Cardiovascular Risk in Primary Hyperparathyroidism and Update

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Abstract

Background: Primary hyperparathyroidism (PHPT) is a common endocrine disorder caused by autonomous overproduction of parathyroid hormone (PTH) from one or more parathyroid glands. It is characterized biochemically by **hypercalcemia, hypophosphatemia,** and **cortical bone loss due to PTH-mediated bone resorption**, as well as e@ects on the renal and gastrointestinal systems. Many patients are asymptomatic and are diagnosed incidentally during routine biochemical screening. In symptomatic individuals, classical features include **fatigue, morning nausea, somnolence, constipation, nephrolithiasis, and fragility (lowtrauma) fractures**. The condition typically presents after the age of 60 and demonstrates a **female predominance**. Primary complications are related to skeletal involvement, with **cortical bone loss leading to increased fracture risk**, as well as **nephrolithiasis**, which may progress to chronic kidney disease. PHPT can also be associated with genetic and syndromic conditions such as **Multiple Endocrine Neoplasia types 1 and 2 (MEN1/MEN2)** and **hyperparathyroidism–jaw tumor syndrome.**

Increasing evidence highlights that PHPT is also associated with **elevated cardiovascular risk and mortality**. Both the direct cardiovascular e@ects of PTH and the chronic e@ects of hypercalcemia contribute to this increased risk. Associated metabolic abnormalities—including **hypertension, impaired glucose tolerance, dyslipidemia, and hyperuricemia**—further exacerbate cardiovascular morbidity.

This evidence-based review aims to emphasize the significance of **cardiovascular risk as a major contributor to morbidity and mortality in patients with primary hyperparathyroidism**, underscoring the importance of early recognition and appropriate management strategies.

Method: This study is a narrative review. Relevant literature was searched from **PubMed-indexed publications** and the **Cochrane Database** covering the period from **2003 to 2023.**

Discussion: Several studies have demonstrated the association between primary hyperparathyroidism (PHPT) and increased cardiovascular morbidity and mortality. In a randomized clinical trial by Kong and colleagues, PHPT was associated with a significant increase in total mortality (relative risk **1.39**, 95% CI **1.23–1.57**) and cardiovascular mortality, while **parathyroidectomy was shown to reduce overall cardiovascular risk.** More recently, in 2023, Iglesias and colleagues analyzed electronic health records of over **699,000 adults** (including 6,515 patients with PHPT) and demonstrated that PHPT is independently associated with higher incidence of **hypertension, stroke, ischemic heart disease, atrial fibrillation, and thromboembolic events** (all $p < 0.001$). Earlier evidence also supports these findings. In 2004, Andersson et al. reported that elevated PTH and hypercalcemia are associated with increased prevalence of **hypertension, left ventricular hypertrophy, and myocardial and valvular calcification.** Furthermore, Brown and colleagues explored both clinical and molecular mechanisms by which PTH a@ects the cardiovascular system and suggested that intervention—medical or surgical—may reverse cardiac remodeling and mitigate cardiovascular risk.

Emerging data by Alay, M., Ercek, B.M., Sonmez, G.M. et al. also links PHPT to vascular and thromboembolic complications. Increased fibrinogen levels have been found in patients with parathyroid adenomas, and fibrinogen is known to be an independent risk factor for atherosclerosis and thrombosis. In one study, patients with PHPT had significantly **higher fibrinogen levels and lower protein S levels** compared with controls, and adenoma volume showed a positive correlation with fibrinogen levels, suggesting a possible mechanism for the increased risk of **atherosclerotic and atherothrombotic cardiovascular disease.**

Conclusion: Primary hyperparathyroidism (PHPT) is one of the most common endocrine disorders encountered in routine clinical practice. Traditionally, clinical focus has centred on bone and renal complications resulting from persistently elevated parathyroid hormone (PTH) levels, which contribute significantly to morbidity and mortality. In this article, I highlight an increasingly recognized yet often under-emphasized aspect of the disease: its impact on the **cardiovascular system.**

Growing evidence from experimental animal models demonstrates that PTH acts directly on cardiomyocytes and the vascular endothelium, exerting **vasodilatory ePects, promoting vascular remodelling, and influencing myocardial contractility and heart rate** (positive inotropic and chronotropic e@ects). Additionally, numerous observational studies, randomized controlled trials, and case reports have shown a consistent association between PHPT and increased cardiovascular risk, including higher prevalence of **hypertension, impaired glucose metabolism, and dyslipidemia.**