ORIGINAL ARTICLE _

Totally implantable central venous catheters of the port-acath type: complications due to its use in the treatment of cancer patients

Miroslav Granic^{1,2}, Darko Zdravkovic^{1,2}, Sandra Krstajic³, Sanja Kostic¹, Aleksandar Simic⁴, Momir Sarac⁵, Nebojsa Ivanovic^{1,2}, Dragan Radovanovic^{1,2}, Srdjan Dikic^{1,2}, Vladimir Kovcin¹

¹University Medical Center "Bezanijska Kosa", Department of Surgical Oncology, Belgrade; ²Faculty of Medicine, University of Belgrade, Department of Surgery, Belgrade; ³Internal Medicine Practice "Oncomed", Belgrade; ⁴Private Practice "Dr Drašković", Belgrade; ⁵Military Medical Academy, Department of Vascular Surgery, Belgrade, Serbia

Summary

Purpose: A multidisciplinary approach to the treatment of patients with malignant diseases requires adequate venous access in order to safely administer chemotherapy, blood transfusion and blood products, antibiotics, rehydratation and total parenteral nutrition. The insertion of the central venous catheter (CVC), its use and its maintenance can be accompanied by multiple complications.

Methods: Fifty cancer patients were retrospectively enrolled in this study. The obligatory inclusion criterion was an implanted CVC of the port-a-cath type, inserted for chemotherapy administration. This study included patients who had their catheters inserted in the period from 2001 to 2012.

Results: The median patient age was 44 years (range 28-68). Thirty five patients (70%) were female and 15 (30%) male. The port-a-cath had been used from 1 to 40 months $(16.8\pm9 \text{ months on average})$. Breast cancer was the most frequent malignancy (18 patients, 36%). The overall incidence of reported complications was 38%. The most common complications were infections and thromboembolic events, each with an incidence of 10 %. The malposition and disconnection of the port-a-cath were in second place, each with an incidence of 6%.

Conclusion: Insertion of the CVC carries the possibility of serious complications (thrombosis, infections, occlusions). However, correct implantation and handling performed by experienced and trained surgical and other medical staff significantly decrease the incidence of these complications. The use of the CVC has greatly improved the quality of life and also decreased the morbidity and mortality of the cancer patients in our study.

Key words: central venous catheter, chemotherapy administration, complications, port-a-cath

Introduction

A modern approach to the treatment of cancer patients involves multiple diagnostic procedures and the administration of different treatment protocols. The treatment of these patients requires, amongst other things, adequate venous access in order to safely administer chemotherapy, transfusion of blood and blood products, antibiotics, rehydratation and, if needed, total parenteral nutrition.

The usage, number and types of CVCs have

significantly increased during the last three decades [1]. The insertion and care of a CVC requires a multidisciplinary approach, meaning the involvement of surgeons, medical oncologists, haematologists, nursing staff and frequently infectologists [2].

The insertion of a CVC, its use and maintenance could be accompanied by a number of complications that require intensive repair measures and in many ways disturb the comfort of the patient. The complications can be divided into early and late. Early complications comprise pneumo-

Correspondence to: Miroslav Granic, MD, PhD. University Hospital Medical Center "Bezanijska Kosa", Faculty of Medicine, University of Belgrade, Bezanijska Kosa BB, 11000 Belgrade, Serbia. Tel: +381 11 3010777, Fax: +381 11 2606520, E-mail: granic@bkosa.edu.rs Received: 17/02/2014; Accepted: 02/03/2014 thorax, haemothorax, injury to large blood vessels, cardiac arrhythmia, air emboli and malposition of the catheter. Late complications include mechanical dysfunction of the catheter, extravasations of cytotoxic drugs, infections, skin necrosis and venous thrombosis [3].

In this article, we would like to present our experience with complications arising from the usage of CVC, which are in keeping with already published literature.

Methods

This study enrolled 50 patients suffering from malignant diseases. The inclusion criterion was an implanted CVC of the port-a-cath type for chemotherapy administration. Patients were treated at two sites: Medical Center "Bezanijska Kosa" and the private clinic "Oncomed", from 2001-2012.

The chemotherapy protocols used were mainly for the treatment of solid tumors, based on anthracyclines, platinum compounds, fluoropyrimidines, taxanes and other. The port-a-cath were implanted subcutaneously, with the silicone membrane on top of the container/ reservoir. These containers, made from polyurethane (most often 8F in diameter) and titanium (6F), had a "hard-base" resistant to damage during needle puncture, thus reducing the possibility of a thrombosis within the system.

These polyurethane and titanium reservoirs are MRI-friendly, meaning that diagnostic procedures such as magnetic resonance imaging are compatible with these systems.

Implantation methods

 Percutaneous implantation method: venous access is most frequently via v.subclavia, under short intravenous anesthesia with analgosedation or under local anesthesia with infiltration. With the help of a metal guide-wire, the catheter is introduced into the superior vena cava with the tip of the catheter entering the right atrium. The position of the catheter needs to be checked with x-rays.

A small skin incision is made on the anterior thoracic wall so the reservoir, connected with the catheter, can be placed and secured under the skin.

2) Surgical (open) method: used when a catheter of a wider diameter (8F or more) needs to be implanted or during re-implantation of a new system if there has been some previous complication.

For the catheter placement we used the vena cephalica in the Mohrenheim's triangle, venous basilica or venous brachialis at the upper arm. The catheter was placed via venesection of 1-2 mm, with the help of a ready-made plastic countered tip blunt ecarter, prepacked with a catheter, for ease of advancement into the vein.

With the help of a metal guide-wire, the tip of the catheter was placed just upstream of the right atrium, which was checked with x-rays. The position allowed infused agents to be spread throughout the body quicky and efficiently. The incision on the skin was used for placement of the reservoir and for the connection of the reservoir and the catheter.

Normal saline was used in both approaches to flush the catheter. After establishing patency, the catheter was flushed with heparinised saline.

The potential complications during the percutaneus implantation method are pneumothorax, and injury to subclavian artery. For both methods, potential complications include disconnetion of the port (reservoir) and the catheter, malposition of the tip of the catheter with or without kinking, thrombosis of the catheter with blockage, and infections.

The left subclavian vein is the preferable site of placement. If not accessable, the right sublacian or brachial veins were used.

During this study, the course of treatment as well as both the early and the late complications that had arisen due to the use of CVC were monitored.

Statistics

Continuous data were expressed as means±standard deviation (SD). For non parametric data median values with range were used. Categorical variables were reported as percentages.

Results

CVCs of a port-a-cath type were implanted into 50 cancer patients. There were 35 (70%) female and 15 (30%) male patients. Their median age was 44 years (range 28-68). The catheters were used from 1 to 40 months (16.8±9 months on average).

Table 1 shows the type and frequency of malignancy for which chemotherapy was indicated.

The implantation and use of the port-a-cath were accompanied by complications in 19 (38%) patients. In 31 (62%) patients there were no complications attributable to the catheters (Table 2).

Early complications included 3 cases of malposition of the port during implantation. In one case, mechanical failure of the chamber was the problem. Because of that surgical removal was required.

The late complications were: A) Skin necrosis and protrusion of the port in 1 patient; after 22 months of use, the port-a-cath was removed, allowing the skin to heal; B) malpuncture of the vein in 1 patient; the intervention was not successful and therefore the port-a-cath was removed

Malignancy	Patients, N	%
Breast cancer	18	36
Lung cancer	9	18
Rectosigmoid cancer	9	18
Uterine cancer	4	8
Rectal cancer	2	4
Colon cancer	2	4
Bone sarcoma	1	2
Ovarian cancer	1	2
Penile cancer	1	2
Prostate cancer	1	2
Stomach cancer	1	2
Non Hodgkin lymphoma	1	2

Table 1. Type and frequency of malignant diseases

Table 2. Early and late complications

···· · · · · · · · · · · · · · · · · ·			
Complications	Patients, N	%	
Early complications			
Port malposition	3	6	
Mechanical dysfunction	1	2	
of the reservoir			
Late complications			
Skin necrosis	1	2	
Wrong puncture	1	2	
Infection	5	10	
Thrombosis	5	10	
Disconnection	3	6	
Total	19	38	

and a new one was implanted; C) infections were noted in 5 patients. One patient developed bacterial endocarditis. Broad spectrum antibiotics were used, and the infections were treated according to the infective microorganism; D) thrombosis was registered in 5 patients. Two patients had a blocked catheter and streptokinase was used successfully for removal of the blockade. One patient had a pulmonary microembolism and another one had deep venous thrombosis. In all cases, the catheters were removed and patients were treated with antithrombotic therapy. E) It is interesting to mention 3 disconnections of the chamber and the catheter when catheters were sucked into the right ventricle. Cardiac catheterisation and extraction of the catheters were performed via the femoral vein.

Discussion

The frequent use of venous catheters for parenteral nutrition was described by Broviac et al. in 1973 [4]. This approach was modified later by Hickmann and his associates in 1979, when the use of these catheters started in oncology [5]. Totally implantable ports came into everyday use in oncology patients in 1982 [6].

Safe and long-term central venous access is of great importance in patients suffering from malignant diseases. However, despite many technical improvements and innovations, the optimal catheter has not been identified so far. The difference lies in the greater or lesser number of disadvantages [7].

The procedure itself is accompanied with a significant number of possible complications, the most frequent being infections, thrombosis, malposition and catheter fracture. During our study, the total percentage of complications was 38%, which is higher compared with results published so far [8].

Implantation of CVC of the port-a-cath type requires maximally sterile conditions. It can be done under local anesthesia. It is necessary that the vein used for the access has the lumen wide enough for appropriate administration of the cytotoxic drugs and to prevent damage to the vein.

The subclavian vein is the most frequently used for percutaneous implantation of venous catheters because it does not require much time to access. Moreover, the distance to the right atrium is short and it does not require incision on the neck, which is sometimes problematic in patients with late-stage malignant disease.

Some other authors prefer the right jugular vein approach, due to anatomical position, which allows straight continuation to the superior vena cava. This approach brings contact of the catheter with a vessel wall to the minimum, decreasing further the possibility of thrombosis [9].

Kock et al. published their findings on 1500 patients with implanted subcutaneous port-acaths for the administration of chemotherapy [10]. The most frequently used access in this study was the subclavian vein for better cosmetic results, wider catheter angulation and easier fixation for the deeper layers of the chest wall. The early complications of this approach were pneumothorax, haematothorax, air emboli, and venous damage (cephalic, external jugular). This approach was used in our study as well.

The fact that the implantation has to be performed under strict sterile conditions and under ultrasound or fluoroscopy control is much more important than whether the procedure is done by an anesthetist, interventional radiologist or surgeon. Following insertion, the position of the port system has to be confirmed by x-rays. The possibility of complications is minized if the operating procedures are strictly followed, both during insertion and during everyday use [9]. In our patients, the catheters were inserted by a surgeon-oncologist and vascular surgeon.

Pneumothorax was seen in 1 to 4% of the cases, if the approach was via the subclavian vein [11]. A thorough knowledge of the anatomy, as well as extensive insertion experience, are the most important predictors in the prevention of this complication during catheterization of the subclavian vein. This complication was not registered during our study.

Cardiac monitoring during the insertion is necessary for the detection of cardiac arrhythmia. A follow-up chest x-rays are needed for a catheter position check.

Complication risk factors include previous extensive surgical interventions in the neck and axilla, radiotherapy in the access field or nearby, previous catheterization, inexperience, high body mass index, and more than 2 puncture attempts in the same area. If there is one puncture attempt, the percentage of the complications is 1.6%. with two attempts the percentage is 10.2%. If there are three or more attempts, the percentage is 43.2%. In summary, combination of the risk factors results in a higher percentage of complications [12].

Infection is the most frequent complication during insertion of the catheter and also the major reason for its removal. The percentage of complications in patients with Hickmann catheter is 11-45%, 0-22% in patients with TICVAP and 7-32% in patients with Goshong catheter [9].

In the present study infections developed in 10.0% of the cases. Catheter insertion-related infections are a very important problem that increases morbidity and even mortality. The results of many studies have indicated that up to 70% of patients with sepsis had CVCs of various types and that it was necessary to follow the guidelines for the prevention and treatment of the infections caused by the insertion of the CVCs [13].

It is necessary to emphasise that the definition of "infection related to the implanted CVC" varies and that it is related to a wide range of infections from bacterial colonization of the catheter, to local infections to septic thrombophlebitis. The most frequent are coagulase-negative staphylococcus, staphylococcus aureus and candida species [14]. Removal of the catheter is considered to be strictly required in case of local complications, persistent sepsis, bacteriaemia, relapse of bacterial infection following antibacterial treatment, clinically unstable patients, systemic complications (thrombosis, emboli, endocarditis) or detection of the above mentioned microorganisms (the presence of which is associated with systemic complications and a very low percentage of success in catheter preservation).

The CVC can be left in place if there are no signs of local infection or metastatic complications and in the case of sterile haemocultures and clinically stable patients (all these criteria have to be met). The treatment of infections requires intensive initial antibiotic therapy (3rd generation cephalosporins, vancomycin). When antibiogram is available, the initial antibiotic treatment has to be corrected.

Thromboembolic complications represent the second most important issue that accompanies the insertion of CVC. Cancer patients are in great risk for thromboembolism, primarily due to the nature of their illness.

Venous stasis, damage to endothelia, the prothrombotic effect of the malignancies and chemotherapy itself all are risk factors in cancer patients. Venous thrombosis can be asymptomatic or presented with ipsilateral pain and swelling in the arm or neck. Furthermore, thrombosis can be partial or complete. Recent studies state that the percentage of symptomatic thrombosis is around 5%, whilst the percentage of asymptomatic thrombosis ranges from 14 to 18% [15]. We registered around 10% of symptomatic thromboses, which is higher than in the above mentioned studies. Taking all these into account, a question arises of the prophylactic use of oral anticoagulant therapy in cancer patients with CVC. However, the results of many studies do not support standard routine prophylaxis with anticoagulants in these patients [16].

The use of CVC of the port-a-cath type has an important role in the treatment of cancer patients. It brings more comfort during the administration of chemotherapy and reduces the possibility of serious damage to the peripheral veins and surrounding tissues [17].

The fear of serious complications during the use of the port-a-cath is realistic (thrombosis, infections, occlusions). However, with correct and safe handling it can be significantly reduced. Infections can be prevented with rigorous aseptic handling techniques. On the other hand, prevention of thrombosis with the regular use of oral anticoagulants is still not standard practice.

In summary, despite the possible complications, the use of CVCs of the port-a-cath type has great significance in the management of cancer patients. It improves their quality of life and also decreases morbidity and even mortality.

References

- 1. Walser EM. Venous access ports: indications, implantation technique, follow-up, and complications. Cardiovasc Intervent Radiol 2012;35:751-764.
- 2. Gallieni M, Pittiruti M, Biffi R. Vascular access in oncology patients. CA Cancer J Clin 2008;58:323-346.
- Nakazawa N. Infectious and thrombotic complications of central venous catheters. Semin Oncol Nurs 2010;26:121-131.
- Broviac JW, Cole JJ, Scribner BH. A silicone rubber atrial catheter for prolonged parenteral alimentation. Surg Gynaecol Obstet 1973;136:602-606.
- 5. Hickman RO, Buckner CD, Clift RA, Sandres JE, Stewart P, Thomas ED. A modified right atrial catheter for access to the venous system in marrow transplant recipients. Surg Gynaecol Obstet 1979;148:871-875.
- 6. Niederhuber JE, Ensminger W, Gyves JW et al. Totally implanted venous and arterial access system to replace external catheters in cancer treatment. Surgery 1982;92:706-712.
- Minassian VA, Sood AK, Lowe P, Sorosky JI, Al-Jurf AS, Buller RE. Long term central venous access in gynecologic cancer patients. J Am Coll Surg 2000;191:403-409.
- De Lucia R, Segreti L, Soldati E, Di Cori A, Zucchelli G, Bongiorni MG. Port-a-Cath complicated by infection or migration not removed by manual traction: usefulness of cardiac pacing leads extraction techniques. Ann Vasc Surg 2013;27:529-536.
- 9. Barbetakis N, Asteriou C, Kleontas A, Tsilikas C. Totally implantable central venous access ports. Analysis of 700 cases. J Surg Oncol 2011;104:654-656.

- Kock HJ, Pietsch M, Krause U, et al. Implantable vascular access systems: experience in 1500 patients with totally implanted venous port systems. World J Surg 1998;22:12-16.
- 11. Ozyuvaci E, Kutlu F. Totally implantable venous access devices via subclavian vein: a retrospective study of 368 oncology patients. Adv Ther 2006;23:574-581.
- 12. Di Carlo I, Pulvirenti E, Mannino M et al. Increased use of percutaneous technique for totally implantable venous access devices. Is it real progress? A 27-year comprehensive review on early complications. Ann Surg Oncol 2010;17:1649–1656.
- 13. Miller DL, O'Grady NP; Society of Interventional Radiology. Guidelines for the prevention of intravascular catheter-related infections: recommendations relevant to interventional radiology for venous catheter placement and maintenance. J Vasc Interv Radiol 2012;23:997-1007.
- 14. Pascual A, Cercenado E, Salavert M et al. Update on pathogenesis and diagnosis of intravascular catheter-related infections. Enferm Infecc Microbiol Clin 2011;4:16-21.
- Schiffer CA, Mangu PB, Wade JC et al. Central venous catheter care for the patient with cancer: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 2013;31:1357-1370.
- 16. Lee AY, Kamphuisen PW. Epidemiology and prevention of catheter-related thrombosis in patients with cancer.J Thromb Haemost 2012;10:1491-1499.
- 17. Chaukiyal P, Nautiyal A, Radhakrishnan S, Singh S, Navaneethan SD. Thromboprophylaxis in cancer patients with central venous catheters. A systematic review and meta-analysis. Thromb Haemost 2008;99:38-43.