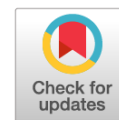


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# Венозный доступ для парентерального питания: что изменилось за последние 12 лет в Европе и Северной Америке?

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## АННОТАЦИЯ

В статье представлен обзор существенных изменений клинической практики, произошедших со времени публикации рекомендаций Европейской ассоциации клинического питания и метаболизма по обеспечению сосудистого доступа для парентерального питания в отношении выбора сосудистого доступа, профилактики и лечения наиболее частых осложнений длительно используемого венозного доступа — катетерассоциированной инфекции кровотока и обструкции внутреннего просвета катетеров.

Предпочитаемый сосудистый доступ при средне- и долговременном парентеральном питании — туннелируемый центральный венозный катетер, периферически имплантируемый центральный венозный катетер или полностью имплантируемая порт-система — теперь в значительной степени определяется основным заболеванием, ближайшим прогнозом жизни и комфортом пациента, а при кратковременном парентеральном питании в стационаре — в большей степени зависит от возможностей конкретного лечебного учреждения. Строгое соблюдение современных стандартных мер инфекционного контроля и ухода за венозным доступом и инфузионными линиями, гигиена рук, а также соответствующее обучение медицинского персонала, пациентов и ухаживающих за ними лиц являются в настоящее время самыми надёжными и эффективными способами профилактики катетерассоциированной инфекции кровотока. В качестве дополнительной меры применяется «замок катетера» тауролидином. Окклюзия внутреннего канала катетера в большинстве случаев может быть устранена лекарственным методом, однако его эффективность непосредственно зависит от соответствия выбранного препарата причине окклюзии.

В целом, произошедшие в последние годы изменения позволили значительно уменьшить частоту и опасность осложнений парентерального питания, связанных с сосудистым доступом.

**Ключевые слова:** венозный доступ; парентеральное питание; катетерассоциированная инфекция кровотока; КАИК; окклюзия венозного катетера.

## Как цитировать

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# Venous access for parenteral nutrition: Changes in Europe and North America over the past 12 years

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## ABSTRACT

This article provides an overview of the significant changes in clinical practices since the publication of the European Association for Clinical Nutrition and Metabolism guidelines on providing vascular access for parenteral nutrition regarding the choice of vascular access and prevention and treatment of the most common and important complications of long-term venous access, the catheter-associated bloodstream infection, and internal lumen obstruction of catheters.

The preferred vascular access for parenteral nutrition for medium- to long-term parenteral nutrition is the tunneled central venous catheter, peripherally inserted central catheter, or a fully implantable port system, which is now largely determined by the underlying disease, near-term prognosis and patient comfort, and short-term parenteral nutrition in a hospital that largely depends on the capabilities of a particular medical institution. Strict adherence to modern standard measures for infection control and care of venous access and infusion lines, hand hygiene, and appropriate training of medical personnel, patients, and their caregivers are currently the most reliable and effective methods to prevent catheter-associated bloodstream infection. Taurolidine “catheter lock” is used as an additional measure.

In most cases, the occlusion of the inner canal of the catheter can be eliminated by drug methods; however, its effectiveness directly depends on the correspondence of the chosen drug to the cause of the occlusion. Generally, changes in recent years have significantly reduced the incidence and risk of parenteral nutrition complications associated with vascular access.

**Keywords:** venous access; parenteral nutrition; catheter-associated bloodstream infection; occlusion/obstruction of the catheter.

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## INTRODUCTION

12 yr have passed since the publication of the guidelines of the European Society for Clinical Nutrition and Metabolism (ESPEN) on vascular access for parenteral nutrition (PN) in 2021 [1].

The Society experts devised recommendations in the form of answers to 12 questions concerning the formation of vascular access (Table, questions 1–5) for PN, prevention and treatment of the most common serious complications of venous access used long-term for PN, namely, catheter-associated bloodstream infection (CABI) (Table, questions 6–9), and obstruction of the internal lumen of the catheters (Table, questions 10–12). It is not surprising that these topics are significant even today. However, it is remarkable that

the answers of ESPEN experts, formulated from more than 10 yr ago, still remain relevant. Regardless, the provisions on venous access for PN did not become a subject of discussion or substantive revision in the most recent publication of the ESPEN guidelines for patients in intensive care units and other clinical groups (which the interested reader can familiarize with on the ESPEN website [2]), and were particularly considered only in relation to home PN [3]. However, general development of technologies, changes in the structure of medical care, and numerous clinical studies conducted in recent years have altered some of the emphases, if not the principles, enshrined in the ESPEN 2009 recommendations, which will improve specific clinical practice in relation to the small cohort of patients receiving home PN in Russia as well as those who receive PN in hospitals.

**Table.** Key issues of venous access for parenteral nutrition (based on [1], initial recommendations are abridged)

1	<i>Can parenteral nutrition be administered through the peripheral access?</i>
	Parenteral nutrition (PN) is recommended through a short peripheral cannula or through a midline catheter under constant close supervision by a medical staff (in hospital) for a short time and only using solutions with osmolarity not exceeding 850 mOsm/L.
2	<i>What is the preferred central venous catheter for parenteral nutrition?</i>
	For inpatient short-term PN, non-tunneled standard central venous catheters and peripherally inserted central venous catheters (PICCs) are used. For medium-term nutrition, PICC, Hohn catheter, tunneled central venous catheters (CVCs), and fully implantable port system are used. For long-term (>3 months) and home PN, tunneled CVCs or fully implantable port system are applied. Tunneled CVCs are preferred when daily access is required.
3	<i>Which access should be avoided when placing a standard central venous catheter?</i>
	Approaches through the femoral veins and “high” approaches to the internal jugular vein are not recommended.
4	<i>How should a central venous catheter be inserted?</i>
	Puncture (percutaneous) cannulation of the vein with dynamic ultrasound support of the procedure is recommended.
5	<i>What is the most appropriate position for the distal end of the central venous catheter for parenteral nutrition? Is a chest X-ray required after central venous catheter placement?</i>
	PN should be given through a catheter, the tip of which is located in the lower third of the superior vena cava, in the cavoatrial junction, or in the upper right atrium. X-ray control is mandatory if (a) the tip position was not validated during the procedure and/or (b) when the device was inserted using a blind subclavian access or other technique with a high risk of damage to the pleura and lung.
6	<i>What can reduce the risk of catheter-associated bloodstream infections?</i>
	The risk of catheter-associated bloodstream infection is reduced with the use of a tunneled CVC and a fully implantable port system (for long-term use), a standard antimicrobial-coated CVC (for short-term use), single-channel catheters (versus multichannel), PICC catheters (compared with a standard CVC without antimicrobial coating), ultrasound examination during access formation; the need to comply with the rules of asepsis and antisepsis during the access formation, as well as its preservation and use, is especially significant. The risk of catheter-associated bloodstream infection (CABI) is not reduced with the use of additional infusion line filters, “scheduled replacement” of the CVC, antibiotic prophylaxis, and filling the catheter with heparin solution.
7	<i>What is the best diagnostic method for catheter-associated bloodstream infection?</i>
	Quantitative or semi-quantitative cultural microbiological methods for examining a catheter removed; paired quantitative or qualitative cultural microbiological methods for examining blood from a peripheral vein and from a catheter with constant control of the time of a positive result of the inoculation.
8	<i>What should be done with a standard central venous catheter in case a catheter-associated bloodstream infection is detected?</i>
	In case of (a) obvious signs of infection at the site of catheter exit from the skin, (b) clinical signs of sepsis, (c) positive catheter culture test result with a guidewire exchange, or (d) positive paired blood cultures, the standard CVC should be removed. After removal of the catheter, appropriate antibiotic therapy must be continued.

**Table.** Ending

9	<i>What should be done with long-term venous access devices if a catheter-associated bloodstream infection is detected?</i>
	A long-term venous access device should be removed in case of (a) tunnel infection or periportal abscess, (b) clinical signs of septic shock, (c) detection of a fungal or highly virulent bacterial infection in paired blood cultures, and/or (d) a CABI complicated by endocarditis, septic thrombosis, or metastatic foci of infection. In other cases, one can try to save the device by inserting a "lock" with an appropriate antibiotic into the inner canal of the catheter.
10	<i>Should the catheter be flushed regularly? What solution should be used? How often should it be used?</i>
	Most central venous catheters for PN can be flushed with saline. If recommended by the device manufacturer, the heparin "lock" of the catheter without a distal valve should be used after flushing with saline when the catheter is in use for no more than 8 hr.
11	<i>How an occlusion of the internal lumen of the central venous catheter can be prevented? What is required in case it is detected?</i>
	Internal lumen occlusion of the catheter can be prevented with appropriate infusion protocols, including the use of infusion pumps.
12	<i>What should be done to prevent thrombotic complications associated with a central venous catheter (at the stage of access formation)? What activities are required in case they are detected?</i>
	The incidence of thrombotic complications can be reduced with ultrasound support for access formation, the choice of the smallest diameter catheter (provided that the patient can receive the necessary infusion therapy), and placement of the distal tip of the catheter in the cavoatrial junction.

## FORMATION OF VASCULAR ACCESS FOR PARENTERAL NUTRITION

In hospitals, a variety of venous accesses are used for PN, ranging from short peripheral catheters to fully implantable port systems (FIPs), due to the extensive variability of clinical scenarios, duration (often unpredictable), and intravenous nutrition regimens for patients in intensive care units or patients receiving treatment for acute or decompensated digestive tract lesions. It is generally used if the patient already has a venous access; e.g., in patients receiving PN in the early postoperative period, the preferred venous access was a standard (non-tunneled) central venous catheter (CVC) placed for intraoperative infusion. Moreover, in cancer patients in Europe or the USA, it was a peripherally inserted central catheter (PICC) or FIPs inserted for anticancer treatment even for short-term PN [4, 5]. In case of absence of suitable venous access, a standard CVC was usually inserted during hospital treatment, which was most likely be utilized not only for PN, but also for drug therapy, blood sampling, and so forth.

In terms of venous access for long-term and home PN, the ESPEN experts who participated in the development of the corresponding recommendations for 2020 unanimously supported the tunneled CVCs with a subcutaneous protective cuff or FIPs, however, considering the use of PICC catheters for the planned duration PN of less than 6 months [3]. Experts from the American Society for Parenteral and Enteral Nutrition (ASPEN) support the use of tunneled CVCs or PICCs for an estimated PN duration of less than 30 days for these indications [6]. However, in practice, the situation at the local level is frequently different. Even in North America, a region with a high adherence to the ASPEN guidelines, PICC (in Canada) or PICC and FIPs (in the USA) are very often used for daily home PN. Furthermore, tunneled CVCs have actually ceased to be the most widely used venous access for home PN in Canada, despite ASPEN recommendations. An analysis of the

Canadian Home PC Registry, which has been collecting data on patients, venous access used, PN programs, and outcomes since 2005, which identified the reasons behind this. The researchers discovered that the share of PICCs used for home PN increased from 21.6% to 52.9% between 2005 and 2008, whereas the share of tunneled CVCs decreased from 64.3% to 38.0% between 2011 and 2014. At the same time, a significant change in the composition of patients was revealed; e.g., the proportion of patients with cancer diseases increased from 16.7% to 37.9% during the same period, while the proportion of patients with short bowel syndrome decreased from 65.5% to 32% [7]. Because the duration of PN in cancer patients is often difficult to predict, and PICCs are the most common central venous access for anticancer drug treatment in Canada, they were simply used for PN when indications appeared without exposing the patients to hospitalization and additional risks associated with the formation of a new, more suitable venous access. A similar situation can be found in the United States and the European countries with high availability of medical care.

## PREVENTION OF CATHETER-ASSOCIATED BLOODSTREAM INFECTION

Apparently, the best results in the prevention of CABI can be achieved by thorough adherence to asepsis and antiseptics when working with components of catheters and infusion lines, contamination of which can lead to the spread of microorganisms into the inner part of the catheter and further into the bloodstream. High adherence to infection control measures and venous access care recommendations, such as hand hygiene, antiseptic treatment of problem areas where infusion lines are connected to catheters, skin of the catheter outlet area, as well as appropriate training of patients and their caregivers, reduces both the overall incidence of CABI and differences in the incidence of infection in different variants of venous vascular access significantly.

In Canada, the overall incidence of CABI for home PN was 1.58 per 1,000 catheter days from 2005 to 2009, while it was 0.97 per 1,000 catheter days in three academic centers that actively trained healthcare workers and patients on the rules of venous access care, not depending on the type of vascular access (more than half of the patients received treatment for short bowel syndrome; the median duration of PN and venous access functioning was 36 months and 281 days; and the frequency of use of tunneled CVCs, PICCs, and FIPSSs was 66.7%, 25.9%, and 7.4%, respectively). The rapid ubiquitous introduction of venous access care protocols led to a decrease in the overall incidence of CABI at home PN to 0.97 per 1,000 catheter days in Canada in the period 2011–2014 [7, 8]. The risk of CABI is considered one of the highest in patients with common types of cancer diseases, due to the duration of the inserted catheter use and their frequent application not only for PN, but also due to non-selective immunosuppression, transient bacteremia in mucositis, and tumor damage to the skin and mucous membranes. However, even in these patients, adherence to the standard measures of asepsis and antiseptics when operating with catheters and infusion lines reduces the incidence of CABI in PN; e.g., in an observational study of 335 cancer patients who received home PN (a total of 408 vascular accesses; FIPSSs, PICCs, and tunneled CVCs in 50.5%, 46.8%, and 2.7% of the cases, respectively), with a median PN duration of 54 days, the frequency of CABI amounted to 0.54 (95% confidence interval 0.32–0.86) per 1,000 catheter days [9].

The risk of CABI has significantly reduced, but still remains, with careful adherence by following the rules of asepsis, there is still interest in methods for sterilizing the internal lumen of catheters by injecting antiseptic solutions into them. A systematic review and meta-analysis of data from individual studies of the efficacy of CABI prevention using different options for washing and filling the internal lumen of catheters after use showed that the regularly using locks with taurolidine solution reduces the incidence of catheter-associated infection significantly [10], as it was reported that within 1 yr, CABI developed in 44% of patients whose catheters were filled with saline solution after use, and only in 12% of patients when using a taurolidine lock. Based on an independent analysis of the same research, ESPEN experts confirmed the desirability and safety of using taurolidine solution for the prevention of CABI in 2020 [3]. Unfortunately, the high price of the drug in Russia reduces its attractiveness and hinders its use significantly. The much cheaper ethanol lock technique using 70% medical alcohol has been demonstrated to be highly effective in several studies [11], although it has not yet received official approval for use with PN catheters.

## PREVENTION AND TREATMENT OF CATHETER OCCLUSION

In recent years, there has been a tendency to refrain from flushing and filling the lumen of PN catheters with

heparin solution, and the main reason for this is an increase in the incidence of CABI. In a study of the incidence of CABI with different compositions of solutions of catheter locks [10], it was revealed that with regular filling of the catheter lumen with heparin solution for 1 yr, 86% of the patients were diagnosed with CABI, i.e., almost twice as often as when the catheter was filled with saline solution (44%), and seven times as often as when the taurolidine solution was used (12%). This finding is not surprising, given that heparin, which is a glycosaminoglycan, is a possible nutrient substrate for microorganisms, promotes biofilm formation, and therefore increases the risk of CABI when the internal lumen of the catheter is contaminated. Some CVC manufacturers recommended a heparin lock, which is traditionally used to reduce the incidence of thrombosis in the internal canal of the catheter due to the “reflux” of blood into it in case of the long-term absence of infusion. With PN, the period without infusion is limited to a few hours, and patients rarely experience significant physical exertion that contributes to a change in the intrathoracic pressure and an active retrograde reflux of blood through the distal end of the catheter into its lumen. In fact, given the increased risks of CABI, an episode of CABI has a significantly higher cost (both in terms of mortality and in terms of material resources required for treatment) when compared with catheter occlusion. ESPEN experts do not recommend the insertion of a heparin lock in case the infusion is temporarily interrupted and after the catheter lumen is flushed with saline solution [3].

Currently, numerous methods are used in clinical practice to eliminate the occlusion of the CVC internal lumen, which are chosen based on both the availability of resources and the alleged cause of the catheter obstruction [12]. Mechanical cleaning of the internal lumen of the catheter with special brushes is a universal and, apparently, most effective method for resolving such problems. In the first comparative study of the efficacy and safety of mechanical and drug elimination of occlusion published in 2015, the rate of restoration of the PN catheter patency using brushes was 86% versus 50% with the thrombolysis technique ( $p < 0.0001$ ) [13].

However, mechanical restoration of the catheter patency is noticeably limited by the low availability of the necessary instruments, making the drug technique still relevant and in demand. This technique involves filling the inner lumen of the catheter with a drug solution that helps dissolve and remove subsequently the clots, precipitates, or other substances that caused the occlusion from the catheter. The effectiveness of the drug method of restoring the catheter patency depends directly on the correspondence of the drug selected to the occlusion cause. Blood clots in the catheter lumen can be eliminated by the administration of thrombolytic drugs; generally, a “lock” with a thrombolytic agent is inserted into the catheter twice, sequentially, with a 30 to 60 min exposure of each dose. The choice of a specific thrombolytic agent is important, as the efficiency

of elimination of the thrombus-associated occlusion of the catheter internal lumen, when using urokinase, is slightly less than 80%, and that of alteplase and reteplase is 86% and 95%, respectively [11]. The precipitates of most drugs dissolve well using “locks” with solutions of sodium hydrochloride (0.1 molar) or citrate. Reduction and complete occlusion of the catheter lumen, associated with the use of fat emulsions, is eliminated well by filling the catheter lumen with 70% ethyl alcohol with an exposure for 30 min or longer (“ethanol lock”). Due to the decrease in the capacity of the catheter internal channel, which is natural for occlusion, the drug solution corresponding to the occlusion cause should be injected slowly, initially in a volume smaller than the volume required for filling the catheter, maintaining a sufficient exposure time for the drug in the catheter lumen and trying to remove the contents from the catheter lumen completely before each repeated insertion of the drug.

## CONCLUSION

The most convenient for the patient and medical personnel and a reliable and safe access option for medium- and long-term PN is a modern tunneled CVC made of polyurethane or silicone and equipped with a subcutaneously fixed cuff that has its distal end inserted in the area of the cavoatrial junction of the superior vena cava, and the outer end is on the skin of the upper chest. Given the current prices of medical devices and medical services in Russia, this is also expedient

from an economic standpoint. At the same time, if the patient has one of the options for medium- or long-term access, other than a tunneled CVC, the need for its replacement seems questionable. The option of venous access for PN is not of fundamental importance for stationary short-term PN and should be selected based on an adequate assessment of the capabilities of a particular medical institution.

The most reliable and effective ways to prevent CABI are strict adherence to standard infection control measures and care for venous access and infusion lines, hand hygiene, and appropriate training for both medical personnel and patients and their caregivers. The taurolidine “catheter lock” can be used as an additional preventive measure for CABI.

In most cases, the occlusion of the catheter inner canal may usually be eliminated using drugs.

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