



# ELISIO™ HX

A NOVEL SHARP CUT-OFF DIALYZER





A novel sharp cut-off,  
next-generation  
HD dialyzer

## Elisio™ HX

Chronic kidney disease (CKD) affects more than 10% of the world's population. For end stage renal disease patients, dialysis is one of the main life-sustaining treatments. However, **dialysis patients have several comorbidities and variable medical needs.**

**Inflammation** is at the core of the CKD leading to protein energy wasting, **anemia, malnutrition and cardiovascular (CV) diseases.**<sup>1</sup>

**Sarcopenia**, characterized by the loss of muscle mass and **frailty** also **increases CV risk and overall mortality.**<sup>2</sup>

With the continuous advancement in dialysis technology, a wider range of uremic toxins can be cleared in patients. High volume HDF has become the gold standard in several countries with superior survival rates.<sup>3</sup>

However, some patients are **not eligible for the HDF treatment** due to:

- unsuitable vascular access

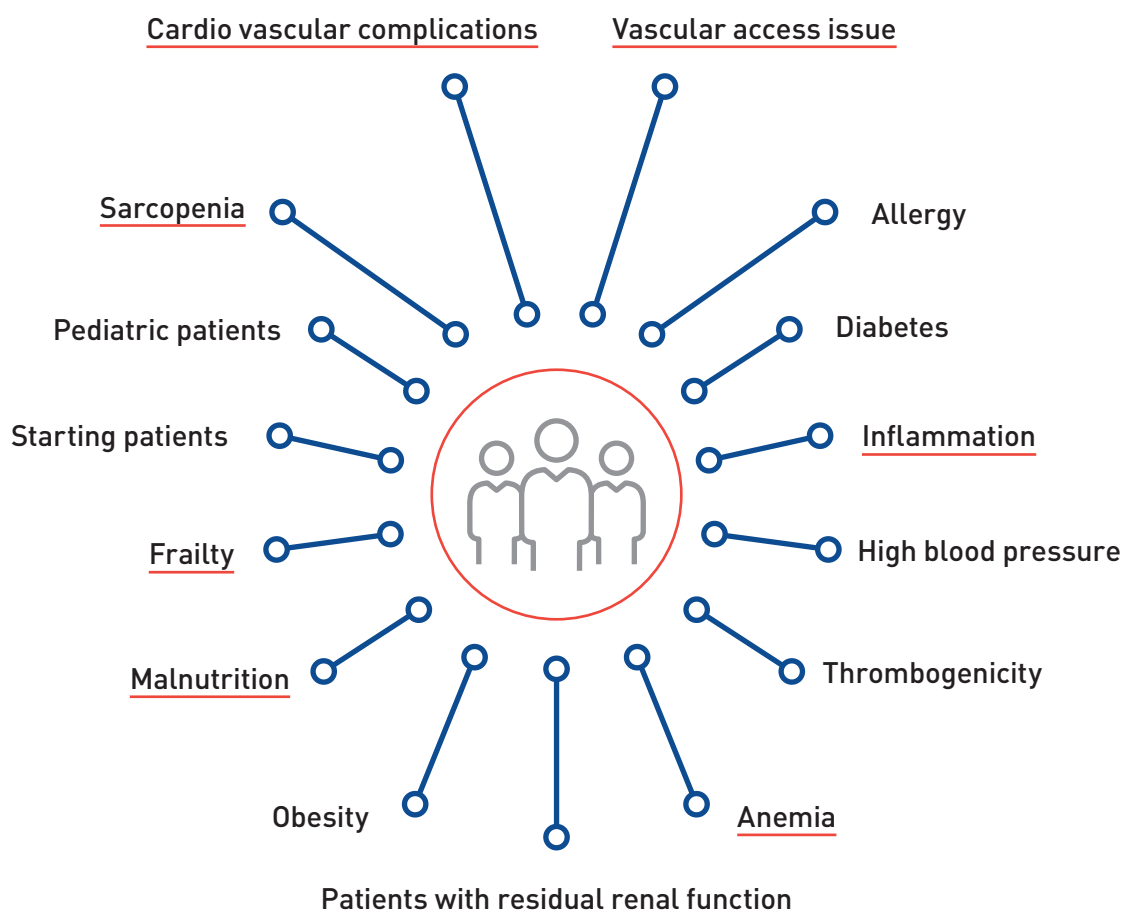
single needle, malfunctioning central venous catheter, new fistula, low access flow not permitting the blood flow of at least 300 mL/min

- inability to reach the efficient convective volumes (> 25 L post dilution)<sup>4</sup>

- clotting problems

- high hematocrit levels

For this wide array of patients with variable medical needs, the best dialyzer should lose minimal albumin while maintaining high clearance of uremic toxins.<sup>1</sup>



Nipro's novel super high flux sharp cut-off dialyzer, Elisio HX, with the combination of a bigger pore size and a specific geometry, is designed to remove a wide range of middle molecule uremic toxins (12-60 kDa) which have serious clinical impact on patients.<sup>2</sup>



## Japanese classification of dialyzers

In the absence of HDF, conventional HD with high flux dialyzers fall short in removing **larger middle molecule uremic toxins**. To overcome this limitation, the **super high flux dialyzers** with bigger pore sizes are introduced. In Japan, this class of dialyzers – also known as high-performance membranes – are used for the treatment of more than 90% of patients on hemodialysis and are associated with **higher survival rates**.<sup>5</sup>

Uremic toxin	Molecular weight
Urea	60 Da
Phosphate	96 Da
PTH	9500 Da
Beta-2 microglobulin	11.8 kDa
Myoglobin	17 kDa
Kappa free light chain	25 kDa
Complement factor D	23.7 kDa
Interleukin-6	24.5 kDa
Alpha-1 microglobulin	33 kDa
YKL-40	40 kDa
Pentraxin 3	41 kDa
Lambda free light chain	45 kDa
Albumin	67 kDa

Low flux class I

Mid-high flux class II and III

High flux class IV + HDF

Super high flux sharp cut-off class V



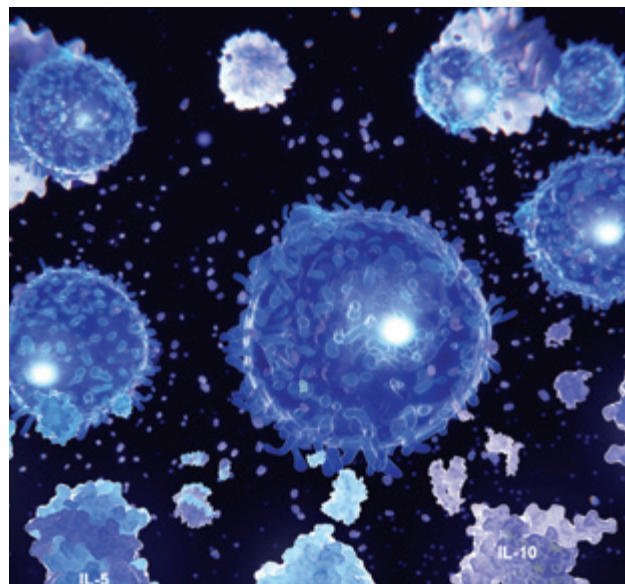
# Efficacy of class V dialyzers in removing clinically impactful middle molecules

## CLINICAL IMPACT OF MIDDLE MOLECULES

### Inflammation

Inflammation is at the **core of the CKD pathology** leading to several complications. A **21% increase of 1<sup>st</sup> year mortality rate** has been shown for **high levels of C-reactive protein**.<sup>6</sup>

The RISCAVID study has demonstrated a higher **CV and all-cause mortality** risk with higher levels of **IL-6 and IL-8**.<sup>7</sup> **IL-18** is also linked with a higher risk of **cardiovascular mortality** in dialysis patients.<sup>8</sup>



### Vascular calcification

An association between **serum Beta-2 microglobulin (B2M) levels** and **vascular calcification** has been observed suggesting the role of B2M in CV events.<sup>9</sup> A study with a follow-up of 6 years demonstrated this molecule as an independent predictor of **all-cause mortality**.<sup>10</sup>

Classically, the elevated B2M can deposit in the form of protein fibrils in various places in patients known as the **dialysis-related amyloidosis**. The effect of accumulated modified B2M is the stimulation of inflammatory molecules in the surrounding tissue leading to **tendonitis, back and neck pain** in patients.<sup>11</sup>

### Maladaptive immunity

Plasma levels of free light chains (FLCs) increase as a result of their diminished removal in CKD patients or their excess production in diseases such as multiple myeloma.<sup>12</sup> The increased serum levels of FLC can interfere with the apoptosis of leukocytes leading to **increased inflammation**.<sup>13</sup> The **free kappa and lambda light chains** are associated with **vascular calcification**, and a higher level of the light chains may be a risk factor for **increased mortality** in CKD patients.<sup>14-15</sup>

## Oxidative stress

In CKD, chronic inflammation, oxidative stress, and accumulation of the uremic toxins lead to the accumulation of the **advanced glycation end products (AGEs)** which can in turn aggravate the **oxidative stress and inflammation**. This vicious circle can lead to decreased muscle mass and the advancement of sarcopenia.<sup>2</sup>

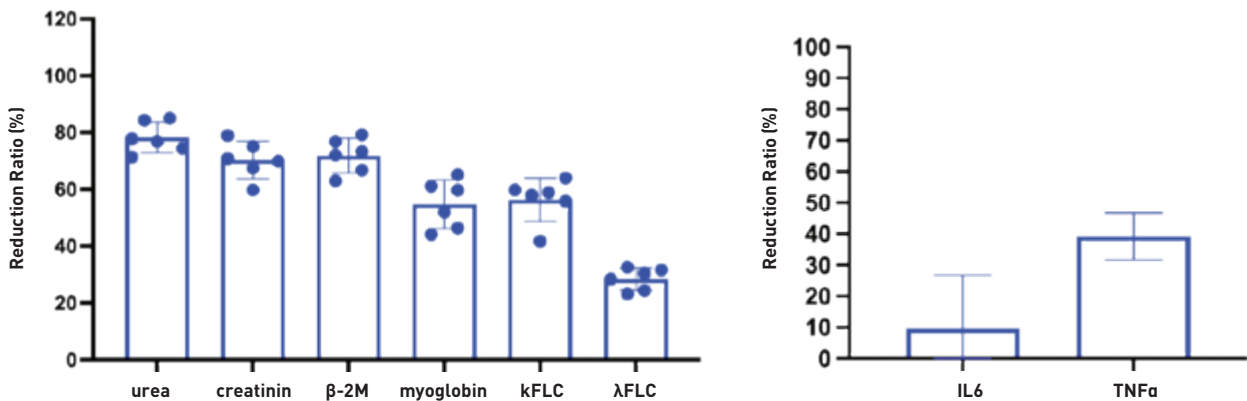
## Dialysis quality dose

The glycoprotein YKL-40, an inflammatory mediator, is a significant predictor of all-cause and CV mortality in dialysis patients.<sup>16</sup>

The **lower serum YKL-40 concentration is associated with the higher dose (Kt/V) in dialysis**.<sup>17</sup> The use of the high convective volumes in this study to increase the efficiency of dialysis highlights that the **removal of middle molecules requires a higher dialysis efficacy**.

# Optimal removal of middle molecule uremic toxins by Elisio HX

The objective of this prospective, single-center study was to determine the performance of the Elisio HX dialyzer in the removal of the following uremic toxins in 6 maintenance hemodialysis patients:<sup>18</sup>



Blood flow rate: 300 mL/min ; Dialysate flow rate: 500 mL/min; Treatment time: 240 min; N=6. Blood was collected pre- and post-dialysis to measure the reduction ratios.

## Removal of high middle molecule uremic toxins:

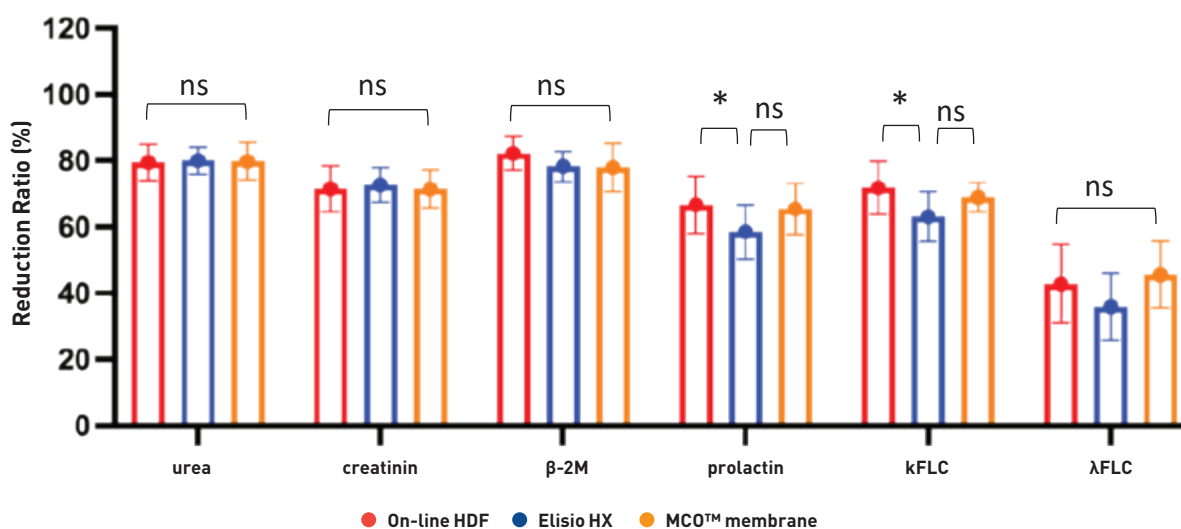
- reduces inflammation and oxidative stress
- improves immune response
- improves cardiovascular co-morbidities
- improves quality of life



## Similar to hemodiafiltration and the medium cut-off membrane

This prospective, randomized, cross-over, single-center study was performed to determine the safety and efficacy of Elisio HX in comparison to a medium cut-off membrane and on-line HDF. 14 patients receiving HDF as baseline treatment were randomized to either Elisio HX or the the medium cut-off membrane for 1 week. The results demonstrate that the removal of the middle molecules was mainly similar between Elisio HX and the medium cut-off as well as between Elisio HX and on-line HDF.<sup>19</sup>

This study indicates that the treatment with Elisio HX is an suitable alternative to on-line HDF and can be utilized for patients for whom HDF treatment is not possible.

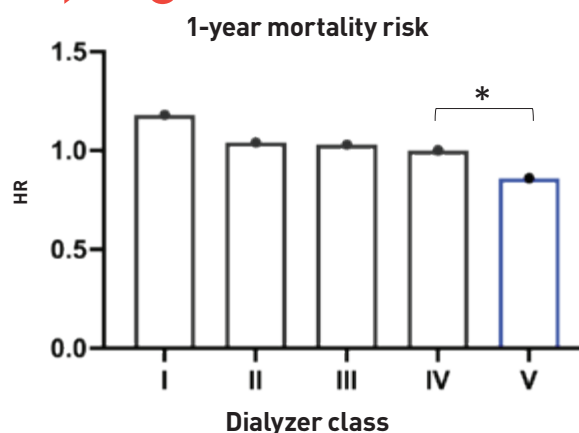


N=14; blood flow > 370 mL/min; replacement volume > 21 L; \*p< 0.05; ns: not significant

## Higher dialyzer performance, higher survival

Japan has been using a distinct 5-grade classification of the dialyzers based on the clearance of B2M at the blood and dialysate flow of 200 and 500 mL/min respectively. Based on this classification, **class IV and V**, also known as **super high flux** dialyzers, are identified by B2M clearance of <70, ≥ 70, and are used for the treatment of more than 90% of patients.

Using the nation-wide data of the Japanese society for dialysis therapy renal data registry in a large cohort of more than 200,000 patients, **this study has revealed a significantly lower risk of all-cause mortality for class V super high flux dialyzers including the sharp cut-off Elisio HX.**<sup>5</sup>

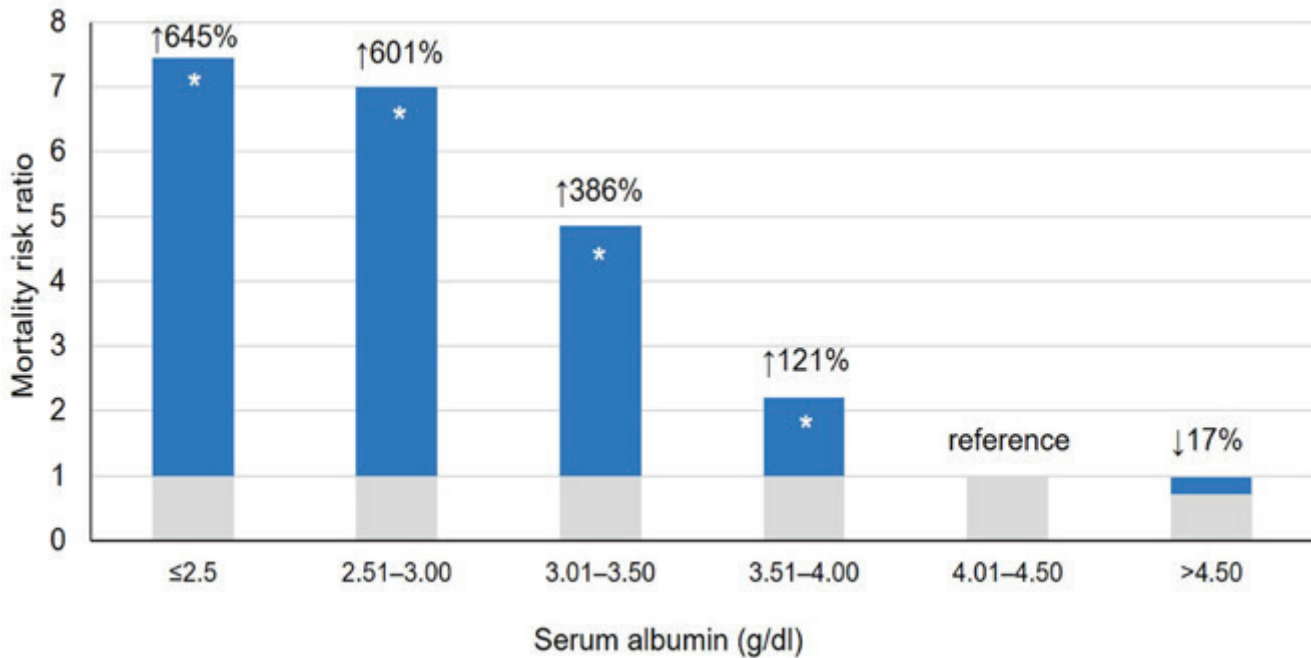


Graph from Abe et al.<sup>5</sup> 1-year all-cause mortality risk compared to class IV as reference. Cox proportional hazard regression. \* p<0.05. Dialyzer classification based on B2M clearance (mL/min): I <10, II <30, III <50, IV <70, V ≥ 70.

# Minimal albumin loss in Elisio HX

Hypoalbuminemia is common amongst the CKD patients and is a **strong predictor of mortality**.<sup>20,21</sup> Dialysis can increase this condition by the extra loss of albumin through the dialyzer's pores.<sup>1</sup>

The type of therapy and the type of membrane can impact the patients' albumin levels.<sup>22, 23</sup>

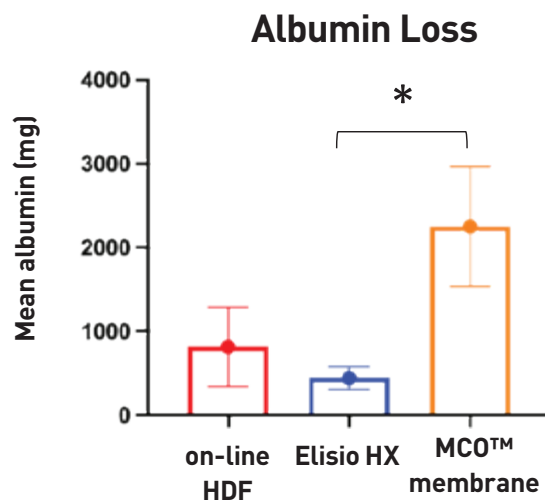


Graph from: <sup>1</sup> Relative risk of death by albumin level among 19,746 patients receiving incenter hemodialysis.<sup>20</sup>

**Elisio HX, thanks to its sharp cut-off, has a significantly lower albumin loss in the dialysate than membranes with higher albumin loss.**<sup>19</sup>

This minimal albumin loss distinguishes Elisio HX as a sharp cut-off membrane in the larger class of medium cut-off membranes.

The sharp cut-off feature of Elisio HX distinguishes this membrane for patients vulnerable to loss of albumin such as patients with malnutrition, frailty, sarcopenia or anemia.



N=14; blood flow > 370 mL/min; replacement volume > 21 L; \*p < 0.05; ns: not significant





# Conclusion

Following the shift of the paradigm from one-size-fits-all to a patient-centric approach, meeting the specific needs of dialysis patients is becoming increasingly important.

HDF, as the gold standard of dialysis removes a wide array of uremic toxins associated with cardiovascular and all-cause mortality.<sup>24</sup> However for patients not medically eligible for HDF, the best qualitative dialysis treatment is necessary.

## **For patients with no access to HDF, a quality dialysis treatment should:**

- remove the larger middle molecules (related to inflammation and CV diseases)<sup>25</sup>
- improve **amyloidosis, restless leg syndrome and pruritis**<sup>26</sup>
- improve the quality of life

The high performance dialyzers known as class IV and V in the Japanese classification, have shown superior survival rates and unharmed albumin losses.<sup>5</sup> In patients with lower capacity for albumin synthesis, or with poor nutrition, retaining sufficient **albumin is vital**.<sup>1</sup>

Elisio HX, with the combination of **bigger pore size and a specific geometry** is able to remove a wide range of middle molecule uremic toxins with **minimal albumin loss**. This provides a **quality dialysis treatment** for both standard and vulnerable patients.

# Performance Data

Clearance: Qf = 0 mL/min*	Qb/Qd (mL/min)	11HX	13HX	15HX	17HX	19HX	21HX
Urea	200/500	191	195	197	198	199	200
	300/500	255	266	275	281	287	290
	400/500	296	313	327	338	348	355
Creatinine	200/500	179	185	190	194	197	198
	300/500	230	244	255	266	275	280
	400/500	260	280	297	310	321	331
Phosphate	200/500	173	180	186	190	194	196
	300/500	212	227	241	252	261	268
	400/500	235	253	272	286	299	310
Vitamin B <sub>12</sub>	200/500	126	139	150	159	167	174
	300/500	146	163	179	192	203	214
	400/500	158	178	196	210	223	235
Myoglobin	200/500	69	80	92	102	112	121
	300/500	76	88	100	110	122	132
	400/500	81	96	108	119	130	142

Clearance Qf = 10 mL/min*	Qb/Qd (mL/min)	11HX	13HX	15HX	17HX	19HX	21HX
Urea	200/500	193	197	199	199	200	200
	300/500	257	268	276	282	288	292
	400/500	298	316	329	341	351	358
Creatinine	200/500	181	188	193	196	198	199
	300/500	233	247	258	270	277	283
	400/500	263	284	300	314	325	334
Phosphate	200/500	175	182	187	191	194	197
	300/500	216	232	245	255	264	271
	400/500	239	256	274	290	302	314
Vitamin B <sub>12</sub>	200/500	129	142	153	162	170	177
	300/500	150	168	183	195	206	217
	400/500	162	182	200	214	226	240
Myoglobin	200/500	74	88	97	108	118	128
	300/500	81	94	105	116	127	139
	400/500	86	100	113	124	137	148

## Ultrafiltration Coefficient

KUF (mL/hr/mmHg)	47	53	60	67	75	82
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## In-Vitro test conditions

Clearance: Qd 500 mL/min, Qf 0 mL/min & Qf 10 mL/min

KUF: Bovine blood (Hct 32 ±2%, Protein 60 g/L, 37°C), Qb 300 mL/min

## Sieving Coefficient\*\*

Vitamin B <sub>12</sub>	1.00	β <sub>2</sub> -microglobulin	1.00	Albumin	0.0024
Inulin	0.97	Myoglobin	0.86		

\* In vitro test condition [EN1283, ISO 8637: 2010]: Qf 0 mL/min, 10 mL/min.

Clearance data obtained in Japan. Clearance data can vary slightly depending on the test setup, lot nr. and production site.

\*\* SC [EN1283, ISO 8637: 2010]: Qb 300 mL/min, Qf 60 mL/min.

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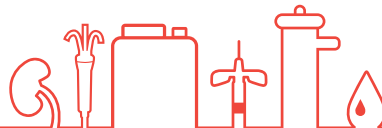
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