The Accuracy of Preoperative Combined Ultrasonography and Sestamibi Scintigraphy in Preoperative Localization of Hyperparathyroidism

Thesis

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George Ibrahem Salama

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List of Abbreviations

3D CT	:	Three dimensional CT
4D CT	:	Four dimensional CT
BNE	:	Bilateral neck exploration
BUN	:	Blood urea nitrogen ratio
Ca	:	Calcium
CaR	:	Calcium ion receptor
CKD	:	Chronic kidney disease
CrCl	:	Creatinine clearance
CT	:	Computed tomography
CUA	:	Calcific uremic arteriolopathy
CVD	:	Cardiovascular disease
ESRD	:	End stage renal disease
FHH	:	Familial hypocalciuric hypercalcemia
FIHPT	:	Familial isolated hyperparathyroidism
HBS	:	Hungry bone syndrome
HPTH	:	Hyperparathyroidism
HPT-JT	:	Hyperparathyroidism-jaw tumor syndrome
IPTH	:	Intra-operative intact parathyroid hormone
Ki _67	:	Ki _67 antibody
Lt	:	Left
MEN	:	Multiple endocrine neoplasia

List of Abbreviations (Cont.)

MEN1	:	Multiple endocrine neoplasia type 1
MEN2A	:	Multiple endocrine neoplasia type 2A
MGD	:	Multiple gland disease
MIRP	:	Minimally invasive radio-guided parathyroidectomy
MRI	:	Magnetic resonance imaging
MTC	:	Medullary thyroid cancer
NIH	:	National Institute of Health
PA	:	Parathyroid adenoma
PET	:	Positron emission tomography
PHPT	:	Primary HPT primary hyperparathyroidism
PT-CA	:	Parathyroid carcinoma
PTH	:	Parathormone hormone
PTHrP	:	Parathyroid hormone-related protein
ROLL	:	Radioguided occult lesion Localization
Rt	:	Right
SHP	:	Secondary hyperparathyroidism
SPECT	:	Single photon emission computed tomography
SVS	:	Selective parathyroid venous sampling
UNE	:	Unilateral neck exploration
US	:	Ultrasonography ultrasound
VATS	:	Video-assisted thoracoscopic surgery

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Introduction

Hyperparathyroidism is a serious metabolic disorder. The incidence of hyperparathyroidism is about one in 20,000 people. It is fairly uncommon actually sort of rare, thus most surgeons only see one or two patients per year or two years. It occurs in female more than male and average age is about 58 years old but it can occur at any age. The types of hyperparathyroidism are primary, secondary and tertiary ***(Russell et al., 2006).***

Most cases of primary hyperparathyroidism are caused by a single parathyroid adenoma (89%). Other causes include hyperplasia of all four glands (6%), double adenomas (4%), and, rarely, parathyroid carcinoma. In most instances, parathyroid adenomas are sporadic.There is an increased incidence of parathyroid hyperplasia in multiple endocrine neoplasia type I and multiple endocrine neoplasia type IIA, although the incidence of these disordersis not sufficiently high to justify screening in all instances of primary hyperparathyroidism ***(Haciyanli et al., 2006).***

Another rare cause of primary hyperparathyroidism is familial hypocalciuric hypercalcemia, an autosomal dominant condition that produces PTH-dependent hypercalcemia. It is associated with mild parathyroid hyperplasia. Primary hyperparathyroidism is considered to be present when serum calcium is elevated and Parathyroid (PTH) is increased or inappropriately normal ***(Krausz et al., 2008).***

Secondary hyperparathyroidism is the excessive production of PTH in response to low blood calcium levels caused by conditions such as renal failure and vitamin D deficiency. The two main strategies for management of this disease include replacement of vitamin D with oral analogues

(1α-calcidiol) and reduction in serum phosphate.While in tertiary hyperparathyroidism the parathyroid glands become autonomous and function independently of calcium levels. This condition is usually associated with increased levels of PTH, calcium, alkaline phosphatase and phosphate ***(Burkey et al., 2007).***

There are numerous, often non-specific, clinical manifestations of hypercalcemia. The most common presenting symptoms include fatigue, hypertension, bone pain, muscle weakness, bilateral recurrent renal stones, pathological fractures and psychiatric illness ***(Ruda et al., 2005).***

The development of unilateral and focused surgical approaches over the past decade, however, has made it even more imperative for imaging to accurately locate abnormal parathyroid glands before surgery. With optimized preoperative mapping, the success rate of these less invasive techniques equals that of the traditional bilateral approach ***(Baliski et al., 2005).***

Several noninvasive preoperative localization modalities are available, including technetium Tc 99m sestamibi scintigraphy, ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), and thallous chloride Tl 201-technetium Tc 99m pertechnetate subtraction scanning. Most recently, four-dimensional CT and positron emission tomography (PET)-CT fusion studies have also been used with success for parathyroid localization ***(Stephen et al., 2006).***

Sestamibi with ^{99m}Tc is the most commonly used radiotracer for imaging the parathyroid glands and has been extensively studied in the setting of hyperparathyroidism. Sestamibi is taken up by both the thyroid and parathyroid glands, but adenomatous and hyperplastic parathyroid tissue

shows more avid uptake of the radiotracer and often retains the radiotracer longer than adjacent thyroid tissue. Thus, initial planar images obtained shortly after the administration of radiotracer will show both thyroid and parathyroid tissue. Asymmetric foci of increased radiotracer uptake on early images can be seen, representing abnormal parathyroid tissue superimposed on the normal thyroid. Delayed images, obtained approximately 2 hours after radiotracer administration, are acquired to look for foci of retained radiotracer characteristic of hyperfunctioning parathyroid tissue ***(Yao et al., 2007).***

Ultrasonography and ^{99m}Tc-Sestamibi scintigraphy are the dominant imaging techniques for preoperative location of hyperparathyroidism. Numerous studies comparing these techniques suggest similar sensitivities and specificities. Localization accuracy is also improved when both studies are obtained preoperatively ***(Melton et al., 2005).***

A preoperative approach that combines both the anatomic information of sonography and the physiologic information of scintigraphy has been shown to predict the presence and location of solitary adenomas more accurately than either technique alone. ***Siperstein et al. (2008)*** predicted 79% surgical success in their prospective study combining both techniques versus 74% for sonography and 68% for scintigraphy alone**.** ***Solorzano et al. (2005)*** who advocate preoperative sonography as the only preoperative location test, found that, used separately, sonography and scintigraphy each correctly predicted uniglandular disease in 77% of patients, but this increased to 90% when the techniques were combined ***(Krausz et al., 2008).***

Over the past decade, the surgical treatment of primary hyperparathyroidism has changed from predominantly a bilateral approach with four-gland explorationin all cases to unilateral and focused approaches guided by preoperative

imaging showing single adenomas. Sonography and ^{99m}Tc-sestamibi scintigraphy have assumed dominant roles in preoperative localization of solitary adenomas, and focused approaches based on concordant findings from both techniques have cure rates equal to that of the traditional approach ***(Grant et al., 2008).***

Aim of the work

The aim of the work is to detect the importance of combination of Ultrasonography and Sestamibi scintigraphy in the preoperative localization of patients with hyperparathyroidism to increase the adoption of minimally invasive parathyroidectomy techniques.