



Comparison of two different time interval protocols for central venous catheter dressing in bone marrow transplant patients: results of a randomized, multicenter study

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ABSTRACT

Background and Objectives. Care of central venous catheter (CVC) in patients undergoing bone marrow transplantation (BMT) raises significant problems related to the high risk of local infections due to the immunodeficient status, which in itself is a predisposing factor for systemic blood-stream infections. Although frequent changes of CVC dressing might theoretically reduce the incidence of infections, they are also accompanied by significant skin toxicity and patient discomfort. No study has yet addressed these points. The objective of this study was to compare two different time interval protocols for CVC dressing in order to assess the effects on local infections and toxicity.

Design and Methods. In a multicenter study, 399 bone marrow transplant (BMT) patients with a tunneled CVC (Group A, 230 pts) or a non-tunneled one (Group B, 169 pts) were randomly allocated to receive CVC dressing changes every 5 or 10 days, if belonging to Group A, or 2 or 5 days, if in Group B. Transparent, impermeable polyurethane dressings were used for all patients. The rate of local infections at the site of CVC insertion was assessed by microbiological assays every 10 days, while the severity of skin toxicity was measured according to the ECOG scale.

Results. Sixty-five per cent of enrolled patients were finally evaluable. Patients (in both Groups) receiving CVC dressing changes at longer intervals did not show a significant increase in the rate of local infections, while those who received dressing every 2 days had a significant increase in local skin toxicity. Longer intervals were accompanied by a reduction in costs.

Interpretations and Conclusions. The results of this study demonstrate that the increase in time interval between CVC dressing changes in BMT patients did not raise the risk of local infections, while significantly reducing patient discomfort and costs.

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Key words: bone marrow transplantation; central venous catheters; infections; catheter dressing; bone marrow nursing

The use of central venous catheters (CVC) in patients with neoplastic diseases has greatly facilitated therapeutic maneuvers and reduced patients' discomfort; however, these devices may also be causes of mechanical and septic complications.¹ Central venous catheters can be divided into two different categories: the *tunneled type* (long-term CVCs, including the Groshong, Hickman, and Leonard types) and the *non-tunneled* ones (short-term type, such as Hohn or Arrow CVCs). The latter differ from the former mainly because they lack a percutaneous tunnel and approach the venous lumen directly; for this reason, the time they can remain *in situ* is shorter than that of catheters with a percutaneous tunnel.

Apart from the mechanical complications (either at the time of insertion or later on) that are common to all patients bearing a CVC irrespectively of the underlying disease,² the use of a CVC in patients undergoing bone marrow transplantation (BMT) poses significant issues that are unique to this category of patients. In fact, these patients receive high-volume fluid infusions for a long period of time (generally, more than one month), including total parental nutrition, and have an exceedingly high risk of infectious complications. These latter can be ascribed to a number of factors, including the profound immunodepressed state consequent to the underlying disease itself, previous treatments, the radio-chemotherapeutic conditioning regimen used in preparation for the BMT, and, in the setting of allogeneic BMT, also to concomitant immunosuppressive drugs given either to prevent or to treat graft-versus-host disease (GvHD).³ Furthermore, susceptibility to infection is increased as a consequence of the loss of cutaneous integrity due to skin toxicity caused by the conditioning regimen, to GvHD skin localization in the allogeneic setting, and possibly other factors.⁴

Management of CVC in BMT patients requires careful aseptic techniques. In most BMT centers in Italy, CVC dressing procedures were performed, at the time of beginning this study, on an alternate-day basis

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using dry sterile gauzes as a covering for the insertion site. However, there is no clear indication in medical or nursing literature about what is the optimal time interval for CVC dressing changes or the most appropriate device for dressing, not even in the *Guidelines for prevention of intravascular device-related infections* recently published by the CDC.⁵ To address these issues, we designed a co-operative, randomized trial to compare two different schedules for CVC dressing in BMT patients using transparent adherent dressings. Patients with both long-term tunneled and non-tunneled CVCs were included in the study, and randomized to receive dressing changes at two different time intervals. The specific aims of the study were to determine: i) the impact of the different time scheduling on infectious complications at the insertion site; ii) the severity of local skin toxicity directly attributable to the dressing procedure itself. Secondary aims were to evaluate the economic implications of the procedures. Seven Italian BMT centers provided patients for the study, in which a total of 399 patients were enrolled.

Design and Methods

Patients

In the period from March 1996 to October 1997, 399 consecutive patients undergoing bone marrow transplantation (either autologous, allogeneic from sibling or unrelated donors, or recipients of autologous peripheral blood stem cells) were enrolled in the study from seven Italian BMT Units. After admission to the BMT Unit, a tunneled CVC was inserted in 230 patients (group A), while in the remaining 169 patients a non-tunneled CVC was inserted (group B). The higher number of patients in the group of tunneled CVC was due to the fact that in some hematology centers (2 out of 7 centers) only long-term, tunneled CVCs are routinely used in BMT patients, irrespective of the type (autologous or allogeneic) of transplant. Patients in group A were randomly selected to have CVC dressing changes at either 5 (112/230 patients) or 10 days (118/230), while for patients in group B the time interval was either 2 days (84/169) or 5 days (85/169). Any additional dressing required for any reason before the scheduled time was recorded on an appropriate form, and the reason was also specified. The two protocols differ in the respective time intervals between two consecutive dressing changes since it has been shown that non-tunneled CVCs have a significantly higher infection rate at the insertion site than tunneled ones.¹⁻⁶ The study was approved by the Ethical Committee of Azienda Ospedaliera Careggi, Florence, Italy. Patients were included in the study after informed, signed consent had been obtained. Randomization was performed in the Florence Center.

Criteria for inclusion and withdrawal from the study

Patients with the following characteristics were not admitted to the study: patients with active cutaneous lesions at the site of CVC insertion at the time of enrollment; patients with known allergy to polyurethane dressings; patients with generalized dermatologic diseases. Patients were withdrawn from the

study for any of the following reasons: skin cultures gave positive results for infectious agents and/or antimicrobial treatment had been started, under medical judgment; significant local skin toxicity (grade II or more); persistent blood loss from the CVC insertion site; spontaneous CVC dehiscence.

CVC maintenance

A detailed protocol for CVC dressing under controlled sterile conditions was prepared, and all nurses involved in CVC maintenance were asked to adhere strictly to it for the whole study period; it was the responsibility of each Center's co-ordinator to ensure the correct performance of the protocol. Sterile polyurethane transparent adherent dressings (Tegaderm™, 3M Company, St. Paul, MN, USA) was used for the CVC dressings.

Skin cultures

Skin swabs were taken from the site of CVC insertion in all patients enrolled in the study at the time of admission to the BMT Unit (*basal sample*) and later on at 10-day intervals during the BMT procedure for the whole period of the patients' stay in hospital. Cultures for bacterial and fungal agents were set up according to established methodologies used in the microbiology department of each Center's central hospital laboratory.

Criteria for cutaneous lesion grading

The following parameters were carefully checked at all dressing changes and at the time of CVC removal: erythema, swelling, tenderness, induration, pain, pruritus, and purulence. Cutaneous lesions were graded according to the ECOG scale (Table 1). A specific data form sheet was made available for recording ECOG grading in each patient for each dressing.

Statistical analysis

Data were registered from participating Centers on pre-printed paper data forms, which were collected and analyzed in the BMT Unit of Florence. Statistical analysis of data was conducted by Pearson's χ^2 test, using the SPSS program (Statsoft, Tulsa, CA, USA) by a person who had not been involved in the clinical study. The level of statistical significance was set at $p \leq 0.05$.

Table 1. ECOG scale of skin toxicity.

Grade	
0	None
1	Scattered macular or papular eruption or asymptomatic erythema
2	Scattered macular or papular eruption or erythema with pruritus or other associated symptoms
3	Generalized symptomatic macular, papular or vesicular eruption
4	Exfoliative dermatitis or ulcerating dermatitis

Table 2. Reasons for patients being withdrawn from the study.

Type of CVC	Patients withdrawn/total enrolled	Because of topical antibiotic use	Because of cutaneous toxicity	Other reasons
Tunneled (Group A)	70/230 (30.4%)	32 (45.7%) ^o	30 (42.8%)	8 (11.4%)
Non-tunneled (Group B)	70/169 (41.4%)	7 (10%)	52 (74.3%)*	11 (15.7%)

* $p < 0.05$; ^o $p < 0.01$.

Results

Of 399 enrolled patients, 259 (65%) completed the study. In the group of patients with tunneled CVC, 160 patients out of 230 (69%) completed the study; 79 patients had been randomly assigned to the 5-day group and 81 patients to the 10-day group. Of the 99 patients with a non-tunneled CVC who completed the study (58% out of a total of 169), 49 patients had been assigned to the 2-day group and 50 patients to the 5-day group. Reasons for withdrawing patients are reported in Table 2. The main reason for withdrawal in the tunneled group was the use of topic antibiotics because of a positive local cutaneous swab, while in the non-tunneled group the most frequent reason was local cutaneous toxicity; in both instances, the difference between the two groups was statistically significant (Table 2).

During the study a total of 415 dressings were performed in the 5-day group of patients bearing an indwelling CVC, of which 40 (9.6%) were additional to the scheduled ones; in the 10-day group, the total

number of dressings was 280, 56 (20%) of which were additional. Among patients with a non-tunneled CVC, there were 293 dressings in the 2-day group, of which 14 (4.7%) were additional, and 200 dressings in the 5-day group, of which 25 (12.5%) were additional. A detailed analysis of the reasons for additional dressings is reported in Table 3; dressing dehiscence requiring a new dressing was by far the most frequent cause in patients enrolled in the 10-day group as compared to the other groups ($p < 0.05$), and alone accounted for 57% of unscheduled dressings.

Classification of patients according to cutaneous toxicity is shown in Table 4. Grade 0 toxicity was recorded in 86% and 87% of redressings in the 5-day group and 10-day group, respectively; the difference between the two groups of patients with indwelling CVC was not significant. In contrast, there was a greater proportion of patients showing grade I-III toxicity in the 5-day non-tunneled group than in the 2-day group (33.5% vs 25%, $p = 0.002$); accordingly, the percentage of patients with grade 0 toxicity was significantly higher in the 2-day group (75%) than in the 5-day group (66%; $p < 0.005$).

Of the 160 patients with a tunneled CVC, a positive swab during the study was recorded in 25 (15.6%); these positive swabs were equally distributed between the two groups (12 in the 5-day group and 13 in the 10-day one). Swab positivity was first documented in the sample collected at ten days in 16 patients and in the remaining 9 patients after twenty days (third swab sampling). Of the 99 patients with a non-tunneled CVC, a positive swab was recorded in 18 (18%), 9 patients in each study arm (2- and 5-days); in 14 patients positivity was documented on the occasion of the second sampling (at ten days) and in 4 patients on third sampling (20 days).

Table 3. Additional dressings.

Type of CVC	Total number of scheduled dressings	Number of additional dressings	Because of dressing deiscence	Because of cutaneous toxicity	Other reasons
Group A, 5-days	375	40 (9.6%)	12 (3.2%)	0	28 (7.4%)
Group A, 10-days	224	56 (20%)*	32 (14.2%)*	3 (1.3%)	21 (9.3%)
Group B, 2-days	279	14 (5.0%)	2 (0.7%)	2 (0.7%)	10 (3.5%)
Group B, 5-days	175	25 (14.2%)	4 (2.2%)	0	21 (12%)

* $p < 0.05$. Other reasons include local hemorrhage, removal of non-adsorbable suture at the site of CVC insertion, patient discomfort such as sine materia pruritus or intolerance.

Table 4. Skin toxicity.

Type of CVC	Total n. of dressings	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Group A, 5-days	415	357 (86%)	50 (12%)	7 (1.7%)	1 (0.2%)	0
Group A, 10-days	280	245 (87%)	25 (9%)	10 (3.6%)	0	0
Group B, 2-days	293	219 (75%)	59 (20%)	14 (5%)	1 (0.3%)	0
Group B, 5-days	200	133 (66%)	62 (31%)	5 (2.5%)	0	0

The two B subgroups were different at the $p = 0.002$ level (Pearson's test).

The agent most frequently isolated from CVC swabs was *Staphylococcus epidermidis* (28/52 positive samples in patients with a tunneled CVC, and 16/18 patients with a non-tunneled CVC). *Staphylococcus aureus* was found in 24 swabs (23 from the tunneled group), while in one case *Streptococcus* was isolated from a patient with a non-tunneled CVC and a fungus from a patient with a tunneled CVC.

Table 5 reports a detailed description of the economic aspects of the two different scheduling protocols, considering both the materials and nursing costs. In the tunneled CVC group, the total cost for the 2-day protocol was about \$66, compared to \$15.5 in the 10-day group; thus there was a greater than 400% saving; in the non-tunneled group, the difference was still significant, the costs being \$33 and \$15.4 in the 2-day and 5-day group, respectively, with about a 50% saving.

Discussion

BMT patients require multiple intravenous infusions and phlebotomies which are routinely performed through a CVC; this latter can be either tunneled or not, depending on the supposed duration that the CVC will remain *in situ*, the type of transplant, personal or surgeon's choices, and so on. Routine care of CVCs in most BMT centers is dry sterile gauze dressings, generally changed on an every-other day basis, and secured to the skin with tapes; the dressings serve as a barrier to bacterial infections but also provide a mechanical protection for the infusion line itself. However, the main drawback of the procedure is cutaneous toxicity at the dressing site, since frequent gauze changes, and also the use of tape, may in themselves cause skin damage, or worsen the effects on the skin of the radio-chemotherapeutic regimen used in preparation for a BMT. This concern has already prompted other studies aimed at evaluating the impact of longer time intervals between catheter dressings in a pediatric BMT unit.⁷ Furthermore, a previous report on adult BMT patients^{8,9} indicated the effectiveness of transparent adherent dressings as compared to the dry technique. These devices provide a barrier impermeable to water and bacteria, and allow for longer time intervals between dressing procedures, without causing an increase in infectious complications. Such properties are of particular interest in the BMT settings for a number of reasons, including a reduction of local skin toxicity resulting from frequent dressing changes, an increased antibacterial protection, and finally a reduction in specialized nursing time with financial savings; also, since they are waterproof, they allow the patient to have showers, and improve catheter stability when compared to the dry dressing technique with gauze.¹⁰ However, as stated in the guidelines published by the *Hospital Infection Control Practices Advisory Committee (HICPAC)*,⁵ the allowed time that transparent dressings can remain on the site of a long-term CVC remains to be established in controlled studies.

The analysis of the data supported the conclusion that patients who had CVC dressings changed at longer intervals (5 vs 2 days in the non-tunneled group; 10 vs 5 days in the tunneled one) were more

Table 5. Economic aspects of the study.

	Tunneled		Non-tunneled	
	Standard*	New ^o	Standard*	New ^f
Nurses' time/patient	280 min	56 min	140 min	56 min
Nurses' cost/patient	\$45.37	\$9.86	\$22.68	\$9.86
Dressing cost	\$16.85	\$4.69	\$8.42	\$4.69
Total cost	\$62.22	\$14.55	\$31.10	\$14.55

*dressing changes on alternate days; ^odressing changes every 10 days.

^fdressing changes every 5 days.

Calculations were made on a exchange rate \$1= 1,700 Italian liras. The actual (net) cost of a nurse in an Italian public hospital is about \$10/hour. Calculations were made based on the assumption that the mean hospital stay for an allogeneic patient with a tunneled CVC was about 40 days (corresponding to a total of 20 dressing changes according to the standard protocol and to 4 changes in the new protocol); the assumption for an autologous BMT recipient with a non-tunneled CVC was about 20 days (corresponding to a total of 10 dressing changes in the standard protocol and 4 with the new one). Median time per dressing was calculated from the scheduled time of PNR (10 min), the Clock Survey from Azienda Ospedaliera Careggi, Florence (20 min), and the time measured at the bedside in the BMT Unit in Florence (13 min).

comfortable in that they experienced cutaneous toxicity less frequently, and to a lesser degree, without being exposed to a higher risk of local infectious complications. In fact, the most frequently identified agent in skin swabs was *Staphylococcus epidermidis*, which can be found almost universally on the skin.¹¹⁻¹³ Finally, these patients required significantly less dedicated nursing time, with substantial money saving.

Some studies have reported an increase of bacterial colonization at the site of CVC insertion in patients with an adherent polyurethane dressing compared to those with sterile gauzes,^{14,15} other studies have failed to confirm these negative results.¹⁶⁻¹⁸ Although it was not the aim of this study to compare transparent versus dry dressings, a retrospective analysis of local infections in a cohort of BMT patients who had received sterile gauzes for CVC dressing did not demonstrate any difference in comparison to the present study with polyurethane devices (personal observations, not reported in detail).

A possible limitation of this study is that patients were analyzed as one group divided only according to the type of CVC inserted, without taking into account the different types of transplant (autologous, allogeneic-related and unrelated, or peripheral-blood stem cell transplant) or the underlying diseases; indeed, the severity of immunodeficiency, and hence the risk of infections, is substantially higher in recipients of allogeneic transplants because of GvHD prophylaxis and/or treatment. However, stratification of patients for these variable would have required an exceedingly high number of subjects to be enrolled. Finally, the incidence of sepsis was not evaluated, since the study group was not sufficiently homogeneous under this respect as concerned other important variables, including the different architectural structures of the hospitals with or without laminar-flow or HEPA-filtered air rooms, different pro-

cedures for fluid infusions, delivery or not of total parental nutrition, use or not of sterile supplies and food, and so on.

Contributions and Acknowledgments

LR was the main investigator, managed and analyzed the data, and wrote the manuscript. D'IM and MM collaborated with LR in collecting and analyzing the data, and in literature revision. AF, BS, GA, AMT, ŽR, PMG, DR, TS, PG, PS, DLT, PG, were responsible, in their respective BMT centers, for enrolling and managing the patients according to the study protocol, and for data collection. The criteria for the order in which the names of the authors appear are based on their contribution to the design, analysis, interpretation of the data, and execution of the study.

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Disclosures

Conflict of interest: none.

Redunant publications: no substantial overlapping with previous papers.

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Potential implications for clinical practice

- ◆ Longer time intervals between CVC dressings do not cause any significant increase in local infectious complications.
- ◆ Longer time intervals between CVC dressings reduce procedure-related local skin toxicity and patient's discomfort.
- ◆ Longer time intervals between CVC dressings allow substantial money and resources saving.

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