

论著·临床研究

# 体外膜肺氧合在院内成人心源性休克和心脏骤停中的应用研究

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**[摘要]** **目的**·评估院内心源性休克和心脏骤停患者使用静脉动脉体外膜肺氧合 (veno-arterial extracorporeal membrane oxygenation, VA-ECMO) 救治对其病死率的影响。**方法**·选择2017年9月—2022年3月期间在上海交通大学医学院苏州九龙医院行VA-ECMO救治的19例心源性休克和心脏骤停患者。根据VA-ECMO实施前是否发生心脏骤停, 将其分为体外心肺复苏组 (extracorporeal cardiopulmonary resuscitation, ECPR) 组 ( $n=9$ ) 和常规VA-ECMO (VA-ECMO for cardiogenic shock, E-CS) 组 ( $n=10$ )。收集2组患者的一般人口学资料、临床资料、序贯器官衰竭评估 (Sequential Organ Failure Assessment, SOFA) 评分、术后并发症及预后指标资料。采用单因素、多因素Cox比例风险回归模型评估各协变量与住院病死率之间的关联性。**结果**·纳入的患者中男性15例 (78.9%), 平均年龄为46.5 (34.5, 61.6) 岁; 术后并发症的发生率依次为: 出血47.4%、急性肾损伤36.8%、感染31.6%、肢体缺血15.8%和脑血管意外5.3%; VA-ECMO持续时间为4.0 (2.0, 6.8) d, ICU监护时间为11.5 (5.8, 26.2) d; ECMO撤机成功率为63.2%, 住院病死率为63.2%。单因素Cox比例风险回归的结果显示, 术前发生急性肾损伤、术后感染和肢体缺血与患者的住院病死率相关 (均 $P<0.05$ )。多因素Cox比例风险回归的结果显示, 术前发生急性肾损伤、术后感染和肢体缺血亦是患者住院病死率的独立危险因素 (均 $P<0.05$ )。**结论**·对于行VA-ECMO救治的心源性休克和心脏骤停患者, 术前发生急性肾损伤、术后感染和肢体缺血与较高的住院病死率独立相关。

**[关键词]** 静脉动脉体外膜肺氧合; 体外心肺复苏; 心源性休克; 心脏骤停; 住院病死率

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## Application of extracorporeal membrane oxygenation to adults with cardiogenic shock and cardiac arrest in hospital

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**[Abstract]** **Objective**·To assess the effect of veno-arterial extracorporeal membrane oxygenation (VA-ECMO) treatment on the mortality rate of patients suffering from cardiogenic shock and cardiac arrest in hospital. **Methods**·A total of 19 patients with cardiogenic shock or cardiac arrest who were treated with VA-ECMO treatment in Suzhou Kowloon Hospital, Shanghai Jiao Tong University School of Medicine from September 2017 to March 2022 were included in the retrospective study. Patients were divided into extracorporeal cardiopulmonary resuscitation (ECPR) group ( $n=9$ ) and VA-ECMO for cardiogenic shock (E-CS) group ( $n=10$ ) according to whether cardiac arrest had occurred. The general demographic data, clinical data, Sequential Organ Failure Assessment (SOFA) scores, postoperative complications and prognostic indicators of the two groups of patients were collected. Univariate and multivariate Cox proportional hazard regression analyses were used to evaluate the correlation between each covariate and hospital mortality. **Results**·Among the included patients, there were 15 males (78.9%), with an average age of 46.5 (34.5, 61.6) years. The incidence of postoperative complications was as follows: bleeding (47.4%), AKI (36.8%), infection (31.6%), limb ischemia (15.8%) and cerebrovascular accident (5.3%). The duration of VA-ECMO was 4.0 (2.0, 6.8) days, and the intensive care duration was 11.5 (5.8, 26.2) days; the ECMO withdrawal success rate was 63.2%, and the hospital mortality was 63.2%. The results of univariate Cox proportional hazard regression analysis showed that AKI (prior to VA-ECMO initiation), postoperative complications of infection

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and limb ischemia were correlated with the hospital mortality of patients (all  $P < 0.05$ ). The results of multivariate Cox proportional hazard regression analysis showed that AKI (prior to VA-ECMO initiation), postoperative complications of infection and limb ischemia were also independent risk factors for the hospital mortality of patients (all  $P < 0.05$ ). **Conclusion** For patients with cardiogenic shock and cardiac arrest treated with VA-ECMO, AKI (prior to VA-ECMO initiation), postoperative infection and limb ischemia are independently associated with higher hospital mortality.

**[Key words]** veno-arterial extracorporeal membrane oxygenation (VA-ECMO); extracorporeal cardiopulmonary resuscitation (ECPR); cardiogenic shock (CS); cardiac arrest (CA); hospital mortality

研究<sup>[1-2]</sup>显示,心源性休克(cardiogenic shock, CS)和心脏骤停(cardiac arrest, CA)患者均有着极高的死亡率。对于该类急性心肺功能严重衰竭的患者,当常规药物治疗失败时,静脉动脉体外膜肺氧合(veno-arterial extracorporeal membrane oxygenation, VA-ECMO)则是挽救其生命的有效治疗手段。临床上,在心血管功能极度受损的情况下,VA-ECMO可为患者的全身组织、器官提供有效的血液动力学支持,即通过膜氧合器将氧合后的血液输送到全身,以维持机体重要器官和周围组织的血液灌注,进而促进心肌细胞的修复、再生以及心脏功能的恢复。但需要注意的是,VA-ECMO的置管过程是一种高风险、较复杂、创伤大的手术操作,术中及术后患者可能会产生多种危及生命的并发症<sup>[3]</sup>。本研究对采用VA-ECMO抢救的CS和CA患者的一般人口学资料、临床资料、序贯器官衰竭评估(Sequential Organ Failure Assessment, SOFA)评分、术后并发症及预后指标进行回顾性分析,以期为后续此类危重症患者的临床救治提供可参考的诊治经验。

## 1 对象与方法

### 1.1 研究对象及分组

选择2017年9月—2022年3月于上海交通大学医学院苏州九龙医院因CS和CA接受了VA-ECMO救治的患者为研究对象。纳入标准:①年龄 $\geq 18$ 岁。②院内发生CS或CA。排除标准:①处于慢性基础疾病终末期或肿瘤晚期。②医疗记录不充分。

最终,本研究共纳入患者19例。根据VA-ECMO实施前是否发生心脏骤停,将其分为体外心肺复苏组(extracorporeal cardiopulmonary resuscitation, ECPR)组( $n=9$ )和常规VA-ECMO(VA-ECMO for cardiogenic shock, E-CS)组( $n=10$ )。

### 1.2 资料收集

收集患者的相关资料,具体如下:①一般人口学资料,包括年龄、性别、体质量指数(body mass index, BMI)。②临床资料,包括既往基础疾病、CS和CA病因、是否联合主动脉内球囊反搏(intra-aortic balloon pump, IABP)治疗、ECMO置管时间、从病情恶化到ECMO开始运行时间(from deterioration to ECMO initiation time, D to I time),VA-ECMO治疗前的血乳酸水平、发生急性肾损伤(acute kidney injury, AKI)、行持续肾脏替代治疗(continuous renal replacement therapy, CRRT)、行呼吸机支持,VA-ECMO治疗后的24 h血乳酸清除率(lactate clearance rate, LCR),以及VA-ECMO持续时间、ECMO撤机成功率、ICU监护时间、住院病死率、脱机后并发症死亡例数(deaths due to complications after ECMO withdrawal, DDCEW)等。③SOFA评分。④术后并发症,包括出血、感染、AKI、肢体缺血和脑血管意外。⑤预后指标,包括出院时脑功能表现分级(cerebral performance category, CPC)、生存出院例数及1年生存率。

### 1.3 临床结局

本研究以CS和CA患者的住院病死率为主要结局,以ECMO撤机成功率为次要结局。其中,将患者在无VA-ECMO支持的情况下,平均动脉压大于60 mmHg(1 mmHg=0.133 kPa)且无需进一步的机械支持48 h以上,定义为VA-ECMO撤机成功。

### 1.4 统计学方法

采用SPSS 22.0统计软件分析数据。符合正态分布的定量资料以 $\bar{x} \pm s$ 表示,不符合正态分布的定量资料以 $M(Q_1, Q_3)$ 表示。定性资料以 $n(\%)$ 表示。分别采用单因素、多因素Cox比例风险回归模型,对VA-ECMO救治的CS和CA患者住院病死率的影响因素进行分析。 $P < 0.05$ 表示差异具有统计学意义。

## 2 结果

### 2.1 患者的资料分析

在本研究纳入的19例接受VA-ECMO治疗的患者中,男性15例(78.9%),平均年龄为46.5(34.5,61.6)岁。对2组患者的一般人口学资料、临床资料

及SOFA评分进行分析,结果(表1)所示E-CS组中有2例患者接受了IABP治疗,ECPR组中则有4例,有12例(63.2%)患者成功撤离了ECMO。对患者的术后并发症及预后指标进行分析,结果(表2)所示生存出院者7例,E-CS组和ECPR组的生存率分别为30.0%和44.4%。

表1 入组患者的一般人口学资料、临床资料及SOFA评分分析

Tab 1 Analysis of general demographic data, clinical data and SOFA scores of enrolled patients

Item	Total (n=19)	E-CS group (n=10)	ECPR group (n=9)
Age/year	46.5 (34.5, 61.6)	50.8 (37.2, 63.5)	43.6 (31.6, 59.8)
Male/n(%)	15 (78.9)	8 (80.0)	7 (77.8)
BMI/(kg·m <sup>-2</sup> )	22.3±2.4	22.5±2.8	22.1±1.9
Previous underlying diseases/n(%)			
Diabetes	4 (21.1)	2 (20.0)	2 (22.2)
Hypertension	5 (26.3)	4 (40.0)	1 (11.1)
Hyperlipidemia	2 (10.5)	1 (10.0)	1 (11.1)
Chronic heart failure	3 (15.8)	1 (10.0)	2 (22.2)
Coronary artery disease	6 (31.6)	5 (50.0)	1 (11.1)
Chronic kidney disease	3 (15.8)	2 (20.0)	1 (11.1)
Etiology of CS and CA/n(%)			
Acute myocardial infarction	8 (42.2)	4 (40.0)	4 (44.4)
Acute severe myocarditis	3 (15.8)	1 (10.0)	2 (22.2)
Heart failure	7 (36.8)	4 (40.0)	3 (33.3)
Cardiomyopathy	1 (5.3)	1 (10.0)	0 (0)
Combined IABP treatment/n(%)	6 (31.6)	2 (20.0)	4 (44.4)
ECMO tube placement time/min	33.8 (25.5, 44.3)	38.5 (27.8, 48.2)	31.5 (25.3, 42.9)
D to I time/min	79.5 (45.8, 98.2)	86.5 (51.3, 116.2)	76.7 (43.5, 96.9)
Before ECMO initiation			
Lactic acid level/(mmol·L <sup>-1</sup> )	10.7±4.0	10.2±4.9	11.1±2.8
AKI/n(%)	11 (57.9)	7 (70.0)	2 (22.2)
CRRT/n(%)	6 (31.6)	4 (40.0)	2 (22.2)
Ventilator support/n(%)	16 (84.2)	9 (90.0)	9 (100.0)
24 h LCR after ECMO initiation/%	67.0 (58.2, 76.3)	63.6 (49.7, 74.6)	69.2 (57.5, 83.4)
Duration of VA-ECMO/d	4.0 (2.0, 6.8)	3.9 (2.5, 5.8)	4.5 (2.6, 6.5)
ECMO withdrawal success rate/n(%)	12 (63.2)	7 (70.0)	5 (55.6)
Intensive care duration/d	11.5 (5.8, 26.2)	10.2 (3.8, 24.5)	11.8 (4.1, 28.0)
Hospital mortality/n(%)	12 (63.2)	7 (70.0)	5 (55.6)
DDCEW/n(%)	5 (26.3)	4 (40.0)	1 (11.1)
SOFA scores/score	14.2±3.7	13.8±4.5	14.8±4.5

### 2.2 住院病死率和ECMO撤机成功率的单因素Cox比例风险回归分析

参考相关文献<sup>[4]</sup>以及体外生命支持组织(extracorporeal life support organization, ELSO)注

册的数据<sup>[5]</sup>,选取年龄、BMI、SOFA评分、ECMO置管时间、从病情恶化到ECMO开始运行时间、VA-ECMO治疗前血乳酸水平、VA-ECMO治疗后24 h LCR、是否联合IABP治疗、术前发生AKI、

表2 入组患者的术后并发症及预后指标分析

Tab 2 Analysis of postoperative complications and prognostic indicators of enrolled patients

Item	Total (n=19)	E-CS group (n=10)	ECPR group (n=9)
Postoperative complication/n(%)			
Bleeding	9 (47.4)	4 (40.0)	5 (55.6)
Infection	6 (31.6)	3 (30.0)	3 (33.3)
AKI	7 (36.8)	3 (20.0)	4 (44.4)
Limb ischemia	3 (15.8)	2 (20.0)	1 (11.1)
Cerebrovascular accident	1 (5.3)	1 (10.0)	0 (0)
Prognostic indicator/n(%)			
CPC 1 to 2 grade	10 (52.6)	5 (50.0)	5 (55.6)
Survival discharge	7 (36.8)	3 (30.0)	4 (44.4)
First year survival rate	4 (21.1)	1 (10.0)	3 (33.3)

术后并发症（感染、出血、肢体缺血）和既往基础疾病等 13 项可能影响患者住院病死率的临床指标，经量化后纳入 Cox 比例风险回归模型开展单因素分析，以考察各单一指标对住院病死率（主要结局）的影响。结果（表 3）显示，术前发生 AKI、术后感染和肢体缺血与患者的住院病死率相关（均  $P < 0.05$ ）；而是否联合 IABP 治疗、术后出血的相对危险度在  $\alpha = 0.05$  水平上接近显著性水平，提示该 2 个指标也可能对住院病死率有较大影响。同时，以上述 13 项指标作为协变量，采用单因素 Cox 比例风险回归模型对 ECMO 撤机成功率（次要结局）的影响进行分析，结果（表 3）显示，年龄、联合 IABP 治疗、术前发生 AKI 与 ECMO 撤机成功率相关（均  $P < 0.05$ ）。

表3 住院病死率和 ECMO 撤机成功率的单因素 Cox 比例风险回归分析

Tab 3 Univariate Cox proportional hazard regression analysis of hospital mortality and ECMO withdrawal success rate

Item	B	S.E	Wald	P value	HR (95.0% CI)
Primary outcome					
Age	0.053	0.058	0.833	0.361	1.054 (0.941–1.181)
BMI	-0.001	0.242	0.000	0.998	0.999 (0.621–1.607)
SOFA scores	0.011	0.064	0.027	0.868	1.011 (0.891–1.147)
ECMO tube placement time	0.032	0.028	1.358	0.244	1.033 (0.978–1.091)
D to I time	-0.005	0.012	0.194	0.659	0.995 (0.972–1.108)
Lactic acid level before ECMO initiation	-0.172	0.155	1.232	0.267	0.842 (0.622–1.141)
24 h LCR after ECMO initiation	0.179	3.937	0.191	0.662	0.179 (0.001–401.203)
Combined IABP treatment	-3.749	2.122	3.120	0.077	0.024 (0.000–1.508)
AKI (prior to ECMO initiation)	3.400	1.606	4.484	0.034	29.960 (1.288–697.195)
Postoperative infection	3.612	1.395	6.706	0.010	37.028 (2.406–569.790)
Postoperative bleeding	1.042	1.120	0.867	0.062	2.835 (0.316–25.444)
Postoperative limb ischemia	3.290	1.378	5.706	0.017	6.853 (1.805–399.524)
Previous underlying diseases	1.739	1.952	0.794	0.373	5.693 (0.124–260.970)
Secondary outcome					
Age	-2.027	1.017	3.973	0.047	1.007 (0.973–1.041)
BMI	-0.007	0.140	0.002	0.962	0.993 (0.755–1.308)
SOFA scores	0.067	0.080	0.760	0.401	1.069 (0.915–1.250)
ECMO tube placement time	0.019	0.035	0.287	0.592	1.019 (0.951–1.092)
D to I time	0.001	0.010	0.023	0.880	1.001 (0.982–1.021)
Lactic acid level before ECMO initiation	-0.034	0.101	0.110	0.741	0.967 (0.793–1.179)
24 h LCR after ECMO initiation	-4.779	2.843	2.849	0.091	0.008 (0.000–2.168)
Combined IABP treatment	2.395	0.821	8.510	0.041	1.674 (1.164–4.769)
AKI (prior to ECMO initiation)	-2.154	1.023	4.433	0.036	1.857 (1.105–8.023)
Postoperative infection	0.063	0.734	0.736	0.391	1.877 (0.445–7.910)
Postoperative bleeding	-0.360	0.714	0.241	0.624	0.698 (0.166–2.940)
Postoperative limb ischemia	1.498	1.416	1.118	0.290	4.472 (0.279–71.807)
Previous underlying diseases	0.122	0.731	0.028	0.867	1.130 (0.270–4.738)

### 2.3 住院病死率和 ECMO 撤机成功率的多因素 Cox 比例风险回归分析

将是否联合 IABP 治疗、术后出血、术前发生 AKI、术后感染和肢体缺血纳入多因素 Cox 比例风险回归模型分析其对主要结局的影响,结果(表4)显示,术前发生 AKI、术后感染和肢体缺血是患者的住

院病死率的独立危险因素(均  $P < 0.05$ )。同时,将年龄、是否联合 IABP 治疗和术前发生 AKI 纳入多因素 Cox 比例风险回归模型分析其对次要结局的影响,结果(表4)显示,联合 IABP 治疗是患者 ECMO 撤机成功率的保护因素( $P = 0.032$ )。

表4 住院病死率和 ECMO 撤机成功率的多因素 Cox 比例风险回归分析

Tab 4 Multivariate Cox proportional hazard regression analysis of hospital mortality and ECMO withdrawal success rate

Item	B	S.E	Wald	P value	HR (95.0% CI)
<b>Primary outcome</b>					
Combined IABP treatment	-1.895	0.980	3.741	0.053	0.150 (0.022-1.026)
Postoperative bleeding	0.002	0.830	0.000	0.998	1.002 (0.197-5.096)
AKI (prior to ECMO initiation)	2.232	0.908	6.040	0.014	9.315 (1.571-55.221)
Postoperative infection	1.863	0.840	4.922	0.027	6.444 (1.242-33.423)
Postoperative limb ischemia	1.749	0.786	4.958	0.026	5.751 (1.233-26.821)
<b>Secondary outcome</b>					
Age	0.009	0.025	0.129	0.719	1.009 (0.961-1.060)
Combined IABP treatment	2.685	0.911	8.687	0.032	0.971 (0.094-10.070)
AKI (prior to ECMO initiation)	-0.338	1.559	0.047	0.828	0.713 (0.034-15.140)

## 3 讨论

本研究回顾性分析了采用传统方法治疗 CS 和 CA 失败后,紧急实施 VA-ECMO 进行挽救治疗的病例情况。结果显示,E-CS 组患者的住院病死率为 70.0%,与文献<sup>[6]</sup>报道的数据(58.0%~75.6%)相一致;ECPR 组患者的住院病死率为 55.6%,则低于文献报道数据(65.9%~86.4%)<sup>[7]</sup>,究其原因,可能是由于在 ECMO 运行前患者已存在多脏器功能不全和严重的组织灌注不足,从而导致最终的抢救失败。临床上,VA-ECMO 救治是否成功取决于对患者的准确筛选;同时,临床医师应谨慎选择 VA-ECMO 的启动时机,对于一些病情过于严重且难以逆转的患者,应主动放弃 VA-ECMO 治疗。而对于最有可能从 VA-ECMO 治疗中获益的急性心肺功能衰竭潜在可逆患者,临床上则应开展积极救治以增加抢救成功率。

本研究结果发现,VA-ECMO 治疗前发生 AKI、术后感染和肢体缺血可增加患者的住院病死率,这与赵帅<sup>[8]</sup>的研究结果一致。CS 和 CA 患者在疾病的进展阶段,其肾脏最先受累,如得不到及时的救治,疾病往往会进展为多器官功能衰竭及严重的组织灌注不足,继而导致更高的死亡率。同时,施行 VA-ECMO 治疗的患者的全身存在多种侵袭性导管,一旦并发感染,会有超过 50% 的感染为血流感染,从而会出现

极高的病死率。本研究结果显示,入组患者的术后感染发生率为 31.6%,低于 CELIŃSKA-SPODAR 等<sup>[9]</sup>报道的感染水平;究其原因,可能与包括重症医学科、心脏内外科、感染科等在内的多学科专家协作以降低术后感染率有关。此外,术后肢体缺血常发生于下肢,多数情况下需经股动脉放置远端灌注管,以避免下肢缺血坏死;而患者一旦出现肢体缺血坏死,坏死的组织将大量释放炎性因子,引起严重的内毒素血症,从而可导致或加速患者死亡。本研究结果显示,入组患者的术后肢体缺血发生率为 15.8%,与 KAUSHAL 等<sup>[6]</sup>的结果相一致。因此,临床医师在进行 VA-ECMO 治疗时应密切关注相关并发症,尽可能在发生不可逆转的器官损伤之前做好充分的干预,以预防、减少严重并发症的发生。

本研究发现,联合 IABP 治疗的患者的 ECMO 撤机成功率优于单独使用 VA-ECMO 的患者。临床上,由 VA-ECMO 提供的血流是与左心室射血方向相反的逆向非搏动性血流,在左心功能严重衰竭时易引起左室超载。而左室超载是 VA-ECMO 治疗中最严重的并发症之一。当发生左室超载时左室后负荷增加,可引起左室过度应变,导致左室扩张,继而影响主动脉瓣开放,最终导致心室内血液淤滞和肺水肿。IABP 则是解决左室超载的有效治疗方法。IABP 治疗不仅可提高主动脉根部舒张压以增加冠脉血供,还可降低左



室后负荷以减少心肌氧耗, 从而为心功能的恢复提供帮助。陈晓华等<sup>[10]</sup>发现, 对于行ECPR的院内CA患者, 联合使用IABP治疗与较高的ECMO撤机成功率相关。因此, 对于院内CA患者, 我们推荐在疾病早期联合使用VA-ECMO和IABP开展治疗, 以提高ECMO撤机成功率及患者的临床获益。

本研究尚存在一定的局限性: ①未随机分组。②未评估在VA-ECMO治疗前患者行药物治疗的种类和剂量、射血分数和心脏指数等指标。③样本量较小, 协变量较多, 可能出现统计学上的偏倚。后续, 我们将扩大样本量并开展长期随访对本研究获得的结果行进一步的验证。

综上, VA-ECMO对传统治疗无效的CS和CA患者是一种有效的挽救疗法。本研究结果对有潜在可逆的心肺功能损害患者开展VA-ECMO挽救治疗提供了一定的临床证据。但在VA-ECMO治疗期间患者易出现出血、感染、肢体缺血等相关并发症, 因此对该并发症的预防和早期识别还需进一步研究。未来, 我们还需开展大样本量、前瞻性、多中心的临床试验, 进一步降低该疗法带来的并发症及住院病死率, 从而为CS和CA患者开展VA-ECMO治疗提供更可靠的诊疗依据。

#### 利益冲突声明/Conflict of Interests

所有作者声明不存在利益冲突。  
All authors disclose no relevant conflict of interests.

#### 伦理批准和知情同意/Ethics Approval and Patient Consent

本研究涉及的所有试验均已通过上海交通大学医学院苏州九龙医院伦理委员会的审核批准(文件号: HG-2023-004)。受试对象或其亲属已经签署知情同意书。

All experimental protocols in this study were reviewed and approved by Ethics Committee of Suzhou Kowloon Hospital, Shanghai Jiao Tong University School of Medicine (Approval Letter No. HG-2023-004). Consent letters have been signed by the research participants or their relatives.

#### 作者贡献/Authors' Contributions

隋明亮、夏大梅负责研究设计和执行, 隋明亮、汤卫兵、夏大梅负责论文写作和修改, 吴长江、黄超发、杨雅迪负责数据收集和分析。所有作者均阅读并同意最终稿件的提交。

The study was designed and conducted by SUI Mingliang and XIA Damei. The manuscript was drafted and revised by SUI Mingliang, TANG Weibing and XIA Damei. The data were collected and analyzed by WU Changjiang, HUANG Chaofa and YANG Yadi. All the authors have read the last version of paper and consented for submission.

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