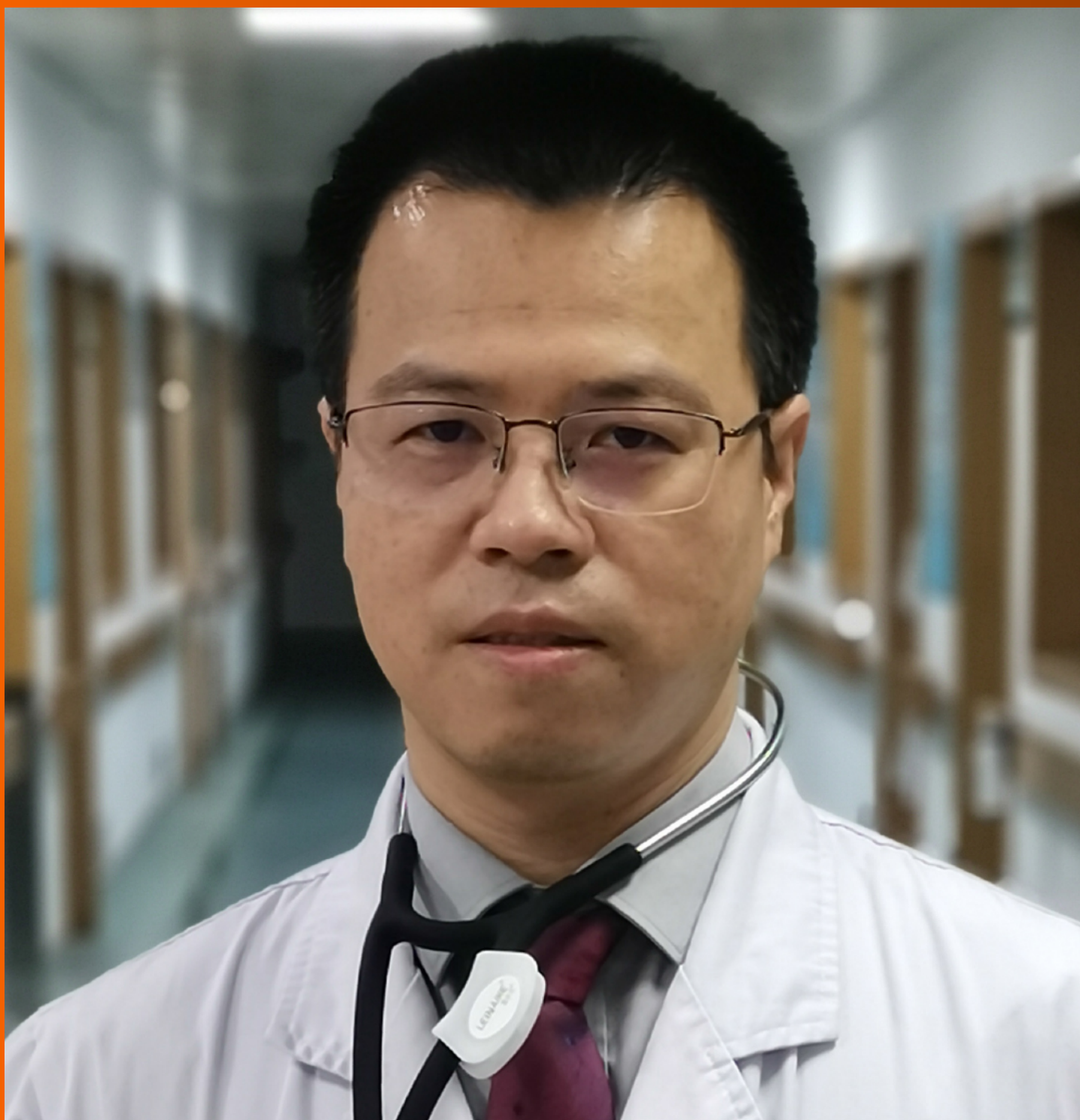


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The primary aim of *Artificial Intelligence in Cancer* (AIC, *Artif Intell Cancer*) is to provide scholars and readers from various fields of artificial intelligence in cancer with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

AIC mainly publishes articles reporting research results obtained in the field of artificial intelligence in cancer and covering a wide range of topics, including artificial intelligence in bone oncology, breast cancer, gastrointestinal cancer, genitourinary cancer, gynecological cancer, head and neck cancer, hematologic malignancy, lung cancer, lymphoma and myeloma, pediatric oncology, and urologic oncology.

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Application of retroperitoneal laparoscopy and robotic surgery in complex adrenal tumors

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Abstract

As a surgical method for the treatment of adrenal surgical diseases, laparoscopy has the advantages of small trauma, short operation time, less bleeding, and fast postoperative recovery. It is considered as the gold standard for the treatment of adrenal surgical diseases. Retroperitoneal laparoscopy is widely used because it does not pass through the abdominal cavity, does not interfere with internal organs, and has little effect on gastrointestinal function. However, complex adrenal tumors have the characteristics of large volume, compression of adjacent tissues, and invasion of surrounding tissues, so they are rarely treated by retroperitoneal laparoscopy. In recent years, with the development of laparoscopic technology and the progress of surgical technology, robotic surgery has been gradually applied to the surgical treatment of complex adrenal tumors. This paper reviews the clinical application of retroperitoneal laparoscopic surgery and robotic surgery in the treatment of complex adrenal tumors.

Key Words: Retroperitoneal laparoscopic; Robotic surgical procedures; Complex adrenal tumors; Clinical application; Robotic

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Core Tip: The posterior laparoscopy does not interfere with the internal organs and has little effect on the function of the gastrointestinal tract, thus widely being used. However, complex adrenal tumors are characterized by large volume, compression of adjacent tissues, and invasion of surrounding tissues. Therefore, they are rarely treated by retroperitoneal laparoscopic surgery. Recently, with the development of laparoscopic techniques and advances in surgical techniques, reports about retroperitoneal laparoscopic adrenalectomy have gradually increased. This article reviews the clinical application of laparoscopy in complex adrenal tumors.

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INTRODUCTION

Adrenal tumors are one of the most common tumors in the urinary system, and surgery is the main method of treatment. Gagner *et al*[1] first reported transabdominal laparoscopic surgery for Cushing syndrome. With the progress of laparoscopic surgery technology and the improvement of equipment, laparoscopic surgery for adrenal diseases has been widely used by urologists. Because of the small space of the retroperitoneum, laparoscopic surgery for the treatment of complex adrenal tumors requires a highly skilled technique. There are few reports regarding retroperitoneal laparoscopic surgery for complex adrenal tumors. Recently, there are more and more reports on robot assisted laparoscopic technology. The Da Vinci surgical robot system provides articulated instruments, three-dimensional (3D) vision, tremor filtering, and stable cameras. It can make up for the defects of traditional laparoscopy.

RETROPERITONEAL LAPAROSCOPY IN ADRENAL TUMORS

In 1992, Gagner *et al*[1] first reported laparoscopic adrenalectomy. Compared with open surgery, laparoscopic adrenalectomy has the advantages of less bleeding, less trauma, faster recovery, and fewer intraoperative and postoperative complications, and soon has been promoted and applied all over the world. Retroperitoneal laparoscopy was first reported by Walz *et al*[2] in 1996. This technology became popular because it can directly and quickly expose the adrenal gland without going through the peritoneal cavity, and does not need to dissect the intraperitoneal structures. In the same year, Mercan *et al*[3] performed eight cases of adrenalectomy and the average operation time was about 150 min. In 2011, Shi *et al*[4] elaborated the surgical methods and skills of anatomical retroperitoneal laparoscopic adrenalectomy. In recent years, with the development of endoscopic technology, robot assisted retroperitoneal laparoscopic technology is gradually increasing. Robot surgery system has the advantages of clear operation field, flexible operation, and fine action and is gradually welcomed[5].

ANATOMIC PATHWAY AND OPERATIVE TECHNIQUE OF RETROPERITONEAL LAPAROSCOPY

However, there are disputes about complex adrenal tumors. It has been found that retroperitoneal laparoscopic anatomical three-layer method has the advantages of less blood loss and shorter operation time in surgery for huge adrenal masses[6].

During the retroperitoneal laparoscopic surgery, the patient usually lies on the healthy side. First, the skin is cut at 1.5 cm above the iliac crest of the midaxillary line, the subcutaneous tissue and fat are separated by fingers, and then an artificial balloon is inserted into the retroperitoneum. After being filled with 500 mL of gas for about 5 min, the balloon is withdrawn, and trocars are inserted for laparoscopy under monitor. After entering the retroperitoneal cavity, the location of Gerota's extraperitoneal cavity is identified, and the adipose tissue outside the Gerota's fascia and peritoneum is sharply separated from the inferior edge of diaphragm to the iliac fossa with an ultrasonic scalpel.

At the first level, the relatively avascular space between the perirenal fat sac above the medial side of the kidney and the anterior layer of Gerota fascia is separated to find the adrenal tumor and expose its anterior surface. At the second level, the relatively avascular space between the perirenal fat sac and the posterior layer of Gerota fascia can be separated to expose the lateral and dorsal side of adrenal tumor. At the third level, the adipose tissue at the bottom of adrenal gland and the surface tissue of renal parenchyma are separated, and the bottom of tumor is exposed by separation of tissue[4].

The right central adrenal vein starts from the apex of the adrenal gland and flows into the back of the inferior vena cava, and attention should be paid to the protection of the inferior vena cava when handling the right vein. The left central adrenal vein starts from the bottom of the left adrenal gland and flows into the left renal vein, and attention should be paid to the protection of the left renal vein[7]. The central adrenal vein and other blood vessels are isolated and ligated with hemo-lock.

DEFINITION AND CLINICAL TREATMENT OF COMPLEX ADRENAL TUMORS

Due to the deep location, complex adrenal tumors are closely related to large blood vessels, the tumor diameter is large, and the pathology is diverse. In recent years, some literature calls adrenal tumors with the following characteristics as complex adrenal tumors: (1) Large adrenal tumors (> 6.0 cm); (2) Adrenal pheochromocytoma; (3) Adrenal tumors with compression or invasion of peripheral blood vessels; (4) Obesity combined with suprarenal gland tumors (body mass index [BMI] ≥ 25 kg/m²); (5) The tumors that need to preserve adrenal tissue during operation; (6) Adrenal malignant tumors; and (7) Having a history of retroperitoneal surgery[8,9].

The growth of the tumor is accompanied by the increase of the degree of malignancy, as well as the internal bleeding and necrosis of the tumor, resulting in the adhesion of the tumor and the surrounding organs, tissues, and blood vessels, which increases the difficulty of operation[10]. Gong *et al*[11] found that all operations were not converted to open surgery by using retroperitoneal laparoscopic technique to remove adrenal tumors larger than 8 cm. At the same time, they temporarily blocked the renal artery to reduce tumor bleeding. After 7-30 mo of follow-up, there was no tumor metastasis and recurrence, which proved that temporary blocking of the renal artery was a feasible and safe method in the treatment of huge adrenal tumors[11].

The pathology of pheochromocytoma can be divided into benign and malignant. Most of them are benign. Benign tumors are round or oval with a smooth surface. Pheochromocytoma can secrete catecholamines, causing hypertension, headache, sweating, palpitation, and other symptoms. Patients usually have persistent or paroxysmal hypertension before treatment. Therefore, perioperative management is an important part of laparoscopic resection of pheochromocytoma[12]. Recently, with the development of laparoscopic technology, the reports of retroperitoneal laparoscopic resection of benign and malignant pheochromocytoma gradually have increased. Costa *et al* performed retroperitoneal laparoscopic surgery on ten cases of adrenal tumors, including two cases of pheochromocytoma and one huge cystic pheochromocytoma (diameter: 14 cm). There were no complications during and after the operation, and the tumor did not recur during the follow-up[13].

Giant pheochromocytoma (> 6 cm) usually has a high degree of malignancy and easy to cause changes in the circulatory system of patients during the operation, resulting in blood pressure fluctuations. Similarly, the advantage of retroperitoneoscopy for giant pheochromocytoma is better than that of laparoscopy[14,15]. Shiraishi *et al*[14] found that in patients with huge pheochromocytoma, compared with laparoscopy, retroperitoneoscopy has obvious advantages in operation time and intraoperative bleeding. No recurrence or metastasis was found in postoperative follow-up. Laparoscopic surgery may be a safe and feasible method for pheochromocytoma treatment, preoperative preparation, intraoperative blood pressure, and postoperative active care.

Because of the hypertrophy of abdominal muscle and fat around the adrenal gland in obese patients, laparoscopic surgery was often contraindicated in the past. In recent years, studies have reported that single obesity is no longer a taboo for laparoscopic surgery[16,17]. When comparing the patients with a BMI > 40 kg/m², bilateral adrenal tumors, and abdominal surgery history who underwent laparoscopy and retroperitoneoscopy in the early stage, Arezzo *et al*[18] found that there was no significant difference in operation time, blood loss, or ambulation time between the two methods, and the eating time and recovery period after retroperitoneoscopy were significantly shortened. When comparing 41 obese patients with adrenal tumor (BMI ≥ 30 kg/m²) and 96 non-obese patients (BMI < 30 kg/m²) who underwent retroperitoneal laparoscopic surgery, it was found that the operation time for obese patients was significantly prolonged, and other parameters had no significant difference. The results showed that retroperitoneal laparoscopic surgery could be performed in obese patients with short recovery time and less bleeding[19]. Dickson *et al*[20] performed retroperitoneal laparoscopic adrenalectomy on 118 patients, 48% of whom had a BMI \geq

30 kg/m², and the patients recovered well without obvious intraoperative and postoperative complications. The above studies show that retroperitoneal laparoscopy is a safe and effective treatment for obese patients with adrenal tumors, which can be carried out in patients according to the clinical experience of surgeons.

Adrenal malignant tumors include adrenal cortical carcinoma, malignant pheochromocytoma, adrenal metastatic carcinoma, and adrenal lymphoma[21]. Most adrenocortical carcinomas are larger than 5 cm in diameter, with hemorrhage and necrosis. At the same time, with the tumor volume increasing, tumor cells are easy to invade the surrounding tissues, blood vessels, and nerves, increasing the difficulty of surgery. In the past, open surgery was recommended for adrenocortical carcinoma, with wide field of vision and complete exposure of tumor tissue, which was convenient for complete resection of the whole tumor tissue. With the development of laparoscopic technology, laparoscopic technology has been applied to adrenal cortical carcinoma. Ma *et al*[22] performed anatomical retroperitoneal laparoscopic surgery on 75 patients with adrenal metastasis. The pathological results showed that clear cell carcinoma and small cell lung cancer were the majority, and the local recurrence rate was 5.3%. Studies have found that BMI, tumor type, and positive margin are independent prognostic factors. Retroperitoneal laparoscopic technique is a safe and effective treatment for adrenal metastases[22].

Adrenal lesions are diverse, including adrenal adenoma, adrenal neuroblastoma, schwannoma, cyst, and other malignant lesions. Most adrenal lesions can be removed by laparoscopic technique[23]. Adrenal lymphangioma is another kind of benign adrenal tumor. Gao *et al*[24] found that no intraoperative or postoperative complications occurred in all patients through retroperitoneal laparoscopic technique for adrenal lymphangioma, and no tumor recurrence occurred during follow-up. Retroperitoneal ectopic pheochromocytoma is an extra adrenal pheochromocytoma below the diaphragm and above the iliac fossa. It has abundant blood supply and is closely related to the peripheral blood vessels. Cai *et al*[25] performed retroperitoneal laparoscopic resection on four cases of retroperitoneal ectopic pheochromocytoma, of which one case was converted to laparotomy. All patients were operated successfully, without obvious intraoperative and postoperative complications, and the postoperative symptoms were significantly improved[25].

RECENT PROGRESS IN SURGICAL TREATMENT OF COMPLEX ADRENAL TUMORS

Recently, there are more and more reports on robot assisted laparoscopic technology. The disadvantages of traditional laparoscopic technology are the limited range of operation, the limited depth perception of 2D video image, and the unstable control of laparoscopic lens. The Da Vinci surgical robot system provides articulated instruments, 3D vision, tremor filtering, and stable cameras. It can make up for the defects of traditional laparoscopy. Surgeons can carry out operations under comfortable conditions[26,27]. In a recent meta-analysis, 1162 patients underwent adrenalectomy (747 patients received robotic adrenalectomy and 415 patients received conventional laparoscopic adrenalectomy). The study found that there were no significant differences in intraoperative and postoperative blood loss or mortality between the two groups. However, the hospital stay associated with robotic surgery was significantly shortened, and the operation time was significantly prolonged. The results showed that robotic surgery was a safe operation[28]. In another meta-analysis, 232 cases and 297 controls were included, including six prospective studies and two retrospective studies. The analysis showed that there was no difference in intraoperative and postoperative complications or mortality between the two groups, while the blood loss was significantly less and hospital stay was significantly shorter in the robot group[29]. Research shows that robotic laparoscopic surgery may be a safe and feasible surgical method for adrenal tumors, but further research is needed to prove it.

Robotic adrenalectomy can be divided into transperitoneal and retroperitoneal approaches. The preoperative preparation, patient position, and instrument channel placement of transperitoneal approach are similar to those of laparoscopic surgery. Transperitoneal approach has larger operation space and obvious anatomical landmarks. Lateral position can push the abdominal viscera to the opposite side, so as to better expose the surgical area. In the supine position, both adrenal glands can be easily found. In the published studies[30,31], most of the patients were in lateral position through the abdominal approach, and the patients were inclined 30-60 degrees. The procedure of transperitoneal approach is similar to that of open surgery.

Table 1 Important papers cited in this manuscript

No.	Ref.	Title	Journal
1	Gagner <i>et al</i> [1], 1992	Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma	<i>N Engl J Med</i>
2	Walz <i>et al</i> [1], 1996	Posterior retroperitoneoscopy as a new minimally invasive approach for adrenalectomy: Results of 30 adrenalectomies in 27 patients	<i>World J Surg</i>
3	Simone <i>et al</i> [5], 2019	Robot-assisted partial adrenalectomy for the treatment of Conn's syndrome: Surgical technique, and perioperative and functional outcomes	<i>Eur Urol</i>
4	Jiang <i>et al</i> [12], 2020	Comparison of the retroperitoneal versus transperitoneal laparoscopic adrenalectomy perioperative outcomes and safety for pheochromocytoma: A meta-analysis	<i>BMC Surg</i>
5	Shiraishi <i>et al</i> [14], 2019	Transperitoneal versus retroperitoneal laparoscopic adrenalectomy for large pheochromocytoma: Comparative outcomes	<i>Int J Urol Off J Japanese Urol Assoc</i>
6	Bai <i>et al</i> [15], 2019	Comparison of transperitoneal laparoscopic versus open adrenalectomy for large pheochromocytoma: A retrospective propensity score-matched cohort study	<i>Int J Surg</i>
7	Dickson <i>et al</i> [20], 2011	Posterior retroperitoneoscopic adrenalectomy: A contemporary American experience	<i>J Am Coll Surg</i>
8	Abraham <i>et al</i> [23], 2014	Laparoscopic extirpation of giant adrenal ganglioneuroma	<i>J Minim Access Surg</i>
9	Ji <i>et al</i> [26], 2020	Retrospective comparison of three minimally invasive approaches for adrenal tumors: perioperative outcomes of transperitoneal laparoscopic, retroperitoneal laparoscopic and robot-assisted laparoscopic adrenalectomy	<i>BMC Urol</i>
10	Conzo <i>et al</i> [28], 2016	Minimally invasive approach for adrenal lesions: Systematic review of laparoscopic versus retroperitoneoscopic adrenalectomy and assessment of risk factors for complications	<i>Int J Surg</i>

The operation does not enter the abdominal cavity, so many intra-abdominal complications are avoided, such as pleural injury, abdominal visceral organ injury, postoperative adhesion, and so on. Therefore, this approach is more suitable for patients with a history of abdominal surgery. But the disadvantage is that the operation space is limited, which increases the difficulty of operation. Kim *et al*[32] found that retroperitoneal robotic adrenalectomy has a shorter learning curve, and for huge adrenal tumors, retroperitoneal robotic adrenalectomy has shorter operation time and less postoperative pain than laparoscopic surgery.

Single port laparoscopic surgery (LESS) is a minimally invasive surgery that is being explored and optimized, that is, the lens and operating instruments are put into the abdominal cavity at the same time through an incision. The utility model has the advantages of small skin trauma, good aesthetic effect, less pain, and less incision complications. The disadvantage is that the cross use of single hole instruments increases the difficulty of the operation[33]. Including a total of 704 cases, a meta-analysis comparing laparoscopic single point adrenalectomy (LESSA) with conventional laparoscopic adrenalectomy. It was found that there were no significant differences in operation time, blood loss, eating time, analgesic dose, perioperative complications, or analgesic drugs between the two techniques, and LESS had a shorter hospital stay and lower postoperative pain score[34]. In another cohort study, 51 obese patients underwent LESS for retroperitoneal laparoscopic adrenalectomy, and the surgical results were compared with those of 65 obese patients who received standard retroperitoneal adrenalectomy by the same surgeon. The study found that there was no significant difference in hospital stay or surgical complications between the two groups, and there was also no significant difference in incision recovery time, postoperative pain requirements, or operation time. However, there were obvious advantages in satisfaction with incision appearance[35]. The results show that single port laparoscopic surgery is a feasible and safe method among experienced surgeons.

CONCLUSION

Laparoscopic adrenalectomy is the gold standard for the treatment of adrenal surgical diseases. At present, there is no unified standard for the surgical treatment of complex adrenal tumors. More and more studies have reported that retroperitoneal laparoscopic adrenalectomy for complex adrenal tumors has good postoperative recovery, exact surgical effect, and increasing application (Table 1). Robot assisted laparoscopy is

a minimally invasive technology developed in recent years. The combination of laparoscopy and robot not only has the advantages of minimally invasive laparoscopy, but also has the characteristics of flexible robot, which has a huge advantage in the treatment of adrenal tumors. However, there are few reports on the treatment of complex adrenal tumors by robot. Further research is needed to determine the role and efficacy of robot in complex adrenal tumor resection. With the progress of science and technology and the continuous improvement of surgeons' technical level, the surgical treatment of complex adrenal tumors will have more obvious advantages and curative effect in the future.

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