Review

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Contemporary Trends in Adrenal Sparing Surgery

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Abstract

Adrenal gland surgery has been practiced by the urologists ever increasingly in line with their interest in this particular field. Total adrenalectomy which is the classical approach for adrenal masses, is replaced by the organ-sparing surgery as soon as the significance of the organ sparing approach is understood as in the case of the renal masses. The partial adrenalectomy which has been in use through open surgery method since 1950's, was adapted to adrenal surgery by Gagner in 1991 and technical advancement was achieved since then with the introduction of the laparoscopic adrenalectomy by Janetschek six years later. Although it is increasingly being used, there still exist ambiguities concerning the technique and indications of the adrenal sparing surgery. In this review, the updated status of the adrenal sparing surgery is discussed with the current literature.
Keywords: Adrenalectomy, partial adrenalectomy, organ-sparing surgery, adrenal mass

Introduction

Adrenal glands are known to be associated with several diseases. In autopsy series, it has been reported that there are anomalies in the adrenal glands at a rate of 9% (1-3). With the widespread use of the computerized tomography (CT), adrenal lesions have been encountered at an approximate rate of 5% in CT scans (1). The rate of detection of the adrenal masses most of which are incidental, varies depending on the age, and the rate is 0.4% at the age of 20 which turns out to be about 7% at the age of 70 (4). It is almost never seen during childhood period. Thus, the adrenal tumors are defined incidentally through the radiological methods in progress and gradually becoming widespread. On the other hand, upon being aware of the symptoms, the tumors are diagnosed during the early stage when the patients consult with the doctor. Such tumors are detected when they are smaller in size when compared with the past (5). The reasons and frequencies of the adrenal masses are given in Table 1 (4,6). There is an increase in rate of diagnosing the adrenal masses by the time. Also, relatively smaller adrenal masses are detected with and a gradual decrease in the preliminary diagnosis of malignity. Hence, the adrenal sparing surgeries are supported in line with the evolutions experienced in the surgeries of the other organs (7). For the patients with high surgical risk, ablative methods have been defined but this is not included within the scope of this article.

Upon execution of the first adrenalectomy by Thornton in 1889, the progresses have been made in adrenalectomy while adrenal sparing surgery was first applied in 1950's for ACHT dependent Cushings' syndrome and bilateral pheochromocytoma thereafter (8). A patient who underwent adrenal sparing surgery in 1950's due to pheochromocytoma showed recurrence after 30 years of partial adrenalectomy in 1984 (9). The first laparoscopic partial adrenelectomy (PA) was made by Janetschek in 1997 with transperitoneal approach and by Walz one year later through retroperitoneal approach (10). Robotic PA was introduced in 2006 while Kumar applied robotic PA for adrenal metastases in 2009 soon after (1,2).

Indications and Contraindications of the Adrenal Sparing Surgery

The traditional method for adrenal masses is the total adrenalectomy (TA). The primary reason for this may include the easiness of this surgical procedure as it is also efficient and safe that the adrenal is the dual functional organ. Since the adrenal diseases show specific behavior, the results may not always be the same. The indications of the adrenal sparing surgery include unifocal, small and unilateral masses on one side, and multifocal, hereditary masses with high recurrence risks on the other side. Ishıdoya et al. (11) showed that more than one adenoma may be observed within the adrenal at a rate of 27% and that the final pathology may not display similar clinical and radiological corelation. The masses greater than 4cm are not deemed to be surgical responsive for adrenal sparing surgery due to the malignity risks and technical reasons. All these reasons display the difficulties and question marks as far

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as the adrenal sparing surgery is concerned and emphasize the significance of the selection of the patients with due diligence along with the preoperative assessment. The indications and techniques of the adrenal sparing surgery have not been fully standardized. Despite the advantages for the patients with solitary adrenal or bilateral involvement, optimal treatment of the small hormonal masses where the other adrenal is normal has not yet been clear while on the other hand the arguments for partial adrenalectomy are not sound. When deciding for adrenal sparing surgery, there should be some sort of balance among the complications similar to the kidney cancer, risk of recurrence and functional and long term results (7).

1- Bilateral adrenal mass

2- Mass on the solitary adrenal

3- Risk of metachromo multiple adrenal tumor.

4- Unilateral, sporadicmasses *

The followings are the current indications for the adrenal sparing surgery:

* (Since the response to stress subsequent to bilateral adrenalectomy is most often failed, PA may be applicable for the unilateral sporadic patients as well as the patients with small mass while the surgical indications gradually increase).

Out of the contraindications of the adrenal sparing surgery, the following can be listed in addition to the contraindications of the laparoscopy:

- Masses larger than 4 cm.

- Metastatic masses

- Doubt of invasive malignity

- Adrenal vein/vena cava inferiorinvolvement

Why Adrenal Sparing Surgery?

Adrenal sparing surgery has been placed in the first priority due to the bilateral involvement of the masses at varying rates, suboptimal response against the stress after the bilateral adrenalectomy, and the risk of Addison crisis -which may be mortal at a rate of 4 %- stemming from failures after the surgery where bilateral adrenalectomy is needed to be done. Many of the adrenal lesions which include especially the hereditary forms such as Von Hippel Lindau (VHL) and MEN-2 syndromestend to be observed in bilateral, multifocal and recurrent forms. On the other hand, the in some cases of pheochromocytoma with nonadrenal residence TA may be insufficient and even insignificant. The rate of bilateral nature of the adrenal masses varies and although it is higher in familial diseases, it is rated to be 7.8% for incidentalome, 35 to 80% for familial MEN syndrome and 40 to 60% for VHL. Table 2 shows the rates of bilateral frequencies of adrenal masses. It should be taken into consideration that the multifunctionality of the adrenal gland and relatively small and fragile nature give way tothe risk of distortion of the adrenal gland in the rest of life. The probability of the lifelong distortion depending on the infections on the adrenal gland, infiltrative diseases, adrenal metastases and such other reasons is only 1% and this rate does not include the adrenal wise distortions during nephrostoma (7). This supports the idea of the use of the adrenal sparing surgery in an appropriate manner. The reasons why the adrenal sparing surgery is of importance are the lifelong replacement requisite due to adrenal failure, hospitalization at a rate of 1/3, the risk of Addison crisis at a rate of 30%. Besides, the risks of serious diseases like osteoporosis, infections and diabetes and insufficient response against stress in the case of bilateral adrenalectomy may also have an impact despite the normality of the other adrenal where no postoperative replacement is required. Therefore, organ sparing approach which gains popularity as time pass by and can be sampled through other urologic tumors, should be prioritized for the adrenal gland.

Technique

One of the most advantageous urologic surgeries is the adrenal surgery where laparoscopy is superior to open surgery. Some studies reveal that minimal invasive approaches such as laparoscopy and robotic laparoscopy used in the adrenal sparing surgery are superior to the open surgery in view of the postoperative pains, complications and cosmetic results as in the case of TA (4,12,13). The recent robotic devices used in the adrenal sparing surgery provide some benefits. The advantages of the robotic surgery may include the minimal mobilization of the normal adrenal tissue during rotatable resection of the entophytic adrenal mass and better control of the adrenal bleeding (14).

Laparoscopic surgery techniques will be summarized here. The position of the patient in laparoscopic partial adrenalectomy and the port locations are almost the same with the laparoscopic adrenalectomy. Based on the experience of the surgeon, the process may be transperitoneal or retroperitoneal. The widely used approach is the transperitoneal approach (4). Prior to dissection of the adrenal gland, inspection is made and the location, dimension of the mass are defined along with the proximity to the adrenal vein. The intraoperative ultrasonography provides benefit for the assessment of the adrenal masses during PA and the intraoperative planning and it is particularly recommended to minimize the risk of residual masses for the diseases with multi nodularity such as pheochromocytoma (15,16). Another method which may assist to define the limits of the masses is the indocyanine green (ICG). There exist very few studies showing the use of the ICG in adrenal sparing surgery. While the pheochromocytoma and lypoadenoma was imaging fluorescent, cortex-induced lesions such as Cushing syndrome imaged hyper fluorescent and this may provide benefits in the complete resection of the mass (17,18). Upon defining the mass and its limits, the adrenal gland and especially the area with the mass are cleared using haemostatic devices such as harmonic scissor, bipolar shutter-cutter. It is recommended to provide protection for the main adrenal vein to the extent possible based on the location of the mass (12). In case the main adrenal vein cannot be protected, it should be resected, however, in such a case, only the location with the mass should be dissected in order not to give way any damage to the minor plexus within the retroperitoneal area to keep the adrenal functionality in order. On the other hand the appropriate section should be mobilized to the extent possible (13,19). Connecting the adrenal vein at the initial stage of the operation has been proven to be preventing the hypertension attacks which are observed more frequently in

PA for pheochromocytoma (20). Some authors suggest direct resection of the mass without dealing with the mobilization of the adrenal gland and the veins (19,20). Walz et al. (21) argued that the most important point to preserve the functionality of the adrenal gland during PA is the protection of the adrenal tissues to the extent possible. The protection of the sound adrenal tissues as much as it can be during PA is sought while the complete excision of the mass is of particular importance. Although there exist studies reporting that 2-3 mm distance as surgical limit is sufficient, in general terms the acceptable distance has always been 5 mm (19,20,22,23). An effective hemorrhage control is made subsequent to excision. During hemostatis the normal adrenal tissue is diligently spared. Hemostatic agents may be used to minimize the potential postoperative hemorrhage

There is no consensus concerning the quantity of the remaining adrenal tissue for the continuity of the physiological functions. There exist some studies suggesting the sparing of 1/3 of the remaining adrenal tissue while some other studies report that 20% of the well perfuzed adrenal is sufficient for preservation (19,24-26).

Results

The most important factors which may have an impact on the options to be made between the TA and the adrenal sparing surgery for the patients with adrenal mass are the ratio of the complications, oncologic results and functional outcomes (trifecta). These are summarized as follows:

Complications

One of the most important points which should be taken into consideration in the case of the patients who are to undergo adrenal sparing surgery is the complications. The complications may be in relation with the overall medical condition of the patient and applicable anesthesia and surgical techniques. The most frequent and significant complication encountered during perioperative and postoperative periods is bleeding (27). It is followed by open wound infection and pneumonia and laxity of the abdominal Wall (28). The study by Walz et al. (21) compared a total of 325 patients who underwent total and partial adrenalectomy. It was observed that average operation time was 80 min with amount of bleeding 29 mL for PA and that no expressive difference was noted when compared with TA Fu et al. (29), in their study with 212 similar cases, reported that there observed no significant difference between the groups in view of the operation time and rates of complication. Wang et al. (27), in their retroperitoneoscopic PA study for adrenal masses of 1 cm and smaller masses, no long term complication was observed and no recurrence was determined over a follow up period of 41 months. The larger the dimension of the mass, the more difficult the PA technique would be. It has been proven that this would have negative effect on the duration of the operation and the amount of hemorrhage. In a recent study comparing the total and partial adrenalectomy made applicable through transperitoneal and retroperitoneoscopic approach for the adrenal masses smaller or larger than five centimeters, it has been observed statistically that the operation period is longer (102.68±30.92 min/9.64±28.39 min, p=0.02) and hemorrhage is higher (451.9±186.3 mL / 286.0±217.5 mL, p=0.02) during retroperitoneoscopic PA for the tumors larger than five centimeters (30). The ratio of transition from PA to TA was determined to be 2.5% in the contents of the study conducted by Kaye et al. (28) with 417 cases. The ratios of perioperative blood transfusion and perioperative complication have been found to be 7.3%, and it was reported that perioperative results are as good as TA.

In case the literature regarding the PA complications are evaluated, it can be argued that although the amount of hemorrhage and duration of the operations are a bit more than the envisaged amount the complications are similar to that of the TA and can be an applicable technique at the experienced medical organizations while it may not always be applicable and possible for every patient.

Oncologic Results

The concerns for oncologic results are the most important factor which may have an effect on the selection of PA by the patients. As specified above, in the case and doubt of the malignity, adrenal sparing surgeryis contraindicated and applied only in benign pathologies despite recurrences observed.

The studies showed the differences in the recurrence rates based on the diseases (9,12,31-33). In particular, it is reported that the rate of recurrence of familial pheochromocytoma tend to be bilateral varies at a wide range like 0% - 100% (9,27,31-33). Referring to the study released by Castinetti et al. (34) in 2016, the rate of recurrence of the hereditary pheochromocytoma is between 0% - 21%. It was stated by Castinetti et al. (34) in their comparative study that the rates of recurrence in the long term follow up is 2.6% for PA and 1.5% for TA while the time for recurrence is stated to 9.5 years (35). The study by Amar et al. (36) regarding the factors affecting the recurrences in pheochromocytoma shows that recurrence is impacted by the dimensions of the tumor, affected location (right side is more likely than the left side) and diagnosis age (recurrence is much more observed amongst the youth). Walz et al. (37), in their study dated back to 2018 in which an assessment was made for the minimal invasive TA and PA for 70 adrenal masses observed on the patients involving 42 children and adolescents with pheochromocytoma and/or paraganlioma, (26 with pheochromocytoma, 11 PGL and 5 pheochromocytoma + PGL) reported that 31 of the patients with pheochromocytoma underwent PA while excision was made for the patients with PGL. During the follow up period of 8.5 years as an average, recurrence was observed in two patients with VHL syndrome in the case of PA and out of five PGL patients with recurrence, four patients had to undergo another operation. As for the Adenoma Secreting Aldosterone (ASA), the rate of recurrence varies between 0% and 2% (7). Out of 212 patients, Fu et al. (29) applied TA on 108 patients and PA on 104 patients and they reported that no recurrence was observed within 96-months follow up period. Kaye et al. (28) reported the overall recurrence rate as 3% in the metaanalysis of the 22 studies they have conducted for the different adrenal diseases. As is seen, the recurrence observed in the benign masses especially the new series are at acceptably low levels except for

the familial pheochromocytoma. In case the patients who may suffer multi-focal cases are assessed carefully and if the adrenal mass is excised through the responsive surgical technique using the intraoperative ancillary technologies (intraoperative ultrasonography, ICG etc.), the oncologic results for PA may be satisfactory.

Functional Results

The functional results of the adrenal sparing surgery can be assessed in two aspects. The first is the recovery of the diseases such as hypertension caused by the hormonal functions of the adrenal mass and the second is the prevention of the steroid dependence of the adrenal function. Ishidoya et al. (11), in their study in the contents of which they compared the results of the TA and PA on 174 patients suffering aldosteronamia, reported that only 2 (6.9%) patients suffered hypertension in view of PA. It has been observed in the study conducted by Fu et al. (29) that the hypertensions of all of the patients suffering ASA in the two groups on whom TA and PA was applied tend to have been recovered while the plasma rennin activities and serum aldosterone levels normalized within the period of 6-months follow up. In both of the groups no Addison crisis was observed and no steroid replacement was deemed to be necessary. Gupta et al. (24) reported that out of 121 cases with PA applied on the pheochromocytoma patients (10 of such surgeries 8 patients with concurrent multiple pheochromocytoma on the similar location), there observed recoveries on the symptoms of all of the patients after 12 months while steroid replacement was a requisite for only one patient with solitary adrenal. In the contents of the study conducted by Chen et al. (30) no hormone replacement was necessary as far as the PA was concerned, while out of 27 patients, replacement was a requisite for 13 patients who underwent TA r (0%/48.15%, p=0.002). In another study, 16 PA and 47 TA for 63 adrenal masses were compared and recuperation was observed in the plasma rennin activity on both side by the end of the year. However, 43.8% of the patients had to undergo anti hypertension treatment for PA. No steroid replacement was deemed to be a requisite on both sides (25). For the durability of the functionality of the adrenal gland, there exist divergent opinions concerning the significance of the preservation of the adrenal vein during PA. The fact that some of the researchers are in the thought that the main adrenal vein should be spared for the continuity of its functions, in the study of Walz et al. (21), it has been argued that the adrenal vein should not be preserved while sufficient adrenal tissue should be spared as possible as it can be, as stated in this study under the title of "Technique". It is observed that the PA and TA results are similar in view of the recovery of the symptoms of the hormonal function of the mass. If examined in view of the preservation of the adrenal functions, PA seems to be advantageous, it should be kept in mind that postoperative replacement may be necessary for the patients with solitary adrenal.

Follow Up

Although recurrence risk after PA does not seem to be statistically higher than TA, more studies should be conducted to find out the time relapsed for recurrence for the patients with pheochromocytoma in particular and the probability for such recurrence. Therefore, periodical biochemical assessments should be made after the surgery as well as the clinical follow-up (6,22). Within 24 hours after the surgical operation, metabolites such as catecholamine and metanephrine fractioned with urine are reviewed and such reviews are repeated for the patients followed up clinically 6 months. Although there exists no consensus concerning the follow-up period, long term follow up protocols are suggested since it can be recurred even after 10 years (28).

Conclusion

Adrenal sparing surgery presents outcome which are similar with TA both in view of the complications and the oncologic results. When reviewed in line with the functional results, it is observed through several studies that despite ongoing antihypertension treatments subsequent to PA, hypertension after PA decreases significantly and steroidplasma is seldom required. Therefore, it can be concluded that the functional results for PA are better than the TA. The adrenal sparing surgery has always been a better surgical alternative for not only the patients with bilateral adrenal mass or solitary adrenal mass along with the patients suffering Familial syndrome with the risk of recurrence and patients with unilateral adrenal mass. Upon completion of the successful preoperative preparations, open surgery or laparoscopic or robotic methods which provide some advantages in comparison with the open surgery, may be applicable.

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Appendix 1. None

Questions

1) Which of the following is not an indication of adrenal sparing surgery?

a. Bilateral adrenal tumor
b. Tumor on the solitary adrenal
c. Metachoronous multiple adrenal tumor risk
d. Uni lateral sporadic tumors
e. Adrenal tumors larger than 4 cm

Correct answer: e

2) Which of the following is false?

a. Open surgery is superior to the minimal invasive methods in adrenal sparing surgery
b. The widely used technique varies based on the experience of the surgeon but it is the laparoscopic transperitoneal approach.
c. It is still being discussed whether or not the adrenal vein is spared during adrenal surgery
d. Minimal mobilization of the adrenal tissueis recommended for the maintenance of the adrenal functions during adrenal sparing surgery.

Correct answer: a

3) Which of the following is true?

a. 1 mm surgical limit is sufficient in adrenal sparing surgery
b. Adrenal sparing surgery is indicated even in the case of any doubt of malignity
c. Recurrence is quite likely after adrenal sparing surgery in the case of ASA.
d. Dependence on the steroid after adrenal sparing surgery is rated to be higher than the total adrenalectomy.
e. For the tumors with multi nodularity such as pheochromocytoma, the devices such as intraoperative ultrasonography helps a lot during adrenal sparing surgery

Correct answer: e

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