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Uniportal Video-assisted Thoracoscopic Talc Pleurodesis in the Treatment of Malignant Pleural Effusions. Is Early Phase Talc Pleurodesis More Effective?

Malign Plevral Efüzyonların Tedavisinde Uniportal Video Yardımlı Torakoskopik Talk Plöredezis. Erken Dönem Talk Plöredezis Daha Etkili midir?

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ABSTRACT

Objective: VATS talk pleurodesis is an effective method for palliatively treating malignant pleural effusion (MPE). This study aimed to compare early and late-phase talc pleurodesis procedures and to determine the factors affecting the success of the uniportal VATS talc pleurodesis procedure.

Materials and Methods: The data of 58 patients who underwent uniportal VATS talc pleurodesis due to MPE were analysed retrospectively. The patients were divided into two groups as early-phase talc pleurodesis (n=23, 48.3%) and late-phase (n=25, 51.7%). Groups were compared using Pearson chi-square test and Mann-Whitney U tests.

Results: Complications developed in 10 patients (17.2%). No significant difference was found between the early-phase talc pleurodesis and the late-phase pleurodesis regarding complication rate (p=0.905), durations of hospitalisation (p=0.821). It was observed that the early-phase talc pleurodesis procedure had higher success than the late -phase talc pleurodesis procedure (Odds ratio=1.425, 95% CI=0.307-6.624), although not statistically significant (p=0.06). It was determined that 86% of the patients who underwent early talc pleurodesis had no hospital readmission due to MPE within the first 3 months.

Conclusion: Uniportal VATS talc pleurodesis is a safe and effective treatment method for malignant pleural effusion, with low complication and high success rates. Early-phase talc pleurodesis procedure significantly reduces recurrent hospitalisations.

Keywords: Dyspnea, malignant pleural effusion, pleurodesis, uniportal VATS

ÖZ

Amaç: VATS talk plöredezis malign plevral efüzyonun (MPE) palyatif tedavisinde etkili bir yöntemdir. Bu çalışmada erken ve geç faz talk plöredez prosedürlerinin karşılaştırılması ve uniportal VATS talk plöredez prosedürünün başarısını etkileyen faktörlerin belirlenmesi amaçlanmıştır.

Materyal ve Metot: MPE nedeniyle Uniportal VATS talk plöredezis uygulanan 58 hastanın verileri retrospektif olarak incelendi. Hastalar erken dönem talk plörodezis grubu (n=23, %48,3) ve geç dönem talk plörodezis grubu (n=25, %51,7) olarak ikiye ayrıldı. Gruplar Pearson ki-kare testi ve Mann-Whitney U testleri kullanılarak karşılaştırıldı.

Bulgular: Komplikasyon 10 hastada (17,2%) gelişti. Erken dönem Uniportal VATS talk plöredezis yapılan grup ile geç dönem Uniportal VATS plöredezis yapılan grup arasında komplikasyon oranı (p=0,905), hastanede kalış süresi (p=0,821) açısından istatistiksel fark saptanmadı (p=0,900). Erken dönemde talk plöredezis prosedürünün geç dönem talk prosedürüne göre daha yüksek başarı gösterdiği görüldü (Odds ratio=1,425, 95%CI=0,307-6,624), fakat istatistiksel olarak anlamlı değildi (p=0,060). Erken dönem talk plöredezis uygulanan hastaların % 86'sının ilk 3 ay içinde MPE nedeniyle hastaneye tekrar başvurusu olmadığı belirlendi.

Sonuç: Uniportal VATS talk plöredezis malign plevral efüzyonlarda komplikasyon oranı düşük, başarı oranı yüksek, güvenli ve etkili bir tedavi yöntemidir. Erken dönemde uygulanan talk plöredezis prosedürü tekrarlayan hastane yatışlarını önemli ölçüde azaltmaktadır.

Anahtar Kelimeler: Dispne, malign plevral efüzyon, plöredez, uniportal VATS

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INTRODUCTION

The presence of malignant pleural effusion (MPE) is a common complication in advanced malignant tumours.[1] MPE is typically accompanied by severe dyspnea that impairs patients' quality of life. The prevalence of MPE among cancer patients ranges from 15% to 39%.[1,2] In addition to developing from pleural metastases, MPE can also result from primary pleura tumours, such as mesothelioma.[3] Lung carcinoma, breast carcinoma, and lymphoma are the most common causes of MPE.[1,3] Survival is considered when designing treatment strategies for patients who have developed MPE. In these advanced cancer patients, where survival expectancy is generally low, the treatment approach can be palliative and aims to improve the patient's quality of life with minimally invasive interventions whenever possible. As part of MPE treatment, it is intended to drain the pleural cavity completely of fluid, to promote lung expansion as much as possible, and to apply interventions to prevent the re-accumulation of fluid. The most widely used approach is pleurodesis with sterile talcum powder.[4] With the advent of video-assisted thoracoscopic surgery (VATS), uniportal (U) talc insufflation, and pleurodesis are now possible.[5] The number of studies investigating the effects of time of application of the talc insufflation procedure and the amount of pleural effusion identified before the procedure on the success of pleurodesis is limited.[5] We hypothesised that the early phase UVATS talc pleurodesis procedure is more effective than the late phase talc pleurodesis procedure and that the early phase talc pleurodesis procedure significantly reduces recurrent hospitalisations.

The study aimed to compare the outcomes of our patients who underwent early and late-phase talc pleurodesis and identify the factors affecting the success of the uniportal VATS (UVATS) talc pleurodesis procedure performed for MPE.

MATERIALS AND METHODS

Ethics Committee Approval: The study was approved by the Ethics Committee of Sakarya University and was conducted in accordance with the principles of the Declaration of Helsinki; (Date: 08/03/2023, decision no: 92). Informed consent was obtained from the patients.

Patient Feature: The records of 235 patients diagnosed with pleural effusion for any reason and who underwent diagnosis and/or treatment VATS at the Department of Thoracic Surgery between 2017 and 2022 were retrospectively analysed. It was determined found that 72 (31%) patients were diagnosed with MPE. A total of 14 patients were excluded from the study, including 8 patients for whom adequate expansion could not be achieved after drainage and three who had previously undergone pleurectomy/pleural abrasion. Patients who had previously undergone talc pleurodesis with a chest drain (n:3) were excluded from the study. Ultimately, 58 patients were included in the study (Figure 1).

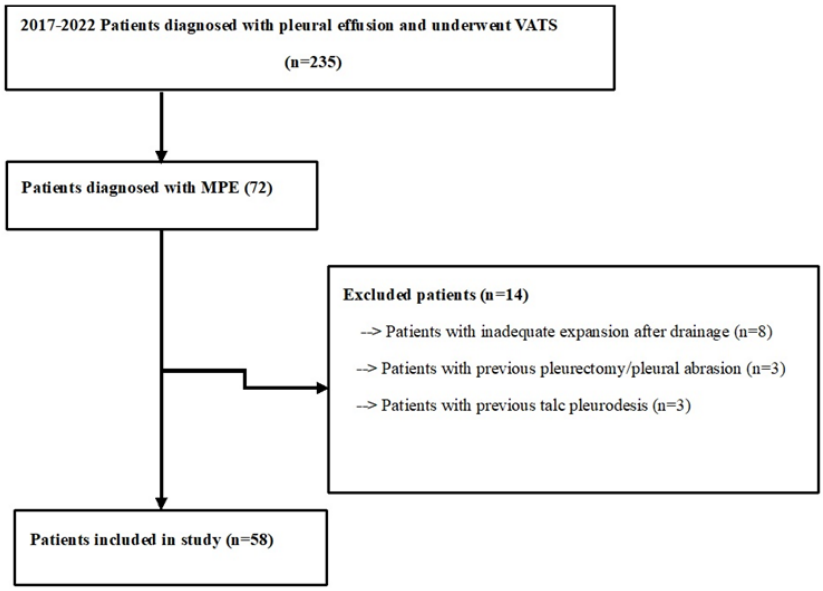

Figure 1. Flow diagram of patient selection and algorithm. MPE: Malignant pleural effusion; VATS: video-assisted thoracoscopic surgery; n: number.

Patients with poor performance status (Karnofsky performance index ≤30) or a life expectancy of less than three months were excluded from the study.[6]

Detection of fluid filling more than two-thirds of the hemithorax on computed tomography (CT) of the thorax was considered massive MPE.[7] Tumours originating primarily from the pleura or lung were defined as "intrathoracic tumours".

In patients with MPE, the application of talc pleurodesis following the first diagnostic pleural procedure was defined as "early-phase talc pleurodesis". If talc pleurodesis was performed after recurrent MPE, it was defined as "late-phase talc pleurodesis". Preoperative complete blood count, coagulation tests, and biochemical tests were routinely evaluated.

Perioperative and Postoperative Periods: In all patients, pleurodesis was performed by UVATS and surgery was performed under general anaesthesia with double-lumen selective intubation.

The pleural cavity was evaluated after drainage with UVATS, and suspicious areas were sampled on both the visceral and parietal pleura. In patients with pleural effusion undiagnosed preoperatively, the malignant pathologic diagnosis was confirmed by intraoperative frozen-section examination. Positive pressure ventilation was used to determine whether the lung had expanded sufficiently after pleural fluid drainage. In patients with sufficient expansion, 4 mg of sterile talcum powder (Steritalc®, Novatech, France) was used for pleurodesis. Talcum powder was distributed evenly on all parenchyma and parietal pleura surfaces by insufflation using a disposable atomiser.[5] The procedure was terminated by placing a single 28- F thoracic drain through the UVATS incision.

In patients with a daily drainage of 100ml/24 h, the drain was terminated when the complete expansion was observed on the posterior-anterior (PA) chest radiograph, and the patients were discharged on the same or the following day.

The patients were routinely scheduled for follow-up at the postoperative day 10, month 1, and month 3 and evaluated by PA chest radiographs. Re-accumulation of pleural fluid in the patient's follow-up was considered a technique failure. The absence of fluid accumulation at subsequent 3-month outpatient clinic visits was considered the procedure's success.

Statistical Analysis: Data were entered into the Statistical Package for the Social Sciences software package (IBM® SPSS Statistics for Windows, version 23.0, Armonk, NY, USA). Descriptive statistics were used, quantitative variables were characterised using mean, maximum (max), and minimum (min) values, while percentages were used for qualitative variables. The normality of the distributions was determined by Kolmogorov-Smirnov analysis. The inter-quantile range (IQR) result was also presented for the values recorded as the median. It was decided to use Student's t-test to compare continuous variables between groups. Pearson's chi-square test was used for the comparative analysis of qualitative variables, whereas Fisher's exact test was used when the sample size was small (≤5). Nonparametric continuous variables were recorded as median and compared using Mann-Whitney U tests. When factors affecting the method's success were identified in the univariate analysis, logistic regression analysis was conducted with these factors.

RESULTS

The mean age of the patients was 62.2±10.7 years (min=22, max=94). Most of the patients included in the study were male (n=36, 62.1%). The clinical manifestations of the patients included dyspnea (n=45, 77.6%), chest pain (n=16, 27.6%), and cough (n=2 3.4%). The cause of MPE was intrathoracic tumours in 56.9% (n=33) and extrathoracic tumours in 43.1% (n=25) of patients. The most common causes of malignant pleural effusions were primary lung cancer (n=25, 43.1%), malignant pleural mesothelioma (n=8, 13.7%), and breast cancer (n=8, 13.7%). Of the patients who underwent talc pleurodesis with UVATS, 28 (48.3%) experienced the early-phase talc pleurodesis procedure. In comparison, 30 patients (51.7%) underwent late talc pleurodesis (n=21 36.2% after the 2nd episode, n=7% after the 3rd episode and n=2 3.4% after the 4th episode). MPE was massive in most patients (n=38, 65.5%). There was no mortality among our patients after UVATS talc pleurodesis. Complications developed in 10 patients (17.2%) after UVATS talc pleurodesis. The most common complication was chest pain (n=4, 6.7%). It was followed by shortness of breath (n=2, 3.4%), arrhythmia (n=2, 3.4%), fever (n=1, 1.7%), atelectasis (n=1, 1.7%), and other complications. The mean duration of hospitalisation was 7.7 days (min=2 days, max=20), and the mean drainage duration was 7.1 days (min=2 days, max=19). The clinicopathologic and demographic characteristics of the patients are summarised in Table 1.

No significant difference was found between these two groups in terms of primary tumour location (p=0.621), complication rate (p=0.905), the success of VATS pleurodesis (p=1.000), duration of hospitalisation, and drainage duration (p=0.821, 0.900, respectively). The comparison of patients who underwent early-phase UVATS pleurodesis and patients who underwent late-phase UVATS pleurodesis is presented in Table 2.

Table 1. Demographic and clinical data of the patients.

Variables		Data
Age, years, mean±SD		62.2±14.1
Sex, n (%)	Female	22 (37.9)
	Male	36 (62.1)
Primary tumour location, n (%)	Intrathoracic	33 (56.9)
	Extrathoracic	25 (43.1)
Tumour subtype, n (%)	Primary lung cancer*	25 (43.1)
	Pleural mesothelioma	8 (13.7)
	Colorectal cancer	4 (6.8)
	Melanoma	1 (1.7)
	Breast cancer	8 (13.7)
	Gastric cancer	4 (6.8)
	Osteosarcoma	2 (3.4)
	Ovarian cancer	3 (5.1)
	Pancreatic cancer	2 (3.4)
	Prostate cancer	1 (1.7)
Mode of diagnosis, n (%)	Pleural biopsy	26 (44.8)
	Cytology	32 (55.2)
Thoracentesis / pathological diagnosis status, n (%)	No	35 (60.3)
	Yes	23 (39.7)
Side, n (%)	Left	39 (67.2)
	Right	19 (32.8)
Surgery after how many recurrences, n (%)	1	28 (48.3)
	2	21 (36.2)
	3	7 (12.1)
	4	2 (3.4)
Amount of malignant pleural effusion, n (%)	Submassive	20 (34.5)
	Massive	38 (65.5)
Smoking, n (%)	No	39 (67.2)
	Yes	19 (32.8)
Comorbidity, n (%)		23 (39.7)
Complication, n (%)		10 (17.2)
Recurrent pleurisy status (success rate), n (%)	Successful	49 (84.5)
	Unsuccessful	9 (15.5)
Length of hospital stay, days, median (IQR)		6 (6.3)
Drainage time, days, median (IQR)		5 (5.3)

IQR: interquartile range; SD: standard deviation; n: number; Primary lung cancer*: lung adenocarcinoma, lung squamous cell cancer, lung small cell cancer

Table 2. Comparison of those who underwent early-phase UVATS talc pleurodesis and late-phase UVATS talc pleurodesis.

Variables		Early-phase UVATS talc pleurodesis (n=28)	Late-phase UVATS talc pleurodesis (n=30)	p-value
Age, years, mean±SD		58.9±13.4	65.3±14.3	*0.080*
Sex, n (%)	Female	9 (32.1)	13 (43.3)	0.380
	Male	19 (67.9)	17 (56.7)	
Primary tumour location, n (%)	Intrathoracic	15 (53.6)	18 (60.0)	0.621
	Extrathoracic	13 (46.4)	12 (40.0)	
Mode of diagnosis, n (%)	Pleural biopsy	8 (28.6)	18 (60.0)	**0.010**
	Cytology	20 (71.4)	12 (40.0)	
Thoracentesis / pathological diagnosis status, n (%)	No	16 (57.1)	19 (63.3)	0.630
	Yes	12 (42.9)	11 (36.7)	
Side, n (%)	Left	12 (42.9)	23 (76.7)	0.113
	Right	16 (57.1)	7 (23.3)	
Amount of malignant pleural effusion, n (%)	Submassive	11 (39.3)	9 (30.0)	0.457
	Massive	17 (60.7)	21 (70.0)	
Smoking, n (%)	No	17 (60.7)	22 (73.3)	0.306
	Yes	11 (39.3)	8 (26.7)	
Comorbidity, n (%)		13 (46.4)	10 (33.3)	0.308
Complication, n (%)		5 (17.9)	5 (16.7)	0.905
Recurrent pleurisy status (success rate), n (%)	Successful	24 (85.7)	25 (83.3)	1.000
	Unsuccessful	4 (14.3)	5 (16.7)	
Length of hospital stay, days, median (IQR)		6 (6.3)	7 (6.5)	0.821
Drainage time, days, median (IQR)		5 (5.5)	6 (5.5)	0.900

The p-value in bold indicates statistical significance. The p-value in italics indicates a trend towards statistical significance. IQR: interquartile range; SD: standard deviation; UVATS: uniportal video-assisted thoracoscopic surgery

VATS talc pleurodesis was successful in 49 patients (84.5%), but not in 9 patients (15.5%), and the effusion recurred during follow-ups. It was determined that 86% of the patients who underwent talc pleurodesis in the early period had no hospital admission due to MPE within the first 3 months. It was found that the evaluated parameters did not affect the success of VATS pleurodesis (Table 3).

Logistic regression analysis of certain variables that may affect the success of VATS talc pleurodesis revealed that smoking was an independent risk factor for failure at a level close to statistical significance (Odds ratio=4.242, 95%CI=0.817-22.032, p=0.08). Early-phase VATS pleurodesis procedure increased the odds of success (Odds ratio=1.425, 95%CI=0.307-6.624, p=0.06), although not statistically significant (Table 4).

DISCUSSION AND CONCLUSION

Primary malignancies of the pleura and many intrathoracic or extrathoracic cancers metastasised to the pleura may cause MPE.[8] In Europe, approximately 100,000 patients are hospitalised annually due to MPE. In contrast, in the United States, the number is estimated to be approximately 126,000.[9] This leads to a dramatic increase in healthcare costs and severe economic losses. Depending on the primary disease, life expectancy ranges from 1 to 12 months on average.[2,10] While it has been reported that the most common cause of MPE is lung cancer, other causes include breast cancer, gastrointestinal system malignancies, hematologic malignancies, and mesothelioma, which is the primary tumour of the pleura.[9,11,12] As a result of our study, we found that primary lung cancer was the most common cause of MPE, followed by mesothelioma and breast cancer

Table 3. Grouping of patients as successful talc pleurodesis and unsuccessful talc pleurodesis according to success status and comparison of these groups.

Variables		Successful pleurodesis (n=49)	Unsuccessful pleurodesis (n=9)	p-value
Age, years, mean±SD		62.2±14.1	63.1±15.1	0.850
Sex, n (%)	Female	20 (40.8)	2 (22.2)	0.291
	Male	29 (59.2)	7 (77.8)	
Primary tumour location, n (%)	Intrathoracic	28 (57.1)	5 (55.6)	1.000
	Extrathoracic	21 (42.9)	4 (44.4)	
Side, n (%)	Left	35 (71.4)	4 (44.4)	0.113
	Right	14 (28.6)	5 (55.6)	
Timing of UVATS, n (%)	Early-phase talc pleurodesis	24 (49.0)	4 (44.4)	1.000
	Late-phase talc pleurodesis	25 (51.0)	5 (55.6)	
Amount of malignant pleural effusion, n (%)	Submassive	17 (34.7)	3 (33.3)	0.937
	Massive	32 (65.3)	6 (66.7)	
Smoking, n (%)	No	35 (71.4)	4 (44.4)	0.137
	Yes	14 (28.6)	5 (55.6)	
CT/RT after pleurodesis, n (%)	No	35 (89.8)	8 (88.9)	1.000
	Yes	5 (10.2)	1 (11.1)	
Comorbidity, n (%)		21 (42.9)	2 (22.2)	0.245
Complication, n (%)		9 (18.4)	1 (11.1)	0.596
Length of hospital stay, days, median (IQR)		6 (5.5)	4 (9.0)	0.248
Drainage time, days, median (IQR)		5 (5.5)	4 (8.0)	0.380

IQR: interquartile range; SD: standard deviation; UVATS: Uniportal video-assisted thoracoscopic surgery; CT: chemotherapy; RT: radiotherapy.

Table 4. Logistic regression analysis of certain variables that may affect the success of pleurodesis with UVATS.

Variable	Odds ratio	95%CI	p-value
Age (for each year)	1.002	0.948-1.059	0.944
Location of the primary tumour (intrathoracic vs extrathoracic)	1.853	0.353-9.718	0.466
UVATS time (early-phase vs. late-phase)	1.425	0.307-6.624	0.651
Amount of malignant pleural effusion (Submassive vs massive)	1.329	0.258-6.842	0.734
Smoking (No vs Yes)	4.242	0.817-22.032	*0.080*

Vs: versus; CI: confidence interval; UVATS: Uniportal video-assisted thoracoscopic surgery.

as other common causes.

Due to their short life expectancy, palliative treatment strategies are typically used in MPE patients. Evacuation of the fluid with closed-system thoracic drainages at diagnosis was accepted as the first approach. Still, after this application, it was observed that the fluid recurred in 60% of the patients within 9 days and in 90% of the patients within a month.[13,14]

For treating MPE, pleurodesis of the pleural cavity is recommended to prevent recurrence.[15] Although agents such as bleomycin, patient's blood, tetracycline, silver nitrate, and iodopovidone, as well as surgical procedures such as pleurectomy/ decortication, can be used for pleurodesis, the most commonly used agent worldwide is sterile talc powder.[4] The aim is to provide adhesion between pleural leaves due to local irritation and inflammation.[16] In a systematic review and meta-analysis, talc pleurodesis with VATS was reported to be more successful than other techniques.[12,17] Hence, we applied the UVATS technique for talc pleurodesis in the patients included in the study. The most commonly reported complications of the technique are chest pain and fever.[4,15] Consistent with the findings in the literature, the most common complication we encountered was chest pain, with an incidence of 17%. There was no difference in complications between early and late-phase VATS talc pleurodesis procedures. Barbetakis et al.18 demonstrated in their study that the most common complication they encountered was prolonged air leak. No prolonged air leak was observed in our series. This may be explained by the fact that decortication was not performed in patients with insufficient lung expansion, and these patients were excluded from the study. In large series, mortality of the procedure has been reported as 0.8-2%.[12,18] Low-performance status and delay between pleural effusion diagnosis and pleurodesis were reported to be statistically significant factors for postoperative mortality.[14,18] Markowiak et al.[19] suggested that 30-day mortality (5.8%) was not related to the procedure but to the primary disease. No early mortality was associated with the procedure in any of our patients. This may be explained by the patients with poor performance status and life expectancy of less than 3 months who were treated with therapeutic thoracentesis or pleural catheter drainage and were excluded from the study.

In the literature, the success rate in patients who underwent VATS talc pleurodesis for MPE was between 76% and 96%.[19,20] Cardillo et al.[14] argued that the early-phase VATS talc pleurodesis procedure increased the chance of success. Meanwhile, Cobanoglu et al.[5] suggested that talc pleurodesis is more likely to be successful when MPE is asymptomatic and a low amount of effusion is detected. Among the patient groups included in our study, we could not see any difference in the success of the procedure between the massive and submassive patient groups. Our success rate in our UVATS talc pleurodesis cases was 84.5%, similar to the literature. Moreover, similar to the literature, when we compared the early-phase talc pleurodesis group with the late talc pleurodesis group, it was found that the early-phase talc pleurodesis procedure increased the probability of success, though not significantly. Based on our study results, the early-phase talc pleurodesis procedure significantly reduced recurrent hospitalisations, supporting our hypothesis. Nevertheless, in contrast to our expectations, there was no significant difference in efficacy between the early and late-phase UVATS talc pleurodesis groups. It was found that 86% of the patients had no hospital admission due to MPE within the first 3 months. For this reason, we think that early-phase VATS talk pleurodesis is important.

In conclusion, it is well established that UVATS talc pleurodesis is a safe and effective treatment modality for MPE, with a low complication and a high success rate. The efficacy of early and late-phase UVATS talc pleurodesis procedures was similar. Early-phase talc pleurodesis procedure significantly reduces recurrent hospitalisations. The study has some limitations. First of all, it was designed as a retrospective study. The MPE patient group is a large heterogeneous group of patients with different survival prospects. However, the fact that it was a single-centre study is a strength regarding the homogeneity of the treatment applied.

Ethics Committee Approval: The study approval was obtained from Sakarya University Faculty of Medicine Local Ethics Committee and was conducted in accordance with the principles of the Declaration of Helsinki; (Date: 08/03/2023, decision no: 92). Informed consent was obtained from the patients.

Conflict of Interest: No conflict of interest was declared by the authors.

Author Contributions: Concept – YA; Supervision – YA, AŞ; Materials – YA; Data Collection and/or Processing – AŞ, YA; Analysis and/or Interpretation – AŞ, YA; Writing –YA.

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