Mid-term results of elective repair of extensive thoracic aortic pathology by the Evita Open Plus hybrid endoprosthesis only.
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Mid-Term Results of Elective Repair of Extensive Thoracic Aortic Pathology by Only the Evita Open Plus Hybrid Endoprosthesis

Running title: Follow-up of the Evita Open Plus

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Abstract

Objectives. To describe the early and mid-term clinical and instrumental results of the frozen elephant trunk procedure (FET) using the recent Evita Open Plus hybrid endoprosthesis for elective one-stage treatment of extensive thoracic aortic disease.

Methods. We reviewed 16 patients undergoing FET for either post-dissection aneurysm (50%), true aneurysm (31%) or other etiologies (19%), through median sternotomy and hypothermic circulatory arrest. An average 14 ± 7.6 months follow-up with regular contrast-enhanced control CT scans was available. Four patients received preliminary carotid-subclavian bypass to improve spinal cord protection. Distal extension through endovascular deployment of stent-grafts into the descending aorta was performed during the same procedure in three patients. Concomitant procedures on the ascending aorta/root were done in 25% of cases.

Results. There were no cases of operative mortality. Neither cases of cerebral stroke nor postoperative paraplegia were observed. Two cases of transient paraparesis and one case of Brown-Séquard syndrome occurred. At follow-up, there were no cases of endoleak or endotension. One patient was reoperated for distal completion (thoracoabdominal aortic replacement).

Conclusions. The FET using the Evita Open Plus device is a reliable and versatile treatment for one-step management of extensive disease of the aortic arch and descending aorta. This strategy should be reserved to patients having limited preoperative comorbidities and good functional status.

KEY WORDS: Aortic operation; Endovascular procedures; Hybrid surgery
Introduction

The treatment of extensive aortic disease involving the arch and the descending segment is a challenge in the domain of aortic surgery. After the earliest experiences [1, 2], the so-called frozen elephant trunk (FET) technique has been introduced in the clinical practice with the aim to reduce the rate of delayed aortic reoperation, late aortic-related morbidity and mortality after repair of acute, chronic dissection or of widespread arch aneurysms [3]. Nonetheless, after the availability of newer hybrid endoprosthesis device (Evita Open Plus, Jotec Inc., Hechingen, Germany) with shorter distal stent-graft portion, a specific follow-up is required, with particular interest to the neurological outcomes. Additionally, the feasibility and follow-up results of endovascular completion concomitant with the FET procedure need to be ascertained.

In the present paper we describe our single-center experience, including mid-term clinical and radiological follow-up, of the Evita Open Plus hybrid endoprosthesis for the elective treatment of extensive thoracic aortic pathology.
Methods

Patients profile.

Starting in February 2009, 16 consecutive patients were treated with the FET technique at our Institution using the Evita Open Plus hybrid endoprosthesis (Jotec Inc., Hechingen, Germany). All patients were affected by extensive thoracic aortic pathology involving the aortic arch with or without extension to the descending or the ascending thoracic aorta, and all cases were done on an elective timing. There were no instances of FET repair in the context of acute aortic dissection in the present series. As part of the N.O.E. (Nouvelle Open des Evita) French National Registry, the pre-, intra- and postoperative data of these patients were prospectively collected within an electronic database, which is checked for completeness and consistency on a monthly basis. In March 2013 we queried the database in order to retrieve both the in-hospital and follow-up information of the patients who received FET within our centre. As institutional policy, the FET procedure was performed only using the Evita Open Plus device. This is composed of a proximal specific woven Dacron tube graft and of a distal self-expandable nitinol stent-graft, which is crimped and mounted on a dedicated deployment system. A broader number of sizes is available compared to its predecessor (Evita Open prosthesis, Jotec Inc., Germany), while the availability of shorter distal stent-graft portion is aimed at minimizing the extent of aortic coverage and the risk of spine cord injury. The Dacron portion of this device is characterized by a tighter texture, aimed at reducing perioperative bleeding.

Mean age of the patients population was 59.3 ± 12 years. The baseline characteristics and the risk profile of our series are summarized in Table 1; two patients had Marfan syndrome and one patient had bicuspid aortic valve. The most common indication to surgery was chronic post-dissection aneurysm (50%), while true aneurysm was present in 31% of cases. Miscellaneous etiologies were observed in the remainders (19%). Previous
cardiac or aortic operation had been accomplished in 5 patients (31%), including Bentall and David root replacement (1 case each), ascending aortic replacement (1 case), isthmus coarctation repair and heart transplantation (1 case each). As well, 6 patients (37%) underwent concomitant procedures at the time of FET performance (3 ascending aortic replacement, 1 Bentall root replacement, 1 mitral valve replacement and 3 distal extension of the aortic repair by deployment of additional stent-grafts into the descending aorta in our staged intervention). The maximum aortic diameter was observed at the level of the arch in four cases and at the level of the proximal descending aorta in the remainders. Cardio-pulmonary bypass time, cardioplegic arrest time and selective cerebral perfusion time were $231 \pm 54$ min, $159 \pm 57$ min and $96 \pm 18$ min, respectively. Indications to surgery were established in compliance with the current guidelines [4].

**Surgical technique.**

The planning of the surgical procedure was performed using the Therenva Endosize software (Therenva Inc., Rennes, France), through elaboration of CT scan-derived images [5]. Preliminary left subclavian-to-left carotid bypass had been performed in 4 patients (25%) one week before the scheduled aortic surgery, in order to improve the spinal cord perfusion both intraoperatively and after completion of the procedure. Carotid-subclavian bypass was systematically performed in patients where concomitant endovascular extension was scheduled. Additionally, the presence of an incomplete polygon of Willis (which was systematically investigated preoperatively by CT scan) was one additional criterion to indicate carotid-subclavian bypass. The aortic arch was accessed by median sternotomy in all instances. Arterial cannulation for cardio-pulmonary bypass was achieved in the right subclavian artery through an interposition graft in 81% of cases and by direct ascending aortic cannulation in the remainders. As part of the routine anesthesiological protocol, patients received intraoperative administration of 1 g of Sodium Thiopental during
systemic cooling, 1 g of Methylprednisolone, 3 g of Magnesium Sulfate and 250 mL of 20% Mannitol before circulatory arrest, adjuncts to hypothermia for neurological protection. Extracorporeal circulation was conducted according to a pH-stat protocol. In 5 patients, an extra-stiff guidewire (Lunderquist, Cook Medical, Bloomington, IN) was advanced into the distal aortic arch under fluoroscopic and/or transesophageal echocardiography guidance. Such strategy facilitates both the correct identification of the true lumen in chronic dissection cases and the optimal positioning of the prosthesis. After accomplishment of systemic hypothermia (26°C rectal temperature) circulatory arrest was performed, the aortic arch was opened and selective antegrade cerebral perfusion (10 mL/kg/min) was established (temperature of the perfusate: 20°C). When preliminary carotid-subclavian bypass had not been performed, the orifice of the left subclavian artery was clamped during the circulatory arrest using a Foley catheter. The hybrid endoprosthesis was usually oversized by 10% to 20% with respect to the landing zone at the level of the arch; oversizing was not performed if Marfan syndrome coexisted. The stent-graft portion of the device was deployed antegradely at the desired level under direct vision; such procedure was assisted by a transfemoral extra-stiff guidewire in 36% of patients (especially in cases where concomitant distal completion was required). In the case of chronic dissection, the distal aortic stump was prepared by obliteration of the false lumen using a running Polypropylene suture. This step maximizes the diameter of the true lumen and therefore reduces the risk of suboptimal deployment of the stented portion, as well as the risk of difficult extraction of the Dacron portion. Subsequently, the distal portion of the Dacron fabric was circumferentially sutured to the proximal descending aorta or to the distal arch between the origin of the left subclavian and left carotid arteries, using a running 4-0 Polypropylene suture. Interrupted pledgetted U-shape stitches were added in the case of tissue fragility. The Dacron fabric graft was then entirely pulled out, and the epiaortic vessels were reimplanted either en bloc with a patch of aortic tissue (87%) or by
interposition Dacron grafts in the event of coexisting aneurysm of their proximal segment (13%). After deairing, the prosthesis was clamped and the cardio-pulmonary bypass restarted. The proximal repair was completed during systemic re-warming. The most frequently size of the implanted hybrid endoprostheses was 28 mm (44%), followed by 24 mm (25%); average diameter of the stent-graft was 28.1 ± 4.1 mm (range: 22-36). Myocardial protection was obtained by antegrade delivery of cold crystalloid cardioplegia (multidose St. Thomas’ solution) plus topical cooling. Concomitant distal extension by deployment of stent-grafts within the descending aorta is feasible both antegradely from the aortic arch (one case in the present series) and retrogradely from the femoral artery (two patients). In both situations, we deployed the stent-grafts before placement of the hybrid endoprosthesis, in order to take advantage from avoided exposure to antegrade flow of the overlap region according to the ‘trombone’ technique. One patient received extension with two stent-grafts and two patients received one additional stent-graft. Cerebrospinal fluid drainage was not systematically instituted immediately before surgery, but it was started later during the postoperative course in event of onset of neurological complications.

**Follow-up.**

All patients were entered in a prospective follow-up program, including pre-discharge control contrast-enhanced CT scan. Follow-up visits were then performed at the third and twelfth postoperative months and every year thereafter. Each visit included physical examination, surface electrocardiography, transthoracic echocardiography and contrast-enhanced CT scan. The CT results were interpreted in consensus by two radiologists experienced in aortic imaging. In case of surgery for chronic dissection, the status of the false lumen was assessed both preoperatively and at follow-up at four given aortic levels: the midpoint of the aortic arch, the proximal descending aorta, the distal descending aorta
(at the level of the diaphragm crura), and the abdominal aorta (at the level of the renal arteries). The false lumen was categorized as patent (homogeneously contrast-enhanced), partially thrombosed (presence of thrombus in any part of it with preserved flow), completely thrombosed (complete lack of blood flow), or regressed (if its thickness was <2 mm or absent). Compliance to follow-up was 100% in the present investigation (average duration 14 ± 7.6 months).
Results

_Early results._

There were no cases of in-hospital mortality, and the planned procedure could be successfully completed in all instances. There were no instances of difficult deployment of the Dacron portion out from the stented part of the device. Major operative complications were surgical revision for bleeding in 3 cases (19%), pulmonary infection in 2 (12%) and adult respiratory distress syndrome (ARDS) in one. There was no case of perioperative cerebral stroke. While we observed no cases of peri- or postoperative paraplegia, we report two cases of transient paraparesis (full recovery was achieved within the same hospitalization) and one case of Brown-Séquard syndrome. Therefore, the entity of overall neurological complications was limited. Among the three patients who received concomitant distal extension of the FET, one displayed transient paraparesis while the remainders had a neurologically uneventful course. Other postoperative morbidity were transient acute renal insufficiency in 4 cases (25%), dysfunction of the recurrent nerve in 2 and sepsis in one.

Pre-discharge CT scan was performed in all patients, and showed optimal positioning of the hybrid endoprosthesis, with no instances of endoleak and complete exclusion of aneurysms without any endotension.

_Late results._

No patient deceased during the follow-up. We recorded one aortic reoperation during the follow-up in a Marfan patients who had received FET for chronic post-dissection aneurysm. He underwent open surgical completion at the fourth postoperative month for repair of type II thoracoabdominal aneurysm, in the context of rapid increase of the aortic diameter at the descending (62 mm) and abdominal (78 mm) levels. During this procedure,
the stent-graft portion of the hybrid endoprosthesis could be shortened in order to facilitate anastomosis with a Dacron graft at a higher level and reimplantation of patent intercostal arteries at the thoracic 8 to 10 levels [6]. No further adverse aortic events were recorded. At the latest available CT scan, we observed no cases of pseudoaneurysm or endoleak, and optimal positioning of the hybrid endoprosthesis in all instances. Complete thrombosis of the false lumen was evident in 55% of the dissection cases. At the latest available follow-up, shrinkage of the aneurysmal sac was documented in 46% of cases, while the aortic diameter remained unmodified in the remaining instances. While preoperatively the false lumen was patent in 100% of cases at all aortic levels, at the latest follow-up we observed that the false lumen was regressed in 20% of cases and completely thrombosed in the remaining 80% at the arch and the proximal descending aorta levels. At the distal descending level, the false lumen was thrombosed in 50% of cases, partially thrombosed in 25% and patent in 25%. At the abdominal level, it was partially thrombosed in 20% of patients and patent in the remainders. No adverse neurological events were observed.
Discussion

The elephant trunk procedure, described initially by Hans Borst and associates [7], has been associated with improved results for the treatment of complex aortic pathology involving the arch and the descending segment. Its major advantages include facilitated proximal cross-clamping and easier proximal anastomosis at the time of the second surgical step. Nonetheless, major series have also underlined that the rate of failure to complete the second step may range between 32% and 60% [8, 9]. Such rate is the cumulated expression of the mortality associated with the first step, the rate of non-returning patients (32% of first step survivors in experienced centers [8]), and the mortality among the non-returning patients (which may reach 36% [8]). A 25% mortality rate among non-returning patients has been indicated by another prominent series [10]. It has been suggested that as many as about 40% of non-returning patients died of aortic rupture [9].

The FET technique was proposed as a mean to improve the long-term prognosis of patients undergoing surgery in the context of aortic dissection, through facilitated obliteration of the residual false lumen and stabilization of the proximal descending aorta. In such circumstances, the FET technique yielded respectable rates of freedom from aortic reoperation and of false lumen thrombosis at 4 years (79% and 96%, respectively), though at the price of non-negligible mortality rates (12%) [11]. In previous literature, mortality associated with the FET procedure was comparable to that of first-stage conventional elephant trunk, and consistently lower than mortality associated with one-stage extensive surgical aortic replacement [12]. Additionally, the strategy based on bypass of all supra-aortic vessels and total stenting of the aortic arch has been questioned due to remarkable mortality-rates [12].

The present paper specifically addresses the follow-up of the Evita Open Plus device for the elective repair of extensive aortic pathology, including both aneurysms and chronic
dissection cases. Large experience has been so far accumulated on its predecessor, i.e. the Evita Open hybrid endoprosthesis (Jotec Inc., Germany) [13]. Conversely, only one previous study has been focused on the clinical results of the Evita Open Plus device [14], which is characterized by a broader spectrum of available sizes and by facilitated hemostasis due to pre-clotting of the prosthetic tube. Our findings indicate that the FET strategy is associated with low rates of perioperative morbidity and optimal freedom from prosthesis-related or aortic complications after one year. We believe that lesions due to some specific etiologies, and globally all cases with upper descending aortic pathology and expected difficulty at proximal cross-clamping through the left thoracotomy access, are good candidates for elective treatment by the FET strategy. These include, but are not limited to, patients presenting with aneurysm of the upper thoracic segment late after repair of isthmus coarctation (Figure 1A), and patients presenting for elective or delayed repair of pseudoaneurysm for traumatic aortic lesion of the isthmus (Figure 1B). In such instances, the sternotomy access allows radical and safer treatment of the lesion through deployment of the hybrid endoprosthesis (Figure 2A and 2B). In particular, the patient in Figure 1B and 2B received the FET approach due to his anatomical features (12 cm-large pseudoaneurysm of the upper descending aorta with surrounding inflammation) which prevented safe proximal cross-clamp through the thoracotomy route. A multimodality and patient-tailored approach is recommended for procedure selection, the endovascular and hybrid solutions being essential part of the surgical armamentarium [15]. As well, the diffusion of endovascular techniques has led to the appearance of a new spectrum of late endoleak- and endotension-related morbidity, which prompts the need for systematic clinical and instrumental follow-up [16].

The neurological outcomes observed among patients treated with the FET technique must challenged with those of the open surgical approach [17], where the possibility to re-implant the patent intercostal arteries exists. Additionally, a continued improvement in
terms of spinal cord injury rates has been observed during recent years [8, 18]. The extension of the diseased segment has been reported as one foremost determinant of the risk of spinal cord injury, regardless of the approach (open surgery vs. endovascular), although other factors have been implicated, such as previous surgery on the distal aorta [18]. Since paraplegia is a dreadful complication, any effort must be done to avoid it [19]. Hence, the decision among alternative procedures must take into consideration the expected risk of spinal cord injury on the basis of anatomical characteristics and imaging features. In the present series we had no cases of paraplegia and two instances of completely resolved paraparesis, which well compare with previous experiences of the FET (rate of paraplegia ranging between 1.3% and 4%) [3, 9, 11]. In the setting of repair of acute aortic dissection by FET, a distal landing zone comprised between the thoracic level 10 and 12 regardless to the dissection entry site, did not determine any instance of spinal cord injury in a recent series of 32 consecutive cases [14]. This is consistent with previous findings, indicating that the sacrifice of more than 12 total segmental arteries or more than 8 segmental arteries originating in the lower thorax is associated with increased paraplegia risk [20]. A distal landing zone at the thoracic 10-12 levels actually entails the sacrifice of less than 12 segmental arteries in the upper thorax. Whenever the diseased segments extend into the distal portion of the descending aorta, a two-stage elephant trunk followed by endovascular completion has been advocated in order to reduce the risk of spinal cord ischemia [20]. In previous experiences, among 31 patients who underwent delayed endovascular completion of a conventional elephant trunk procedure, 6.4% presented paraparesis and none developed paraplegia, while the distal extent of stent-graft coverage reached the thoracic level 8 in 45% of patients, and the thoracic level 9 or lower in 19% of cases [21]. Hence, we systematically performed preliminary carotid-subclavian bypass in patients scheduled for distal endovascular extension. Additionally, we believe that such strategy allows confident perfusion of the spinal cord both intra- and
postoperatively, despite obliteration of the ostium of the left subclavian artery. The absence of a third perfusion cannula facilitates suturing, and continued postoperative flow may minimize the risk of delayed paraplegia. Our patients systematically received evaluation of the polygon of Willis at preoperative CT scan; incompleteness of this circulation together with anticipated need for obliteration of the right subclavian artery, was the criterion to indicate preliminary carotid-subclavian bypass. Different lengths of the stent-graft portion of the hybrid endoprosthesis are available, ranging from 110 to 160 mm. This facilitates the adaptation of the surgical strategy to individual patients on the basis of their anatomy and localization of segmental arteries, and helps minimizing the risk of spinal cord injury. In our experience, the sizing of the hybrid endoprosthesis was performed on the basis of preoperative CT scan with the aid of an automated three-dimensional navigation software (Endosize, Therenva Inc., Rennes, France), which has yielded minimal interobserver variability in planning the endovascular aortic repair [5]. Such applications not only facilitate the sizing process, but also may constitute a documental basis to support the operative choices in a medical-legal environment. It is therefore useful for all phases of treatment of this complex patients, from sizing to storing of data and following of late evolution through facilitated comparison of historical images. Our series presents a quite remarkable average antegrade selective cerebral perfusion time (96 min). We believe that this is attributable to the poor quality of the aortic tissue in several patients, which obliged to laborious suturing at the level of the distal aortic stump, to obliterate the false lumen in chronic dissection cases and to the need to reconstruct the epiaortic vessels by interposition grafts in two patients. These elements are likely to increase the selective cerebral perfusion time. Additionally, the absence of perioperative cerebral strokes in our series essentially confirms the reliability of this technique for cerebral protection, despite considerable circulatory arrest times.
In a series of endovascular elephant trunk completion, the rates of type III endoleak and of device migration were 4.5% and 9%, respectively [17]. Additionally, these Authors reported a 6.4% rate of endoleak and a 9.4% rate of caudal migration of the endoprosthesis requiring open surgery during the follow-up. A ‘distal first’ strategy, entailing deployment of stent-grafts just immediately performance of the FET procedure and creation of a 5-8 cm overlap region, may help minimize the risk of such complications on the basis of the ‘trombone’ mechanism (abolished exposure of the joint region to antegrade blood flow). Deployment of stent-grafts may be achieved either antegradely from the arch or retrogradely from the femoral artery. We did not observe any case of stent-graft migration or endoleak in the follow-up of our patients receiving combined FET and endovascular completion, although such finding needs confirmation in larger patient subsets. Overall, the present series underlines the versatility of the hybrid endoprosthesis. In fact, it allows both combined endovascular completion, and shortening of its distal portion whenever required at the time of surgical completion on the downstream aorta [6]. The latter feature is of predominant interest in Marfan patients, who have increased likelihood of late aortic reoperation. Moreover, concomitant repair of more proximal disease is also feasible, without significant increase in operative morbidity (herein, ascending aortic/root replacement and valve replacement). Nonetheless, few data are available so far over the effectiveness of the FET strategy in Marfan patients. The FET cannot be recommended for the routine use in Marfan cases due to the risk of late aortic complication, unless other options are less viable, depending on the clinical context.

Despite the complex baseline profile of our patients (high rate of previous cardiac operations and of concomitant procedures) and the nature of the operation, entailing prolonged hypothermic arrest, we had no operative mortality and acceptable rates of morbidity. Such difference versus previous series, which reported mortality-rates ranging between 3.2% and 13.4% [3, 11, 22], may be due to the characteristics of our population.
Our patients were all elective and received surgery at a slightly younger age (average 59.3 years) than previous series (up to 67.9 years [3]), and we have no patients undergoing surgery in the setting of acute dissection [9]. Previous experiences of arch surgery based on the policy of accepting patients with advanced age, multiple comorbidities and critical perioperative state have yielded remarkable rates of mortality (11.6%) and permanent neurological dysfunction (9.6%) [23]. In this same investigation, advanced age, compromised renal function, peripheral vascular disease and markers of critical perioperative state were strong predictors of mortality at multivariate analysis. This is evident despite recent advancements in anesthesiological techniques and availability of antegrade selective cerebral perfusion with moderate core hypothermia [24]. Hence, despite the use of hybrid techniques and devices, the treatment of extensive aortic pathology remains significantly morbid. Adequate patients’ selection is critical to ensure both tolerability of the operation and long-term benefits [25]. This should raise a reflection over the opportunity to recruit morbid and elderly patients for arch surgery. The major limitation of the present paper consists in the little size of the population; therefore, sample bias is possible with respect to operative mortality and to the rate of perioperative neurological complications. Larger nationwide series will be able to address these issues more in detail. Nonetheless, the present series includes only patients receiving the Evita Open Plus device, and its specific follow-up represents an element of originality with respect to previous papers, which were focused on the predecessor device.

In conclusion, the FET strategy using the Evita Open Plus device is a feasible and versatile solution to allow one-step treatment of complex aortic disease of the arch and of the descending aorta, with or without involvement of the proximal aortic segments. Such strategy remains anyway reserved to patients with low rates of comorbidities and limited perioperative risk.
References


**Figure Legends.**

**Figure 1.** Three-dimensional contrast-enhanced CT scan imaging with volume-rendering.  

**Figure 2.** Three-dimensional contrast-enhanced CT scan.  **A.** Postoperative imaging of the patient in Figure 1A.  **B.** Postoperative imaging of the patient in Figure 1B.  Both controls show optimal positioning of the hybrid endoprosthesis and the absence of complications.
**Table 1.** Baseline characteristics of the study population (N=16). COPD: Chronic Obstructive Pulmonary Disease. LVEF: Left Ventricular Ejection Fraction. Renal insufficiency was defined as creatinine clearance <60 mL/min (as calculated by the Cockcroft-Gault equation). TIA: Transient Ischemic Attack. BMI: Body Mass Index. *As measured at the level of the bifurcation of the pulmonary artery.

<table>
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<td>Age (years)</td>
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<tr>
<td>Gender (Male/Female, %)</td>
<td>81% / 19%</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>61.9 ± 6.4</td>
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<td>COPD</td>
<td>2 (12%)</td>
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<tr>
<td>Renal insufficiency</td>
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<tr>
<td>Previous cerebral TIA</td>
<td>2 (12%)</td>
</tr>
<tr>
<td>Previous cord TIA</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Marfan syndrome</td>
<td>2 (12%)</td>
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<tr>
<td>Diameter of descending aorta* (mm)</td>
<td>45.9 ± 14.6</td>
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