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*Intravascular thrombosis as a result of central venous access*

The central venous access is in many cases an indispensable element of patient treatment. It allows constant possibility of the measurement of central venous pressure; it is the optimal way of intravenous administration of drugs, fluids, high-osmolar solutions of parenteral nutrition or cytostatic factors. It is indispensable for carrying out a dialysis therapy or haemofiltration.

Unfortunately, beside numerous benefits resulting from the presence of a catheter in the central vein, one should face the possibility of complications. The main and clinically most essential are: venous thrombosis and local infections or general ones (12). The upper limb venography performed in a long-term catheterization of central vessels reveals in 26% to 67% of cases the presence of thrombi in the vascular lumen. The natural course of venous thrombosis predicts three types of its descent: 1) complete thrombus dissolution resulting from the action of fibrinolytic physiological mechanisms, 2) thrombus growth up to the total vessel occlusion with later possible recanalization, 3) abruption of a part of a thrombus into the pulmonary circulation with a clinical picture of pulmonary embolism.

The latter complication may have a disastrous consequences and ruin the whole therapeutic procedure. Pulmonary embolism is described in approximately 17% cases of central vein thrombosis (6).

Considering clinical significance of possible complications, the aim of this study was quantitative and qualitative evaluation of the thrombotic complications of central vascular access.

## MATERIAL AND METHODS

The study was carried out in the Public Clinical Hospital and involved patients who had central venous cannulation performed during the course of their treatment therapy regardless of its purpose. The patients to whom vascular access was performed by non-anaesthesiologists were excluded.

Size 7F one-channel, non-heparinized catheters were used and they were introduced into the vessel by means of the Seldinger method. The occurrence of clinical symptoms of the impaired vascular flow in the region of access or the lack of the free flow through the cannule despite the correction of its position were qualified as a threat of intravascular thrombosis. In such cases the vascular catheter was removed and the course of the disease and treatment were submitted to a detailed retrospective analysis and prospective evaluation.

## RESULTS

The analysis included 887 patients who had central vascular access performed between January and December 1999. Five cases of thrombosis were noted: four of them concerned patients treated in the Department of Haematooncology; one of them concerned a patient of the Department of Intensive Therapy.

Case I. The patient M. Cz. aged 28, treated since 1997, with a diagnosis of Hodgkin's disease. In the course of the treatment she was three times subjected to radiotherapy aimed at mediastinum and axillary lymph nodes bilaterally. In computer tomography of the chest performed in the period prior to vein cannulation, traits of anterior mediastinum fibrosis were noted as well as single lymph nodes on the level of aortic arch and a bundle of lymph nodes in the region of the pulmonary cone. The catheter was inserted into the right subclavian vein for apheresis purpose. 20 days later pyrexial episodes as well as complaints concerning the supraclavicular region and the right one occurred. The ultrasonography revealed the extensive thrombus which involved the right subclavian vein up to the axillary vein, brachiocephalic trunk and jugular vein up to its division. The right jugular internal and external veins were free due to collateral circulation.

Case II. The patient Z. P. aged 50, with a diagnosis of acute granulocytic leukaemia. In the course of cytostatic therapy a catheter was inserted into the left subclavian vein. During the cannulation, the level of thrombocytes was  $735 \text{ K}/\mu\text{l}$ . After 7 days an extensive oedema occurred in the area of the neck and subclavicular fossa. The ultrasonographic investigation showed thrombosis, which involved left axillary and brachial veins, left venous angle and left internal jugular vein. Blood and catheter cultures revealed the presence of methicillin resistant strain of *Staphylococcus aureus*.

Case III. The patient Z. P. aged 49, with a diagnosis of acute granulocytic leukaemia. Treated with amphotericin B because of pulmonary aspergillosis. Prior to the cannulation of the right internal jugular vein, an extensive thrombotic and inflammatory changes were detected in both limbs as a result of peripheral vein cannulation. Two days after the catheterisation the patient complained of dyspnoea and the X-ray investigation suggested disseminated pulmonary embolism. It was confirmed later by the scintigraphic examination. 5 days' period of maintaining the catheter in the jugular vein caused inflammation in the region of the supraclavicular fovea, painful and with visible discoloration. In the Doppler ultrasonography the thrombosis involved right external and internal jugular as well as subclavian veins.

Case IV. The patient W. H. aged 50 treated because of the acute lymphocytic leukaemia since 1998. The cannulation of the subclavian vein took place parallelly to the treatment of the intensive metrorrhagia. The patient received thrombocyte transfusion, hormonal drugs and cyclonamine. The external traits of the thrombosis occurred after 14 days. The ultrasonographic examination confirmed the presence of thrombosis which involved subclavian and axillary veins, the proximal part of the internal jugular vein and venous angle on the right side.

Case V. The patient T. M. aged 60, hospitalized in the Department of Intensive Therapy Clinic because of the respiratory and renal failure which required a dialysis. In the course of a long-term treatment both jugular veins constituted dialysis venous access. Subclavian veins were used for fluid and nutrition. On the 72th day of hospitalization, bilateral swelling of the neck and supraclavicular region were observed.

The ultrasonographic examination (Figs 1, 2) revealed the presence of the parietal thrombus in both internal jugular veins (3 cm long on the right side, 5 cm long on the left side). Both venous angles with no thrombotic changes but with visible blood cells flotation suggested disturbances of the venous flow distally to the side of obstruction. Central veins venography did not reveal any pathological changes within the superior caval vein.

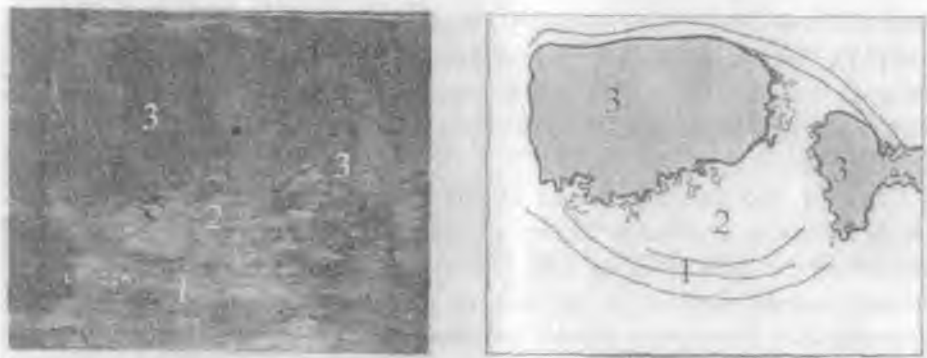


Fig. 1. Transverse cross-section of the left internal jugular vein with thrombosis in the lumen; 1) vessel wall, 2) parietal thrombus, 3) vein lumen

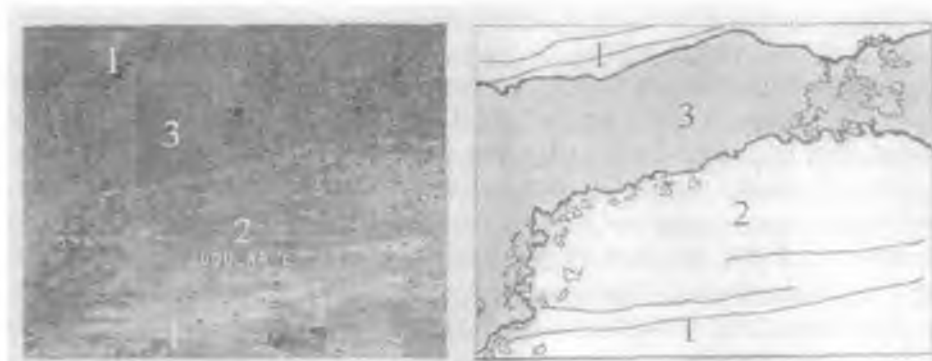


Fig. 2. Longitudinal cross-section of the left internal jugular vein with thrombosis in the lumen; 1) vessel wall, 2) parietal thrombus, 3) vein lumen

The diagnosis of central vein thrombosis obliged to remove the catheters from vessels of majority of the patients. The treatment comprising high doses of low-molecular heparin and antiaggregation drugs was introduced in each case. Following the next several months it was noticed that the patients of the Department of Haematooncology had recanalization of the occluded vessels except one who created collateral circulation.

No guided therapy was assumed in the patient T. M. treated in the Intensive Therapy Clinic. The parietal thrombus did not occlude the flow from the region of the neck and head. At the time when the clinical symptoms were revealed, the intravascular thrombus was solid and the risk of pulmonary embolism was low. During the whole period of hospitalization the patient received low-molecular heparin in prophylactic doses. His age and several episodes of bleeding from chronic duodenal ulcer were essential contraindication to the thrombolytic therapy.

## DISCUSSION

A small number of patients, who had intravascular thrombosis diagnosed within one year as a result of the performed venous access, do not reflect the actual scope of the problem. Our own material includes only three cases in which intravascular changes were verified by the records of the ultrasonographic examination. However, asymptomatic central vein thrombosis occurs more often than it is generally expected. Balestri et al. (1) examined urologic patients with a short-term or a long-term central vascular access, with no clinical symptoms of the axillary-subclavian thrombosis. They confirmed the presence of incomplete venous thrombotic stenosis in 45% cases including fully asymptomatic in 10% patients. Others (3) claim that the range of the asymptomatic upper limb thrombosis involves 90% of all cannulations and the remaining 10% are symptomatic ones. They

are closely related to central vein thrombosis, thrombophilia or lower limb vein thrombosis which the patients had before.

There are limited data on thrombosis formation because of the insufficient number of systematic, randomized clinical investigations. Our study confirms that thrombosis may be formed along the catheter on its wall, it may also be localized parietally along the vessel in which the catheter is placed. In each described case the growth of the thrombus may lead to blood flow occlusion and to formation of superior caval vein syndrome with all its consequences. It may also cause subclavian vein or brachiocephalic trunk occlusion and, which is obvious, the loss of venous access.

The symptoms of central vein thrombosis that occur in consequence of its cannulation are extremely varied. The occlusion of the venous catheter together with the arm swelling is the most frequent. Sometimes it is accompanied by pain of the neck, brachialgia or extensive filling of the external jugular veins. Late symptoms are: fever, changes in the skin temperature and discoloration. The diagnosis tends to be easy if the patient shows all symptoms of the complete occlusion of the unilateral venous flow. It is difficult when symptoms are incomplete.

The superior caval vein thrombosis most frequently resulted from the spread of subclavicular and brachiocephalic vein thrombosis and accompanied mediastinal tumours, penetrating injuries and irradiation (15). The latter was the cause of complications in the first described patient.

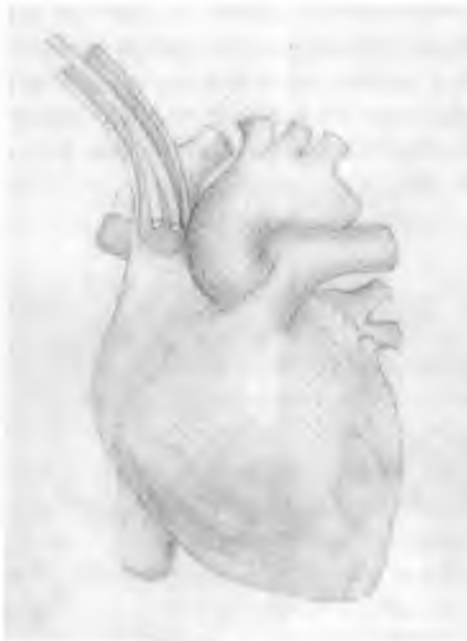


Fig. 3. Diagram of the catheter localization in the superior vena cava – the effect of “striking”

The most recent reports pointed out the role of local factors having influence on the thrombus formation. These are, among others: the quality of material the catheter was made of, its size in relation to vein lumen, position of the catheter tip in vein and the site of the catheter insertion (5, 6, 11). It is assumed that improper localization of the catheter distal part in the vein lumen may lead to the formation of a mural thrombus: the changes in the intravascular pressures generated by the respiratory rhythm, may cause "striking" of the catheter against vein endothelium (Fig. 3) leading to its damage (5).

More common places for thrombus formation are the left subclavian vein and the left internal jugular vein. It was venographically confirmed, that the left brachiocephalic vein enters into superior caval vein at a sharper angle than the one on the right side (11). That is why at the time of cannulation ("push him") the vessel endothelium is more easily damaged both by the guide-wire and by the catheter. At worst, the vein wall may be ruptured and the pericardiac tamponade may follow. Such complication was noted when Groshnog's catheters were used (2). In our study only one patient had the left subclavian vein canalization because of previous long-term cannulation of central veins on the right side. So far, no correlation between the concentration of fibrinogen in the plasma and the venous thrombosis was proved to exist. However, there is no doubt that this factor is essential for normal blood viscosity maintenance. Therefore, it can be assumed that the elevated fibrinogen concentration essentially increases the risk of venous thrombosis, especially when the venous blood flow is already slowed down.

The ethiopathology of intravascular thrombosis at the site of venous access is often complex. It is of special importance in the intensive therapy where both primary pathological disturbances and employed diagnostic and therapeutic procedures may favour such complication. Our observations confirm such risk, as in patient T. M. – not only existing uraemia was responsible for the thrombus formation. Numerous haemodialyses might have also led to decreasing of serum concentration of protein C which is an important coagulation inhibitor (15). Moreover, previous thrombosis of the lower limb deep veins and numerous vessel cannulations made the risk of thrombosis extremely high (3). Eventually, not only the systemic changes but also infection at the site of injection (MRSA and *Pseudomonas aeruginosa* resistant to ceftazidym were isolated) could itself lead to the local activation of the intravascular coagulation in this patient (8, 9).

The scope of the accessible investigation to confirm central vein thrombosis is wide. The basic diagnostic procedure is chest radiogram which does not allow directly to estimate vessel patency, but it is useful for defining the placement of the catheter tip, its displacement or bending. Contrast venography is a standard method for detecting of the thrombosis. Its use allows to evaluate the localization and the extent of thrombus according to a IV-grade scale: I – the lack of a visible thrombus, II – small thrombus restricting the vein lumen less than a half, III – large thrombus restricting the vein lumen more than a half, IV – the thrombus completely closing the vein lumen. In our study, in all patients who were cannulized for haematological purpose, the IV-grade occlusion was detected, which means the complete closure of the lumen of one or several central veins.

Administration of a contrast medium through the catheter which is "one-way" occluded is helpful to exclude parietal thrombosis and to employ therapy of fibrin thrombus of the cannule tip. In case of the parietal change, this method enables the evaluation of the blood flow proximally to the occlusion (6).

Our study confirmed that the ultrasonographic examination of the venous vascular bed (7, 10) is also a useful diagnostic method, especially when it is performed in two projections (duplex Doppler). The diagnostic value of this examination depends mainly on the localization of changes: it is the highest in the symptomatic thrombosis of proximal veins (sensitivity 94%, specificity 96%) and limited or unsatisfactory in the thrombosis of deep veins, for example, behind the sternum (6, 15).

The rules of the therapy of central vein thrombosis caused by its cannulation are not uniform. Conservative procedure involves the removal of the catheter and employing antithrombotic therapy (to prevent the enlargement of thrombus and to decrease the risk of pulmonary embolism). It is more and more frequently replaced by the fibrinolytic therapy, which does not demand the removal of the catheter (as far as it is not the source of inflammation) (9, 14). The safety, effectiveness and costs of fibrinolysis remain on account of the thrombotic agent used (urokinase, streptokinase, rt PA- in commonly known dosage) (3).

Facing the threat of permanent organ disturbances, the prophylaxis of central vascular access complications should be taken into consideration in every individual case. It is especially important in reference to the population of patients treated from myeloproliferative diseases, where the occurrence of intravascular thrombosis is related not only to vein cannulation. It seems that the routine antithrombotic prophylaxis may decrease the frequency of such complications in the whole population of patients (3, 6, 13). The use of high quality catheters with heparinized covers should be the supplement of such procedure in high risk patients, however, it does not seem to be absolutely reliable protection (4, 8, 9).

## CONCLUSIONS

1. Clinically evident intravascular thrombosis is a rare complication of central vein cannulation.
2. Bed-side ultrasonography is a useful diagnostic method for evaluation of the site and range of intravascular pathology.
3. Early diagnostics and the employment of antithrombotic therapy allow partial or full restoration of vessel patency in a large number of cases.

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## SUMMARY

Central venous access represents one of the most basic therapeutic procedures in modern medicine. Unfortunately, numerous advantages that result from maintaining a central venous line are accompanied by some complications among which the venous thrombosis is the most significant clinically. The study was designed to assess frequency and natural history of this complication in the setting at a multi profile clinical hospital. Central venous cannulation was performed by a fully qualified anaesthesiologist in every case. There were 887 cannulations and only 5 patients with clinically significant venous thrombosis.

The analysis of the collected data allowed us to state that the frequency of intravascular thrombosis is low, but this complication is often associated with extensive impairment of patency of the central veins. Full recanalization is not always achieved regardless of the treatment applied. Pulmonary embolism in the course of central venous thrombosis was diagnosed in one patient only and appeared as a multiple and fine X-ray infiltrates. It seems that in the presence of permanent or even life threatening complications of central venous thrombosis their risk should be minimized by frequent examination of the cannulation site and early initiation of antithrombotic treatment.

#### Zakrzepica wewnątrznaczyniowa jako następstwo centralnego dostępu naczyniowego

Centralny dostęp naczyniowy stanowi obecnie w wielu dziedzinach medycyny jeden z podstawowych elementów postępowania leczniczego. Liczne korzyści wynikające z obecności cewnika w żyłę głównej górnej wiążą się niestety z możliwością wystąpienia powikłań, z których zakrzepica żylna jest najbardziej istotna klinicznie. Celem pracy było ustalenie rocznej liczby i naturalnego przebiegu tego powikłania u chorych wieloprofilowego szpitala klinicznego. Kaniulacji naczyń centralnych dokonywali lekarze anestezjododzy. Przeprowadzono 887 kaniulacji, jawną klinicznie zakrzepicę żył centralnych stwierdzono u 5 chorych. Analiza zebranego materiału pozwoliła na stwierdzenie, że zakrzepica wewnątrznaczyniowa jest powikłaniem rzadkim, najczęściej związanym z rozległym upośledzeniem drożności centralnego układu żylnego. Mimo zastosowanej terapii nie zawsze dochodzi do pełnej rekanalizacji naczyń. Zatorowość płucna w przebiegu zakrzepicy naczyń centralnych wystąpiła tylko u jednego pacjenta i miała charakter mnogich drobnych zmian. Wydaje się, że wobec groźby trwałych i niebezpiecznych dla życia powikłań zakrzepicy należy dążyć do zminimalizowania ryzyka przez dokładną obserwację miejsca wprowadzenia kaniuli i wczesne wdrożenie leczenia przeciwzakrzepowego.