

Oncology Treatment Discovery

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Oncology Treatment Discovery

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The Impact of Timing of Laparoscopic Cholecystectomy after Percutaneous Transhepatic Gallbladder Drainage on the Final Therapeutic Effect in Patients with Acute Calculous Cholecystitis

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Abstract: *Objective:* To explore the therapeutic effect of laparoscopic cholecystectomy (LC) after percutaneous transhepatic gallbladder drainage (PTGBD) in the treatment of acute calculous cholecystitis (ACC). *Methods:* A total of 50 ACC patients treated from January 2022 to January 2025 were selected as samples and randomly divided into two groups. Group A received LC after PTGBD, while Group B received LC only. Surgical indicators, inflammatory factors, liver function indicators, complications, and conversion to open surgery rates were compared between the two groups. *Results:* The operation time, postoperative abdominal drainage time, postoperative anal exhaust time, and hospital stay in Group A were shorter than those in Group B, and the intraoperative blood loss was lower than that in Group B ($P < 0.05$). The levels of procalcitonin (PCT), C-reactive protein (CRP), and interleukin-6 (IL-6) in Group A were lower than those in Group B ($P < 0.05$). The levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TBiL), and amylase (AMY) in Group A were lower than those in Group B ($P < 0.05$). The complication rate and conversion to open surgery rate in Group A were lower than those in Group B ($P < 0.05$). *Conclusion:* LC after PTGBD for the treatment of ACC can accelerate postoperative recovery, inhibit inflammatory factors, improve liver function, and is safe and efficient.

Keywords: Acute calculous cholecystitis; Laparoscopic cholecystectomy; Percutaneous transhepatic gallbladder drainage

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1. Introduction

ACC is an acute inflammatory disease related to bile excretion disorders caused by gallstone blockage of the cystic duct. Long-term inflammatory stimulation can damage the gallbladder mucosa, requiring surgical treatment. LC is the preferred treatment option for ACC patients. However, some ACC patients have multiple comorbidities and poor physiological status, which increases the risk of LC surgery, and postoperative complications such as

infection and bile leakage are prone to occur^[1]. In addition, LC is not suitable for ACC patients with gallbladder necrosis or perforation, and some patients may require conversion to open surgery due to critical intraoperative conditions. In recent years, PTGBD has been gradually used in the treatment of ACC, which can quickly control acute inflammation. Performing LC after PTGBD can improve the surgical success rate while reducing surgical risks. Based on this, this article explores the treatment effect of LC after PTGBD using 50 ACC patients treated from January 2022 to January 2025 as samples.

2. Materials and methods

2.1. Materials

Fifty ACC patients treated from January 2022 to January 2025 were selected as samples and randomly divided into two groups. There was no significant difference in baseline data between Group A and Group B ($P > 0.05$) (**Table 1**).

Table 1. Analysis of baseline data of ACC patients

Group	<i>n</i>	Gender		Age (years)		Duration (days)		Number of stones	
		Male	Female	Range	Mean	Range	Mean	Single	Multiple
Group A	25	15 (60.00)	10 (40.00)	28–64	46.18 ± 2.86	1–3	1.61 ± 0.42	19 (76.00)	6 (24.00)
Group B	25	16 (64.00)	9 (36.00)	28–65	46.21 ± 2.79	1–4	1.59 ± 0.46	18 (72.00)	7 (28.00)
χ^2/t	-	0.0849		0.0375		0.1605		0.1040	
<i>P</i>	-	0.7708		0.9702		0.8731		0.7471	

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) laboratory and imaging results suggestive of acute calculous cholecystitis (ACC); (2) compatibility with the 2016 World Emergency Surgery Association Guidelines^[2] for ACC; (3) informed consent; (4) presence of surgical indications. Exclusion criteria: (1) history of abdominal surgery; (2) coagulation disorders; (3) mental disorders; (4) endocrine disorders.

2.3. Treatment methods

Group A: PTGBD followed by LC

- (1) Patients were placed in a supine position, and color Doppler ultrasonography was used to identify the puncture site. The gallbladder was targeted, and a local anesthetic was administered for puncture at the closest point on the skin, maintaining a 90° angle of needle insertion and avoiding blood vessels. The needle tip was inserted through the liver tissue into the center of the gallbladder, and successful puncture was indicated by the smooth flow of bile after withdrawing the needle core. An appropriate amount of bile was collected for testing, and a drainage bag was connected and secured.
- (2) B-mode ultrasonography was performed 4–12 weeks after PTGBD. When the gallbladder wall thickness was found to be less than 0.4 cm, LC was performed. General anesthesia with endotracheal intubation was administered, and a pneumoperitoneum of 12–15 mmHg was created. A 10 mm Trocar was inserted after puncture to explore the abdominal cavity, observe the physiological structure and condition of the gallbladder, and analyze the relationship between the gallbladder and adjacent tissues. The laparoscope assistant and surgeon stood on the left side of the ACC patient. A 1 cm primary operating port was opened

under the xiphoid process of the upper abdomen, and a 0.5 cm secondary operating port was opened at the right mid-clavicular line rib margin. The gallbladder tissue was carefully explored. After completing the above operations, the cystic artery was clamped after dissociating the gallbladder triangle, and then the cystic duct was cut to remove the gallbladder. A drainage tube was placed and secured.

Group B: LC operation was the same as Group A.

2.4. Observation indicators

- (1) Surgical indicators: Operating time, postoperative abdominal cavity drainage time, postoperative anal exhaust time, hospital stay, and intraoperative blood loss were recorded.
- (2) Inflammatory factor indicators: 3 ml of fasting venous blood was collected before surgery and 1 day after surgery, centrifuged at 3000 r/min for 15 minutes, and the supernatant was taken. PCT, CRP, and IL-6 levels were monitored by enzyme-linked immunosorbent assay (ELISA).
- (3) Liver function indicators: 6 ml of fasting venous blood was collected before surgery and 1 day after surgery, and serum was obtained. AST, ALT, TBiL, and AMY levels were monitored using an automatic biochemical analyzer.
- (4) Complications and conversion to open surgery: Incision infection, incision bleeding, fat liquefaction, bile leakage, and conversion to open surgery were recorded.

2.5. Statistical analysis

SPSS 23.0 was used for data processing. Count data were recorded as percentages (%) and analyzed using the chi-square test (χ^2 test). Measurement data were recorded as mean \pm standard deviation (SD) and analyzed using the *t*-test. Statistical differences were considered significant at $P < 0.05$.

3. Results

3.1. Surgical indicators

The surgical indicators of Group A were better than those of Group B, with $P < 0.05$ (Table 2).

Table 2. Comparison of surgical indicators for ACC patients (mean \pm SD)

Group	Operating time (min)	Postoperative abdominal drainage time (d)	Postoperative anal exhaust time (h)	Hospitalization time (d)	Intraoperative bleeding (mL)
Group A ($n = 25$)	67.19 \pm 1.26	2.71 \pm 0.48	20.39 \pm 1.58	5.71 \pm 1.05	54.61 \pm 3.25
Group B ($n = 25$)	84.22 \pm 1.81	7.62 \pm 0.86	29.48 \pm 2.16	9.05 \pm 1.11	76.44 \pm 3.49
<i>t</i>	38.6101	24.9267	16.9831	10.9298	22.8878
<i>P</i>	0.0000	0.0000	0.0000	0.0000	0.0000

3.2. Inflammatory factor indicators

One day after surgery, the levels of PCT, CRP, and IL-6 in Group A were lower than those in Group B, with $P < 0.05$ (Table 3).

Table 3. Comparison of inflammatory factors in ACC (mean \pm SD)

Group	PCT (ng/L)		CRP (mg/L)		IL-6 (ng/L)	
	Preoperative	Postoperative 1d	Preoperative	Postoperative 1d	Preoperative	Postoperative 1d
Group A ($n = 25$)	10.49 \pm 1.28	14.32 \pm 1.05	16.79 \pm 2.42	31.82 \pm 1.29	45.44 \pm 3.26	53.29 \pm 1.81
Group B ($n = 25$)	10.44 \pm 1.31	17.42 \pm 1.11	16.82 \pm 2.39	40.11 \pm 1.86	45.36 \pm 3.29	64.12 \pm 2.06
t	0.1365	10.1444	0.0441	18.3119	0.0864	19.7469
P	0.8920	0.0000	0.9650	0.0000	0.9315	0.0000

3.3. Liver function indicators

One day after surgery, the levels of AST, ALT, TBIl, and AMY in Group A were lower than those in Group B, with $P < 0.05$ (Table 4).

Table 4. Analysis of liver function indicators in ACC before and after treatment (mean \pm SD)

Group	AST (U/L)		ALT (U/L)		TBIl (μ mol/L)		AMY (U/L)	
	Before	After	Before	After	Before	After	Before	After
Group A ($n = 25$)	85.79 \pm 2.12	40.18 \pm 1.75	130.58 \pm 8.81	46.88 \pm 3.26	20.71 \pm 3.26	12.81 \pm 1.51	241.62 \pm 5.16	124.62 \pm 3.26
Group B ($n = 25$)	85.81 \pm 2.14	50.81 \pm 1.89	130.61 \pm 8.79	59.03 \pm 4.47	20.69 \pm 3.29	16.06 \pm 1.87	241.59 \pm 5.19	186.06 \pm 4.68
t	0.0332	20.6346	0.0121	10.9806	0.0216	6.7609	0.0205	53.8616
P	0.9737	0.0000	0.9904	0.0000	0.9829	0.0000	0.9837	0.0000

3.4. Complication indicators

The complication rate and conversion to open surgery rate were lower in Group A compared to Group B, with $P < 0.05$ (Table 5).

Table 5. Comparison of complications and conversion to open surgery indicators ($n, \%$)

Group	Incision infection	Incision bleeding	Fat liquefaction	Bile leakage	Incidence	Conversion to laparotomy
Group A ($n = 25$)	0 (0.00)	0 (0.00)	1 (4.00)	0 (0.00)	1 (4.00)	0 (0.00)
Group B ($n = 25$)	2 (8.00)	2 (8.00)	1 (4.00)	1 (4.00)	6 (24.00)	4 (16.00)
χ^2	-	-	-	-	4.1528	4.3478
P	-	-	-	-	0.0416	0.0371

4. Discussion

ACC is an abdominal emergency related to the blockage of the cystic duct by stones. After the occurrence of ACC, the typical symptom is right upper abdominal colic, which can spread to the right shoulder and back, and the pain may intensify during the night, after eating fatty foods, or after a full meal. As the pain persists, patients may experience nausea and vomiting, with the vomit mostly consisting of stomach contents. Additionally, patients with less severe ACC may experience low-grade fever and mild jaundice, while those with more severe conditions

may have high fever, chills, and icterus of the sclera and skin. Therefore, early surgical treatment is necessary for ACC, and LC is a commonly used surgical method characterized by minimal trauma and good prognosis. However, the surgery requires dissection of the Calot's triangle, and due to the adhesion of local tissues caused by gallbladder edema in ACC patients, the difficulty of dissecting the Calot's triangle increases, thus raising the surgical difficulty. This is especially true for middle-aged and elderly patients with underlying diseases, where the risk of LC treatment is higher and can affect prognosis. Therefore, to ensure the safety of ACC patients, it is necessary to explore combined surgical treatment ^[3]. PTGBD is an alternative treatment for ACC, offering advantages such as mature technology and simple operation. Guided by ultrasonography, the puncture operation is performed to quickly drain purulent bile out of the body, relieving the high-pressure state of the gallbladder, avoiding bile continuously stimulating the gallbladder wall, which may cause rupture, and preventing the body from absorbing large amounts of toxins that can induce adverse reactions. This lays a favorable foundation for subsequent LC surgery ^[4]. In the data presented in this article, Group A had shorter operation time, postoperative abdominal drainage time, postoperative anal exhaust time, and hospital stay, as well as lower intraoperative blood loss compared to Group B ($P < 0.05$). The reason for this may be that in the early stages of ACC, there is adhesion in the gallbladder triangle, and for those with severe inflammatory reactions, edema and congestion are severe, increasing the difficulty of LC operation and potentially increasing blood loss in tissues adjacent to the gallbladder, thereby prolonging operation time and increasing intraoperative blood loss. In this article, PTGBD was performed before LC, which quickly controlled infection and relieved local edema of the gallbladder, inhibiting inflammation progression. After 4-12 weeks, B-ultrasound was performed, and LC was performed at an appropriate time, facilitating the positioning and separation of the gallbladder by the surgeon. Therefore, the difficulty of the operation was reduced, intraoperative blood loss was decreased, and operation time was shortened. Additionally, the combined surgery had minimal trauma, which was beneficial for the patient's prognosis ^[5].

For patients with ACC, LC treatment after PTGBD still involves invasive procedures that can stimulate the body to secrete large amounts of inflammatory factors, potentially exacerbating the body's stress response and even affecting postoperative recovery from ACC. PCT, a protein, provides objective feedback on the inflammatory response, and its level is positively correlated with inflammation. CRP is an acute-phase reactant protein that can rise rapidly in response to traumatic stimuli or adverse external factors. IL-6 binds to relevant receptors in the human body, accelerating the progression of inflammatory responses; the longer the surgery and the greater the trauma, the higher the level of IL-6 ^[6]. The data in this article shows that the levels of PCT, CRP, and IL-6 in Group A were lower than those in Group B, with $P < 0.05$. The reason for this is that LC treatment after PTGBD utilizes imaging technology to observe the condition of the lesion and the physiological anatomy of the gallbladder, which can avoid a series of complications induced by unnecessary trauma and improve patients' physical and mental health. Performing PTGBD before LC can also reduce the pressure in the gallbladder cavity, inhibit the body's absorption of toxins, and thereby control local inflammation and lower the levels of various inflammatory factors ^[7].

Another set of data indicates that the AST, ALT, TBiL, and AMY indicators in Group A were lower than those in Group B, with $P < 0.05$. The reason for this is that LC after PTGBD in the treatment of ACC patients can avoid potential risk events associated with emergency surgery, reduce gallbladder edema pressure, inhibit local inflammation, and relieve obstruction. Simultaneously, it can reduce the risk of perforation and necrotizing fasciitis in the affected area, thereby buying time for surgical treatment of ACC patients and benefiting liver function protection ^[8]. Furthermore, LC after PTGBD can completely drain pus from the gallbladder, avoiding liver function damage caused by pneumoperitoneum during LC and further reducing the risk of perioperative liver

function impairment. Hence, various liver function indicators recover well after surgery^[9].

The final set of data shows that the complication rate and conversion to open surgery rate were lower in Group A compared to Group B, with $P < 0.05$. The small incision of the PTGBD procedure causes minimal damage to ACC patients and does not induce a severe stress response. Additionally, LC after PTGBD facilitates precise dissection of the lesion by the surgeon, reduces surgical difficulty, avoids complications caused by unnecessary trauma, and lowers the risk of intraoperative conversion to open surgery, resulting in high overall surgical safety^[10]. To promote recovery after LC following PTGBD, it is essential to maintain clean and dry wounds, avoid contamination or exposure to water, regularly evaluate the wounds for redness, swelling, or bleeding, monitor body temperature, and immediately report any abnormalities. Patients should also follow medical advice on dressing changes and avoid touching the wound or removing sutures independently to prevent infection.

5. Conclusion

In summary, LC treatment after PTGBD for ACC patients can reduce surgically induced inflammation, shorten postoperative recovery time, and result in fewer perioperative complications, making it worthy of promotion. However, due to the small sample size of ACC cases included in this study, there may be bias in the treatment effect of LC after PTGBD. Therefore, it is recommended to increase the number of ACC cases in future studies and analyze long-term postoperative prognosis.

Disclosure statement

The authors declare no conflict of interest.

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Pharmacological Study of Azithromycin Combined with Cephalosporins in the Treatment of AECOPD

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Abstract: *Objective:* To analyze the efficacy of azithromycin combined with cephalosporins in the treatment of patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD). *Methods:* A total of 62 AECOPD patients who visited the hospital from January 2024 to December 2024 were selected as samples and randomly divided into two groups using the lottery method. Group A was treated with azithromycin and cephalosporins, while Group B was treated with cephalosporins only. The efficacy, lung function, inflammatory factors, and adverse reactions were compared between the two groups. *Results:* The efficacy of AECOPD treatment in Group A was higher than that in Group B ($P < 0.05$). The forced vital capacity (FVC), peak expiratory flow (PEF), and forced expiratory volume in 1 second (FEV1) in Group A were all higher than those in Group B ($P < 0.05$). The levels of interleukin-6 (IL-6), interleukin-8 (IL-8), and tumor necrosis factor- α (TNF- α) in Group A were all lower than those in Group B ($P < 0.05$). *Conclusion:* The combination of azithromycin and cephalosporins in the treatment of AECOPD can inhibit inflammatory factors and improve lung function, with safety and high efficiency.

Keywords: AECOPD; Cephalosporins; Azithromycin; Pharmacological analysis

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1. Introduction

AECOPD is characterized by airflow limitation, and under the influence of the disease, sputum secretion increases, which can lead to respiratory mucosal edema and impairment of lung ventilation function. AECOPD is often associated with infection, has a high incidence and fatality rate, and requires prompt anti-infective treatment. After the occurrence of AECOPD, patients experience exacerbation of symptoms such as wheezing, shortness of breath, and cough in a short period of time, accompanied by increased sputum production and purulent sputum. A few patients may also experience fever, insomnia, and lethargy, requiring early medication management. Cephalosporins are commonly used in the clinical treatment of AECOPD for their anti-infective effects, but the

efficacy of monotherapy is limited. Azithromycin can effectively inhibit bacteria, and since P450 enzymes are not involved in its metabolic process, it can reduce the risk of antibiotic-related gastrointestinal reactions and liver damage ^[1]. Based on this, this article explores the pharmacological effects of azithromycin combined with cephalosporins using 62 AECOPD patients who visited our hospital from January 2024 to December 2024 as samples.

2. Materials and methods

2.1. Materials

A total of 62 AECOPD patients who visited our hospital from January 2024 to December 2024 were selected as samples and randomly divided into two groups using the lottery method. There was no statistically significant difference in AECOPD data between Group A and Group B ($P > 0.05$) (Table 1).

Table 1. Analysis of AECOPD data

Group	<i>n</i>	Gender (%)		Age (years old)		Course of disease (years)	
		Male	Female	Range	Mean	Range	Mean
Group A	31	16 (51.61)	15 (48.39)	42–68	57.19 ± 1.88	2–6	4.11 ± 0.25
Group B	31	17 (54.84)	14 (45.16)	43–69	57.21 ± 1.91	2–7	4.13 ± 0.31
χ^2/t	-	0.0648		0.0416		0.2796	
<i>P</i>	-	0.7991		0.9670		0.7807	

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Comply with the AECOPD criteria in the “Practical Guideline for Clinical Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease in Elderly Chinese” ^[2]; (2) Signed informed consent; (3) Lung function indicators and CT results suggest AECOPD. Exclusion criteria: (1) Accompanied by mental illness; (2) History of malignant tumors; (3) Disease has entered a stable phase.

2.3. Treatment methods

Group A received oral administration of Cefixime Tablets (Jiangsu Zhengda Qingjiang Pharmaceutical Co., Ltd., National Medical Approval Number H20061245, 0.1 g), 0.1 g per time, twice a day; and Azithromycin Tablets (Zhejiang Jingxin Pharmaceutical Co., Ltd., National Medical Approval Number H20058315, 0.25 g), 0.25 g per time, twice a day. The medication was administered for 10 days. Group B received the same Cefixime Tablets regimen as Group A.

2.4. Observation indicators

- (1) Efficacy: Complete resolution of cough, expectoration, and dyspnea, with X-ray indicating inflammation absorption of $> 70\%$ was considered as markedly effective; improvement of symptoms and X-ray indicating inflammation absorption of $> 30\%$ was considered as effective; no change was considered as ineffective.
- (2) Lung function: Lung function tester was used to monitor indicators such as PEF, FVC, and FEV1.
- (3) Inflammatory factors: Fasting venous blood was collected, and indicators such as IL-6, IL-8, and TNF- α

were detected using enzyme-linked immunosorbent assay.

(4) Adverse reactions: Occurrences of dizziness, abdominal pain, nausea, and vomiting were recorded.

2.5. Statistical analysis

Data were processed using SPSS 23.0. χ^2 test was used for counting data (recorded as %), and t -test was used for measurement data (recorded as mean \pm SD). Statistical significance was set at $P < 0.05$.

3. Results

3.1. Efficacy

The efficacy of AECOPD treatment in Group A was higher than that in Group B, $P < 0.05$ (Table 2).

Table 2. Analysis of AECOPD patient efficacy (n , %)

Group	Marked effective	Effective	Ineffective	Total effective rate
Group A ($n = 31$)	20 (64.52)	10 (32.26)	1 (3.23)	30 (96.77)
Group B ($n = 31$)	13 (41.94)	12 (38.71)	6 (19.35)	25 (80.65)
χ^2	-	-	-	4.0260
P	-	-	-	0.0448

3.2. Lung function

After treatment, the FVC, PEF, and FEV1 indicators of AECOPD patients in Group A were all higher than those in Group B, $P < 0.05$ (Table 3).

Table 3. Analysis of lung function indicators for AECOPD patients (mean \pm SD)

Group	FVC (L)		PEF (L/s)		FEV1 (L)	
	Before medication	After medication	Before medication	After medication	Before medication	After medication
Group A ($n = 31$)	2.17 \pm 0.42	3.51 \pm 0.57	2.36 \pm 0.33	3.47 \pm 0.52	1.51 \pm 0.15	2.59 \pm 0.33
Group B ($n = 31$)	2.16 \pm 0.41	2.79 \pm 0.51	2.38 \pm 0.35	2.79 \pm 0.43	1.53 \pm 0.14	2.01 \pm 0.26
t	0.0949	5.2413	0.2315	5.6110	0.5427	7.6866
P	0.9247	0.0000	0.8177	0.0000	0.5893	0.0000

3.3. Inflammation level

After treatment, the IL-6, IL-8, and TNF- α indicators of AECOPD patients in Group A were all lower than those in Group B, $P < 0.05$ (Table 4).

Table 4. Analysis of inflammatory factor indicators for AECOPD patients (mean \pm SD)

Group	IL-6 (ng/L)		IL-8 (μ g/L)		TNF- α (pg/mL)	
	Before medication	After medication	Before medication	After medication	Before medication	After medication
Group A ($n = 31$)	28.41 \pm 1.81	9.58 \pm 1.11	36.61 \pm 1.62	24.11 \pm 1.49	18.27 \pm 1.58	9.21 \pm 1.02
Group B ($n = 31$)	28.39 \pm 1.79	16.21 \pm 1.46	36.59 \pm 1.68	30.21 \pm 1.62	18.25 \pm 1.61	13.06 \pm 1.35
t	0.0437	20.1273	0.0477	15.4307	0.0494	12.6689
P	0.9653	0.0000	0.9621	0.0000	0.9608	0.0000

3.4. Adverse reactions

The adverse reactions of AECOPD patients in Group A were lower than those in Group B, $P < 0.05$ (Table 5).

Table 5. Analysis of adverse reactions in AECOPD patients (n , %)

Group	Dizziness	Abdominal pain	Nausea and vomiting	Incidence rate
Group A ($n = 31$)	0 (0.00)	0 (0.00)	1 (3.23)	1 (3.23)
Group B ($n = 31$)	2 (6.45)	1 (3.23)	3 (9.68)	6 (19.35)
χ^2	-	-	-	4.0260
P	-	-	-	0.0448

4. Discussion

The typical pathological feature of AECOPD is airflow limitation, which obstructs the respiratory tract and can induce symptoms such as chest tightness, wheezing, and expectoration. It may even lead to secondary dyspnea and respiratory failure, posing a significant threat to patients' lives and health. AECOPD is associated with respiratory system infections, which can cause acute and progressive exacerbation of respiratory symptoms. Additionally, climate change and exposure to air pollution can stimulate airway spasms, further exacerbating AECOPD symptoms. As AECOPD progresses, continuous stimulation of airway secretion of sputum leads to respiratory mucosal edema, increases the difficulty of sputum excretion, and aggravates the impairment of airway ciliary movement. This can result in decreased airway ventilation function and worsened respiratory failure^[3]. Furthermore, when AECOPD patients are infected with *Mycoplasma pneumoniae*, it stimulates the body to release large amounts of antigenic components into the blood circulation system. These antigens bind to pre-existing antibodies, forming circulating immune complexes that can induce further release of cytokines, leading to chronic inflammation. Therefore, in addition to routine management and control of AECOPD, anti-infective treatment should be emphasized. Cephalosporins are commonly used in the treatment of AECOPD due to their anti-infective properties and ability to enhance disease control efficacy. When combined with azithromycin, they can achieve a stable antibacterial effect. After oral administration of azithromycin, the active ingredients bind to the bacterial ribosome's 50S subunit, inhibiting the synthesis of RNA proteins in the body and exerting antibacterial activity. Additionally, azithromycin has strong acid stability, which reduces adverse gastrointestinal stimulation associated with oral administration, resulting in high medication safety^[4].

Based on the data presented in this article, the efficacy of AECOPD treatment in Group A was higher than that in Group B, with $P < 0.05$. The reason for this may be attributed to the use of cefixime tablets, which can inhibit

transpeptidase and achieve a bactericidal effect by blocking the process of bacterial cell wall synthesis. When used in the treatment of AECOPD patients, it exhibits high antibacterial activity against Gram-negative and Gram-positive bacteria in the patient's body. Analyzing the pharmaceutical characteristics of cefixime tablets, this drug has a broad antibacterial spectrum, can inhibit the activity of various respiratory infection-causing pathogens, and has excellent efficacy. Additionally, it has strong tissue penetrability, allowing it to quickly reach the respiratory tract lesion after oral administration. The high local blood drug concentration can enhance the antibacterial effect and shorten the course of AECOPD patients^[5]. The combination of azithromycin, a macrolide drug, can improve patients' lung function. Azithromycin has a similar structure to erythromycin. When taken orally, it inhibits bacterial protein synthesis, offering advantages such as high bioavailability and antibacterial efficacy. Furthermore, this drug has a wide tissue distribution and can stably exert its pharmacological effects in an acidic environment, making it suitable for the treatment of AECOPD^[6]. The combination of these two drugs exerts synergistic effects through different pathways.

Another set of data indicates that the FVC, PEF, and FEV1 indicators in Group A were higher than those in Group B, with $P < 0.05$. The reason for this may be that AECOPD patients experience reduced lung elasticity and impaired lung retraction due to factors such as overinflation of the lungs and airway obstruction. As a result, patients cannot completely exhale the air in their lungs, leading to a decrease in FVC. The magnitude of this decrease is positively correlated with the degree of impairment of lung ventilation function. Monitoring changes in FVC can provide insights into prognosis. As the inflammation in the lungs of AECOPD patients worsens, continuous inflammatory factor stimulation increases airway resistance and aggravates smooth muscle spasms, leading to impaired airway patency and a decrease in PEF. Monitoring changes in PEF can help analyze the severity of chronic obstructive pulmonary disease. FEV1 provides feedback on the degree of airflow limitation. If airway obstruction intensifies in AECOPD patients, it can lead to a decrease in FEV1. Monitoring FEV1 indicators can guide clinical adjustments to treatment plans. The occurrence of AECOPD can continuously damage patients' lung function, which is related to airway inflammation caused by infection or exposure to air pollution. This stimulates smooth muscle contraction, increases mucus secretion, and aggravates mucosal edema. Inflammatory factors stimulate the airways, increasing airway secretion and leading to the formation of local mucus plugs, resulting in airway obstruction. Restricted exhalation airflow increases residual lung volume, which can lead to excessive lung inflation and damage to lung elastic retraction^[7]. Additionally, carbon dioxide retention or long-term hypoxia in AECOPD patients can aggravate respiratory muscle fatigue, leading to impaired exhalation function. In this article, cefixime tablets were chosen for treatment due to their broad antibacterial spectrum. They inhibit the malignant reproduction of pathogens by disrupting cell walls. After oral administration, the active ingredients quickly enter the cerebrospinal fluid, inhibiting inflammatory reactions and reducing respiratory reactivity. Azithromycin has strong antibacterial effects and can inhibit *Mycoplasma pneumoniae*. It is quickly absorbed after oral administration^[8]. Therefore, the combination of azithromycin and cephalosporins can improve patients' respiratory status and rapidly enhance their lung function.

Another set of data shows that IL-6, IL-8, and TNF- α levels in Group A were lower than those in Group B, with $P < 0.05$. The reason for this may be that IL-6 is a pro-inflammatory factor. When the body is infected with bacteria or viruses, continuous stimulation of bronchial epithelial cells can increase the release of IL-6 and aggravate inflammation in the body. IL-8 is mainly produced by airway epithelial cells and macrophages. Increased IL-8 levels in AECOPD patients induce the accumulation of neutrophils in the airways, leading to an "inflammatory cycle" that further impairs lung function. TNF- α provides feedback on the degree of inflammatory reaction and is

positively correlated with lung tissue damage. The combined drug treatment used in this study includes cefixime tablets, which inhibit bacterial cell wall synthesis. Although they do not have a direct anti-inflammatory effect, they can indirectly reduce the production of inflammatory factors in the body through antibacterial pathways. Azithromycin can regulate the body's immune function, reduce inflammation, block the NF- κ B signaling pathway, inhibit the expression of inflammatory factors, and block neutrophil chemotaxis pathways, thereby enhancing the control of airway inflammation^[9]. Additionally, the combined drug treatment has a broader antibacterial spectrum, effectively managing patients with mixed infections, and synergistically exerting anti-inflammatory effects to prevent excessive expression of inflammatory factors.

Finally, another set of data indicates that the adverse reactions in Group A were lower than those in Group B, with $P < 0.05$. The reason for this is that combined drug treatment can improve the prognosis of AECOPD patients and has high medication safety. Cefixime tablets quickly distribute in the patient's body after oral administration, exerting pharmacological effects in multiple areas such as skin tissue, the urinary system, and the respiratory tract. The high blood drug concentration in the lungs is beneficial for managing respiratory tract infections. This drug is metabolized in the liver and has a long half-life, allowing it to exert a stable pharmacological effect. Azithromycin inhibits bacterial protein synthesis with a half-life of 6-8 hours and low liver toxicity, balancing efficacy and safety and promoting disease prognosis^[10]. During treatment with azithromycin and cephalosporins, AECOPD patients should be advised to follow medical advice, correctly adjust medication frequency, time, and dosage, and avoid making changes to the medication regimen themselves. During medication, patients should be observed for nausea, vomiting, dyspnea, itching, or adverse gastrointestinal reactions. Additionally, liver and kidney function and blood routine should be rechecked to assess physiological and pathological states and adjust medication accordingly. Patients should also adjust their daily diet, avoiding greasy and spicy foods, as these can increase the burden on the gastrointestinal tract and affect drug metabolism. In summary, the combination of azithromycin and cephalosporins for the treatment of AECOPD can inhibit inflammation progression, reduce adverse reactions, and improve lung function, making it a viable treatment option.

Disclosure statement

The author declares no conflict of interest.

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Pulmonary Myelolipoma in NSCLC with EML4-ALK Fusion: A Case Report and Literature Review

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Abstract: Pulmonary or bronchial myelolipomas are rare, and no cases of genetic testing have been clinically reported, which limits research on their pathogenesis and the scientific basis of diagnosis and treatment. A 52-year-old Asian male presented with a two-week history of paroxysmal cough and blood-streaked sputum. The patient reported no additional symptoms and had no history of smoking. A chest computed tomography (CT) scan conducted two years prior revealed a 10 mm × 18 mm nodule in the right lower lung, which had increased to 32 mm × 16 mm on the current scan. In addition, an enlarged lymph node measuring 18 mm × 10 mm was observed in the right lower pulmonary hilum, along with a pulmonary bulla. A whole-body 18F-fluorodeoxyglucose positron emission tomography (18F-FDG PET) scan demonstrated increased metabolic activity in both the mass and the enlarged lymph node. A thoracoscopic right lower lobectomy was performed, and the pulmonary bulla was removed concurrently. Pathological examination confirmed non-small cell lung carcinoma (NSCLC) in the mass, while the tissue surrounding the pulmonary bulla revealed mixed components, including bone, adipose, and hematopoietic tissues. Postoperative tumor mutation testing identified an EML4-ALK fusion gene variant. The patient recovered well following surgery, and a follow-up chest X-ray showed a resolution of atelectasis in the right lower lung. Adjuvant therapy with alectinib is planned.

Keywords: Myelolipoma, Pulmonary, NSCLC, EML4-ALK, CT

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1. Background

Myelolipoma is a rare benign tumor composed of light yellow mature adipose tissue and red-brown normal hematopoietic tissue ^[1]. It is most commonly found in the adrenal glands but can also occur in extra-adrenal locations, including the liver, spleen, thorax, retroperitoneum, presacral region, stomach, thyroid, nasal cavity,

and bones ^[2,3]. The incidence of myelolipomas in these extra-adrenal tissues is estimated to be 0.08%-0.2%, with approximately 3% occurring in the thoracic region ^[4]. Notably, only 24 cases of pulmonary or bronchial myelolipomas, including the present case, have been reported worldwide. Pulmonary myelolipomas are often asymptomatic and are typically discovered incidentally during physical examinations or autopsies ^[2]. Due to their benign nature and low incidence, genetic testing data are limited, and their molecular mechanisms remain poorly understood. The EML4-ALK fusion gene is one of the most significant pathogenic genes identified in non-small cell lung carcinoma (NSCLC), occurring in approximately 3–5% of cases ^[5]. ALK, a membrane-bound receptor, activates several signaling pathways, including the PI3K-AKT, JAK-STAT, and MAPK pathways, which play essential roles in tumorigenesis and cancer progression ^[6]. Herein, we report a case of pulmonary myelolipoma in a patient with NSCLC harboring the EML4-ALK fusion, accompanied by a review of the literature on pulmonary and bronchial myelolipoma cases.

2. Case presentation

A previously healthy 52-year-old Asian male presented with a two-week history of paroxysmal cough and blood-streaked sputum. Initial treatment with carbazochrome Tablets at a local hospital led to symptom alleviation, and a chest computed tomography (CT) scan revealed a 32 mm × 16 mm mass in the basal segment of the right lower lung, accompanied by bilateral pleural thickening.

The patient subsequently sought further evaluation at our hospital. A previous chest CT (computed tomography) performed two years earlier during a routine physical examination had identified a 10 mm × 18 mm nodule in the same region of the right lower lung. The patient reported no additional symptoms or smoking history. Laboratory investigations at admission included lung tumor marker analysis, which showed an elevated carcinoembryonic antigen (CEA) level of 22.00 ng/mL (reference value ≤ 5.00 ng/mL). Routine blood tests and coagulation function tests were within normal limits. Contrast-enhanced chest CT confirmed significant enhancement of the lesion, along with an enlarged lymph node measuring 18 mm × 10 mm in the right lower pulmonary hilum and a pulmonary bulla in the posterior segment of the right upper lung (**Figure 1**). To further evaluate the possibility of lung cancer, a whole-body 18F-fluorodeoxyglucose positron emission tomography (18F-FDG PET) scan and EGFR mutation testing were performed. The PET scan revealed increased metabolic activity in the mass and the lymph node (**Figure 2**), while EGFR mutation testing was negative. Thoracoscopic right lower lobectomy, right upper lung apex bullectomy, and hilar and mediastinal lymph node dissection were subsequently performed.

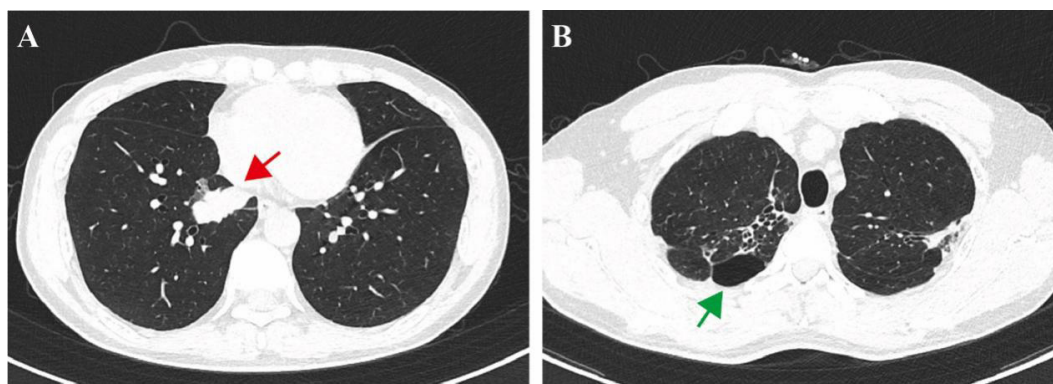


Figure 1. (A) Chest CT image demonstrating a high-density mass (red arrow) located in the basal segment of the right lower lung. (B) Chest CT reveals a lymph node shadow (green arrow) at the right lower pulmonary hilum.

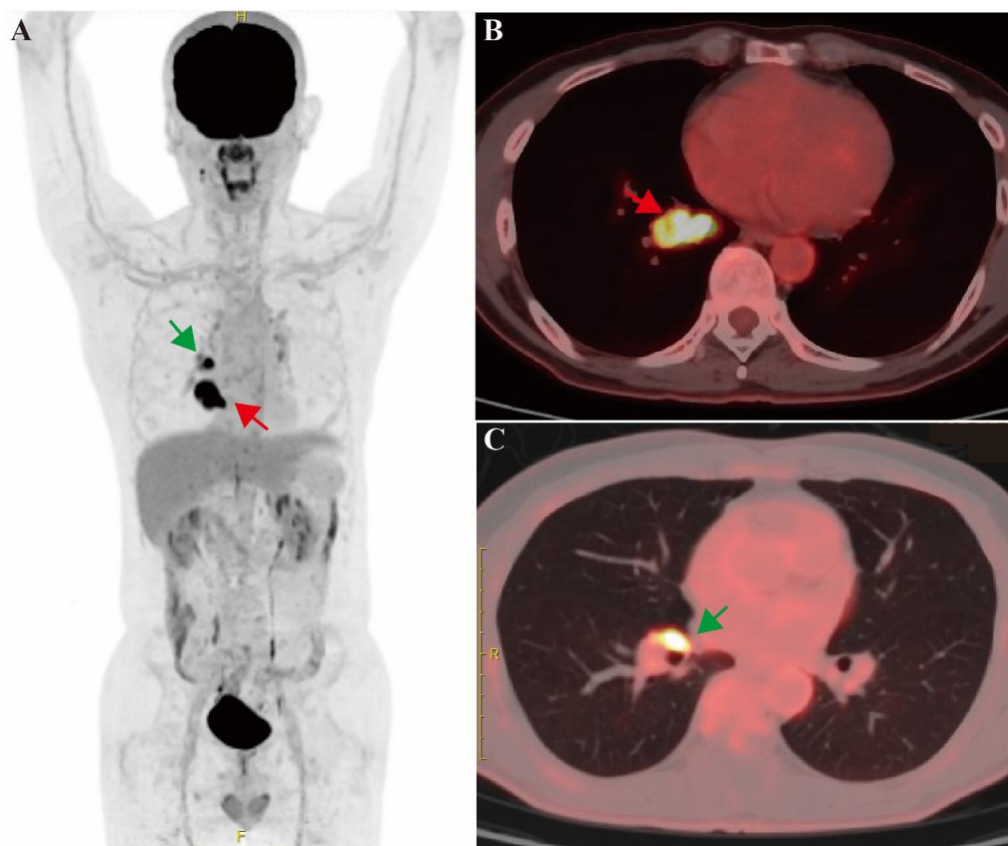


Figure 2. Whole-body 18F-FDG PET image showing increased FDG uptake in the mass (red arrow) and the lymph node (green arrow).

The excised right lower lung lobe contained a mass measuring 38 mm × 26 mm × 22 mm. Pathological examination confirmed poorly differentiated invasive lung adenocarcinoma (**Figure 3**). Immunohistochemistry revealed positive ALK, TTF-1, BRG1, SMARCA2, and INI-1 expression. Pathology analysis of the tissue surrounding the lung bulla revealed mixed components, including bone, adipose, and hematopoietic tissues (**Figure 4**), confirming the diagnosis of lung myelolipoma. Radiological evaluation indicated no parenchymal involvement of the myelolipoma on CT. Clinically, the patient exhibited no hematologic disorders, such as anemia or thrombocytopenia, and no endocrine abnormalities were noted.

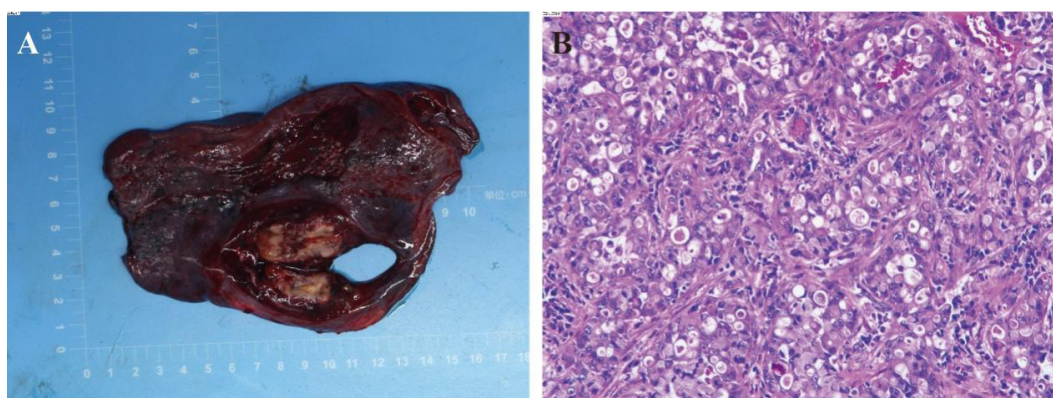


Figure 3. (A) The excised right lower lung lobe contained a mass measuring 38 mm × 26 mm × 22 mm. (B) Histological examination of the specimen revealed invasive lung adenocarcinoma (hematoxylin and eosin [H&E] staining, × 400).

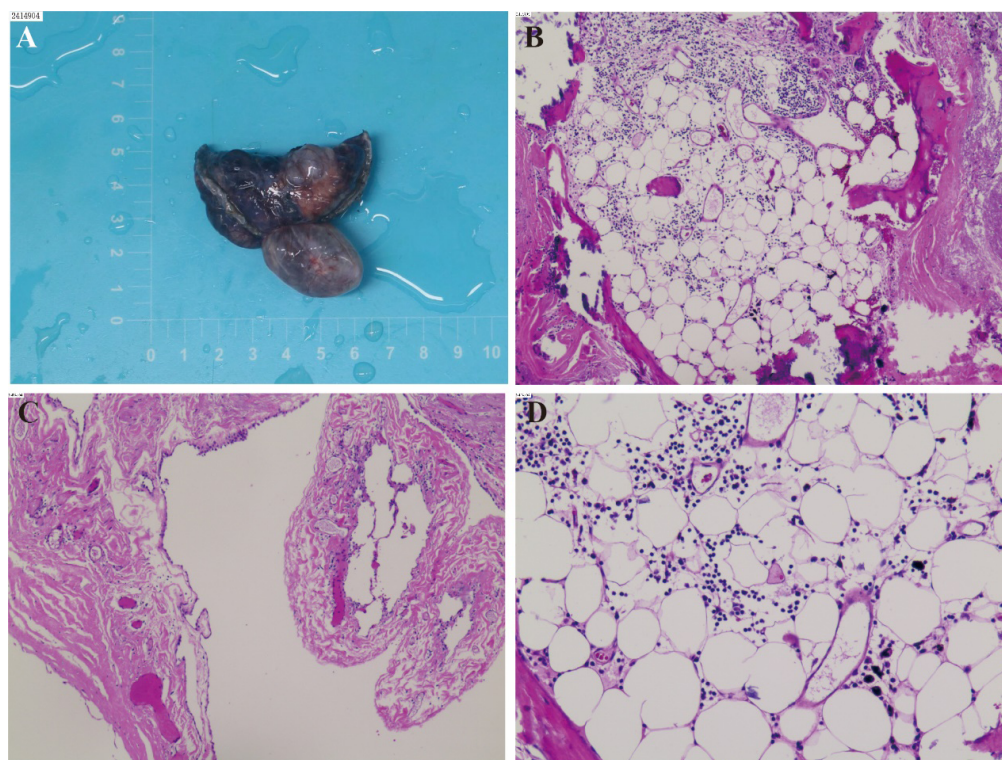


Figure 4. (A) The excised lung tissue from the right upper lobe displayed two vesicles on the pleural surface. (B) Microscopic examination of the specimen (H&E staining, $\times 100$). (C) The specimen showed bone tissue, adipose tissue, and dilated thin-walled blood vessels (H&E staining, $\times 100$). (D) Scattered hematopoietic tissues were observed within the specimen (H&E staining, $\times 400$).

Postoperative tumor mutation gene testing identified the presence of EML4-ALK fusion, MDM2 amplification, and NSD1 mutation. Chest radiographs taken the day after surgery showed improvement in atelectasis in the right lower lung, accompanied by the resolution of symptoms such as cough, sputum production, and dyspnea. A follow-up chest X-ray taken 10 days later confirmed the complete resolution of the lung atelectasis. Given the diagnosis of resected EML4-ALK fusion NSCLC and lung myelolipoma, the patient is scheduled to receive alectinib as targeted therapy ^[7].

3. Discussion

Pulmonary or bronchial myelolipoma is an exceptionally rare condition, with only 23 cases documented to date. Here, we present the 24th case and summarize clinicopathological features (**Table 1**). Patients with pulmonary or bronchial myelolipomas commonly experience concurrent pneumonia (4 cases, 16.7%) or atelectasis (3 cases, 12.5%). Notably, only one patient with a history of lung cancer has been reported. There was no specific predilection for tumor location, although 4 cases (12.5%) were confined exclusively to the bronchus without involving the lung parenchyma.

Abnormal imaging findings were reported on X-ray or CT in 19 cases (79.2%). CT imaging features previously described include a fatty- and soft-tissue-density mass ^[8], a smooth and well-defined lesion ^[9], a solitary nodule with rim-like calcification ^[10], a patchy high-density shadow ^[11], and a mixed calcification mass ^[12].

To date, there is no established imaging feature study for pulmonary myelolipoma. The reported cases suggest that myelolipomas in the thorax typically appear as elliptical or flattened masses with well-defined boundaries. The tumor density observed on CT and the gross morphology of mediastinal and pulmonary myelolipomas are influenced by the relative proportions of adipose tissue (low-density) and bone marrow hematopoietic tissue (slightly higher density) within the tumor ^[11].

In mediastinal myelolipomas, the predominant myeloid element may exhibit high attenuation on CT images, which can be enhanced following intravenous administration of iodinated contrast material ^[13]. In our patient, the tumor's maximum diameter was 0.3 cm, making abnormalities challenging to detect on CT images. Coincidentally, the presence of a pulmonary bulla facilitated its removal and subsequent identification. We hypothesize that this condition results from local bronchial obstruction and inflammation.

Table 1. Patient and tumor characteristics of reported pulmonary myelolipomas

First author (year)	Other disease (s)	Tumor location	Size (cm)	Abnormal imaging examinations
Saleeby/1925	Pneumonia	Peripherally	Φ2.5	/
Hunter <i>et al.</i> /1992	Rheumatoid arthritis	Peripherally	No measured	X ray, CT
Ziókowski <i>et al.</i> /1996	Pneumonia	LLL	7.0 × 5.0 × 5.0	/
Ziókowski <i>et al.</i> /1996	/	RLL	Φ2.0	/
Zunarelli <i>et al.</i> /1999	Bronchial carcinoid tumor	RLL	No measured	/
Sabate and Shahian/2002	Hypercholesterolemia	LUL	Φ2.5	X ray, CT
Lu <i>et al.</i> /2003	Pneumonia	LUL	Φ1.5	X ray, CT
Sato <i>et al.</i> /2007	Lung cancer	LLL	Φ2.0	X ray, CT
Lin <i>et al.</i> /2009	/	LUL	4.5 × 3.5 × 2.3	X ray, CT
Liu <i>et al.</i> /2012	/	LMB	2.0 × 1.0 × 0.5	CT
Xing <i>et al.</i> /2012	/	RML	Φ1.5	X ray, CT
Huang <i>et al.</i> /2012	Atelectasis	LLL	2.3 × 1.2 × 1.0	CT
Huang <i>et al.</i> /2012	Bronchiectasis	RLL	Φ1.6	CT
Silvija <i>et al.</i> /2017	/	RLL	Φ3.0	/
Chung <i>et al.</i> /2019	Pneumonia	RB	2.0 × 1.3	CT
Wang <i>et al.</i> /2019	/	RLL	2.5 × 2.0 × 2.0	CT
Zhan <i>et al.</i> /2020	/	LLL	1.4 × 1.3	CT
Zhang <i>et al.</i> /2021	Cervicodynia	RLL	7.0 × 4.0 × 3.5	CT
Yang <i>et al.</i> /2023	/	RML	0.8 x 0.7	CT
Liu <i>et al.</i> /2023	/	RML	2.5 × 2.1	CT
Ji <i>et al.</i> /2023	Bronchiectasis	BB	0.6 x 0.4 x 0.3	CT
Su <i>et al.</i> /2024	Atelectasis	RML	1.7 x 1.5 x 1.0	CT
Yan <i>et al.</i> /2024	Atelectasis	LMB	9.0 x 8.0 x 3.0	CT
Present case	Lung cancer	RUL	Φ0.3	CT

*LLL, left lower lobe; LUL, left upper lobe; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe; LMB, left main bronchus; RB, right bronchus; BB, bilateral bronchi.

The exact pathogenesis of myelolipoma remains unclear. Hypotheses regarding the cause of extra-adrenal myelolipomas include degenerative changes in hyperplastic tumor cells, metaplasia of primary stem mesenchymal cells of the adrenal cortex, and displacement of differentiated bone marrow cells during embryogenesis^[14]. The current understanding suggests that pulmonary myelolipomas originate from mesenchymal cells in the bronchial wall, which may differentiate into bone marrow hematopoietic tissue under specific conditions, such as tissue damage, chronic infection, or abnormal levels of endocrine hormones^[15]. To our knowledge, this is the first case of pulmonary myelolipoma associated with NSCLC and EML-ALK4 fusion. This novel association may offer new perspectives and directions for exploring the etiology of pulmonary myelolipoma at the genetic level.

4. Conclusion

The presence of a pulmonary bulla identified on CT and during surgery led to the discovery of this case of pulmonary myelolipoma. The occurrence of NSCLC with an EML4-ALK fusion in this patient offers new insights into the understanding of pulmonary myelolipoma, paving the way for improved preventative strategies and treatment approaches.

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Authors' contributions

Data analysis – Xin Zhang and Zhan Ye

Manuscript drafting – Xin Zhang, Zhan Ye and Xuwei Chen,

Manuscript editing – Xin Zhang and Xuwei Chen

Manuscript revision – Zhan Ye, Xin Zhang, Ao Lin, Junjun Fu and Jieyu Xie

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An Endoscopic Surgical Auxiliary Belt Value in Endoscopic Submucosal Dissection of Colorectal Lateral Developmental Tumors

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Abstract: *Objective:* To explore the value of an auxiliary band for endoscopic surgery in endoscopic submucosal dissection of colorectal lateral developmental tumors, with a view to providing a new method for the early diagnosis and treatment of such tumors, and thus improving the prognosis of patients. *Methods:* The clinical data of 60 patients who underwent endoscopic submucosal dissection of colorectal LST in the hospital between June 2022 and June 2024 were retrospectively analyzed. The patients were categorized into the auxiliary belt group ($n = 30$) and the control group ($n = 30$) according to whether or not the auxiliary belt for endoscopic surgery was used during the operation. The operation time, the number of intraoperative hemostasis, the number of titanium clips used, the success rate of ESD, the incidence of postoperative complications, the length of hospitalization and the hospitalization cost of the two groups were compared. *Results:* The operation time of the patients in the auxiliary belt group was slightly longer than that of the control group, but the difference was not statistically significant ($P > 0.05$); the number of intraoperative hemostasis and the number of titanium clips used in the auxiliary belt group was less than that of the control group, but the difference was not statistically significant ($P > 0.05$); the success rate of ESD in the auxiliary belt group was 93.33%, which was higher than that of the control group, which was 90.00%. The ESD success rate in the auxiliary belt group was 93.33%, which was higher than the ESD success rate of 90.00% in the control group, but the difference was not statistically significant ($P > 0.05$); the incidence of postoperative complications in the auxiliary belt group was lower than that in the control group, but the difference was not statistically significant ($P > 0.05$); the length of hospital stay in the auxiliary belt group was significantly shorter than that of the control group, and the difference was statistically significant ($P < 0.05$); and the hospitalization cost of patients in both groups was comparable, with no significant difference ($P > 0.05$). *Conclusion:* The auxiliary belt for endoscopic surgery has certain application value in endoscopic submucosal dissection of colorectal lateral developmental tumors, which can assist the surgical operation, may reduce intraoperative bleeding and the use of titanium clips, shorten the patient's hospitalization time, and does not increase the hospitalization cost.

Keywords: Auxiliary band for endoscopic surgery; Lateral developmental tumor of the colorectum; Endoscopic surgery

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1. Introduction

Lateral developmental tumor of the colorectum (LST) is a rare colorectal precancerous lesion, but has a high risk of malignant transformation and is highly susceptible to clinical underdiagnosis and misdiagnosis. According to the literature, about 60% of patients with LST develop metastasis, which mainly manifests as metastasis to distant organs, including the liver, lung, and bone, and has a poor prognosis ^[1]. Therefore, early diagnosis and treatment of such tumors have been a hot issue of clinical concern. The traditional endoscopic submucosal-derived esophageal dissection (ESD) of colorectal LST is cumbersome, time-consuming, and prone to bleeding ^[2]. With the continuous updating of endoscopic techniques and equipment, the use of assistive tapes in ESD has been gradually adopted in clinical practice ^[3]. Several types of assistive tapes have been used in colorectal LST surgery, but there is a lack of large randomized controlled studies. In this study, we retrospectively analyzed the value of an auxiliary band for endoscopic surgery in colorectal LST, and investigated whether it could reduce intraoperative bleeding and the number of titanium clips used, shorten the patient's hospital stay, and reduce the cost of hospitalization. It provides a new method for the early diagnosis and treatment of such tumors.

2. Information and methods

2.1. General information

Sixty patients, including 35 males and 25 females, aged 30–75 years old, with an average of (47.5 ± 10.6) years old, who were treated with colorectal LST endoscopic submucosal dissection in the hospital from June 2022 to June 2024, were selected and all of them were confirmed by pathology. The 60 patients were divided into the auxiliary band group and the control group, and there was no difference ($P > 0.05$) in the comparison of the general information of the two groups, such as gender, age, tumor type, tumor infiltration depth, and so on, which was comparable (Table 1).

Table 1. General information

Groups		Auxiliary belt group ($n = 30$)	Control group ($n = 30$)	t/x^2	P
Gender (cases, %)	Male	18 (60.00%)	17 (56.67%)	0.067	0.796
	Female	12 (40.00%)	13 (43.33%)		
Age (years)		47.53 ± 10.55	47.47 ± 10.65	0.021	0.983
Tumor type (cases, %)	Adenoma (glandular tumor)	20 (66.67%)	19 (63.33%)	0.071	0.790
	Non-adenomatous tumor	10 (33.33%)	11 (36.67%)		
Depth of tumor infiltration (mm)		5.12 ± 1.23	5.08 ± 1.27	0.125	0.901

2.2. Methodology

All patients were treated with endoscopy and submucosal dissection under general anesthesia. Intraoperative application of an auxiliary band assisted in stripping the mucosa and completing tumor resection; the control group was operated on only with conventional endoscopic surgical tools. The endoscopic diagnosis and treatment system is EVO Plus, which consists of an image acquisition device, a bendable catheter, a syringe pump, a display and a joystick, among which the display is 26 cm wide and 10 cm high, with a resolution of 1080×1080 , a maximum field of view angle of up to 90° , and adopts an integrated design, which can effectively minimize the complications caused by the movement of endoscopic instruments. The operation method of the endoscopic diagnosis and

treatment system is referred to as “ESD Preoperative Preparation and Selection of Operative Procedures” (3rd edition) [4].

2.3. Observation indicators

Comparing the two groups of patients, the operation time (calculated from the beginning of entering the operating room), the number of intraoperative hemostasis, the number of titanium clips used, the success rate of ESD, the incidence of postoperative complications (including nausea, vomiting, abdominal pain, diarrhea, bleeding, etc.), the length of hospitalization (calculated from the beginning of the processing of admission to the end of the processing of discharge) and hospitalization costs (all the costs, including the bed fee, surgical cost, nursing costs, medical costs, etc.) and other indicators.

2.4. Statistical methods

SPSS 21.0 statistical software was used to process the data, and the measurement data were expressed as mean \pm standard deviation (SD) by *t*-test, and the count data were expressed as percentage (%) by χ^2 test, and the difference was regarded as statistically significant at $P < 0.05$.

3. Results

3.1. Comparison of operation time, number of intraoperative hemostasis, and number of titanium clips used between the two groups of patients

The operation time of the patients in the auxiliary belt group was slightly longer than that of the control group, but the difference was not statistically significant ($P > 0.05$); in terms of the number of intraoperative hemostasis and the number of titanium clips used, the auxiliary belt group was less than the control group, but the difference was not statistically significant ($P > 0.05$) (Table 2).

Table 2. Comparison of operative time, number of intraoperative hemostasis, and number of titanium clips used between the two groups (mean \pm SD)

Groups	Surgical time (h)	Number of intraoperative hemostasis (times)	Number of titanium clips used (pcs)
Auxiliary belt group ($n = 30$)	1.25 ± 0.35	2.10 ± 0.45	3.50 ± 0.75
Control group ($n = 30$)	1.30 ± 0.40	2.15 ± 0.50	3.60 ± 0.80
<i>t</i>	0.532	0.421	0.487
<i>P</i>	0.596	0.675	0.628

3.2. Comparison of ESD success rate and postoperative complication rate between two groups of patients

The ESD success rates of the auxiliary belt group were all 93.33% higher than the ESD success rates of the control group were all 90.00%, but the difference was not statistically significant ($P > 0.05$); the postoperative complication rate of the auxiliary belt group was lower than that of the control group, but the difference was not statistically significant ($P > 0.05$) (Table 3).

Table 3. Comparison of ESD success rate and postoperative complication rate between the two groups [n (%)]

Groups	ESD Success Rate	Postoperative complication rate
Auxiliary belt group (<i>n</i> = 30)	28 (93.33%)	3 (10.00%)
Control group (<i>n</i> = 30)	27 (90.00%)	4 (13.33%)
χ^2 value	0.218	0.152
<i>P</i> -value	0.641	0.697

3.3. Comparison of hospitalization time and hospitalization cost between the two groups of patients

The hospitalization time of the auxiliary belt group was significantly shorter than that of the control group, and the difference was statistically significant ($P < 0.05$); the hospitalization costs of the patients in the two groups were comparable, with no significant difference ($P > 0.05$) (Table 4).

Table 4. Comparison of hospitalization time and hospitalization cost between the two groups (mean \pm SD)

Groups	Length of hospitalization (d)	Hospitalization costs (\$)
Auxiliary belt group (<i>n</i> = 30)	4.50 \pm 1.20	12500.50 \pm 1500.75
Control group (<i>n</i> = 30)	6.00 \pm 1.50	12800.25 \pm 1600.50
<i>t</i>	4.123	0.685
<i>P</i>	0.001	0.496

4. Discussion

In recent years, with the development of gastrointestinal endoscopic technology, endoscopic submucosal dissection (ESD) for laterally spreading tumors of the colorectum has been widely used in the clinic as an effective treatment option. Although this procedure has the advantages of small trauma and fast recovery, there are many risks and complications, such as mucosal bleeding and perforation, and how to reduce the complication rate has been a hot issue in clinical research. Foreign scholars have proposed the “double belt” method to solve this problem, i.e., to fix the mucosal tissues with double wires and strengthen their protection during the operation, which can prevent bleeding; at the same time, the increased pressure can also reduce the edema of the intestinal wall caused by the tumor compression, and create better conditions for the subsequent operation. However, the double-band method has not yet been popularized in China and is expensive, so how to minimize its use under the premise of ensuring surgical safety and thus reducing medical costs has become an urgent clinical problem.

An auxiliary band is a tool that enables the separation of tissue into the surrounding submucosal layer under direct endoscopic vision in the direction of the mucosal surface. The main role of the assistive tape is to reduce the difficulty of surgical operation, reduce intraoperative bleeding, reduce the operation time, and improve patient comfort. At present, there are three types of assistive belts applied to colorectal LST in the clinic: (1) metal clips based on electric knife and titanium clips; (2) EST based on electric knife, titanium clips, and metal clips; (3) EST based on electric knife and titanium clips. Among them, metal clips are the traditional assistive belts, but due to their cumbersome, time-consuming, and easy-to-bleed operation, they are rarely applied in the clinic at present. In recent years, with the development of endoscopic equipment and technology, more and more doctors have

begun to use auxiliary bands to assist surgical operations. By expanding the endoscopic resection scope to the surrounding submucosa through the auxiliary belt, both the resection rate and intraoperative bleeding are improved and the postoperative recovery time is shortened. The auxiliary band for endoscopic surgery reported in this paper is a new type of auxiliary band for endoscopic surgery. It is mainly composed of two parts: a metal clip and a support belt, in which the metal clip is made of titanium steel and is used to hold tissues during intraoperative operation. The instrument rotates the titanium clip by rotation so that it is located under the mucosa. The support band is made of nylon fibers, and its function is to adjust the scope of tissue removal by adjusting the support band during the operation. The combination of the two can improve surgical efficiency, reduce intraoperative bleeding, and postoperative recovery time to a certain extent. Endoscopic treatment is currently the most commonly used minimally invasive surgical procedure for colorectal lateral developmental tumors, which has the advantages of less trauma, faster recovery, and fewer complications. However, because these tumors are located in the lower part of the rectum or colon, adjacent to the anus, and lacking normal tissue structure and vascular distribution in the surrounding area, complications such as bleeding, perforation, and stenosis are prone to occur when endoscopic submucosal dissection (ESD) is performed.

Although several studies have demonstrated the therapeutic value of the use of endoscopic surgical adjuvant tapes in early stage colorectal laterally developed tumors with mucus secretion^[5]. However, the use of endoscopic surgical adjuvant tapes is still in the clinical exploratory stage, and there are not enough randomized controlled studies to support the clinical value of endoscopic surgical adjuvant tapes in the treatment of this type of tumor. In addition, the length of hospitalization and hospitalization costs were comparable between the two groups, with no significant differences.

The results of this study showed that the auxiliary belt for endoscopic surgery has certain application value in colorectal lateral developmental tumors. The operation time of patients in the auxiliary belt group was slightly longer than that of the control group, but the difference was not statistically significant ($P > 0.05$); in terms of the number of intraoperative hemostatic times and the number of titanium clips used, the auxiliary belt group was less than that of the control group, but the difference was not statistically significant ($P > 0.05$); the success rate of ESD of the auxiliary belt group was 93.33% in all cases was higher than that of the control group which was 90.00% in all cases, but the difference was not statistically significant ($P > 0.05$); the incidence of postoperative complications in the auxiliary belt group was lower than that in the control group, but the difference was not statistically significant ($P > 0.05$); the hospitalization time of the auxiliary belt group was significantly shorter than that of the control group, and the difference was statistically significant ($P < 0.05$); the hospitalization costs of the two groups were comparable, with no significant difference ($P > 0.05$). It indicates that the use of an auxiliary belt for endoscopic surgery can effectively reduce the amount of intraoperative bleeding in patients, shorten the hospitalization time of patients, and not increase the hospitalization cost. This result is consistent with the findings of Li *et al.*^[6], Ren *et al.*^[7], and Chen *et al.*^[8]

At present, the endoscopic submucosal dissection (ESD) technique for colorectal lateral developmental tumors is still immature in China. Although some international studies have shown that the use of auxiliary tape can significantly reduce the occurrence of bleeding and perforation, the lack of a unified standardized operating procedure and the limitations of surgical instruments and auxiliary devices mean that the application of auxiliary tape still has certain risks and problems in the process^[9]. By analyzing the application of auxiliary belt in the clinic, this study found that it cannot only improve the clarity of intraoperative vision and reduce the difficulty of operation, but also effectively control the amount of intraoperative bleeding and improve the patient's

postoperative recovery status, which has a good application prospect. At the same time, compared with European and American countries, endoscopic surgery in China started late, and the level of physicians varies, so how to standardize and promote this technology is a key issue to be solved^[10]. Therefore, the study suggests that in future clinical work, a reasonable method of using auxiliary belts should be formulated with the condition of specific patients, and the relevant operation specification should be continuously improved so that it can be safely and effectively applied in clinical practice.

Due to the limited number of cases in this study, the specific mechanism regarding the therapeutic effect of adjuvant bands for endoscopic surgery on this type of tumor is currently unclear. Therefore, the value and advantages of adjuvant bands for endoscopic surgery in endoscopic submucosal dissection of colorectal lateral developmental tumors and the differences and distinctions between them and traditional titanium clips in combination with therapeutic strategies need to be further explored in future studies. In addition, further validation is required to determine whether the results of this study have some generalizability.

5. Conclusion

In conclusion, the auxiliary belt for endoscopic surgery has certain application value in endoscopic submucosal dissection of colorectal lateral developmental tumors, which can reduce the risk of intraoperative hemorrhage, improve the success rate of the operation, and shorten the patient's hospital stays without increasing the cost of hospitalization.

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Disclosure statement

The authors declare no conflict of interest.

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Healing Mechanism and Therapeutic Prospects of Immediate Implant Placement Combined with Guided Bone Regeneration (GBR) Technique in Oral Cavity

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Abstract: *Objective:* To explore the healing mechanism and effectiveness of immediate implant placement combined with Guided Bone Regeneration (GBR) technique in the oral cavity. *Methods:* A retrospective analysis was conducted on 93 patients treated at Yongning Dental Clinic (Nanning Xinlantian Medical Investment Co., Ltd.) from September 2021 to September 2024. The patients, aged between 28 and 60, met the criteria for immediate implant placement combined with GBR treatment. The alveolar bone contour plumpness score, osseointegration status, implant stability score, postoperative aesthetic effect, and patient satisfaction score were compared at 1, 3, and 6 months postoperatively. *Results:* At 1, 3, and 6 months postoperatively, the patients' alveolar bone contour plumpness was higher than preoperative levels. Postoperatively, osseointegration and implant stability (ISQ value) were improved, and the aesthetic effect was superior to preoperative levels ($P < 0.05$). The patient satisfaction score was 92.34 ± 3.12 , with 94.4% of patients willing to undergo similar treatment again and 97.8% willing to recommend it to others. *Conclusion:* Immediate implant placement combined with the GBR technique demonstrates significant advantages in promoting postoperative jaw morphology recovery, enhancing osseointegration and implant stability, improving the aesthetic effect of implant restoration, and boosting patient satisfaction. This approach provides a new therapeutic option in the field of oral implantology.

Keywords: Oral implantology; Immediate implant placement; Guided Bone Regeneration (GBR) technique; Alveolar bone morphology; Aesthetic effect; Patient satisfaction

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1. Introduction

Oral implant technology, especially the advanced technique of immediate implant placement (simultaneous implant placement during tooth extraction), has garnered widespread attention and praise due to its ability to

effectively shorten the overall treatment cycle and significantly reduce patient discomfort during the treatment process. In recent years, the number of patients with tooth loss has been increasing year by year, manifesting in difficulties chewing food, noticeable changes in facial morphology, and other specific symptoms. Failure to perform timely implant restoration surgery after tooth extraction may lead to serious problems, such as jaw bone resorption and aesthetic collapse of the face, greatly affecting patients' quality of life ^[1]. Research indicates that GBR technology, as a core means of promoting bone regeneration, effectively reduces the overall cycle of dental implant surgery and provides patients with a superior treatment plan when combined with immediate implant placement ^[2,3]. Furthermore, the healing mechanism of immediate implant placement combined with GBR is clear and well-defined, demonstrating excellent clinical potential and significant value. This approach has important guiding and practical significance for significantly improving the success rate of immediate implant placement surgery and enhancing patient satisfaction, offering more diversified treatment options for patients requiring tooth extraction.

2. Materials and methods

2.1. General information

A retrospective analysis was conducted on 93 patients who were diagnosed and treated with immediate implant placement and the Guided Bone Regeneration (GBR) bone augmentation technique at Yongning Dental Clinic of Nanning Xinlantian Medical Investment Co., Ltd. (located on the first floor, 45 Caihong South Road, Yongning District, Nanning City) from September 2021 to November 2024. Among them, 46 were male patients and 47 were female patients, with an age range of 28 to 60 years old and an average age of (44.0 ± 5.5) years old. The inclusion criteria were: (1) age range of 28–60 years old; (2) confirmed diagnosis of immediate implant placement after tooth extraction; (3) agreement to receive GBR bone augmentation technique. Exclusion criteria were: (1) suffering from severe systemic diseases; (2) unable to cooperate with treatment and follow-up; (3) having contraindications for implant surgery.

2.2. Methods

During the preoperative preparation stage, local infiltration anesthesia was carefully performed using Articaine Hydrochloride and Epinephrine Tartrate Injection (1.7 mL: 68 mg) to ensure that the patients were in a painless state throughout the surgery. The surgical equipment included a carefully selected dental implant machine from the Woodpecker company, along with a set of dental implant surgical instruments (Straumann) provided by Straumann Group, which contained crucial surgical equipment such as implant drills and implants. Sterilized gloves, medical masks, protective hats, and surgical gowns were prepared to ensure a sterile surgical environment.

The surgical procedure began with the patient lying in a supine position, followed by thorough cleaning and disinfection of the oral cavity. Then, medical staff used Articaine Hydrochloride and Epinephrine Tartrate Injection to perform precise local infiltration anesthesia on the specified area. Using professional dental implant machinery and surgical instruments, the surgeon precisely extracted the affected tooth through a minimally invasive approach and immediately placed an implant of the appropriate size (diameter and length) that was prepared based on preoperative CBCT measurements. GBR bone augmentation was performed around the implant, using 0.25 grams of precisely measured bio-oss bone powder from Switzerland, which was carefully applied to the surface of the implant. A bio-gide membrane was then placed to protect the surgical site and accelerate bone regeneration.

Patients were provided with Amoxicillin Capsules (0.25 g) and 0.2% Compound Chlorhexidine Oral Gargle during the postoperative management stage to prevent potential infections. Ibuprofen Sustained-Release Capsules (0.3 g) were administered to control and alleviate postoperative pain. Patients were required to attend follow-up appointments at 1 week, 1 month, 3 months, and 6 months postoperatively. The stability of the implant was evaluated through changes in the value of the implant stability quotient (ISQ) measured by a dental implant stability meter. Advanced imaging techniques, such as fine-detail oral CT scans, were used to observe the degree of alveolar bone resorption and changes in bone density around the implant, allowing for a detailed evaluation of the alveolar bone contour, bone regeneration, and osseointegration.

2.3. Observation indicators

- (1) Comparison of alveolar bone contour fullness scores: Specific changes in the alveolar bone contour fullness scores in horizontal and vertical directions were compared before surgery and at 1 month, 3 months, and 6 months postoperatively. The VAS score, ranging from 0 to 10, was used for detailed observation, with higher scores indicating better fullness.
- (2) Comparison of osseointegration and implant stability scores: The stability of the implant was evaluated using the ISQ value (within the normal range of 50–75). Changes in bone density around the implant, observed through X-rays, were used to assess osseointegration.
- (3) Postoperative aesthetic evaluation indicators: Facial aesthetic assessment criteria were used to measure the facial aesthetic improvements achieved through immediate implant placement combined with GBR bone augmentation surgery. These criteria included facial symmetry evaluation, tooth alignment regularity, gingival health status score, and occlusal efficiency score, all with a maximum score of 10. Higher scores indicated better aesthetic results.
- (4) Comparison of patient satisfaction scores: Patient satisfaction was evaluated based on surgical results, postoperative recovery process, and pain management. The total score was 100. Scores for willingness to undergo treatment again and recommendation willingness were also assessed, with a maximum score of 100. Higher scores indicated greater satisfaction.

2.4. Statistical processing

SPSS 22.0 software was used as the dedicated data processing tool for this study. All measurement data were verified to follow a normal distribution and were presented as mean \pm standard deviation (SD). The *t*-test and *F*-test were used for statistical analysis. Count data were expressed as the number of cases (*n*) and percentages (%) and were analyzed using the χ^2 test. A *P*-value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of alveolar bone contour fullness scores

The alveolar bone contour fullness scores of patients at 1 month, 3 months, and 6 months postoperatively were higher than those before surgery ($P < 0.05$) (**Table 1**).

Table 1. Comparison table of alveolar bone contour fullness scores (scores, mean \pm SD)

Time	Cases (<i>n</i>)	Alveolar bone contour fullness
Pre-operation	93	45.23 \pm 4.15
1 month post-operation	93	55.34 \pm 5.91
3 months post-operation	93	60.78 \pm 6.11
6 months post-operation	93	65.89 \pm 6.72
F		215.934
P		< 0.001

3.2. Comparison of osseointegration and implant stability scores

The osseointegration and implant stability (ISQ value) of patients after surgery were higher than those before surgery ($P < 0.05$) (Table 2).

Table 2. Comparison of osseointegration and implant stability scores (scores, mean \pm SD)

Time	Cases (<i>n</i>)	Implant stability (ISQ value)	Osseointegration bone density score	Implant looseness	Peri-implant soft tissue inflammation
Pre-operation	93	58.4 \pm 4.95	3.2 \pm 0.31	1.0 \pm 0.21	1.52 \pm 0.44
Post-operation	93	69.3 \pm 5.19	8.1 \pm 1.72	0.19 \pm 0.07	0.87 \pm 0.38
<i>t</i>		14.656	27.038	35.288	10.782
P		< 0.001	< 0.001	< 0.001	< 0.001

3.3. Comparative analysis of postoperative aesthetic effects

The aesthetic effects of patients after surgery were better than those before surgery ($P < 0.05$) (Table 3).

Table 3. Comparative analysis of postoperative aesthetic effects (mean \pm SD)

Time	Cases (<i>n</i>)	Facial symmetry score (m)	Tooth alignment score (n)	Gingival soft tissue health score (o)	Occlusal function score (p)
Pre-operation	93	3.02 \pm 0.51	2.57 \pm 0.41	2.85 \pm 0.31	2.03 \pm 0.81
Post-operation	93	4.55 \pm 0.61	4.55 \pm 0.50	4.57 \pm 0.41	8.04 \pm 0.71
<i>t</i>		18.557	29.530	32.270	53.808
P		< 0.001	< 0.001	< 0.001	< 0.001

Measurement unit notes: (m) Measurement unit is score, (n) Measurement unit is score, (o) Measurement unit is score, (p) Measurement unit is score.

3.4. Analysis of patient satisfaction scores

The patient satisfaction score was (92.34 \pm 3.12 points), with a high proportion of 94.4% of patients willing to receive similar treatment again, and 97.8% willing to recommend it to others.

4. Discussion

The immediate implant placement technique in oral surgery, combined with GBR (Guided Bone Regeneration) bone augmentation technology, represents a cutting-edge innovation in the field of oral implantology. Its application primarily addresses issues such as tooth looseness that is difficult to retain and requires extraction, leading to atrophy of the alveolar bone due to long-term tooth loss^[4]. This technology, with its unique advantages, can significantly reduce the treatment time required, effectively alleviate the physical and psychological burden on patients, and promote positive improvements in jaw morphology^[4]. Comprehensive nursing measures that cover crucial aspects such as active prevention of postoperative infections, meticulous pain management, and regular and thoughtful follow-up visits for patients are essential^[5]. This study deeply reveals that the combination of the immediate implant placement technique and GBR has demonstrated significant effectiveness in promoting effective recovery of postoperative alveolar bone morphology. The results are highly consistent with conclusions drawn from numerous similar studies, both domestically and internationally.

The findings indicate that the fullness of the alveolar bone contour of patients after surgery has significantly improved, validating the effectiveness of the immediate implant placement combined with GBR technology in restoring jaw morphology. Statistical analysis results at 1 month, 3 months, and 6 months postoperatively all showed significant differences ($P < 0.05$), which strongly demonstrates the continuous and positive improvement and development of the fullness of the jaw contour. The improvement in alveolar bone contour fullness is not a short-term phenomenon but is accompanied by an enhancement in implant stability^[6]. Detailed assessments of implant stability (ISQ value) at 3 and 6 months postoperatively revealed significant improvements ($P < 0.05$), and the osseointegration status also progressed from a good state at 1 month postoperatively to a more optimal and stable level at 6 months postoperatively. This suggests that the significant improvement in alveolar bone contour fullness and the enhancement of implant stability have formed a virtuous cycle, complementing each other and jointly becoming indispensable key aspects of postoperative recovery^[5]. The fullness of the alveolar bone facilitates the neat arrangement of implant-supported dentures and adjacent natural teeth, enhancing the patient's biting and chewing function. Additionally, it improves the aesthetic contour of gingival soft tissues and the continuity of the smile line, enhancing the overall facial aesthetics.

In terms of patient satisfaction, not only has the satisfaction score increased significantly, but patients' willingness to undergo treatment again and their recommendation intentions have also strengthened notably^[7,8]. At 3 months postoperatively, the patient satisfaction score increased significantly to 92.34 ± 3.12 points ($P < 0.05$), showing a clear positive trend. Among them, the proportion of patients willing to receive similar treatment again in the future accounted for up to 94.4%, while the proportion of patients willing to recommend this treatment experience to others reached 97.8%. These data show in detail the remarkable advantages of the immediate implant placement combined with GBR technology in greatly improving patient satisfaction and gaining widespread recognition^[9,10].

5. Conclusion

The combination of the immediate implant placement technique and the GBR bone augmentation method in oral surgery has played a significant role in postoperative jaw morphology recovery. It has greatly enhanced the stability of implants, effectively controlled pain and infection, and significantly improved patient satisfaction.

Disclosure statement

The author declares no conflict of interest.

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Research Progress on Malignant Peritoneal Effusion in Gastrointestinal Tumors

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Abstract: Malignant Peritoneal Effusion (MPE) in gastrointestinal tumors can affect the prognosis of patients with advanced cancer. It is associated with multiple factors such as abnormal angiogenesis, a damaged lymphatic system, and an inflammatory response. After the onset of the disease, tumor cells invade the peritoneum, and changes in the peritoneal microenvironment can increase vascular permeability. Additionally, factors such as the high number of neovascularizations in patients with malignant tumors, lymphatic circulation disorders, and intensified inflammatory responses in the body create a vicious cycle, leading to increased production of ascites. Clinically, imaging techniques, cytological techniques, and biomarker detection techniques are commonly used to diagnose MPE, and treatment options and prognostic factors are explored through clinical practice. This study analyzes the diagnosis and treatment methods of MPE from multiple perspectives, providing a basis for summarizing new diagnosis and treatment methods for MPE in the later stage.

Keywords: Gastrointestinal tumors; Malignant peritoneal effusion; Diagnostic methods; Treatment methods

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1. Introduction

MPE is a common complication of advanced gastrointestinal tumors (such as gastric cancer, colorectal cancer, pancreatic cancer, etc.), with about 15%-50% of patients with advanced disease developing peritoneal effusion ^[1]. This type of effusion grows rapidly and can cause symptoms such as abdominal pain, abdominal distension, oliguria, and dyspnea. It may also lead to serious complications such as water and electrolyte imbalance, infection, and pulmonary embolism. The appearance of MPE indicates that the disease has entered its terminal stage, with a median survival time of only 3-6 months for patients. With the advancement of molecular biology and imaging technology, significant progress has been made in the diagnosis and treatment of MPE, but challenges such as high drug resistance still exist. Therefore, in-depth research on MPE is extremely important for developing new treatment strategies, relieving patient symptoms, and improving prognosis. This article aims to systematically review the research results on the pathophysiological mechanism, diagnostic methods, treatment strategies, prognostic factors, and palliative and supportive treatment of malignant peritoneal effusion

in gastrointestinal tumors, providing references for clinical treatment and further research.

2. Current research status of malignant peritoneal effusion in gastrointestinal tumors

In recent years, domestic and foreign research has focused on exploring the molecular mechanisms of MPE and developing precision treatment strategies. For example, Hua Chan Su injection reduces the production of ascites in colon cancer by inhibiting Vasculogenic Mimicry (VM), with a clinical effective rate of 61.5%^[2]. In targeted therapy, anti-VEGF drugs (such as Bevacizumab) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) significantly reduce serum VEGF levels in patients with ovarian cancer and ascites. Immunotherapy, such as PD-1 inhibitors, can achieve a response rate of 20%-30% in gastric cancer ascites^[3]. Additionally, liquid biopsy techniques (such as circulating tumor cell detection) have shown potential in the early diagnosis and efficacy monitoring of MPE.

3. Pathophysiological mechanisms of malignant peritoneal effusion in gastrointestinal tumors

3.1. Interaction between tumor cells and the peritoneal microenvironment

3.1.1. Characteristics of tumor cells and peritoneal metastasis

Gastrointestinal tumor cells exhibit strong invasion and metastasis capabilities. Through epithelial-mesenchymal transition (EMT), these cells acquire invasiveness, expressing adhesion molecules like integrin $\alpha v \beta 3$ and CD44, which facilitate peritoneal implantation. The tumor cells can also secrete a series of cytokines that promote the production and maturation of the extracellular matrix. Inflammatory factors can enhance their adhesion and implantation abilities, ultimately enabling them to reach the abdominal cavity via lymphatic or blood circulation, adhere, proliferate, and form metastases. For instance, ovarian cancer cells can secrete MMP-2/9 to degrade the extracellular matrix, leading to the formation of metastatic lesions.

3.1.2. Impact of the peritoneal microenvironment on tumor cells

The peritoneal microenvironment, consisting of various cellular components, extracellular matrix, and specific local physicochemical properties, forms a complex but relatively stable environment. In this setting, multiple cell types can be induced by cancer cells, participating in and facilitating tumor growth, invasion, and peritoneal metastasis. For example, tumor-associated macrophages (TAMs) secrete IL-10 and TGF- β to suppress immune responses and release VEGF to promote vascular leakage^[4], thereby enhancing tumor cell proliferation and metastasis. Caspase-1, by cleaving the PPAR γ protein, induces TAM lipid metabolism reprogramming, exacerbating ascites formation.

3.2. Angiogenesis, lymphatic system, and inflammatory responses

3.2.1. Role of angiogenesis in the formation of peritoneal effusion

In the formation of malignant peritoneal effusion, angiogenesis is abnormally active. The newly formed tumor vessels are immature and have increased permeability, providing rich nutrient supply and oxygen support to tumor cells. Vascular endothelial growth factor (VEGF) promotes increased vascular permeability, extracellular matrix denaturation, vascular endothelial cell migration, proliferation, and angiogenesis. For instance, VEGF-A

upregulates vascular permeability, allowing plasma proteins to infiltrate into the abdominal cavity, while VEGF-C/D drives lymphatic hyperplasia, leading to lymphatic return dysfunction. ANGPT2 acts synergistically with VEGF to promote vascular leakage ^[5].

3.2.2. Lymphatic system dysfunction and peritoneal effusion

Under normal circumstances, the lymphatic system absorbs excess fluid and macromolecular substances, returning them to the blood circulation to prevent edema. In malignant peritoneal effusion, the lymphatic system function is often impaired, leading to fluid accumulation. Additionally, tumors can secrete certain factors that interfere with the normal function of the lymphatic system, further exacerbating the formation of peritoneal effusion.

3.2.3. Inflammatory responses and peritoneal effusion

Inflammation alters the tumor microenvironment (TME) through various mechanisms, affecting the production of cytokines and proinflammatory mediators, angiogenesis, and tissue remodeling, thereby participating in tumor development ^[6]. For example, inflammatory factors such as tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) are elevated in malignant peritoneal effusion, closely related to its formation and progression.

4. Diagnostic methods for malignant peritoneal effusion in gastrointestinal cancer

4.1. Imaging examination

Computed tomography (CT) and positron emission tomography-computed tomography (PET-CT) can clearly show tumor lesions, the amount of effusion, and tumor metastasis in the abdominal cavity. Ultrasonography is economical, convenient, and noninvasive, making it a useful tool for initial screening. Additionally, ultrasound fusion techniques (such as US-CT/MRI), which combine real-time dynamic imaging with high-resolution tomography, can accurately locate peritoneal metastases. Enhanced magnetic resonance imaging (MRI) can detect small amounts of ascites (< 100 mL) and peritoneal thickening.

4.2. Cytological examination

Cytological examination is one of the gold standards for diagnosing malignant peritoneal effusion. It mainly includes abdominal paracentesis and cell smear examination. Furthermore, the examination of free cancer cells in the abdominal cavity and peritoneal lavage fluid can also improve diagnostic accuracy. However, cytological examination has low sensitivity, and multiple examinations may be required for some patients.

4.3. Biomarker detection

Biomarkers include tumor markers, inflammatory factors, and other related indicators. Serum tumor markers such as CEA, carbohydrate antigen 125 (CA125) ^[25], and carbohydrate antigen 19-9 (CA19-9) can suggest the possibility of tumor metastasis and peritoneal effusion. For example, elevated levels of CEA and CA19-9 in the serum of patients with colorectal cancer may indicate the presence of tumor metastasis and peritoneal effusion. Additionally, some emerging biomarkers, such as circulating tumor cells (CTC) and exosomes, have shown potential diagnostic value in research ^[7].

5. Treatment progress of malignant peritoneal effusion in gastrointestinal cancer

5.1. Systemic chemotherapy

Commonly used chemotherapy drugs include cisplatin, fluorouracil, oxaliplatin, and paclitaxel. Systemic chemotherapy can cover multiple tumor lesions in the body. However, it also has significant limitations, such as low drug concentration in the abdominal cavity, which makes it difficult to effectively control local lesions. Due to limitations in chemotherapy drug dosage and side effects, such as the peritoneal-plasma barrier, intravenous chemotherapy cannot effectively control the occurrence and progression of free cancer cells (FCC) in the abdominal cavity.

5.2. Paracentesis for ascites drainage and intraperitoneal drug administration

Paracentesis for ascites drainage is a commonly used method for treating malignant peritoneal effusion (MPE) with proven efficacy. However, simply draining the ascites can lead to its recurrence in a short period of time, and repeated drainage can cause hypoproteinemia, electrolyte imbalance, peritonitis, and hypovolemic shock in patients. Through technical improvements, paracentesis catheter drainage can achieve one-time puncture and multiple drainage of ascites, reducing patient discomfort and facilitating intraperitoneal drug administration for the treatment of MPE.

5.3. Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

HIPEC can directly target intra-abdominal lesions while providing local chemotherapy, hyperthermia, and peritoneal lavage for residual tumor nodules, micrometastases, and free cancer cells. This technique has become a mature clinical application and has unique efficacy in preventing peritoneal metastasis and associated malignant peritoneal effusion in abdominal malignancies such as colorectal cancer, gastric cancer, liver cancer, and pancreatic cancer. A recent study has shown that HIPEC can significantly improve the median survival time in patients with terminal gastrointestinal tumors ^[8].

5.4. Targeted therapy and immunotherapy

Targeted therapy acts specifically on particular molecular targets on tumor cells, such as VEGF receptors and EGFR, enabling more precise inhibition of tumor growth and angiogenesis. Representative drugs include bevacizumab and cetuximab. For instance, the ToGA trial demonstrated that trastuzumab, as a first-line treatment, can improve survival rates in patients with advanced gastric cancer ^[9]. Immunotherapy, which activates the body's own immune system to fight cancer, has gained significant attention in recent years.

6. Factors influencing the prognosis of malignant peritoneal effusion in gastrointestinal tumors

6.1. Tumor-related factors

The type, stage, metastasis, and biological characteristics of the tumor cells significantly impact the prognosis. Generally, early-stage gastrointestinal tumors have a better prognosis if detected and treated effectively. However, advanced tumors, especially those with peritoneal metastasis, have a poorer prognosis.

6.2. Patient's general condition

Factors such as age, physical condition, nutritional status, and comorbidities also affect the prognosis. For example, patients with malnutrition or chronic diseases may have poor tolerance to treatment, thereby affecting the overall efficacy ^[10].

7. Palliative and supportive treatment for malignant peritoneal effusion in gastrointestinal tumors

7.1. Symptom control

For patients with malignant peritoneal effusion due to gastrointestinal tumors, symptom relief is a crucial aspect of palliative care. Currently, ascites drainage is the primary clinical method to control ascites, rapidly alleviating symptoms caused by ascites compression. For patients with significant pain, the appropriate use of analgesic drugs is essential. For some patients who cannot achieve symptom relief through medication or interventional therapy, palliative surgery (such as peritoneal drainage) can effectively reduce symptoms and improve quality of life.

7.2. Improvement of physical and mental conditions

For patients with ascites caused by hypoproteinemia, strict control of sodium and water intake is essential, along with planning a daily diet and intravenous infusion of albumin to increase plasma colloidal osmotic pressure. Additionally, psychological support, pain management, and rehabilitation exercises cannot be ignored. Patients with malignant intraperitoneal fluid often suffer from psychological issues such as anxiety and depression, making psychological intervention and social support crucial components of palliative care.

7.3. Multidisciplinary Treatment Model (MDT)

The Multidisciplinary Treatment Model (MDT) offers significant advantages in the palliative care of patients with advanced cancer. By integrating resources from various disciplines such as surgery, internal medicine, traditional Chinese medicine, and nursing, MDT provides individualized treatment plans for patients.

8. Conclusion

Malignant peritoneal effusion in gastrointestinal tumors is a severe complication in the late stages of the disease, significantly impacting patients' quality of life and survival prognosis. Although recent research has made progress in understanding its pathophysiology, diagnostic methods, and treatment strategies, leading to better diagnosis and treatment options, many challenges remain. In terms of diagnosis, there is a need to further improve accuracy and sensitivity. Regarding treatment, each approach has limitations, necessitating the exploration of more effective integrated treatment plans.

In the future, more intensive research should be conducted on the pathogenesis of malignant peritoneal effusion in gastrointestinal tumors to identify new therapeutic targets. Additionally, multi-center, large-sample clinical studies should be carried out to provide high-level, evidence-based medical evidence for various treatment methods and optimize treatment plans. Furthermore, with the development of precision medicine and artificial intelligence technology, personalized treatment is expected to be achieved, further improving patients' survival rates and quality of life.

Disclosure statement

The authors declare no conflict of interest.

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Clinical Study on the Short-term Efficacy Evaluation of Proton Radiotherapy after Surgery for Medulloblastoma in Children

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Abstract: *Objective:* To explore the short-term efficacy and safety of proton radiotherapy as an adjuvant treatment for medulloblastoma in children, focusing on evaluating its impact on local tumor control rate, neurocognitive function, and pituitary-thyroid axis. *Methods:* Thirty children with medulloblastoma who completed surgery between May 2023 and May 2024 were included in the study. The patients were randomly assigned to two groups: the experimental group received proton radiotherapy, while the control group underwent conventional photon radiotherapy. Both groups followed a standard dose regimen: 36Gy for the whole brain and spinal cord, and 54Gy for the tumor bed. Observation indicators included the local tumor control rate, acute radiotherapy-related toxicities, and changes in pituitary-thyroid function within 6 months. *Results:* The local tumor control rate was better in the proton radiotherapy group compared to the control group, with no significant increase in acute toxic side effects. In neurocognitive assessments, children in the experimental group showed more stable cognitive function maintenance. Endocrine monitoring revealed that the pituitary-thyroid axis function was relatively stable in the proton group, and the risk of impairment was significantly lower than that in the photon group. *Conclusion:* Proton radiotherapy has significant clinical advantages as an adjuvant treatment for medulloblastoma in children. Its precise dose delivery reduces exposure to normal brain tissue, significantly reducing the risk of neurocognitive and endocrine function impairment. This therapy not only improves local tumor control but also balances the quality of life for the children, providing a more ideal treatment option. Future studies need to expand the sample size and extend follow-up time to verify long-term safety and durability of efficacy. The results of this study provide a solid clinical basis for the promotion and application of proton radiotherapy in the treatment of pediatric brain tumors.

Keywords: Medulloblastoma; Proton radiotherapy; Efficacy and safety

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1. Introduction

Medulloblastoma is one of the most common malignant intracranial tumors. The occurrence of this disease is

related to various factors such as genetics and the environment, affecting the central nervous system function of patients and bringing great misfortune to patients and their families. Surgical resection is the preferred method for treating this disease. However, due to the incomplete resectability of the surgery, effective adjuvant radiotherapy is a common treatment method for patients after surgery. Although traditional photon radiotherapy can kill tumor cells, it cannot avoid giving radiotherapy doses to brain cells, especially in important areas of brain function development, such as the hippocampal region and important endocrine glands, leading to irreversible damage to patients. In longer-term follow-up, many surviving patients experience varying degrees of cognitive decline, and endocrine changes such as growth hormone deficiency are also common. Such injuries are directly related to the radiotherapy dose, and the incomplete distribution of the radiotherapy dose results in the complete exposure of normal brain regions being excluded from the impact. However, proton beams, unlike photons, have a more significant ability to kill tumor tissue and have a significantly smaller impact on non-target normal tissue. They can better achieve precise positioning of the dose peak in the tumor target area, greatly reducing the dose to important normal brain tissue such as the hippocampal region and endocrine glands. Currently, dosimetry studies also indicate that it can reduce the dose burden on important brain function areas such as the hippocampal region and endocrine glands. However, there is no objective verification in clinical practice whether proton radiotherapy reduces neurocognitive and endocrine function damage in children. There are also no specific reports on acute toxic reactions in children after radiotherapy. We can evaluate neurocognitive and endocrine function damage caused by proton radiotherapy through multi-modal assessment methods, such as diffusion tensor imaging (DTI) and detailed neurocognitive assessment indicators, to provide an objective interpretation of proton radiotherapy's damage to brain structure and function. This research plans to compare the short-term efficacy and safety of the radiotherapy group and the proton radiotherapy group through a prospective randomized controlled approach. To explore the reduction of cognitive impairment and endocrine function changes by proton radiotherapy, and to analyze and study brain function after radiotherapy. The research results will not only guide the optimization of clinical radiotherapy plans but also provide scientific support for improving the long-term survival quality of children with brain tumors, which has important clinical and social significance^[1].

2. Materials and methods

2.1. General information

Thirty pediatric patients with medulloblastoma treated at our hospital from May 2023 to May 2024 were selected. After pathological examination, patients with postoperative residual lesion diameters less than 1.5 cm and no distant metastasis were included in the study. Inclusion criteria: Karnofsky score of 70–90, excluding those with a history of radiotherapy and craniocerebral surgery, patients with Gorlin syndrome, and those with significant liver and kidney dysfunction. Stratified random control grouping was used based on age, with 8 males and 7 females in the control group, aged 6.2 (range 3–12) years old. The study group consisted of 9 males and 6 females, aged 5.8 (range 4–11) years old. Tumor volumes were 28.6 ± 5.1 and 27.9 ± 4.8 cm³, respectively, and the proportions of SHH molecular subtypes were 53.3% and 46.7%. There was no statistically significant difference between the two groups ($P > 0.05$)^[2].

2.2. Methods

2.2.1. Control group

The control group received 6 MV X-ray volumetric modulated arc therapy (VMAT) for craniospinal irradiation with a total dose of 36 Gy delivered in 20 fractions, and a boost dose of 54 Gy to the tumor bed delivered in

30 fractions. Target delineation included the postoperative tumor bed and 1cm surrounding area, with a 0.5 cm expansion of the spinal cord CTV. Strict dose control was required for critical organs: the maximum dose to the brainstem was ≤ 54 Gy, and lens exposure was controlled at ≤ 5 Gy. This protocol achieved an optimal balance between preserving function and inhibiting the tumor. Reasonable dosing and appropriate target range minimized the risk of radiation-induced neurological damage while providing sufficient dosing to ensure the lowest recurrence rate ^[3]. Unlike proton therapy, VMAT offered certain advantages in dose uniformity and irradiation range, but still had limitations in protecting normal deep organs. Treatment plans needed to be tailored to individual patient conditions, balancing benefits and risks for optimal therapeutic effect ^[4].

2.2.2. Experimental group

The experimental group received proton beam scanning radiotherapy with a planned dose of 36 Gy RBE to the brain and spinal cord and 54 Gy RBE to the tumor bed. The irradiation range was set according to the control group, and multi-field optimization was employed to keep the dose to the hippocampal region below 10 Gy RBE and the maximum dose to the pituitary gland below 20 Gy RBE. This dosing ensured efficacy while reducing exposure to critical brain regions, thereby effectively avoiding cognitive and endocrine damage ^[5]. Weekly CT scans were used for positioning during treatment, with a margin of error within 2 mm to ensure treatment safety. This highlighted the advantages of proton beam scanning radiotherapy for postoperative radiotherapy of pediatric medulloblastoma and its unique role in protecting normal brain regions ^[6].

2.3. Observation indicators

- (1) Clinical efficacy was comprehensively evaluated using RANO criteria. Progression-free survival was determined by MRI at 6 months post-surgery. During treatment, results were analyzed based on tumor stability, reduction, or progression, excluding subjective estimation factors to ensure objective, reliable efficacy ^[7].
- (2) Acute radiation-induced cerebral edema was graded according to CTCAE 5.0, using CT scans and clinical symptoms as grading criteria. Myelosuppression was graded based on hematological results, reflecting treatment-related myelosuppression injury ^[8].
- (3) The Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV) was used to assess changes in children's cognitive function before and after treatment. WISC-IV accurately reflected cognitive dysfunction characteristics, patterns, and recovery across various scales and items.
- (4) Continuous monitoring of free thyroxine (FT4) and insulin-like growth factor-1 (IGF-1) levels before and after treatment allowed early detection of endocrine disorders after radiotherapy, guiding subsequent adjustments ^[9].

2.4. Statistical analysis

SPSS 26.0 was used for statistical analysis. Survival analysis was performed using the Kaplan-Meier method and Log-rank test. Cognitive scores were analyzed using repeated measures ANOVA. Categorical variables were tested using Fisher's exact test. Statistical significance was set at $P < 0.05$.

3. Results

3.1. Comparison of tumor control and imaging indicators between the two groups

The experimental group showed superior local control rates at the tumor bed (100% vs. 80%) and better

preservation of white matter fiber bundle integrity (FA value decrease of 1.2% vs. 8.7%) compared to the control group ($P < 0.05$). See **Table 1** for a comparison of tumor control and neuroimaging changes.

Table 1. Comparison of tumor control and neuroimaging changes

Parameter	Control group ($n = 15$)	Experimental group ($n = 15$)	Statistic (χ^2/t)	P -value
6-month PFS (%)	73.3 (11/15)	93.3 (14/15)	$\chi^2 = 3.75$	0.018
Local tumor bed control (%)	80.0 (12/15)	100 (15/15)	$\chi^2 = 4.62$	0.031
Δ DTI-FA (%)	-8.7 ± 2.3	-1.2 ± 0.9	$t = 11.34$	< 0.01
Mean hippocampal dose (Gy)	32.1 ± 3.2	9.5 ± 1.8	$t = 23.67$	< 0.01
Tumor bed conformity index (CI)	0.78 ± 0.05	0.92 ± 0.03	$t = 8.94$	< 0.01
Max spinal cord dose (Gy)	41.3 ± 1.5	36.0 ± 0.9	$t = 12.85$	< 0.01

3.2. Comparison of acute toxic reactions and endocrine function between the two groups

The incidence of Grade 3 myelosuppression in the experimental group decreased by 60%, and the TSH abnormality rate improved significantly ($P = 0.026$) (**Table 2**).

Table 2. Comparison of toxic reactions and endocrine indicators

Parameter	Control group ($n = 15$)	Experimental group ($n = 15$)	Statistic (χ^2/t)	P -value
Grade 3 myelosuppression (%)	33.3 (5/15)	13.3 (2/15)	$\chi^2 = 2.14$	0.143
Acute radiation-induced brain edema (%)	40.0 (6/15)	6.7 (1/15)	$\chi^2 = 5.23$	0.018
TSH abnormality (> 5 mIU/L, %)	46.7 (7/15)	13.3 (2/15)	$\chi^2 = 4.32$	0.026
Δ IGF-1 reduction (ng/mL)	-35.2 ± 8.1	-12.6 ± 4.3	$t = 9.27$	< 0.01
Hearing loss (\geq Grade 2, %)	26.7 (4/15)	6.7 (1/15)	$\chi^2 = 2.86$	0.043
Nausea/Vomiting (\geq Grade 2, %)	53.3 (8/15)	20.0 (3/15)	$\chi^2 = 4.13$	0.042

3.3. Comparison of neurocognitive and quality of life scores between the two groups

The decrease in working memory scores in the experimental group was reduced by 76.5% compared to the control group ($P = 0.003$) (**Table 3**).

Table 3. Comparison of neuropsychological evaluation results

Measure	Control group ($n = 15$)	Experimental group ($n = 15$)	t -value	P -value
FSIQ change	-8.2 ± 2.1	-2.5 ± 1.3	8.94	< 0.01
Working Memory Index (WMI)	-10.5 ± 3.2	-2.4 ± 1.1	9.23	< 0.01
Processing Speed Index (PSI)	-7.8 ± 2.7	-3.1 ± 1.5	5.67	< 0.01
Parent-Reported Executive Function (BRIEF-T)	68.3 ± 5.2	57.1 ± 4.8	5.82	< 0.01
Physical functioning (PedsQL)	62.4 ± 6.3	78.9 ± 5.1	7.35	< 0.01
Emotional problems (SDQ)	14.2 ± 2.5	9.8 ± 1.7	5.43	< 0.01

4. Discussion

This study investigated the short-term efficacy and safety of adding proton radiotherapy to adjuvant radiotherapy after surgery for pediatric medulloblastoma. The results showed that the local tumor control rate in the proton group reached 100%, which was significantly better than the 80% in the conventional photon group. This suggests that proton radiotherapy is more accurate and effective in local target control, while minimizing damage to adjacent normal brain tissue. The impact of diffusion tensor imaging (DTI) on white matter fiber integrity in the proton group was only slightly reduced, indicating that the proton group can more effectively reduce nerve fiber damage compared to the conventional photon group, suggesting a greater neuroprotective effect of the proton group. This directly reflects the potential advantages of proton radiotherapy for protecting the nervous system of children.

Comparing the proton group with the photon group, the mean dose to the hippocampal region was lower in the proton group, suggesting that proton irradiation can minimize the radiation exposure to important brain regions while ensuring the radiotherapy dose. The hippocampus is the main structure responsible for cognition, so reducing the radiation dose to the hippocampus may be related to improved neurocognitive function. From the clinical manifestations of neurocognitive function, the comparison between the proton group and the photon group suggests that the proportion of children with neurocognitive dysfunction after treatment is lower in the proton group than in the photon group (mainly working memory and processing speed), enhancing the perception of imaging dosimetry. It can be considered that proton therapy reduces tumor residue and provides a guarantee for the long-term quality of life of children.

From the perspective of toxic reactions, the incidence of Grade 3 myelosuppression and acute radiation-induced brain edema was lower in the proton group. In particular, the pituitary-thyroid axis function showed a significant improvement trend, with a lower TSH abnormality rate and more stable IGF-1, indicating that proton therapy has a better endocrine protective effect. Endocrine system damage often has a severe impact on children's growth and development as well as their long-term quality of life. Thus, the results suggest that proton therapy can contribute to the long-term physiological recovery of children.

Patient quality of life scores, including life function, activity, and emotional ability, were higher in the proton treatment group compared to the control group. Parent ratings of executive function were also lower in the proton treatment group, suggesting that proton therapy not only controls the tumor well but also improves overall function and emotions. It has a good effect on this group of children. It is suggested that more attention should be paid to the care of children after the end of treatment, and proton therapy may improve the quality of life of children.

On the other hand, the uniform dose distribution characteristic of proton radiotherapy also brings enlightenment to the development of pediatric oncology treatment. The dilemma of how to reduce the radiation dose to normal tissues while reducing treatment-related toxicity has always troubled us. The results of this study undoubtedly provide clinical evidence for this clinical dilemma, pointing out the importance of technological development for the comprehensive treatment of pediatric tumors. Follow-up studies still need to focus on the long-term follow-up of proton radiotherapy, studying its long-term development impact on neurocognitive, endocrine, and social adaptability to provide optimized treatment plans^[10].

5. Conclusion

Proton radiotherapy demonstrates significant clinical advantages as an adjuvant treatment for pediatric medulloblastoma. Its precision in dose delivery minimizes radiation exposure to healthy brain tissue, thereby

substantially lowering the risks of neurocognitive and endocrine dysfunction. This approach not only enhances local tumor control but also improves long-term quality of life for pediatric patients, offering a superior therapeutic option compared to conventional radiotherapy. However, further large-scale studies with extended follow-up periods are warranted to validate its long-term efficacy and safety. The findings of this study strongly support the broader clinical adoption of proton radiotherapy in the management of pediatric brain tumors.

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Disclosure statement

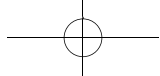
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- Ethics
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