

Short-Term and Mid-Term Outcomes of Video-Assisted Thoracic Surgery in Patients with Early-Stage Non-Small Cell Lung Cancer

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Background: Mid-term outcomes of video-assisted thoracoscopic surgery (VATS) lobectomy for early stage non-small cell lung cancer (NSCLC) in Vietnam should be evaluated and discussed.

Methods: This prospective descriptive study was conducted on 94 patients with NSCLC under stages I–IIA who were treated with VATS from November 2011 to July 2014.

Results: The median patient age was 55.5 ± 10.8 years. The rate of successful VATS for NSCLC treatment was 98.9%, and the conversion rate (from VATS to thoracotomy) was 1.1%. The operative time was 143.8 ± 38.9 minutes, the amount of blood loss was 194.8 ± 150.5 mL, and the postoperative complication rate was 10.6%. The ICU length stay was 2.8 ± 1.0 days, and the postoperative hospital length stay was 7.7 ± 2.1 days. Among the 89 patients with successful follow-up, one (1.1%) had a recurrent tumor, and ten (11.8%) had metastasis. The 1- and 2-year relative survival rates were 95.9% (3 deaths) and 80.8% (9 deaths), respectively.

Conclusion: VATS treatment for early stage NSCLC is an effective method with safe outcomes. The mid-term outcomes were acceptable with 1- and 2-year relative survival rates of 95.9% and 80.8%, respectively.

Keywords: video-assisted thoracoscopic surgery, VATS, non-small cell lung cancer, NSCLC, early-stage, short-term outcomes, mid-term outcomes

Introduction

Surgical therapy in the early stage of disease plays an important role in the multimodal therapy of lung cancer treatment. Among which, thoracotomy is an effective method, but its complication rate, extended hospital stay, and postoperative pain are still of foremost concern. Thoracoscopic surgery was developed to overcome these points and showed high safety and feasibility.^{1,2} However, video-assisted thoracic surgery (VATS) is inferior to thoracotomy as a NSCLC treatment regarding long-term outcomes and recurrence and overall survival rates.^{3–5} The reason is that in patients with NSCLC, VATS can accomplish difficult oncologic resection with restricted handling of surgical instruments.

Although the short-term outcomes of VATS are advantageous with respect to postoperative complications and hospital length stay, reports on its mid- and long-term outcomes are insufficient,^{6,7} especially in Vietnam. In this study, VATS as treatment for NSCLC in stages I and IIA was examined. The short- and mid-term results may provide meaningful information for NSCLC surgical treatment.

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Materials and Methods

This prospective, descriptive study was conducted on 94 patients with NSCLC who were treated by VATS from November 2011 to July 2014. Inclusion criteria were as follows: patients with NSCLC diagnosed based on histopathological results (transbronchial biopsy, computed tomography [CT]-guided biopsy, VATS biopsy, and histopathological result after surgery) and appropriate information in the medical record and were treated by VATS. Exclusion criteria were as follows: patients treated by VATS who have a different histopathological result from NSCLC; those lacking information in the medical record; and patients who refused to participate in this study. The flowchart of this study is shown in Figure 1.

Research Procedure

(1) Clinical examinations and laboratory tests

(2) Indications of VATS⁸ lobectomy treating NSCLC:

+ NSCLC with the clinical stage is from the clinical stage from I to IIA.

+ Computed tomography image features tumor size < 6 cm without invasion and non-calcified hilar nodes.

(3) Preparing patients for surgery:

Patients are instructed on breathing exercises, nutrition, and personal hygiene prior to surgery. General anesthesia is applied, and selective lung ventilation is performed with double-lumen intubation in the lateral decubitus position. The surgical team consists of one leading surgeon and two assistant surgeons. A video monitor is positioned on the left of the operating table and slightly elevated at 15°–30° on the surgeon's opposite side.

(4) Technique of VATS

Step 1: Trocar insertion.

Step 2: Evaluate injuries, including pleural space, pleural thickening classification, features of fissures, and tumor position.

Step 3: Lung biopsy, including tumor biopsy and wedge resection.

Step 4: Lobectomy and lymph node dissection.

- Pulmonary lobectomy: Technique of pulmonary lobectomy according to Gottsot D. (2010).⁹

- Lymph node dissection: Investigate and remove visible lymph nodes according to American Cancer Society guidelines.¹⁰

Step 5: Collecting samples, final checks, insert a chest tube (under thoracoscopic guidance), and close the incisions. In the Department of Pathology, specimens were

handled following a procedure and identified according to the WHO recommended classification of NSCLC in 2004.¹¹

(5) Postoperative care

- Regular monitoring for all patients. Chest tubes are connected to a drainage system device. Postoperative pain management is initiated after epidural analgesia in the operating room, by administering local anesthesia (Bupivacaine 0.5/20 mL and Sufentanyl 50 mg in NaCl 9⁰ /₀₀) maintained using the patient-controlled analgesia device. When the patient is moved to the ward, epidural analgesia is replaced with oral Paracetamol 0.5 * 2 per day. Postoperative complications, such as hemorrhage, prolonged air leak, chylothorax, arrhythmia, atelectasis, and pneumothorax after drain removal, are managed.

After discharge, the follow-up regimen is in accordance with the guidance of ACCP (2007)¹² and BTS (2010).¹³ Patients are checked at the following time points: 1, 3, 6, 12, 18, and 24 months after surgery and at the end of research in the outpatient clinic of Phạm Ngọc Thạch Hospital.

Data Analysis

Information of patients is filled in parameter estimates table of SPSS 16.0 statistical software. We are using statistical formulas. Analytics: (χ^2) is used to compare the qualitative parameters in two groups. In case of the shortage of data or 1 in 4 parameters of 2×2 table less than 5, Fisher's equation is used instead of (χ^2). To evaluate a quantitative value: drain duration, length of stay of hospital after surgery. We use T - student, Mann-Whitney, and Kruskal-Wallis equations. Accreditation is significant (either difference or relations) if $p < 0.05$.

Ethics in Research

Approved by Ethical Committee of Phạm Ngọc Thạch Hospital.

Results

General Characteristics

The median age was 55.5 ± 10.8 years. The common symptoms were chest pain (59.8%), dry cough (43.6%), hemoptysis (20.2%), and locally decreased lung sounds (22.3%). Approximately 14.9% of patients had no Image in symptoms. CT images showed 100% peripheral tumors with 2.1/1 ratio of the right lung/the left lung. The largest tumor was 5 cm in diameter. Biopsy prior to pulmonary lobectomy by VATS can

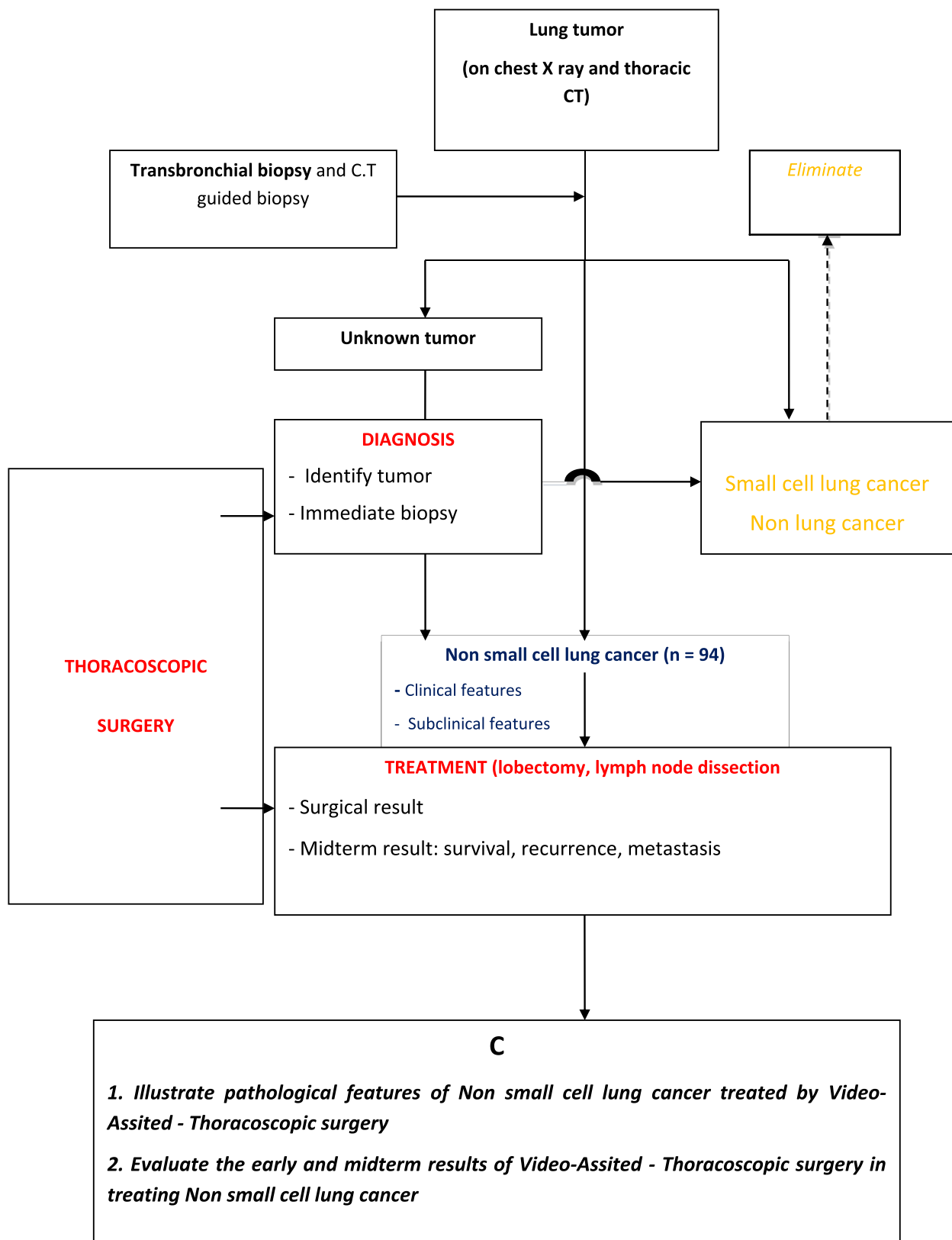


Figure 1 Flowchart of study.

be classified as transbronchial biopsy (12.8%), trans-thoracic wall under computed tomography biopsy (46.8%), and during VATS (40.4%). Clinical TNM staging was from IA to IIA with stage IA rate of 54.3% and IB rate of 40.4%.

Surgical Characteristics

The rate of VATS lobectomy for NSCLC treatment was 98.9%, and the conversion rate (from VATS to thoracotomy) accounted for 1.1% (one case of severe bleeding). During the operation, the rates of severe complications and blood transfusion were 3.2% and 5.3%, respectively. The operative time was 143.8 ± 38.9 minutes, and the amount of blood loss was 194.8 ± 150.5 mL. In the upper lobe resection, the blood loss during surgery (229.6 ± 176.5 mL, $p < 0.05$) and the rate of blood transfusion ($p < 0.05$) were statistically significant. Detailed information is shown in Table 1. The postoperative complication rate was 10.6% (8/9 mild cases accounting for 88.9%). The prolonged air leak was the highest with 5.3% (Table 2).

Table 3 shows the postoperative characteristics. The amount of pleural fluid drainage decreased gradually from the 1st to the 2nd day after surgery. Drain duration after surgery was identified in 93 patients (one case was converted to thoracotomy). Drain removal in the first 3 days was accomplished in 59.1% of patients. The average duration of using epidural anesthesia for pain relief was 2.6 ± 0.8

days. The mean VAS score on the 5th day after surgery was 2.7 ± 1.0 . The ICU length stay was 2.8 ± 1.0 days, and the postoperative hospital length stay was 7.7 ± 2.1 days.

Midterm Results

At the end of this study, communication was continued with 89/94 patients (94.7%). Among them, the survival rate was 81.9%, and the death rate was 12.8%.

One case (1.1%) had a recurrent tumor. Ten cases (11.8%) had metastasis, and the mean detection time was 10.7 ± 9.7 months after surgery. The relationship among lesion macroscopically, pathology, and metastasis is shown in Table 4.

The twelve 1-year relative survival rate was 95.9% (3 deaths), and the 2-year relative survival rate was 80.8% (9 deaths). The median survival time was 30.8 ± 1.2 months (min-max: 26.6–43.5, CI 95% = 28.52–33.09). The factors associated with the survival rate are listed in Table 5. Details on the disease-free survival according to TNM stages after surgery are shown in Table 6.

Discussion

A high rate of lung cancer is associated with advanced age,¹⁴ with estimates of 0.02% at the age of 40 years and up to 2.0% at the age of 80 years.¹⁵ In this study, 84.0% of patients were aged 40–69 years, which is close to the 81.8% of lung cancer occurring in individuals aged 54–84 years.¹⁵ Smoking is one of the leading risks of lung cancer.¹⁶ In this work, the general rate of smoking was 40.4%. Among which, 79.2% were male, and no female had history of smoking. The male/female ratio for NSCLC was 1/1, indicating that in addition to smoking, many other risk factors contribute to this disease. The status of passive smoking in female patients has not been evaluated in this research. When choosing a surgical method, female patients often agree to endoscopic surgery related to aesthetics and postoperative pain. VAST was considered as suitable treatment for NSCLC in the early stage. Among the 1015 NSCLC cases undergoing VATS, those at Phase I accounted for 87.9%.¹⁷ In some cases, VATS was only used in patients at stage I with non-hypertrophic N1 and N2 lymph nodes.^{18,19}

In the present study, the surgical time was 143.8 ± 38.9 minutes, which is similar to the results of Swanson et al²⁰ at 130 minutes, Tomaszek et al at 139 minutes,²¹ Congregado M. at 153 minutes,¹⁸ and Marty–Ane at 152 minutes.²² Other authors showed relatively long surgical time of up to 200,²³ and 258.1 minutes.²⁴ The surgical

Table 1 Intra-Operative Result

Criteria	Result
Operating time (minute)	143.8 ± 38.9
The amount of blood loss (mL)	194.8 ± 150.5
Severe hemorrhage rate (%)	3.2
Blood transfusion rate (%)	5.3

Table 2 Postoperative Complications

Complication	Number of Patients (n = 94)	Rate %
Prolonged air leak	5	5.3
Chylothorax	1	1.1
Pneumothorax after drain removal	1	1.1
Arrhythmia	1	1.1
Atelectasis	2	2.1
Total	10	10.6

Table 3 Postoperative Characteristics

		Mean $\pm$ SD	Min – Max Number (Percentage)
The amount of pleural fluid drainage (mL) P - values < 0.0001 ^w	POD 1	358.7 $\pm$ 151.7	20–800
	POD 2	216.1 $\pm$ 110.8	40–500
The duration of chest tube	Mean	3.7 $\pm$ 2.1	
	$\leq$ 3 days		55 (59.1)
	4–6 days		29 (31.2)
	$\geq$ 7 days		9 (9.7)
Duration of epidural anesthesia (day)		2.6 $\pm$ 0.8	1–5
VAS scale point on POD 5		2.7 $\pm$ 1.0	2–6
Length of stay (day)	In ICU	2.8 $\pm$ 1.0	1–6
	In total	7.7 $\pm$ 2.1	4–7

Abbreviations: w, Wilcoxon test; POD, postoperative days.

Table 4 Relationship Among Lesion Macroscopically, Pathology and Metastasis

Lesion Macroscopically, Pathology		Metastasis		P - values
		Yes	No	
Lesion macroscopically				
Visceral pleura puckering over tumor	Yes	1	17	0.611
	No	9	58	
Chest wall adhesions	Yes	0	5	> 0.05
	No	10	70	
Parietal pleura invasion in macroscopically	Yes	2	1	0.035*
	No	8	74	
The average size of tumor (cm)		3.4 ± 1.1	3.4 ± 1.3	0.962
Pathology				
N1 lymph nodes metastases		5	3	< 0.001*
N2 lymph nodes metastases		3	7	
No metastasis		2	65	
Postoperative TNM staging	I	2	58	0.0009*
	II	5	10	
	IIIA	3	7	

Note: *Statistical significant.

time showed positive trends with blood loss and blood transfusion during surgery. In the present work, the amount of blood loss during surgery was 194.8 $\pm$ 150.5 mL, which was lower than previous values, such

as 253.2 mL,²⁴ and 672 mL,²⁵ but higher than those in other studies such as 100²³ and 150 mL.²¹ During surgery, the amount of blood loss dramatically depends on the type of surgery, the lesion's characteristics, the medical equipment, and the surgeon's experience. No effective hemostatic devices, such as the ultrasonic systems (Harmonic® scalpel) and the electrothermal bipolar-activated devices (Ligasure™) that can be a risk factor for increasing blood loss surgery, were applied in the current work. Another risk factor was pulmonary blood congestion due to the ligation of the pulmonary vein before the artery. Severe bleeding during the operation is a serious complication in pulmonary lobe surgery. Vascular injury is a common etiology.^{1,26,27} Atrial injury and bronchial artery injury rarely happen but have also been recorded.^{1,27} In the case of failure to control the bleeding, thoracotomy is the next step in the procedure. The rate of changing to thoracotomy in VATS for NSCLC treatment varies from 0% to 14.7%.^{2,17,23,24,26} Among the 94 cases in the present study, 3.2% (3 cases) had severe bleeding caused by upper lobal segmental artery injury. In two cases, bleeding was successfully controlled using a clamping clip of blood vessels. One case (1.1%) was transferred to thoracotomy.

The rate of postoperative complications was 10.6%, including prolonged air leak (5.3%), atelectasis (2.1%), chylothorax (1.1%), arrhythmia (1.1%), and pneumothorax after chest tube removal (1.1%). Shortening the hospitalization time is the advantage of VATS. In this study, the hospitalization time was 7.3 $\pm$ 2.2 days, which was higher than that in

Table 5 Survival Associated with Several Factors

		Mean	Rate (%)		P - value
		Time (Months) (95% CI)	12 Months	24 Months	
Pathological TNM staging	I (n = 61)	33.2 (30.9–35.4)	97.8	93.7	0.001*
	II (n = 16)	26.9 (22.8–31.1)	92.3	70.3	
	IIIA (n = 12)	23.5 (17.4–29.6)	91.7	68.8	
Lymph nodes metastases	N0 (n = 69)	33.0 (30.9–35.1)	98.1	88.0	<0.001*
	N1 (n = 09)	22.2 (17.4–26.9)	87.5	43.8	
	N2 (n = 11)	24.5 (17.6–31.3)	90.9	75.8	
Age	≤ 60 (n = 62)	31.4 (29.1–33.8)	97.9	85.1	0.208
	> 60 (n = 27)	29.6 (24.3–34.9)	90.9	71.1	

Note: *Statistical significant.

Table 6 Disease-Free Survival According to Pathological TNM Stages

Pathological TNM Stages	Mean	Percentage (%)		P - values
	Time (Months) (95% CI)	12 Months	24 Months	
I (n = 61)	33.2 (31.0–35.5)	97.8	91.9	0.003*
II (n = 16)	25.8 (20.6–31.1)	87.1	62.2	
IIIA (n = 12)	22.5 (15.2–29.9)	83.3	71.4	

Note: *Statistical significant.

some studies, such as 4²⁸ and 6.5 days.²⁹ One of the reasons is that the homes of almost all the patients are located far from our hospital. Hence, they want to extend the hospitalization time to achieve a stable condition prior to discharged and coming home. Postoperative care also remarked with chest tube drainage and postoperative pain. The chest tube duration was 3.7 ± 2.1 days, with 59.1% removed during the first 3 days. The pleural fluid at postoperative day 1 and 2 was 358.7 ± 151.7 and 216.1 ± 110.8 mL, respectively. These results were similar to those in other studies.^{24,29} Postoperative pain management is another crucial factor affecting recovery and quality of life.^{30,31} The time of analgesia infusion was 2.6 ± 0.8 days, and the VAS score at postoperative day 5 was 2.7 ± 1.0 . These values indicate promising results in pain management.

Mid-Term Results

Recurrence and metastatic evaluation is fundamental in cancer monitoring. Kelsey et al showed that the mean duration of local recurrence and metastasis was 14.1 and 12.5 months,

respectively.³² With 36 months of follow-up after surgery, no statistically significant difference in recurrence rate and distant metastasis was observed between thoracoscopy and thoracotomy.⁷ A long-term study on phase I lung cancer with follow-up time of 91 months showed that recurrence was mainly observed in 60% of patients during the first 2 years after surgery.³³ In the present work, one case (1.3%) had local recurrence 3 months after surgery. Ten cases (11.8%) showed metastatic detection time of 11.7 ± 9.7 months after the surgery. These recurrence and metastatic rates were considered low. A large sample size with a long follow-up time is required for paranomical evaluation. The current work also revealed several factors related to metastasis. The tumor with parietal pleural invasion had higher metastatic rate than that without invasiveness (20.0% vs 1.3%, $p < 0.05$). The (distant) metastasis rate was statistically significant for the stages of lymph node metastasis with N1-metastasis at 62.5%, N2-metastasis at 30%, and with no lymph node metastasis at 3.0%.

Overall survival rate is a key in evaluating the effectiveness of treatment from oncological perspectives.⁷ In patients with NSCLC stage I, the overall survival after resection did not differ between those receiving thoracotomy and VATS.^{7,34,35} In general, the 5-year relative survival rate of NSCLC ranges from 58% to 97%.³⁶ A 3-year follow-up study reported that the 1-, 2-, and 3-year relative survival rates for NSCLC were 85%, 82.2%, and 73.5%, respectively.²³ In the current work, the 1- and 2-year relative survival rates were 95.9% and 88.0%, respectively. These rates were acceptable and in line with previous results on early stage.³⁷ The survival rate also varied

under different disease stages, that is, the 3-year relative survival rate of stage I was 87.2%, and that of stage II–III was 58.4%.⁷

Conclusion

VATS as an early stage NSCLC treatment is an effective method with safe outcomes. Its mid-term outcomes were acceptable with 1 and 2-year relative survival rates of 95.9% and 80.8%, respectively.

Data Sharing Statement

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The Ethics Committee of Pham Ngoc Thach Hospital approved the study protocol (QD/HVQY) and authorized its conduct and follow-up. The study was in line with the Declaration of Helsinki. Individual patient consent for inclusion in the study was obtained. Before treatment, written informed consent was provided to all participants after a thorough explanation of the purpose of this study. Patients had signed in written informed consent. Patients had the right to discontinue at any time during the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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