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GUIDELINE

Guidelines for Central Venous Port Placement and Management (Abridged Translation of the Japanese Version)

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Abstract:
The central venous port has been widely used for patients who require long-term intravenous treatments, and the number of palcement has been increasing. The Japanese Society of Interventional Radiology developed a guideline for central venous port placement and management to provide evidence-based recommendations to support healthcare providers in the decision-making process regarding the central venous port. The guideline consisted of two parts: (i) a comprehensive review of topics including preoperative preparation, techniques for placement or removal, complications, and maintenance methods and (ii) recommendations for the six clinical questions regarding blood vessels for central venous port placement, port implantation site, prophylactic antibiotic therapy, imaging guidance for puncture, disinfectant prior to accessing the central venous port, and the optimal procedure at the end of drug administration via the central venous port, generated on the basis of the rating quality of evidence by systematic review.

Keywords:
central venous port, central venous catheter, guidelines

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1. Introduction

The central venous (CV) port has been used for administering intravenous medications to patients who require long-term treatment. The number of placement has been increasing mainly due to the increase in the number of patients with cancer who require intravenous medical treatments and the widespread use of CV port in outpatient settings. The Japanese Society of Interventional Radiology (JSIR) developed a practice guideline for CV port placement and management to provide evidence-based recommendations addressing the palcement techniques and management issues of CV ports. This guideline also aims to provide support for the decision-making of medical professionals in clinical settings and does not compel medical professionals to follow the recommendations presented. The target audience includes medical professionals, such as physicians, nurses, and pharmacists, involved in the clinical practice using CV ports in Japan. The target patients include those scheduled for CV port placement and those who require CV port management following CV port placement. This guideline is focused on placement procedures and postprocedural management provided by healthcare providers. Drug therapy and drug-related adverse events and management by the patient and their family members are not covered by this guideline.

The certainty of evidence and classification of the strength of recommendations was determined using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system (**Table 1** and **2**) [1-14]. The recommendation type was classified into five types as

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Table 1. Graded Scale of Outcome Importance.

Grade scale								
1	2	3	4	5	6	7	8	9
Least important								Most important
Not important for decision-making (not included in the evidence profile)			Important for decision-making but not critical (included in the evidence profile)			Critical for decision-making (included in the evidence profile)		

Table 2. Classification of Evidence Certainty.

High	Moderate	Low	Very low
⊕⊕⊕⊕	⊕⊕⊕	⊕⊕	⊕

presented in **Table 3**. Furthermore, when the recommendation is weak, the term "weak" can be confused with evidence weakness; therefore, it can be replaced with "with conditions," "optional," and "limited." In this guideline, we will use the term "with conditions," or in other words, "recommendation subject to the setting, available resources, and patient sense of values" [1-14].

This guideline is based on its Japanese version, which was published in 2020 on the website of JSIR [15], and the publication of the current English version has been approved by JSIR.

2. Table of Clinical Questions and Recommendations (Table 4)

Clinical questions and recommendation are displayed in **Table 4**.

3. Clinically Important Matters in CV Port Placement and Management

3.1. What is a CV port?

The concept of CV port ("reservoir" in the Japanese article) was reported separately at the same time in 1982 in Japan and the United States [16, 17]. A CV port can be defined as medical equipment that satisfies the following three conditions: (1) connecting to a catheter inserted in the central vein enables long-term subcutaneous implantation of the overall system; (2) there is a space (chamber) communicating with the catheter lumen, and percutaneously puncturing this chamber enables repeat intravenous injection of a drug solution; and (3) the system itself does not have a pump function such as that for a continuous infusion [18]. CV ports are advantageous in that (1) they enable administration of drugs to the central vein easily and safely, (2) there is a low incidence of infection compared with CV catheters; and (3) there is no specific protection needed in daily life, and it has a discreet external appearance [18]. Conversely, disadvantages include (1) psychological stress caused by implantation of a foreign object, (2) the need for maintenance, and (3) adverse events caused by port fracture or inappropriate use [18]. Therefore, the indication of a CV port should be determined upon considering the balance between these advantages and disadvantages.

3.2. Preoperative preparation for CV port placement

As with CV catheter (CVC) insertion, it is extremely important to be aware that CV port placement can at times cause fatal complications. To avoid complications, options that do not involve CV port placement should be considered and alternative means should be considered for each individual patient, such as a usual CVC or a peripherally inserted central catheter [19]. Moreover, to place a CV port safely, it is preferable that the details involving the methods, procedure, management methods, and informed consent are standardized among institutions and medical departments. Additionally, there should be appropriate educational guidance and safe management systems within institutions and hospitals.

Before performing CV port placement, patient (age, gender, underlying illness, medical history, height, and weight) and test data (blood data and imaging findings) information should be collected as much as possible. Reported patient-specific risk factors for the onset of central vein puncture complications include obesity (body mass index (BMI) >30, underweight (emaciation, BMI <20), edema, blood coagulation disorder, surgical wound at the puncture site, respiratory function disorder, and a history of difficult-to-secure CVC [19, 20].

For the risk of hemorrhage, it is recommended that the platelet count is ≥50,000/μL, and the prothrombin time and internationalized normalized ratio is maintained at <1.5; however, these risks of hemorrhage have not been evaluated by a prospective randomized-controlled trial (RCT) [19, 20].

The withdrawal of antithrombotic agents (antiplatelet agents and anticoagulants) should be determined for each individual patient considering the balance with expected thromboembolism and the risk of bleeding after the procedure [21, 22]. With regard to antiplatelet agents, the procedure can be performed without a washout period for low-dose aspirin monotherapy. When two or more agents are used, each patient should be treated carefully, on a case-by-case basis [21-25]. It is thought that CV port placement can be performed after discontinuing edoxaban for 24 h and the thrombin inhibitor dabigatran and the direct factor Xa in-

Table 3. Recommendation Type.

Strength of recommendation	Strong	Weak	Weak	Weak	Strong
Recommendation	Recommended to "perform intervention"	Recommended to "perform intervention" with conditions	Recommended to either "perform or not perform intervention" with conditions	Recommended to "not perform intervention" with conditions	Recommended to "not perform intervention"

Table 4. Clinical Questions and Recommendations.

CQ number	CQ	Recommendation
1	Which blood vessels are used for a central venous access port?	Access via the internal jugular, subclavian, and brachial veins is recommended with conditions. Ancillary condition: Using image guidance for vascular access (see CQ 4). Children were excluded from the study. [Strength of recommendation: weak (with conditions), confidence of evidence: moderate]
2	Which port implantation site is suitable for CV port placement?	The site can be selected from the anterior chest region, lateral chest region, and upper limb depending on the patient's condition. [Strength of recommendation: weak, confidence of evidence: very low]
3	Is antimicrobial prophylaxis needed at the time of CV port placement?	No high-quality evidence that indicates the effectiveness of antimicrobial prophylaxis at the time of CV port placement is presented, and considering the increased risk of an allergic drug reaction caused by simple antimicrobial usage and the increased risk of antimicrobial-resistant microorganisms, the use of antimicrobial prophylaxis is not recommended. [Strength of recommendation: weak, confidence of evidence: moderate]
4	Is image guidance useful for CV port placement?	It is recommended to use ultrasound guidance for venipuncture at the time of CV port placement. (In particular, it is preferable to perform venipuncture while confirming the target vein and puncture needle in real time using two-dimensional ultrasound.) [Strength of recommendation: strong, confidence of evidence: moderate]
5	What disinfectant is used during puncture for the CV port?	Unless contraindicated, it is suggested to use an alcohol-based disinfectant. [Strength of recommendation: weak, confidence of evidence: low]
6	What is the procedure upon completion of drug administration via the CV port?	After flushing with physiological saline upon completion of drug administration via the CV port, it is recommended to lock with positive pressure using physiological saline or physiological saline with heparin. [Strength of recommendation: weak, confidence of evidence: low]

hibitors rivaroxaban and apixaban for 48 h. Generally, heparinization is unnecessary during the preoperative washout period of direct oral anticoagulants; however, in the group at high risk of stroke, it is thought that heparinization is necessary [21-25].

Apart from antithrombotic agents, agents that require caution include vascular endothelial growth factor inhibitors such as bevacizumab [21, 26]. Although it is thought that the same extent of caution is unnecessary for CV port placement as that for major surgery such as organ resection, it should be understood that delayed wound healing can occur. Although it has been reported that CV port placement is possible during bevacizumab therapy, it has also been reported that a washout period of approximately 1 week should be allowed; as such, opinion is controversial [21, 26].

3.3. Actual techniques of CV port placement

Central vein puncture includes surface landmarks, ultrasound guidance, vein angiography, and venous cut down (venesection) [21]; however, it is recommended to use some type of image guidance (CQ 4). Furthermore, realtime ultrasound-guided puncture should be performed upon understanding the characteristics and pitfalls of ultrasound. The subclavian, internal jugular, and brachial or forearm veins are generally used as blood vessels to be punctured (CQ 1). The basic CV port placement method for a typical access vessel using ultrasound guidance is described as follows [19-21]:

①CV port placement is to be performed at a location where aseptic manipulation can be ensured such as in an operating theater or angiography room. Pretreatment and premedication are essentially unnecessary except for pediatric or agitated patients. (For antimicrobial prophylaxis, refer to CQ 3.)

②Ultrasound examination of the target vein is performed (at 5-7.5 MHz for superficial use), and the positional relationship of the vein and artery, vascular diameter, and presence or absence of thrombosis are evaluated.

③In compliance with the maximal barrier precaution, the practitioner puts on sterile gloves and a sterile gown, after which they prime CV port and catheters and prepare equipment in advance, such as setting the suture thread in the needle holder.

④Disinfection of the planned suture site is performed at least twice, and a sterile drape is placed over the patient (CQ 5). The ultrasound probe is also covered with a sterile cover.

⑥While confirming the vein via ultrasound, a local anesthesia is injected from the skin to near the surface of the vein.

⑦The vein is punctured under ultrasound guidance. After puncturing the vein and confirming venous blood suction using a syringe, a guidewire is carefully inserted.

⑧In the event of over-the-wire type equipment, a peel-away sheath is inserted intravascularly along the guidewire, and after leaving the guidewire and removing the sheath inner tube, a catheter is inserted, and the sheath outer tube and guidewire are removed.

⑨The position of the catheter tip is verified via fluoroscopy.

⑩A subcutaneous pocket is created. Then, the catheter is cut at an appropriate length and is connected to the port, and the port is implanted in the subcutaneous pocket. If necessary, the catheter is passed through the subcutaneous tunnel and/or the port is fixed with two sutures to the subcutaneous adipose tissue or the pectoral fascia.

⑫The skin is sutured to close the incised wound of the skin pocket, and the port is locked with positive pressure using physiological saline or heparinized physiological saline. Last, the absence of bending or abnormal positioning of the catheter and complications, such as pneumothorax, is confirmed via fluoroscopy.

The operators of CV port placement should pay attention to the catheter tip position because serious complications can occur depending on its position. It has been reported that the incident rate of complications, including tip malposition, thrombus formation, and pleural effusion, is high when the CVC tip position is higher than the tracheal bifurcation site [27-30]. Furthermore, when the tip is in the right atrium, cardiac tamponade and thrombus formation have been reported [19, 31, 32]. It is thought that the appropriate catheter tip position lies between the tracheal bifurcation site and the cavoatrial junction. Furthermore, it has been found that the tracheal bifurcation site usually lies superior to the cavoatrial junction, and although the distance between the tracheal bifurcation and cavoatrial junction differs depending on the modality, it is said to be approximately 3.5-5 cm. Therefore, it is considered valid to position the catheter tip 2 to 3 cm on the cardiac side (caudal side) from the tracheal bifurcation.

3.4. Intraoperative complications of CV port placement

The incidence rate of arterial puncture is approximately 5%-10% in blind puncture cases using the landmark method, which is higher than that in ultrasound-guided puncture cases. Hematoma removal is indicated when the trachea and/or nerve were compressed or hematoma infection occurred.

It has been reported that pneumothorax has an incidence rate of 0.5%-2% and 0.2%-0.5% in subclavian and internal jugular vein puncture cases, respectively [33]. When symptoms are severe, chest drainage can be indicated. Air embolism is the state of air migration in the venous system via the catheter or sheath and occurs in 0.3% of cases [34]. The migration of air in small amounts is not a problem; however, when large amounts of air migrate, symptoms such as cyanosis, increased respiratory rate, hypotension, and cardiac murmur are observed. When symptoms are severe, hyperbaric oxygen therapy is indicated [35]. Depending on the injured nerve, symptoms observed in nerve injury include pain running through the tips of the fingers and toes, numbness, and difficulty in breathing [36]. Discontinuing the procedure will improve the symptoms. In left subclavian vein puncture, thoracic duct injury can occur on extremely rare cases. Lymphorrhea into the thoracic cavity causes chylothorax [37]. When the leakage cannot be stopped, suturing or embolization of the thoracic duct is needed in some instances. Iatrogenic arteriovenous fistula is a rare complication caused by intravenous insertion of the catheter through the artery. Arrhythmia occurs as a result of sinus node contact with the catheter. Arrhythmia can be avoided by intraoperative electrocardiographic monitoring and catheter insertion under fluoroscopy. It has been reported that heart and major vessel injuries occur extremely rarely as a result of blind or careless catheter manipulation; with device improvements, such injuries are no longer seen in recent years. Although rare, there have been reports of fatalities associated with central vein puncture. The causes of such deaths are reported to include asphyxiation caused by hematoma in the neck region associated with internal jugular vein puncture, superior mediastinal, and right pleural hemorrhage caused by vertebral artery injury, changes in hemodynamics caused by pneumothorax, and fatal arrhythmia secondary to cardiac tamponade caused by perforation of the right ventricle with the catheter [19, 38].

3.5. Complications following CV port placement

Complications after CV port placement include catheter-related bloodstream infections (CRBSI; refer to Section 3.6), fibrin sheaths (see Section 3.7), thrombophlebitis (see Section 3.8), subcutaneous extravasation of anticancer agents (see Section 3.9), catheter deviation, catheter fracture (pinch-off syndrome), and catheter removal difficulty [35, 39, 40]. Catheter deviation can occur as a result of postural changes, and it has been reported that a catheter tip located in the left brachiocephalic or azygos vein is prone to thrombus formation. When deviation is observed, the catheter needs to be replaced or repositioned. Catheter fracture due to compression (pinching off) occurs using the subclavian vein approach. Catheters compressed between the clavicle and the first rib can be damaged by mechanical wear and tear. When catheter fracture is observed, the catheter should be removed at the earliest.

3.6. Diagnosis and treatment of CRBSI

The diagnosis and treatment of CRBSI already have several guidelines, which will be described in this study based

on guideline descriptions.

As suggested by the Centers for Disease Control and Prevention (CDC), catheter-related infection (CRI) can be subdivided into catheter colonization, local CRI, infusate-related BSI, and catheter-related BSI [41, 42]. In the Japanese Association for Infectious Diseases/Japanese Society of Chemotherapy guidelines for management of infectious diseases 2017, sepsis and CRBSI [43], the following is a summary regarding CRBSI in adult patients:

・The same organism grows from at least one set of percutaneous blood and catheter tip cultures is required for the diagnosis of CRBSIs. Furthermore, diagnosis is determined on the basis of percutaneous blood sampling and blood culture collected from the catheter [44-47].

・Typical pathogenic microorganisms include coagulase-negative *Staphylococcus*, *Staphylococcus aureus* (including methicillin-resistant *S. aureus*, MRSA), *Candida* genus, *Enterococcus*, and gram-negative bacillus (*Escherichia coli*, *Enterobacter* genus, *Pseudomonas aeruginosa*, *Klebsiella* genus, etc.) [48, 49].

・Antibiotic therapy is initiated after performing blood culture of two sets or more whenever possible [44]. (One set is defined as catheter blood sampling.) However, antibiotic therapy must not be delayed to prioritize blood culture [50, 51].

・As empiric therapy, the combined use of anti-MRSA agents and broad-spectrum antimicrobials is recommended [52].

・For definitive therapy, antimicrobial drugs are selected on the basis of the pathogen.

Infection is also a major complication related to CV ports. If infection develops, it can result in sepsis with serious deterioration of the patient's condition, and port removal will be required. According to Crnich et al. [53], the mean incidence rate of BSI related to a CV port is 0.2 infections per 1,000 days in 13 prospective studies. To manage the infected CV ports, accurate and early diagnosis is mandatory [54]. Blood culture should be collected when CRBSI is suspected [55]. Antibiotic therapy will be continued or ceased according to the clinical courses including results of blood culture and other infective complications [56]. CV port removal is sometimes impossible because of the risk of hemorrhagic complications or lack of alternative blood access routes [41]. For these cases, continuous administration of antibiotics is required for a longer period [55]. Port infection in the subcutaneous pocket without BSI can be treated with local treatment such as port removal combined with antibiotic therapy [41, 44, 55-57]. Empirical systemic administration of antibiotics should be initiated when CRBSI is suspected, and it can be modified depending on the results of blood culture or other microbiological examinations. Additionally, metastatic infective diseases, such as endocarditis, are investigated [41, 55].

Treatment methods for patients with BSIs related to long-term indwelling CVCs and CV ports can be found in other guidelines regarding the diagnosis and management of intravascular CRI [44].

3.7. Diagnosis and treatment of fibrin sheaths

Immediately after catheter placement, thrombi start to form at the catheter tip as a result of intravascular protein and cell deposition, and within 24 h, albumin, lipoproteins, and fibrinogen form a protein sleeve around the catheter. As a result, coagulation factors and platelets aggregate, a fibrin sheath is formed, and the catheter is wrapped in it [58, 59].

Contrast injection via the port is useful for diagnosing fibrin sheaths and intracatheter thrombi, whereas ultrasound examination and venography are useful for diagnosing mural thrombi and venous thrombosis [60]. Fibrin sheaths are first suspected when injections can be made but suctioning is impossible via the port, and they are diagnosed via contrast injection via the port. Fibrin sheaths characteristically present "pseudoenlargement signs" of the catheter during contrast injection. Linear flux or a jet of contrast medium, or both, is observed along the catheter. A fibrin sheath can also form a pouch distal to catheter tip, which can be filled with contrast medium. Furthermore, catheter adherence to the vessel wall is suspected when its tip does not move with heart motion and patient movement and moves closely with vessel wall movement [61]. Other diagnostic imaging includes ultrasound examination, X-ray, and computed tomography (CT) [62-64].

Treatments for CVC malfunction caused by fibrin sheaths include intracatheter infusion of a thrombolytic agent, fibrin sheath stripping, balloon angioplasty, catheter exchange, and catheter replacement [65-72]. Infusion of a thrombolytic agent is minimally invasive, safe, inexpensive, and can be performed in the hospital ward; thus, it is preferred by patients and is an easier option than stripping. In urokinase infusion, urokinase of 40,000 units per hour or 60,000 units per hour is administered for 6-12 or 4 h, respectively [67-70]. It has been reported that the success rate of urokinase infusion was 76%-97% and that there were no complications [67-71]. A large-scale prospective study reported that the success rate of using tPA was 86%-93% for various CVCs and 79% for CV ports, and the overall 30-day catheter patency rate was 74% [66]. Stripping is a method of grasping and pulling the catheter using a snare accessed via the femoral or brachial vein to strip away substances surrounding the catheter that cause occlusion. This procedure has the risk of making embolic substances flow into the pulmonary artery [59]. Although stripping has a reported success rate of 92%-98%, which is slightly better than that of thrombolytic agent infusion, the patency period is comparable with that of thrombolytic agent infusion [59, 61]. In a prospective trial comparing urokinase infusion and stripping as treatments for fibrin sheath around dialysis catheters, Gray et al. reported success rates in the urokinase and stripping groups (improved flow rate) of 97% and 89%, respectively. The 30-day patency rates of the urokinase and stripping groups were 63% and 52%, respectively, and the median patency periods of the urokinase and stripping groups were 42 and 32 days, respectively, with no significant difference in the patency period on the patency curve [67].

3.8. Diagnosis and treatment of thrombophlebitis

Thrombophlebitis is a condition that is particularly commonly observed in superficial veins. Pressure pain, redness, and swelling are found at the affected site of the vein, and it is called superficial thrombophlebitis (STP). When sudden swelling and pain are observed in the upper arm and head and neck regions on the side of port placement, thrombophlebitis and venous thrombosis are suspected. When thrombus formation is sudden, anticoagulant therapy is indicated [73]. In general, the prognosis of thrombophlebitis is considered good [74]. However, when thrombi progress in a central direction, it is called ascending thrombophlebitis and can cause deep venous thrombosis (DVT) and pulmonary embolism, which require emergency treatment [75, 76].

There are no reports with robust evidence regarding thrombophlebitis in CV ports, and most reports are of retrospective case studies. There are many reports of thrombophlebitis involving CV access catheters, and it is considered that such reports should be referenced for CV port placement.

It has been reported that ultrasound examination is useful for evaluating thrombophlebitis and determining catheter removal [77]. In a multicenter prospective trial, 458 CVCs (including CV ports) of 416 patients with cancers of the blood were investigated. CVC-related DVT, lower limb DVT, pulmonary embolism, CVC-related STP, thrombus-induced CVC occlusion or malfunction, and atherothrombotic disease were observed in 1.5%, 0.4%, 1.3%, 3.9%, 6.1%, and 1.1% of blood cancer cases, respectively [78].

3.9. Treatment of subcutaneous extravasation of anticancer agents

A CV port is placed to administer anticancer agents safely; however, malfunction of the CV port system can cause complications such as subcutaneous extravasation of anticancer agents.

Drug extravasation is caused by technical factors at the time of puncture and by defects in the CV port system. Technical factors include erroneous needle puncture, inadequate puncture needle fixation, and the use of a needle with inappropriate length. In these instances, bodily motion can cause displacement of the needle followed by drug extravasation. Causes attributed to CV port system defects include catheter pinch-off syndrome when the catheter is compressed between the clavicle and rib, port septum damage, catheter falling out of the port, secondary reflux caused by fibrin sheath or thrombosis, and the catheter tip being pulled out subcutaneously [79, 80].

A risk factor of subcutaneous extravasation is a high BMI (>30). Patients with a high BMI have thick subcutaneous adipose tissue; therefore, it is considered possible that they are susceptible to puncture needle withdrawal and catheter displacement [79].

It has been reported that the incidence of subcutaneous drug extravasation was 0.2%-1.2% [79, 81, 82].

Furthermore, CV port system damage cannot be diagnosed by imaging with contrast injection via the port, and when CV port system damage is suspected, it is important to remove the CV port and replace it with a new CV port before complications become serious [83].

When patients notice symptoms such as pain, it is possible that time has passed since the onset of extravasation. Early detection and treatment of extravasation helps to minimize subsequent damage; therefore, it is important to instruct patients to notify their medical institution immediately upon experiencing symptoms. In the event of subcutaneous extravasation of small amounts of irritant and nonvesicant drugs, conservative treatment (follow-up observation, steroid ointment application, and local steroid injection) is a therapeutic option. In the event of subcutaneous extravasation of vesicant drugs, such as anthracyclines, vinca alkaloids, mitomycin C, and taxanes, some cases are resistant to the aforementioned conservative treatments. In such cases, early removal of the CV port (within 48 h of subcutaneous extravasation) and wound lavage (2,000 mL) should be performed. Forty-eight hours after subcutaneous extravasation, CV port removal and, depending on the situation, debridement plus skin flap will be needed [79]. At the time of extravasation of anthracycline anticancer agents, intravenous administration of dexrazoxane is also considered. When extravasation of vesicant drugs occurs, ulceration and necrosis of the skin can develop; therefore, the departments of dermatology and plastic surgery should be consulted. In reports to date, there are no evidences to support the recommendation of treating extravasation of anticancer agents by applying cold or hot compress; however, such treatments are often performed as symptomatic treatment. Furthermore, the effectiveness of raising the affected limb has not been demonstrated [84].

3.10. CV port system removal

Situations to consider CV port removal are broadly divided into when (1) a clinical reason to use a CV port is no longer present, (2) the CV port has been indwelling over a long period, and (3) complications caused by the CV port appear. Although there is no clear definition of long-term placement, it has been reported to cause difficulty in CVC removal at an incidence rate of 0.3%-2.0%, and removal becomes difficult in children with indwelling catheters over 20 months or with blood disease. When the clinical reason for using a CV port is lost, it should be removed without delay.

The basic procedure for CV port removal involves making a skin incision near the port indwelling site and then removing the port, after which it is simple to pull out the catheter attached to the port, and usually, hemostasis can be achieved by applying pressure alone. Furthermore, blood can easily accumulate in the pocket area where the port was inserted; therefore, postoperative compression should be applied.

Removal difficulties are broadly divided into port and catheter removal difficulties [85]. Port removal difficulties can be caused by strong adhesion between the port and subcutaneous tissue. In patients with ports for long-term usage, in many instances, the area of subcutaneous tissue with the

adhesion becomes thin and the skin also becomes fragile; therefore, careful manipulation is needed to avoid skin damage. Catheter removal difficulty is primarily caused by adhesion between the catheter and blood vessel [86, 87]. It is believed that thrombi around the catheter or between the catheter and the vascular endothelium are replaced by tissue including collagen, fibrin, and vascular endothelial cells, leading to strong adhesion between the catheter and vascular intima [88]. In the removal of difficult-to-remove catheters, to mechanically separate adhesion of the catheter and vascular intima without catheter tear, various methods have been attempted such as pushing the catheter, inserting a guidewire into the catheter and rotating it, inserting a guidewire and catheter into the adhesion site, inserting a coaxial sheath, and separating the adhesion site using a balloon catheter. However, in the event of long adhesions, it is common for removal to be extremely difficult. When the catheter cannot be removed despite attempting these manipulations, consider extracting the port only and leaving the catheter. Several reports have indicated that when there is no infection, leaving the catheter will cause no clinical problem, and when the risk of catheter removal is high, leaving the catheter is a permissible option from a clinical risks-benefits perspective [85, 89]. Conversely, when there is infection, the catheter needs to be removed, and in such instances, catheter removal via surgical procedures involving vascular resection and vascular dissection should be considered.

4. Clinical Questions

4.1. CV port placement

CQ 1: Which blood vessels are used as an access site for CV port placement?

Recommendation:

The internal jugular, subclavian, and brachial veins are conditionally recommended as access sites.

Ancillary condition: Using image guidance for vascular access (see CQ 4). Children were excluded from this CQ.

[Strength of recommendation: weak (with conditions), confidence of evidence: moderate, agreement rate: 100%]

Commentary

The primary access sites for CV port placement include the internal jugular, subclavian, brachial, cubital, and femoral veins; however, there is no robust evidence to recommend which vein to use. In a single RCT comparing CV port access sites and methods, it has been reported that the technical success rate for vascular access was significantly higher for ultrasound-guided subclavian vein access than for internal jugular vein access using the landmark method and surgical (cut down) cephalic vein access. In terms of complications, there was no significant difference observed in short-term (mechanical) and long-term complications [90, 91]. Several RCTs of CVC [92-94] and a Cochrane review with four RCTs including the aforementioned RCT of CV ports [91] have been published. According to the Cochrane review, among long-term complications, there was no significant difference between internal jugular and subclavian vein access sites in the risks of CRBSI and venous thrombosis, whereas less colony formation at the catheter tip and thrombosis were observed with the subclavian venous access compared with the femoral venous access. For patients with cancer who require long-term usage of CV ports, no significant difference in the risk of complications was demonstrated for the internal jugular and subclavian veins. Given the assumption of long-term usage of CV ports, long-term complications that interrupt usage are important factors to be considered. Also, mechanical complications at the time of placement should be considered when selecting the access site. In the Cochrane review, unsuccessful placement and mechanical complications were significantly more frequent in the subclavian vein; however, in all studies, image guidance was not used and the landmark method was used. The usefulness of image guidance is described in detail in CQ 4. In this guideline, image-guided vascular access is endorsed, and the internal jugular, subclavian, and upper limb veins are recommended as the access sites of CV port placement, considering few unsuccessful placements and few mechanical complications in ultrasound-guided subclavian vein access [90] although the strength of its recommendation is weak. The femoral vein is not recommended if other veins can be used, because a significantly high risk of infection was reported with the femoral venous access.

CQ 2: Which port implantation site is suitable for CV port placement?

Recommendation:

The site can be selected from the anterior chest region, lateral chest region, and upper limb depending on the patient's condition.

[Strength of recommendation: weak, confidence of evidence: very low, agreement rate: 100%]

Commentary

As a result of secondary screening, 26 articles from PubMed were included in the evaluation. The articles selected for these screening operations were all "case reports" or "case series" and provided a very low strength of evidence.

According to these articles, the site of port implantation primarily included the anterior chest region, lateral chest region, and upper limbs, for which the incidence of complications (wound infection, skin ulcer, systemic infection, phlebitis, and thrombi, etc.) varied from 0% to 33%. However, there was great discrepancy in the observation period and patient condition at baseline among these reports. Few articles indicated a significant difference according to implantation site. Although there are reports indicating a significantly frequent incidence of thrombophlebitis in upper limb implantation [95, 96], this is thought to be affected by the catheter length and vein diameter, and it is unclear whether the frequency of complications increases in relation to the implantation site itself. It has been reported that complications are frequent in port placement on the caudal side of the breast [97]. Although there are reports of port placement in the abdominal and femoral regions [98], it is difficult to compare the incidence of complications with other sites be-

cause only few cases were included.

With regard to the esthetic outcomes and patient satisfaction level, it has been reported that there is less discomfort with forearm ports when performing specific activities compared with the discomfort with chest wall ports [96]. Additionally, it has been reported that puncturing is difficult with abdominal wall ports [98], and a case has been reported in which the chest wall port was damaged by a seatbelt during a traffic accident [99]; however, each report included only one case.

Additionally, in the Cochrane review, no evidence was found with regard to port implantation site.

CQ 3: Is prophylactic antibiotic therapy needed for CV port placement?

Recommendation:

There is no robust evidence presented that indicates the effectiveness of antimicrobial prophylaxis at the time of CV port placement, and considering the increased risks of an allergic reaction caused by aimless antimicrobial drug usage and resistant microorganisms, the use of antimicrobial prophylaxis is not recommended.

[Strength of recommendation: weak, confidence of evidence: moderate, agreement rate: 100%]

Commentary

There are few reports that examined antimicrobial prophylaxis at the time of CV port placement. Many previous reports also investigated CVC placement. Reports with robust evidence restricted to CV ports are limited to two RCTs [100, 101] and one meta-analysis [102]. Other reports are recommendations integrating retrospective studies and expert opinions [103-108]. Furthermore, the type of antimicrobial used and the definition of infective complications have not been standardized between these studies.

In CV port placement, the incidence of early infective complications (within 30 days) is low and at 0%-3% in the group without antimicrobials [100-102]. Furthermore, in the group with antimicrobial prophylaxis used at the time of CV port placement, the incidence rate of early infective complications is 0%-2.5%, and no evidence supporting that antimicrobial prophylaxis reduces the risk of early infection has been found in either randomized trials or meta-analyses. In a retrospective controlled study (n = 459), it was reported that the incidence rates of CRBSI that required port removal were 0% and 2% in the groups with (n = 103 patients) and without (n = 356 patients) antimicrobial prophylaxis, respectively; however, the difference was not statistically significant (p = 0.218) [104].

Although no evidence has been found in the aforementioned reports indicating the benefits of antimicrobial prophylaxis at the time of CV port placement and the harm of prophylactic antimicrobial therapy, frequent use of antimicrobials without a specific reason increases the risks of drug allergy and resistant microorganisms; therefore, the prophylactic use of antimicrobials is not recommended in these guidelines. Antimicrobial prophylaxis at the time of CV port placement should be administered in a limited manner considering the patient risk, such as that in patients who are immunosuppressed [102].

CQ 4: Is image guidance useful for CV port placement?

Recommendation:

It is recommended to use ultrasound guidance for venous puncture in CV port placement. (In particular, it is preferable to perform venous puncture while confirming the target vein and puncture needle in real time using two-dimensional ultrasound.)

[Strength of recommendation: high, confidence of evidence: moderate, agreement rate: 100%]

Commentary

Venous puncture has conventionally been performed using the landmark method, whereby bones and parallel-running arteries are palpated to estimate the position of the target vein anatomically. However, with developments in diagnostic imaging modalities, image-guided puncture, such as fluoroscopy guidance in which the delineated vein using venography is punctured upon fluoroscopically and ultrasound guidance in which the target vein is delineated using ultrasound and then punctured, has gained popularity. In particular, ultrasound guidance is noninvasive and inexpensive and is widely used in clinical practice. In reports to date, ultrasound-guided puncture includes the methods of (1) puncture while observing the target vein and puncture needle in real time on two-dimensional ultrasound, (2) confirming the location of the vein in advance on ultrasound and not using ultrasound during puncture, and (3) using Doppler ultrasound. In Japan, method (1) is most commonly used at the time of venous puncture [109].

Veins typically punctured in CV port placement include the subclavian, internal jugular, arm, and femoral veins (refer to CQ 1). These are selected similarly as veins selected for CVC; therefore, in this CQ, the literature regarding CVC placement was screened and evaluated as subjects.

As related evidence, 2 Cochrane reviews, 2 meta-analyses, and 10 RCTs were confirmed. The results of the Cochrane reviews and meta-analyses differed slightly; however, it was found that the incidence of complications caused by ultrasound-guided puncture was low and the success rate of venous cannulation was high, with unconfirmed evidence indicating the superiority of the landmark method [110-114].

4.2. CV port management

CQ 5: What disinfectant should be used prior to accessing the CV port?

Recommendation:

Unless contraindicated, the use of an alcohol-based disinfectant is proposed.

[Strength of recommendation: weak, confidence of evidence: low, agreement rate: 100%]

Commentary

Twelve articles (6 articles in PubMed and 6 articles in the Japan Medical Abstract databases) that described disinfection prior to CV port puncture were found. Among these, many articles described disinfection at the site of CV port placement and CVC insertion just before the procedure although few articles mentioned disinfection prior to port

puncture.

We found four RCTs of skin disinfection at the site of intravascular indwelling catheter insertion [115-118]. In an RCT of skin disinfection at the site of intravascular indwelling catheter insertion in patients with hematologic disease [118], chlorhexidine (CHG) 1% and povidone iodine (PI) 10% were compared, and CHG was found to be superior for preventing catheter infection than PI. In an RCT of skin disinfection at the site of intravascular indwelling catheter insertion [116], octenidine hydrochloride, a new agent used for eradicating MRSA with comparable efficacy as CHG, was found to be superior for preventing catheter infection than conventional disinfection with ethanol. In an RCT of disinfection at the site of intravascular indwelling catheter insertion of adult patients in the intensive care unit [117], PI 10%, CHG 2%, and CHG 5% were compared and both CHG 2% and CHG 5% were found to be superior for preventing catheter infection than PI 10%. In RCT [115], with regard to disinfection at the site of intravascular indwelling catheter insertion, a meta-analysis was conducted of disinfection using CHG and PI 10%, and the conclusions was that CHG is effective for the prevention of catheter infection, though the concentration of CHG was not standardized. Therefore, on the basis of three RCTs [115, 117, 118], the CHG solution exhibited a greater preventive effect against infection than PI. Furthermore, in an observational study [119] with regard to skin disinfection at the site of intravascular indwelling catheter insertion, compared to disinfection with PI 10%, disinfection with CHG 1% reduced microbial colonization at the site of catheter insertion and reduced the risk of bloodstream infection.

There is 1 observational study on disinfection prior to CV port puncture [120]. In this study, CHG 1% was compared with ethanol and PI 10%, resulting in no statistically significant difference in the CV port infection rate between the three disinfectants.

Therefore, on the basis of the literature regarding disinfection at the site of intravascular indwelling catheter insertion and the 2017 CDC guidelines for preventing surgical site infection [121] regarding disinfection prior to CV port puncture, unless contraindicated, the use of alcohol-based disinfectants is proposed (described below).

CQ 6: What is the optimal procedure at the end of drug administration via the CV port?

Recommendation:

At the end of drug administration via the CV port system, flushing with 0.9% normal saline followed by positive pressure locking with 0.9% sodium chloride or diluted heparin solution is recommended.

[Strength of recommendation: weak, confidence of evidence: low, agreement rate: 100%]

Commentary

To prevent system occlusion at the end of drug administration via the CV port, the system needs to be flushed. Generally, when completing drug administration, it is recommended to flush the system with 0.9% normal saline to wash out the drugs followed by positive pressure locking with heparinized saline injection and then remove the injection needle. However, the content and volume of the lavage fluid recommended for flushing and locking vary depending on the manufacturers. There is no clear evidence for the procedure at the end of drug administration via the CV port system, which is mainly documented in several guidelines and consensus statements [122-125].

There are two procedures at the end of drug administration: (1) completely washing out administered drugs from the system (flushing) to prevent drug deposition and system occlusion and (2) preventing thrombotic occlusion of the system during the nonuse period by locking the system with positive pressure infusion of solution (positive pressure locking). For flushing the system, ≥10 mL of 0.9% normal saline is primarily used, and when blood sampling was performed or intravenous fat emulsion was administered via the system, flushing the system using ≥20 mL of 0.9% normal saline may be required. For the flushing procedure, pulsatile and intermittent flushing by injecting 0.9% normal saline is recommended [126-128]. Furthermore, the port catheter system has a pressure-resistance limit, and system corruption can occur when pressure exceeds ≥25 psi [124, 125]. The excessive pressure heightens the risks of catheter rupture and port disruption when using a smaller volume of a syringe for flushing and locking, and the procedures should be performed using a syringe with volume of ≥10 mL.

For positive pressure locking, it is documented that the use of diluted heparin solution can prevent thrombus formation within the system and catheter in the guidelines and consensus statement [122-125]. Diluted heparin solution at concentrations from 10 to 1,000 U/mL has been shown to be effective for preventing system occlusion; however, no optimal concentration of the solution is recommended [129]. In clinical practice, diluted heparin solution is widely used for positive pressure locking; however, it should be noted that heparin can occasionally induce serious complications, such as thrombocytopenia, bleeding, and infection [122-125]. Although positive pressure locking is performed following flushing at the end of drug administration, the locking procedure is recommended every 4 weeks to avoid system occlusion even when the CV port is not in use for a long period [130, 131]. Anticoagulant therapies, including oral warfarin and systemic low-molecular-weight heparin, are not allowed for preventing system occlusion due to lack of evidence [55, 132].

Conversely, in an RCT comparing the locking procedures of diluted heparin solution (300 U/3 mL) and 0.9% normal saline (10 mL) in patients with an indwelling CV port, the inability of blood aspiration from the system were 3.9% and 3.7%, respectively, with no significant difference between the two groups, and the incidence of CRBSI was also equivalent [133]. In a Cochrane Database of Systematic Reviews comparing the two locking procedures of diluted heparin solution and 0.9% normal saline for the maintenance of CVCs, no conclusive evidence showed significant differences between the procedures in terms of the prevention of catheter occlusion and safety [134, 135].

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