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# Clinical Application and Research Progress of Accelerated Rehabilitation Surgery in Perioperative Period of Advanced Gastric Cancer in the Elderly

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## Abstract

Enhanced recovery after surgery (ERAS) has been used in various surgical professions in recent years and is widely accepted by doctors. This concept not only helps patients speed up postoperative recovery, reduce the incidence of related complications and shorten hospital stays, but also has been proved to be effective and safe in the perioperative application of gastric cancer. This article reviews the clinical application and research progress of enhanced recovery after surgery in the perioperative period of advanced gastric cancer in the elderly.

## Keywords

Enhanced Recovery after Surgery, Elderly Patients, Advanced Gastric Cancer, Perioperative Period, Clinical Application, Research Progress

## 1. Overview

According to GLOBOCAN data in 2018 [1] [2], the number of gastric cancer patients worldwide is about 103 million. Gastric cancer has become the fifth most common malignant tumor and one of the third most deadly tumors. New cases of gastric cancer are added every year. About 5.7% of all new cancer cases. In China, although the incidence and mortality of gastric cancer have declined in recent years, it accounted for about 11 percent of all cancers and 12.8 percent of all deaths. It is still the third leading cause of cancer death in China, after lung cancer and colorectal cancer. In the elderly, the incidence of gastric cancer is

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higher [3], because the clinical symptoms of early gastric cancer are not obvious, patients often do not pay enough attention. In addition, due to the lack of effective methods for early screening of gastric cancer, the detection rate of early gastric cancer is only about 10% [4]. Has entered the advanced stage, so surgery is currently recognized as the best treatment.

In China, in recent years, the population structure tends to be aging, the proportion of the elderly (>60 years old) is increasing, and the corresponding elderly patients are gradually increasing. As the body immunity of the elderly declines, the adaptability to the internal and external environment decreases. Often combined with chronic diseases, such as hypertension, diabetes, heart disease, etc. [5], the tolerance and resilience to surgery and its postoperative decline, prone to a series of complications, and even life-threatening. How to reduce stress response and speed up postoperative recovery is a hot and difficult point.

Based on evidence-based medicine, ERAS is a multidisciplinary collaboration that reduces post-stress and accelerates postoperative recovery. It was first proposed by Danish surgeon Kehlet *et al.* [6] in 1997 and in China by 2007. Professor Zhiwei's application in gastric cancer [7] has been widely used in various surgical fields. This concept runs through preoperative, intraoperative and postoperative operations. The focus is on preoperative consultation, optimized nutrition, standardized analgesia, and reduction. The use of opioids to minimize electrolyte and fluid imbalances and promote early activity and feeding [8]; there is clear evidence [9] [10] that accelerating rehabilitation surgery is safe and effective for elderly patients, supporting accelerated surgical surgery applications. In elderly patients, this article reviews the clinical application and research progress of accelerated rehabilitation surgery in elderly patients with advanced gastric cancer during gastric surgery.

## **2. Application of Eras in Perioperative Period of Advanced Gastric Cancer in the Elderly**

### **2.1. Preoperative Preparation**

#### **2.1.1. Preoperative Communication and Consultation**

Before surgery, the patient physiologically responds to stress. The central nervous system mediates this process, producing stress hormones and inflammatory mediators [11], and strengthens effective communication with patients before surgery. It can be written and spoken. The above agreement provides individualized counseling to patients and psychologically prepares them for what they are doing, thereby reducing the anxiety and fear of patients, improving recovery, improving patient compliance with the plan, and promoting eating. Early exercise, pain control and respiratory function, reduce the occurrence of complications [8] [12]; for elderly patients, often combined with chronic diseases, to actively treat diseases that affect the recovery of patients, such as hypertension, diabetes, blood pressure Achieve a stable state with blood glucose before surgery, and actively improve nutrition for malnourished patients, so that the patient's

body reaches an optimal state before surgery.

### **2.1.2. Preoperative Nutritional Improvement**

For elderly patients with gastric cancer, often combined with malnutrition, is the main clinical problem of gastrointestinal malignant tumors, malnutrition in hospitalized patients reached 50% - 60%, up to 71% in cancer patients [13]; malnutrition led to hospitalization Prolonged time, increased postoperative complications, slow recovery of postoperative bowel function, high readmission rate, high postoperative mortality; evidence [14], preoperative nutritional status is a key determinant of optimal outcome in gastrointestinal surgery avoid preoperative fasting before surgery, optimize preoperative nutrition, oral nutritional supplements and immunonutrient preparations; Sonvi research shows [15], preoperative oral immunonutrition preparations, postoperative complications are lower, it is recommended that all preoperative The patient underwent 5 to 7 days of on-site immunonutrition [16].

### **2.1.3. Gastrointestinal Preparation**

Inadequate mechanical bowel preparation before surgery has been shown to cause dehydration and imbalance of fluids and electrolytes, especially in elderly patients. Mechanical bowel preparation is to remove solid excretion from the large intestine and reduce the amount of bacteria. Liquefaction of feces increases the risk of surgical spillage [8]; there is no need to fast for one night before surgery. The current guidelines recommended by the American Society of Anesthesiologists [17], fasting solid foods 8 hours before surgery, 2 hours before the ban According to the Cochrane study [18], the risk and incidence of inhalation were not increased compared with traditional requirements; prolonged fasting (>12 h) resulted in hypovolemia, increased metabolic stress and insulin resistance, insulin resistance It is a key factor for long-term rehabilitation and increased morbidity; a data suggest that [19], decreased insulin sensitivity, will lead to increased complication rate, postoperative hyperglycemia, increased risk of postoperative infection by 30%; 2 - 3 day before surgery Drinking 300 - 400 ml of carbohydrates a day can not only reduce pre-operative thirst, hunger, anxiety and postoperative insulin resistance, but also reduce postoperative nitrogen and protein loss, better maintain capacity and muscle mass, and exhaust time. With hospitalizationShortening, however, for patients with diabetes and delayed gastric emptying, gastrointestinal motility disorders with the exception of patients [8].

### **2.1.4. Gastrointestinal Decompression Tube**

The nasogastric tube is not routinely used. According to the Cochrane conclusion [18], the nasogastric tube is not routinely used, the pulmonary complications are significantly reduced, the early feeding is improved, and the hospital stay is shortened. The use of the nasogastric tube has a certain effect on the nasopharyngeal mucosa. The stimulation, which leads to increased complications in the pharynx and lungs, also exerts pressure on the patient's psychology, and

also has an effect on the patient's early bed-out activities; a randomized trial [20], no patients who received the nasogastric tube, there was no difference in postoperative nausea, vomiting, and recovery of bowel function.

## **2.2. Intraoperative Application**

### **2.2.1. Intraoperative Anesthesia**

The anesthesia program will promote the recovery of gastrointestinal motility and is the key to speeding up recovery. For elderly patients, the anesthesia should be avoided too deeply, and the depth of anesthesia is bis  $< 45$ , not only to minimize the anesthetic, but also to prevent convulsions, promote rapid arousal and recovery [21]; anesthesia is a stress response that limits surgery to fluid balance and pain [22]; intraoperative intravenous anesthesia combined with epidural anesthesia, anesthesia induction and continuous anesthesia are generally selected for short-acting anesthetics (propofol, cis Lacurium, fentanyl, to reduce sympathetic nerve stimulation and postoperative anesthesia, combined anesthesia combined with general anesthesia onset, intraoperative anesthesia and epidural anesthesia can promote postoperative gastrointestinal function recovery, postoperative analgesia The advantages can not only achieve the desired anesthetic effect, but also accelerate the recovery of patients after surgery, inhibit the occurrence of postoperative intestinal paralysis, accelerate the recovery of gastrointestinal function, and provide conditions for early postoperative feeding [21].

### **2.2.2. The Use of Preventive Antibiotics**

The use of prophylactic antibiotics can reduce the incidence of postoperative infections; studies have shown [23] that prophylactic antibiotics are effective against possible anaerobic and aerobic infections, 30 minutes to 1 hour before skin incision Dosage can be administered repeatedly according to the half-life of the drug and the operation time during the operation.

### **2.2.3. Surgical Operation**

The safety and efficacy of laparoscopic radical gastrectomy have been confirmed [24]; there is evidence [14] that laparoscopic surgery can reduce trauma, reduce intraoperative blood loss, and reduce surgical stress response compared with conventional laparotomy Postoperative pain and discomfort, postoperative intestinal adhesions, low incidence of intestinal obstruction, early recovery of bowel function, reduced hospital stay, and a high degree of synergy with eras.

### **2.2.4. Liquid Management**

Liquid management is an important part of eras. It can maintain normal blood volume by pre-operative, intraoperative and postoperative methods. Whether it is a large amount of infusion or a limited amount of infusion, it can significantly impair organ function and will increase postoperative complications ( $P < 0.05$ ). Symptoms and prolonged hospital stay [25]; there is evidence [8], a large number of fluid replacement, delayed recovery of gastrointestinal function, wound



healing and anastomotic healing, affecting tissue oxygenation, leading to prolonged hospital stay; intraoperative fluid management is maintained. There is sufficient circulation at the end of the organ, low blood volume leads to hypoperfusion, increased risk of organ failure, high blood volume leads to peripheral and pulmonary edema, and the incidence of postoperative intestinal obstruction increases [18]; intraoperative fluid should be zero-balanced. For the purpose of high-risk patients or large-scale abdominal surgery should be targeted to use liquid therapy, using objective parameters, according to hemodynamics, such as cardiac output, pulse pressure changes, etc., to make patients' fluid recovery more accurate, reduce postoperative bowel obstruction, promote the recovery of bowel function, thereby reducing hospital stay [26]; postoperative, early oral fluid, limiting postoperative intravenous rehydration, can reduce hospital stay, reduce concurrency, such as the occurrence of intestinal obstruction [8].

### **2.2.5. Intraoperative Temperature**

In gastric cancer surgery, due to anesthesia leading to abnormal body temperature regulation, a large number of infusions, and prolonged exposure to the wound, cold water flushing the abdominal cavity, often lead to hypothermia, especially in elderly patients [7]; According to studies [8], maintaining a normal body temperature can reduce wound infections and heart complications. bleeding and blood transfusion requirements, shorten postoperative recovery time; it is recommended to use room temperature at 24°C, through the upper body forced air heating, insulation blanket, heated intravenous infusion, warm water to wash the abdominal cavity and other measures to make the patient's body temperature keep at around 36°C to avoid complications and improve intraoperative and postoperative safety [27].

### **2.2.6. Drainage Tube**

Abdominal drainage tube should not be used routinely. Abdominal drainage tube does not reduce the incidence of complications, but increases the risk of infection and postoperative fistula [28]; a rct experiment shows [29], two groups in wound infection and there was no significant difference in postoperative pus. The incidence of postoperative complications and hospitalization time were lower in the non-drainage group; if it was in some special cases, such as anastomotic blood supply, cancerous ascites, weak constitution, nutritional status. If the difference is poor, the drainage tube should be placed according to the intraoperative condition. The amount and nature of the drainage fluid should be closely observed after operation, and the tube should be extubated as soon as possible to reduce the tube stimulation and complications.

## **3. Postoperative Application**

### **3.1. Multimodal Analgesia**

Postoperative multimodal analgesia, preventive analgesia, the purpose of early

mobilization, promote the recovery of gastrointestinal function; multimodal analgesia is the use of more than one pain control mode to achieve effective analgesia, including systemic administration, Regional, epidural analgesia, axonal pattern, and a variety of drugs designed to reduce the use of opioids and reduce the side effects caused by opioids; opioids cause intestinal obstruction, respiratory depression, causing nausea, vomiting, especially in the elderly Large doses of opioids increase the risk [30]; multimodal analgesia also incorporates prophylactic analgesia, which is the treatment of pre-drugs that reduce pain or pain before surgery. It has been shown to reduce pain, inflammation, nausea, vomiting [31]; effective pain control is the basis for early bed-out activities, gastrointestinal recovery, and multi-mode combined analgesia is effective, not only reduces the occurrence of related complications, but also promotes early stage Bed activity, shortened hospital stay.

### **3.2. Early Diet**

Early (<24 h) diet accelerated recovery of gastrointestinal function, reduced complication rate and mortality, and contributed to wound healing and anastomotic strength, which has been shown to be safe [16] [32]; 6 - 24 h began to take a small amount of warm boiled water, if the patient does not have discomfort such as bloating, the next day after surgery, gradually overdue from a fluid diet to a normal diet; early return to a normal diet, that is, provide the corresponding energy and protein, and can reduce the cause of hunger Insulin resistance [8]; according to Carr *et al.* [18], intestinal mucosal permeability was not increased in patients receiving early feeding; RCT experiments performed according to EINakeeb *et al.* [33], early diet promotes intestinal function Recover, reduce intestinal edema, shorten the time of exhaust and stool, reduce the risk of various forms of infection, thereby shortening the length of hospital stay, and recommend early diet.

### **3.3. Prevention of Nausea and Vomiting**

25% - 35% of patients have postoperative nausea and vomiting. By administering prophylactic antiemetic drugs, 40% of postoperative nausea and vomiting can be reduced. Patients should be advised to give preventive antiemetic drugs [12] in advance; prevention of nausea and vomiting More meaningful than analgesia, reduce the risk of anastomotic leakage, promote early feeding, early bed-out activities; prevent postoperative nausea and vomiting, can be given dexamethasone sodium phosphate at the beginning of surgery or serotonin antagonism at the end of surgery Agent [8].

### **3.4. Venous Thrombosis Prevention**

A common complication of venous thromboembolism, a higher incidence in elderly patients, but effective prevention strategies, including pharmacological or non-pharmacological aspects, can significantly reduce the incidence; for patients

with epidural analgesia, should Careful use of antithrombotic drugs, before the use of low molecular weight heparin, needle should be introduced, the catheter should be taken at the lowest point of drug action (before the next scheduled dose), the subsequent dose should be given at least 2 hours after extubation, for Patients with a body mass index (>30) should consider using higher doses of low molecular weight heparin [33].

### 3.5. Catheter

The urinary catheter should be pulled out as soon as possible after the operation, and pulled out on the first or second day after surgery to promote the patient to get out of bed early after surgery, without increasing the incidence of urinary tract infection, but pay attention to patients with benign prostatic hyperplasia, uterus Patients with a history of resection and cesarean section need to strengthen the frequency of observation after surgery. When patients have urinary dysfunction, they should be treated in time [6].

### 3.6. Get out of Bed Early

Long-term bed rest can lead to atelectasis, insulin resistance, thromboembolism, decreased exercise capacity, and in the case of effective analgesia, it is possible to get out of bed early; it is recommended to start appropriate activities the next day after surgery. It not only reduces related complications, but also promotes intestinal function recovery, strengthens blood circulation, promotes wound healing, and shortens hospital stay [12].

## 4. Summary and Outlook

The clinical application of accelerated rehabilitation surgery in perioperative period of elderly gastric cancer has been proved to be safe and effective, reducing stress response and postoperative complications, improving postoperative nutritional status, speeding up recovery, shortening hospital stay and reducing costs. However, there is still little evidence on how eras can benefit patients in the long term [8]; for the application of accelerated rehabilitation surgery, it is not possible to generalize the application of individualized conditions; the current clinical application of accelerated rehabilitation surgery still exists. The challenge is that the surgeon is accustomed to the traditional concept and lacks understanding of the eras. Second, the lack of effective communication between the doctor and the patient leads to insufficient compliance and compliance. The third is to accelerate the lack of standardization in rehabilitation surgery, and some aspects are still controversial. Lack of evidence to enable surgeons to obtain effective guidance in application; fourth, accelerating rehabilitation surgery is a multi-disciplinary collaboration, including anesthesia, nursing, etc., which leads to difficulties in application; I believe that the concept of accelerated rehabilitation surgery will continue to improve in the future. And development, widely used to benefit patients.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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# Isolated versus Drug Combined Vestibular Rehabilitation for the Treatment of Metabolic Dizziness

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## Abstract

**Introduction:** Systemic processes and inappropriate use of medications may affect vestibular adaptation. **Objectives:** To assess the efficacy of isolated and combined drug therapy for treating metabolic dizziness and to determine the effect of multidrug treatment. **Methodology:** We analyzed 100 questionnaires of patients diagnosed with dizziness of metabolic origin. **Results:** The group treated with vestibular rehabilitation alone showed improvement with 9 months of therapy ( $p = 0.01$ ). The group treated with vestibular rehabilitation and medication showed improvement with 45 days of therapy ( $p = 0.01$ ). The group treated with a single type of drug did not show significant improvement. The group treated with several drugs showed improvement with 45 days of therapy ( $p = 0.03$ ). **Conclusion:** Combined vestibular rehabilitation resulted in immediate improvement of symptoms without contributing to long-term compensation. Vestibular rehabilitation alone resulted in improvement of symptoms over time. Multidrug treatment was beneficial for immediate relief of dizziness.

## Keywords

Dizziness, Metabolism, Vestibular Rehabilitation

## 1. Introduction

Metabolic dysfunctions are considered responsible for labyrinthine changes [1]. Metabolic disorders may act as the main etiological factor in vestibular dysfunction or as an aggravating factor in preexisting vestibular disease [2].

The inner ear is distinguished by its intense metabolic activity; however, it has

no energy reserve. Small glycemic variations influence its function, causing changes in balance. Metabolic changes in the inner ear cause displacement of potassium from endolymph to perilymph; sodium is concomitantly displaced in the opposite direction. This mechanism causes vertigo, tinnitus, hypoacusis, and auricular plenitude [3].

Vestibular rehabilitation, indicated for treating metabolic dizziness, is influenced by comorbidities in the final response to treatment. In these cases, the objective is integrated otoneurologic therapy with the goal of resolving etiologic factors; this involves rational use of antivertiginous drugs and the application of individualized therapeutic techniques to reduce patient symptoms.

Anti-vertigo medication is currently used as part of combined otoneurologic therapy; however, many researchers caution against the use of multidrug treatments that may cause impairment in vestibular compensation through unintended drug interactions [4]. Thus, our study was undertaken to analyze the outcome of treatment of dizziness of metabolic origin with vestibular rehabilitation in isolation, compared with vestibular rehabilitation combined with medications, and to evaluate the effect of multidrug treatment on the final outcome of vestibular rehabilitation.

## 2. Materials and Methods

This retrospective, observational study was performed by using questionnaire analysis. Data were collected from internal questionnaires administered to patients who attended the vestibular rehabilitation clinic. Only questionnaires of patients with a medical diagnosis of dizziness of metabolic origin were included in the study; questionnaires with incomplete information were excluded from the study. The diagnosis of metabolic dizziness was carried out by the outpatient medical team composed of otolaryngologists. The questionnaires used were designed according to the clinical experience of the researchers, addressing signs and symptoms involved in dizzying crises, social characteristics of the patients, medications in use and objective questions to assess the effectiveness of vestibular rehabilitation therapy.

A total of 642 questionnaires completed between 2002 and 2014 were evaluated; to generate the sample for analysis, 100 questionnaires were randomly selected.

To assess the outcome of vestibular rehabilitation, the response of each patient upon return to therapy was considered. Responses were either “improvement,” “worsening,” or “maintenance” of dizziness. Five service sessions were evaluated: 30 days, 45 days, 3 months, 6 months, and 9 months after beginning rehabilitation.

## 3. Results and Analysis

We adopted a significance level of  $p < 0.05$  in all analyses. We used parametric methods because all variables exhibited a normal distribution (Kolmogorov-Smir-



nov test). Fisher's exact test for non-paired samples was used to compare groups. For intra-group analyses at different times of therapy, Fisher's exact test was used.

The sample was composed of 100 questionnaires. The age distribution of subjects according to gender (mean and standard deviation) is described in **Table 1**.

The number of subjects with a diagnosis of dizziness of metabolic origin who also exhibited a metabolic disease was 55% (N = 55) in the population studied; metabolic alterations reported were diabetes (28%), hypothyroidism (24%), and cholesterol (18%); 15% of subjects had more than one metabolic alteration.

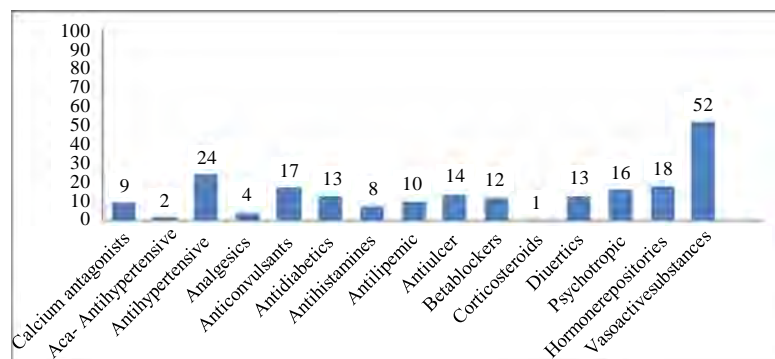
**Figure 1** shows the drugs used by the study population. A total of 80% (N = 80) of the subjects used medication; 62% (N = 62) of the subjects underwent combination therapy with two or more pharmacological agents.

The group using medication was composed of 81 patients; 70 of these patients returned for further vestibular rehabilitation. The non-medicated group comprised 19 patients; 14 of these patients returned for further vestibular rehabilitation.

The group treated with vestibular rehabilitation alone exhibited a significant reduction in the symptom of dizziness at the 9-month follow-up ( $p = 0.01$ ) (**Table 2**). The group treated with vestibular rehabilitation and medication showed a significant reduction in dizziness at the 45-day follow-up ( $p = 0.01$ ). In a comparison between groups, there was a significant reduction in dizziness at the 9-month follow-up ( $p = 0.01$ ) for the group treated with vestibular rehabilitation and medication (**Table 3**).

Notably, 19 patients were using only one type of drug; 18 of these patients returned for further vestibular rehabilitation. Sixty-two patients were using two or more types of drugs; 52 of these patients returned for further vestibular rehabilitation.

The group using one type of drug did not exhibit a significant reduction in dizziness. The group using several drugs showed a significant improvement at the 45-day follow-up ( $p = 0.03$ ) (**Table 4**). There was no statistically significant difference between the groups (**Table 5**).



ACa Antihypertensive = Antihypertensive calcium antagonists.

**Figure 1.** Pharmacological distribution according to its occurrence in the study population.

**Table 1.** Age distribution of subjects according to gender: mean and standard deviation.

Gender	N	%	Mean Age	Standard Deviation	Coefficient of Variation
Female	69	69%	52.72	16.97	32.18
Male	31	31%	55.83	15	26.86
Total	100	100%	53.69	16.31	30.3

**Table 2.** Analysis of vestibular rehabilitation outcome according to follow-up time in groups with and without medication.

	30 days vs. 45 days		30 days vs. 3 months		30 days vs. 6 months		30 days vs. 9 months	
	N		N		N		N	
<b>G1</b>								
Improvement	8	8	8	7	8	10	8	12
No reply	6	6	6	7	6	4	6	0
P	1.2964		1		0.6946		<b>0.0171*</b>	
<b>G2</b>								
Improvement	37	49	37	31	37	31	37	32
No reply	33	17	33	23	33	28	33	17
P	<b>0.0127*</b>		0.7163		1		0.1918	

Legend: G1 = Group without use of medication; G2 = Group using medication. Fisher exact test.

**Table 3.** Comparison between groups with and without medication according to the outcome of vestibular rehabilitation.

	30 days		45 days		3 months		6 months		9 months	
	G1 vs. G2		G1 vs. G2		G1 vs. G2		G1 vs. G2		G1 vs. G2	
	N		N		N		N		N	
Improvement	8	37	8	49	7	31	10	31	12	32
No reply	6	33	6	17	7	28	4	23	0	17
P	1		0.2104		1		0.379		<b>0.0142*</b>	

Legend: G1 = Group without use of medication; G2 = Group using medication. Fisher exact test.

**Table 4.** Analysis of vestibular rehabilitation outcomes according to follow-up times in groups with a single type of medication and with multiple medications.

	30 days vs. 45 days		30 days vs. 3 months		30 days vs. 6 months		30 days vs. 9 months	
	N		N		N		N	
<b>G1</b>								
Improvement	8	11	8	7	8	9	8	12
No reply	10	5	10	7	10	3	10	0
P	0.1854		1		0.1414		0.2543	
<b>G2</b>								
Improvement	29	38	29	24	29	22	29	25
No reply	23	12	23	21	23	20	23	14
P	<b>0.0382*</b>		0.8403		0.8358		0.5189	

Legend: G1 = Group with single medication; G2 = Group with multiple medications. Fisher exact test.

**Table 5.** Comparison between groups using one and more types of medications with the result of vestibular rehabilitation.

	30 days		45 days		3 months		6 months		9 months	
	G1 vs. G2		G1 vs. G2		G1 vs. G2		G1 vs. G2		G1 vs. G2	
	N	N	N	N	N	N	N	N	N	N
Improvement	29	8	38	11	24	7	22	9	25	7
No reply	23	10	12	5	21	7	20	3	14	3
P	0.4272		0.7433		1		0.2003		1	

Legend: G1 = Group with single medication; G2 = Group with multiple medications. Fisher exact test.

#### 4. Discussion

The distribution of the sample regarding gender and average age (**Table 1**) showed that dizziness was prevalent in female patients in this study, consistent with prior literature [5] [6]. Women seek medical care more frequently than men, regardless of factors such as the variation of the monthly hormonal cycle and menopause, which exhibits dizziness as a primary symptom [7] [8].

Anti-vertigo drugs are used as vestibular rehabilitation allies for treating dizziness; however, many professionals are concerned with the side effects described in the literature, among them impairment in vestibular compensation.

We sought to characterize the vestibular rehabilitation outcome by using an isolated and combined approach with medications, and to analyze the effect of the multidrug treatment in subjects who used two or more types of drugs.

We analyzed a group of individuals using medication and another group without; however, both performed vestibular rehabilitation. In the analysis between groups, there was a significant improvement in dizziness with 9 months of treatment for the group using drugs combined with therapy. For better understanding, intra-group analysis was performed, which indicated that this time effect was attributed to vestibular rehabilitation therapy.

The effect of the combined treatment of vestibular rehabilitation and medications was significant for relieving symptoms of dizziness at 45 days of follow-up, but the improvement did not remain significant over time. This indicates that the drug helps in immediate reduction of symptoms, but does not contribute to long-term compensation. We verified that vestibular rehabilitation as an isolated treatment resulted in a significant improvement in symptom of dizziness at 9 months of follow-up, indicating that it is an effective treatment and has an effect over time.

Snifer *et al.* (2004) [9] evaluated the response of patients with vestibular disorder to treatment with vestibular rehabilitation and medication, both combined and in isolation. They found that patients treated with vestibular rehabilitation alone, or in combination with medication, showed clinical improvement and significant differences in the Dizziness Handicap Inventory. The group treated with medication alone did not show clinical improvement and a significant difference in the Dizziness Handicap Inventory. In that study, the use of a single vasodilator drug was evaluated.

The works of Shoair *et al.* (2011) [10] and Pinheiro *et al.* (2013) [11] concluded that multidrug treatment is associated with increased risk of dizziness and injury in vestibular compensation. For the treatment of vertigo of vestibular origin, two or more types of drugs are used because there is no specific drug that acts on the vestibular system [12].

Considering the drug interactions and various side effects, among them the increased of dizziness, we sought to characterize the difference between the group using a single type of medication and another group using multiple drugs. We found that the group using a single type of medication did not show significant improvement in dizziness during the time period of the study. The group with drug interactions showed significant improvement in dizziness after 45 days of treatment.

The use of drug interactions was beneficial with an immediate effect for the relief of dizziness; however, a long-term effect was not observed.

Although drug interactions do not contribute to long-term central compensation, in this study it was possible to identify a positive action at the beginning of treatment, with a reduction in symptoms, which is necessary because the patient benefits from the immediate relief of dizziness to initiate the vestibular rehabilitation exercises. Caution should be taken to indicate the correct dosage of drugs and the time of use.

The factors that interfere in the evolution of cases of metabolic vestibulopathy and the success of short-term vestibular rehabilitation are inadequate eating habits, sedentary lifestyle, sleep disturbances, delay in the control of underlying disease and, in the case of women, hormonal variations and menopause. Other factors, such as failure to perform proposed exercises and/or inadequate performance, are common during vestibular rehabilitation, regardless of the etiology of dizziness, and also occurred in the study population.

## 5. Conclusions

Vestibular rehabilitation combined with medication for the treatment of dizziness resulted in immediate improvement of dizziness symptoms, and did not contribute to long-term compensation. Vestibular rehabilitation alone in the treatment of dizziness resulted in improvement of symptoms over time.

Multidrug treatment was beneficial for immediate relief of dizziness but did not contribute to long-term compensation.

The use of medications aids in early stages of rehabilitation of disorders of the peripheral vestibular system, which are complemented and sedimented by vestibular rehabilitation exercises.

## Acknowledgements

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## Ethical Standards

This study was approved by the ethics council of the authors' institution. In this study, we followed the norms advocated by the ethics and research commission with respect to human research, ethical secrecy, and biosafety norms.

Only the researchers had access to the information provided by the questionnaires.

The authors state that all procedures that contributed to this work complied with the ethical standards of the relevant national and institutional guidelines on human experimentation, and with the Declaration of Helsinki of 1975, as revised in 2008.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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# The Clinical Effect of Percutaneous Transforaminal Endoscopic Discectomy in the Treatment of Low Lumbar Single Segment Disc Herniation

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## Abstract

**Objective:** To observe the clinical effect percutaneous transforaminal endoscopic discectomy (PTED) in the treatment of single lumbar disc herniation. **Methods:** From August 2017 to June 2019, 42 patients with low lumbar single segment lumbar disc herniation were treated with percutaneous transforaminal endoscopic discectomy surgery in our hospital. The operation time, incision size, bleeding volume and hospitalization time were recorded respectively. The patients were evaluated before operation, 1 month and 6 months after operation. Visual analogue scale (VAS) and assessment were used to evaluate the lumbocrural pain. The JOA score and the Oswestry disability index (ODI) were used to evaluate the lumbar function, and the modified macnab score was used to evaluate the clinical effect in the last follow-up. **Results:** All the 42 patients successfully completed the operation without any other operation. There were no severe complications such as dural injury and nerve root injury. The operation time was  $(76.98 \pm 8.58)$  min, the incision size was  $(8.45 \pm 1.2)$  mm, the bleeding volume was  $(20.14 \pm 2.93)$  ml, and the hospitalization time was  $(4.55 \pm 1.13)$  d. One month and six months after the operation, the visual analogue scale (VAS), the evaluation of lumbar function (Oswestry) and the disability index (ODI) were significantly improved compared with those before the operation ( $P < 0.05$ ). The last follow-up evaluation of the clinical effect of modified macnab: excellent in 30 cases, good in 8 cases, fair in 3 cases and poor in 1 case. The excellent rate was 90.47%. One patient developed back pain and discomfort. One case recurred. **Conclusion:** The treatment of low lumbar but segmental lumbar disc herniation with percutaneous intervertebral foramen, with small incision, less

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bleeding and quick recovery, can improve the pain and dysfunction of patients.

## **Keywords**

Lumbar Disc Herniation, Percutaneous Transforaminal Endoscopic Discectomy, Clinical Effect

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## **1. Introduction**

Lumbar disc herniation is one of the most common orthopedic diseases, and single segment disease is more common. Non-surgical treatment can alleviate the symptoms of most patients, and a small number of patients need surgical treatment [1]. At present, the median approach is the most common after the operation, but it is easy to cause FBSS (failed back surgery syndrome). Therefore, in 1968, Wihse proposed the approach through the longest muscle and multi split muscle space. However, there are still some disadvantages, such as the greater damage in the operation area, spinal injury, adhesion of the surrounding tissues and so on. Then with the progress of science and technology and spine surgery, percutaneous transaminal endoscopic surgery can reach the target area for surgery, which not only effectively avoids the shortcomings of the traditional surgery, but also has the advantages of small amount of bleeding, short operation time and quick recovery. And this operation can be carried out under local anesthesia, the patients stay awake during the operation, keep in touch with the patients during the operation, and effectively avoid serious complications such as nerve injury. From August 2017 to June 2019, 42 patients with single level lumbar disc herniation were operated with percutaneous transaminal endoscopic surgery, and the postoperative effect was satisfactory. The report is as follows.

## **2. Data and Methods**

### **2.1. General Information**

From August 2017 to June 2019, 42 patients with single lumbar disc herniation in our hospital were selected, all of whom were 24 males and 18 females, aged 27 - 68 years with an average age of 48.5 years. After more than 3 months of regular conservative treatment, it was ineffective. There was no previous operation history; exclusion criteria: 1) Lumbar instability, lumbar fracture, lumbar tuberculosis, lumbar tumor, and infection of intervertebral space; 2) Lumbar surgery history, sacral canal sealing treatment history; 3) Patients with multiple segments.

### **2.2. Operation Method**

#### **2.2.1. Preoperative Preparation**

Prepare the preoperative reading film (X-ray film, CT, MRI) and physical ex-



amination to determine the lumbar disc herniation segment and the relative position with the nerve root. During the close to the shoulder of the superior articular process. Fluoroscopy confirmed that the puncture needle was located at the shoulder of the superior articular process. 2 ml of 1% lidocaine hydrochloride was injected to anesthesia around the articular process. Then, the puncture needle enters the intervertebral disc of the protruding part, where the prepared contrast agent (iohexol and methylene blue) can be injected. Insert the guide wire and pull out the puncture needle. At this time, pay attention to maintain the position of the guide wire. No. 11 scalpel made an incision operation, the patient took the prone position, the chest and abdomen cushion C-arm positive and lateral position fluoroscopy to locate the responsible segment, adjust the body position, make the lumbar spine forward, and bend the hip and knee, so as to expand the intervertebral foramen. After positioning, the marker marks the needle feeding point.

### **2.2.2. Operative Procedure**

The operation of this study was completed by the same senior chief physician, taking L4/L5 as an example, the conventional operation area disinfection towel. 1% lidocaine hydrochloride was used for local infiltration anesthesia. The puncture needle was inserted about 8 mm long at the puncture point. The catheter should be placed along the guide wire and expanded step by step. It should be confirmed that the catheter is close to the articular process at each step. At the same time, the catheter can be rotated clockwise to reduce the pain of the patient. The anterior end of the circular saw shall not exceed the line between the pedicle and the medial margin at any time. Put in the guide rod, establish the working channel and then put into the intervertebral foramen system. The blue stained nucleus pulposus was removed and radiofrequency ablation was performed to confirm that the nerve roots were fully released. When loosening the nerve root, the patient can be communicated. If the nerve symptom is relieved, 40 mg triamcinolone acetonide and 2 ml 1% lidocaine can be injected and the intervertebral foramen system can be pulled out. After washing with normal saline, the incision was sutured layer by layer and the drainage tube was retained.

### **2.2.3. Postoperative Management**

The drainage tube can be pulled out 24 hours after operation, and a small amount of waist circumference can be worn to get out of bed. Weight bearing and strenuous exercise should be avoided within 3 months after operation, and standing and sitting for a long time should be avoided.

## **2.3. Observation Indicators**

The operation time, incision size, bleeding volume and hospital stay were evaluated by visual analogue scale (VAS). The higher the score of 0 - 10, the more serious the pain was. The JOA score and Oswestry disability index (ODI) were used to evaluate the lumbar function. ODI included 10 items such as lumbago

and leg pain, walking and standing. Each item had 5 points and 50 points in total.  $ODI = \text{total score}/50 \text{ points} \times 100\%$ , the higher the score, the more serious the obstacle [2]. The final follow-up evaluation of clinical efficacy was performed with modified macnab efficacy score. Specific evaluation criteria: excellent: straight leg elevation  $> 70^\circ$ , lower extremity sensation and movement are normal, muscle strength is normal, and lumbocrural pain disappears; good: straight leg elevation is  $30^\circ$  higher than that before operation, but  $< 70^\circ$ , muscle strength grade IV, occasionally with slight lumbocrural pain but not affecting work and life; can: straight leg elevation is  $15^\circ$  higher than that before operation, but  $< 70^\circ$ , muscle strength grade III, lumbocrural pain is less than that before operation, and painkillers are occasionally used; poor There is no change or even aggravation before and after the operation, so it is necessary to take painkillers [3].

## 2.4. Statistical Analysis

SPSS 22.00 software is used, the counting data is expressed in rate (%), and the measurement data is expressed in mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ) indicated that the operation time, incision size, bleeding volume and hospitalization time were recorded respectively, and the paired sample t-test was used before operation, 1 month and 6 months after operation, and the last follow-up was compared with that before operation. The difference was statistically significant ( $P < 0.05$ ).

## 3. Result

### 3.1. Perioperative Conditions

3.2 patients successfully completed the operation without any other operation. There were no severe complications such as dural injury and nerve root injury. The operation time was  $(76.98 \pm 8.58)$  min, the incision size was  $(8.45 \pm 1.2)$  mm, the bleeding volume was  $(20.14 \pm 2.93)$  ml, and the hospitalization time was  $(4.55 \pm 1.13)$  d.

### 3.2. Follow-Up Results

One month and six months after the operation, the visual analogue scale (VAS), the evaluation of lumbar function (Oswestry) and the disability index (ODI) were significantly improved compared with those before the operation ( $P < 0.05$ ; **Table 1**). The last follow-up evaluation of the clinical effect of modified macnab was excellent in 30 cases, good in 8 cases, fair in 3 cases and poor in 1 case. The excellent rate was 90.47%. One of the patients suffered from back pain and discomfort after operation. The above symptoms were relieved by NSAIDs and physiotherapy. There was no recurrence during the follow-up period after the pain symptom was eliminated. **Figure 1** is the imaging data of surgical patients.

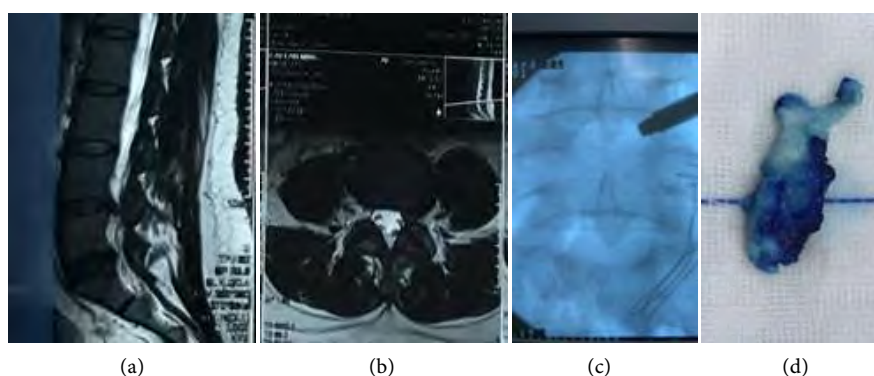
## 4. Discussion

Lumbar disc herniation is one of the most common causes of low back and leg pain. It is a syndrome caused by degeneration of lumbar disc, rupture of fiber

**Table 1.** Comparison of observation indexes before and after operation ( $\bar{x} \pm s$ ).

time	Low back pain VAS (sub)	Lower limb pain VAS (sub)	JOA score	ODI (%)
Preoperative	6.64 + 1.14	6.71 + 0.97	12.07 + 2.25	70.33 + 4.95
1 month after operation	2.93 + 0.51a	2.57 + 0.59b	20.14 + 2.67c	35.05 + 2.69d
6 months after operation	1.21 + 0.47a	0.91 + 0.43b	23.33 + 2.19c	22.43 + 1.76d
Last follow-up	0.60 + 0.63a	0.64 + 0.62b	24.55 + 2.14c	21.45 + 2.12d

Note: a compared with preoperative, the difference was statistically significant,  $P < 0.05$ ; b compared with preoperative, the difference was statistically significant,  $P < 0.05$ ; c compared with preoperative, the difference was statistically significant,  $P < 0.05$ ; d compared with preoperative, the difference was statistically significant,  $P < 0.05$ .



**Figure 1.** (a) The sagittal MRI of the lumbar spine showed 4/5 lumbar disc herniation; (b) the transverse MRI of the lumbar spine showed 4/5 lumbar disc herniation; (c) During the operation, the puncture needle entered along the lumbar 4/5 intervertebral foramen; (d) the nucleus pulposus of the extracted intervertebral disc.

ring, extrusion of nucleus pulposus and stimulation of lumbosacral nerve root and cauda equina nerve. The following lumbar lesions are common, of which L4/5 and L5/S1 account for more than 90% [4]. Traditional open surgery can relieve the pain and dysfunction of the patients' waist and legs, but it can damage the tissues around the operation area and affect the stability of the lumbar spine. Tissue adhesion can also increase the difficulty of reoperation [5].

With the development of society and aging, the incidence rate of lumbar disc herniation is increasing and younger. After more than 3 months of formal non-surgical treatment are invalid, we can consider the operation. The principle of surgical treatment is to relieve the nerve compression and remove the protruding nucleus pulposus [6]. The percutaneous transforaminal endoscopic discectomy surgery, which starts from the "kambin triangle" [7], can protect the original structure of the spine as much as possible, and can hardly damage the posterior structure of the spine, such as muscles, ligaments, lamina and facet processes. At the same time, it can remove the diseased tissue and release the compressed nerve root. In addition, under local anesthesia, the patient is in a conscious state, which reduces the occurrence of important nerve injury. Be-

cause of the advantages of small trauma and fast recovery, it is accepted by more and more patients with lumbar disc herniation [8].

In this study, 42 patients successfully completed the operation, the operation time was  $(76.98 \pm 8.58)$  min, and the rotation and movement of the working pipe increased the operation time. Yeung *et al.* Analyzed 307 cases of lumbar disc herniation treated with percutaneous foramen, the excellent and good rate was 89.3% [9]. Hermantin *et al.* [10] compared traditional open surgery with percutaneous endoscopic surgery in the treatment of lumbar disc herniation, the results showed that the satisfaction rate of the traditional open group was 93.0%, and that of the percutaneous endoscopic group was 97.0%. The excellent and good rate is 90.47%, which is consistent with the previous reports.

Although there are many advantages mentioned above, we should also correctly recognize and prevent the occurrence of complications such as infection of intervertebral space and dural tear. The incidence of infection of intervertebral space after traditional operation is about 1% - 5%. Because of the small wound and the large amount of liquid used in the operation, the infection rate was greatly reduced to 0.12% [11].

To sum up, the clinical efficacy of this study is satisfactory, and percutaneous transforaminal endoscopic discectomy surgery is safe and minimally invasive, which is worthy of clinical promotion. The indication of operation should be strictly controlled to reduce the occurrence of postoperative complications. The learning curve of the technique itself is long [12], which can only be carried out after the surgeon is familiar with the anatomical structure and strict training.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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# Evaluation of Empty Nose Syndrome Scores in Patients Undergoing Extended Endoscopic Transnasal Sellar Surgery

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## Abstract

**Background:** Several large series have established endoscopic transnasal sellar surgery as the procedure of choice for removal of tumors in the sellar area. Although this procedure provides a less invasive approach to the sella, it entails complications such as nasal bleeding, impaired olfactory function, atrophic rhinitis, synechia, etc. No studies have yet reported potential morbidities such as empty nose syndrome (ENS), although patients have a relatively empty nasal cavity after surgery. Therefore, we sought to verify the percentage of patients who truly met the diagnostic criteria for ENS after endoscopic transnasal sellar surgery, determine the variation between pre- and postoperative scores in each Empty Nose Syndrome 6-Item Questionnaire (ENS6Q) item, and further evaluate the symptoms that may affect the patients the most after surgery. **Methods:** Between March 2015 and January 2019, eventually 11 patients who underwent extended endoscopic transnasal sellar surgery in Shin Kong Wu Ho-Su Memorial Hospital, a tertiary referral medical center in Taipei, Taiwan, were enrolled. The patients completed the recently validated ENS6Q after surgery. **Results:** One patient met the objective diagnostic criteria for ENS (score  $\geq 11$  in ENS6Q). Significant differences were observed in the pre- and postoperative total ENS6Q scores. The pre- and postoperative scores of “nose feeling too open” and nasal crusting showed statistically significant differences. Further, compared with the other items, the postoperative score of nasal crusting increased most obviously, and it may be the most apparent operation-related symptom. **Conclusion:** This study is the first to report the possibility of developing ENS after endoscopic transnasal sellar surgery. Although the transnasal endoscopic approach is a safe

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and minimally invasive procedure for the treatment of sellar lesions, possible complications such as ENS should be considered.

## Keywords

Endoscopic Transnasal Sellar Surgery, Empty Nose Syndrome, ENS6Q, Nasal Crusting, Aerodynamics of Nasal Airflow

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## 1. Introduction

Empty nose syndrome (ENS) is an infrequent, late complication of sinonasal procedures, especially turbinate surgery. Paradoxical nasal obstruction, nasal crusting, nasal dryness, and a persistent feeling of dyspnea are the most common symptoms [1]. Although the etiology of ENS remains uncertain, anatomical changes leading to alterations in local environment and excessive nasal permeability affecting neurosensitive receptors and humidification and conditioning of inhaled air are strongly implicated [1]. The diagnosis of ENS is frequently associated with the presence of paradoxical nasal obstruction despite an objectively patent nasal airway. Patients with ENS exhibit varied prominent symptoms, including dyspnea, nasal and pharyngeal dryness, facial or nasal pain, crusting, hyposmia, and depression. ENS significantly influences the quality of life of the patients, and the associated psychological factors are responsible for patient discomfort [2].

Endoscopic transnasal sellar surgery has been validated as a safe and effective method for removing tumors in the sellar region [3]. Although it is a popular approach to treat sellar lesions, the procedure still entails some complications such as nasal bleeding, impaired olfactory function, atrophic rhinitis, synechiae, etc. [3] [4]. To the best of our knowledge, no study has yet demonstrated potential morbidities such as empty nose syndrome, despite the fact that these patients are under an empty status in their nasal cavity after the extended endoscopic transnasal surgery. Thus, through this study, we aimed to evaluate the correlation of ENS with extended endoscopic transnasal surgery.

## 2. Materials and Methods

### 2.1. Patient Selection

Between March 2015 and January 2019, 32 patients with sellar tumors who underwent transnasal sellar surgery in Shin Kong Wu Ho-Su Memorial Hospital were recruited.

### 2.2. Exclusion Criteria

The records of the 32 patients were retrospectively analyzed. Patients who were undergoing microscopic transnasal sellar surgery ( $n = 6$ ), those who had tumors without cavernous sinus extension ( $n = 13$ ), those unavailable for regular fol-

low-ups ( $n = 7$ ), and those unable to finish the questionnaire ( $n = 3$ ) were excluded.

### 2.3. Preoperative Survey and Postoperative Follow-Up

Ultimately, 11 patients (6 men and 5 women, age range: 18 - 81 years, median age: 59 years) who underwent extended endoscopic transnasal surgery owing to bulky tumor size and cavernous sinus or optic chiasm extension were enrolled. None of them had undergone nasal surgery earlier. For each patient, the symptom score was assessed using the Empty Nose Syndrome 6-Item Questionnaire (ENS6Q); the ENS6Q is a recently validated questionnaire consisting of six items that quantify the symptoms associated with ENS, and each item is rated on a score from 0 (*no symptoms*) to 5 (*severe symptoms*) [5]. The patients completed the ENS6Q, for which a Chinese translation has also been validated, 6 months after the surgery (Table 1).

### 2.4. Operative Setting

Patients were placed supine on the operating table, under general anesthesia and orotracheal intubation. The procedure consisted of sinus and sellar stages performed using rigid endoscopes (Karl Storz, GmbH and Co, Tuttlingen, Germany) with a diameter of 4 mm and length of 18 cm, at angles of 0°, 30°, 45°, and 70°. Topical 4% xylocaine or Bosmin-soaked cotton pledgets were placed into each naris, and 1% lidocaine with 1:100,000 epinephrine was injected into the nasal mucosa, with particular consideration to the septum on the side of planned nasoseptal flap harvest. The natural ostium of the sphenoid sinus was identified bilaterally. A pedicled nasoseptal flap was then harvested. Bilateral sphenoidotomies were performed, with particular attention to preserving the vascular pedicle to the contralateral nasoseptal flap. A posterior septectomy (15 - 20 mm) was performed for binarial access to the sphenoid sinus. Left ethmoidectomy was performed and a part of the middle turbinate was removed to create the corridor. The mucosa of the sphenoid sinus was totally removed to avoid postoperative mucocele formation. Moreover, the sphenoid sinus septations and rostrum of the sphenoid sinus were drilled down to create the surgical space. Key anatomical landmarks including the dorsum sella, tuberculum sella, sella, bilateral optico-carotid recesses, and clinoidal carotid protuberances were thereafter identified. The bone over the sella was removed using a diamond burr and Kerrison rongeurs. Tumor debulking was performed using ring curettes, suction, and an aspirator. As soon as the tumor resection was completed, the area was irrigated and hemostasis was achieved. Finally, the sellar floor was reconstructed in a graded manner, depending on the extent of the skull base defects. The exposed area in the nasal cavity after the procedure is shown in Figure 1.

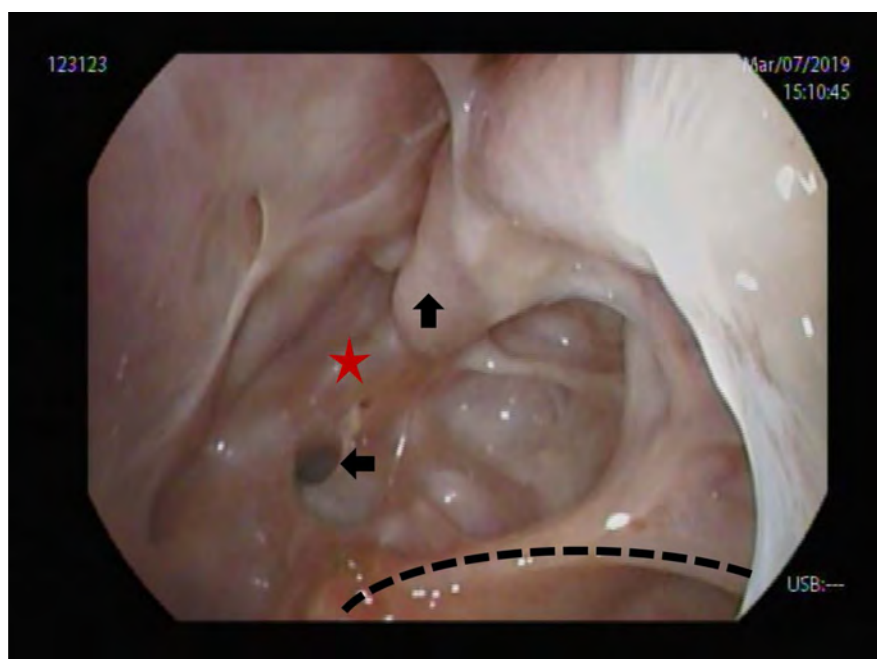
### 2.5. Statistical Analyses

Initially, the total score of the ENS6Q with a score cutoff of 11 was analyzed as



**Table 1.** The Empty Nose Syndrome 6-item Questionnaire (ENS6Q).

Symptom	No problem	Very mild	Mild	Moderate	Severe	Extremely severe
Dryness	0	1	2	3	4	5
Sense of diminished airway	0	1	2	3	4	5
Suffocation	0	1	2	3	4	5
Nose feels too open	0	1	2	3	4	5
Nasal crusting	0	1	2	3	4	5
Nasal burning	0	1	2	3	4	5



**Figure 1.** Endoscopic view after extended endoscopic transnasal sellar surgery. - -: Posterior border of the left maxillary sinus opening. ★: Nasoseptal flap. ↑: Remnant of the left middle turbinate. ◀: Opening of the sphenoid sinus.

an objective diagnostic criterion for ENS [5]. Subsequently, the variation between the scores of each ENS6Q item before and after surgery was analyzed. A Wilcoxon test was applied to calculate the  $p$ -values;  $p < 0.05$  was defined as statistically significant. All statistical analyses were performed on a personal computer by using the statistical package MedCalc for Windows (Version 19.0.7, MedCalc manual).

### 3. Results

**Table 2** shows the demographic results of the 11 patients who underwent extended endoscopic transnasal surgery from March 2015 to January 2019. Macroadenoma was the major component of the total pathologies (6/11). All patients exhibited invasion of cavernous sinus part of the internal carotid artery, and 10 of them showed compression at the optic chiasm.

**Table 2.** Patient pathologies and demographic characteristics.

Patient (No.)	Gender	Age	Pathology
1	Male	76	Metastatic adenocarcinoma
2	Male	53	Adenoma
3	Female	81	Adenoma
4	Male	66	Adenoma
5	Male	68	Adenoma
6	Female	18	Rathke cleft cyst
7	Female	29	Rathke cleft cyst
8	Male	52	Craniopharyngioma
9	Male	76	Adenoma
10	Female	59	Adenoma
11	Female	76	Rathke cleft cyst
Median		59	

The ENS6Q questionnaire was applied to evaluate the diagnosis of ENS. **Table 3** shows that one of the total 11 patients met the diagnostic criteria for ENS (total score  $\geq 11$ ) after surgery. Although the postoperative ENS6Q scores of other patients did not satisfy the diagnostic criteria, the patients still showed increased severity of symptoms after surgery, compared with their preoperative scores. **Figure 2** shows significant differences in the total ENS6Q scores of the patients before and after surgery ( $p < 0.05$ ). **Table 4** reveals that two items (nose feeling too open and nasal crusting) showed statistically significant difference between the preoperative and postoperative scores when the Wilcoxon test was applied. To determine the item that may have been the most bothering symptom after undergoing the surgery, the postoperative score of each item in the ENS6Q questionnaire was further analyzed by applying the Kruskal-Wallis test. The result showed that compared with the other items, the score of nasal crusting increased most obviously after surgery, suggesting that it may be the most apparent operation-related symptom.

#### 4. Discussion

In the past decades, several large series have established the endoscopic transphenoidal approach as the procedure of choice for treating pituitary tumors, demonstrating better outcomes and fewer major complications than those associated with a transcranial approach [6] [7]. Although the endoscopic approach is safe and efficient, several studies in the literature have discussed complications arising from the surgery, including nasal bleeding resulting from the approach itself, impaired olfactory function, atrophic rhinitis, synechia, mucoperiosteal flap necrosis, and external nasal deformities [4]. However, little has been explicitly stated about the potential morbidity of ENS, despite the presence of more than adequate intranasal airspace after transnasal endoscopic sellar surgery.

**Table 3.** Pre- and postoperative ENS6Q scores.

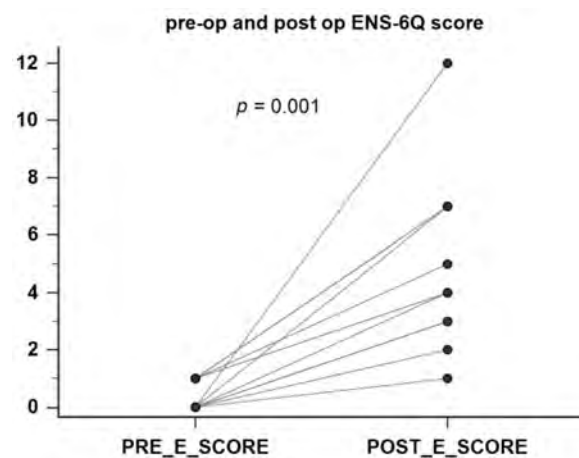
Patient (No.)	Pre-op (score)	Post-op (score)
1	1	7
2	1	5
3	1	4
4	0	2
5	0	12*
6	0	3
7	0	1
8	0	4
9	0	3
10	1	7
11	0	7

\*A score cutoff of 11 as an objective diagnostic criterion for empty nose syndrome.

**Table 4.** Analysis of the differences in pre- and postoperative scores of individual items in the ENS6Q.

Pre-op and post-op differences	Median difference	95% Confidence interval	<i>p</i> -value
ENS-6Q score	4.25	2.5000 to 7.0000	0.0010*
Dryness	0.75	0.0000 to 2.5000	0.0625
Sense of diminished nasal airflow	0.5	0.0000 to 1.0000	0.125
Suffocation	0	0.0000 to 0.0000	0
Nose feels too open	1	0.0000 to 2.0000	0.0313*
Crusting	1	0.5000 to 2.0000	0.0039*
Burning	0	0.0000 to 0.5000	NA

\**p* < 0.05 was considered statistically significant.

**Figure 2.** Pre- and postoperative ENS6Q scores. A tendency of increased total ENS6Q score was observed after the operation. The differences in the pre- and postoperative ENS6Q scores were statistically significant.

ENS, a term originally coined by Eugene Kern and Moore in 1994, described the empty space in the region of the inferior and middle turbinates on coronal computed tomography images of patients who had undergone partial or total inferior and middle turbinectomy [8]. ENS is a diagnosis of exclusion, as it must be differentiated from chronic rhinosinusitis, autoimmune diseases of the nose, and primary atrophic rhinitis. ENS is empirically diagnosed according to the presence of a history of turbinate surgery, clinical examination, and relevant symptoms including varying degrees of nasal crusting, dryness, paradoxical nasal obstruction, thick nasal discharge, postnasal drip, or facial pain [1] [2].

In this study, the ENS6Q was applied as a subjective measure of symptoms that were highly correlated with ENS. The ENS6Q is a recently validated and widely used disease-specific questionnaire to discriminate patients suspected of having ENS [5]. The questionnaire can be completed in approximately 2 min and constitutes a good marker for ENS.

According to our past experience with endoscopic transnasal sellar surgery, even several patients who did not meet the diagnostic criteria of the ENS6Q developed nasal symptoms similar to those listed in the diagnostic items of ENS. This provoked our interests in evaluating the potential links between ENS and extended endoscopic transnasal surgery. In this study, we found that one of the included patients met the diagnostic criteria of ENS6Q (Table 3). In addition, the total score (Figure 2) and two (nose feeling too open and nasal crusting) of the six items in the ENS6Q showed significant differences before and after surgery (Table 4). The *p*-values for two (suffocation and burning sensation) of the remaining four items that showed no statistical significance in the Wilcoxon test were unavailable owing to the characteristics of the data. As no patient experienced suffocation before or after the surgery, the *p*-value remained 0 after applying Wilcoxon test. Meanwhile, owing to the high homogeneity of the preoperative and postoperative scores with regard to a burning sensation, *p* values for the included patients were unavailable.

In our surgical practice, in order to create the surgical corridor and expose the whole sellar anatomy, we partially resected the left middle turbinate and created a posterior septal window. This distorts the anatomy of the nasal cavity. Dayal *et al.* applied virtual surgery and computational fluid dynamics to simulate the aerodynamics of nasal airflow before and after turbinectomy. They found that the efficiency of humidification significantly decreased after both inferior turbinectomy and middle turbinectomy [9]. Decreased humidification function may predispose nasal dryness, facilitating crust formation in the nose and a sense of airflow change. Houser describes four subtypes of ENS: 1) ENS secondary to inferior turbinate resection (ENS-IT); 2) ENS secondary to middle turbinate resection (ENS-MT); 3) ENS secondary to both inferior and middle turbinate (ENS-both); and 4) ENS after turbinate-sparing procedures [10] [11]. Therefore, we speculate that the partial middle turbinectomy and posterior septectomy may play certain roles in influencing the items in the ENS6Q, especially in patients undergoing extended endoscopic transnasal sellar surgery.

Despite the anatomical factor, the neurosensory mechanism has a role in the sensation of the nasal cavity. TRPM8 is a well-known specific trigeminal cool thermoreceptor involved in the sensation of nasal patency [11]. This thermoreceptor is activated when high-speed air passes through the nostril and induces the evaporation of water from the mucosa. Adequate mucosal cooling achieved by effective turbulent airflow activates the thermoreceptors. In patients who undergo endoscopic transnasal sellar surgery, the alterations of the aerodynamics from turbulent airflow to laminar airflow due to turbinate resection may fail to activate the thermoreceptors. Loss of neural sensitivity further aggravates compromised mucosal cooling; consequently, the sensation of nasal patency is not elicited.

Besides the nasal symptoms, patients with ENS suffer from extra-sinonasal symptoms, including reduced concentration; chronic fatigue; and mood problems such as frustration, irritability, anger, and depression owing to the constant abnormal breathing sensations [1] [2]. However, these psychologic burdens may be balanced off by other more distracting factors. We believe that concerns over the skull base tumor and recovery may have distracted the focus of the patients from the symptoms of empty nose. This may also explain the limited links between ENS and extended endoscopic transnasal sellar surgery in this study.

The study limitations relate to the fact that it was performed retrospectively. In addition, this is a relatively small sample size study due to the limited number of patients who were indicated for endoscopic transnasal sellar surgery generally. Though a small number of subjects may limit statistical power, our study elucidates the potential link between ENS and extended endoscopic transnasal sellar surgery.

## 5. Conclusion

This study is the first to report the relationship of ENS with extended endoscopic transnasal sellar surgery in a tertiary referral medical center. Although this is a safe and effective procedure, possible complications such as ENS should be considered.

## Author Contribution

Yu-Hsuan Kuo: study design, composed main manuscript, data analysis; Chia-Jung Lee: collected the data, performed the analysis; Hsing-Mei Wu: contributed data collection and analysis tool; Chung-Yu Hao: contributed substantially to the conception, surgical technique verified; Yung-Hui Liu: surgical technique verified; Yih-Jeng Tsai: study design, revised and verified the manuscript, provided final approval of the version to publish, general coordinator.

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## Research Involving Human Participants and/or Animals

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

## Informed Consent

Informed consent was obtained from all individual participants included in the study.

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- Clinical Transplantation
- Clinical Trials
- Clinical Ultrasound
- Clinical Virology
- Complementary Therapies in Clinical Practice
- Consulting and Clinical Psychology
- Contemporary Clinical Trials
- Controlled Clinical Trials
- Diabetes Research and Clinical Practice
- Evaluation in Clinical Practice
- Fundamental & Clinical Pharmacology
- Hereditary Cancer in Clinical Practice
- Human Psychopharmacology: Clinical and Experimental
- Innovations in Clinical Neuroscience
- Laboratory and Clinical Medicine
- Neurophysiologic Clinique/Clinical Neurophysiology
- Nutrition in Clinical Practice
- Pacing and Clinical Electrophysiology
- Psychiatry in Clinical Practice
- Therapeutics and Clinical Risk Management
- Veterinary Clinical Pathology

We are also interested in short papers (letters) that clearly address a specific problem, and short survey or position papers that sketch the results or problems on a specific topic. Authors of selected short papers would be invited to write a regular paper on the same topic for future issues of the **IJCM**.

## Notes for Intending Authors

All manuscripts submitted to IJCM must be previously unpublished and may not be considered for publication elsewhere at any time during IJCM's review period. Paper submission will be handled electronically through the website. All papers are refereed through a peer review process. Additionally, accepted ones will immediately appear online followed by printed in hard copy. For more details about the submissions, please access the website.

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