# RESEARCH



# Comparative study of single-port singlechannel and single-port multi-channel adrenalectomy in various maximum tumor diameters

Pengcheng Zhang<sup>1</sup>, Yuhan Pei<sup>1</sup>, Yunlai Zhi<sup>1</sup>, Fanghu Sun<sup>1</sup> and Ninghong Song<sup>2\*</sup>

# Abstract

**Background** Investigating the application of single-port single-channel and single-port multi-channel adrenalectomy in various maximum tumor diameters.

**Methods** Retrospective analysis of clinical data from 218 adrenal tumors treated with single-port retroperitoneoscopic adrenalectomy at Lianyungang Clinical Medical College of Nanjing Medical University from September 2018 to November 2023. All adrenal tumors are benign lesions classified as T1 stage. Tumors were classified into three groups based on their maximum diameter:  $\leq 3 \text{ cm}$  (Group A), > 3 cm and  $\leq 4 \text{ cm}$  (Group B), and > 4 cm and  $\leq 5 \text{ cm}$  (Group C). Based on the surgical approach, patients were divided into single-port single-channel and single-port multi-channel groups. Group A had an average tumor diameter of  $(2.32 \pm 0.45)$  cm with 46 single-port single-channel and 53 single-port multi-channel cases; Group B had  $(3.42 \pm 0.31)$  cm with 33 single-port single-channel and 23 single-port multi-channel cases; Group C had  $(4.60 \pm 0.28)$  cm with 18 single-port single-channel and 23 single-port multi-channel cases. Comparisons were made between single-port single-channel and single-port multi-channel cases. Comparisons were made between single-port single-channel and single-port multi-channel cases. Comparisons were made between single-port single-channel and single-port multi-channel cases. Comparisons were made between single-port single-channel and single-port multi-channel cases. Comparisons were made between single-port single-channel and single-port multi-channel cases. Comparisons were made between single-port single-channel and single-port multi-channel cases. Comparisons were made between single-port single-channel and single-port multi-channel cases. Comparisons were made between single-port single-channel and single-port multi-channel groups in terms of operation time, hospital stay, intraoperative bleeding, postoperative pain score, surgical complications, incision length (total length of all incisions), and the need for additional puncture holes for each tumor size group.

**Results** All 218 surgeries were successfully completed without conversion to open surgery. In Group A, no significant difference was observed between single-channel and multi-channel groups in terms of operation time and blood loss (P > 0.05), but significant differences were found in hospital stay, pain score, subcutaneous emphysema incidence, and incision length (P < 0.05). In Group B, there was no significant difference between single-channel and multi-channel groups regarding operation time and blood loss (P > 0.05), but significant differences were observed in hospital stay, pain score, subcutaneous emphysema incidence, and incision length (P < 0.05). In Group C, no significant difference was observed between single-channel and multi-channel groups in terms of hospital stay, blood loss, pain score, incision length, vascular injury, and subcutaneous emphysema incidence (P > 0.05), but significant differences

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were found in operation time and the incidence of additional puncture holes (P < 0.05). Postoperative follow-up ranged from 4 to 22 months, with an average of 11.5 months, and no complications were observed.

**Conclusions** Single-port single-channel laparoscopy has significant advantages in surgeries for tumors with a maximum diameter  $\leq 4$  cm, as it can directly reach the target organ, reduce separation operations, cause less damage, and has good cosmetic effects. For adrenal tumor surgeries with a maximum diameter > 4 cm, the multi-channel technique is superior to the single-channel technique in terms of shorter hospital stay and the need for additional punctures.

Keywords Laparoscopic surgery, Single-port laparoscopic surgery, Adrenal tumor

# Background

Adrenal diseases such as adrenal tumors and adrenal hyperplasia are common and prevalent in urology. With the development and popularization of diagnostic technologies such as CT, an increasing number of patients are diagnosed. Most patients with adrenal tumors and some with adrenal hyperplasia require adrenalectomy, making it one of the most common procedures in urology. Reducing surgical trauma and complications is a general trend in surgical development. The laparoscopic techniques in urology have been widely adopted with the advancement of laparoscopic surgery. Retroperitoneal laparoscopic techniques, due to their retroperitoneal approach, direct access to the unilateral adrenal gland and urinary system, minimal interference with intra-abdominal organs, short surgical duration, and quick recovery, are increasingly recognized and widely performed.

Laparoscopic adrenalectomy is the standard procedure for treating adrenal tumors. With the development of laparoscopic surgery and the expansion of minimally invasive concepts, single-port laparoscopic surgery has gained increasing attention and importance among experts and scholars [1]. Compared to traditional retroperitoneoscopy, single-port retroperitoneoscopy presents challenges in visual field exposure and complex operations, demanding higher levels of skill, concentration, precision, and team coordination from the surgeon, thus affecting its widespread clinical adoption [2]. In recent years, single-port laparoscopic technology has flourished, mainly divided into single-port single-channel and single-port multi-channel approaches [3]. We conducted single-port single-channel laparoscopic adrenalectomy and compared it with single-port multi-channel laparoscopic adrenalectomy, and report the findings as follows.

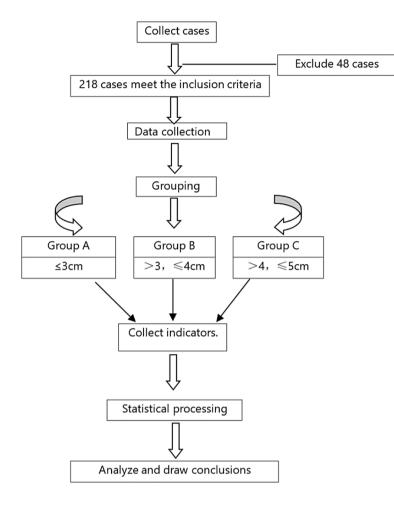
# Methods

# **Clinical information**

Retrospective analysis of clinical data from 218 adrenal tumors treated with single-port retroperitoneoscopic adrenalectomy at Lianyungang Clinical Medical College of Nanjing Medical University from September 2018 to November 2023. Tumors were classified into three groups based on their maximum diameter:  $\leq 3 \text{ cm}$  (Group A), >3 cm and  $\leq 4 \text{ cm}$  (Group B), and >4 cm and  $\leq 5 \text{ cm}$  (Group C). (Fig. 1)Based on the surgical approach, patients were divided into single-port single-channel and single-port multi-channel groups. Group A had an average tumor diameter of  $(2.32\pm0.45)$  cm with 46 single-port single-channel and 53 single-port multi-channel cases (Table 1); Group B had  $(3.42\pm0.31)$  cm with 33 single-port single-channel and 45 single-port multi-channel cases (Table 2); Group C had  $(4.60\pm0.28)$  cm with 18 single-port single-channel and 23 single-port multi-channel cases (Table 3).

Inclusion criteria: ① Benign adrenal lesions; ② Body Mass Index (BMI)<30 kg/m<sup>2</sup>; ③ No history of related abdominal surgery, no severe cardiopulmonary complications; ④ American Society of Anesthesiologists (ASA) classification grade I or II. Exclusion criteria: ① Patients with severe renal disease; ② Malignant adrenal tumor.; ③History of previous abdominal surgery as well as severe cardiopulmonary complications; ④ Patients with coagulation disorders; ⑤ Other significant underlying diseases, etc.

All patients underwent CT or MRI for localization diagnosis. Preoperative hormonal and CT examinations suggesting pheochromocytoma were treated with phenoxybenzamine to dilate blood vessels for 2 weeks to control blood pressure; if ineffective, nifedipine controlled-release tablets and metoprolol tartrate were added to control blood pressure and heart rate, respectively. Perioperative blood pressure was controlled at 120-140/70-80 mmHg (1 mmHg=0.133 kPa) and heart rate around 80 beats/min, with crystalloid and colloid expansion starting 3 days before surgery. Patients considered preoperatively to have primary hyperaldosteronism were treated with spironolactone and antihypertensive drugs to correct blood potassium and control blood pressure and potassium within normal ranges. For preoperative suspicion of Cushing's syndrome, blood pressure was controlled below 140/90 mmHg, blood sugar below 10 mmol/L, and electrolyte acid-base balance corrected. For patients considered preoperatively to have non-functional adenomas, no special preparation was required before surgery.



# Fig. 1 Research flowchart

**Table 1** Comparison of General Information and SurgicalOutcomes of Group A patients

| Parameter                          | Single-Port<br>Single-<br>Channel<br>Group( <i>n</i> = 46) | Single-Port<br>Multi-Channel<br>Group( <i>n</i> = 53) | <i>p-</i><br>val-<br>ue |
|------------------------------------|--|---|-------------------------|
| Age (years)                        | 48.6±6.9   | 49.8±5.7  | 0.88                    |
| Male/Female (n)                    | 22/24  | 25/28   | 0.96                    |
| Body Mass Index (kg/m²)            | $26.4 \pm 4.5$   | $26.9 \pm 3.3$  | 0.43                    |
| Left/Right (n)                     | 20/26  | 26/27   | 0.52                    |
| Pheochromocytoma                   | 2  | 3   | —                       |
| Aldosteronoma                      | 18   | 17  | —                       |
| Non-functional Tumor               | 21   | 26  | —                       |
| Cushing's Syndrome                 | 5  | 7   |                         |
| Surgical duration/min              | $58.00 \pm 6.79$   | $56.00 \pm 5.89$                                      | 0.09                    |
| Hospital Stay/days                 | $4.26 \pm 1.34$  | $6.45 \pm 1.28$                                       | < 0.01                  |
| Blood Loss/mL                      | $35.25 \pm 5.83$   | $38.00 \pm 4.16$                                      | 0.89                    |
| Postoperative VAS Score/<br>points | 3.56±0.52  | 5.32±0.61   | <0.01                   |
| Subcutaneous Emphysema             | 0  | 3   | 0.04                    |
| Incision Length/cm                 | $3.18 \pm 0.36$  | $5.45 \pm 0.50$                                       | < 0.01                  |
| Additional Puncture Holes          | 0  | 0   |                         |

| Table 2         Comparison of General Information and Surgical |
|--|
| Outcomes of Group B patients                                   |

| Parameter                          | Single-Port<br>Single-<br>Channel<br>Group( <i>n</i> =33) | Single-Port<br>Multi-Channel<br>Group( <i>n</i> = 45) | <i>p-</i><br>val-<br>ue |
|------------------------------------|---|---|-------------------------|
| Age (years)                        | $52.35 \pm 8.12$  | $53.00 \pm 9.01$                                      | 0.53                    |
| Male/Female (n)                    | 15/18   | 20/25   | 0.11                    |
| Body Mass Index (kg/m²)            | $26.91 \pm 1.34$  | $26.41 \pm 2.45$                                      | 0.31                    |
| Left/Right (n)                     | 14/19   | 19/26   | 0.61                    |
| Pheochromocytoma                   | 4   | 5   | —                       |
| Aldosteronoma                      | 9   | 14  | —                       |
| Non-functional Tumor               | 17  | 21  | _                       |
| Cushing's Syndrome                 | 3   | 6   |                         |
| Surgery Duration/min               | $65.24 \pm 7.56$  | $62.15 \pm 6.03$                                      | 0.11                    |
| Hospital Stay/days                 | $4.93 \pm 1.34$   | 6.23±1.27   | <0.01                   |
| Blood Loss/mL                      | $36.96 \pm 2.23$  | 36.84±5.21  | 0.89                    |
| Postoperative VAS Score/<br>points | 3.47±0.64   | 5.45±0.61   | <0.01                   |
| Subcutaneous Emphysema             | 0   | 4   | 0.03                    |
| Incision Length/cm                 | $3.95 \pm 0.41$   | $5.42 \pm 0.51$                                       | <0.01                   |
| Additional Puncture Holes          | 2   | 0   | _                       |

| Table 3         Comparison of general information and sur | gical |
|---|-------|
| outcomes of group C patients                              |       |

| Parameter                            | Single-Port<br>Single-<br>Channel<br>Group( <i>n</i> = 18) | Single-Port<br>Multi-Channel<br>Group( <i>n</i> = 23) | <i>p-</i><br>val-<br>ue |
|--------------------------------------|--|---|-------------------------|
| Age (years)                          | $55.86 \pm 6.21$   | $53.75 \pm 6.89$                                      | 0.33                    |
| Male/Female (n)                      | 10/9   | 13/10   | 0.83                    |
| Body Mass Index (kg/m <sup>2</sup> ) | $27.28 \pm 3.21$   | $26.89 \pm 3.61$                                      | 0.75                    |
| Left/Right (n)                       | 8/10   | 9/14  | 0.21                    |
| Pheochromocytoma                     | 5  | 7   | _                       |
| Aldosteronoma                        | 4  | 9   | _                       |
| Non-functional Tumor                 | 7  | 6   | _                       |
| Cushing's Syndrome                   | 2  | 1   | _                       |
| Surgery Duration/min                 | $83.43 \pm 8.52$   | $75.65 \pm 7.92$                                      | < 0.01                  |
| Hospital Stay/days                   | $6.35 \pm 0.88$  | 6.71±1.21   | 0.07                    |
| Blood Loss/mL                        | 56.21±8.31   | $61.42 \pm 9.54$                                      | 0.52                    |
| Postoperative VAS Score/<br>points   | 5.25±0.61  | 5.49±0.91   | 0.14                    |
| Subcutaneous Emphysema               | 1  | 3   | 0.31                    |
| Incision Length/cm                   | $5.50 \pm 0.64$  | $5.69 \pm 0.82$                                       | 0.08                    |
| Additional Puncture Holes            | 7  | 0   | <0.01                   |

The study was conducted in accordance with the Declaration of Helsinki. The study was approved by the Institutional Review Board of the first People's Hospital of Lianyungang. And the reference number is 2016-LYYL-20. Investigators provided subjects or their legal guardians with detailed information about the purpose, methods, risks, and benefits of the study. Subjects or their legal guardians signed and dated informed consent after fully understanding and consent.

# **Operation procedure**

Single-port single-channel group surgical method: Under general anesthesia, the patient is positioned in a healthy lateral decubitus position with a slightly elevated waist bridge. A 1.2 cm transverse incision is made under the 12th rib on the posterior axillary line, and after locating the adrenal tumor with ultrasound, an 18G Veress needle is inserted towards the tumor until it reaches the tumor capsule. Methylene blue solution is injected as the needle is withdrawn (diluted to 0.25 mg/ml) (Fig. 2A). The closed puncture technique [4] is used to enter the retroperitoneal space and gas is injected to expand this space. A 12 mm trocar is inserted along the direction of the puncture needle, with an intra-abdominal pressure of 10-15mmHg. A side-view 0° laparoscope (with a 6 mm diameter channel for the operating forceps) is inserted (Fig. 2B). Under the pneumoperitoneum pressure, fat tissue in the retroperitoneal space appears island-like, connected by translucent connective tissue (Fig. 3A). Under direct vision, the trocar is advanced along the methylene blue marker to the Gerota's fascia, where a small hole is made (Fig. 3B), and the laparoscope continues towards the adrenal tumor, forming a retroperitoneal tunnel [5] (Fig. 4A), reaching the tumor (Fig. 4B). During the procedure, the trocar and the body of the laparoscope can be used to push aside the surrounding adrenal tissue to appropriately expand the operating space. If difficulties arise due to patient obesity or other reasons, additional punctures can be made to complete the surgery. The specimen is placed in a specimen bag, one end of which is removed through the incision (Fig. 5A), the specimen is then removed (Fig. 5B), a retroperitoneal drainage tube is placed, and the incision is sutured.

Single-port multi-channel group surgical method: Under general anesthesia, the patient is positioned in a healthy lateral decubitus position. A 3.5 cm transverse incision is made under the 12th rib on the mid-axillary line, through the external oblique muscle. The muscles and lumbodorsal fascia are separated using a vascular clamp to enter the retroperitoneum, and fingers are used to separate and expand the retroperitoneal space. A single-port multi-channel operating sleeve is inserted



Fig. 2 Injection of methylene blue solution for localization (A); Insertion of a 0° lateral-view laparoscope (B)

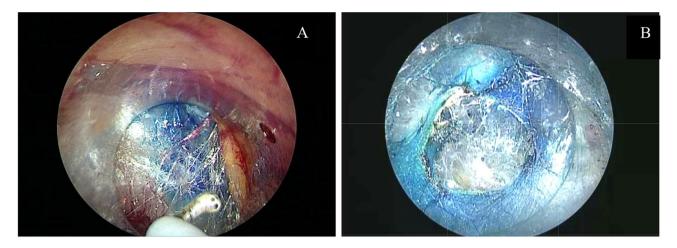


Fig. 3 The adipose tissue is visible in an island-like distribution, connected by transparent connective tissue, with visible methylene blue markings (A). Dissect along the methylene blue markings to the Gerota's fascia and create a small opening (B)

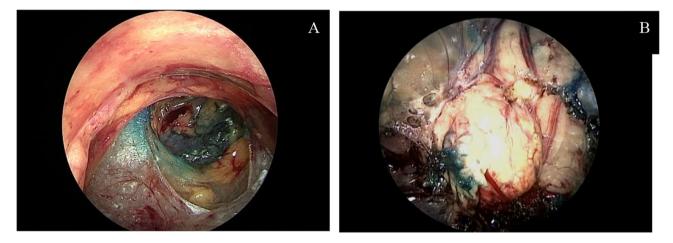


Fig. 4 Forming a retroperitoneal tunnel (A). reaching the tumor (B)



Fig. 5 Pull out one end of the specimen bag through the incision (A), the specimen is removed (B)

(Fig. 6A), pneumoperitoneum is established, and a laparoscope is inserted (Fig. 6B). Gerota's fascia is incised, the kidney is mobilized dorsally and ventrally, and the perirenal fat is incised to expose the adrenal gland and tumor. The vascular pedicle surrounding the tumor is separated and excised. the tumor was removed and then the drainage was inserted.

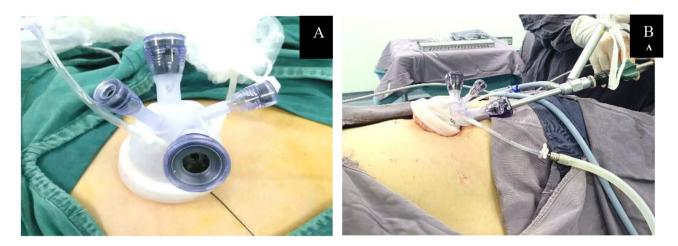


Fig. 6 Insertion of a single-port multi-channel sheath(A). Insertion of the laparoscope (B)

#### Data and statistics

Primary objective: length of hospital stay. Secondary objectives: gender, age, body mass index (BMI), surgical duration, intraoperative blood loss, postoperative visual analog scale (VAS) for pain, incision length (total length of all incisions), and the need for additional puncture holes. Statistical analysis was performed using SPSS 27.0. Normally distributed data were presented in the form of Mean±SD, while non-normally distributed data were represented using Median (P25, P75). Categorical variables were presented as numbers and percentages. Data comparisons between the two groups was performed using t-test, rank sum test, chi-square test, and Fisher's exact test: Student's t-test was used for normal distribution data, Mann-Whitney U test was used for non-normally distribution data, chi-square test and Fisher's exact test were used for categorical variables data. Missing data were handled using BOCF. Results are presented with 95% confidence intervals. A p-value<0.05 was considered statistically significant.

# Results

All surgeries were successfully completed without major bleeding or associated organ damage. In group A, no significant differences were observed between the single-port, single-channel group and the single-port, multichannel group in terms of gender, age, BMI, surgical duration, and blood loss (P>0.05). However, significant differences were found in hospital stay, VAS score, subcutaneous emphysema rate, and incision length (P < 0.05) (Table 1). In group B, there were no significant differences between the single-port, single-channel and singleport, multi-channel groups in gender, age, BMI, surgical duration, and blood loss (P>0.05). Significant differences were found in hospital stay, VAS score, subcutaneous emphysema rate, and incision length (P < 0.05) (Table 2). In group C, no significant differences were found between the single-port, single-channel group and the 
 Table 4
 Key findings between the two groups of surgical techniques

| Parameter                 | Single-Port<br>Single-Chan- | Single-Port<br>Multi-Chan- | <i>p-</i><br>val- |
|---------------------------|-----------------------------|----------------------------|-------------------|
|                           |                             |                            |                   |
| Group A                   |                             |                            |                   |
| Hospital Stay/days        | $4.26 \pm 1.34$             | $6.45 \pm 1.28$            | <0.01             |
| Postoperative VAS Score/  | $3.56 \pm 0.52$             | $5.32 \pm 0.61$            | < 0.01            |
| points                    |                             |                            |                   |
| Incision Length/cm        | 3.18±0.36                   | $5.45 \pm 0.50$            | < 0.01            |
| Group B                   |                             |                            |                   |
| Hospital Stay/days        | $4.93 \pm 1.34$             | $6.23 \pm 1.27$            | < 0.01            |
| Postoperative VAS Score/  | $3.47 \pm 0.64$             | $5.45 \pm 0.61$            | < 0.01            |
| points                    |                             |                            |                   |
| Incision Length/cm        | $3.95 \pm 0.41$             | $5.42 \pm 0.51$            | < 0.01            |
| Group C                   |                             |                            |                   |
| Surgery Duration/min      | $83.43 \pm 8.52$            | $75.65 \pm 7.92$           | < 0.01            |
| Additional Puncture Holes | 7                           | 0                          | < 0.01            |

single-port, multi-channel group in terms of gender, age, BMI, hospital stay, blood loss, VAS score, incision length, and subcutaneous emphysema rate (P>0.05). There were significant differences in surgical duration and the rate of additional puncture holes required (P<0.05)(Table 3).

In summary: the single-channel technique is superior to the multichannel technique for tumors less than 4 cm in terms of hospital stay, postop VAS score, and incision length, whereas for tumors greater than 4 cm, the multichannel technique is superior to the single-channel technique in terms of shorter hospital stay and the need for additional punctures (Table 4). Postoperative pathology was consistent with preoperative diagnoses. Follow-up ranged from 4 to 22 months, averaging 11.5 months, with no recurrence or related complications observed.

## Discussion

Laparoscopic adrenal surgery has now become the gold standard for treating adrenal tumors. With the improvement of surgical experience, techniques, and instruments, laparoscopic adrenal surgery has made significant progress in tissue dissection, bleeding control, and tumor localization [6, 7]. Traditional retroperitoneoscopic adrenal surgery first establishes a retroperitoneal space (formed by artificial separation with a balloon or instruments), then inserts relevant operative instruments and a camera, and based on inherent anatomical landmarks within the retroperitoneum, separates, cleans, and expands the retroperitoneal tissue to expose the adrenal tumor. Compared to open surgery, there is less damage to the abdominal wall, but the anatomical separation operations within the retroperitoneum are not reduced. In recent years, single-port retroperitoneoscopic adrenalectomy has rapidly developed and gradually gained acceptance among patients due to its minimally invasive effects better meeting patients' cosmetic demands [8–12].

Single-port retroperitoneoscopic adrenal surgery can be divided into single-port multi-channel and single-port single-channel surgeries. Single-port multi-channel laparoscopic surgery uses a single-port multi-channel trocar, which, compared to traditional laparoscopy, has a relatively lower risk of bleeding and incisional hernia during the creation of channels, and allows for direct specimen extraction without the need to extend the incision. However, the operative process of single-port multi-channel laparoscopic adrenal lesion resection in the retroperitoneum is similar to that of traditional retroperitoneoscopy, with no reduction in the anatomical separation operations within the retroperitoneum, leading to separation injuries. Using a large single port, all instruments operate through a parallel channel, violating the "triangulation principle" of laparoscopic operation [13, 14], leading to the "chopstick effect" [15], where frequent conflicts occur between the operating instruments and the laparoscope lens.

Through the practice of single-port, single-channel laparoscopic surgery, we found that the adrenal glands are located deep within the body, requiring a long path in the retroperitoneum to locate them, advancing layer by layer based on relevant anatomical landmarks. In this process, only when the upper layer is fully opened can deep anatomical confirmation and opening be facilitated, reducing the obstruction of the retroperitoneal tissue to the field of view. In the retroperitoneum, the operative space from the abdominal wall to the adrenal tumor is a process of gradual narrowing, which inevitably causes damage to the normal retroperitoneal tissue. The process of operating from the abdominal wall to the adrenal tumor is merely to establish a space to reach the tumor. Once the adrenal tumor is located, the operations such as anatomical separation are focused on the tumor, rendering most of the operative space redundant. Therefore, we use ultrasonography for localization and methylene blue to mark the adrenal tumors, creating a direct path to them. This allows us to perform separation operations directly on the adrenal tumors without fully opening and separating each layer of retroperitoneal normal tissue, reducing retroperitoneal separation injuries and related complications [16]. However, due to the small operating space, it is more challenging to handle complex cases such as larger adrenal tumors. Therefore, we need to consider which patients are suitable for single-port, singlechannel or single-port, multi-channel surgeries.

In the literature on retroperitoneoscopic surgery, surgeons often select adrenal tumors with a diameter of <4 cm for surgery [17–20]. Fewer surgeons opt for single-port retroperitoneoscopic surgery for adrenal tumors with a diameter of >4 cm. In the initial stages of performing single-port retroperitoneoscopic adrenal tumor surgery, our hospital also selected smaller tumors with a diameter of 2–3 cm, gradually increasing the size of the tumors as proficiency in the single-port laparoscopic technique was achieved. In our study, we found that for tumors smaller than 4 cm, single-channel technique is superior to multi-channel technique in terms of hospital stay, postoperative VAS scores, and incision length. However, for tumors larger than 4 cm, multi-channel technique is superior to single-channel technique in terms of hospital stay and additional punctures.

In single-port retroperitoneoscopic surgery for tumors with a diameter >4 cm, it was found that the increased diameter of the tumor created a broader free space, requiring a larger operating range for the instruments, making the use of a single-port, single-channel laparoscope more difficult. This is especially true for pheochromocytomas, which are rich in blood vessels and adherent to surrounding structures, causing large intraoperative blood pressure fluctuations and higher surgical risks. Often, it is necessary to add auxiliary ports to aid in exposure and separation, and to be prepared to switch to traditional laparoscopy. This study has some limitations and shortcomings: the number of cases is still insufficient, and the research results need more cases to be further confirmed. The follow-up time is short, and the long-term effects of the operation are still pending to be determined by longer follow-up.

# Conclusions

When performing adrenal tumor surgery, both doctors and patients prefer a less invasive approach, but it's also worth considering what size of tumor can maximize patient benefits when operated on with a single-port, single-channel laparoscope. The single-port, singlechannel laparoscope has a distinct advantage in surgeries where the tumor's maximum diameter is  $\leq 4$  cm, as it can directly reach the target organ, reducing separation operations, causing less damage, and having a good cosmetic effect. In surgeries for adrenal tumors with a maximum diameter >4 cm, the multichannel technique is superior to the single-channel technique in terms of shorter hospital stay and the need for additional punctures.

#### Abbreviations

- BMI Body Mass Index
- ASA American Society of Anesthesiologists
- VAS Visual Analogue Scale
- BOCF Baseline Observation Carried Forward
- CT Computed Tomography

#### Acknowledgements

The authors would like to thank all our participants in this study.

#### Author contributions

PCZ and FHS conceived of the study. NHS, YHP and YLZ participated in the design, analysis and drafted the manuscript of the study. They contributed equally to the study, and all authors gave final approval for the manuscript and agree to be accountable for all aspects of the work herein.

#### Funding

This work was supported by Lianyungang Health young Doctor Science and Technology Project (QN202405), Young Talents Project of Lianyungang First People's Hospital (QN2413), Lianyungang Cancer prevention and Treatment Science and Technology Development Program Project (QN202405), Lianyungang city science Association soft project (Lkxyb24188).

#### Data availability

No datasets were generated or analysed during the current study.

#### Declarations

#### Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. The study was approved by the Institutional Review Board of the first People's Hospital of Lianyungang. And the reference number is 2016-LYYL-20. Informed consent was obtained from of all subjects and/or their legal guardian(s).

#### **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare no competing interests.

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## Received: 18 December 2023 / Accepted: 26 December 2024 Published online: 06 January 2025

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