

# **Special Program**



■ Orlo H Clark

Cornell University Medical School, USA

In 1850, Sir Richard Owen identified a parathyroid gland in an Indian one horned Rhinoceros. Twenty-nine years later, Ivar Sandstrom first identified parathyroid glands both grossly and microscopically in animals and man. In 1925, Dr. Felix Mandel performed the first successful parathyroidectomy, but his patient, Albert, subsequently developed recurrent hyperparathyroidism. In 1926, Captain Charles Martel had his first of seven operations for primary hyperparathyroidism (PHPT), but unfortunately had persistent disease until his elusive mediastinal parathyroid tumor was removed. This was obviously an ominous beginning to the treatment of patients with PHPT. PHPT is a common problem effecting at least one in 500 women and one in 2,000 men. Many patients with PHPT have a form of premature aging and have more cardiovascular disease, osteoporosis, cancer and kidney dysfunction. Many patients with PHPT have increased fatigue, depression, weakness, gastrointestinal disorders and a shortened life expectancy. Although most patients are successfully treated at their initial operation, some have persistent and others develop recurrent PHPT. The reasons for a failed parathyroidectomy include: surgeon inexperience, inaccurate preoperative localization tests, multiple or ectopically situated tumors, subtotal tumor resection or fracturing the parathyroid tumor, or familial PHPT and parathyroid cancer. Factors that make parathyroid operations more difficult include: previous thyroid or parathyroid operations, negative or equivocal localization studies, multiple abnormal parathyroid glands or ectopic tumor location, large and nodular goiters, extensive lymphadenopathy, bleeding disorders, and brown fat.

Localizing studies are essential for patients with persistent and recurrent PHPT as is reviewing the previous operative and pathology reports. Sestamibi and ultrasound scanning are the most sensitive preoperative localization studies. MRI and CT scans can also be helpful especially for patients with relatively large mediastinal and paratracheal tumors. Highly selective venous catheterization for PTH is helpful when non invasive localization studies are equivocal, conflicting or negative. The results of venous catheterization depend upon parathyroid function rather than size.

Patients with persistent or recurrent HPT who have had a previous focused approach, and patients with sporadic PHPT are generally easier to “cure” than are patients after a bilateral exploration by an experienced surgeon or with familial disease. We generally use a unilateral or “back door” approach for reoperations when tumors are localized as it provides the best exposure of the recurrent laryngeal nerve and there may be less scar tissue. When a parathyroid tumor is localized preoperatively we use the same criteria for reoperation (after direct laryngoscopy) as in patients having an initial exploration. When there is a risk of permanent hypothyroidism, parathyroid tissue should be cryopreserved or autotransplanted. In patients with negative localizing studies observation or treatment with Sensapar® may be helpful. Overall, the success rate of reoperative parathyroidectomy by an experienced parathyroid surgeon is about 93 to 95% with a complication rate of about 2%.

To conclude, recurrent and persistent PHPT should be avoided; the indications for reoperation are similar to those for the initial operation in most patients, and preoperative localization tests are essential.

■ Leigh W Delbridge

Department of Surgery, The University of Sydney, Australia / International Association of Endocrine Surgeons

The last decade has seen a paradigm shift in Western society in the surgical management of differentiated thyroid cancer, specifically in relation to the role of surgery for regional cervical lymph nodes. This change has, in fact, followed the lead of surgical practice of many Asian endocrine surgical units, where routine cervical lymph node dissection has been standard of care for many years. The minimalist approach of former times in western society (hemithyroidectomy alone as sufficient treatment for papillary cancer), has now been recognised as inadequate treatment for many patients, with high rates of recurrent or persistent disease. That approach has been replaced by a comprehensive surgical strategy based on two principles, namely: that completeness of surgical resection is an important determinant of outcome; and that residual metastatic lymph nodes represent the most common site of persistence/recurrence. As such, all patients undergoing surgery with malignant findings on cytology require a preoperative ultrasound examination of the cervical nodes, including the lateral neck nodes. Nodal involvement that is apparent either clinically pre-operatively or intra-operatively, or on pre-operative imaging (clinically N1a) mandates a “therapeutic” neck dissection, which may include the lateral compartment of the neck (Level 5) or the retromanubrial compartment down to the innominate vein (Level 7) in addition to the central compartment. For patients with no clinical or radiological evidence of lymph node involvement (clinically N0) the surgical approach recommended in most published guidelines is total thyroidectomy and routine “prophylactic” central neck dissection. However there has never been consensus on what constitutes an appropriate “central” neck dissection for this disease, with numerous published definitions, and considerable variation in clinical practice. A recently published consensus statement by Carty and colleagues (1) reviews the relevant anatomy of the central compartment and defines a consistent terminology relevant to central compartment neck dissection. A “central” neck dissection is defined as including a comprehensive, compartment-oriented removal of the pre-laryngeal nodes, the pretracheal nodes and at least one of the paratracheal lymph node basin. Removal of one paratracheal compartment on the side of the tumour constitutes a “unilateral central lymph node dissection” whereas removal of both paratracheal compartments constitutes a “bilateral central lymph node dissection”. However the guidelines do not address the issue of whether a prophylactic bilateral or unilateral neck dissection is superior and there are no evidence-based data to support one or other approach. As always the balance lies between increased risk of complications including recurrent nerve palsy and permanent hypoparathyroidism with bilateral dissection but a more limited node clearance. Data from our own unit (2) has demonstrated that prophylactic unilateral central node dissection significantly reduces the post-operative thyroglobulin levels without any increase in complications, and would appear a reasonable approach to prophylactic central neck dissection for papillary thyroid cancer. Other recent data from our own unit has shown that BRAF positive tumours in Stage II/III patients have a higher propensity for local nodal recurrence and are less sensitive to radioiodine ablation. This would imply that patients with BRAF positive tumours should be considered for more extensive initial lymph node surgery.

1. Carty SE, Cooper DS, Doherty GM et al. Consensus Statement on Terminology and Classification of Central Neck Dissection for Thyroid Cancer. *Thyroid* 2009;19:1153-1158.
2. Sywak M, Cornford L, Roach P, Stalberg P, Sidhu S, Delbridge L. Routine ipsilateral level VI lymphadenectomy reduces postoperative thyroglobulin levels in papillary thyroid cancer. *Surgery*. 2006, 140:1000-5

■ Yoshihide Fujimoto

Division of Head and Neck, Cancer Institute Ariake Hospital, Japan

How to treat of papillary thyroid cancer(PTC) has been controversial issue. Currently general trend is toward radical treatment, consisting of total thyroidectomy followed by radioiodine ablation and TSH suppression. Twenty years have passed since Cady and Hay declared the two biologically different risk groups in patients with PTC, and final prognosis of patients was not influenced by extent of thyroidectomy, extent of lymphnode dissection and postoperative adjuvant therapies. Several other discrimination systems for low or high cancer death risk have been developed and all of them stressed the importance of age, extracapsular invasion and distant metastasis. Thus far minute lung metastasis was occasionally undetectable by the usual chest x-ray, and accuracy of low-risk determination at the time of initial operation was 96-98%. We can expect, however, that the use of lung CT scan will decrease the false negative result.

In 1997 we performed a long-term (35-45 year) follow-up study of patients who had undergone thyroid surgery during a 11-year period (1950-1960) at University of Tokyo Hospital. Of 49 patients with low-risk PTC, only one male patient died of lumber spine metastasis 28 years after he first noted bilateral cervical lymphnode metastases at age 15. Childhood PTC should be considered differently from adult ones. No other patients presented any evidence of malignant transformation from a low-risk to high-risk cancer. Three patients presented small cancer recurrence in the remnant thyroid and/or regional lymphnodes at the long follow-up study, which were left untreated without showing of any further enlargement.

We have shown our experience at Tokyo Women's Medical College Hospital that, when 15 % of all patients with low-risk PTC were selected by preoperative ultrasonography to undergo total thyroidectomy because of bilateral cancer involvement, only a few (0.5%) recurrence was seen in the remnant thyroid in a total of 343 patients who received hemithyroidectomy. The cancer specific survival rates of patients with low-risk PTC were 99% at 10 and 15 years postoperatively.

We have also experienced in other patients recently that there have been no enlargement of recurrent nodal metastasis during various terms of conservative observation. They tended to stop further enlargement after the node became at maximum 2 cm in the size.

Based on our experiences stated above, we propose that, so long as the patient is judged as of low-risk one, (1) an indication of total thyroidectomy can be determined selectively by preoperative ultrasonography, (2) postoperative adjuvant therapy including radioiodine ablation and TSH suppression are not necessary, and (3) postoperative nodal cancer recurrence of the size less than 2cm may safely be followed up conservatively. This treatment strategy certainly elevates QOL and reduces medical cost in patients with a low-risk PTC.

## **PL-1-1** | **SURGICAL MANAGEMENT OF ASYMPTOMATIC PRIMARY HYPERPARATHYROIDISM**

■ Chung Yau Lo

Breast & Endocrine Surgery Centre, Hong Kong

Primary hyperparathyroidism (PHPT) is the third most common endocrine disorder, with the highest incidence in postmenopausal women. Somatic manifestations of hypercalcemia include abdominal pain, nephrolithiasis, osteopenia, and mental status changes. In addition, PHPT is also associated with nephrolithiasis, metabolic bone diseases, increased cardiovascular disease, and decreased survival. Symptomatic or severe diseases arise less frequently now than it did 20-30 years ago. Asymptomatic diseases are most often diagnosed when routine biochemical testing shows an elevated serum calcium level. On the other hand, the modern day “asymptomatic” patient may present with much more subtle neurocognitive symptoms including fatigue, lethargy, muscle weakness, depression, and cognitive impairment that may be unmasked after successful parathyroidectomy. Furthermore, reduced bone density and increased fracture risk can be improved with parathyroidectomy. The demonstrated prevalence of nonclassical symptoms and their reversibility, the evidence of “asymptomatic” but harmful effects reversible by surgery, and the accumulating evidence for surgical reduction of increased long-term mortality risk have substantially supported the argument for need of treating this condition. Added to these reasons has been the introduction of minimally invasive parathyroidectomy (MIP) with the aim of making surgical treatment much simpler and faster.

Medical management of mild disease is possible with bisphosphonates, hormone replacement therapy, and calcimimetics but surgical excision of adequate amount of functioning parathyroid tissue remains the most effective treatment for this condition. Excision of a solitary adenoma cures the condition but is inadequate for patients with multiglandular hyperplasia. Since the first parathyroidectomy performed in 1925, the surgical strategy for treatment of pHPT has undergone a continuous evolution. Advances in imaging technology, intraoperative parathyroid hormone measurement, and surgical technique now allow parathyroidectomy to be performed using a focused approach without the absolute need of a four-gland exploration. In contrast to conventional cervical exploration, noninvasive localization studies including ultrasound and sestamibi scans are often employed, especially in anticipation of focused explorations. Invasive localization studies should be reserved for remedial explorations where noninvasive imaging has been unsuccessful. Preoperative imaging studies should only be performed to plan the operation, and negative imaging should never preclude surgical referral although it may have an implication for the size of adenoma and underlying pathology. When performed by expert parathyroid surgeons, parathyroid surgery is safe, cost-effective, and associated with very low perioperative morbidity. MIP appears to be as effective as the classic bilateral cervical exploration approach and is increasingly accomplished under local anesthesia on an outpatient basis. MIP can be accomplished through a unilateral or focused exploration with a small incision or the use of specialized instruments or videoscope. The availability of quick parathyroid hormone assay serves to facilitate the confirmation of surgical success after excision of a solitary adenoma and the identification of patients with multiglandular disease even when a single gland is erroneously located by preoperative localization. A >50% decline in quick PTH assay at 10-15 minutes compared with induction or pre-excision level is commonly employed as the criteria for surgical success and to identify patients with hyperplasia for conversion to bilateral exploration. Although there are numerous types of MIP and no firmly established method has been accepted as the standard technique, MIP has become the preferred approach during surgical management of patients with pHPT. On the other hand, bilateral cervical exploration remains procedure of choice for multiglandular diseases and is complimentary to MIP in the presence of negative or equivocal localization.

## PL-1-2 | SURGICAL EXPERIENCE FOR SECONDARY HYPERPARATHYROIDISM

■ Yoshihiro Tominaga

Department of Transplant and Endocrine Surgery, Nagoya Red Cross Hospital 2, Japan

Secondary hyperparathyroidism (HPT) is a common complication in patients with chronic kidney disease (CKD) and it is often associated with morbidity and sometimes mortality. Hyperphosphatemia, hypercalcemia and high level of parathyroid hormone (PTH) contribute to mortality due mainly to vascular and valvular ectopic calcification. At present many modalities including calcimimetics are available for medical treatment of secondary HPT and majority of patients with secondary HPT can be managed by these treatments. However, the medical treatment does not always provide control of the parathyroid disorder. Some patients require surgical treatment: parathyroidectomy (PTx). Successful PTx often results dramatic drop in the PTH level, relieves the patients from clinical symptoms, and reduces mortality.

The clinical condition after PTx in secondary HPT is quite different from in primary HPT. In fact, except for multiple endocrine neoplasia, in primary HPT, the risk of recurrent HPT is extremely low. In secondary HPT, pathogenetic factors, ie. hypocalcemia, hyperphosphatemia, deficiency of active vitamin D ect, persist after the initial surgery, therefore it is very difficult to avoid recurrent HPT and re-operation. To prevent re-operation, removal of all parathyroid glands at the initial operation should be required. However, it is sometimes difficult to detect all parathyroid glands at surgery, because parathyroid glands sometimes are located ectopically and supernumerary. Surgeons should be familiar with anatomy and embryology of the small organs.

There are different methods of PTx, including subtotal PTx, total PTx with autograft and total PTx without autograft. To avoid recurrent HPT, some surgeons prefer total PTx without autograft. However, it is not clarified that hypoparathyroidism after the operation is acceptable or suitable for patients with CKD. Low level of PTH may induce adynamic bone disease and may contribute to progression of ectopic calcification and influence mortality. It has been reported that after total PTx without autograft recurrent HPT sometimes occurred due mainly to residual parathyroid nest located in thymus.

Subtotal PTx and total PTx with forearm autograft are widely accepted for secondary HPT. We prefer total PTx with forearm autograft because at recurrence removal of autograft is less invasive than the re-neck exploration after subtotal PTx.

Between July 1973 and November 2009, 2743 patients underwent total PTx with forearm autograft for secondary HPT in our department. In our series, 10 years survival rate after the initial operation was 77.6%. Our definition of recurrence is that a PTH level drop under 60 pg/mL after the initial PTx and then PTH level is re-elevating and re-operation is required. In our experience cumulative frequency of recurrence was about 20% at 10th year after initial PTx.

At recurrence, it is very important to detect the responsible lesion of over-secreting PTH. Usually graft dependent recurrence can be diagnosed by high PTH gradient and detection of swollen autograft by MRI or US. By removal of autograft en-bloc with surrounding muscle, PTH level usually decreased under 300pg/ml and secondary HPT could be controlled by medical treatment in our study.

Other possible origins of PTH over-secretion are residual gland in the neck or mediastinum, parathyromatosis and metastasis of parathyroid carcinoma. In our series the frequency of recurrence depend on residual gland was 1.4% and re-neck or mediastinal exploration was required.

Parathyromatosis and metastatic parathyroid carcinoma are very problematic. At the parathyromatosis en-bloc resection of small parathyroid nodules with thyroid lobe was performed, however it was often difficult to control recurrent HPT by surgical treatment. To prevent parathyromatosis injury of parathyroid capsule should be avoided at the initial surgery. Sometimes Cinacalcet HCl was useful to control recurrent HPT induced by parathyromatosis. Parathyroid carcinoma in hemodialysis patients is very rare. We encountered five hemodialysis patients with distant metastasis of parathyroid carcinoma. Unfortunately three patients died of hypercalcemia or calciphylaxis. It has been reported Cinacalcet HCl also was effective to control hypercalcemia due to metastatic parathyroid carcinoma which could not be resected surgically.

In conclusion, Recurrent HPT can not be avoided after PTx for secondary HPT. It is easier and safer to remove residual parathyroid tissue from the forearm than to perform re-neck exploration, total PTx with forearm autograft is preferable for patient who has to continue hemodialysis for long period.

## PL-2-1 | DIAGNOSIS AND CLINICAL WORKUP OF SUBCLINICAL CUSHING'S SYNDROME

■ Yutaka Oki

Second Division (Endocrinology & Metabolism), Department of Medicine, Hamamatsu University School of Medicine, Japan

Cushing's syndrome (CS) can be a lethal disease as it causes excess exposure to endogenous glucocorticoid, if not diagnosed and treated appropriately. CS is classified into two types, ACTH-dependent and -independent. In the past 20 years, the clinically silent form of endogenous cortisol excess has been investigated and named as subclinical CS (SCS) including both adrenal and pituitary types.

Most patients with SCS start to be examined due to incidentally discovered adrenal mass. In some patients, the detailed endocrine tests for diabetes, hypertension or dyslipidemia can be opportunities of diagnosis of SCS. We perform low dose dexamethasone suppression test (DST) as an initial screening test. The Endocrine Society (US) published clinical guidelines for CS including SCS in 2008, and 1 mg DST, determination of late salivary cortisol or urinary free cortisol is recommended as the initial screening test. To achieve high sensitivity, the cortisol cut-off value of 1 mg DST is reduced to 1.8 µg/dL, which is quite lower than the previous one (5 µg/dL). However, it has been suggested that 1 mg DST is too strong to suppress plasma cortisol levels in Asian patients, because they are leaner than patients in Western countries. Recently, it has been reported that 0.5 mg DST with a cortisol cut-off level of 3 µg/dL is more sensitive and specific than 1 mg DST for the diagnosis of ACTH-dependent CS. This method can be also applied to ACTH-independent CS with the same cortisol cut-off value. The determination of late salivary cortisol levels is a very nice diagnostic tool for overt CS but is not useful for the diagnosis of SCS. To prove the suppression of the pituitary ACTH secretion and the normal adrenal gland, we use corticotropin-releasing hormone (CRH) test and/or adrenal scintigraphy. If plasma ACTH does not respond to CRH, the glucocorticoid replacement therapy will be necessary after adrenalectomy. We sometimes care patients with bilateral adrenal lesions, e.g. ACTH-independent macronodular adrenal hyperplasia (AIMAH). When the patient with AIMAH shows subclinical, we usually recommend removing the larger side, which is determined with computed tomography. Patients with SCS do not show any typical feature of CS, e.g. round face, but they usually have cardiovascular risk factors such as glucose intolerance, dyslipidemia and hypertension. In addition, it has been reported that the prevalence of osteoporosis is high in patients with SCS.

Although it is very difficult to define who should undergo adrenalectomy, the removal of adrenal mass frequently improves diabetes mellitus and hypertension. In this lecture, current consensus of diagnosis and clinical workup of SCS will be discussed.

## **PL-2-2** | **MANAGEMENT OF SUBCLINICAL CUSHING'S SYNDROME - LAPAROSCOPIC SURGERY VS CONSERVATIVE TREATMENT**

■ Brian H Lang

University of Hong Kong (HKU), Hong Kong

Subclinical Cushing's syndrome is believed to be the commonest hormonal abnormality detected in patients with adrenal incidentalomas. Its prevalence has been quoted between 5 to 20% of all adrenal incidentalomas, depending on the referral type, study design and diagnostic criteria. Owing to the increasing use of routine imaging modalities, the ageing population as well as the improved sensitivity of biochemical assays, it is expected that this condition will pose an increasing problem for clinicians.

In terms of management, it still remains largely empirical as there remains a lack of prospective, randomized clinical trials for evidence-based medicine. For surgeons, one of the most important and relevant issues is whether surgery is beneficial and leads to better outcomes than medical treatment alone. Earlier data suggest that adrenalectomy may ameliorate the cardiovascular risk profile of patients who have subclinical Cushing's syndrome, but data remain inconsistent and conflicting.

However, with improved techniques in laparoscopic adrenalectomy, surgery has become a relatively low-risk procedure and therefore, it is an attractive treatment option for these patients. Since the first description of laparoscopic adrenalectomy by Higashihara from Tokyo and Gagner from Montreal in 1992, there have been numerous reports showing continuous improvement in surgical outcomes. Compared with conventional open surgery, laparoscopic surgery is associated with less pain, shorter hospital stay and faster return to normal daily activities. However, unlike overt Cushing's syndrome, the issue of whether all patients with subclinical Cushing's syndrome should be managed by laparoscopic adrenalectomy is far more complex. This is because firstly, the diagnosis of subclinical Cushing's syndrome is still difficult to define. So far, there has been no standardized test or agreed diagnostic criteria available. Furthermore, recent data suggest that the degree of hypercortisolism is distributed continuously among different patients, implying the fact that there is a spectrum of variability from non-functioning adenoma to autonomous cortisol-producing adrenal adenoma. There is even some evidence to suggest that in "normal" non-obese, normoglycemic patients with adrenal incidentaloma, they too have a higher frequency of impaired glucose tolerance, elevated blood pressure and reduced insulin sensitivity compared to age-, sex- and BMI-matched controls. Secondly, the long-term detrimental impact of subclinical cortisol excess remains largely unknown as there are few studies with long-term follow-up. Intuitively, one may presume that over a long period, the classic complications of full blown Cushing's syndrome such as arterial hypertension, obesity, diabetes and osteoporosis will manifest. Thirdly, along with the improvement in surgical techniques and outcomes, the effectiveness of medical treatment and lifestyle changes will continue to improve with time. Nevertheless, a recent randomized trial found that laparoscopic adrenalectomy when performed by skilled surgeons was a better treatment option in patients with subclinical Cushing's syndrome than conservative treatment. More importantly, it confirmed that successful laparoscopic adrenalectomy could reverse some of the cardiovascular risk factors including diabetes mellitus, arterial hypertension, lipid profile problems and high body mass index. However, the impact of laparoscopic adrenalectomy on long-term outcomes and quality of life in subclinical Cushing's syndrome were not addressed and will be important in future studies.

■ Abdullah N Hisham

Department of Breast and Endocrine Surgery, Hospital Putrajaya, Malaysia

Thyroid surgery for a simple and large endemic goitre is a common surgical procedure in Malaysia. Nonetheless the challenge of thyroid surgery is in providing safe surgical benchmark for retrosternal goitres. The definition of retrosternal goiter is not uniform and varies among authors. The most widely applied definition of retrosternal goiter is when more than 50% of the thyroid gland is located below the suprasternal notch.

Over the years a multitude of classification systems has been introduced to categorize the retrosternal goitres. Often Substernal goiters are classified into two groups: a direct substernal extension and a truly intrathoracic or aberrant goiter. Goitres extending into the thorax frequently compress onto important vital structures resulting in significant compressive symptoms. These effects clearly increase the difficulties and hazards of surgery. Based on Zylak system of categorizing the mediastinum into 3 longitudinal compartments from the level of thoracic inlet to diaphragm we propose a classification of retrosternal goiter taking into the account the contralateral extension of anterior and posterior retrosternal goiter coupled with anterior posterior extension or vice versa. Careful attention is paid to fundamental points of the classification, surgical technique and approach of surgery. Although in most instances the operation is usually straightforward and accomplished without much difficulty, it is important that all surgeons understand the types and various approaches to retrosternal goiters. Most retrosternal goitres can be removed through an entirely cervical approach with a low complication rate. It is only on rare occasions a median sternotomy will be required to permit a safe and complete removal of retrosternal goitres.

We reviewed our experience of substernal goiters from December 1998 to May 2008 where 140 consecutive patients who met the required criteria were included in this prospective non randomized study. The incidence of substernal goiters in our series is 6.95% (140/2015) with the mean age of 53.3 years (ranged 14 to 78 years). The female and male ratio was 3.7 to 1.0. At least 60% of our patients have some form of significant compressive symptoms and 16 cases were done under emergency surgery. From our series only 10 patients (7.2%) needed a sterna split and one patient (0.7%) had a right posterior lateral thoracotomy. 85.7% of the retrosternal goiter was located in the anterior compartment and 14.3% in the posterior compartment.

The presence of a retrosternal goiter is an indication for removal in view of the potential risk of critical airway compression and the risk of malignancy. In the majority of cases most of the goiters can be removed via the classical cervical approach and from our series 92% of retrosternal goiter can be safely removed via a classical cervical incision.

## **PL-4-1** | **FAMILIAL PHEOCHROMOCYTOMA IN JAPAN: A NATIONAL REGISTRY DATA ANALYSIS**

■ Tsuneo Imai

Department of Breast & Endocrine Surgery, Nagoya University, Japan

[Introduction] Despite advances in diagnostic methods including genetic analysis and surgical techniques, differences in the management of multiple endocrine neoplasia type 2 (MEN2) patients are evident in Japan, thus differences in patient outcome may result. In order to establish national guidelines for MEN2 management, a registry of MEN management regimes was compiled by the Japanese study group (MEN Consortium of Japan) in 2009.

[Patients and Methods] Data on pheochromocytoma in MEN2 was collected from 11 institutions in Japan. The questionnaire included the following questions: 1) Was there a positive diagnosis of pheochromocytoma? If yes; age at diagnosis. 2) Was surgical intervention performed? If yes; age at surgery. 3) Was there unilateral or bilateral involvement? 4) Which particular surgical procedures were performed? 5) Was there a pathological diagnosis? 6) Were multiple surgeries performed?

[Results] The total number of patients registered with MEN2 in November, 2009 was 243. There were 204 (84%) MEN2A and 6 (2.5%) 2B patients with the remaining 33 (13.5%) presenting with familial medullary thyroid carcinoma (FMTC). Pheochromocytoma was detected in 101 (48%) of the 210 MEN2 patients. The mean age for the diagnosis of pheochromocytoma was 41 years (range: 14–83 years) and 55 patients (55%) were women. Adrenal surgery was performed on 84 of the 101 patients (83%). Unilateral adrenalectomy was performed in 33 patients. Bilateral adrenalectomy was performed in 48 patients, 36 patients had one stage bilateral adrenalectomy and 12 patients had two stage bilateral adrenalectomy. Laparoscopic surgery was performed in 29 patients. Pathological diagnosis confirmed pheochromocytoma in all but one case of malignant pheochromocytoma. Multiple operations were performed in 14 patients.

[Discussion] The number of nominated institutions in the MEN Consortium has increased to 25, all of which treat MEN patients. This fact-finding survey of prevalence and treatment of MEN2 in Japan will provide important information for the development of national guidelines for the efficient management of MEN2.

## **PL-4-2** | **MULTIPLE ENDOCRINE NEOPLASIA (MEN) TYPE 1 IN JAPAN: ESTABLISHMENT AND ANALYSIS OF A MULTICENTER DATABASE**

■ Shinichi Suzuki<sup>1</sup>, Akihiro Sakurai<sup>2</sup>, Shinya Uchino<sup>3</sup>, Masayuki Imamura<sup>4</sup>, Shinji Kosugi<sup>5</sup>, Tsuneo Imai<sup>6</sup>, Hiroshi Kaji<sup>7</sup>, Masanobu Yamada<sup>8</sup>, Shohei Hirakawa<sup>9</sup>, Hiroshi Takeyama<sup>10</sup>, Kazuo Shimizu<sup>11</sup>, Iwao Sugitani<sup>12</sup>

<sup>1</sup>Department of Breast Endocrine Thyroid Surgery, Fukushima Medical University School of Medicine, Japan, <sup>2</sup>Department of Medical Genetics, Shinshu University School of Medicine, Japan, <sup>3</sup>Noguchi Thyroid Clinic and Hospital Foundation, Japan, <sup>4</sup>Department of Surgery, Osaka Saiseikai Noe Hospital, Japan, <sup>5</sup>Department of Medical Ethics, Kyoto University Graduate School of Public Health, Japan, <sup>6</sup>Department of Breast and Endocrine Surgery, Nagoya University School of Medicine, Japan, <sup>7</sup>Division of Diabetes, Metabolism and Endocrinology, Department of Internal Medicine, Kobe Graduate School of Medicine, Japan, <sup>8</sup>Department of Medicine and Molecular Science, Guma University Graduate School of Medicine, Japan, <sup>9</sup>Department of Surgery, Yokohama City University, Japan, <sup>10</sup>Department of Surgery, Jikei University Daisan Hospital, Japan, <sup>11</sup>Department of Surgery 2, Nippon Medical School, Japan, <sup>12</sup>Department of Head and Neck Surgery, the Cancer Institute, Japan

We established a multiple endocrine neoplasia (MEN) research consortium (MEN Consortium of Japan) for the purpose of the clarifying of the situation and accumulating evidence on MEN over the last one year in Japan. We report MEN1 cases in Japan collected from the MEN Consortium of Japan.

The subjects were 208 MEN1 cases involving 20 registered institutes in this consortium. Of the 208 MEN1 cases, there were 102 men and 106 women, with an average age of 55.6±15.1 years at the initial diagnosis. The frequencies of typical diseases of each endocrine organ were: 191 hyperparathyroidism (92%), 94 pituitary adenomas (45%), 110 pancreatic duodenal tumors (53%), 44 adrenocortical tumors (21%), 18 carcinoid tumors (8.6%), and 36 skin tumors (17%). Familial and sporadic cases comprised 169 (81%) and 39 (19%) respectively, involving probands of MEN1 families in 65 cases (38%). Operations were performed in 76% of MEN1 cases with parathyroid disease, 35% with pituitary disease, 56% with pancreatic duodenal tumors, 30% with adrenocortical tumors, and 88% with carcinoid tumors.

Genetic testing involved 169 examples (81%). Of these, 135 cases (80%) showed the mutation of MEN1, and 34 cases (20%) had exhibited the wild-type of the MEN1 gene.

We examined the current state, prognosis, treatment, and correlation with the geno- and phenotype in MEN1 in Japan. It is necessary to analyze the data of this consortium, and use the results to advance the diagnosis and treatment of MEN1 in Japan.

## **PL-5-1** | **MANAGEMENT OF LOW-RISK PAPILLARY THYROID CARCINOMA: UNIQUE CONVENTIONAL POLICY IN JAPAN AND OUR EFFORTS TO IMPROVE THE LEVEL OF EVIDENCE**

■ Iwao Sugitani, Kazuhisa Toda, Yoshihide Fujimoto

Division of Head and Neck, Japanese Foundation for Cancer Research, Cancer Institute Hospital, Japan

Papillary thyroid carcinoma (PTC) accounts for over 90% of all thyroid cancer in Japan. The majority of patients with PTC are categorized into low-risk group according to the recent risk-group classification schemes and they have excellent outcomes. Several management guidelines for thyroid cancers have been published in Western countries these days, and Japanese guidelines for management of thyroid tumors will be published soon. However, the optimal therapeutic options for PTC remain controversial and high-level clinical evidence to resolve the issues is lacking. Moreover, socio-economical differences in medical care exist; therefore, conventional policies for the treatment of PTC have been different between Japan and foreign countries. This presentation focuses on the unique policy in Japan preferring to treat patients with low-risk PTC by less-than-total thyroidectomy without adjuvant therapies rather than total thyroidectomy with radioactive iodine (RAI), in an attempt to maintain patients' quality of life. In addition, we introduce our institutional efforts to improve the level of evidence for the management of PTC.

### *(1) Our own risk-group classification system for cancer-specific survival in PTC patients*

We retrospectively analyzed a total of 604 patients who had undergone initial surgery for PTC (tumor diameter, >1 cm) between 1976 and 1998. Mean duration of follow-up was 11 years. Multivariate analysis for cause-specific survival (CSS) identified distant metastasis as the only significant risk factor for younger patients (age, <50 years). For older patients (age, ≥50), distant metastasis, extrathyroidal invasion, and large nodal metastasis (≥3 cm) showed relative importance. From these results, younger patients with distant metastasis and older patients with any of the three factors were defined as high-risk, while all other patients were defined as low-risk. Overall, 106 high-risk patients (18%) and 498 low-risk patients (82%) displayed 10-year CSS rate of 69% and 99%, respectively.

### *(2) Dual policy for the extent of thyroidectomy and informed decisions by patients*

Since 2005, we have started to explain 2 policies for treatment to patients with low-risk PTC: 1) total thyroidectomy followed by RAI ablation and TSH suppression; and 2) conservative thyroidectomy without any adjuvant therapies. We then request that patients make an "informed decision" about which policy they choose. As of 2008, there were 240 patients diagnosed with low-risk PTC, excluding 56 patients for whom total thyroidectomy was unavoidable. Among these 240 patients, 8 (3%) wanted to receive total thyroidectomy with adjuvant therapy and 201 (84%) chose conservative surgery. The remaining 31 patients (13%) could not decide by themselves and left the matter up to the doctor.

### *(2) Randomized controlled trial (RCT) for the effects of TSH suppression therapy*

In 1996, we started a single-center, open-label, prospective RCT on the effectiveness of TSH suppression therapy. The primary endpoint was clinical recurrence. The trial was designed as a noninferiority study to demonstrate that disease-free survival (DFS) for patients without TSH suppression therapy was not inferior to that for patients with the therapy. By 2005, the planned sample size of 204 patients for each group was accumulated. In 2009, the mean duration of follow-up reached 7 years and the final report will be published.

### *(3) Prospective outcomes of selective lymph node dissection based on preoperative ultrasonography (US)*

Since 1993, we have performed cervical lymph node dissection based on preoperative suspicion of lymph node metastasis by US. Prospective analysis was conducted for 361 consecutive patients with PTC who received initial surgery between 1993 and 2001. Central compartment node dissection only was performed for patients with lymph node metastasis in the central zone only and for patients with no nodal metastasis detected by US. Nodal recurrences were seen in 18 patients (8%) and 10-year nodal DFS was 91%. Among the risk factors that could be diagnosed preoperatively, distant metastasis and large primary tumor were the most important factors under multivariate analysis.

### *(4) Non-surgical observation trial for asymptomatic papillary microcarcinoma (PMC)*

According to our previous retrospective review of 178 patients with PMC who underwent surgery between 1976 and 1993, the most significant risk factors affecting cancer-specific survival were clinical symptoms at presentation due to either invasion or metastasis. Distant metastasis and cancer-specific death were never seen postoperatively for 148 cases (83%) of asymptomatic PMC without clinically apparent (≥1 cm) lymph node metastasis or recurrent nerve palsy. Since 1995, we have been conducting a prospective clinical trial of non-surgical observation for asymptomatic PMC. As of 2008, 230 of 244 candidates (94%) have decided to accept this policy. Non-surgical observation for a mean of 5 years (range, 1-17 years) for 300 lesions of asymptomatic PMC revealed that 22 (7%) had increased in size, 269 (90%) were unchanged and 9 (3%) had decreased. No patients developed extrathyroidal invasion or distant metastasis. Three patients (1%) who developed apparent lymph node metastasis and 9 patients (4%) in whom tumor increased in size eventually received surgery after 1-12 years of follow-up. No recurrences have been identified postoperatively.

## PL-5-2 | INVESTIGATION FOR HIGH-RISK AND LOW-RISK CASES OF PAPILLARY THYROID CARCINOMA IN JAPAN BASED ON UICC TNM CLASSIFICATION AND STAGING SYSTEM

■ Yasuhiro Ito, Akira Miyauchi

Department of Surgery, Kuma Hospital, Japan

*Background;* Papillary thyroid carcinoma generally has an indolent nature, but cases demonstrating certain features are progressive. UICC TNM classification is the most widely adopted system to evaluate the biological behavior of this carcinoma, but it is doubtful whether this system can efficiently discriminate high-risk cases from others. In this study, we investigate high-risk cases of papillary carcinoma using a revised UICC TNM classification.

*Methods;* We investigated the prognoses of 5911 patients with papillary carcinoma without distant metastasis at diagnosis who underwent initial surgery between January 1987 and January 2005 and evaluated the utility of prominent staging systems such as UICC Stage, MACIS score ( $> 7$  and  $\leq 7$ ), AMES and CIH classification.

*Results;* Disease-free survival (DFS) and cause-specific survival (CSS) of patients with Stage IVA were better than those of patients with high MACIS score or those of patients diagnosed as high-risk based on AMES and CIH classification. We then established iStage by revising the UICC TNM classification. Patients aged 55 yrs or older were classified into iStage IVA if they had tumors larger than 2 cm with massive extrathyroid extension not only on preoperative but also on intraoperative findings or had regional node metastasis larger than 3 cm or extranodal tumor extension on intraoperative findings. Five-year and 10-year DFS and CSS rates of iStage IVA patients were not only worse than those of patients classified as Stage IVA on the original UICC but also worse than those of patients with high MACIS score and high-risk cases based on AMES and CIH classification.

*Conclusion;* Patients with papillary carcinoma 55 yrs or older were classified as high-risk if they have any of the following characteristics: 1) tumor larger than 2 cm with massive extrathyroid extension: 2) regional node metastasis larger than 3 cm: and 3) regional node metastasis with extranodal tumor extension requiring at least partial excision of adjacent organs. Patients 55 yrs or older and having any of following three characteristics can be regarded as intermediate risk showing high recurrence rate but low mortality: 1) tumor larger than 4 cm without massive extrathyroid extension: 2) tumor 2 cm or less with massive extrathyroid extension: 3) preoperatively detected regional node metastasis measuring 3 cm or smaller without extranodal carcinoma extension.

■ Masayuki Imamura

Osaka Saiseikai Noe Hospital, Japan

Localization of gastro-entero-pancreatic neuroendocrine tumors (GEPNET) has been almost established by the development of both SASI test (Selective arterial secretagogue injection test) and SRS (Somatostatin receptor scintigraphy). These two techniques are specific for GEPNET and useful for preoperative localization of curative resection surgery. These two methods have promoted curative resection surgery for GEPNET.

Characteristic pathological findings have been accumulated as the number of resection surgery has increased, and have been used for deciding the modus of resection surgery of GEPNET. For example, the rate of hepatic metastases from pancreatic gastrinoma is more than 60%, but rate of hepatic metastases from duodenal is less than 10%. Thus pancreatic gastrinoma should be resected as soon as possible for preventing hepatic metastases. Gastrinoma have easily metastasized to the regional lymph nodes. So, it is now well known that intensive dissection of regional lymph node is necessary for curative resection of gastrinoma. We know now that Zollinger-Ellison syndrome is caused more often by the duodenal gastrinoma rather than by the pancreatic gastrinoma. Sporadic duodenal gastrinoma is often single, although duodenal gastrinoma associated with multiple endocrine neoplasia type 1 (MEN 1) are often multiple and sometimes numerous. There are multiple and microscopically numerous GEPNET in the pancreas of patients with MEN 1, but gastrinomas has been always located in the duodenum and pancreatic gastrinoma has been coexisted in 13% cases.

G-cell hyperplasia in and /or close to the duodenal Brunner's glands has been observed in almost all the duodenum in our cases with MEN 1 and ZES. That has been described as a precursor lesion of duodenal gastrinoma in MEN 1 and ZES by Kloppel et al. We think that one of the reasons why recurrence of ZES took place higher rate in these cases may be in this precursor lesion. We now perform pancreas preserving total duodenectomy (PPTD) for prevention of unresected minute microgastrinomas and /or de novo gastrinomas that may develop from duodenal precursor lesions due to menin gene mutations in MEN 1 and ZES.

Thus, curative resection surgery for GEPNET is principally a complete resection of the main tumors with dissection of regional lymph nodes guided by localization with SASI test and SRS. For resection of a benign GEPNET like an insulinoma, intraoperative ultra-sonography (US) is useful for estimation of the distance between a tumor and the main pancreatic duct. As far as the tumor was apart more than 5mm from the main pancreatic duct, enucleation can be safely performed. For other GEPNET like gastrinoma or glucagonoma or VIPoma which are potentially malignant, modus of curative resection surgery includes the resection of the pancreas, such as distal pancreatectomy, pancreaticoduodenectomy, pylorus preserving pancreaticoduodenectomy and central resection of the pancreas. Sporadic duodenal gastrinoma can be curative ly resected by local resection of the tumor through duodenotomy and aggressive dissection of the regional lymph nodes is recommended. In cases with MEN 1 and ZES, gastrinomas are located in the duodenum which are often multiple and sometimes numerous, so we have recommended partial duodenectomies or PPPTD for en bloc curative resection not to leave any gastrinomas behind.

Treatment strategy for hepatic metastases of GEPNET has not been standardized, although many surgeons have recommended mass reduction surgery for countable numbers of hepatic metastases. Chemotherapy for hepatic metastases of GEPNET has been performed with a variety of regimens, and each department has a few cases in whom hepatic metastases were completely cured with streptozotocine alone or with 5FU. Now, European Neuroendocrine Tumor Study Group (ENETS) recommends cisplatin with etoposide for poorly differentiated rapidly growing GEPNET, and STZ with 5-FU for rapidly growing well differentiated GEPNET.

Recent topic in medical therapy for GEPNET is the introduction of somatostatin analogs for inhibition of growth of GEPNET. Recently, PROMID-study-group statistically proved that the time to tumor progression of metastatic midgut GEPNET was significantly prolonged in the group treated with octreotide LAR compared to the group treated with placebo. So, octreotide LAR is recommended for slow growing metastatic GEPNET by the ENETS.

## **SY-1-1** | “DELTOPECTORIAL FLAP RECONSTRUCTION” WITH PREOPERATIVELY TRANSPLANTED AURICULAR CARTILAGE FOR THYROID PAPILLARY CANCER INVADING THE TRACHEA

■ Masayuki Tori<sup>1</sup>, Toshirou Nishida<sup>1</sup>, Hiroki Akamatsu<sup>1</sup>, Katsuhide Yoshidome<sup>1</sup>, Tsukasa Oyama<sup>1</sup>, Shigeyuki Ueshima<sup>1</sup>, Takeshi Omori<sup>1</sup>, Takuya Hamakawa<sup>1</sup>, Masaaki Nakahara<sup>1</sup>, Motomu Maeda<sup>2</sup>

<sup>1</sup>Surgery, Osaka Police Hospital, Japan, <sup>2</sup>Plastic Surgery, Osaka Police Hospital, Japan

**Background and Aim:** Majority of thyroid papillary cancers are slow growing and show good prognosis, however some of them are aggressive and might exhibit so-called oncologic emergencies such as bulky tracheal bleeding and/or occlusion of airway, which lead to life-threatening status. Therefore, proper and novel procedure for reconstruction of the tracheal defect after resection in the operation of thyroid papillary cancer was examined in terms of the site and area of invasion, and moreover, novel operative procedure, deltopectorial (DP) flap reconstruction was estimated if the method could be applied to various type of invasion and standardized as reconstruction. (Estimation of invasion) ultrasonography, CT, MRI, and bronchofiber were preoperatively performed. If invasion was estimated beyond extramucosal layer, shaving was tried first during operation. **Patients and methods:** For the past 7 years, 80 cases were operated diagnosed as differentiated papillary thyroid cancer invasive to the trachea. Those are divided into 5 groups in terms of operative procedures. (A) shaving; 57 cases, (B) wedge resection; 4 cases, (C) window resection with DP flap reconstruction; 9 cases, (D) cylindrical resection with direct suture; 6 cases, (E) total laryngectomy; 4 cases. All cases were examined histopathologically and the perioperative complications and outcome of each case was retrospectively searched. **Result:** In (A)(B) group, all cases survived without recurrence and/or metastasis. There were no complications. (C) One case suffered from lung metastasis 2 years after the operation. The others survived without recurrence. **Complication;** one minor leakage. (D) One case suffered from recurrence in half and a year after the operation, when total laryngectomy was performed. There was one case with minor leakage. (E) Two papillary carcinoma cases survived without recurrence. There was one case with cerebral infarction after the operation. We developed the procedures of DP flap reconstruction. When the site of invasion is at the level of the cricoid cartilage, flap is pulled through the tunnel underneath the skin and raised to cover the defect of trachea and tracheostomy was made just above the sternal notch, on the other hand, if the site of invasion is rather low, the skin is cut and divided longitudinally to put the DP flap on the “skin-crevasse”. By such device, postoperative management of airway control is achieved safely. **Conclusion** Shaving might be applied to most of the cases, and if invasion reach the mucosa, novel method, i.e. window resection with tracheostomy could be safe and be standardized as reconstructive procedure in that respiratory risk is very low and QOL of patients after operation is excellent.

## **SY-1-2** | **MANAGEMENT OF ADVANCED THYROID CANCER WITH MEDIASTINAL INVASION**

■ Hang-Seok Chang, Cheong Soo Park

Department of Surgery, Yonsei University College of Medicine, Korea

The advanced thyroid cancers with extensive metastasis to mediastinum are extremely rare, but are frequently associated with high morbidity and mortality.

The mechanism of mediastinal metastasis from thyroid cancer has not been yet fully understood. However, the lymphatic connection from central compartment to lower mediastinum can be supposed as the main pathway.

As for other malignant diseases, the principles of treatment are complete surgical removal of all metastatic foci and appropriate adjuvant therapy. However, because of the highest degree of surgical difficulty, postoperative morbidity, and mortality, most of previous studies indicated that the surgical treatment would be impossible.

When the metastatic foci are confined to anterior-superior mediastinum, the majority can be removed via transcervical approach. However, in cases of metastasis located at lower than aortic arch level, with extensive invasion to vital organs in mediastinum, and irradiated neck and mediastinum, a full midline sternotomy is needed. The choice of surgical options should be that offer the lowest morbidity, as well as the highest long-term remission rate.

High dose radioiodine therapy should be done in all indicated cases. However, because advanced thyroid cancers may transform to less differentiated type, the role of radioiodine in this setting can be limited. If the effects of surgery and radioiodine therapy is unlikely, external beam radiation therapy should be considered.

In summary, mediastinal metastasis from thyroid cancers may result in local failure, as well as decreased overall survival. The surgical treatments should focus on complete removal with leaving minimal morbidity, and maintaining the functions.

## **SY-1-3** | **VASCULAR PROBLEMS IN THE NECK SURGERY: ANATOMICAL AND TECHNICAL ASPECTS**

■ Masami Ochi

Division of Cardiovascular Surgery, Nippon Medical School, Japan

Vascular problems in the endocrine neck surgery may include the involvement of neck vessels by the invasive neoplastic tumor and occasionally inadvertent injury of these vessels during the neck dissection. The jugular veins and the carotid arteries run with thyroid gland in a side-by-side manner. Laterally, subclavian arteries lie just behind the clavicle. When a surgeon needs to dissect down behind the upper border of the sternum, he sometimes encounters the brachiocephalic trunk. To overcome these vascular problem, it is better way to know how to handle the blood vessels and to manage difficulty when it should occur. Details of vascular anatomy around the neck as well as the basic techniques of vascular surgery will be discussed.

## **SY-1-4** | **ADVANCED THYROID CANCER - LARYNGOPHARYNGEAL INVASION**

■ Soo Khee Chee

National Cancer Centre Singapore, Singapore

There are several dilemmas in the management of advanced local/regional thyroid cancers. These include understaging and underestimating of cartilage/visceral invasion, the need for sacrifice of recurrent laryngeal nerve, the role of ablation of larynx and pharynx when invasion of these structures are detected and the role of concurrent treatment of neck nodal disease in the presence of advanced local disease. Visceral involvement can be suspected if there is concurrent vocal cord paralysis, fixation to skin, fixation to the middle compartment of the neck or when there is intra luminal extension detected endoscopically or radiologically. We will discuss the management principles based on publication by others and our institutions' experience.

## **SY-1-5** | MANAGEMENT OF RECURRENT LARYNGEAL NERVE INVADED BY THYROID CANCER

■ Akira Miyauchi

Center for Excellence in Thyroid Care, Kuma Hospital, Japan

The recurrent laryngeal nerve (RLN) is one of the major concerns in thyroid cancer surgery. Thyroid cancer often invades the RLN causing vocal cord paralysis (VCP). In such cases, resection of part of the RLN is usually necessary. Even in patients with functioning vocal cords preoperatively, the RLN may be found being invaded by thyroid cancer during surgery. In such cases, we should try to preserve the nerve with sharp dissection, although resection of the nerve may be necessary in many cases. Resection of the unilateral RLN causes permanent VCP. Symptoms are hoarseness, aspiration and short phonation because of waste of air during phonation. Aspiration can be dangerous especially in elderly persons. I will report several methods of RLN reconstruction to improve phonation. The methods frequently used include direct anastomosis, free nerve grafting, and ansa cervicalis-to-RLN anastomosis, and vagus-to-RLN anastomosis was done in two cases. The thyroid cancer often invades the RLN at its laryngeal entry point. In such cases, you might think that nerve reconstruction is impossible, since you do not see the distal stump of the nerve. However, if you cut the inferior pharyngeal constrictor muscle, you can find the distal branches of the RLN, and a nerve anastomosis can be made behind the thyroid cartilage. In patients with extensive node metastases involving the ansa cervicalis, the ansa on the opposite side can be used for nerve reconstruction.

Following any type of nerve reconstruction, the vocal cords on the side of reconstruction do not restore normal movement because of misdirected regeneration among the adductor and abductor nerve fibers. The condition of the vocal cords is not paralysis. It is better expressed as synkinesis, simultaneous contraction of the adductor and abductor muscles. Therefore, the vocal cords recover from atrophy and restore tension during phonation. Thus, patients' voices recover.

Since the vocal cords on the side of nerve reconstruction do not restore normal motions, laryngoscopic examination is not suitable to evaluate vocal cord function. The most practical and simplest way is measuring maximum phonation time (MPT) periodically after surgery. Patients with VCP had significantly shorter MPT than normal subjects, and patients who underwent RLN reconstruction achieved MPT of nearly normal value one year after surgery. Male subjects had significantly longer MPT than female subjects. MPT / vital capacity ratio should indicate laryngeal function of converting unit volume of exhaled air to a certain length of phonation. Thus, we call this value phonation efficiency index (PEI). When we calculate PEI, difference by gender disappears, indicating this value is suitable in evaluating vocal cord function regardless of gender. Patients who underwent RLN reconstruction achieved PEI of nearly normal value one year after surgery regardless of presence or absence of VCP preoperatively.

In conclusion, reconstruction of the RLN should be performed, if the nerve was resected regardless of presence or absence of vocal cord paralysis preoperatively.

## **SY-2-1** | **SURGICAL MANAGEMENT OF GRAVES' DISEASE -SURGICAL OUTCOME AND CURRENT POLICY IN OUR INSTITUTION -**

■ Kiminori Sugino, Koichi Ito, Mitsuji Nagahama, Wataru Kitagawa, Hiroshi Shibuya, Keiko Ohkuwa, Yukiko Yano, Junko Akaishi, Takashi Uruno, Kunihiko Ito  
Surgical Branch, Ito Hospital, Japan

Although the treatment policy varies between countries, surgical treatment for Graves' disease has not been considered as a common therapy. Because of occurrence of surgical complications and economical issue, surgery becomes obsolete. In Japan, surgical treatment was performed more often at former days, however, at present time, first-line treatment is antithyroid drug or radioiodine therapy. There still exist several advantages of surgery and it is not absolutely abandoned treatment. Controversy also exists, concerning whether subtotal or total thyroidectomy is suitable as surgical therapy for Graves' disease. No patient is expected to have recurrence of hyperthyroidism after total thyroidectomy. However, all patients are permanent hypothyroidism. Subtotal thyroidectomy had been performed as a standard procedure for Graves' disease in our hospital. We previously reported our surgical outcome and relapse rate of hyperthyroidism was too high to be accepted. The size of thyroid remnant is the most powerful factor to predict postoperative relapse. To reduce the relapse rate, we prospectively and gradually changed thyroid remnant size smaller for ten years. As a result, reduction of relapse rate could be achieved; however, more patients had hypothyroidism. We concluded subtotal thyroidectomy could not provide satisfactory outcome. Recently, we recommend total or near total thyroidectomy for the treatment of choice. In this report, we present our previous results for Graves' disease treated by subtotal thyroidectomy, which made us alterations to latest surgical strategy, with special reference to surgical outcome for patients with large goiter and childhood Graves' disease because surgery is often indicated for these patients.

## **SY-2-2** | **SURGICAL MANAGEMENT OF GRAVES' DISEASE, PAST AND FUTURE**

■ Hitoshi Noguchi, Shinya Uchino, Hiroto Yamashita, Tsukasa Murakami, Yasushi Noguchi, Shiro Noguchi  
Endocrinology, Noguchi Thyroid Clinic and Hospital Foundation, Japan

The Noguchi Thyroid Clinic and Hospital Foundation has surgically treated Graves's disease since 1911, preceding the discovery of thyroid suppressing effects of iodine tincture by Henry Plummer. Thyroid function was suppressed by a primitive form of external radiation which offered a window of euthyroid opportunity for surgery. Since then, the Foundation has thrived mainly as a treatment center for thyroid and parathyroid diseases. Counting only from 1966, we have performed roughly 55,000 thyroid surgeries, more than 22,000 of which were for Graves' disease. We have a computerized database for more than 6000 cases of recent surgery. With wider application of radioiodine ablation, earlier diagnosis and improved medical treatment, the indication for surgery has decreased. Some patients, however are still recommended to undergo surgery. Patients indicated for surgery will always exist. Careful selection of therapeutic modality for each patient is in order. We discuss the risks and benefits of surgical therapy for Graves' disease and what it may mean for the future of thyroid surgery.

## **SY-2-3** | SURGICAL MANAGEMENT OF GRAVES' DISEASE UP-TO-DATE IN TAIWAN

■ Chen-Hsen Lee

Department of Surgery, Taipei Veterans General Hospital / School of Medicine, National Yang-Ming University, Taiwan

Current management for Graves' disease (Toxic diffuse hyperthyroidism) consists of antithyroid drugs, radioiodine, and surgery. There are regional variations in clinical practice. For example, radioiodine therapy is commonly used in North America and antithyroid medication is favored nearly everywhere else. Surgery is seldom recommended as primary treatment in North America, but it has been an important therapeutic option in other countries.

In Taiwan, approximately 10,000 thyroid operations were annually performed. Since fine needle aspiration cytology is widely used, thyroid neoplasm was the main indication for surgery (39%). Thyrotoxicosis was the second most frequent indication (20%), with two thirds cases involving failure of medical control.

In Taiwan, thyroidectomy for hyperthyroidism is done for patients who have failed antithyroid drug or radioiodine therapy or recurrence, who have large goiter with symptoms of mechanical compression (e.g., dysphasia, dyspnea, or voice change), who have cosmetic concerns, who need a rapid reversal of hyperthyroidism (e.g. during pregnancy), who fear the exposure to radiation therapy, and who have concomitant thyroid nodule suspected of malignancy. At presentation, 67% of patients with hyperthyroidism had failure of medical treatment (defined as recurrence after discontinuation of antithyroid drug), 19% had intolerance of long-term medication, 14% had recommendation for evaluation of indications for thyroidectomy by a physician, and 1% had unsuitable radioiodine treatment.

Although surgical resection is the quickest therapy for Graves' disease, there is still no consensus in surgical techniques at present. Unilateral total and contralateral subtotal thyroidectomy and bilateral subtotal thyroidectomy are two major subtotal modalities. In consideration of hypothyroidism, recurrent hyperthyroidism and postoperative complications, some endocrine surgeons favor unilateral total and contralateral subtotal thyroidectomy.

Total thyroidectomies were considered in the hyperthyroid patients combined with thyroid cancer, severe thyroid ophthalmopathy, higher level of anti-Thyroid stimulation hormone antibody, or other autoimmune disorders involved.

In the operative technique other than total thyroidectomy, the remnant size will undoubtedly affect surgical outcome. In general, a 4-8g of thyroid remnant is recommended for a subtotal thyroidectomy. It is recommended to preserve more thyroid tissue in patients with higher preoperative AMA (anti-microsomal antibody). The remnant thyroid is usually left over the smaller lobe from the intraoperative or preoperative ultrasonographic findings.

Thyroid uptake and scintigraphy are widely employed in the diagnosis and management of hyperthyroidism. It was our practice to select the thyroid remnant on the less uptake side after a separated radioiodine uptake of each lobe was tested.

According to previous reports worldwide, the reported prevalence of thyroid cancer with concurrent hyperthyroidism varies from 0.76% to 9.9% and the rate has increased in recent surveys, perhaps as a result of more detailed examinations. In Taiwan, the incidence was around 13.3% with female predominant. Papillary thyroid carcinomas were found in 95.1%. Most thyroid cancers with concurrent Graves' disease were less than 10 mm. A subtotal thyroidectomy with complete resection of the cancer bearing lobe is usually adequate for patients with concurrent carcinoma 10 mm or smaller.

## **SY-2-4 | SURGICAL TREATMENT OF GRAVES' DISEASE IN EGYPT**

■ Amr A Mohsen, Hany M Mikhail, Abdrabo Mashehour, Mohamed Raslan  
Department of General Surgery, Cairo University Medical School, Egypt

This presentation aims at giving an overview of the surgical treatment of Graves' disease in Egypt. Such information represents an essential foundation upon which the participants in the symposium can discuss better ways of improving service of our patients.

The data were collected from different sources that included the medical records at Cairo University hospitals, an internet survey among Egyptian surgeons, journal publications and theses dissertations.

The presentation addresses such issues as the choice of patients for surgery, preoperative preparation, the extent of thyroid resection and management of special situations. It also demonstrates the change of attitude towards management of Graves' disease over the last decade.

## **SY-2-5** | SURGICAL MANAGEMENT OF GRAVES' DISEASE IN AUSTRALIA

■ Robert F Parkyn

Discipline of Surgery, University of Adelaide, Australia

All disciplines of Medicine have their own bias for various treatments of various diagnoses. Where there are viable options available it is perhaps not surprising that the treatment recommended and advocated reflects the particular skills of that clinician. Endocrinologists prescribe, Radiotherapists administer, and Surgeons operate! But where, as in Australia, the “gatekeeper” is the Endocrinologist not surprisingly the majority of patients are treated medically or with subsequent radioiodine. Even where there is overt ophthalmopathy only 27% of Endocrinologists surveyed in Australia recommend surgery but trends are changing and there is a steady recognition of the value of surgery where there were significant eye symptoms.

If referred from an Endocrinologist most patients would be assessed by a dedicated Endocrine or Thyroid Surgeon. Once referred, most endocrine surgeons would advocate a total thyroidectomy This is based upon the premise that most patients referred would have a special circumstance such as ophthalmopathy, pregnancy, compressive symptoms or cosmetic issues from a very large goiter. In addition some ethnic groups within Australia have their own bias against radioactive iodine and failed medical management equates to a request for surgery.

Surgery on a toxic patient would be very uncommon without complete pre operative preparation establishing a euthyroid state. Carbimazole would be the most common antithyroid treatment in Australia. Treatment with beta blockade alone would be exceptional and confined to very special circumstances such as non compliant patients needing urgent surgery. This can be an issue with our indigenous population.

Lugol's iodine is used by some surgeons but this is now less frequent.

Pre operative imaging would not be usual apart from diagnostic nuclear scans performed at the initial diagnosis, but again with the increase in the use of Surgeon performed Ultrasound (SPU) and with the recognition of a small risk of coincidental concomitant thyroid cancer there is an emerging trend for regular SPU.

At surgery, general anaesthesia would be normal with the use of cervical nerve block and local anaesthesia with sedation being used only on the most unusual circumstances. “Sutureless surgery” is strongly gaining favour. Division of the strap muscles is frequent except where the thyroid is small and readily accessed. Parathyroid autografting is used liberally. The recurrent laryngeal and superior laryngeal nerves are identified and protected. The use of Intra operative neuro-monitoring would be most uncommon and reserved for special circumstances.

Post operative management is frequently in a high dependency area or at least in a dedicated “thyroid “ward. The majority of patients would be discharged within 24 hours with the early monitoring of PTH levels being used as a guide to post operative hypocalcaemia.

Longer term follow-up and thyroxine replacement monitoring would be performed by the referring endocrinologist and the patient's general practitioner, with ongoing monitoring of any associated ophthalmopathy by the relevant eye surgeon.

## **SY-2-6 | MANAGEMENT OF GRAVES' DISEASE IN SRI LANKA**

■ Ranil Fernando<sup>1</sup>, A Pathmeswaran<sup>2</sup>, M Willaraarchchi<sup>1</sup>

<sup>1</sup>Surgery, Faculty of Medicine, University of Kelaniya, Sri Lanka, <sup>2</sup>Dept of Public Health Faculty of Medicine University of Kelaniya, Sri Lanka

Sri Lanka is a developing country with a population of 20 million people. Goitre is endemic. Surgery for thyroid disease is common. Thyroid surgery is done by general surgeons and some E.N.T surgeons. Graves disease is managed by physicians, as well as surgeons. The two main indications for surgery are large goitres and poor control of toxicity with medication.

**Method:** A study was done to assess the practice of thyroid surgery among a total of 33 general and ENT surgeons using a questionnaire. Direct questions regarding management of Graves' disease were included in the questionnaire.

**Results:**

The level of experience was found to range from 2 to 38 years - Mean 19. Number of thyroidectomies in the past year ranged from 0 to 130, mean - 53. For Graves' disease 35% Performed total thyroidectomy, 35% performed near total thyroidectomy, &13%performedsubtotal thyroidectomy. Interestingly 17% did not offer surgery. The level of experience influenced decision making. If the surgeon had less than 15 years experience they did more total thyroidectomies than surgeons with more than 15 years experience.

**Conclusions:**

The management trends in Graves' disease in Sri Lanka are similar to the global pattern

Younger surgeons tend to undertake total thyroidectomy

## **SY-3-1** | **GASLESS ENDOSCOPIC THYROID SURGERY (VANS): OUR RECENT TECHNIQUE AND NEWLY-DESIGNED U-KELLY FORCEPS**

■ Yoshiyuki Usui, Ichiro Akiyama, Hironori Kunisue, Hideaki Mori, Shuji Ichihara  
Department of Surgery, Okayama Medical Center, Japan

Since 1999 approximately 200 cases of gasless endoscopic thyroid surgery (video-assisted neck surgery, VANS) have been performed in our hospital. Various modifications have been made to facilitate its operative procedure, such as a new retractor (2000) and a camera trocar (2005). This procedure has become a surgical option for benign unilateral thyroid tumors due to its safety and satisfactory cosmetic results.

To improve the procedure further, an even better designed Kelly forceps (U-Kelly) was made in 2008. Conventional Kelly forceps are used to dissect the surrounding tissues of the thyroid and to stabilize the tissues between their tips in gasless endoscopic thyroid surgery. Conventional Kelly forceps need the operator's fingers to keep the tips open. The new forceps can be kept open in the desired position (circa 8mm) without the need of the operator's fingers. Their shape is similar to that of conventional forceps except for their ratchet. Space between the tips of the U-Kelly produces a buffer area, which might prevent heat injury induced by the ultrasonically activated scalpel.

To make a subplatismal tunnel, tumescent local anesthesia is being used recently. This could make the working space more easily and lessen minor bleeding during dissection and might decrease postoperative wound pain.

Various modifications and newly-designed surgical instruments made this operation easier to perform and safer.

## **SY-3-2** | THE CURRENT TECHNICS OF ENDOSCOPIC THYROIDECTOMY IN THAILAND

■ Suchart Chantawibul

Department of Surgery, Rajavithi Hospital, Rangsit University, College of Medicine, Thailand

After endoscopic technics of the thyroid gland were published in various surgical journals in about last ten years, Thai surgeons also moved forward with the current trend. The first case was performed in 2001. The technic was modified from three ports axillary approach to four ports approach with carbon dioxide insufflation. By the end of 2009, we had 30 surgeons performed endoscopic thyroidectomy. Most are general surgeons except three ENT surgeons. The most popular technic was axillary approach (27 among 30 surgeons), and the rest (3 surgeons) used breast or anterior chest wall approach. There was no surgeon who used gasless technic in Thailand today.

At our hospital, from April 2001 to November 2009 we performed 420 cases of axillary approach. The conversion rate was about 1%, no permanent recurrent laryngeal nerve injury found. On the way from the first case, there were many modifications and changes to refine the details of this method. The current technic was start by open dissection until reaching the anterior border of the sternocleidomastoid muscle followed by carbon dioxide insufflation (4-6 mmHg) and full endoscopic dissection after that.

Recently, we try to conduct an axillary approach via a single incision. The early experience was promising with a small number of patients.

### **SY-3-3** | A DILEMMA FOR THE DECISION OF SURGICAL STRATEGY IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

■ Daishu Miura

Department of Breast and Endocrine Surgery, Toranomon Hospital, Japan

**Background:** The surgical strategies in patients with primary hyperparathyroidism (PHPT) are removal of abnormal parathyroid gland or glands. Although there has been a recent development of preoperative localization studies, the differentiation between parathyroid adenoma and hyperplasia is relatively difficult and base on the surgeon's skill. Our strategy for PHPT is that some patients of which US and MIBI showed one parathyroid tumor with concordance, undergo video-assisted focused parathyroidectomy (VAFP) and the others do general bilateral exploration. In general, symptomatic patients have bigger parathyroid tumors that is likely well-localized by US and MIBI than those of asymptomatic patients, consequently can receive less invasive surgery. The goal of this investigation is to determine the success rates of each procedure and the association between clinical symptoms and probability to receive the minimally invasive surgery.

**Materials and Methods:** Between 94 to 07 consecutive 238 patients with PHPT who underwent parathyroidectomy were analyzed. Operative success was defined as documented cure of hypercalcemia at least 6 months after the operation. Preoperative US was studied in all patients and MIBI in 237 patients.

**Results:** Over 80 % of all cases were asymptomatic according to NIH guideline 2002. Pathological findings revealed 73% in solitary adenoma, 11% in hyperplasia, 2% in multiple adenomas, and 0.8% in carcinoma. 65 patients underwent focused parathyroidectomy including 32 VAFP cases after 2002, 129 in bilateral approach, and 44 in unilateral approach. The average weight of parathyroid tumors removed was 938mg. Success rate in VAFP was 99%, one had persistent hypercalcemia after VAFP, and that in bilateral or unilateral approach was 100%.

## **SY-3-4** | **FOCUSED PARATHYROIDECTOMY FOR GIANT BENIGN PARATHYROID ADENOMAS**

■ Amit Agarwal, Sushil Kumar Gupta, Prateek Mehrotra, Gyan Chand, Anjali Mishra, Gaurav Agarwal, Ashok Kumar Verma, Saroj Kumar Mishra

Endocrine Surgery, Sgpgims, India

**Aim:** To evaluate the safety and efficacy of focused parathyroidectomy in large parathyroid adenomas seen in our patients of primary hyperparathyroidism with advanced skeletal disease.

**Patient and methods:** 125 patients of primary hyperparathyroidism were operated during the period 1990-2009. Clinical, biochemical parameters, operative details, histopathology & follow-up data was reviewed. Patients with single localized gland with concordant MIBI and USG were selected for focused parathyroidectomy using oblique incisions of size ranging from 2 to 2.5 cm.

**Results:** 79.2% patients had classical osteitis fibrosa cystica with mean PTH levels of 863 pg/ml and ALP levels of 1240IU/L. There was one case of temporary recurrent laryngeal palsy but no case of permanent RLN palsy. 42 patients developed symptomatic hypocalcaemia requiring intravenous calcium infusion. The mean weight of parathyroid adenoma was 4959gm and mean size was 2.9cm. 8 required conversion. The hospital stay was 10.37 days. The cure rate was 94.8%.

**Conclusion:** Focused parathyroidectomy is feasible even in large parathyroid adenomas. Though the advantages in terms of cosmesis and patient satisfaction are evident, the incidence of post-operative hypocalcaemia is still high.

## **SY-3-5** | SINGLE-PORT ADRENALECTOMY FOR ALDOSTERONOMA

■ Wei Keat Cheah, C.T.K. Tan, D. Lomanto

Department of Surgery, National University Hospital, Singapore

Single-port laparoscopic surgery is gaining popularity as the number of incisions and ports are reduced to potentially gain superior recovery after surgery. Such surgeries are already performed for cholecystectomy, appendicectomy, inguinal hernia repair, gastric surgery, thyroidectomy, and adrenalectomy.

We present our initial series of single-port adrenalectomy for 5 patients with Conn's syndrome who had unilateral benign cortical tumours. The approaches were; transabdominal lateral approach (left side) and retroperitoneal approach (right and left sides). The Covidien SILS™ (single incision laparoscopic surgery) port was used in all cases. Through the port, multiple instrument access into the abdominal cavity was possible. Carbon dioxide insufflation was used in all cases. Ultrasonic dissector was also used.

When the 5 cases were compared to the traditional methods of performing laparoscopic adrenalectomy, there were no differences in outcomes. These results, as well as video demonstrations, will be discussed and shown in the lecture session.

Single-port laparoscopic surgery is feasible for certain procedures such as adrenalectomy. Further studies are required to show superior benefits over the traditional laparoscopic methods.

## **SY-3-6** | **LAPAROSCOPIC ADRENALECTOMY: DEVELOPMENT, CURRENT STATUS AND FUTURE DIRECTIONS**

■ Tadashi Matsuda

Department of Urology and Andrology, Kansai Medical University, Japan

Laparoscopic adrenalectomy (LAX) was first performed by Japanese urologists in the beginning of 1992. Due to the minimal invasiveness of laparoscopic surgery as compared to an open adrenalectomy, LAX has become the standard for small adrenal tumors. According to several nation-wide surveys in Japan, 60% of adrenalectomies were performed by urologists, whereas 40% were done by endocrine surgeons. Fifty percent of the surgeries were performed laparoscopically in 2007. LAX is useful not only for aldosterone producing adenomas and Cushing's syndrome, but also for pheochromocytomas and small adrenal cancers or metastatic tumors. The operative outcomes of LAX were reported to be very similar among these diseases.

According to a nation-wide survey of laparoscopic surgeries in Japan, the major complication and open conversion rates of 6,362 LAX procedures were 6.7 % and 3.3%, respectively. The frequent complications included bleeding, injury to the adrenals, and injury to the adjacent organs. The complication and conversion rates gradually decreased over these 16 years when divided into 3 periods, from 8.4% to 3.7% and from 4.2% to 1.9%, respectively. One fatal case was reported.

Four different methods were developed to approach the adrenal gland; transperitoneal anterior, transperitoneal lateral, retroperitoneal lateral and retroperitoneal posterior. Currently, the transperitoneal lateral and retroperitoneal lateral approaches are the most widely-used globally, and both methods showed equal results with regard to the operative outcomes and postoperative recovery. In Japan, 84% were approached transperitoneally and 15% underwent the retroperitoneal lateral approach.

To reduce the invasiveness of LAX, needlescopic surgery using 2-3mm ports and laparoendoscopic single site surgery through only one wound have been recently developed. Further improvements in operative instruments, including surgical robots, will make these procedures easy and acceptable for the majority of adrenal surgeons.

## **SY-3-7** | **LAPAROSCOPIC DISTAL PANCREATECTOMY FOR NEUROENDOCRINE TUMOR OF THE PANCREAS**

■ Yoshiharu Nakamura<sup>1</sup>, Eiji Uchida<sup>1</sup>, Satoshi Matsumoto<sup>1</sup>, Yoshio Jo<sup>2</sup>, Toshiki Inoue<sup>2</sup>, Takashi Tajiri<sup>1</sup>, Kazuo Shimizu<sup>1</sup>

<sup>1</sup>Department of Surgery, Nippon Medical School, Japan, <sup>2</sup>Hogy Medical Co., Ltd., Japan

### **Introduction:**

Since the approval of laparoscopic pancreatic resection in January 2004 by the Ethics Committee of Nippon Medical School, the use of this procedure has been introduced in our department, and to date we have conducted a total of more than 50 procedures for laparoscopic distal pancreatectomy (Lap-DP) and laparoscopic pancreaticoduodenectomy (Lap-PD). In this conference, we would like to show the techniques of Lap-DP for neuroendocrine tumor of the pancreas; especially, about laparoscopic spleen-preserving distal pancreatectomy with conservation of the splenic artery and vein (Lap-SPDP), and will demonstrate those clinical outcomes including our published data<sup>1-3</sup>).

### **Patients & Procedure:**

A total of 13 patients with neuroendocrine tumor of the pancreas (5 of insulinomas and 8 of non-functioning islet cell tumors) who underwent Lap-DP from January 2004 to October 2009 were enrolled in this symposium. The average age was 52 years (range: 31-85 years), and there were six men and 7 women with an average body mass index (BMI) of 23.1 kg/m<sup>2</sup> (range: 17.1-28.2 kg/m<sup>2</sup>). The main tumor location was the pancreatic body in 8 patients and the pancreatic tail in 5 patients. The average tumor size was 2.6 cm (range: 1.3-7.0 cm). When conserving the spleen, the splenic artery and vein were conserved in all patients, and Warshaw and colleagues' procedure was not employed. Of these, the spleen was conserved in 9 patients. In all 13 patients, pancreatic resection was performed using only endoscopic linear stapler. The average follow-up periods was 30.1 months (range: 2-69 months).

### **Results:**

The postoperative data were as follows: median operating time was 285 minutes (range: 225-635 minutes), and median blood loss was 170 ml (range: 10-1020 ml). No transfusions were given during or after surgery in any of the patients. In all patients, oral intake was started within five days of surgery, and the median value was 2 days after surgery. There were pancreatic fistula in 53.8% (grade A: 46.1%, grade B: 7.6%, grade C: 0%), and there were no other postoperative complications. The median hospital stay was 8 days (range: 7-10 days), and none of the patients died perioperatively.

### **Conclusion:**

In neuroendocrine tumor arising in the distal pancreas, we surely think that Lap-DP might be feasible and safe procedure.

### **Reference**

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## **SY-3-8** | MINIMALLY INVASIVE SURGERY IN PANCREAS

■ Ho-Seong Han

Department of Surgery, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Korea

Since the introduction of laparoscopy, application on laparoscopic surgery for pancreas is increasing these days. There are several kinds of laparoscopic surgical procedure including distal pancreatectomy, pancreaticoduodenectomy, central pancreatectomy, enucleation, etc. Although, laparoscopic pancreaticoduodenectomy is still controversial due to its difficult techniques, laparoscopic distal pancreatectomy is frequently used as an optional treatment method for the lesions in body and tail of pancreas, when the lesion is considered benign or premalignant. Laparoscopic enucleation is an also good treatment modality when the lesion is presumed to be benign and small such as insulinoma. Central pancreatectomy is moderately difficult in terms of technique, and it is occasionally used for the lesion in the neck to preserve the volume of the pancreas as much as possible. The application of laparoscopic technique to malignancy is still contraindicated and still there are few reports on this disease entity.

We retrospectively analyzed of the clinical outcome of 78 patients who underwent laparoscopic pancreas surgery from June 2004 to October 2008. As regards to the technique of distal pancreatectomy, preservation of splenic vessels and spleen was tried unless the tumor was very close to splenic hilum or malignancy was suspected in preoperative radiologic studies. For pancreaticoduodenectomy, both laparoscopy assisted method and totally laparoscopic method have been used. Operation types were 55 cases of distal pancreatectomy, 10 cases of pancreaticoduodenectomy, 6 cases of central pancreatectomy, 4 cases of enucleation and 3 other operations. Among them, 10 patients were endocrine tumor. Out of 10 patients with endocrine tumor, one patient proved to have invasive endocrine carcinoma. The patient is still alive for 52 months with recurrence of tumor at postoperative 21 months. Our experiences show that laparoscopic pancreas surgery is becoming attractive option for pancreas disease including endocrine tumor.