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Comparison of Serum Selenium Levels Between Patients with Newly Diagnosed Atrial Fibrillation and Normal Controls

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Abstract
Atrial fibrillation (AF) is the most common sustained dysrhythmia in the elderly population. It is estimated to affect more than 30 million people worldwide. AF occurs when abnormal electrical impulses start to activate in the atria and override the heart's natural pacemaker, which can no longer control the heart's rhythm. Since atrial contractility is impaired in AF, blood flow in the atria becomes stasis over time and causes thrombus formation. This thrombus causes the risk of embolism and causes complications such as stroke. Therefore, it is a fundamental cause of cardiovascular mortality and morbidity. The diagnosis of AF is usually made with the help of electrocardiography (ECG). The absence of P waves in ECG and irregular R-R interval is sufficient for diagnosis. AF is most commonly associated with advanced age, hypertension, diabetes mellitus, thyroid dysfunction, obesity, alcohol use, physical inactivity, and underlying ischemic heart diseases. As well as to all these usual risk factors, electrolyte disorders and mineral deficiencies also play an essential role in the etiology of AF. Previous studies have clearly demonstrated that serum electrolyte changes have a role in the etiology of AF. These include electrolytes such as serum magnesium, calcium, potassium, and chloride. However, there is not enough information in the literature about the effects of trace elements on AF. Selenium is a trace element that plays an important role in many systems in the human body. It has a vital role in inflammation, regulation of antioxidant reactions, and fibrosis of tissues in both animals and humans. It is known that selenium deficiency causes many cardiovascular diseases such as heart failure, coronary artery disease, and arrhythmia. Our study aimed to compare serum selenium levels in newly diagnosed AF patients with the healthy control group.

Keywords Atrial fibrillation · Dysrhythmia · Selenium · Trace element

Introduction

Atrial fibrillation (AF) is a type of supraventricular arrhythmia characterized by rapid, irregular stimulation of the atria and irregular activation of the ventricles. This arrhythmia is one of the most common types of cardiac arrhythmia in adult clinical practice [1]. Due to the irregular rhythm, the blood flow in the heart becomes turbulent and causes stasis within the atria, causing thrombus to form. This thrombus causes embolism, especially in the central nervous system, leading to strokes. Electrocardiography (ECG) is the most widely used and most practical method in diagnosing AF. The absence makes the diagnosis of P waves representing atrial depolarization on the ECG and the unequal R-R intervals (Fig. 1). Risk factors for AF include advanced age, hypertension (HT), diabetes mellitus (DM), underlying heart and lung disease, congenital heart disease, and increased alcohol consumption [2]. Another important risk factor is electrolyte disturbances. In previous studies, it has been reported that the incidence of cardiac arrhythmias is increased in mineral deficiencies such as magnesium, calcium, sodium, and potassium [3–8].

Selenium is an essential trace element in the human body and has important roles in many systems. For example, its antioxidant properties prevent the activation of reactive oxygen species (ROS) and protect the body from oxidative damage caused by ROS in cells and tissues [9]. In humans, selenium deficiency is associated with acute and chronic

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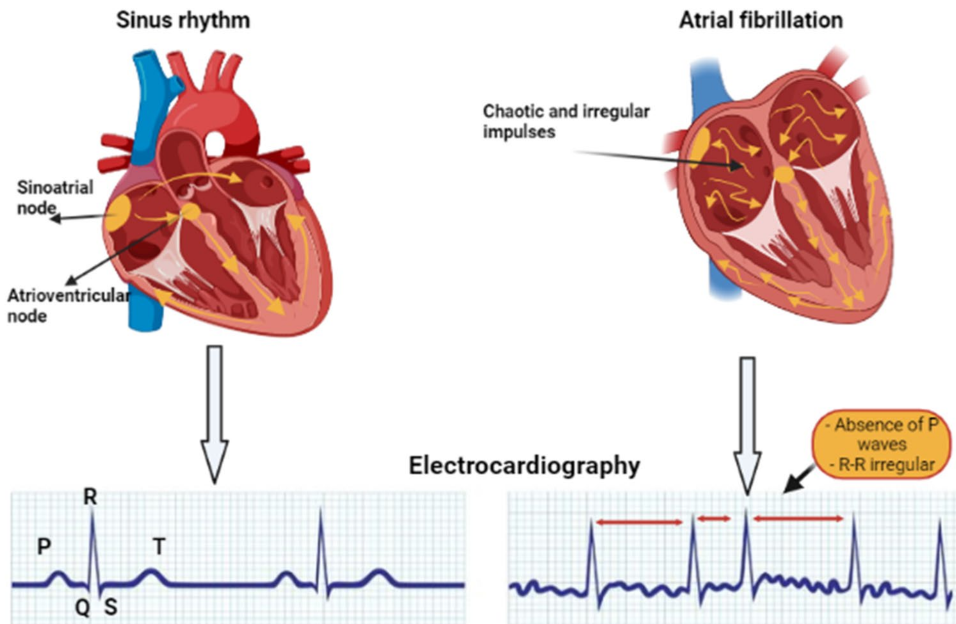

Fig. 1 Conduction system and ECG images of sinus rhythm and atrial fibrillation

pathological conditions such as systemic inflammation, cardiovascular diseases, autoimmune diseases, diabetes mellitus, and various cancers [10–13].

Numerous studies support the importance of providing the recommended selenium intake for maintaining proper body function and homeostasis [14, 15]. Selenium has been shown to be cardioprotective in previous studies, and it is known to reduce infarct size, reduce arrhythmias, and contribute to contractile recovery after ischemia/reperfusion injury [16–19]. The adverse cardiac effects of selenium deficiency first appeared in the Keshan region of Heilongjiang province. The disease was named Keshan disease, after the region where it was discovered. Clinically, this disease demonstrated an acute or chronic episode of heart disease characterized by cardiogenic shock, heart enlargement, and congestive heart failure [20]. Animal experimental and basic scientific studies have also shown that selenium deficiency may be associated with an increased risk of atherosclerotic cardiovascular disease [21, 22].

As far as we know, there is no study in the literature on the relationship between selenium deficiency and AF. Therefore, our study aimed to compare serum selenium levels in newly diagnosed AF patients with healthy control groups.

Material and Methods

Study Population

This prospective and cross-sectional study included 91 consecutive patients (51 females and 40 males) with newly diagnosed AF, aged 35–75 years, who presented to the cardiology outpatient clinic between March 2021 and July 2021. As the control group, 91 healthy volunteers with normal sinus rhythm (SR) age- and sex-matched were included. A complete physical examination was performed by questioning the medical histories of all participants in the study group. After resting for at least 10 min, arterial blood pressure measurements were made, and the data were recorded. Waist circumference, height, and weight of all participants were measured. Body mass indexes (BMIs) were calculated using the formula BMI = weight (kg)/[height (meter)]^2. Atatürk University Faculty of Medicine Ethics Committee approved this study. The study was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained for the anonymized information of the patients to be published in this article. The algorithm for selecting the patient group is shown in Fig. 2.

Exclusion Criteria of the Study

- Known history of coronary artery disease
- Heart failure with reduced ejection fraction (HFrEF) = (EF < 40%)
- Heart failure with mildly reduced ejection fraction (HFmrEF) = (EF = 40–49%)
- Moderate and severe heart valve diseases
- Hypertrophic cardiomyopathy
- Pericardial disease
- Use of implanted cardiac device for arrhythmias
- Use of anti-arrhythmic drugs (beta-blockers, calcium channel blockers, amiodarone, etc.)
- Active malignancy and malnutrition
- Hyperthyroidism, hypothyroidism

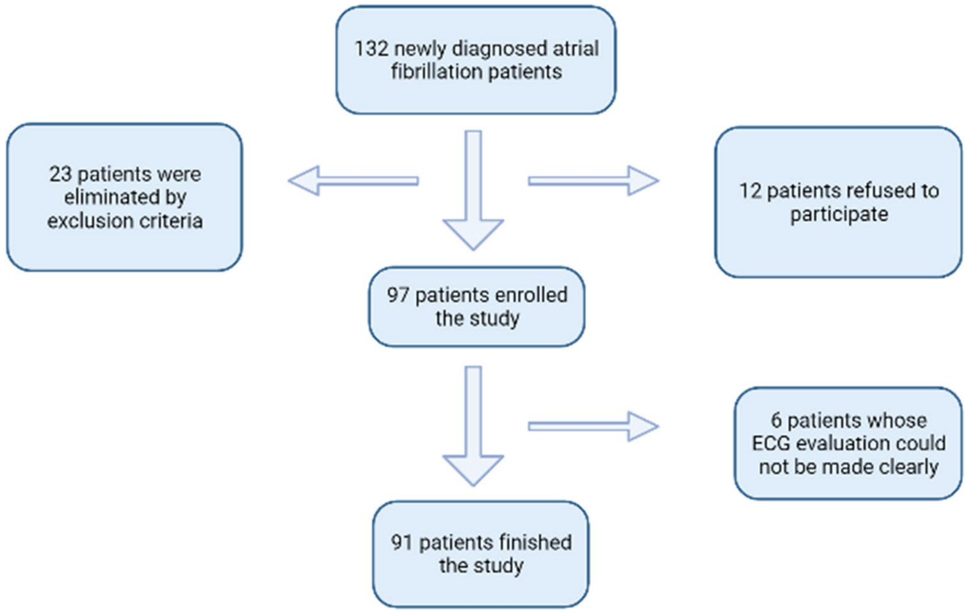

Fig. 2 Designing the patient group in the study

- Renal failure (GFR < 60 ml/min)
- Severe anemia (Hg < 11 gr/dl)
- Infectious diseases in the last 6 months
- Excessive amounts use of alcohol
- Those whose ECG evaluation cannot be made clearly

ECG and Echocardiographic Evaluation

Recordings were taken via 12-lead superficial ECG at a paper speed of 50 mm/s and a voltage of 10 mm/mV using the Nihon Kohden (Tokyo, Japan) ECG recorder of all participants. All ECGs were taken at least 10 min after rest and in the supine position in a regular breathing pattern. The absence of P waves on ECG and irregular R-R intervals were defined as AF. Two different cardiologists who could not see the study participants analyzed the ECG data and calculated their relevant parameters. Inter-observer and inter-observer variation coefficients are 2.6% and 3.1%, respectively.

Transthoracic echocardiography was performed on all participants in the study group. Echocardiographic examinations were performed in the Department of Cardiology Echocardiography Laboratory using the EPIQ 7 echocardiography device (Philips, Amsterdam, Netherlands). Measurements were made in the left lateral decubitus position as recommended by the American Society of Echocardiography. In addition, left atrium, ascending aorta diameter, left ventricular end-systolic and end-diastolic diameters, interventricular septum, and posterior wall were measured with parasternal long-axis imaging. In addition, the left ventricular ejection fraction was measured with the modified Simpson's method.

Laboratory Analyses

Venous blood samples were taken after 8 h of fasting for biochemical analysis of the participants. Fasting blood glucose, kidney function tests, liver function tests, thyroid function tests, and serum electrolyte levels were measured in biochemical analysis. Serum selenium levels were studied in the Agilent Technologies 7700 Series ICP-MC atomic absorption device in the Department of Medical-Biochemistry Laboratory. To measure the selenium level, the vein blood obtained from the patient and control groups was taken into the original 5-mL biochemistry tubes with yellow caps. Serums were obtained by centrifugation at 3500 rpm, 4 °C for 10 min in a centrifuge device. The obtained sera were used for selenium analysis. One hundred microliters of serums was put into 10-mL plastic falcon tubes with caps used in the ICP-MS device. Five hundred microliters of nitric acid and hydrogen peroxide mixture solution, which was prepared and kept in advance, was added, and the lids were closed tightly. The tubes were burned at 100 °C for 1 h and 45 min in a special microwave incinerator. After the combustion process was completed, the caps of the tubes were opened and 9.5 mL of distilled water was added to them, and they were prepared for analysis. 6 standard mixtures at different concentrations were prepared for the device. These are blends of Blak, 0.625 ppb, 1.25 ppb, 2.5 ppb, 5 ppb, 10 ppb, and 20 ppb, respectively. After all the solutions were ready, the tubes were placed in the appropriate parts of the device, and the device was made ready. After the preparation of the device, the tubes with the serum samples whose incineration process was completed were also placed in the device, and the machine was started. The number of samples to be processed as specified on the device's monitor, and the samples were coded. After the device made the measurement automatically, the results were recorded.

Statistical Analysis

The statistical analyses were given as mean ± standard deviation (SD). Unpaired *T*-test (one-tailed *P*-value), as well as ordinary two-way ANOVA using Sidak's multiple comparisons test, was utilized to compare the study groups. The comparison was done in GraphPad Prism 8.0.1 (GraphPad Software, San Diego, CA, USA) software. The degree of significance was denoted as $^{**}P < 0.01$, $^{***}P < 0.001$, and $^{****}P < 0.0001$.

Receiver operating characteristics (ROC) analysis was performed to choose a cutoff value that separates "normal" from "abnormal" Se concentrations (mg/dL). The analysis was accomplished using GraphPad Prism 8.0.1 (GraphPad Software, San Diego, CA, USA) software. To help make the decision, a tradeoff of sensitivity versus specificity was plotted as a ROC curve. Sensitivity measures the fraction of people with the disease that the test correctly identifies as positive. On the other hand, specificity means the fraction of people without the disease that the test correctly identifies as negative. The mean area under the entire curve (AUC) ± standard error (SE) of 95% confidence was evaluated, which quantifies the overall ability of the test to discriminate among patients and healthy individuals.

A Pearson's correlation test was conducted to measure the linear correlation between Se concentrations (mg/dL) and risk factors such as HT% and DM% in AF patients. Accordingly, Pearson's correlation coefficients (PCC/*r* and R^2 values) were computed using the two-tailed *P*-value option and 95% confidence level.

Results

The mean age in the study group was 66.81 ± 9.56 years. There was no significant difference between the groups in terms of age and gender (Fig. 3a). As expected, the number of patients with HT and DM was significantly higher in the AF group. In biochemical analyses, selenium levels were significantly lower in the AF group compared to the control group (69.30 ± 19.86 mg/dL vs. 79.92 ± 22.86 mg/dL, $P < 0.0005$, respectively) (Fig. 3b). The comparison of demographic and clinical information of the groups is shown in Table 1.

Specificity was found to be significant in ROC curve analysis ($P < 0.01$). Area under ROC curve (AUC) was = 0.63 ± 0.04 (Fig. 3c). When analyzed according to genders, serum Se levels were significantly lower in men

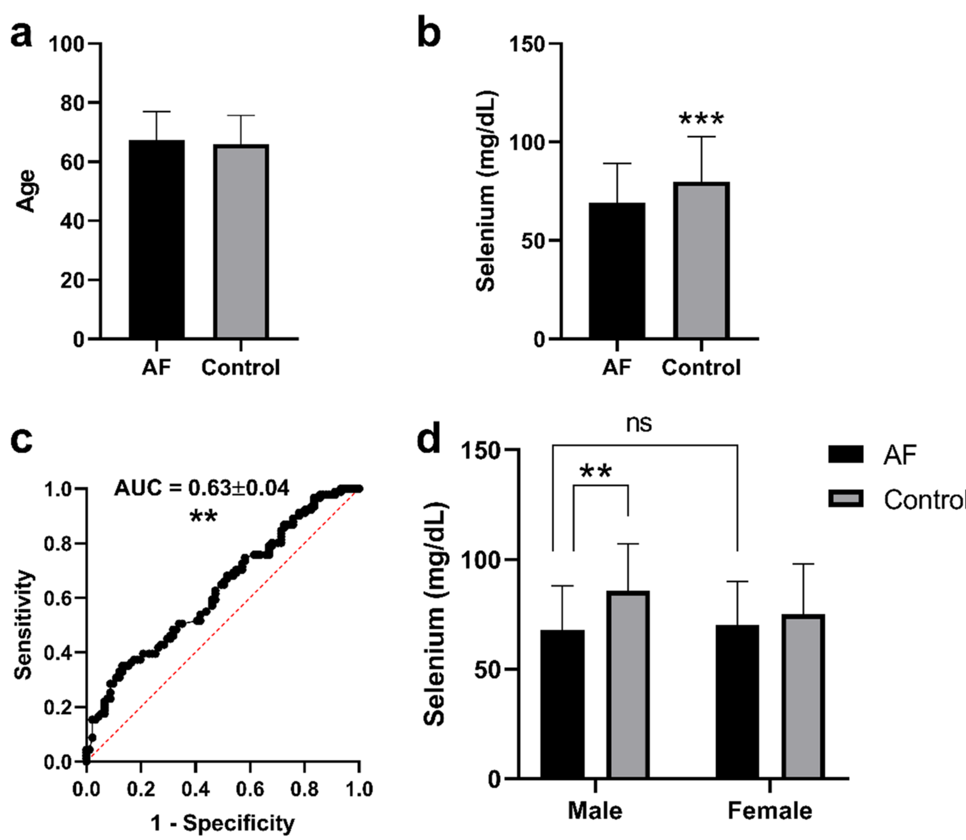

Fig. 3 Demographic, clinical, and laboratory parameters in study groups. The comparison of **a** ages (years), **b** Se concentrations, **c** the ROC curve of Se, and **d** sex-based Se concentrations between patients and control groups. AF Atrial fibrillation, AUC area under ROC curve, Se selenium. The degree of significance was denoted as: $^{**}P < 0.01$ and $^{***}P < 0.001$

Table 1 Demographic, clinical, and laboratory parameters in study groups

Parameter	AF group (mean ± SD) ($n = 91$)	Control (mean ± SD) ($n = 91$)	*P*-value
Age, years	67.47 ± 9.56	65.92 ± 9.79	0.1408
Smoking, *n* (%)	18 (19.78)	18 (19.78)	0.4806
HT, *n* (%)	45 (49.45)	32 (35.16)	< 0.0001
DM, *n* (%)	24 (26.37)	15 (16.48)	< 0.0001
BMI (kg /m^2)	27.07 ± 2.61	26.45 ± 2.89	0.2108
Se, mg/dL	69.30 ± 19.86	79.92 ± 22.86	< 0.0005

AF atrial fibrillation, *Se* selenium, *HT* hypertension, *DM* diabetes mellitus, *SD* standard deviation, *BMI* body mass index

with AF compared to the control group (67.88 ± 20.05 mg/dL vs 85.63 ± 21.61 mg/dL, $P = 0.0012$, respectively), but no significant difference was observed in women (70.36 ± 19.64 mg/dL vs 75.02 ± 22.97 mg/dL, $P = 0.8472$, respectively) (Table 2) (Fig. 3d).

In the Pearson correlation test performed to test whether there is a linear relationship between serum levels according to risk factors, it was observed that there was no significant difference between the groups in terms of HT and DM (Table 3).

Discussion

This study's most important new finding is the statistically significantly lower serum selenium level in newly diagnosed AF patients compared to healthy control subjects. These results provide important evidence explaining the etiology of selenium deficiency in newly diagnosed AF patients. This is also the first study in the literature to report that serum Se levels in newly diagnosed AF patients are lower than in the healthy control group.

AF has been the subject of more research than other arrhythmias, and its pathogenesis has been tried to be clarified. Thanks to the histopathological and electrophysiological studies on the disease, the disease has been better understood, and treatment possibilities have improved. However, there are still many unanswered questions regarding the formation of the disease. Many factors such as aging, HT, DM, genetic disorders, and nutrition play a role in the pathogenesis of arrhythmia [23]. Studies on nutrition have

Table 3 A Pearson correlation test for atrial fibrillation patients

Correlation	Se vs. HT%	Se vs. DM %
Pearson r	0.1008	0.1026
R^2	0.01016	0.01053
P-value	0.3417	0.3330
Significant? (alpha = 0.05)	No	No

Se selenium, *HT* hypertension, *DM* diabetes mellitus

shown that multiple dietary components and minerals are protective for AF [24]. It has also been shown that deficiencies in many minerals and elements may be a risk factor for AF. There are studies in the literature about the formation of AF and increased recurrence in the deficiency of elements such as iron, copper, zinc, and magnesium [3–8]. However, there is no study in the literature showing the relationship between selenium deficiency and newly diagnosed AF. For this reason, we aimed to compare the selenium levels of newly diagnosed AF patients with healthy individuals in our study.

In 2016, McDonald C et al. reported that low preoperative selenium levels were associated with postoperative atrial fibrillation in their study of patients undergoing coronary artery surgery [25]. Our study determined coronary artery disease and previous heart surgery as exclusion criteria. As it is known, cardiac arrhythmias can frequently occur after major surgery. Possible reasons for this include increased catecholaminergic activity and perioperative loss of fluid and electrolytes. Another study showed that in patients with paroxysmal AF attacks and sinus rhythm after cardioversion, the selenium level on the 1st day and 1st month did not change significantly compared to the healthy group [26]. However, unlike this study, the patient group in our study was chronic patients defined as permanent AF, and it was the group that could not achieve normal sinus rhythm with cardioversion. In addition, our study group consisted of more participants. Another difference was that we compared selenium levels between the patient and control groups according to gender in our study. As a result, there was no significant difference in selenium levels between the patient and healthy groups in females. We thought that the possible reason for this might be the differences in nutrition and accompanying risk factors in females.

Selenium is a trace element with antioxidant properties, prevents the formation of reactive oxygen species

Table 2 Sex-based selenium concentrations between patients and control groups

Gender	AF group (mean ± SD) ($n = 91$)	Control (mean ± SD) ($n = 91$)	*P*-value
Males (Se, mg/dL)	67.88 ± 20.05 ($n = 40$)	85.63 ± 21.61 ($n = 42$)	0.0012
Females (Se, mg/dL)	70.36 ± 19.64 ($n = 51$)	75.02 ± 22.97 ($n = 49$)	0.8472

AF atrial fibrillation, *Se* selenium, *SD* standard deviation

(ROS), and prevents their potentially harmful effects on tissues. ROS are unstable, highly reactive molecules that can transform other molecules with which they interact. As a result, high amounts of ROS are produced during oxidative stress (i.e., an imbalance between oxidant and antioxidant agents), a condition in which proteins, carbohydrates, lipids, and nucleic acids are adversely affected [27, 28].

In recent years, oxidative stress has been investigated as a potential underlying mechanism in the development of AF. ROS produced through oxygen metabolism has a multifaceted effect on cells found in heart tissue [29]. Tahhan et al. recently demonstrated that the prevalence and incidence of AF are associated with oxidative stress markers [30]. Studies have shown that over-produced ROS can disrupt ion channels and directly affect the action potential propagation [31]. ROS formation in the myocardium has been attributed to many enzymatic sources. Among these, NADPH oxidase has a critical role in the progression of AF [32]. Recent studies have shown that ROS has a pro-arrhythmic effect. One of the mechanisms described is that ROS alters the heart's normal electrical activity, and another is that ROS causes structural remodeling of the atria [33, 34]. It is known that fibrosis and necrosis develop in many tissues in the absence of selenium, which has antioxidant properties [35]. An experimental study in mice showed that selenium deficiency leads to myocardial fibrosis by affecting the redox-methylation balance [36].

As a result, we believe that antioxidant elements such as antioxidant enzymes and selenium may be beneficial in primary and secondary prevention of arrhythmic conditions such as AF by preventing ROS formation. Furthermore, selenium is protective in many cardiac diseases such as heart failure, coronary artery disease, and hypertension and in arrhythmic conditions such as AF. Therefore, we think that adequate selenium intake with food or supplements should be provided in individuals with risk factors for AF. In addition, it has been reported that the Mediterranean diet, which is known to have protective properties against oxidative stress, reduces the formation of AF and facilitates the conversion to spontaneous sinus rhythm [37].

Limitations

Our study has several limitations. The main limitation is that it is unknown how long the patients were alone with the disease before being diagnosed with AF. In addition, because patients may also have AF before they apply to us, the relatively small number of patients is another limitation. Finally, there is no follow-up showing how AF patients affect their selenium levels in the long term.

Conclusion

Selenium, which plays a role in many events, such as enzymatic antioxidant defense and regulation of the immune system, is a trace element that participates in various enzymes as a cofactor. Selenium performs its antioxidant function mainly as a component of selenoenzymes that detoxify ROS, such as glutathione peroxidase, thioredoxin reductase, and selenoprotein P. Oxidative stress, inflammatory mediators, and the fibrotic process they cause predispose to arrhythmias. By eliminating or minimizing these factors, the occurrence of AF can be reduced. One of the most reliable and inexpensive methods of this can be to encourage the use of antioxidants such as selenium. As a result of our study, it was concluded that low selenium levels are a factor leading to newly diagnosed AF. We have contributed to the literature and can be a reference for future studies on this subject.

Declarations

Ethics Approval and Consent to Participate Informed consent was obtained from all participants, and the Institutional Ethics Committee approved the study (Approval number: 2019–03/32–22 April 2019). The study was conducted in accordance with the Declaration of Helsinki.

Conflict of Interest The authors declare no competing interests.

References

1. Kornej J, Börschel CS, Benjamin EJ, Schnabel RB (2020) Epidemiology of atrial fibrillation in the 21st century: novel methods and new insights. Circ Res 127(1):4–20
2. Thakur RK, Natale A (2021) Atrial fibrillation risk factors. Card Electrophysiol Clin 13(1):xvii
3. Wodschow K, Villanueva CM, Larsen ML, Gislason G, Schullehner J, Hansen B, Ersbøll AK (2021) Association between magnesium in drinking water and atrial fibrillation incidence: a nationwide population-based cohort study, 2002–2015. Environ Health 15;20(1):126
4. Dai W, Kesaraju S, Weber CR (2021) Transcriptional factors in calcium mishandling and atrial fibrillation development. Pflugers Arch 473(8):1177–1197
5. Larsson SC, Drca N, Michaëlsson K (2019) Serum magnesium and calcium levels and risk of atrial fibrillation. Circ Genom Precis Med 12(1):e002349
6. Tu SJ, Elliott AD, Hanna-Rivero N, Gallagher C, Mishima RS, Lyrtzis E, Wlochowicz D, Clarke NA, Roberts-Thomson KC, Stokes MB, Emami M, Lau DH, Sanders P, Wong CX (2021) Rationale and design of the IRON-AF study: a double-blind, randomised, placebo-controlled study to assess the effect of intravenous ferric carboxymaltose in patients with atrial fibrillation and iron deficiency. BMJ Open 9;11(8):e047642
7. Hoppe LK, Muhlack DC, Koenig W, Carr PR, Brenner H, Schöttker B (2018) Association of abnormal serum potassium levels with arrhythmias and cardiovascular mortality: a systematic

review and meta-analysis of observational studies. Cardiovasc Drugs Ther 32(2):197–212
8. Cavusoglu Y, Kaya H, Eraslan S, Yilmaz MB (2019) Hyponatremia is associated with occurrence of atrial fibrillation in outpatients with heart failure and reduced ejection fraction. Hellenic J Cardiol 60(2):117–121
9. Cai Z, Zhang J, Li H (2019) Selenium, aging and aging-related diseases. Aging Clin Exp Res 31(8):1035–1047
10. Al-Mubarak AA, van der Meer P, Bomer N (2021) Selenium, selenoproteins, and heart failure: current knowledge and future perspective. Curr Heart Fail Rep 18(3):122–131
11. Fontenelle LC, de Paiva Sousa M, Dos Santos LR, Cardoso BEP, de Sousa TGV, da Cunha Soares T, de Sousa Melo SR, Morais JBS, da Silva Dias TM, de Oliveira FE, Braz DC, de Castro E Sousa JM, Torres-Leal FL, Henriques GS, do Nascimento Marreiro D (2022) Relationship between selenium nutritional status and markers of low-grade chronic inflammation in obese women. Biol Trace Elem Res Epub ahead of print
12. Vinceti M, Filippini T, Rothman KJ (2018) Selenium exposure and the risk of type 2 diabetes: a systematic review and meta-analysis. Eur J Epidemiol 33(9):789–810
13. Kalimuthu K, Keerthana CK, Mohan M, Arivalagan J, Christyraj JRSS, Firer MA, Choudry MHA, Anto RJ, Lee YJ (2022) The emerging role of selenium metabolic pathways in cancer: New therapeutic targets for cancer. J Cell Biochem 123(3):532–542
14. Rayman MP (2020) Selenium intake, status, and health: a complex relationship. Hormones (Athens) 19(1):9–14
15. Mohammadifard N, Humphries KH, Gotay C, Mena-Sánchez G, Salas-Salvadó J, Esmaillzadeh A, Ignaszewski A, Sarrafzadegan N (2017) Trace minerals intake: risks and benefits for cardiovascular health. Crit Rev Food Sci Nutr 59(8):1334–1346
16. Yang HB, Lu ZY, Yuan W, Li WD, Mao S (2021) Selenium attenuates doxorubicin-induced cardiotoxicity through Nrf2-NLRP3 pathway. Biol Trace Elem Res Epub ahead of print
17. Gunes S, Sahinturk V, Karasati P, Sahin IK, Ayhanci A (2017) Cardioprotective effect of selenium against cyclophosphamide-induced cardiotoxicity in rats. Biol Trace Elem Res 177(1):107–114
18. Venardos KM, Perkins A, Headrick J, Kaye DM (2007) Myocardial ischemia-reperfusion injury, antioxidant enzyme systems, and selenium: a review. Curr Med Chem 14(14):1539–1549
19. Ali Kelani AI, El-Deen Mohammed HS, Soliman MM, Sayed M, El-Badre HM, Fathi BSc MA (2018) Serum selenium level in acute myocardial infarction. Egypt J Intern Med 30; 28–34
20. Wang S, Yan R, Wang B, Meng P, Tan W, Guo X (2019) The functional analysis of selenium-related genes and magnesium-related genes in the gene expression profile microarray in the peripheral blood mononuclear cells of Keshan disease. Biol Trace Elem Res 192(1):3–9
21. Xiao J, Li N, Xiao S, Wu Y, Liu H (2021) Comparison of selenium nanoparticles and sodium selenite on the alleviation of early atherosclerosis by inhibiting endothelial dysfunction and inflammation in apolipoprotein E-deficient mice. Int J Mol Sci 22(21):11612
22. Xiao S, Mao L, Xiao J, Wu Y, Liu H (2021) Selenium nanoparticles inhibit the formation of atherosclerosis in apolipoprotein E deficient mice by alleviating hyperlipidemia and oxidative stress. Eur J Pharmacol 902:174120
23. Sagris M, Vardas EP, Theofilis P, Antonopoulos AS, Oikonomou E, Tousoulis D (2021) Atrial fibrillation: pathogenesis, predisposing factors, and genetics. Int J Mol Sci 23(1):6
24. Koh LY, Hwang NC (2020) Serum electrolyte concentrations and their association with postoperative atrial fibrillation: a long-standing myth or reality? J Cardiothorac Vasc Anesth 34(5):1160–1161
25. McDonald C, Fraser J, Shekar K, Clarke A, Coombes J, Barnett A, Pearse B, Fung L (2016) Low preoperative selenium is associated with postoperative atrial fibrillation in patients having intermediate-risk coronary artery surgery. Eur J Clin Nutr 70(10):1138–1143
26. Negreva M, Georgiev S, Vitlianova K, Georgieva R (2015) Selenium status in paroxysmal atrial fibrillation. Int J Med Pharm 3:17–26
27. Xie Z, Hou H, Luo D, An R, Zhao Y, Qiu C (2021) ROS-dependent lipid peroxidation and reliant antioxidant ferroptosis-suppressor-protein 1 in rheumatoid arthritis: a covert clue for potential therapy. Inflammation 44(1):35–47
28. Zhang M, Wang D, Geng Z, Li P, Sun Z, Xu W (2017) Effect of heat shock protein 90 against ROS-induced phospholipid oxidation. Food Chem 240:642–647
29. Zhang D, Li Y, Heims-Waldron D, Bezzerides V, Guatimosim S, Guo Y, Gu F, Zhou P, Lin Z, Ma Q, Liu J, Wang DZ, Pu WT (2018) Mitochondrial cardiomyopathy caused by elevated reactive oxygen species and impaired cardiomyocyte proliferation. Circ Res 122(1):74–87
30. Samman Tahhan A, Sandesara PB, Hayek SS, Alkhoder A, Chivukula K, Hammadah M, Mohamed-Kelli H, O'Neal WT, Topel M, Ghasemzadeh N, Ko YA, Aida H, Gafeer M, Sperling L, Vaccarino V, Liang Y, Jones DP, Quyyumi AA (2017) Association between oxidative stress and atrial fibrillation. Heart Rhythm 14(12):1849–1855
31. Sovari AA, Dudley SC Jr (2012) Reactive oxygen species-targeted therapeutic interventions for atrial fibrillation. Front Physiol 3:311
32. Barangi S, Hayes AW, Karimi G (2018) The more effective treatment of atrial fibrillation applying the natural compounds; as NADPH oxidase and ion channel inhibitors. Crit Rev Food Sci Nutr 58(7):1230–1241
33. Tytman K, Kaczmarek K, Lipińska S, Wranicz JK (2016) Rola wolnych rodników tlenowych w patogenezie zaburzeń rytmu serca [The role of reactive oxygen species (ROS) in arrhythmogenesis]. Pol Merkur Lekarski 40(235):32–35
34. Miura M, Taguchi Y, Handoh T, Hasegawa T, Takahashi Y, Morita N, Matsumoto A, Sato H, Shindoh C (2018) Regional increase in ROS within stretched region exacerbates arrhythmias in rat trabeculae with nonuniform contraction. Pflugers Arch 470(9):1349–1357
35. Fu YX, Wang YB, Bu QW, Guo MY (2022) Selenium deficiency caused fibrosis as an oxidative stress-induced inflammatory injury in the lungs of mice. Biol Trace Elem Res Epub ahead of print
36. Metes-Kosik N, Luptak I, Dibello PM, Handy DE, Tang SS, Zhi H, Qin F, Jacobsen DW, Loscalzo J, Joseph J (2012) Both selenium deficiency and modest selenium supplementation lead to myocardial fibrosis in mice via effects on redox-methylation balance. Mol Nutr Food Res 56(12):1812–1824
37. Pastori D, Carnevale R, Bartimoccia S, Nocella C, Tanzilli G, Cangemi R, Vicario T, Catena M, Violi F, Pignatelli P (2015) Does Mediterranean diet reduce cardiovascular events and oxidative stress in atrial fibrillation? Antioxid Redox Signal 23(8):682–687