

CrossMark
click for updates

Cardiac effects of parathyroid hormone excess; an updated mini-review

Ardeshir Tajbakhsh¹, Kamran Shirbache², Ali Shirbacheh³, Venus Shahabi Rabori⁴, Shahab Chaman⁵, Elahe Zaremoghadam⁶

Abstract

Hyperparathyroidism causes high levels of PTH, which can lead to a variety of cardiovascular problems that can pose a significant risk to an individual's overall health. In more severe cases, such as high blood calcium levels due to primary hyperparathyroidism, the individual may also experience increased risks of kidney stones, bone fractures, and osteoporosis.

Keywords: Cardiovascular disease, Hyperparathyroidism, Parathyroid hormone, Parathormone, Atherosclerosis, PTH excess, Endothelial dysfunction, Parathyroid glands, Hypertension

Please cite this paper as: Tajbakhsh A, Shirbache K, Shirbacheh A, Shahabi Rabori V, Chaman S, Zaremoghadam E. Cardiac effects of parathyroid hormone excess; an updated mini-review. J Parathyroid Dis. 2023;11:e11218. doi:10.34172/jpd.2023.11218.

Copyright © 2023 The Author(s); Published by Nickan Research Institute. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Cardiovascular risk factors are a noteworthy concern in end-stage kidney disease on dialysis. Diseases of the heart and vessels are the directing cause of mortality in hemodialysis and are accountable for the increase in mortality in dialysis (1). The impact of parathormone on myocardial structure and function is appealing for more attention since the effects of parathormone on heart function is the most critical outcome of secondary hyperparathyroidism in kidney failure (2). Left ventricular hypertrophy is a common heart complication in end-stage renal disease individuals. Left ventricular hypertrophy has a negative prognostic effect since this condition leads to dysrhythmia, diastolic dysfunction, congestive cardiac failure, and death (3). Parathyroid hormone (PTH) plays a vital role in calcium homeostasis. When the body detects low calcium levels, the parathyroid glands release PTH, which leads to increased calcium levels by releasing calcium from the bones, promoting calcium absorption from foods, across reducing the excretion of calcium in the urine (4). Hyperparathyroidism can affect many aspects of health, including cardiovascular, renal, and musculoskeletal systems and other body organs (5). One of these common effects is cardiac effects such as endothelial dysfunction, which cause impairment in the endothelium's ability to constrict and dilate blood vessels.

(6). This dysfunction is implicated in the development of atherosclerosis, a condition that causes the narrowing of arteries due to the buildup of plaque. Hyperparathyroidism also has been linked to oxidative stress, which can lead to damage to cells and negatively affect organ functions. Moreover, excessive parathormone levels have also been associated with calcification of the coronary arteries, which may result in the development of heart disease and heart attacks (7). Meanwhile, excessive parathormone concentration leads to protein synthesis and the release of fibroblasts that can lead to changes in the heart's structure. This process is called cardiac remodelling and can result in changes in ventricular chamber sizes, contractility, and other structural abnormalities (2,8). In this mini-review, we aimed to review the cardiac effects of PTH excess in primary and secondary hyperparathyroidism.

Study method

This review collected materials through a search of international databases such as PubMed to obtain relevant information. The keywords of conducted for this study were hyperparathyroidism, parathyroid hormone, cardiovascular disease, parathormone, atherosclerosis, PTH excess, end-stage kidney disease, endothelial dysfunction, parathyroid glands, end-stage renal disease, hypertension and left ventricular hypertrophy.

Received: 20 May 2023, Accepted: 6 July 2023, ePublished: 29 July 2023

¹Anesthesia Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. ²Independent Researcher, 40 Av de Charles de Gaulle, 79000 Niort, France. ³Niort Hospital, Niort, France. ⁴Department of Cardiology, Seyed-Al-Shohada Cardiology Hospital, Urmia University of Medical Sciences, Urmia, Iran. ⁵Department of Cardiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. ⁶Department of Internal Medicine, School of Medicine, Birjand University of Medical Sciences, Birjand, Iran.

*Corresponding author: Elahe Zaremoghadam, Email: dr.elahe.zaremoghadam.65@gmail.com

■ Implication for health policy/practice/research/medical education

The long-term effects of hyperparathyroidism, especially on the cardiovascular system, can be severe. When left untreated, hyperparathyroidism may result in significant heart problems such as hypertension, increased risk of heart disease or heart attacks, cardiac arrhythmias, or left ventricular hypertrophy.

Impact of parathyroid hormone excess on heart function and structure

PTH can increase the production of renin and aldosterone hormones in the adrenal glands, leading to hypertension. Likewise, persistent hyperparathyroidism can result in atherosclerosis, which may manifest in the form of peripheral arterial disease or heart attacks (9). In addition, high PTH concentration has been connected to the prolongation of the QT interval, which can lead to the beginning of cardiac dysrhythmias, comprising torsades de pointes (10). Several investigations showed excessive PTH can lead to left ventricular hypertrophy, a circumstance where the cardiac left side increases in size. Individuals with left ventricular hypertrophy have an increased risk of cardiac failure. Likewise, individuals with primary hyperparathyroidism might be at increased risk of stroke due to hypertension, cerebral artery calcification, and endothelial dysfunction (11,12). Additionally, in this condition, an abridged heart output exists. High PTH levels can reduce heart output, which is associated with fatigue, shortness of breath, and other symptoms of heart failure. Accordingly, hyperparathyroidism is also associated with vascular calcification (5,12). Primary hyperparathyroidism affects the calcium metabolism in the body, leading to calcification of arteries and blood vessels. When the vessels become stiff, blood pressure can increase, potentially leading to stroke or aneurysm. In advanced conditions, if left untreated, hyperparathyroidism can lead to the progressive failure of the cardiac muscles. Finally, the weakened heart muscles can result in congestive heart failure (5,13).

In rare conditions, there was an increased risk of atrial fibrillation. Atrial fibrillation is an irregular heartbeat that can be accompanied by blood clots, stroke, and heart failure. Besides, there is a chance for an increased risk of myocardial infarction. Cases with hyperparathyroidism may be more likely to develop coronary artery disease and a higher risk for a heart attack (1-7). Finally, there is a risk of mitral valve prolapse. Hyperparathyroidism can increase the risk of developing of mitral valve issue (14).

Discussion

In a previous study, Al Salmi et al reported the association of PTH with mortality in hemodialysis. The mean patient age of their patients was 55 years. Median PTH ranged from 259 pg/mL to 437 pg/mL; they concluded that secondary hyperparathyroidism is highly prevalent

among their patients on hemodialysis. They showed a strong U-shaped PTH /mortality association at PTH <300 pg/mL and >450 pg/mL (15). A previous study by Nasri et al on 73 hemodialysis patients with the age of 46.5 ± 16 years showed a significant inverse association of serum alkaline phosphatase with the percent of left ventricular ejection fraction, this study also showed a significant inverse association among serum parathormone value with of left ventricular ejection fraction in non-diabetic cases (16). Shaltout et al assessed the association of parathormone level with left ventricular mass in 40 hemodialysis cases. They showed hyperparathyroidism is a primary determinant of left ventricular hypertrophy in end-stage kidney disease patients on hemodialysis (17). Previously Saleh et al studied 27159 subjects of the general population. About 2700 were assessed for serum parathormone measurement and left ventricular mass calculation by echocardiography. They showed parathormone is an independent predictor of left ventricular mass in males older than 59 years and women younger than 60 years (11).

Conclusion

In summary, when left untreated, hyperparathyroidism may result in significant heart problems such as blood pressure elevations, increased risk of heart disease and heart attacks, cardiac arrhythmias, or left ventricular hypertrophy. Therefore, it is essential to manage hyperparathyroidism to prevent complications that could lead to heart problems. Regular follow-ups with your healthcare provider, proper lifestyle habits, and management of underlying health conditions alongside parathyroid management are essential. In addition, regular cardiovascular check-ups are very important to monitor progress and intervene early in case of cardiovascular events.

Authors' contribution

Conceptualization: KSh.

Validation: Ash.

Investigation: ShCh

Resources: AT.

Data curation: EZ and VSh.

Visualization: Ash.

Supervision: EZ.

Funding Acquisition: All authors.

Writing–original draft : KSh, ASH, EZ, and VSh.

Writing–review and editing: AT and ShCh.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

None.

References

1. Sakhaee K. Is there an optimal parathyroid hormone level in end-stage renal failure: the lower the better? *Curr Opin Nephrol Hypertens.* 2001; 1:421-7. doi: 10.1097/00041552-200105000-00020.
2. Brown SJ, Ruppe MD, Tabatabai LS. The Parathyroid Gland and Heart Disease. *Methodist Debakey Cardiovasc J.* 2017;1:49-54. doi: 10.14797/mdcj-13-2-49.
3. Coimbra S, Catarino C, Sameiro Faria M, Nunes JPL, Rocha S, et al. The Association of Leptin with Left Ventricular Hypertrophy in End-Stage Kidney Disease Patients on Dialysis. *Biomedicines.* 2023;1:1026. doi: 10.3390/biomedicines11041026.
4. Khan M, Jose A, Sharma S. Physiology, Parathyroid Hormone. [Updated 2022 Oct 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.
5. Brown SJ, Ruppe MD, Tabatabai LS. The Parathyroid Gland and Heart Disease. *Methodist Debakey Cardiovasc J.* 2017;1:49-54. doi: 10.14797/mdcj-13-2-49.
6. Gambardella J, De Rosa M, Sorriento D, Prevete N, Fiordelisi A, Ciccarelli M, et al. Parathyroid Hormone Causes Endothelial Dysfunction by Inducing Mitochondrial ROS and Specific Oxidative Signal Transduction Modifications. *Oxid Med Cell Longev.* 2018;2018:9582319. doi: 10.1155/2018/9582319.
7. Dube P, DeRiso A, Patel M, Battepati D, Khatib-Shahidi B, Sharma H, et al. Vascular Calcification in Chronic Kidney Disease: Diversity in the Vessel Wall. *Biomedicines.* 2021;9:404. doi: 10.3390/biomedicines9040404.
8. Krysiak R, Bartecka A, Okopień B. Rzadkie zaburzenia funkcji przytarczyc i działania receptorowego parathormonu [Rare abnormalities of parathyroid gland function and parathyroid hormone receptor action]. *Przegl Lek.* 2014;71:36-47. Polish.
9. Milicic Stanic B, Ilincic B, Zeravica R, Milicic Ivanovski D, Cabarkapa V, Mijovic R. The Importance of Correlation between Aldosterone and Parathyroid Hormone in Patients with Primary Hyperparathyroidism. *Int J Endocrinol.* 2022;2022:3804899. doi: 10.1155/2022/3804899.
10. Muzurović E, Medenica S, Kalezić M, Pavlović S. Primary hyperparathyroidism associated with acquired long QT interval and ventricular tachycardia. *Endocrinol Diabetes Metab Case Rep.* 2021;2021:21-0016. doi: 10.1530/EDM-21-0016.
11. Saleh FN, Schirmer H, Sundsfjord J, Jorde R. Parathyroid hormone and left ventricular hypertrophy. *Eur Heart J.* 2003;24:2054-60. doi: 10.1016/j.ehj.2003.09.010.
12. Randon RB, Rohde LE, Comerlato L, Ribeiro JP, Manfro RC. The role of secondary hyperparathyroidism in left ventricular hypertrophy of patients under chronic hemodialysis. *Braz J Med Biol Res.* 2005;38:1409-16. doi: 10.1590/s0100-879x2005000900016.
13. Walker MD, Silverberg SJ. Cardiovascular aspects of primary hyperparathyroidism. *J Endocrinol Invest.* 2008;3:925-31. doi: 10.1007/BF03346443.
14. Stefenelli T, Abela C, Frank H, Koller-Strametz J, Globits S, Bergler-Klein J, et al. Cardiac abnormalities in patients with primary hyperparathyroidism: implications for follow-up. *J Clin Endocrinol Metab.* 1997;82:106-12. doi: 10.1210/jcem.82.1.3666.
15. Al Salmi I, Bieber B, Al Rukhaimi M, AlSahow A, Shaheen F, Al-Ghamdi SMG, et al. Parathyroid Hormone Serum Levels and Mortality among Hemodialysis Patients in the Gulf Cooperation Council Countries: Results from the DOPPS (2012-2018). *Kidney360.* 2020;1:1083-1090. doi: 10.34067/KID.0000772020.
16. Nasri H, Baradaran A, Naderi AS. Close association between parathyroid hormone and left ventricular function and structure in end-stage renal failure patients under maintenance hemodialysis. *Acta Med Austriaca.* 2004;31:67-72.
17. Shaltout AH, Samir S, Lashin FI, Sherif MH, Aboelnasr MS. Correlation of parathyroid hormone level with left ventricular mass in patients with end-stage kidney disease on hemodialysis. *J Egypt Soc Nephrol Transplant* 2021;21:124-9. doi: 10.4103/jesnt.jesnt_1_21