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Research Article

MEDICAL OUTCOMES OF PARATHYROIDECTOMY

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Abstract:

Hyperparathyroidism (HPT) is considered an endocrine disorder characterized by the hyperfunctioning of one or more parathyroid tissues and overproduction of the parathyroid hormone – a polypeptide hormone with 84 amino acids. Prolonged over-secretion of parathyroid hormone causes an elevation in serum calcium levels. HPT presents with a wide range of moderate to severe symptoms and no symptoms at all. Some common symptoms indicated of HPT include musculoskeletal symptoms (loss of muscle strength, painful joints), gastrointestinal issues (constipation), and neuropsychiatric symptoms (depression, anxiety, mood disorders, fatigue). Parathyroidectomy is considered the only curative and definitive option for treating HPT with high success rates. In parathyroidectomy, the overactive parathyroid tissues, involving one or more of the four parathyroid glands, are removed surgically. This surgical procedure aims to remove hyperplasia or adenoma(s) by exploring all of the four parathyroid glands with an overproduction of parathyroid hormone. Although parathyroidectomy is a safe procedure, some serious medical outcomes may still arise. This review article explores the common outcomes associated with parathyroidectomy, including postoperative hypocalcemia, hypoparathyroidism, hematoma, laryngeal nerve injury, prolonged length of stay, and recurrent HPT. To minimize serious medical outcomes of parathyroidectomy, a team of healthcare professionals, including surgeons, nursing staff, anesthesiologists, pathologists, and radiologists must be established.

Keywords: *Hyperparathyroidism, parathyroidectomy, serum calcium, parathyroid hormone, recurrent HPT.*

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INTRODUCTION:

Hyperparathyroidism (HPT) is a clinical endocrine condition described as the overproduction of the serum parathyroid hormone (PTH). The condition occurs when the parathyroid tissue, involving one or more parathyroid glands, hyperfunctions, resulting in too much secretion of parathyroid hormone[1]. This results in osteoclastic bone resorption, renal tubular reabsorption, and abnormal calcium homeostasis (hypercalcemia). Furthermore, the overproduction of parathyroid hormone increases renal activation of vitamin D, which then promotes increased absorption of intestinal Ca^{2+} [2]. Normocalcemic hyperparathyroidism is considered a variant form of primary hyperparathyroidism (PHPT). It is a condition, which is suspected when serum calcium levels are persistently normal despite pathologic parathyroid overactivity [3].

After thyroid disease and diabetes mellitus, HPT has become as the third most prevalent health concern in general public. This common endocrine disorder is two times more prevalent in women than men, and more frequent in the elderly than the young[4]. Annually, HPT affects approximately 77 cases in men and 176 cases in women per 100,000 persons[5]. Due to a dramatic change in the clinical spectrum of HPT given the routine biochemical screening, the number of asymptomatic HPT patients has subsequently increased than before [6]. Over the last few decades, the prompt hypercalcemia detection has changed the clinical picture of HPT, which frequently characterizes as a mildly symptomatic or asymptomatic disease. The symptoms indicative of HPT, in most cases, are non-specific and diverse. The most common ones include gastrointestinal discomfort, such as constipation, neuropsychiatric symptoms, such as fatigue, mood changes, depression, memory problems & anxiety, and musculoskeletal symptoms, such as painful joints and declined muscle strength[7]. These symptoms may potentially contribute to the low quality of life (QoL).

In patients with HPT, multichannel analyzers identify hypercalcemia as the only finding, which occurs as a consequence of osteoporotic fragility fractures and renal calculi [8]. The leading and potentially curative treatment option for HPT is the surgical resection of parathyroid glands in order to minimize the risk of hypercalcemia. Surgical intervention is also preferred for decreasing the chances of further complications in patients with history of hypercalcemia (1mg/dl above than normal), low glomerular filtration rate, kidney stones, osteoporosis, and fractures [9]. Parathyroidectomy remains to be the successful surgical options. There are many surgical options

available for curing HPT, including bilateral neck exploration, minimally invasive parathyroidectomy, endoscopic parathyroidectomy, total endoscopic parathyroidectomy, and directed parathyroidectomy[10].

Parathyroidectomy:

Parathyroidectomy (PTx) is the definitive treatment, which involves removing one or more of the parathyroid glands to permanently stop the hyperfunctioning of parathyroid tissues. In most of the cases, hyperparathyroidism is characterized by a single parathyroid adenoma. However, double adenomas are also present in a significant minority (more than 10%), while hyperplasia of all four parathyroid glands is also found in a few cases[11]. In the traditional parathyroidectomy, all of the four parathyroid glands are explored and the adenoma(s) are removed, depending on the clinical spectrum of parathyroid glands' size. Parathyroidectomy should be preferred when hyperparathyroidism cannot be controlled with medical therapy. This surgical intervention is indicated for HPT patients with reported symptoms, including osteoporosis (with a <-2.5 bone density score), vertebral compression fracture or fragility fracture, hypercalciuria, nephrocalcinosis or nephrolithiasis, neuropsychiatric symptoms, polyuria, neurocognitive dysfunction, and polydipsia[12].

With advanced interventions for medical treatment of hyperparathyroidism, the indications of parathyroidectomy could be reduced to[13]:

- Patients with HPT who do not respond to the treatment with calcimimetics.
- Patients with PTH serum levels of more than 500 pg/mL and calciphylaxis refractory to oral and intravenous calcimimetics.
- Primary HPT characterized by non-suppressed PTH levels and non-iatrogenic hypercalcemia in young patients with CKD.
- Severe refractory hyperphosphatemia.
- Severe secondary HPT in patients who do not respond to combined medical treatment for more than a year (medical treatments include the association of P binders, vitamin D derivatives, and cinacalcet).
- Complications of Severe secondary HPT, such as refractory anemia, severe bone pain, and tedious rupture.
- Patients with kidney transplantation having high PTH with uncontrolled hypercalcemia, having poor response to oral and IV calcimimetics.

For asymptomatic patients with hyperparathyroidism, the indications of parathyroidectomy include[1]:

- Serum calcium levels of greater than 1 mg/dL.
- Patients having the age of less than 50 years.
- Bone density of greater than 2.5 (forearm, hip, or lumbar spine).
- A reduction in creatinine clearance by more than 30% in comparison with other patients of the same age group.
- Urinary calcium excretion of less than 400 mg per day.
- No possibility or chances of medical surveillance.
- Surgical resection chosen by the patient.

Secondary hyperparathyroidism, in most cases, is managed with medical therapy. If a patient presents with severe symptoms or refractory secondary hyperparathyroidism with hyperphosphatemia or hypercalcemia, then parathyroidectomy is recommended. Parathyroidectomy is indicated to 15% of patients with refractory hyperparathyroidism after five to ten years on dialysis[14]. Another indication of parathyroidectomy is for patients who are diagnosed with tertiary hyperparathyroidism accompanied by symptomatic hypercalcemia. Medical therapy is also recommended, higher cure rates have been reported with surgical interventions for tertiary hyperparathyroidism[15]. For treating tertiary hyperparathyroidism with subtotal or limited parathyroidectomy, the primary objective is to maintain serum calcium levels within six months post-surgery[16].

Medical Outcomes of Parathyroidectomy:

There continues to be a debate over the appropriate management of hyperparathyroidism involving multiple parathyroid glands because a very little information on the outcomes following parathyroidectomy is reported in literature. Furthermore, the availability of information is largely based on a combination of outcomes for patients with primary, secondary, or tertiary HPT, multiple parathyroid adenomas, and both four-gland hyperplasia. However, the possible outcomes of parathyroidectomy reported in literature are as followed:

1. Prolonged Length of Stay (LOS) After the Surgery:

Although several studies report that patients after undergoing parathyroidectomy can safely be discharged on the day of the surgery or one day after the surgery[17]. A prolonged length of stay (LOS) is

referred to as the duration of hospitalization between the patient's admittance to hospital and discharged greater than six days. Prolonged hospital stay following parathyroidectomy is only secondary to complications occurring after the surgery, such as respiratory conditions[18], hungry bone syndrome, hypocalcemia, significantly high phosphatase levels, and subperiosteal bone resorption[19]. It has also been reported that prolonged LOS after parathyroidectomy could result in adverse outcomes, thus leading to increased morbidity [20]. The variations in length of stay and readmissions to hospital can be eliminated by encouraging multidisciplinary approaches regarding the estimated hospital journey, postsurgical care, and criteria for safe discharge from the hospital. These factors can contribute to significant reduction in the LOS to only 1.5 days[21].

2. Recurrence of Hyperparathyroidism (HPT):

Even after successful parathyroidectomy, persistent serum levels of parathyroid glands may often result in recurrent HPT. This may represent an "incomplete" parathyroidectomy. Recurrent HPT occurs when a patient fails to achieve normal serum calcium levels within six months of a subsequent follow-up. It is characterized by abnormally elevated and non-suppressed secretion of parathyroid glands along with hypercalcemia of greater than 10.2 mg/dL following parathyroidectomy. Some studies report that the primary reason for recurrent HPT is due to the involvement of more than one parathyroid glands at the time of surgery, which later become hyperfunctioning and release too much of serum PTH. Factors that contribute to the high prevalence of recurrent HPT still remain unclear. However, in one study, patients with recurrent HPT were of old age (>50 years) and had slightly higher parathyroid glands, high serum PTH levels, lower postoperative calcium levels, higher creatinine levels, lower vitamin D levels, and more bone disease[22].

One study published in the Journal of Surgical Research reported that patients with double adenomas (DAs) had persistently recurrent HPT, which raises the need for immediate intervention for long-term cure of primary HPT [23]. Common risk factors associated with the high prevalence rate of recurrent HPT include surgeries performed by inexperienced parathyroid surgeons, abnormal location of hyperfunctioning parathyroid tissue(s), and hyperplasia of unrecognized four glands[24].

3. Mortality Rates:

Many studies found in scientific literature report different death rates after the HPT surgery. One study

reported that mortality rates were significantly lower in hemodialysis patients who received parathyroidectomy and higher in patients who did not receive parathyroidectomy [25]. Similarly, another study published in the World Journal of Surgery demonstrated that minimally invasive parathyroidectomy is a safe surgical intervention due to its higher cure rates and lower mortality rates [26]. In another study, parathyroidectomies for secondary HPT were examined from 2002 to 2011. It was found that in-hospital mortality rates after parathyroidectomy were reduced from 1.7% to 0.8% in 2022. However, patients with peripheral vascular disease and heart failure, after parathyroidectomy, exhibited higher mortality rates as compared to patients with kidney transplantation[27]. Another study was conducted to evaluate medical outcomes of parathyroidectomy after one year in patients who were receiving hemodialysis. The study involved 4435 patients. Among these patients who had parathyroidectomy, 2.0% mortality rate was reported immediately after parathyroidectomy [28].

4. Calcium Abnormalities:

Parathyroidectomy is considered a successful treatment for primary hyperparathyroidism. The success of parathyroidectomy is predicted when serum parathyroid hormone levels decrease by 50% or more. Serum calcium levels are also expected to return to their normal range a day or two after the surgery. But in some cases, hypercalcemia remains persistent despite the surgery. This happens in 10% of the patients who exhibit a persistent delay in calcium normalization[29]. Another frequent calcium complication that occurs immediately after parathyroidectomy is postoperative hypocalcemia. Postoperative hypocalcemia occurs as a result of parathyroid removal and inadvertent parathyroid devascularization, due to which postoperative hypothyroidism is also induced [30]. Other factors contributing to this process include hungry bone syndrome, an increase in serum calcitonin levels, and vitamin D deficiency. Hungry bone syndrome (HBS) is known as a major complication of parathyroidectomy and is characterized by persistent and severe hypocalcemia. The symptoms indicative of HBS include seizures, tetany, Chvostek's sign, fingertip paresthesia, perioral numbness, Trousseau's sign, and cardiac dysrhythmia[31].

5. Postoperative Hematoma and Bleeding:

Neck hematoma after parathyroidectomy is a rare but serious outcome of the surgery, leading to significant morbidity, stroke, cardiac arrest, or tracheostomy. If the symptoms develop, it can be a life-threatening condition for the patient. The hematoma and

excessive bleeding may cause tracheal obstruction and subsequent airway compromise. To alleviate airway compression, surgical exploration and wound opening must be performed to prevent further complications. Furthermore, they should not be any delay in intubation.

6. Laryngeal Nerve Injury:

Another most feared complication of parathyroidectomy is recurrent laryngeal nerve injury, which can lead to an increased risk of aspiration, stridor or hoarseness, palsy of the vocal cord, and airway occlusion. When this occurs, occasional tracheostomy or reintubation becomes necessary. Most patients present with temporary recurrence laryngeal nerve injuries. However, 1.1% of patients are reported with permanent paresis of the vocal cord following the surgery. Patients with temporary recurrence of laryngeal nerve injury are recovered from vocal cord paresis within a few months [32].

CONCLUSION:

In patients diagnosed with primary hyperparathyroidism, parathyroidectomy remains to be the excellent and curative treatment. Based on the scientific evidence from literature, parathyroidectomy has been associated with high success rates accompanied by low mortality rates. Despite the high success rates of parathyroidectomy, patients can still experience some adverse outcomes even after a subsequent follow-up. Such complications include postoperative hypocalcemia, hungry bone syndrome, recurrent hyperparathyroidism, laryngeal nerve injuries, neck hematoma, and hypoparathyroidism. In order to achieve the best clinical outcomes, accurate patient management and the involvement of a multidisciplinary team is necessary.

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