population has led to a higher prevalence of AS, as its incidence increases with age[1,5]. Second, advances in diagnostic techniques and easier access to them allow earlier detection of aortic valve disease. Moreover, earlier intervention has become more common after publications demonstrating that treatment of asymptomatic patients with severe AS diagnosed in echocardiography significantly reduces the risk of sudden cardiac death, which may otherwise be the first clinical manifestation of the disease[6–8]. Additionally, improvements in procedural safety and the development of

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TAVI have enabled high-risk patients - previously considered unsuitable for standard SAVR - to undergo these procedures[9]. However, it remains uncertain whether these factors alone fully account for the rapid increase in patients with aortic valve disease undergoing interventional procedures.

Among patients requiring valve replacement, the pathological progression of valve calcification and degeneration is associated with complex biochemical and structural changes, including the deposition of minerals[10]. Although macroelements such as sodium (Na), potassium (K), calcium (Ca), magnesium (Mg), and phosphorus (P) play crucial roles in cellular homeostasis, mineralization processes, and overall cardiovascular health[11], their altered distribution within aortic valve tissues influences the mechanical properties and may lead to pathological progression of valve degeneration[12]. However, the specific contributions of macroelement levels to disease progression and their profiles in degenerated valves remain insufficiently understood[13]. Ca and P are particularly known to be implicated in AS by promoting aortic valve calcification, contributing to its stiffness and impaired function; thus, their ratio can be used as markers of the mineralization process[14,15]. However, other macroelements such as K and Mg, which can act as natural calcification inhibitors, and P, which is essential in Ca phosphate deposition, may also play significant roles in the pathological mineralization process[16]. Na and K, primarily involved in osmotic balance and cellular electrochemical gradients, can potentially also influence the disease state, especially since the increased Na/K ratio is a risk factor for hypertension and could exacerbate valve dysfunction due to increased vascular pressure and promotion of left ventricular hypertrophy[17,18].

Epicardial adipose tissue, located between the myocardium and the visceral layer of the pericardium, has been increasingly recognized as a metabolically active tissue capable of influencing cardiovascular diseases[19]. It is known to secrete adiponectin, adrenomedullin, adipokines, several proinflammatory cytokines, monocyte chemoattractant protein-1, nerve growth factor, resistin, plasminogen activator inhibitor-1, and free fatty acids[20]. Importantly, epicardial fat is in direct anatomic and functional proximity to the myocardium and coronary arteries, allowing it to potentially influence the progression of cardiovascular pathologies, including AS. Understanding whether mineral composition of this tissue mirrors or modulates valvular mineralization could potentially provide new insights into the local pathophysiological processes contributing to AS progression.

Despite this, little is known about the mineral profile of epicardial adipose tissue in patients with AS and how it correlates with mineral levels in the valve or systemic circulation. Despite increasing interest in the biochemical composition of degenerative aortic valves, detailed quantitative analyses of macroelement levels in these tissues are still scarce, and little is known about the mineral profile of epicardial adipose tissue[21]. A comprehensive understanding of their concentrations, ratios, and interactions within the context of valve pathology could offer insights into the mineralization processes driving disease progression, especially as it is known that aortic mineralization does not result from passive deposition but rather from complex cellular and biochemical alterations[22]. Such information could also help identify potential therapeutic targets to modulate mineral homeostasis within valve tissue.

This study aimed to quantify the content of Na, K, Ca, Mg, and P and their ratios (Ca/P, Na/K) in aortic valves collected from patients undergoing SAVR due to degenerative AS and to understand whether valvular mineral levels correlate with their concentrations in serum and epicardial fat as well as the number of clinical parameters. By providing a detailed profile of macroelement levels, this research seeks to enhance the understanding of mineral element dynamics in AS and their potential contributions to valve calcification and degeneration pathophysiology.

Results

The main characteristics of patients from whom samples were collected during the aortic valve replacement procedure are provided in Table 1. They had a mean age of 68.9 ± 7.4 years, were represented by the majority of men, and had a high prevalence of obesity, coronary artery disease, arterial hypertension, and diabetes mellitus (Table 1).

Table 2 summarizes the determined levels of elements and their ratios in serum, epicardial fat, and aortic valves. The mean concentration of minerals decreased in the following order: Na > K > Ca > P > Mg (serum), Ca > Na > P > K > Mg (epicardial fat), and Ca > P > Na > Mg > K (aortic valve). Significantly higher concentrations of elements were found in aortic valves than in epicardial fat (Table 2).

The content and ratios of elements in epicardial fat did not correlate with those in serum and aortic valves. In turn, the serum and valve Na/K ratios were positively related (Fig. 1). Moreover, serum K concentration revealed negative correlations with the aortic valve's content of Ca, Na, and P. Serum K and Mg levels were also negatively associated with the valve's Ca/P ratio (Fig. 1).

The patient's age was positively correlated with the Ca, Mg, Na, and P content in aortic valves and a higher Ca/P ratio (Table 3). Furthermore, patients aged ≥ 70 revealed a higher valvular Ca/P ratio than those aged < 70 (mean $\pm$ SD 2.60 ± 0.04 vs. 2.72 ± 0.05, $p = 0.003$). In the case of the mineral content in the epicardial fat, no significant associations were found with patient age and no difference between < 70 and ≥ 70 years. Moreover, the valvular Ca/P ratio correlated with the patient's BMI (Table 3) and was higher in obese individuals compared to those with BMI < 30 (mean $\pm$ SD 2.72 ± 0.05 vs. 2.66 ± 0.03, $p = 0.03$). Creatinine and Lp(A) levels correlated positively with valvular K content and Ca/P ratio, respectively, while high-density lipoprotein cholesterol concentration was positively associated with Ca, Mg, and P content in epicardial fat (Table 3). The mean transvalvular pressure gradient was positively correlated only with valvular Na content, and patients with values exceeding 50 mm Hg were found to have significantly higher levels of this mineral (Fig. 2). Maximum transvalvular pressure gradient did not correlate with serum, valvular, and epicardial fat levels of studied minerals.

Preoperative data	
Age (years), mean ± SD	68.9 ± 7.4
< 70 years, % (n)	50 (10)
≥ 70 years, % (n)	50 (10)
Male/Female, % (n)	70/30 (14/6)
BMI, kg/m^2	29.4 ± 4.6
Obesity (BMI > 30 kg/m^2), % (n)	45 (9)
Coronary artery disease, % (n)	35 (7)
Acute coronary syndrome in history, % (n)	10 (2)
Heart Failure in NYHA III and IV, % (n)	50 (10)
Atrial fibrillation, % (n)	5 (25)
Ascending aortic aneurysm, % (n)	35 (7)
Arterial hypertension, % (n)	85 (17)
Peripheral artery disease, % (n)	15 (3)
Diabetes mellitus, % (n) Treated with insulin, % (n)	45 (9) 15 (3)
Chronic kidney disease (class 3 and more), % (n)	10 (2)
eGFR, mL/min/1.73 m^2	86.4 ± 25.9
Preoperative echocardiography (M + 2D + Doppler)	
Mean systolic pressure gradient [mmHg]	53.9 ± 15.9
Peak systolic pressure gradient [mmHg]	82.3 ± 23.9
Mean systolic pressure gradient > 50 mmHg, % (n)	35 (7)
Surgical details	
Isolated SAVR, % (n)	50 (10)
SAVR + CABG, % (n)	10 (2)
SAVR + AAR, % (n)	35 (7)
SAVR + MVR, % (n)	5 (1)

Table 1. The selected clinical data of the studied group of patients ($n = 20$). *AAR* ascending aortic replacement (if diameter exceeded 4.5 cm), *BMI* Body Mass Index, *CABG* coronary artery bypass grafting, *eGFR* estimated glomerular filtration rate, *SAVR* Surgical aortic valve replacement, *MVR* mitral valve replacement, *NYHA* New York Heart Association scale.

	Serum	Epicardial fat	Aortic valve	
	Concentrations			
Parameter	[mg/L]	[mg/g]	[mg/g]	Fat vs. Valve (*p*-value)
Ca	108.0 ± 13.4 (80.8-147.1)	0.77 ± 1.12 (0.05–3.80)	112.0 ± 36.6 (21.8-169.5)	< 0.0001
K	208.2 ± 33.9 (123.4-273.1)	0.28 ± 0.16 (0.11–0.69)	0.38 ± 0.08 (0.27–0.54)	0.01
Mg	31.0 ± 2.7 (26.4–36.3)	0.036 ± 0.025 (0.006–0.12)	1.3 ± 0.40 (0.25–1.9)	< 0.0001
Na	3410.2 ± 320.6 (2976.9-4148.5)	0.52 ± 0.29 (0.10–1.37)	4.6 ± 0.9 (1.9–5.9)	< 0.0001
P	97.1 ± 15.1 (65.5-124.6)	0.33 ± 0.43 (0.09–1.98)	41.7 ± 13.9 (8.1–64.3)	< 0.0001
	Ratios			
Ca/P	1.1 ± 0.1 (0.8–1.4)	1.3 ± 0.6 (0.3–2.1)	2.7 ± 0.05 (2.6–2.8)	< 0.0001
Na/K	16.7 ± 2.8 (13.5–25.9)	2.0 ± 0.7 (0.9–3.9)	12.4 ± 3.2 (6.4–18.0)	< 0.0001

Table 2. Levels of macroelements in serum, epicardial fat, and aortic valve in patients undergoing aortic valve replacement ($n = 20$). Data presented as mean ± standard deviation (min-max).

Discussion

This study examined the distribution of Ca, K, Na, Mg, and P levels and their ratios in aortic valves in patients undergoing their surgical replacement, as well as the relationship between valvular mineralization and concentrations of elements in serum and epicardial fat. The reported findings add to a general understanding of the potential mechanisms behind valvular calcification, a common and severe cardiovascular problem, and provide insights into systemic or localized factors that contribute to valve degeneration. Such knowledge may help potentially identify biomarkers for early diagnosis and guide research on novel treatments for patients with valvular heart disease.

Notably, the investigated elements were more concentrated in the aortic valves than in epicardial fat, suggesting localized mineral accumulation within valve tissue. To the best of our knowledge, this is the first

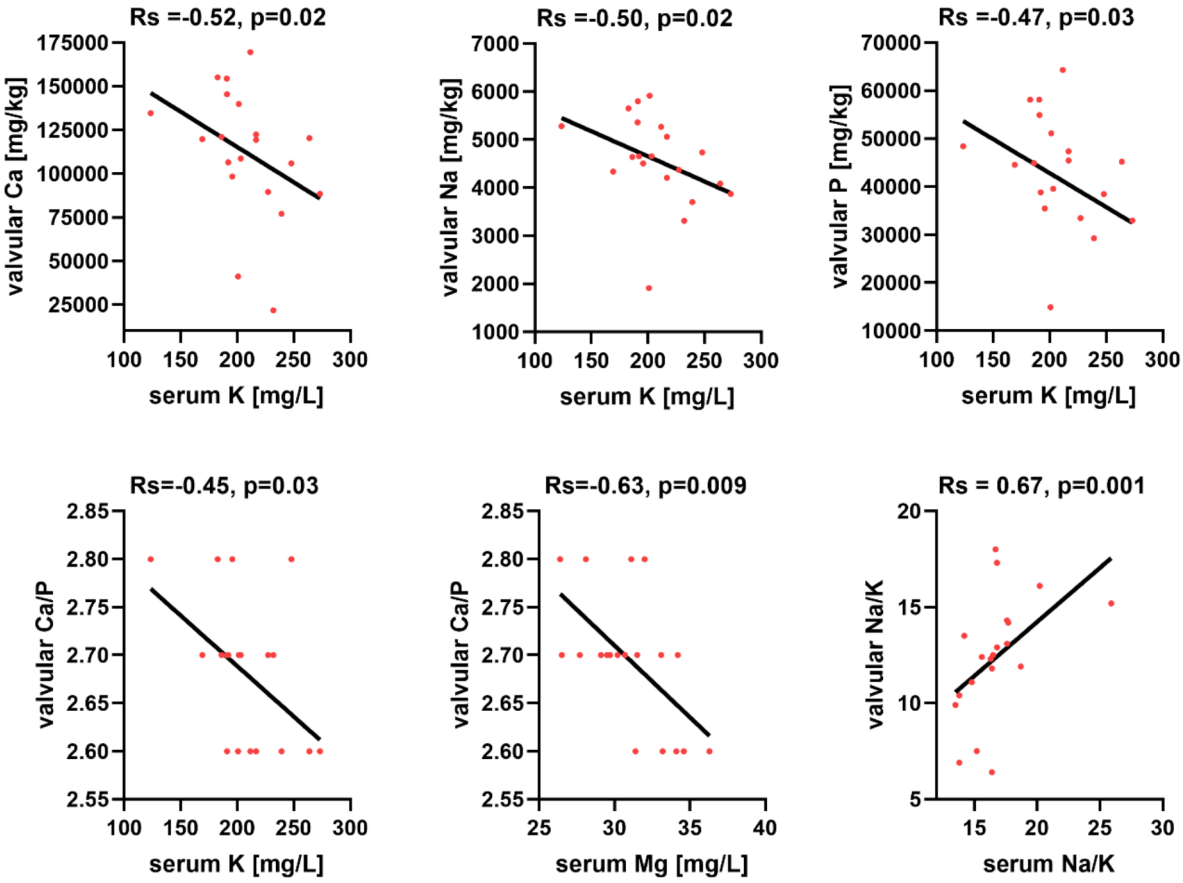

Fig. 1. The statistically significant correlations (Spearman's correlation coefficient, Rs) between serum and valvular mineral content in patients undergoing aortic valve replacement ($n = 20$).

time the profile of macroelements in human epicardial adipose tissue has been reported. The lack of correlation between the content of minerals in this tissue and their serum and aortic valve levels suggests distinct regulatory processes in epicardiac fat compared to systemic and valvular compartments. Moreover, the accumulation of macroelements in the aortic valves did not follow the gradient observed in serum or epicardial fat and was mainly driven by Ca and P deposits. That confirms previous observations that valvular mineralization does not result from a simple passive accumulation of circulating elements but involves active processes, including the emergence of osteoblast-like bone-forming cells, endothelial-to-mesenchymal transition, and formation of matrix vesicles giving rise to microcalcific nodules[10,22]. Interestingly, even though valvular Ca and P contents between particular patients, the Ca/P ratio remained uniform at the 2.6–2.8 level. These values imply intensive valve calcification and the presence of crystallized hydroxyapatite variants, possibly also with carbonate and Mg substitutions[23,24].

The study also uncovered a novel association between transvalvular systolic pressure gradient and valvular Na content. Specifically, the mean transvalvular pressure gradient was positively correlated with the Na content of aortic valves, and patients with values exceeding 50 mm Hg had significantly higher levels of Na within their valves. This finding suggests that Na deposition may contribute to the hemodynamic burden observed in severe AS, potentially through effects on valve stiffness and calcification. This observation highlights the need to investigate whether localized Na accumulation could exacerbate the biomechanical and structural alterations characteristic of advanced AS.

Our analysis also shows that the patient's age was positively correlated with levels of particular elements, i.e., Ca, K, Mg, P, and Ca/P ratio. This is consistent with the epidemiological observations documenting that aging contributes to degenerative, calcific, and valvular disease, affecting over 25% of patients aged over 65 years with a risk doubling every 10 years of life in the elderly when adjusting for confounding clinical factors[25–27]. This is because, along with aging, valve interstitial cells tend to differentiate pathologically into myofibroblasts and osteoblast-like phenotype, leading to calcium crystals being laid in the valve matrix and organized in structures similar to lamellar bone[28]. However, one should note that our study did not investigate valvular mineralization in individuals of contrasting ages but in a rather narrow range, with a mean of 69 years, which is typical for those requiring AVR[29]. In addition, the valvular Ca/P ratio also increased with the patient's BMI, which is consistent

Element	Age	BMI	Creatinine	eGFR	Cholesterol	LDL	HDL	TG	Lp(A)	Fibrinogen
Aortic valve										
Na	0.37	− 0.18	0.31	− 0.07	0.07	0.11	− 0.21	0.33	− 0.27	− 0.14
Mg	**0.53**	− 0.11	0.36	0.02	0.03	0.09	− 0.16	0.25	0.03	− 0.04
P	**0.45**	0.02	0.29	0.13	0.08	0.16	− 0.25	0.29	0.08	0.00
K	0.11	0.15	**0.57**	− 0.19	− 0.01	0.02	− 0.14	0.27	− 0.07	0.19
Ca	**0.48**	0.08	0.30	0.17	0.10	0.20	− 0.29	0.38	0.08	0.01
Na/K	0.23	− 0.21	− 0.10	0.03	− 0.04	− 0.03	− 0.13	0.04	− 0.19	− 0.22
Ca/P	**0.30**	**0.49**	− 0.37	− 0.18	0.10	− 0.08	0.34	0.05	**0.49**	− 0.14
Epicardial adipose tissue										
Na	0.04	− 0.21	− 0.15	− 0.04	− 0.01	− 0.14	0.16	0.01	− 0.10	− 0.05
Mg	0.22	− **0.47**	− 0.27	− 0.28	0.02	− 0.25	**0.47**	− 0.15	− 0.25	− 0.11
P	0.21	− 0.24	− 0.27	− 0.14	0.08	− 0.15	**0.50**	− 0.18	− 0.25	− 0.29
K	0.18	− 0.23	− 0.17	− 0.16	0.32	0.09	0.45	− 0.02	− 0.21	− 0.26
Ca	0.36	− 0.19	− 0.41	− 0.02	0.04	− 0.10	**0.68**	− 0.37	− 0.21	− 0.39
Na/K	0.15	0.11	0.16	− 0.21	− 0.40	− 0.41	− 0.23	0.02	− 0.16	0.11
Ca/P	− 0.04	0.16	0.01	0.05	0.45	0.45	0.04	0.12	0.43	− 0.27

Table 3. Correlations (Spearman's rank coefficient, rs) between patient's clinical characteristics and mineral composition of the aortic valve and epicardial fat in patients undergoing aortic valve replacement ($n = 20$). Statistically significant correlations ($p < 0.05$) are bolded. *BMI* Body Mass Index, *eGFR* estimated glomerular filtration rate, *LDL* low-density lipoprotein, *HDL* high-density lipoprotein, *TG* total glycerides, *Lp(a)* lipoprotein (a).

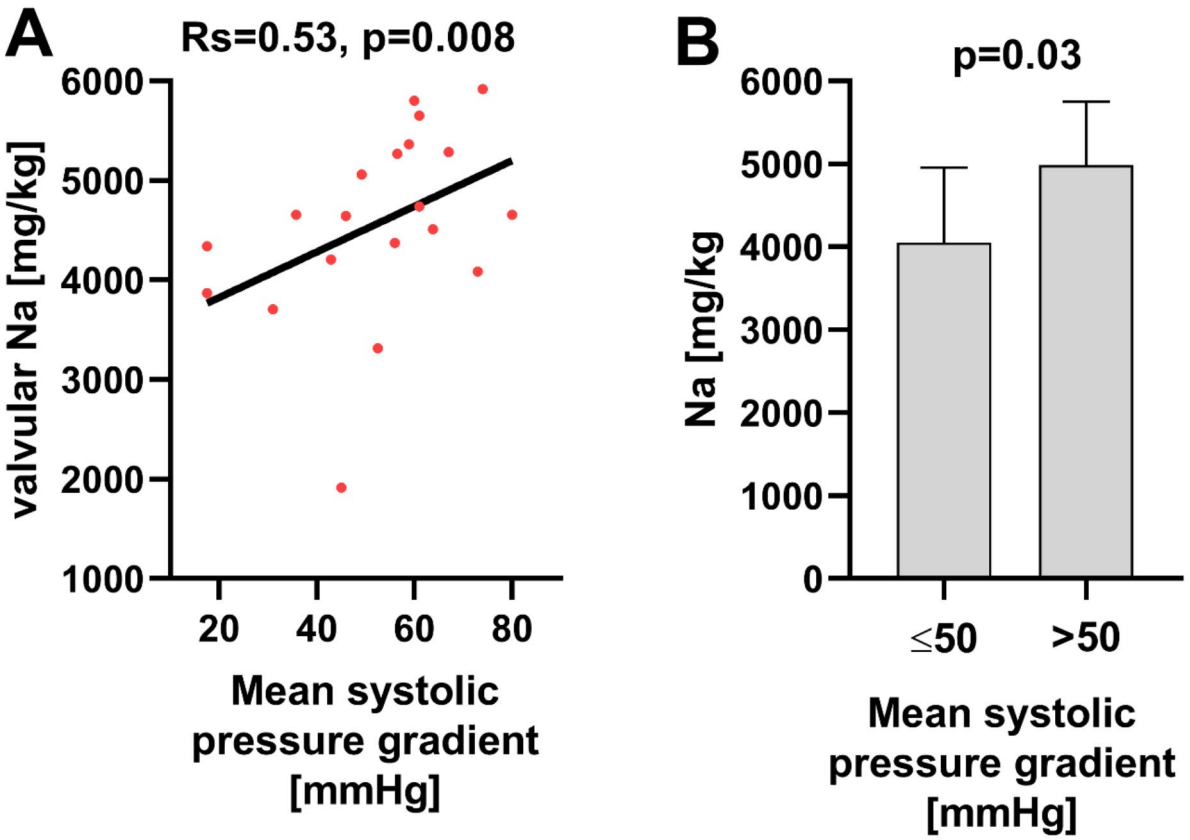

Fig. 2. The relationship between mean transvalvular systolic pressure gradient and valvular Na content in patients undergoing aortic valve replacement ($n = 20$).

with previous findings that increased body mass is an independent risk factor for AS[30,31] and that calcified aortic valves are more common in individuals with obesity[32].

The present study also reports on certain associations between serum concentrations of minerals and their valve levels, indicating that systemic electrolyte balance might influence valvular mineralization patterns. As shown, serum K levels revealed significant negative correlations with Ca, Na, and P content in aortic valves. It is known that K may play a role in limiting calcification in the aortic valve, which results from the deposition of calcium phosphate minerals. As shown in vivo, reduced dietary K promoted atherosclerotic vascular calcification and increased aortic stiffness[33]. Higher K concentrations could reduce Na and Ca uptake into tissues such as the aortic valve, firstly by affecting Na^+/K^+-ATPase activity and subsequently leading to decreased tissue Na levels, to ultimately alter the Na^+/Ca_2^+ exchanger activity, thereby affecting Ca deposition[34–36]. These assumptions are further supported in the present study by the decreased valve's Ca/P ratio, a marker of calcification, in patients having higher serum concentrations of K. Similar association was also found for serum Mg, which is also known to prevent vascular calcification by inhibiting hydroxyapatite crystal formation[37]. These findings contribute to a growing body of evidence on the role of mineral metabolism in cardiovascular disease and suggest potential biomarkers or therapeutic targets related to tissue mineralization.

Interesting associations between valvular mineralization and selected biochemical markers were found. Serum creatinine was positively correlated with K content. This potentially indicates the renal system may play a broader role in the mechanisms influencing valvular calcification beyond the presence of renal insufficiency[38]. The observed positive correlation between serum creatinine and both K content and Ca/P ratio in valves highlights the possibility of such complex renal involvement, particularly since the majority of the studied patients had a normal estimated glomerular filtration rate. It is known that renal dysfunction can alter systemic mineral metabolism, potentially leading to changes in calcium-phosphate homeostasis and increased chronic inflammation, both of which play a role in calcification processes[39,40]. This underscores the need for further research into renal contributions, including mechanisms independent of outright renal insufficiency.

In turn, lipoprotein (a) concentrations were positively correlated with the Ca/P ratio. The elevated level of the former is a marker of impaired kidney function, which is closely linked to aortic valve calcification and AS due to disturbances in Ca-P metabolism and chronic inflammation[41,42]. In turn, increased lipoprotein (a) levels have been associated with the onset and progression of aortic valve calcification and the need for AVR[43–45] by infiltrating the inner layers of the valve and stimulating the expression of osteoblastic transcription factors, runt-related transcription factor 2 and bone morphogenetic protein 2 in the valvular interstitial cells[46–48]. In addition, the present study found a correlation between serum high-density lipoprotein concentration and levels of Ca, Mg, and P in epicardial fat. As previously found, this lipoprotein can affect mineral metabolism, e.g., by increasing intracellular Ca levels in human endothelial cells[49]. However, further studies are required to determine whether the same phenomenon occurs in the case of epicardial adipose tissue.

While this study provides valuable insights into the mineral element dynamics in AS, it has several limitations that must be stressed. First, the study is limited by its cross-sectional design, which restricts our ability to draw causal conclusions about the relationship between mineral levels and valve degeneration. The observed relationships between serum, epicardial fat, and valve tissue element levels are associative, so further research is needed to clarify the underlying mechanisms linking systemic mineral homeostasis and valve calcification. Additionally, the analysis was conducted on samples collected exclusively from patients undergoing valve replacement for severe aortic valve calcific degeneration, which may not represent the mineral dynamics in earlier disease stages or in healthy individuals. Another limitation is the relatively small sample size, which might reduce the generalizability of the findings across diverse populations. Furthermore, while the study focused on macroelements such as Na, K, Ca, Mg, and P, other trace elements or molecular factors involved in valve pathology were not examined and may also play significant roles in the calcification processes.

Conclusions

This study enhances our understanding of mineral element dynamics in aortic valve calcification, highlighting the complex interplay between systemic and localized factors in valvular degeneration. The findings emphasize the distinct mineral profiles in aortic valves compared to epicardial fat and serum, with valvular calcification primarily driven by Ca-P deposition and associated with aging, BMI, and selected biomarkers, i.e., creatinine, and lipoprotein (a). Additionally, the observed relationships between serum K and Mg levels and reduced calcification markers suggest potential roles for these elements in mitigating mineral accumulation. These insights underscore the importance of further research into mineral metabolism and its implications for early diagnosis and novel therapeutic strategies targeting aortic valve calcification.

Materials and methods

Patients

This study involved 20 adult patients who underwent elective SAVR as isolated or combined procedures in a single cardiac surgical department (Table 1). Patients were qualified for surgery following clinical assessment and analysis of imaging examinations (echocardiography, coronary angiography, and computed angiographic tomography (CTA) if indicated). All operations were done under general anesthesia and in standard cardiopulmonary bypass (CPB).

The study was approved by the Local Bioethical Committee of the Poznan University of Medical Sciences, Poznan, Poland, and has been performed according to the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Every recruited patient undersigned a written informed consent.

Sample collection

Blood samples were collected once patients reached the operating theatre before surgery, left to clot, and centrifuged at 2,000 x g for 10 min to collect serum. Additional blood samples were collected for analysis of biochemical markers (creatinine, estimated glomerular filtration rate, total cholesterol, low-density lipoprotein, high-density lipoprotein, total glycerides, lipoprotein (a), and fibrinogen) at an accredited hospital laboratory. A small portion (approximately 1 to 2 cm^3) of fatty tissue covering the anterior part of the pericardium was harvested soon after sternotomy, while all degenerated aortic cusps were collected following aortic cross-clamping, cardioplegic cardiac arrest and aortic valve exposure.

Samples preparation

Following the collection, the aortic valves and epicardial fat samples were profusely rinsed with sterile distilled water to remove blood remnants and stored in cryogenic Nunc™ tubes (ThermoScientific, USA) at -40°C until further processing. Serum samples were stored under similar conditions. Thawed valves and fat were weighted and digested with concentrated 65% HNO_3 (Sigma-Aldrich, USA) in closed Teflon containers in the microwave digestion system Mars 6 Xpress (CEM Corporation, USA) by ramping to 180 °C for 20 min and holding for 30 min. Serum samples (1 mL) were digested similarly in 3 mL 65% HNO_3. After mineralization, samples were filtered and diluted with MilliQ water (Millipore, Germany) to a total volume of 15.0 mL in the case of valve and lipid samples and 5.0 mL in the case of serum.

Macroelements determination

The elemental composition of samples has been determined using inductively coupled plasma mass spectrometry (PlasmaQuant MS Q; Analytik Jena, Germany). The following instrument's settings were applied: nebulizer gas flow 1.05 L/min, plasma gas flow 9.0 L/min, auxiliary gas flow 1.5 L/min, and radio frequency power 1.35 kW. The signal was measured in 5 replicates (10 scans each). The interferences were reduced using the integrated collision reaction cell working sequentially in three modes: without gas addition, with helium as collision gas, and hydrogen as reaction gas. A reflexION ion mirror was used to adjust the sensitivity to increase the range of concentrations. Detection limits were as follows: Ca − 78 µg/L, K – 36 µg/L, Na − 15 µg/L, Mg − 3,2 µg/L, and *P* − 10 µg/L. The analytical procedure was validated using multiple certified reference materials (BCR-668, DB001, BCR-185R, ERM-BB184, Seronorm-L1, DA-120a, BCR-627). The analytical process has been controlled using certified reference material ERM-BB184 bovine muscle (European Commission Joint Research Centre (JRC), Geel, Belgium) and standard addition procedure. The recovery of 80–120% has been considered acceptable.

Statistical analyses

The results were analyzed with Statistica v.13.3 (StatSoft, USA). Demographic and selected preoperative clinical data were expressed as either mean with standard deviation (SD) (if continuous) or numbers (n) with percent (%) (if categorical variables). Due to non-Gaussian data distribution (evaluated with Shapiro-Wilk's test), non-parametric Mann-Whitney U test was used to evaluate the differences in elemental composition between groups, while Spearman's rank correlation coefficient was employed to assess interrelationships among elements and their association with patient's age. A p-value below 0.05 was deemed statistically significant.

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author upon reasonable request.

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Author contributions

Barbara Poniedziałek: conceptualization; methodology; formal analysis; resources, investigation, writing—review and editing. Bartłomiej Perek: conceptualization methodology; sample collection; formal analysis; writing—review and editing. Aleksandra Orłowska: investigation. Anna Komosa: formal analysis; writing—review and editing. Przemysław Niedzielski: methodology; formal analysis investigation; writing—review and editing. Piotr Buczkowski: sample collection. Marek Jemielity: sample collection; resources; supervision. Piotr Rzymski: conceptualization; methodology; formal analysis; resources, investigation, supervision; writing—original draft.

Declarations

Competing interests

The authors declare no competing interests.

Ethics approval

The study was approved by the Local Bioethical Committee of the Poznan University of Medical Sciences, Poznan, Poland (approval number 518/23 issued on 29 June 2024).

Additional information

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