

## Modern Possibilities of Interventional Radiology Methods in the Treatment of Patients in Cancer Center

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### Abstract

This article presents an analysis of the immediate and long-term results of interventional radiology methods in oncological practice at the premises of South - Kazakhstan Regional Oncologic Dispensary for a 17-year period (2004-2020).

Since 2004, the first attempts to introduce intraarterial chemotherapy for cervical cancer have been started in South- Kazakhstan Regional Oncologic Dispensary. Currently, the specialists of Regional Oncologic Dispensary widely perform such endovascular (interventional) operations as: angiography, regional intraarterial chemotherapy, chemoembolization, placement of infusion port systems, percutaneous drainage of bile and urinary ducts, etc.

For 17 years (2004-2020), in Shymkent, there were treated more than 3700 patients with tumor diseases of various localization using endovascular methods. Currently, about 300 endovascular procedures are performed annually in City Cancer Center, more than 150 of them are performed as tertiary health care. The immediate and long-term results of the use of X-ray surgical methods of treatment in cancer patients showed that the control over recurrent glioblastomas was achieved in 72% of patients up to 18 months. As the initial stage of treatment of head and neck squamous cell carcinoma, intraarterial chemotherapy allowed the completion of radical therapy in more than 73% of patients. After treatment of patients with lung cancer by X-ray surgical methods, the 5-year survival rate was 14.3% ( $p < 0.05$ ). The 7-year survival rate was 11.4% ( $p < 0.05$ ). The 10-year survival rate was 5.7% ( $p < 0.05$ ). In liver cancer, the one-year mortality began to decrease intensively from 2007 for the period from 2008 to 2018, the one-year mortality of patients decreased by 32.4%. The total mortality of patients over the past 10 years has decreased by 2 times (5.7 per 100 thousand of population in 2004, and in 2018, this indicator was 2.5 per 100 thousand of population).

Thus, X-ray endovascular methods of diagnosis and treatment in oncological practice may and should be widely used in order to improve the treatment outcomes, prolonging survival and improving the quality of life of oncologic patients. The use of such highly specialized methods of treatment makes it possible to meet the requirements set by the head of state and the government in the field of modern healthcare development and to maintain a course aimed at studying, supporting and widely introducing advanced technologies for the treatment of serious cancer patients.

**Keywords:** Experience; Organization; Endovascular Oncology; Chemotherapy; Implementation of Methods

## Introduction

Diagnosis and treatment of malignant tumors remains the most urgent problem of clinical medicine; today, in the Republic of Kazakhstan, oncological diseases occupy the second place in the disease incidence after cardiovascular pathology.

More often, the only method that allows long-term survival in malignant tumors of various localization is surgery. However, by the time of diagnosis, eradication of tumor is possible only in 5-15% of patients, and the remaining patients are undergone to palliative treatment, i.e., systemic chemotherapy and radiation therapy; unfortunately, non-surgical methods of treatment do not always give the desired result and often treatment is ineffective. The search for minimally invasive and at the same time, effective methods of therapy stimulated the development of intravascular interventions done under X-ray control [1,2,5].

The first attempts of such therapeutic procedures were made in Neurosurgery in the mid-1920s. The fundamentals for the further development of this area were the development of percutaneous puncture approach by S. Seldinger technique in 1953 and creation of radiopaque catheters by P. Odman in 1959. The first scientific society that got its name from the new area of medicine, namely Interventional radiology, was established in 1975 [2,13,14].

For more than 30 years, along with radiodiagnosis and radiation therapy, X-ray surgery (syn. - Interventional radiology, Endovascular surgery) has been defined as an independent branch of Radiology, closely related to Surgery, Oncology, Gastroenterology and other related specialties. X-ray surgery is the sequential performance of diagnostic and therapeutic procedures under the control of X-ray examination, ultrasound investigation, computerized tomography and magnetic resonance imaging. In addition to a variety of X-ray endovascular procedures, its scope includes performing various types of biopsies, percutaneous local therapy, drainage, balloon dilation, prosthetics (stenting) of non-vascular structures [2,4,7].

Currently, there is a rapid development of interventional radiology and minimally invasive surgery. According to foreign studies, the number of diagnostic and therapeutic interventional radiological procedures performed is increasing by more than 10% per year. At the same time, the role of these interventions in the treatment of malignant tumors of various localization is noticeably increasing. The probability of further progress in modern Clinical Oncology, in addition to the creation of new effective drugs, is associated with the widespread locoregional methods of treatment [2,6,8,11].

The experience of percutaneous interventions in various tumor localities allows us to formulate the advantages of this method over other therapeutic effects or in combination with them, namely

- Low invasiveness. The vast majority of procedures are performed using percutaneous puncture approach under regional anesthesia; in this regard, there is no need for laparotomy and general anesthesia.
- Selectivity of treatment. In most cases, chemotherapeutic drug is injected directly into the arteries that supply blood to the tumor. As a result of the so-called "first pass" effect, about 50% of the cytostatic drugs remain in this region and only 50% enters the general bloodstream. This results in an increase in the concentration of drug in tumor and at the same time, a decrease in systemic toxicity. Arterial embolization is performed at a more distal level than surgical ligation, and therefore, it is a more reliable method of interrupting blood flow. Methods of local therapy (percutaneous ethanol injections, radiofrequency ablation, cryodestruction) are also aimed at direct destruction of tumor without significant damage to surrounding healthy tissues [9,10,12,13,15].

The other advantages of X-ray endovascular therapy techniques are as follows:

- Shorter recovery period compared to surgical treatment.
- Reducing the number of complications.
- Improving the effectiveness of antitumor effects.
- Possibility of repeated courses.
- Using in combination with other types of treatment (systemic chemotherapy, radiation, surgery, etc.).

More than 30 thousand new patients with malignant tumors are detected annually in Kazakhstan. Of these, in 30-40% of cases, different interventional procedures can be used as a part of combination therapy.

In some localizations, interventional methods are - and, or may be one of the leading methods of combination therapy of cancer patients, for example

- Liver cancer up to 80%
- Isolated secondary metastases of various liver tumors up to 80%

- Pancreatic cancer up to 50%
- Bone sarcomas up to 70%
- Cervical cancer up to 30%
- Kidney cancer up to 20%

Below are the main types of endovascular (interventional) procedures used in Oncology

- Angiography
- Regional intraarterial chemotherapy
- Chemoembolization
- Radioembolization
- Placement of infusion port systems
- Percutaneous drainage of bile and urinary ducts
- Stenting of hollow organs through a tumor
- Radiofrequency thermoablation (RFT) [2]

The objective of our research was to analyze the immediate and long-term results of interventional radiology methods in oncological practice at the premises of South - Kazakhstan Regional Oncologic Dispensary for a 17-year period (2004-2020).

## Materials and Methods

Since 2005, the first attempts to introduce intraarterial chemotherapy for cervical cancer have been started in South- Kazakhstan Regional Oncologic Dispensary (since 2018 - Shymkent City Cancer Center (CCC)), the technique was studied by the doctors Makhmutov N.T. and Arybzhhanov D.T. at Kazakh Research Institute of Oncology and Radiology of the Ministry of Health of the Republic of Kazakhstan. In June 2004, there was invited a specialist directly involved in this technique namely Shulyak V.V., Candidate of Medical Science, an angiosurgeon from Kazakh Research Institute of Oncology and Radiology, and the technique was introduced into everyday practice. In the future, methods of intraarterial chemotherapy were widely introduced (Arybzhhanov D.T.) in combination therapy of patients with pulmonary cancer, sarcomas of the limbs, pelvic tumors, etc.

In 2008, the specialists of Regional Oncologic Dispensary were trained at the Russian Research Center of Radiology and Surgical Technologies (RRCRST, St. Petersburg), and thus, Oncologic Dis-

pensary of South-Kazakhstan region was one of the first medical institutions that introduced the methods of chemoembolization for liver cancer, kidney cancer and cervical cancer.

Since 2009, after master class of Professor, Doctor of Medicine Ivshin V.G. (Tula), the technique of percutaneous interventions for obstructive jaundice in patients with obturation syndrome of biliary tract tumors was mastered and introduced into everyday practice.

In 2010, the methods of endovascular treatment of tumors such as intraarterial chemotherapy, chemoembolization, were included in the list of procedures performed as a technology of tertiary care (TC), and in 2011, Regional Oncologic Dispensary, the first institution among other cancer care facilities, established The Department of Chemotherapy and Endovascular Oncology by adding 60 hospital beds; this fact stimulated the development and wider implementation of interventional radiology methods in combination therapy of patients with various oncopathologies, there were implemented the methods of radiofrequency thermoablation, regional chemoinfusion into the vessels of the brain in glioblastomas, implantation of venous and arterial port systems, stenting of hollow organs through a tumor, etc.

Currently, the following main types of endovascular (interventional) procedures are widely used in Shymkent City Cancer Center:

- Angiography
- Regional intraarterial chemotherapy
- Transcatheter arterial chemoembolization (TACE)
- Placement of infusion port systems
- Percutaneous drainage of bile and urinary ducts
- Stenting of hollow organs through a tumor
- Radiofrequency thermoablation (RFT)

Currently, about 300 endovascular procedures are performed annually in Shymkent Cancer Center, more than 150 of them are performed as TC, using the Shimadzu X-ray diagnostic unit (Japan). By 2020, more than 3,700 intervention operations and X-ray surgical interventions have been successfully performed in our medical institution. Currently, there are 50 hospital beds at The Department of Chemotherapy and Endovascular Oncology, 8 doctors work there, among them 3 doctors mastered the technique and work in

this area (1 of them is a Candidate of Medical Science). All of them are trained at the Russian Research Center of Radiology and Surgical Technologies (St. Petersburg) within the program of Continuing Professional Development of South - Kazakhstan Health Department. In 2021, it is expected to use a biplane angiograph, which will significantly increase the number of procedures performed.

### The Outcomes and their Discussion

Below we present some data (on the example of a number of tumor localizations, including disease recurrences), which clearly show our achievements with the introduction of Endovascular surgery (Oncology) methods in Shymkent and South -Kazakhstan region

- The treatment outcomes of patients with recurrent grade III glioblastomas of the brain for 10 years (2011 - 2020) with the use of regional intraarterial chemotherapy in intracranial vessels
- There were studied the treatment outcomes of 22 patients with recurrent brain tumors. Women - 7, men - 15, aged 19-65 years. Morphologically, 20 patients had malignant brain tumors, 2 patients had malignant lymphoma.

All patients previously got combination therapy - surgery, radiation therapy (cumulative dose 60-70 Gray), 6-8 courses of Temozolamide chemotherapy. At the time of treatment, some patients had tonic-clonic muscle activity that was poorly treated by anti-seizure medications, some patients did not control the functions of pelvic organs and had general cerebral symptoms of compression of various brain structures. All patients were undergone the following chemotherapy: 1 day- Bevacizumabum (400mg miv), 2 day - intraarterial chemoinfusion into the internal carotid artery trunk - Cisplatinum (100mg/m2) + Dacarbazine (1000mg) (Figure 1).

Patients with malignant lymphoma were treated by Methotrexatum (1.5mg/kg), Carboplatinum (150mg/m2) - intraarterial introduction, Cyclophosphamidum (100mg miv) (infusion time of drugs diluted in 400ml NaCl 0.9% - 3 hours). The chemotherapy courses were repeated every 28 days, for a total of 4-6 courses.

Patients were observed for 1.5 years (18 months). During the follow-up period, CT and MRI showed partial regression of 7 (31.8%) patients, 9 (41%) patients showed stabilization, and 4 patients - progression 4 (18.2%). Complete tumor regression of patients with malignant lymphoma was showed after three chemotherapy courses.

Pelvic organ functions of 4 patients were restored, brain symptoms were reversed, and tonic-clonic muscle activity was regressed.

3 patients died 5 months after the treatment from progression of the core process by hemorrhagic tumors.

1 patient returned to receive specialist treatment after 9 months because of the process progression.

The average life expectancy of patients was 11.5-15 months. Only one patient lived for more than 20 months.

**Figure 1:** Angiograms of a. carotica int. during intraarterial preoperative chemotherapy into the Brain vessels.

The immediate treatment outcomes of patients with head and neck squamous cell carcinoma for 2 years (2018 - 2020) using regional intraarterial chemotherapy

During this period, we treated 42 patients at the age of 27-75 years suffering from head and neck squamous cell carcinoma by using intraarterial preoperative chemotherapy. In all patients, the process was within T2-3N1M0. There were 17 women (40.47%) and 25 men (59.53%). A locally advanced process prevailed in 31 (73.8%) patients. According to the tumor localization, the patients were grouped as follows: oral mucosal cancer-11 (26.2%) patients, tongue cancer - 6 (14.3%) patients, laryngopharyngeal cancer - 13 (31%) patients, nasopharyngeal cancer - 11 (26.2%) patients. All patients had morphological diagnosis verification, while 100% of patients had squamous cell carcinoma. Intraarterial preoperative chemotherapy was performed by femoral artery catheterization by

the Seldinger technique and selective catheterization with angiographic catheters of the external carotid artery supplying the tumor lesion area (Figure 2).

There was used a generally accepted chemotherapy regimen - Cisplatinum (80mg/m<sup>2</sup>) + Paclitaxelum (175mg/m<sup>2</sup>). Non-adjuvant chemotherapy consisted of 3 courses. The interval between the courses was 3 weeks (21 days).

The following outcomes were showed during dynamic follow-up period after 3 courses of intraarterial preoperative chemotherapy: 20 (47.6%) patients - significant regression of the process, 11 (26.2%) patients - partial regression of the process, 11 (26.2%) patients - stabilization of the process. There was no progression of the process. The treatment outcome showed that 73.8% of patients had a positive effect of treatment with a decrease in the size and prevalence of the tumor, which allowed them to subsequently undergo definitive radiation therapy (single tumor dose 2 Gray, total radiation dose 60 Gray).

Thus, the immediate outcomes of intraarterial preoperative chemotherapy as the initial stage of treatment of head and neck squamous cell carcinoma allow the completion of definitive therapy in more than 73% of patients. Its use in patients in late IIIa, IIIb stages allows contributing to the achievement of partial regression after 3 courses of therapy. Despite the effectiveness of intraarterial preoperative chemotherapy, it is only a stage preceding radiation or surgical treatment, so the method should be used as an initial, important link in combination treatment of head and neck cancer.

**Figure 2:** Angiogram of the left external carotid artery of the patient A., 43 years old, during intraarterial preoperative chemotherapy for head and neck squamous cell carcinoma (Diagnosis: cancer of the oral cavity (on the left, stage 3).

The treatment outcomes of patients with lung cancer T2N2-2M0 - T3N1-2M0 (the IIIa - IIIb stages) for 15 years (2004-2019) using intraarterial polychemotherapy.

There were treated 70 patients at the age of 42 - 77 years suffering from non-small cells lung cancer (NSCLC) (IIIa, b stages). Among them, 50 patients were treated by intraarterial preoperative chemotherapy. Morphologically, 5 patient had adenocarcinoma, 65 patients - squamous cell lung cancer. A chemotherapy regimen was used in standard dosages of EP scheme (Etoposide (120 mg/m<sup>2</sup>) + Cisplatinum (80 mg/m<sup>2</sup>) and TP (Docetaxelum (75 mg/m<sup>2</sup>) + Cisplatinum (75 mg/m<sup>2</sup>). Tumor regression after 2 courses of intraarterial preoperative chemotherapy (partial) - 47 (67.2%), stabilization - 15 (21.3%), progression - 8 (11.5%). The possibility of radical surgery in 49 (70%) patients, completion of beam therapy - 20% (p < 0.05). The 5-year survival rate was 14.3% (p < 0.05). The 7-year survival rate was 11.4% (p < 0.05). The 10-year survival rate was 5.7% (p < 0.05).

#### Possibilities of bronchial artery embolization in lung cancer

There was analyzed an experience of treating 12 patients at the age of 32-65 years suffering from locally advanced, central lung cancer (T3-4N1-2M0). Morphologically, 2 patients had adenocarcinoma, 8 patients had squamous cell lung cancer.

All patients underwent polychemotherapy courses due to inoperability. 8 patients - according to EP scheme: Etoposide (120 mg/m<sup>2</sup>), Cisplatinum (80 mg/m<sup>2</sup>), 2 patients - according to TP scheme: Taxotere (75 mg/m<sup>2</sup>), Cisplatinum (75 mg/m<sup>2</sup>). 12 patients (from the moment of treatment) had complaints of significant hemoptysis, especially with a severe cough with clots and scarlet blood in sputum.

After preliminary conservative hemostatic therapy, all patients underwent mechanical bronchial artery embolization (MBAE). The procedure was tolerated satisfactorily.

The treatment outcomes of patients with cervical cancer T2-3N0-1M0 (the IIa, IIb, IIIa stages) for 15 years (2004-2019) using intraarterial polychemotherapy

There were treated 100 women at the age of 23-59 years suffering from cervical cancer, 48 patients of the IIa-IIb stage, 52 patients of the IIIa stage.

- Tumor regression (significant + partial) at the stage II - 66%, at the stage III - 50%.
- The possibility of radical surgery at the stage II - 62%, at the stage III - 42% (p < 0.05).

- The 3-year survival rate at the stage II- 89.3%, at the stage III - 66,9% ( $p < 0.05$ ).
- The 5-year survival rate at the stage II - 82.3%, at the stage III - 61.7% ( $p < 0.05$ ).
- The 5-year survival rate in the presence of N1 in both stages - 26.5% ( $p < 0.05$ ).

The treatment outcomes of patients with cervical cancer T2-3N0-1M0 (the IIa, IIb, IIIa stages) for 12 years (2008-2019) using combination therapy with chemoembolization of uterine arteries

- There were treated 60 women aged from 28 to 57 years suffering from cervical cancer, 20 patients of the IIa- IIb stage, 40 patients of the IIIa stage.
- Tumor regression (significant + partial) at the stages II and III -71.7%.
- The possibility of radical surgery at the stage II - 53.8%, at the stage III-42.3% ( $p < 0.05$ ).
- The 3-year survival rate at the stage II - 86.7%, at the stage III- 63,3% ( $p < 0.05$ ).
- The 3-year survival rate in the presence of N1in both groups - 55.7% ( $p < 0.05$ ).

The treatment outcomes of patients suffering from cervical cancer with tumor bleeding for 12 years (2008-2020) using combination therapy with embolization of the great vessels

There were treated 17 women at the age of 33- 42 years suffering from the stage III cervical cancer with bleeding.

- The time of admission from the beginning of bleeding is 24-72 hours.
- The probability of posthemorrhagic anemia of 2-3 degrees - 100% (Hb 45-80g/l).
- The time of the urgent uterine artery embolisation is 1-1.5 hours from the moment of admission to the Regional Oncologic Dispensary.
- The procedure duration is 25-40 min. The time to arrest bleeding from the beginning of the procedure and "4-hands" working (2 angiosurgeons) is 7-15 minutes (depends on the anatomy of internal iliac artery). The efficacy of mechanical hemostasis is 100% (Figure 3, 4). The possibility to continue specialist treatment in more than 80% of cases (mainly combined radiation therapy).

According to the results of the work performed, there is a decrease in the one-year mortality from cervical cancer by 4.8% and the total mortality of female population by 1.2 per 100,000 thousand of population (in 2009 - 3.6, in 2020 - 2.4). There is an increase in the 5-year survival rate of patients with cervical cancer over the past 6 years by 3.9% (in 2014 - 49.3%, in 2020 - 53.2%).

**Figure 3:** Angiogram of the patient K., 47 years old. Diagnosis: cervical cancer of stage 3, total embolization of internal iliac artery on the left (with metal spirals and a hemostatic sponge).

**Figure 4:** Angiogram of the patient K., 47 years old. Diagnosis: cervical cancer of stage 3, total embolization of internal iliac artery on the right (with metal spirals and a hemostatic sponge).

The treatment outcomes of patients suffering from kidney cancer for 12 years (2008-2020) using transarterial embolization of renal artery



From 2008 to 2020, we have an experience of treating 27 patients with advanced kidney cancer T3NxM1, who underwent transcatheter chemoembolization of the tumor within the combination therapy.

- The age of patients is from 35 to 87 years. Men - 19, women - 8.
- On presentation, 7 patients had a solitary kidney.
- 9 patients had skeletal metastases, 12- lung metastases, and 6 -liver metastases.
- At the start of treatment, the Karnofsky Performance Status was estimated at 70-80%.

The first stage of kidney tumor embolization was made with a hemostatic sponge and polyvinyl alcohol particles, 7 patients underwent superselective tumor embolization of a solitary kidney. Further, all patients controlled by ultrasound investigation underwent a trepanbiopsy for diagnosis verification.

In order to relieve pain syndrome for spinal metastases, 5 patients received palliative radiation therapy in a total radiation dose (TRD) of 25 Gray. The second stage comprises palliative nephrectomy for the purpose of cytoreduction (3 patients).

8 patients (2008-2013) underwent 4-6 courses of immunotherapy by Vincristine (2mg) intravenously on the 1<sup>st</sup> and the 8<sup>th</sup> day + Roferon 4.5 million MU subcutaneously, 1-10 days + Bonefos (1500 mg) intravenously on the 1<sup>st</sup> day, then 1600mg orally from the 2<sup>nd</sup> day continuously for 1 year. As the second stage of treatment, 4 patients underwent immunotherapy and took bisphosphonates (Intron (3mln. MU subcutaneously + Zometa (4mg) once a month) in combination with targeted therapy by Avastin (400mg) intravenously, once in 21 days, 6 courses. 19 patients (from 2013 and thereafter) received targeted therapy- Sunitinib (50mg/per day), long -term administration, or Sorafenib (800mg/per day), long -term administration, the 2<sup>nd</sup> line drugs - Pazopanibum, Everolimus.

The treatment outcomes of patients with liver cancer for 15 years (2005-2020) using transarterial chemoembolization of the hepatic artery (TACE)

Endovascular methods of patients' treatment suffering from liver cancer were started in August 2005 with the technique of regional intraarterial chemoinfusion directly into the hepatic artery,

then, in July 2008, after relevant training of personnel, there was implemented the technique of chemoembolization of liver tumors (Figure 5,6).

Currently, we have treated 424 patients aged 25 to 82 years with hepatocellular carcinoma of III-IV stages. TACE was performed in a standard way using Lipiodol and Doxorubicinum (50-100mg). The interval between TACE courses is 1.5-2 months (6-8 weeks). Tumor regression after 3-6 courses of HACE (partial) - 112 (26.4%), stabilization - 190 (44.8%). Progression of hepatocellular carcinoma during treatment with fatal case (within 6-8 months) is 122 (28.7%).

The 1-year survival rate (all patients) were 260 (61.3%). The 3-year survival rate of patients of class B by Child-Pugh score, stage A-B according to the Barcelona classification were 157 (37%), class C by Child-Pugh score (early-stage C) - 89 (21%),  $p < 0.05$ .

The median survival: stage A-B according to BCLC-  $21 \pm 1.2$  months ( $p < 0.05$ ). The median survival: stage C according to BCLC-  $13 \pm 3$  months ( $p < 0.05$ ).

The outcomes of patients with liver cancer treated by chemoembolization are shown in figure 5-7. The analysis of the work performed showed that the survival rate of patients with liver cancer after TACE was 36.8%. For the first time in the last 10 years, there was observed a positive dynamic of one-year mortality and total mortality of patients with liver cancer in South- Kazakhstan region and Shymkent. Thus, the one-year mortality rate began to decrease intensively from 2007.

**Figure 5:** Liver angiogram before embolization.

**Figure 6**

For the period from 2008 to 2018, the one-year mortality rate of patients decreased by 32.4%. The total mortality of patients over the past 10 years has decreased by 2 times (5.7 per 100 thousand of population in 2004, in 2018, this indicator was 2.5 per 100 thousand of population). In general, it can be noted that the outcomes of transarterial chemoembolization in the treatment of inoperable patients with liver cancer in South Kazakhstan were fairly good and long-term ones; currently, there is a positive balance between the incidence of disease and mortality of the population from liver cancer.

**Figure 7:** Survival rate of patients with hepatocellular carcinoma after transarterial chemoembolization for 2008-2018 (according to the data of Shymkent City Cancer Center).

## Conclusions

Thus, X-ray endovascular methods of diagnosis and treatment in oncological practice may and should be widely used in order to improve the treatment outcomes, prolonging survival and improving the quality of life of oncologic patients. The use of such highly specialized methods of treatment makes it possible to meet the requirements set by the head of state and the government in the field

**Figure 8:** Indicators of the one-year mortality of patients with hepatocellular carcinoma in South Kazakhstan and Shymkent for 2004-2018 (15 years).

of modern healthcare development and to maintain a course aimed at studying, supporting and widely introducing advanced technologies for the treatment of serious cancer patients.

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