PERIPHERAL VENOUS CATHETER-RELATED INFLAMMATION
A Randomized Prospective Trial

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ABSTRACT • BACKGROUND: Peripheral venous catheter-related inflammation (PVCRI) is a serious health and economic issue. It is mainly linked to peripheral venous catheter (PVC) duration and other risk factors.

METHODS: PVCRI was prospectively evaluated in a 3-month-study according to PVC duration. Other risk factors were also studied such as age, gender, diabetes, intravenous steroids and antibiotics. 221 patients admitted to 3 different departments in a university hospital were randomized to undergo a 72 hours versus 96 hours PVC. The primary endpoint was to evaluate if this prolonged duration would increase the incidence of lymphangitis. The secondary endpoints were to evaluate if other risk factors such as age, gender, diabetes, intravenous steroids and antibiotics, have a direct impact on lymphangitis. Fever, local inflammatory signs and date of occurrence have been noted by two different nurses.

The Stata 8.0 program, and the Pearson chi-square test to compare percentages ($\alpha = 0.05$) were used.

RESULTS: PVCRI occurred in 20.4% of all studied patients. PVCRI incidence did not differ between the patients who kept the catheter for 72 hours and those who kept it for 96 hours, but we found a significantly increasing incidence of PVCRI while comparing 24 hours versus 48 hours duration and 24-48 hours duration versus 72-96 hours duration respectively. Age, as well as intravenous antibiotic showed to be a significant risk factor for PVCRI. As for diabetic patients, there was a trend towards a higher incidence of PVCRI. Intravenous steroids showed to have a beneficial effect. It is to be noted that the rate of PVCRI was significantly higher in the internal medicine/infectious diseases department compared to the two other departments.

CONCLUSION: No difference on PVCRI risk was found between 72 and 96 hours catheter duration. However the risk seems to increase between the first and the third day of catheterization. We suggest that an adapted duration of the PVC to the patient risks would be more cost-effective.

RÉSUMÉ • INTRODUCTION: La phlébite liée au cathétérisme veineux périphérique (PLCVP) ou lymphangite est un problème de santé et de surcoût, lié à la durée du cathétérisme veineux périphérique et à d’autres facteurs de risques.

MÉTHODE: La phlébite liée au cathéter veineux périphérique (CVP) a été étudiée pendant 3 mois, en fonction de la durée de cathétérisme. D’autres facteurs de risque ont été évalués tels que l’âge, le sexe, le diabète, l’antibiothérapie et la corticothérapie intraveineuses. 221 patients admis dans 3 services différents d’un hôpital universitaire ont été randomisés pour la pose d’un CVP pour deux durées différentes: 72 heures versus 96 heures.

L’objectif primaire était de savoir si l’extension de la durée du CVP augmentait l’incidence de lymphangite. Les objectifs secondaires étaient d’évaluer l’impact des autres facteurs de risque tels que l’âge, le sexe, le diabète, et les médicaments administrés par voie intraveineuse, sur l’inflammation. La fièvre, les signes inflammatoires locaux et leurs dates d’apparition ont été notés par deux infirmières.

Le programme statistique Stata 8.0 et le test Pearson chi-square pour comparer les pourcentages ($\alpha = 0.05$) ont été utilisés.

RÉSULTATS: L’incidence de la lymphangite liée au CVP était de 20,4% chez les malades inclus. Cette incidence ne semble pas varier entre 72 et 96 heures de cathétérisme. Cependant, cette incidence semble augmenter entre J1-J2 d’une part et entre J3-J4 d’autre part. L’âge, l’antibiothérapie intraveineuse et le diabète sont corrélés à une plus forte incidence de lymphangite alors que la corticothérapie intraveineuse semble la réduire. L’incidence de cette complication a été plus élevée dans l’unité de Médecine interne - Maladies infectieuses.

CONCLUSION: Nous n’avons pas mis en évidence une élévation de l’incidence de lymphangite entre 72 et 96 heures de cathétérisme et nous suggérons que le changement du cathéter veineux périphérique s’effectue selon les facteurs de risques de chaque patient.
Incidence of peripheral venous catheter-related complication is estimated between 20 and 35% of hospitalized patients [1-2]. This incidence is variable among studies because of discrepancies between definitions: phlebitis or lymphangitis or peripheral venous catheter-related inflammation (PVCRI) accounts for 1 to 35% of complications (mean 20%), colonization for 3 to 35% (mean 10%), catheter-related infection for 1 to 8% (mean 5%), catheter-related bacteremia for 0.2 to 0.5% [3-17].

Phlebitis is defined clinically by the presence of two or more of the following signs or symptoms on examination of the catheter insertion site: pain, tenderness, erythema, swelling, purulence, and a palpable venous cord [14, 17-18].

Peripheral venous catheter (PVC) related infection is defined by a phlebitis associated to catheter colonization. PVC-related bacteremia is defined as catheter colonization associated to a positive peripheral hemoculture regarding the same bacteria [17].

Microbiologically, catheter contamination is defined by a positive quantitative catheter culture less than 10^5 CFU/ml, whereas catheter colonization is defined by a positive qualitative catheter culture equal to, or more than 10^5 CFU/ml [2].

Although infection is thought to be a frequent PVC complication, many studies show that the major complication remain an inflammation at the site of infusion or what is called phlebitis or lymphangitis [1, 14, 17, 19-21].

PVC-related phlebitis is primarily a physicochemical phenomenon [17]. Risk factors include: canula material (tetrafluoroethylene-hexafluoropropylene (FEP) or Teflon is more phlebitogenic than polyetherurethane (PEU) or Vialon); length (12-inch > 2-inch), and bore size (large > small); operator skills in insertion, the anatomic site of canulation; the frequency of dressing changes; the infusate (such as glucose-containing admixtures, aminocids and lipid emulsion, potassium chloride, vancomycin, amphotericin B, beta-lactam antibiotics, benzodiazepines, barbiturates, phenytoin, vasoactive pressor amines and chemotherapeutic agents); host factors such as patient age (≥ 55 years), Caucasian race, female gender, and the underlying diseases such as diabetes and patients who already developed phlebitis with a first catheter [2, 4, 17]. Randomized controlled trials have shown that adding hydrocortisone [22-23], heparin [22-24], or both to infusate, or topically applying a corticosteroid [25] or transdermal glyceryl trinitrate [26-27] at insertion site can reduce the risk for PVC-related phlebitis. However, these data are not strong enough in order to recommend the routine use of these drugs to prevent phlebitis [17].

Risk factors for peripheral venous catheter-related colonization include age (≥ 55 years), the duration of canulation (≥ 72 hours) and the anatomic site of canulation (external jugular vein, near the joints) [2, 14]. At Hôtel-Dieu de France University Hospital, peripheral venous catheter-insertion obeys to a strict protocol based on international recommendations (see Appendix pp. 144-145). Every PVC is systematically changed after 96 hours of insertion according to CDC guidelines. However, we believe that in our institution, we should have our proper recommendations concerning peripheral venous catheter insertion and care. We conducted a randomized controlled trial. The primary endpoint was to compare the incidence of PVCRI between two groups of hospitalized patients: the first group having PVC changed systematically after 72 hours of insertion, and the second group having PVC changed systematically after 96 hours of insertion. The secondary endpoints were to find out and analyze any risk or protective factors regarding PVCRI.

METHODS

During a 3-month study period, 221 patients (124 men and 97 women) have been included in our randomized prospective controlled trial. These patients were admitted to three different departments of the Hôtel-Dieu de France University Hospital: the Internal Medicine/Infectious Diseases department, the Pneumology/Gastroenterology department, and the General Internal Medicine department.

The inclusion criterion was: any patient admitted to the above mentioned departments during the 3-month study period and having a PVC. The exclusion criteria were: any patient who is hospitalized for less then three days or has his PVC removed for any other reason than PVCRI before the randomized time-limit (72 hours versus 96 hours after PVC-insertion).

During the study, the hospital nurses insert the PVC to the patients according to the protocol (Appendix). PVC’s were made of PEU (Optiva®). The time-limit setting for systematic removal of PVC in every patient (72 hours versus 96 hours after insertion) is randomized in a mono-blind fashion. The nurses monitor the insertion site regularly every six hours and when needed. The information concerning every included patient were written on a card index: name, age, gender, diabetic status, date of PVC-insertion, local inflammation signs (heat, erythema, pain, induration, swelling) and systemic signs such as fever and rigors and their date of occurrence, medications and solutions received through the PVC and finally, admission diagnosis.

![Figure 1](image-url)
We did not perform blood cultures neither PVC-tip culture because the recommendations regarding catheter culturing techniques are still debatable [28] and because PVCR1 is considered as a medical event in which infection is not usually implicated and will rarely lead to sepsis. Data have been collected on a statistic computer program : Stata 8.0. The Pearson chi-square test is used to compare percentages (with $\alpha = 0.05$).

RESULTS

Two hundred seventy-three patients were admitted to the three above-mentioned departments. Fifty-two patients were excluded according to criteria. Among the 221 patients included in our study, 124 (56.1%) were men and 97 (43.9%) were women. Thirty patients (13.6%) were 29 years, 67 patients (30.3%) were between 30 and 59 years, and 124 patients (56.1%) were above 60 years old.

Fifty-nine patients (26.7%) had diabetes mellitus. Randomly, 108 patients (48.9%) were assigned to the 72 hours group (group 1) and 113 patients (51.1%) were assigned to the 96 hours group (group 2). Forty-five patients (20.4%) developed PVCR1 with at least two local signs of inflammation. Fourteen (31.1%) of these patients developed inflammation on day 1 after PVC-insertion; 20 patients (44.4%) developed inflammation on day 2; 6 patients (13.3%) developed inflammation on day 3; 5 patients (11.1%) developed inflammation on day 4 (Fig. 1). Signs of inflammation were found as follows: 28 patients (62%) developed fever, erythema, heat and pain, 10 patients (22%) developed fever, erythema, heat, pain and induration, 2 patients (4.4%) developed fever, pain and swelling and 5 patients (11%) developed erythema and pain. It is to be noted that 18 patients (40%) presented fever 24 hours before the appearance of local signs of inflammation. The fever has been linked to PVCIR only after exclusion of other sites of infection (chest X-Ray, urine and blood culture) and the resolution of fever after changing the IV line.

Statistically significant differences are noted between “day 1-day 2 group” and “day 3-day 4 group” ($p = 0.038$), as well as between day 1 group and day 2 group ($p = 0.033$) while no significant difference was shown ($p = 0.741$) by comparing the incidence of PVCR1 in the 72 hours (group 1) and 96 hours (group 2) groups (Fig. 2). A trend towards higher PVCR1 was depicted in diabetic subgroup (27% of PVCRI in 59 diabetic patients versus 17.9% in the non-diabetic subgroup) even though no statistical significance could be demonstrated ($p = 0.132$).

Age was stratified into three categories: less than 29 years, between 30 and 59 years and more than 60 years (Fig 3). The incidence of PVCRI in the three groups was 3.33%, 23.88% and 22.58% respectively and the difference was statistically significant ($p = 0.044$).

25.8% of women developed PVCRI, and 16.1% of men. Women seem to have a higher trend towards increased incidence of PVCRI, but no significant statistical difference could be depicted ($p = 0.077$).

One hundred eight patients (48.86%) were receiving intravenous antibiotic therapy. Twenty-eight of them (25.9%) developed PVCRI compared to 15% in the group not receiving antibiotics with a significant difference ($p = 0.045$) (Fig. 4).

37.8% of patients were admitted to the Internal Medicine/Infectious Diseases department, 13.3% were admitted to the Pneumology/Gastroenterology department, and 48.9% were admitted to the General Internal Medicine department (Fig. 5). The first department had a higher incidence of PVCRI compared to the second
and the third department respectively (p = 0.015). The patients admitted to the Internal Medicine/Infectious Diseases department were more frequently receiving intravenous antibiotic therapy through the PVC (64.2%) compared to the two other departments, with a statistically significant difference (p = 0.009% and p = 0.008% respectively). The relative risk for developing PVCRI is still significant (RR = 0.38 [0.166-0.876]), higher in the Internal Medicine/Infections diseases compared to Pneumology/Gastroenterology departments, even after adjustment on antibiotic intake.

Nineteen (8.59%) patients received intravenous corticosteroid therapy through the PVC; 10.5% of these patients developed PVCRI; 21.3% of patients not receiving corticosteroid developed PVCRI. The difference seems noteworthy but is not statistically significant (p = 0.265).

**COMMENT**

The incidence of PVCRI in our patients was 20.4% which is similar to the results seen in the literature. We did not find any significant statistical difference for the risk of developing PVCRI between the patients who kept their PVC for 72 hours and those who kept their PVC for 96 hours. But we found significant statistical difference for the risk of developing PVCRI between the 24 hour-duration-PVC and the 48 hour-duration-PVC as well as the 24/48 hour-duration-PVC and the 72/96 hour-duration-PVC.

These data concur with those of Maki [17] as he found that the incidence of phlebitis increased markedly between 24 and 48 hours after catheterization whereas the risk for each remaining day was similar to that on day 2. Thus, the day-specific risk for phlebitis would remain relatively constant each day thereafter and the cumulative risk would ultimately become very high [17]. This observation could confirm the notion that PVC-related inflammation is at least initially, a noninfectious phlebitic process.

The idea could be further enhanced by the fact that in our study, and in other trials [22-23], corticosteroids decreased or at least had a tendency to decrease the risk of PVCRI.

As other studies did [17, 27, 29-31], our study showed that the administration of intravenous antibiotics through a PVC increases the risk of PVCRI. This iterates the potential chemical phlebitogenic effect of intravenous antibiotics [19, 21, 32-33].

We noticed that, even after adjustment on antibiotic intake, the department of Internal Medicine/Infectious Diseases still had a significantly higher rate of PVCRI which raised different issues, such as the quality of insertion and surveillance of PVC by an overworked nursing staff.

Age proved, as in other studies, to be an important and significant risk factor for PVCRI. Diabetic patients had only a higher trend towards developing PVCRI. This might be related to the small number of diabetic patients included in our study. A new trial including a higher number of diabetic and immunosuppressed patients would be of great interest to elaborate more adapted PVC-duration protocols per category of patients.

PVCRI is obviously a serious health and economic problem. The results of this study showed a heterogeneity between different groups of patients regarding phlebitis. It suggests that there should not be a unique protocol regarding PVC-duration to all categories of patients. Patient-group adapted protocol should be more cost-effective. We recommend the conduction of a large observational epidemiologic study in order to elaborate a predictive clinical rule that will permit the stratification of patients according to their risk of developing phlebitis; this will allow us to decide whether a group of patients will need a rigorous surveillance of their insertion site and a more frequent catheter change.

Finally, we noticed that fever might be the only sign of PVCRI, and could be quite problematic in initially infected patients receiving antibiotics. It would be of great interest to see in future trials, if changing systematically the PVC every 48 hours would be cost-effective in such patients.

**REFERENCES**

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انتهاء متعلق بقذفاعة محبطية ورودية تجربة عشوائية مستقبلية

موجز - انهاج الوريد سبب قطرة محبطية ورودية أو انهاج العروق الملفانية مشكلة صحية وله علاقة بمرة بداية القذفاعة وعوامل خطر أخرى

الطريقة - درس 32 شهور للأنهاج الوريد المحتوي على علاجات بقذفاعة ورودية تم دفعها. وقد قمت عننا بعرض أخرى للكمرب المرض والجنس والداء السكري والعلاقة بالأحماض الحيوية والشربين وريدية، 31 مريضاً أطلقوا على مستشفى جامعي في ثلاثة أقسام مختلفة عشوائياً ووضع لهم قناعات ورودية لمدة 22 ساعة. الموضوع الأولي كان تعريفاً ان طول زمن القذفاعة تزيد من حينث أنهاج العروق الملفانية وكانت الواضح إشاراتياً بالدماغ، وانهاج الرعوم الأخرى ك الأمر المرض ورمجمه وأصابته بالسكري، والأدوات التي تختلف فيها ورودية وعلاجه بالانهاج سجلت الحمز وعلمات الانهاج الملفانية وتأخير ظهورها من قبل مرضى. استعمال البرنامج

خاص

20 Khi، اختيبر برسون 2 كمعادلة النسبة المئوية

النتائج - كان حصول انهاج العروق الملفانية بسبب القذفاعة 45.2% عند المرضى ونسبة الط(isseth) 1726 لساعة مختلفة من عمق القذفاعة 22 و 97 ساعة. مع ذلك فإن هذه النسبة تنفرد بين النورم الأولياً من جهة وبين النورم الثالث والرابع من جهة أخرى. الأمر والبداية بالمضادات الحيوية ورودياً والداء السكري، فإنها علاجة كبيرة لأنهاج العروق الملفانية بينما المداواة بالمضادات ورودياً يقتصرها وكانت الاختلافات غير محدود الطب الباطني والأمراض الأنتانية.

الخلاصة - تم الرصاب حول انهاج العروق الملفانية بين 22 و 97 ساعة مرة بدءاء القذفاعة وتوصي بأن يتم تغيير القذفاعة استناداً إلى عوامل الخطر عند كل مريض.
PERIPHERAL VENOUS CATHETER INSERTION PROTOCOL APPLIED AT HÔTEL-DIEU DE FRANCE UNIVERSITY HOSPITAL

1. Objective
   • Dispose a permanent and reliable peripheral venous access.
   • Consider a precise, quick and efficient therapeutic impact.
   • Prevent peripheral venous catheter-related complications and infections, by skillful and aseptic insertion and manipulation technique.

2. Indications
   PVC insertion is done based on physician prescription orders, and has specific therapeutic and/or diagnostic targets.

3. Anatomic site of canulation
   The choice of the site depends upon the nurse, while considering the following criteria:
   • Prefer the left hand and upper arm in right-handed patients and vice versa.
   • Avoid inserting a catheter in a limb that has been subject to an arterio-venous fistula, a lymphatic curage, a cutaneous infection, or an orthopedic foreign device.
   • Avoid inserting a catheter in lower limbs.

4. Devices
   • Draw-sheets, elastic garrot, disposable non-sterile gloves.
   • Sterile compresses, Leukoplast®.
   • Transparent adhesive dressing.
   • Broad-spectrum dermal antiseptic: Betadine dermique®, (10% povidone iodine solution), Bétadine moussante® (foamy), sterile saline serum, hydro-alcoholic solution (S pitaderm®).
   • Short peripheral venous catheter (PEU-Optiva®) with multiple gauge options.
   • Perfusion and serum-filled line, triple-lumen tap.
   • Multipurpose metallic container, needle waste container.
   • Perfusion post.

5. Technique
   • Perform a simple hand washing.
   • Prepare the devices and products on a clean and disinfected table.
   • Perform an antiseptic hand washing.
   • Locate the appropriate anatomic site for venous catheter insertion.
   • Install a draw-sheet under the patient’s arm.
   • Depilate the site of catheter insertion.
   • Install the elastic garrot.
   • Clean the skin with foamy providone iodine (Bétadine moussante®) soaked compresses; rinse; dry.
   • Apply a dose of hydro-alcoholic solution on the nurse’s hands.
   • Put on the gloves.
   • Perform an antiseptic (povidone iodine 10% solution) cleansing of the catheter insertion site from the center towards the periphery.
   • Wait for a one minute contact.
   • Choose the caliber (gauge) of the catheter according to the vein-calibre, the solution-type, and the perfusion flow.
   • Remove the elastic garrot.
   • Throw the mandrin in the needle waste container.
   • Connect the line provided with the triple-lumen tap.
   • Allow the flow of the perfusion solution.
   • Remove any trace of blood or oozing by sterile compress buffering; then dry correctly.
   • Fix the catheter with a sterile adhesive to avoid any vein mobilization.
   • Install a sterile adhesive and occlusive dressing on the insertion site.
   • Check the flow-back and fix the appropriate perfusion flow as noted by the physician.
   • Remove the gloves, put away the devices and outfit, clean the garrot, and wash hands.
   • Note down the catheter insertion date on the dressing and on the nursing-file.
6. Catheter Handling
- Perform an antiseptic hand washing.
- Keep the catheter-system closed.
- Reduce catheter-manipulations to the strict minimum.
- Employ antiseptic soaked sterile compresses for manipulating the tap.
- Put the lumen-cap on a povidone soaked compress.
- Use if necessary a sterile cap
- Keep the lines and connections free and away from any source of contamination.
- Replace systematically the lines after administering blood, blood-derived products, and lipidic solutions.

7. Looking after the catheter
- Check the insertion point at least every 8 hours.
- Detect evocative signs of inflammation and infection (inspection and palpation).
- Check the local aspect: erythema, œdema, heat, suppuration.
- Check the general aspect: fever, rigors, sweating.
- Replace immediately and aseptically the dressing if it is dirty, humid, or unstuck; and re-note down on the dressing the date of catheter-insertion.

8. Removal of the catheter
Removal of the PVC and its line and taps is compulsory:
- Every 96 hours.
- In case of local or regional reaction.
- In case of fever or rigors.
- If the catheter is obstructed.
For catheter removal:
- Wear non-sterile gloves.
- Exert pressure with a sterile compress for 2 minutes, on the insertion site after catheter removal.
- Put a sterile and dry dressing on the insertion site.