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Mechanical thrombectomy in COVID-19-associated ischaemic stroke: patient characteristics and outcomes in a single-centre study

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ABSTRACT

Introduction. The aim of this study was to assess the clinical profiles and outcomes of patients with confirmed COVID-19 infection and acute ischaemic stroke (AIS) treated with mechanical thrombectomy (MT) at the Comprehensive Stroke Centre (CSC) of the University Hospital in Krakow.

Clinical rationale for the study. COVID-19 is a risk factor for AIS and worsens prognosis in patients with large artery occlusions. During the pandemic, the global number of MT has dropped. At the same time, studies assessing outcomes of this treatment in COVID-19-associated AIS have produced divergent results.

Material and methods. In this single-centre study, we retrospectively analysed and compared the clinical profiles (age, sex, presence of cardiovascular risk factors, neurological deficit at admission), stroke size (measured using postprocessing analysis of perfusion CT with RAPID software), time from stroke onset to arrival at the CSC, time from arrival at the CSC to groin puncture, treatment with intravenous thrombolysis, length of hospitalisation, laboratory test results, and short-term outcomes (measured with Thrombolysis in Cerebral Infarction scale, modified Rankin Scale and National Health Institute Stroke Scale) in patients with AIS treated with MT during the pandemic. A comparison between patients with and without concomitant SARS-CoV2 infection was then performed.

Results. There were no statistically significant differences between 15 COVID (+) and 167 COVID (-) AIS patients treated with AIS with respect to clinical profiles (p > 0.05), stroke size (p > 0.05) or outcomes (NIHSS at discharge, 8.1 (SD = 7.1) vs. 8.8 (SD = 9.6), p = 0.778, mRS at discharge 2.9 (SD = 2) vs. 3.1 (SD = 2.1), p = 0.817, death rate 6.7% vs. 12.6%, p = 0.699). There was a significant difference between patients with and without COVID-19 concerning time from arrival at the CSC to groin puncture [104.27 (SD = 51.47) vs. 97.63 (SD = 156.94) min., p = 0.044] and the length of hospitalisation [23.7 (SD = 11.9) vs. 10.5 (SD = 6.9)]days, p < 0.001].

Conclusion. In AIS patients treated with MT, concomitant SARS-CoV2 infection did not affect the outcome. Our observations need to be confirmed in larger, and preferably multicentre, studies.

Key words: acute ischaemic stroke, COVID-19, mechanical thrombectomy, large artery occlusion

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Introduction

The majority of hospitalised patients with SARS-CoV2 experience neurological symptoms of varying severity [1]. COV-ID-19 is proven to be a risk factor for acute ischaemic stroke (AIS) [2]. AIS in patients with a SARS-CoV2 infection is associated with a more severe neurological deficit and higher in-hospital mortality [3]. The incidence of AIS in patients with COVID-19 is estimated at around 1.5%, although this percentage is higher among critically ill patients [4].

Mechanical thrombectomy (MT) is an endovascular method of stroke treatment that has revolutionised the outcomes of patients with emergent large artery occlusion (LAO). Recent studies suggest that AIS in COVID-19 patients is more commonly associated with LAO [5], and that concomitant SARS-CoV2 infection increases mortality in patients with LAO [6]. At the same time, during the COVID-19 pandemic a decline in the global number of stroke hospitalisations and MT procedures has been observed [7].

Clinical rationale for the study

The literature on the outcomes of COVID-19-associated AIS patients treated with MT is scarce, and the studies show divergent results. These have been summarised in a recent systematic review [8]. The characteristics and treatment results of this group of patients still need to be evaluated.

Therefore, the aim of this study was to assess the clinical profiles and outcomes of patients with a confirmed COV-ID-19 infection and AIS treated with MT at the University Hospital in Krakow,Poland and to compare them to those of AIS patients treated with MT at the same time, but without a concomitant SARS-CoV2 infection.

Material and methods

In this retrospective study, we analysed the medical documentation of patients who had undergone MT for AIS in the Comprehensive Stroke Centre (CSC) of the University Hospital in Krakow, Poland during the COVID-19 pandemic between March 2020 and May 2021. Included were patients with a COVID-19 infection confirmed by a positive SARS-CoV2 PCR or antigen test from a nasopharyngeal swab obtained at admission or in the referring hospital, or before hospitalisation (if the patient did not match the criteria for recovery). The control group consisted of 167 AIS patients treated with MT in the CSC between March 2020 and February 2021, who tested negative for SARS-CoV2 at admission. Excluded were patients who were negative for COVID-19 at admission but who tested positive during hospitalisation, or those who were transferred to another centre and therefore lost to follow-up.

The procedures for acute stroke causative treatment in Małopolska Voivodship, where our centre is located, have

been described elsewhere [9]. AIS patients with and without COVID-19 followed the same pathway of care. MT patients without SARS-CoV2 infection were admitted to the Stroke Unit, while those with a confirmed COVID-19 infection were transferred to a specialised Neurology Ward for COVID-19 (+) patients, where they were treated by neurologists from the same centre, with the same level of experience in acute stroke care. The guidelines for treatment of COVID-19 changed during the course of the pandemic, so the patients with SARS-CoV2 infection were treated according to the international recommendations pertaining at the time of their hospitalisation.

The patients who qualified for the study were followed according to the standard protocol of the Krakow Stroke Data Bank, as described in previous publications from our centre [10]. For the purposes of this study, we analysed the patients' age, sex, the presence and number of cardiovascular risk factors, time from stroke onset to the arrival at the CSC, time from arrival at the CSC to groin puncture, number of days of hospitalisation, treatment with intravenous thrombolysis, the immediate radiological effect of thrombectomy (measured using Thrombolysis in Cerebral Infarction scale, TICI), the neurological deficit (measured using National Institute of Health Stroke Scale, NIHSS) at admission and discharge from our centre, the functional outcome (measured using modified Rankin Scale, mRS) at discharge, and in-hospital mortality. Where available, the computed tomography perfusion imaging parameters at admission calculated using RAPID software (a postprocessing tool used for qualification for MT in DAWN and DEFUSE-3 trials) [11, 12] were also analysed. We also analysed the available laboratory test results — fibrinogen, D-dimer, lactate dehydrogenase (LDH), lymphocyte count, and C-reactive protein (CRP).

The results were compared between groups of AIS patients with and without a COVID-19 infection. Statistical analysis was performed using a PS Imago Pro 6.0 program. We presented categorical data as counts and percentages, and continuous data as mean and standard deviation (SD) or median and interquartile range (IQR). Categorical data was compared between groups using a Chi-square test. We tested continuous variables for normality with a Shapiro-Wilk test and compared them between groups using a t-Student test for normally distributed data and, in other cases, using a Mann-Whitney U test. We considered a two-sided p-value of less than 0.05 to be statistically significant.

In patients with COVID-19, we also noted the clinical and radiological symptoms of lung involvement. HRCT (high resolution computed tomography) images were analysed by the artificial intelligence technology software YITU Healthcare to automatically measure the relative (%) volume of inflammation in both lungs (the methodology was as described in a previous work from our centre) [13]. The chest X-ray images were assessed by a radiologist using a semiquantitative chest X-ray severity score [14].

The study was approved by the Bioethics Committee of the District Medical Council in Krakow (opinion number 143/KBL/OIL/2020) and conducted in accordance with the Declaration of Helsinki. As a part of the CRACoV-HHS project it was also approved by the Bioethics Committee of the Jagiellonian University in Cracow (opinion number 1072.6120.333.2020 dated December 7, 2020).

Results

We identified 16 patients with a COVID-19 infection and AIS who received treatment with MT in the CSC between March 2020 and May 2021. One patient was transferred after procedure to an Intensive Care Unit of another hospital, lost to follow-up, and not included in the final analysis. Four patients were diagnosed with COVID-19 before the onset of stroke, and two of them had already been hospitalised when the stroke occurred. The patients' individual characteristics, including their SARS-CoV2 infection clinical picture, are set out in Table 1.

The patients were aged 49 to 85 with a median age of 70 years (IQR = 17). Eight (53.3%) were female. The most common cardiovascular risk factor was arterial hypertension, found in 13 (86.7%) patients. There were no statistically significant differences between groups of patients with and without COVID-19 with respect to age, sex, the presence of individual cardiovascular risk factors, or the total amount of cardiovascular risk factors (Tab. 2).

CT perfusion with post-processing analysis with RAPID software was performed in 11 and 138 patients with, and without, COVID-19 infection respectively. There were no statistically significant differences in the volumes of total ischaemia, penumbra or necrosis between patients with and without COVID-19 infection (Tab. 2).

Patients with COVID-19 had a longer time from stroke onset to arrival at the Comprehensive Stroke Centre [307.3 (SD = 183.7) vs. 227.3 (SD = 115.7) minutes], but this difference was not statistically significant (p = 0.062). They also had a longer time from arrival at the CSC to groin puncture: this difference was small but statistically significant [104.27 (SD = 51.47) vs. 97.63 (SD = 156.94) minutes, p = 0.044] (Tab. 2). There were no statistically significant differences between the compared groups with respect to the severity of neurological deficit at admission and discharge (measured using the NI-HSS scale), the functional outcome at discharge (measured using the mRS scale), the percentage of patients treated with intravenous thrombolysis, the percentage of successful reperfusions (defined as TICI 2b-3), or in-hospital mortality. There was a statistically significant difference between the groups concerning the number of days of hospitalisation: 23.7 (SD = 11.9) for COVID (+) patients versus 10.5 (SD = 6.9) for COVID (-) patients, p < 0.001.

The levels of CRP and LDH were significantly higher, and the lymphocyte count significantly lower, in COVID (+) patients

compared to the control group (see Tab. 2). There was no statistically significant difference in D-dimer level, but this may be due to the fact that it is not routinely assessed in COVID (–) stroke patients in our centre, in fact only when thrombosis is suspected. It was impossible to compare fibrinogen levels due to the small data sample.

All our results are summarised in Table 2.

Discussion

To the best of our knowledge, this study is the first in Poland to present the characteristics of patients with COV-ID-19-associated AIS after MT. It is also the first study to compare stroke size in MT-treated patients with and without COVID-19 using CT-perfusion imaging with post-processing analysis with RAPID software.

LAO in COVID-19 patients seems to be associated with higher mortality than in patients without SARS-CoV2 infection [6]. However, previous studies on the outcomes of COVID-19 patients treated with MT produced mixed results, as presented in a recent systematic review [8]. Some of the research has shown poor outcomes in such patients. A study by Escalard et al. including 10 patients showed an in-hospital mortality rate of 60% [15]. A recent multicentre study by Cagnazzo et al. which included 93 COVID (+) patients showed a 30-day mortality of 29% [16]. A study by Pop et al. involving 13 COVID (+) patients reported mortality of 15.3% and a high incidence of in-hospital thrombotic complications in this group [17].

On the other hand, some studies have reported similar outcomes of COVID (+) and COVID (-) patients. A prospective international study by al Kasab et al. compared 13 COVID (+) MT-treated patients to a group of 445 COVID (-) MT-treated patients. This revealed that patients with a SARS-CoV2 infection had a higher NIHSS score at admission, but did not differ in respect to in-hospital mortality, number of days of hospitalisation, or functional outcome measured with mRS at discharge. At the same time, COVID (+) patients were significantly younger than COVID (-) ones, which may have influenced the results [18].

In our study, the MT-treated AIS patients with a SARS-CoV2 infection also presented with similar outcomes to patients without COVID-19 (including mortality 6.7% vs. 12.6%).

We speculate that this may be due to several reasons.

Firstly, there were no clinical differences at admission parameters between our COVID (+) and COVID (-) MT-treated AIS patients. There was a similar age distribution, gender ratio, and number of cardiovascular risk factors. Moreover, there were no significant differences in stroke volume (as counted by perfusion CT analysis with RAPID software). Secondly, there was no statistically significant difference between groups when it came to the time from stroke onset to arrival at the CSC. The difference between groups concerning time from arrival at the CSC to groin puncture was statistically significant, but

 Table 1. Individual characteristics of COVID-19-associated MT patients treated with MT in CDC between March 2020 and May 2021

Outcome	NIHSS = 17 mRS = 5	NIHSS = 16 mRS = 5	NIHSS = 2 mRS = 1	NIHSS = 2 mRS = 1	Deceased	NIHSS = 6 mRS = 2	NIHSS = 16 mRS = 5	NIHSS = 22 mRS = 5
Complica- tions	Haemorrhagic transformation Brain oedema Pneumonia Splenic haematoma	Deep vein thrombosis	1	Deep vein thrombosis	Haemorrhagic transformation Subarachnoid haemorrhage	RICA dissection Pneumonia	Clostridium difficile infection	Haemorrhagic transformation Pneumonia
Days of hospita- lisation	20	30	10	15	7	88	82	21
Treatment of COVID-19	Passive oxygen therapy dexamethasone LMWH	ГММН	ГММН	ГММН	Passive oxygen therapy	Passive oxygen therapy Dexamethasone LMWH	Passive oxygen therapy LMWH	Passive oxygen therapy Dexamethasone LMWH
COVID-19 clinical and radiological symptoms	Sore throat Fever Cough Desaturation Lung involvement (HRCT) = 14.21%	— Chest X-ray severity score = 15	Lung involvement (HRCT) = 9.24%	Cough Fever Chest X-ray severity score = 7	Cough desaturation Chest X-ray severity score = 8	Desaturation Chest X-ray severity score = 4	Desaturation Lung involvement (HRCT) = 1.82%	Desaturation Chest X-ray severity score = 10
달	0	0	m	m	m	m	m	m
Perfusion CT parameters (as calculated by RAPID software)	CBF < 30% = 62 mL Tmax > 6 s = 215 mL Mismatch volume = 153 mL	I	CBF < 30% = 20 mL Tmax > 6 s = 61 mL Mismatch volume = 41 mL	I	CBF < 30% = 34 mL Tmax > 6 s = 151 mL Mismatch volume = 117 mL	I	I	CBF < 30% = 7 mL Tmax > 6 s = 95 mL Mismatch volume = 88 mL
Intra- venous throm- bolysis (0 = no, 1 = yes)	0	0	-	-	-	-	-	0
LAO locali- sation	M1-LMCA	RICA	M1-RMCA	LICA	M1-RMCA	M1-RMCA	LACA +	M1-LMCA
NIHSS at admis- sion to CSC	16	15	16	7	20	51	21	21
Time from stroke onset to arrival (mins)	490	174	518	0	102	300	250	729
Comorbidities	Arterial hypertension Aortic aneurysm Atrial fibrillation Peripheral atherosclerosis	Metastatic breast cancer Arterial hypertension Atrial fibrillation Peripheral atherosclerosis Dyslipidemia	Arterial hypertension Dyslipidemia Breast cancer	Arterial hypertension Chronic kidney disease Kidney transplant in 2002 GERD Skin melanoma in the past	Arterial hypertension History of stroke Hypothyroidism Dementia	Arterial hypertension Peripheral atherosclerosis Diabetes mellitus Obesity History of smoking Alcohol abuse Gout	Arterial hypertension Atrial fibrillation Peripheral atherosclerosis Dyslipidemia Diabetes mellitus Obesity	Arterial hypertension Atrial fibrillation Dyslipidemia Peripheral atherosclerosis Dementia
Age, sex	66, M	79, F	56, F	49, M	82, F	62, M	83, F	85, F
	-	7	m	4	70	φ	_	∞

Table 1 cont. Individual characteristics of COVID-19-associated MT patients treated with MT in CDC between March 2020 and May 2021

Outcome	NIHSS = 4 mRS = 2	Outcome	NIHSS = 1 mRS = 0	NIHSS = 2 mRS = 2	NIHSS = 12 mRS = 5	NIHSS = 6 mRS = 1	NIHSS = 2 mRS = 1	NIHSS = 5 mRS = 2
Complica- tions	Haemorrhagic transformation Pneumonia	Complications	Haemorrhagic transformation Pneumonia	Humerus fracture	Pneumonia Clostridium difficile infection	UTI Urinary retention	Pneumonia	RICA dissection
Days of hospita- lisation	8	Days of hospita- lisation	36	21	30	32	32	15
Treatment of COVID-19	LMWH	Treatment of COVID-19	Passive oxygen therapy Dexamethasone LMWH	Passive oxygen therapy Dexamethasone LMWH Remdesivir	Passive oxygen therapy Dexamethasone LMWH	Passive oxygen therapy Dexamethasone LMWH Remdesivir	Passive oxygen therapy Dexamethasone LMWH Remdesivir	ГММН
COVID-19 clinical and radiological symptoms	Lung involvement (HRCT) = 2.08%	COVID-19 clinical and radiological symptoms	Desaturation Lung involvement (HRCT) = 44.12%	Desaturation Lung involvement (HRCT) = 19.52%	Desaturation Lung involvement (HRCT) = 49.79%	Desaturation Lung involvement (HRCT) = 0.41%	Dyspnoea Fever Lung involvement (HRCT) = 17.53%	— Lung involvement (HRCT) = 2.28%
TICI	m	DH 1	m	m	m	2b	m	0
Perfusion CT parameters (as calculated by RAPID software)	CBF < 30% = 0 mL Tmax > 6 s = 16 mL Mismatch volume = 16 mL	Perfusion CT parameters	CBF < 30% = 0 mL Tmax > 6 s = 141 mL Mismatch volume = 141 mL	CBF < 30% = 0 mL Tmax > 6 s = 8 mL Mismatch volume = 8 mL	CBF < 30% = 22 mL Tmax > 6 s = 59 mL Mismatch volume = 37 mL	CBF < 30% = 0 mL Tmax > 6 s = 36 mL Mismatch volume = 36 mL	CBF < 30% = 5 mL Tmax > 6s = 85 mL Mismatch volume = 80 mL	CBF < 30% = 0 mL Tmax > 6 s = 32 mL Mismatch volume = 32 mL
Intravenous thrombolysis (0 = no, 1 = yes)	0	Intravenous thrombolysis	-	0	-	0	0	0
LAO locali- sation	M2-LMCA	LAO	M2-LMCA	V1-RVA	ПСА	M1-LMCA	LICA	RICA
NIHSS at admis- sion to CSC	4	NIHSS at admission	17	_	20	17	∞	5
Time from stroke onset to arrival (mins)	276	Time from stroke onset to arrival (mins)	265	485	282	288	296	154
Comorbidities	Arterial hypertension Atrial fibrillation Dyslipidemia Hypothyroidism Thrombocytopenia	Comorbidities	Arterial hypertension Chronic heart failure Atrial fibrillation Prostate hypertrophy Peripheral atherosclerosis	Arterial hypertension Atrial fibrillation Peripheral atherosclerosis Dyslipidemia Diabetes mellitus Double mastectomy (2010)	Arterial hypertension Coronary artery disease Peripheral atherosclerosis History of TIA Dyslipidemia Diabetes mellitus	Arterial hypertension Diabetes mellitus Coronary artery disease Peripheral atherosclerosis Biological heart valve	Peripheral atherosclerosis History of smoking	Peripheral atherosclerosis Bladder cancer Kidney cancer
Age, sex	72, F	Age, sex	78, M	70, F	70, M	68, M	55, M	65, F
	Q		10	=	12	13	4	15

Table 2. Comparison of COVID (+) and COVID (-) patients with AIS treated with MT

	COVID (+)	COVID (-)	P-value
Demographics	N = 15*	N = 167*	
Age (years)	70 (IQR = 17)	70 (IQR = 17)	p = 0.965
Female sex (%)	8 (53.3%)	83 (49.7%)	p = 1.000
Cardiovascular risk factors	N = 15*	N = 167*	
Arterial hypertension (%)	13 (86.7%)	115 (68.9%)	p = 0.237
Coronary artery disease (%)	2 (13.3%)	38 (22.8%)	p = 0.528
Artificial heart valve (%)	0 (0%)	4 (2.4%)	p = 1.000
Atrial fibrillation (%)	7 (46.7%)	69 (41.3%)	p = 0.787
Peripheral artery atherosclerosis (%)	11 (73.3%)	129 (77.2%)	p = 0.751
History of stroke/TIA (%)	2 (13.3%)	16 (9.6%)	p = 0.647
Dyslipidemia (%)	7 (46.7%)	56 (33.5%)	p = 0.396
Diabetes mellitus (%)	5 (33.3%)	34 (20.4%)	p = 0.320
Obesity (%)	2 (13.3%)	14 (8.4%)	p = 0.626
History of smoking (%)	2 (13.3%)	39 (23.4%)	p = 0.526
Chronic kidney disease (%)	1 (6.7%)	15 (9%)	p = 1.000
Total sum of risk factors	3.5 (SD = 1.6)	3.2 (SD = 1.5)	p = 0.575
CT perfusion parameters	N = 11	N = 138	
CBF < 30% [mL]	13.6 (SD = 19.8)	21.0 (SD = 32.9)	p = 0.560
Tmax > 6 s [mL]	81.7 (SD = 64.4)	121.1 (SD = 82.6)	p = 0.096
Mismatch volume [mL]	68.1 (SD = 50.8)	100.0 (SD = 71.5)	p = 0.117
Disease course	N = 15*	N = 167*	
Time from stroke onset to admission (min)	307.3 (SD = 183.7)	227.3 (SD = 115.7) N = 166	p = 0.062
Time from admission to groin puncture	104.27 (SD = 51.47)	97.63 (SD = 156.94)	p = 0.044
NIHSS score at admission	13.3 (SD = 6.6)	15.5 (SD = 8)	p = 0.505
Intravenous thrombolysis (%)	7 (46.7%)	105 (62.9%)	p = 0.270
Full reperfusion (TICI 2b-3) (%)	12 (80%)	148 (88.6%)	p = 0.398
NIHSS at discharge	8.1 (SD = 7.1) N = 14	8.8 (SD = 9.6) N = 145	p = 0.778
mRS at discharge	2.9 (SD = 2)	3.1 (SD = 2.1)	p = 0.817
In-hospital mortality (%)	1 (6.7%)	21 (12.6%)	p = 0.699
Days of hospitalisation	23.7 SD = 11.9)	10.5 (SD = 6.9)	p < 0.001
Laboratory tests results			
Fibrinogen [g/L]	4.07 (SD = 1.88) N = 2	2.87 (SD = 1.09) N = 146	Analysis impossible, sample too small
D-dimer [mg/L]	10.1 (SD = 12.36) N = 14	7.46 (SD = 9.56) N = 16	p = 0.580
Ldh [u/L]	330.92 (SD = 158.58) N = 12	224.62 (SD = 55.69) N = 13	p = 0.015
Lymphocyte count [1 x 10 ³ /uL]	1.09 (SD = 0.50) N = 14	1.60 (SD = 0.64) N = 60	p = 0.003
CRP [mg/L]	39.77 (SD=38.02) N = 15	17.80 (SD = 23.25) N = 162	p = 0.004
unless specified atherwise			

*unless specified otherwise

small. This is probably due to the standardised pathway of care that was implemented for both groups of patients during the pandemic, including a separate part of the Emergency Department and CT laboratory, as well as transport pathways

for COVID (+) patients. Thirdly, after the procedure both groups of patients were treated in highly specialised wards (the Stroke Unit or the Neurology/COVID-19 ward) with specialists trained in stroke care present in both of them. What

is more, good outcomes of our patients may also be a result of their relatively mild COVID-19 course. None of our patients required intensive care or mechanical ventilation. In 2020 and 2021 (up to the time of writing), there were seven disqualifications of COVID (+) patients from mechanical thrombectomy in our centre, and none of the seven was due to severe general condition caused by COVID-19; they were all based on the neurological criteria. Four patients were disqualified due to recanalisation of the artery after intravenous thrombolysis, two patients due to predominance of irreversible ischaemic changes in neuroimaging, and one patient due to haemorrhagic transformation of the stroke.

Our study has some limitations. Firstly, it was a retrospective analysis and the study group was relatively small. Secondly, the patients had a mild-to-moderate COVID-19 course which might also have an important impact on their outcomes. Thirdly, the small group of patients with COVID-19 treated with MT did not allow for multivariable analysis.

Clinical implications / future directions

Our research suggests that in patients with MT-treated AIS associated with COVID-19 who do not require intensive care, the outcome may be similar to that in MT-treated AIS without concomitant SARS-CoV2 infection. Not only the patients' clinical profiles, but also efficient organisation and the implementation of standardised pathways of care, seem to play important roles in the final result of the treatment.

The outcomes of COVID-19-associated AIS patients treated with MT should be reported in larger, and preferably prospective and multicentre, studies.

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Conflicts of interest: None.

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