Recanalization and Mortality Rates of Thrombectomy With Stent-Retrievers in Octogenarian Patients with Acute Ischemic Stroke

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Abstract

Background Our objective was to evaluate the effect of treatment with stent-retrievers in octogenarians suffering an acute ischemic stroke.

Methods A total of 150 consecutive patients with acute stroke who were treated with stent-retrievers between April 2010 and June 2012 were retrospectively reviewed. Patients were divided into those <80 years old ($n = 116$) and those ≥ 80 ($n = 34$). Baseline characteristics, procedure data, and endpoints (postprocedural NIHSS, death, and mRS at 3 months) were compared.

Results High blood pressure, atrial fibrillation, and anticoagulation were more frequent in octogenarians ($p = 0.01$, 0.003 , and 0.04 respectively). There were no differences between both groups regarding previous intravenous thrombolysis (32.4 vs. 48.3 %, $p = 0.1$), preprocedural NIHSS (18.1 vs. 16.8 , $p = 0.3$), procedure time (74.5 (40–114) min vs. 63 (38–92) min, $p = 0.2$), revascularization time (380.5 (298–526.3) min vs. 350 (296.3–452.8),

$p = 0.3$), $\text{TICI} \geq 2\text{B}$ (88.2 vs. 93.9 %, $p = 0.1$), and symptomatic haemorrhage (5.9 vs. 2.6 %, $p = 0.3$). Discharge NIHSS was higher in octogenarians (9.7 vs. 6.5 , $p = 0.03$). Death and 3-month mRS ≥ 3 were more frequent in octogenarians (35.3 vs. 17.2 %, $p = 0.02$ and 73.5 vs. 37.1 %, $p = 0.02$). ICA-involvement and prolonged revascularization involved higher mortality (66.7 vs. 27.6 %, $p = 0.03$) and worse mRS (50 vs. 24.4 %, $p = 0.06$) in octogenarians.

Conclusions In our series, treatment with stent-retrievers in octogenarians with acute ischemic stroke achieved good rates of recanalization but with a high mortality rate. ICA involvement and revascularization times beyond 6 hours associated to a worse prognosis. These data might be of value in the design of prospective studies evaluating the clinical efficacy of the endovascular treatments in octogenarians.

Keywords Neurointerventions · Endovascular treatment · Stroke therapy · Thrombectomy · Brain/neurological/nervous system · Stroke

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Introduction

During the past years, there has been a significant increase in the proportion of acute ischemic stroke patients receiving revascularization by endovascular treatment, with patients aged ≥ 80 years having the lowest rate of utilization [1]. This tendency might be partly explained by the results of previous studies, which show that the mortality rate after different treatments (intravenous thrombolysis, intra-arterial thrombolysis, mechanical thrombectomy with classic retrievers) is higher in octogenarians than in younger patients, conveying increased age a higher rate of

stroke-related death [2–4]. In the past years, stent-retrievers seem to have opened a new window in the field of mechanical thrombectomy, achieving better angiographic and clinical outcomes than classic retrievers [5, 6], but their effect and security in the older patients have scarcely been reported [7]. We present the results of a series of octogenarians patients who were treated with stent-retrievers, compare them with a control group, and discuss the topic of endovascular treatment of acute stroke in octogenarians.

Patients and Methods

General Design of the Study

All patients with acute stroke that were treated with mechanical thrombectomy using stent retrievers between April 2010 and June 2012 were retrospectively reviewed from our centre's stroke database. For the purpose of this study, patients were divided into those <80 and those ≥80 years old. Baseline characteristics (age, high blood pressure, diabetes mellitus, dyslipemia, atrial fibrillation, smoking habit, anticoagulant treatment), stroke parameters (stroke subtype, occluded vessel, previous intravenous thrombolysis, preprocedural National Institute of Health Stroke Scale (NIHSS), procedure and revascularization times, and outcome (NIHSS at discharge, modified Rankin Scale at 3 months, and death) were subsequently compared.

Stroke subtype was established according to the aetiology into atherothrombotic, cardioembolic, arterial dissection, or undetermined (when no aetiology for the stroke could be found or when two or more possible etiologists were found). Location of the occluded vessel was established by catheter angiography and divided into extracranial internal carotid (ECA), intracranial internal carotid (ICA), middle cerebral artery (MCA), vertebrobasilar (VB), or tandem occlusion (TO). Procedural time was defined as the time between the groin puncture and angiographic revascularization of the vessel correspondent to $\text{TICI} \geq 2\text{B}$. Revascularization time was the time between symptom onset and an angiographic revascularization $\text{TICI} \geq 2\text{B}$.

End Points

The end point of the study was to determine whether there were differences in the clinical outcome between both groups of patients. Clinical outcome was defined by postprocedural NIHSS, death, and modified Rankin scale 3 months postprocedure. Patients were followed up by neurologists in external consultation 3 months after discharge. In those cases which in-person follow-up was not possible (patient refusal, great disability), consultation was made by phone.

Patient Transferral

Our hospital is the only endovascular stroke centre in the region, covering an area of 11,313 square kilometres and a population of approximately 1,470,000 people. It is situated in south of the region, and the patients to be considered for mechanical treatment who do not come directly to our emergency room are transferred to our centre either from the mobile emergency units that operate through the region or from the emergency rooms of the other six hospitals in the area. In one of these centres a neurologist on call evaluates the stroke patient, and in the other five centres and mobile emergency units the initial neurologic evaluation is performed by the emergency physicians. Each case considered subsidiary of mechanical thrombectomy is communicated by phone to the staff neurologist and neurointerventionist on call at our centre, and a decision to transfer the patient or not is made. The same vehicles then transfer those selected patients that had been initially attended by mobile units to our centre, and the nearest ambulance transfers those who have been attended in the emergency units of other hospitals.

Stroke Protocol and Selection Criteria

Once in our centre, patients are selected for mechanical thrombectomy after an imaging and clinical protocol that is performed in all stroke patients who are considered candidates for intravenous thrombolysis and/or mechanical thrombectomy and includes urgent nonenhanced CT, CT angiography, and CT perfusion. Candidates for intravenous thrombolysis are selected according to the National Institute of Neurological Disorders [8] and Stroke and the Third European Cooperative Acute Stroke Study criteria [9, 10]. Indications for mechanical thrombectomy include 1) rescue therapy, performed in those patients in whom intravenous thrombolysis is not accompanied by a clinical response (improvement in NIHSS score ≥ 4) in the first 60 minutes after treatment, and 2) direct thrombectomy, which is performed in those patients in whom intravenous thrombolysis is contraindicated and in those with large vessel stroke that arrive at our hospital between 4.5 and 8 hours after symptom onset [11–15].

Exclusion criteria for mechanical thrombectomy included: presence of cerebral haemorrhage, an ASPECTS score of less than 7 in anterior circulation strokes or evidence of established large cerebellar and brain stem infarction in posterior circulation strokes in the nonenhanced CT, absence of large vessel vascular occlusion in the CT angiography, or any medical conditions that preclude a general anaesthesia. For those strokes beyond 6 hours since symptom onset, a CT perfusion mismatch greater than 50 % was also requested.

Procedure

Before angiography and mechanical thrombectomy, all patients or relatives gave informed consent. All of the procedures were performed under general anaesthesia. Angiography was performed via a femoral approach using a 9F sheath and a diagnostic catheter, generally a JB 4F (Cordis, Miami Lakes, FL). Once the location of the clot was identified, the diagnostic catheter was removed and an 8F balloon guide catheter (Concentric Medical, Mountain View, CA) was advanced and placed in the internal carotid artery (anterior circulation strokes) or in the vertebral artery (posterior circulation strokes). For those cases in which the placement of an 8F catheter was not possible due to the diameter of the vertebral artery, a Neuron 6F (Penumbra Inc., Alameda, CA) was placed instead. A Rebar-18 microcatheter (ev3 Neurovascular, Irvine, CA) with a 0.014-inch Traxcess guidewire (MicroVention, Tustin, CA) was then advanced distally to the clot. The microwire was then removed and a stent-retriever Solitaire AB 4 or 6 mm, FR 4 or 6 mm (ev3 Neurovascular), Trevo 4 mm, Trevo Pro 4 mm (Concentric Medical), or Capture 3 or 4 mm (MindFrame, Irvine, CA) was used to engage and snare the clot. Once the clot was captured, the balloon guide catheter was inflated to temporally arrest forward flow while the clot was being withdrawn. The clot was first pulled into the catheter guide and then completely out of the body while aspirating with a 50-mL syringe. The balloon was then deflated, and the flow was restored. Recanalization was assessed on the control angiogram following TICI classification [16].

Postprocedure Management

Once the procedure was finished, the patients were admitted to the intensive care unit for 24 hours and then to the stroke unit. Antiplatelet or anticoagulation therapy was initiated after the initial postprocedural scan had ruled out symptomatic haemorrhage. The choice of therapy depended on the suspected aetiology of the stroke. Initial anticoagulation with intravenous heparin and a posterior switch to acenocoumarol was used for inferred cardioembolism in the setting of atrial fibrillation, whereas antiplatelet therapy (aspirin, 200 mg/day, or clopidogrel, 75 mg/day) was preferred in the setting of atherothrombotic aetiologies. Control of blood pressure, fever, hyperglycaemia, aspiration risk, deep venous thrombosis prophylaxis, and all other essential aspects in acute stroke management were performed following current stroke guidelines [17].

Statistical Analyses

Continuous variables were tested for normality by the Kolmogorov–Smirnov test. Continuous variables are presented

as a mean $\pm$ standard deviation (SD) or median (25th and 75th percentiles), as appropriate, and categorical variables as a percentage. Univariate analyses were performed, including the Student (or Mann–Whitney *U* test if appropriate) for the continuous variables and the Chi-square test for the categorical variables. We explored the influence of different variables on prognosis, in particular hypertension, internal carotid involvement, revascularization time beyond 6 hours, oral anticoagulation, and presence of atrial fibrillation. For determining the differences between the octogenarians group and those younger than 80 years, all variables with a $p < 0.1$ on the univariate level were included into a multiple binominal regression analysis (p to enter = 0.05, p to leave = 0.1). Logistic regression models were used for dichotomous outcomes (e.g., mRS ≥ 3 and death). A value of $p < 0.05$ was considered significant. Statistical analyses were performed using a statistical software package (Statistical Package for the Social Sciences, Version 17.0; SPSS, Chicago, IL).

Results

Baseline Characteristics

In Table 1, we show the clinical characteristics of the present cohort, comparing between octogenarians and younger patients. Hypertension, atrial fibrillation, and oral anticoagulation were more frequent in the octogenarian patients than in those patients younger than 80 years (88.2 vs. 65.5 %, $p = 0.01$; 73.5 vs. 44.8 %, $p = 0.003$; and 23.5 vs. 10.3 %, $p = 0.04$, respectively). Smoking habit was more frequent in the younger patients (32.8 vs. 8.8 %, $p = 0.005$). Diabetes mellitus, coronary disease, and dyslipemia showed no statistical differences between both groups. No differences were either detected regarding stroke subtype ($p = 0.8$), location of the occluded vessel ($p = 0.7$), previous intravenous thrombolysis (32.4 vs. 48.3 %, $p = 0.1$), and preprocedural NIHSS (18.1 vs. 16.8 %, $p = 0.3$)

Procedure Data

In Table 2, procedure and clinical outcome data are shown. There were no differences in the procedure times between both groups (63 (38–92) minutes in those younger than 80 years and 74.5 (40–114) minutes in the octogenarian patients, $p = 0.2$). Revascularization times also showed no difference between both groups (350 (296.3–452.8) minutes and 380.5 (298–526.3) minutes, respectively, $p = 0.3$). Time from symptom onset to groin puncture was 280 (235–365) minutes in patients younger than 80 years and 298 (247.5–421.3) minutes in octogenarians ($p = 0.2$). Postprocedure TICI score $\geq 2B$ was reached in 93.9 % of the patients younger than 80, and 88.2 % of the octogenarians,

Table 1 Baseline characteristics of octogenarians and younger patients

	<80 years (n, %)	≥80 years (n, %)	p value
Male sex	66 (56.9)	12 (35.3)	0.03
High blood pressure	76 (65.5)	30 (88.2)	0.01
Diabetes mellitus	33 (28.4)	11 (32.4)	0.7
Coronary disease	14 (12.1)	5 (14.7)	0.7
Atrial fibrillation	52 (44.8)	25 (73.5)	0.003
Dyslipemia	45 (38.8)	16 (47.1)	0.4
Smoking	38 (32.8)	3 (8.8)	0.005
Anticoagulants	12 (10.3)	8 (23.5)	0.04
Occluded vessel	EICA 8 (6.9)	EICA 4 (11.8)	0.7
	IICA 21 (18.1)	IICA 8 (23.5)	
	MCA 55 (47.4)	MCA 13 (38.2)	
	TO 15 (12.9)	TO 3 (8.8)	
	VB 17 (14.7)	VB 6 (17.7)	
Stroke subtype	AT 39 (33.6)	AT 11 (32.4)	0.8
	CE 44 (37.9)	CE 14 (41.2)	
	AD 3 (2.6)	AD 0	
	UN 30 (25.9)	UN 9 (26.5)	
Previous IV thrombolysis	56 (48.3)	11 (32.4)	0.1
Preprocedure NIHSS	16.8	18.1	0.3

EICA extracranial internal carotid artery, *IICA* intracranial internal carotid artery, *MCA* middle cerebral artery, *TO* tandem occlusion, *VB* vertebrobasilar, *ATS* atherothrombotic, *CE* cardioembolic, *AD* arterial dissection, *UN* undetermined, *NIHSS* National Institute of Health Stroke Scale

Table 2 Procedure data and clinical outcome

	<80 years (n, %)	≥80 years (n, %)	p value
NIHSS at discharge	6.5	9.7	0.03
Time of procedure	63 (38–92)	74.5 (40–114)	0.2
Time of revascularization	350 (296.3–452.8)	380.5 (298–526.3)	0.3
Time from symptoms onset to groin puncture	280 (235–365)	298 (247.5–421.3)	0.2
Postprocedure TICI ≥ 2B	109 (93.9)	30 (88.2)	0.1
Symptomatic haemorrhage	3 (2.6)	2 (5.9)	0.3
mRS ≥ 3	44/102 (43.1)	25/29 (86.2)	<0.0001
mRS 3–5	23/102 (22.5)	13/29 (44.8)	0.03
Death	20/150 (17.2)	12/150 (35.3)	0.02
Causes of death	SP 14 (70)	SP8 (66)	0.08
	VR 0	VR 1 (8.3)	
	SH 2 (10)	SH 2 (16.7)	
	SC 4 (20)	SC 1 (8.3)	

NIHSS National Institute of Health Stroke Scale, *mRS* modified Rankin Scale, *TICI* thrombolysis in cerebral infarction

without statistical difference between both groups ($p = 0.1$). The percentage of symptomatic haemorrhage after thrombectomy was similar in both groups (5.9 and 2.6 %, $p = 0.3$). There were no differences in the distribution of any of the stent-retrievers between older and younger patients (Solitaire 4: $p = 0.4$, Solitaire 6: $p = 0.09$, Trevo: $p = 0.4$, Capture: $p = 0.5$).

End Points

Postprocedural NIHSS was statistically higher in the octogenarians group than in younger patients (9.7 and 6.5, $p = 0.03$). Death rate was more frequent in the

octogenarians patients than in the younger group (35.3 vs. 17.2 %, $p = 0.02$). In the octogenarians patients group, deaths were secondary to stroke progression (defined as a worsening of NIHSS ≥ 4–15) in eight cases (66.7 %), symptomatic haemorrhage in two (16.7 %), and systemic complication (pneumonia) and vessel rupture in one case each (8.3 %). In those patients younger than 80, deaths were caused by stroke progression in 14 cases (70 %), systemic complications in 4 (20 %, corresponding to 1 pulmonary thromboembolism, 1 acute renal failure, and 2 sepsis of urinary and pulmonary origin), and 2 symptomatic haemorrhages (10 %). There were no statistically significant differences between both groups ($p = 0.08$).

Table 3 Multivariate analysis for mRS and death

	<i>p</i>	Odds ratio (95 % CI)		<i>p</i>	Odds ratio (95 % CI)
mRS 3–5 AT 3 months			Death		
Male sex	0.9	0.92 (0.4–2.2)	Male sex	0.4	1.45 (0.6–3.5)
High blood pressure	0.01	5.05 (1.4–18.4)	High blood pressure	0.3	1.73 (0.6–4.8)
Atrial fibrillation	0.6	0.8 (0.3–19.3)	Atrial fibrillation	0.3	1.54 (0.6–3.8)
Smoking	0.06	0.31 (0.1–1.1)	Smoking	0.8	1.18 (0.4–3.5)
Oral anticoagulation	0.7	0.82 (0.3–2.7)	Oral anticoagulation	0.3	1.73 (0.6–4.9)

NIHSS National Institute of Health Stroke Scale, mRS modified Rankin Scale, SH symptomatic haemorrhage, SP stroke progression, SC systemic complication, TICI thrombolysis in cerebral infarction, VR vessel rupture

Table 4 Subgroup analysis by occluded vessel and time of revascularization

	<80 years old	≥80 years old	<i>p</i>
Occluded vessel			
ICA (extra or intracranial)	29	12	0.23
Other vessels	87	22	
Carotid occlusion			
mRS≥3	2/22 (9.1)	2/10 (20.0)	0.56
Death	8/29 (27.6)	8/12 (66.7)	0.03
Other vessels			
mRS≥3	21/78 (26.9)	11/19 (57.8)	0.01
Death	12/87 (13.8)	4/22 (18.2)	0.6
Time of revascularization			
<6 hours	56	10	0.21
>6 hours	48	20	
<6 hours			
mRS≥3	13/50 (26.0)	5/9 (55.6)	0.12
Death	9/56 (16.1)	2/11 (18.2)	1.00
>6 hours			
mRS≥3	10/41 (24.4)	8/16 (50.0)	0.06
Death	9/48 (18.6)	6/19 (31.6)	0.25

ICA internal carotid artery, mRS modified Rankin Scale

A modified Rankin Scale at 3 months ≥ 3 was significantly more frequent in the octogenarians group than in those younger than 80 years of age (86.2 vs. 43.1 %, $p < 0.0001$). The effect of thrombectomy on survivors also was studied by performing a new analysis in which those patients with modified Rankin Scale = 6 (death) were excluded. In those patients with a 3-month modified Rankin Scale = 3–5, a statistical difference between octogenarians and younger patients also was found ($p = 0.03$).

All variables with a $p < 0.1$ on the univariate level (high blood pressure, atrial fibrillation, oral anticoagulation, and smoking) were included into a multiple logistic regression analysis (Table 3). A previous history of hypertension independently associated to a modified Rankin Scale 3–5 at 3 months ($p = 0.01$).

As shown in Table 4, no differences in the distribution of ICA/other vessels were found between both groups ($p = 0.23$). However, ICA occlusion was associated with higher mortality in octogenarians than in younger patients ($p = 0.03$), without differences in the 3-month mRS ($p = 0.56$). Regarding the time of revascularization, no differences in the distribution below or beyond 6 hours were found between both groups ($p = 0.21$). A trend to a worse mRS at 3 months was observed in those octogenarians treated beyond 6 hours, but it did not reach statistical significance ($p = 0.06$). There was no difference in mortality ($p = 0.25$).

Discussion

The purpose of our study was to test the effect of mechanical thrombectomy with stent-retrievers in octogenarians with acute ischemic stroke. Our results indicate that the use of these devices achieve good rates of recanalization in elderly patients (88.2 %) but still with a remarkably high mortality rate (35.3 %) and poor clinical prognosis (NIHSS at discharge, 3 months mRS) compared with younger patients.

Previous studies have already shown that poor outcomes after ischemic stroke are more frequent in octogenarians than in younger patients and that age ≥ 80 years is a predictor of higher mortality and poorer functional outcome compared with younger patients after intravenous thrombolysis [2]. In the field of the endovascular therapy prior to stent-retrievers (Table 5), Kim et al. [3] obtained a recanalization rate of 68 % by using intraarterial thrombolysis with urokinase or tPA, with a mortality of 43 % and a tendency to higher mortality rates and lower functional outcomes in the octogenarians group compared with younger patients. Loh et al. [4] reported recanalization rates of 81 % and a mortality of 48 % in acute stroke octogenarians treated with the Merci thrombectomy device. Mono et al. [18] treated 53 patients with intra-arterial thrombolytics plus optional mechanical therapy with aspiration, clot retrieval, angioplasty, and/or stenting, with

Table 5 Endovascular treatment of acute stroke in octogenarians. Most relevant previous studies and current series

Type of endovascular therapy	Number of patients ≥ 80	TICI $\geq 2B$	Symptomatic Hemorrhage	mRS ≥ 3	Mortality
UK, rTPA (3)	33	68 %	7 %	73 %	43 %
UK, rTPA, AS- AP- ST (18)	53	65 %	6 %	72 %	40 %
Classic retrievers: Merci (4)	31	81 %	11 %	79 %	48 %
Classic retrievers: Merci, Penumbra (19)	34	71 %	4 %	97 %	58 %
Stent-retrievers: Solitaire FR (7)	50	74 %	14 %	89 %	44 %
Stent-retrievers: Solitaire FR, Trevo, Capture (our center)	34	88 %	5 %	73 %	35 %

TICI thrombolysis in cerebral infarction; *mRS* modified Rankin Scale; *UK* urokinase; *rTPA* recombinant tissue plasminogen activator *MR* mechanical recanalization; *AS* clot aspiration; *AP* angioplasty; *ST* stenting

similar results, and Chandra et al. [19] reviewed 34 patients treated with the Merci retriever or the Penumbra aspiration device, finding a mortality of 58 % and mRS ≥ 3 at 3 months of 97 %. Previous studies with stent retrievers in patients older than 80 years include Gratz et al. [7], who studied 50 octogenarian patients with anterior circulation strokes treated exclusively with Solitaire FR, with a recanalization rate of 74 %, mRS ≥ 3 at 3 months of 89 %, and mortality of 44 %. Other articles analyzed the general impact of age in the clinical response to mechanical thrombectomy [20–22], but these papers did not focus on the subgroup of octogenarians and included other mechanical therapies different to stent-retrievers.

Our series differ from Gratz's in that both patients with anterior and posterior circulation strokes have been included and up to four different stent-retrievers (not only Solitaire FR) could be chosen for treatment by the neuro-interventionist in charge. However, the similar results obtained seem to confirm that, despite the high rates of recanalization, thrombectomy with stent retrievers in octogenarians are still associated with high mortality and morbidity rates. This bad clinical evolution is probably due to the vascular fragility of these patients, which is favoured by age and the higher incidence of related risk factors, but some modifiable factors also might be influencing.

In this sense, our results suggest that three main factors may influence the worst prognosis observed in the group of octogenarians: (1) higher incidence of risk factors, such as high blood pressure ($p = 0.01$), atrial fibrillation ($p = 0.003$), or anticoagulants intake ($p = 0.04$), (2) the location of the occluded vessel (ICA occlusion associate to higher mortality in octogenarians than in younger patients ($p = 0.034$), and (3) the revascularization time, which shows an association trend with worst 3-month mRS in those octogenarians treated beyond 6 hours (Table 3). This seems to indicate that these three conditions (associated cardiovascular risk factors, ICA involvement, and revascularization time > 6 hours) are especially harmful for the elderly patients and could be taken into account to adapt selection

criteria and procedural and postprocedural management approaches and avoid futile recanalization in this group of age.

The main drawbacks of our study are related with the prolonged revascularization times, which are due to the big area/population covered by our centre and an inefficient patient transfer system, which is currently being improved with measures, such as a bigger mobile unit's fleet or a 24-hour stroke ambulance located in each of the six big main hospitals of the region. These prolonged times are observed in both arms of the study (octogenarians and younger patients, $p = 0.4$), which makes the differences found in mortality and clinical outcome still of value.

Also of interest, our procedure times seem to be slightly beyond what is considered optimal. At our centre, stroke thrombectomies are performed under general anaesthesia, a situation that allows us to work in a more controlled situation but may carry a longer preparation of the patient. Our current results seem to indicate that sedation might be a better option to save critical time in the elderly patients. Prospective studies are needed to test this and the previous aspects suggested by our results.

Conclusions

In our series, treatment with stent-retrievers in octogenarians with acute ischemic stroke achieved good rates of recanalization but worse clinical outcome than younger patients. A higher incidence of risk factors, ICA involvement, and revascularization times beyond 6 hours were associated to a worse prognosis. These data might be of value in the design of prospective studies evaluating the clinical efficacy of the endovascular treatments in octogenarians.

Conflict of interest All authors declare that they have no conflict of interest.

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