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Hemodynamic Consequences during minimally Invasive Adrenalectomy for Pheochromocytoma: Robot-assisted *vs* Conventional Laparoscopic Approach

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BACKGROUND AND AIMS

Minimally invasive surgery of the adrenal gland is widespread. Although reports demonstrate the safety and feasibility of robot-assisted adrenalectomy, the objective benefits are still unclear, compared to those of conventional laparoscopy. Recently, robot-assisted approach has also become possible for pheochromocytoma resection. Since cardiopulmonary changes during robot-assisted dissection of the pheochromocytoma patient has not been studied in detail, we aimed to assess these concerns, compared to the routine laparoscopic technique.

METHODS

In this case-control study, 19 consecutive robot-assisted adrenal resections were compared with a control group consisting of 14 conventional laparoscopic adrenalectomy. Patient characteristics and intraoperative hemodynamic and respiratory parameters were assessed. Groups were compared using the χ^2 test for categorical variables and Student's t-test for continuous variables. Significance was considered $p < 0.05$.

RESULTS

The robot-assisted procedure was performed successfully in all patients, except one. The duration of the robot-assisted procedure, compared to the conventional laparoscopy group, was significantly longer ($p < 0.05$). Intraoperative blood loss was significantly less in the robot-assisted group ($p < 0.05$). Dissection of pheochromocytoma showed a significant difference between the groups, according to the incidence of intraoperative blood pressure fluctuations ($p < 0.05$). The robot-assisted approach resulted in less incidents. Other hemodynamic and respiratory parameters did not differ between groups significantly. There were no perioperative deaths. Complication rates and postoperative hospital stays were not significantly different.

CONCLUSION

Robot-assisted adrenalectomy is a safe and technically feasible procedure for a pheochromocytoma patient. Robot-assisted resection of pheochromocytoma minimized the occurrence of intraoperative blood pressure fluctuations and blood loss.

Predictors of Malignancy in Patients with Pheochromocytoma: A Single-institution Experience

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BACKGROUND AND AIMS

Malignant pheochromocytomas are rare tumors accounting for about 10% of all pheochromocytomas. Clinical, biochemical, and histological features cannot reliably distinguish malignant from benign tumors. The goal of this study is to find predictors in differentiating benign from malignant pheochromocytomas.

METHODS

We retrospectively reviewed 118 patients who were diagnosed with pheochromocytomas and paragangliomas in Putrajaya Hospital from 2002 to 2014. Demographic data, functionality of tumor, tumor location, size, and recurrence were reviewed. Data were analyzed using the Pearson chi-square and linear-by-linear association.

RESULTS

The mean age of patients was 36 years (8–73 years). The median tumor size was 60 mm (5–200 mm). Out of 118 patients, 99 (83.9%) had benign and 19 (16.1%) had malignant pheochromocytomas. Age, gender, race, and tumor size have no significant association with malignancy (p-value > 0.05). There is an association between functioning tumor toward benign tumor ($p = 0.04$). Tumor bilaterality shows an association with benignity as all bilateral adrenal tumors are benign ($p = 0.001$). Tumor recurrence is more associated with malignancy ($p < 0.001$). Comparing pheochromocytomas and paragangliomas (extra-adrenal pheochromocytomas), it was revealed that pheochromocytomas are more associated with being benign ($p = < 0.001$).

CONCLUSION

Functioning bilateral adrenal pheochromocytomas are more associated with benign tumors, while the presence of recurrence is more associated with malignancy.

Trends of Genetic Screening in Patients with Pheochromocytoma: 15-year Evaluation in a High-volume Tertiary Referral Center

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BACKGROUND AND AIMS

There is increasing attention for genetic testing in patients with pheochromocytoma. Early establishment of a hereditary syndrome enables a close follow-up of high-risk patients and screening and treatment of syndromic manifestations in their relatives. We sought to determine the trend of performing genetic testing and its consequences in a high-volume tertiary referral center.

METHODS

An institutional database of consecutive patients undergoing adrenalectomy for pheochromocytoma and paraganglioma between January 2000 and July 2015 was used. Specific information was collected regarding genetic testing. To evaluate a possible trend, patients were divided based on the year of diagnosis: 2000 to 2005 (group 1), 2006 to 2010 (group 2), and 2011 to 2015 (group 3).

RESULTS

A total of 129 patients were included, subdivided into 35 (group 1), 44 (group 2), and 50 (group 3) patients. The mean age of the study population was 47 years, and 72 (56%) were women with no significant difference between groups. Patients from groups 2 and 3 were more frequently referred for genetic consultation than from group 1 (70 and 92% *vs* 25; both $p < 0.001$); The p-value was < 0.001 between groups 1 and 2 and between groups 1 and 3. Actual follow-up for consultation was done in 58% of the patients. The percentage of patients with a genetic syndrome was comparable between the groups, with 23, 28, and 22% respectively; however, diagnosis in group 1 was more often based on clinical presentation and family history in 63% *vs* 17 and 27% in groups 2 and 3. Seven patients had a positive genetic test, without a positive family history or syndromic presentation. An overview of results is presented in Table 1.

CONCLUSION

Recommendation of genetic counseling has significantly increased in the past 15 years; however, actual follow-up by patients is only half. More effort should be taken by clinicians to improve this rate, since a selection of patients presents without syndromic symptoms and has negative family history.

Table 1: Patients' characteristics, clinical presentation, and genetic information of each group

	Group 1 2000–2005	*Group 2 2006–2010*	*Group 3 2011–2015*	
Total (n)	*35*	*44*	*50*	*p-value**
Age	45 ± 15.5	49 ± 15.7	47 ± 17	0.8
Sex				
Female	21 (60%)	24 (54%)	27 (54%)	0.8
Tumor type				
Pheochromocytoma	32 (91%)	41 (93%)	44 (88%)	
Paraganglioma	3 (9%)	3 (7%)	6 (12%)	0.7

(Cont'd)

(Cont'd)

	Group 1 2000–2005	*Group 2 2006–2010*	*Group 3 2011–2015*	
Total (n)	*35*	*44*	*50*	*p-value**
Clinical presentation				
Classical	24 (69%)	22 (50%)	28 (56%)	
Syndromic	2 (5.5%)	6 (13.5%)	3 (6%)	
Incidentaloma	6 (17%)	13 (29.5%)	18 (36%)	
Genetic screening	3 (8.5%)	3 (7%)	1 (2%)	0.4
Genetic syndrome				
Total	8 (23%)	12 (27%)	11 (22%)	
MEN2A	2	6	5	
MEN2B		1		
VHL	2		2	
SDH-B	2	3	2	
NF	1	1	1	
Other	1	1	1	
Number of patients				
Referred for genetic consultation	9 (25%)	31 (70%)	46 (92%)	<0.001
Went for consultation	7	11	32	
Got genetic test	5	16	21	0.015
Test result				
Positive	3 (60%)	10 (63%)	8 (38%)	
Negative	2 (40%)	4 (37%)	10 (62)	

*p-values were calculated using chi-square for dichotomous variables and ANOVA for continuous variables

Left-ventricular Mass and Left-ventricular Mass Index Changes in Pheochromocytoma and their Reversal following Surgical Cure: A Prospective Case-control Study

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BACKGROUND AND AIMS

Cardiovascular (CV) dysfunction can cause perioperative morbidity in pheochromocytoma (PCC) patients. In the past, we have described functional-humoral CV changes in a PCC cohort, and their reversal following the cure of PCC (Agarwal G et al. Surgery 2011; vol. 150). Left-ventricular mass (LVM) and LVM index (LVMI) are sensitive indicators of structural cardiac changes and independent prognostic factors. In a case-control study, we evaluated LVM and LVMI alterations in PCC patients, before and after curative PCC surgery.

METHODS

In 32 PCC patients, echocardiography (2D-ECHO) and body surface area (BSA; DuBois method) were recorded at diagnosis, 2 weeks post-alpha-blockade with prazosin; 7 to 10 days postoperatively; and at 3- and 6-month follow-ups. Controls (8 normotensive non-PCC adrenalectomy patients; 8 essential hypertensives) were evaluated only once. The LVM and LVMI were calculated using the Devereux formula, and data analyzed using Statistical Package for the Social Sciences (SPSS) version 17.0.

RESULTS

The mean age of the PCC cohort (36.5 ± 16.3 years) was comparable with that of the control group ($p = 0.43$). Four (12.5%) PCC patients were normotensive. Post surgery, biochemical cure was documented in all. Of the 28 hypertensive PCC patients, 26 (92.8%) became normotensive by 6 months post surgery. When compared with controls, PCC patients exhibited significantly poorer LVM and LVMI ($p < 0.05$). Following preoperative alpha-blockade and after-curative PCC surgery, LVM and LVMI showed significant improvement ($p < 0.05$) and normalization within 3 to 6 months.

CONCLUSION

Pheochromocytoma results in functional as well as structural cardiac derangements. Structural ventricular changes due to PCC can be objectively assessed and monitored using 2D-ECHO-based LVM and LVMI estimation. Following surgical cure of PCC, the functional as well as structural changes are reversed in PCC patients over 6 months and show continued improvement in further follow-ups. Such studies may help in the reduction of perioperative morbidity and monitoring cardiac recovery in PCC.

Evolving Localization Techniques in Insulinoma: Experience at a Tertiary Referral Center in India

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BACKGROUND AND AIMS

Preoperative localization techniques for insulinoma continue to evolve. The aim of this study was to study the sensitivity of various preoperative localization modalities used in insulinoma over the last two and half decades in our center.

METHODS

This retrospective study (January 1990 and October 2015) includes 35 patients of organic hyperinsulinemic hypoglycemia. The correlation between radiologic, operative, and histology findings was noted.

RESULTS

The median age of the patients was 45 years (M:F = 1:1.7). MEN1, islet cell hyperplasia, and malignancy were noted in 14.3, 11.4, and 2.8% patients respectively. The median duration of symptoms was 36 months (15 days to 120 months). A total of 82.8% insulinomas could be localized preoperatively. The sensitivity for localizing insulinoma for ultrasound, CT scan, MRI, and selective arterial calcium stimulation with hepatic venous sampling (ASVS) was 25, 71, 60, and 85.7% respectively. Preoperative localization rate was 61.5 and 95.4% before and after the year 2005. The sensitivity of triple-phase CECT was 88.8% in the last decade, and ASVS and transhepatic selective venous sampling helped in regionalization of occult insulinoma and islet cell hyperplasia. Bi-digital palpation and intraoperative ultrasonography (IOUS) was accurate in 96.8% cases. Surgery was successful in all but one case (97.1%). Two cases of hyperplasia missed on first exploration needed re-operation. A total of 14 enucleations and 21 pancreatic resections were performed.

CONCLUSION

The sensitivity of preoperative localization techniques for insulinoma has improved greatly in the last one decade. Almost all the remaining insulinomas missed on preoperative localization can be detected peroperatively by an experienced surgeon and IOUS performed by an expert.

Safety of Laparoscopic Surgery for Pheochromocytoma Patients Who developed Catecholamine-induced Cardiomyopathy

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BACKGROUND AND AIMS

Pheochromocytoma is a rare tumor that develops from chromaffin tissue of the adrenal grands. Catecholaminergic crisis by pheochromocytoma sometimes causes catecholamine-induced cardiomyopathy (CICM), which causes severe heart failure. A standard surgical procedure for pheochromocytoma is laparoscopic surgery; however, pneumoperitoneum for patients with a history of cardiac dysfunction has usually been avoided. Thus far, few literatures discussing the safety of laparoscopic surgery for patients with pheochromocytoma who developed CICM are available. The aim of this study is to verify the safety of laparoscopic surgery for patients with pheochromocytoma who developed CICM.

METHODS

We operated laparoscopically six patients with pheochromocytoma who developed CICM between September 2001 and April 2014 (CICM group). During the same period, we operated 59 patients with pheochromocytoma without CICM (non-CICM group). These two groups were compared retrospectively in terms of intra- and postoperative complications. Data were analyzed statistically using the Mann–Whitney U and Fisher's exact test.

RESULTS

Patients in the CICM group underwent surgery after remission of CICM, and improvement of their ejection fractions to the normal level was confirmed at the time of operation. There were no differences between these two groups in terms of characteristics of the tumor and patients and intraoperative circulation dynamics. The CICM group had longer operation time and more blood loss

than the non-CICM group, but there was no statistical significance. No patient required transfusion. There were no significant differences of postoperative course and complications between these two groups (Table 1).

CONCLUSION

We consider that patients with pheochromocytoma can undergo laparoscopic surgery safely even if they had a history of acute heart failure due to CICM.

Table 1: Postoperative course and complications between the groups

	CICM	*Non-CICM*	*p-value*
Number	6	59	
Age at operation	49.5	51	0.71
Gender (female:male)	5:1	34:25	0.39
Left:Right	4:2	31:28	0.68
Body mass index (kg/m^2)	22.8	21.6	0.29
Tumor size (mm)	36.5	42	0.39
Preoperative ejection fraction (%)	69.5	69.3	0.65
Operation time (min)	178.5	151.4	0.60
Pneumoperitoneum time (min)	134.7	124.7	0.73
Blood loss (mL)	123.5	80.5	0.64
Intraoperative circulation dynamics			
highest blood pressure (mm Hg)	169.3	178.7	0.48
lowest blood pressure (mm Hg)	74.2	80.8	0.20
fastest heart rate	104.8	98.6	0.62
slowest heart rate	65.2	57.7	0.19
Total volume infusion (mL)	3266	2820	0.43
Beginning of diet (postoperative day)	2	1.9	0.47
Hospital stay (postoperative day)	8.2	7.5	0.77

Laparoscopic Adrenalectomy *vs* Radiofrequency Ablation for Aldosterone-producing Adenoma: A Multicenter Prospective Randomized Controlled Trial

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BACKGROUND AND AIMS

While laparoscopic adrenalectomy (LA) is the conventional treatment for primary aldosteronism (PA) due to aldosterone-producing adenoma (APA), radiofrequency ablation (RFA) has recently been developed as a new treatment option. The safety and efficacy of RFA in treating APA were proven to be promising. Whether RFA can produce comparable outcomes with those of LA has never been prospectively evaluated.

METHODS

This was an open-labeled, multicenter, prospective randomized controlled trial aiming to compare the treatment outcomes between LA and RFA. Hypertensive subjects with unilateral APA (size < 3 cm) were randomized to receive either lateral transperitoneal LA or CT-guided percutaneous RFA (a maximum of two successive sessions). Their postoperative outcomes, complication profiles, and treatment success rates were compared.

RESULTS

Between January 2013 and June 2015, 30 patients were randomized to receive LA (n = 16) and RFA (n = 14). Both groups were comparable for all preoperative variables. In treating APA, RFA had significantly shorter operating time (12.9 ± 3.9 *vs* 105.5 ± 18.8 minutes, $p < 0.001$), lower pain score (VAS 7 *vs* 50, $p < 0.001$), lower parenteral analgesic consumption (14.3 *vs* 50.0%, $p = 0.03$), shorter hospital stay (2.0 ± 0.0 *vs* 3.6 ± 1.1 days, $p < 0.001$), and earlier resumption of daily activities (2.2 ± 0.7 *vs* 5.7 ± 3.4 days, $p < 0.001$) when compared to LA. Operative morbidity (28.6 *vs* 25.0%, $p = 0.82$), mortality (0 *vs* 0, $p = 1.0$), patient satisfaction (VAS 83.4 ±

16.5 *vs* 88.2 ± 10.9, p = 0.65), and surgeon satisfaction (VAS 85.7 ± 7.5 *vs* 78.8 ± 15.2, p = 0.47) were comparable between RFA and LA. As for treatment efficacy after a single treatment, persistent PA was absent in LA group but was found in three RFA patients who required a second RFA session. The final treatment success rates were comparable (100 *vs* 100%, p = 1.0).

CONCLUSION

In treating APA, RFA compares more favorably than LA for short-term perioperative outcomes and recovery. Resolution of PA is highly effective after LA, but multiple RFA sessions may be needed to achieve the same biochemical cure.

Is Laparoscopic Adrenalectomy for Adrenal Metastasis more Difficult than for Nonfunctional Benign Tumor?

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BACKGROUND AND AIMS

Owing to the advancement of technical skills and devices, laparoscopic surgery for metastatic adrenal tumor has become widespread in spite of the risk of bleeding, tumor rupture, and dissemination. We investigated whether laparoscopic adrenalectomy for metastatic tumor is more difficult than for nonfunctional benign tumor and the oncological safety of this procedure.

METHODS

Between 2008 and 2015, 204 patients underwent laparoscopic adrenalectomy in our department. Nine (right: 3, left: 6) cases were for metastatic tumors (group A) and 12 (right: 7, left: 5) cases were for nonfunctional benign tumors (group B). Adrenalectomies for functional tumors were excluded. Medical records of these cases were analyzed retrospectively.

RESULTS

In group A, the primary lesions were lung cancer (7 cases), uterine cervix cancer (1 case), and renal cell cancer (1 case). In group B, pathological diagnoses were cortical adenomas (8 cases), myelolipomas (2 cases), ganglioneuroma (1 case), and cavernous hemangioma (1 case). The mean tumor size was 32.0 mm (22–55) in group A and 54.7 mm (30–70) in group B (p = 0.01). All cases underwent laparoscopic surgery. In one case in group A (metastasis of renal cell cancer), conversion to open surgery was required due to strong adhesion and intractable bleeding. Median operating time and amount of bleeding was 153 minutes (84–404) and 6 ml (0–24) in group A and 138 minutes (106–214) and 9 ml (1–166) in group B (NS). In group A, one postoperative complication (duodenal ulcer) developed, which required open surgery. Neither local nor port site recurrence developed in both groups.

CONCLUSION

This report showed no significant differences between the two groups with regard to the operating time, amount of bleeding, and postoperative hospital stay. This report also showed oncological safety of laparoscopic surgery for metastatic adrenal tumors. However, higher vascularity and thick adhesions surrounding tumors were observed in some cases with metastatic adrenal tumor. Laparoscopic surgery could also be the treatment of choice for metastatic adrenal tumors under the condition that careful maneuver is warranted.

A Prognostic Nomogram to predict Levothyroxine Therapy Withdrawal after Hemithyroidectomy for Patients with Differentiated Thyroid Carcinoma

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BACKGROUND AND AIMS

There were no criteria regarding the degree and duration of levothyroxine therapy to prevent thyroid cancer recurrence after hemithyroidectomy in patients with differentiated thyroid carcinoma (DTC). And the incidence of subclinical hypothyroidism after levothyroxine withdrawal remains unclear. The aim of this study was to create a nomogram able to predict subclinical hypothyroidism after levothyroxine withdrawal in patients who underwent hemithyroidectomy for DTC.

METHODS

We retrospectively reviewed 574 patients who underwent hemithyroidectomy for DTC from October 2005 to December 2010. Patients were divided into two subgroups according to levothyroxine withdrawal or not (230 *vs* 344). The withdrawal group

was used for developing a nomogram for subclinical hypothyroidism. Preoperative TSH, TSH at withdrawal time, and resected tissue weight were included in a multivariable logistic regression model to predict subclinical hypothyroidism. External patient cohort was used for validating the nomogram by discrimination [or the area under curve (AUC).

RESULTS

The overall median follow-up period was 75 months. In the withdrawal group, the mean levothyroxine maintenance and withdrawal period were 40 and 36 months respectively. There were 38 (16.5%) patients who developed subclinical hypothyroidism after levothyroxine withdrawal. The variables with the strongest predictive value were preoperative TSH ($p < 0.001$) and TSH at withdrawal time ($p < 0.001$). The final nomogram had good discrimination of 0.733 (95% confidence interval 0.653–0.814) with appropriate calibration, supported by an external validation point estimate of 0.698 (95% confidence interval 0.616–0.779).

CONCLUSION

A validated nomogram utilizing readily available pre- and postoperative variables has been developed to give a predicted probability of subclinical hypothyroidism after levothyroxine withdrawal in patients who underwent hemithyroidectomy for DTC. This nomogram may help guide decision making for levothyroxine withdrawal after hemithyroidectomy in DTC.