Tumori, 96: 690-694, 2010

Central venous catheter-associated thrombosis in the perioperative period: a frequent complication in cancer patients that can be detected early with Doppler examination

Kerim Bora Yilmaz[1], Melih Akinci[1], Lutfi Dogan[2], Zeynel Yologlu[2], Can Atalay[2], and Hakan Kulacoglu[1]

[1]Department of General Surgery, Diskapi Education and Research Hospital, Diskapi - Ankara; [2]Ankara Oncology Education and Research Hospital, Ankara, Turkey

ABSTRACT

Aims and background. The aim of the study was to determine the incidence of venous thrombosis in cancer patients with central venous catheters inserted perioperatively.

Methods and study design. A prospective analysis was performed with 68 patients in whom central venous catheters were placed perioperatively. Cancer patients with planned central venous catheters had prophylaxis with low-molecular-weight heparin. Patient characteristics, procedure-related complications and venous thrombosis related to central venous catheters were recorded. In order to detect the venous thrombosis, color Doppler sonography was used after removal of the central venous catheter.

Results. The median age of the 68 patients was 55 years (range, 24-83). The median duration of catheter placement in patients was 9 days (range, 1-24). Venous thrombosis was detected in 45 (66.2%) patients: at the superficial veins (jugular and subclavian veins) in 27 patients, stretching from superficial veins into the vena cava in 8 cases, in the vena cava in 2 cases, in the right atrium in 2 cases, and at more then one place in 6 patients. Total thrombosis was detected only in 3 patients.

Conclusions. Cancer patients have a high central venous catheter-related thrombosis risk perioperatively despite prophylactic anticoagulation. Color Doppler sonography is a rapid and noninvasive technique and it is accurate in the diagnosis of venous thrombosis. Early detection of venous thrombosis is important to prevent the systemic and fatal complication of the thrombosis. Free full text available at www.tumorionline.it

Introduction

Thrombosis is an important complication of intravascular catheters, especially in patients with cancer, and it is a source of considerable morbidity[1]. Catheter-related thrombosis is an under-diagnosed and under-treated condition, so that the true incidence of thrombosis associated with central venous catheters is difficult to estimate[2,3]. The published data are conflicting due to different definitions, different methods for detection of the central venous catheter-associated thrombosis, and the use of the different catheters[3].

The present study sought to determine the incidence of venous thrombosis (VT) in cancer patients with central venous catheters (CVC) and to detect VT by ultrasonography before clinical symptom and complications.

Materials and methods

Ethics committee approval and informed consent of patients were obtained for this prospective study. Patients were eligible if they had a histologically confirmed diag-

Key words: cancer, central venous catheter, venous thrombosis.

Correspondence to: Melih Akinci, 1424. Cadde 1435.Sokak 4/14, 06520 Cukurambar/Ankara, Turkey.
Tel +90-505-6253175;
fax +90-312-3454979;
e-mail melihakinci@yahoo.com

Received December 12, 2009;
accepted May 28, 2010.

nosis of cancer, needed CVC insertion, and were at least 16 years of age. Patients were excluded if they had a contraindication for antithrombotic prophylaxis or if they were already on warfarin or any other anticoagulation therapy for other indications.

Sixty-eight consecutive cancer patients in whom CVC were placed were included in the study. Double-lumen catheters (Certofix Duo V 720, Braun, Melsungen, Germany) were inserted into either the right internal jugular vein or subclavian vein by the Seldinger method under sterile technique. Polyurathane dual-lumen CVC (0.8 Fr, 12 cm long) were used. Cancer patients had antithrombotic prophylaxis with low-molecular-weight heparin (LMWH) (Enoxaparin anti-Xa 5000 IU per day, Clexan, Sanofi-Aventis, Paris, France) starting on the first postoperative day until totally mobile or discharge from the hospital.

Patient characteristics, procedure-related complications and VT related to CVCs were recorded. Standard postprocedure chest radiograph was used to detect malposition and mechanical complications. The correct position of the catheter tip (at the junction of the superior vena cava and right atrium) was checked by chest radiography after CVC insertion. In order to detect the VT, color Doppler sonography (CDS) was used after removal of the CVC. VT characteristics such as size and vessel localization were noted. When a VT was detected, the patient underwent a standard medical therapy protocol to prevent systemic VT. The standard treatment included increasing the doses of LMWH and warfarin.

All statistical analyses were performed with SPSS (version 11.5) software (SPSS, Inc, Chicago, ILL, USA). Continuous values are expressed as mean ± standard deviation and nominal variables as counts (percentages). The patients with and without thrombosis were compared with chi-square and t tests. P <0.05 was considered as significant.

Results

The mean age of the 68 patients was 55 years (range, 24-83). Seven patients had an urgent and 61 patients had a planned procedure. The mean duration of catheter placement in patients was 9.2 days (range, 1-24). Twenty-eight (41.2%) patients had stomach-esophagus, 26 (38.2%) had colon-rectum, 2 (2.9%) had breast, and 2 (2.9%) had intra-abdominal masses, and 10 (14.7%) had urgent non-malignant operations. Staging: 19 (27.9%) patients were stage II, 23 (33.8%) were stage III, and 16 (23.5%) were stage IV. Fifty-three (77.9%) patients underwent organ resection. The indication of the CVC was for major surgery in 54 (79.4%) cases, to support therapy in 6 (8.8%) cases, for complications after the surgery in 5 (7.4%) cases, and to deliver blood products and drugs in 3 (4.4%) cases. CVC-related mechanical complications were pneumothorax in 1 (1.5%) patient and arterial puncture in 4 (5.9%) patients. Malposition was detected as the left jugular vein in 2 (2.9%) cases and the right jugular vein in 1 (1.5%) case.

VT was detected in 45 (66.2%) patients with CDS, but no clinical complication was detected. Table 1 compares the patients with and without thrombosis. There were no statistically significant differences between the patients with and without CVC-related thrombosis as regards demographics, clinical characteristics, site of insertion and complications of the CVC (Table 1). The CVC with VT stayed longer than the catheters without thrombosis, although the difference did not reach statistical significance.

The mean length of the thrombosis was 1.05 cm (range, 0.1-4). The VT was at the superficial veins (jugular and subclavian veins) in 27 (37.9%) patients. The VT stretched from superficial veins into the vena cava in 8 (11.8%) cases, it was located at the vena cava in 2 (%2.9) cases, and at the right atrium in 2 (2.9%) cases (Figures 1-4). In 6 (8.8%) cases, the VT was located at more then one place. Total thrombosis was detected only at 3 (4.4%) patients (Figure 2).

Discussion

CVC placement increases the risk of thrombosis in cancer patients perioperatively. Thrombosis often necessitates removal of the CVC, resulting in treatment delays and thrombosis-related morbidity and mortality.

In the present study, using Doppler ultrasonography, we detected CVC-related thrombosis in 66% of the patients with cancer despite prophylactic anticoagulation. In a study with Doppler ultrasonography, in 81 patients undergoing cardiac surgery, thrombi were found in 56% of patients with short-term (3-4 days) catheterization in spite of routine heparin administration[4]. Another study performed in an ICU detected thrombi after removal of the catheter in 64% of patients[5]. Ultrasonic evaluation was performed after removal of CVC because sleeve-like thrombi could not be identified with the catheter in the vein[4]. The rate of CVC thrombosis in cancer patients ranged from 3% to 62%, especially when assessed with sophisticated tools such as ultrasound or venograms[1,2,6-8]. In our study, the thromboses were detected early, before any symptoms developed. Therefore, perioperative central VT incidence is higher than symptomatic long-term catheter-related thrombotic events, whose incidence has recently been reported to be 6% in cancer patients with or without warfarin thromboprophylaxis[2]. In future studies, it would also be interesting to compare the outcome of patients with cancer *versus* patients harboring non-neoplastic diseases regarding the CVC thrombosis rate perioperatively.

Venograms have been seen as the gold standard, but they are expensive and complex to conduct and require

Table 1 - Clinical characteristics and complications of central venous catheter insertion in cancer patients with and without Doppler-detected thrombosis after removal of the central venous catheter

	No thrombosis, n = 23	Thrombosis, n = 45	*P*
Age (yr)	57 ± 13	54 ± 14	0.354
Male/Female	15/8	31/14	0.483
Emergency/elective operation	2/21	5/40	0.559
Type of operation: stomach-esophagus, colon, breast, intra-abdominal mass, emergency non-malignant	10, 10, 0, 1, 2	18, 16, 2, 1, 8	0.773
Surgical organ resection	17	36	0.390
Stage II, III, IV	11, 4, 6	8, 19, 10	0.97
ICU stay (n)	19	42	0.169
Duration of ICU stay, days (range)	1 (0-2)	1 (0-12)	0.12
Internal jugular, subclavian vein (n)	7, 16	14, 31	0.64
Complications during CVC insertion: arterial puncture, pneumothorax (n)	1, 0	3, 1	0.582
Malposition: left jugular vein, right jugular vein (n)	0	2, 1	0.21
Complications during catheter stay: skin infection, obstruction (n)	1, 0	3, 3	0.38
Duration of the CVC (no. of days)	7.9 ± 4	9.9 ± 5	0.08

ICU, Intensive Care Unit; CVC, central venous catheter.
Data are given as number of patients (n), mean ± standard deviation or median (minimum-maximum).

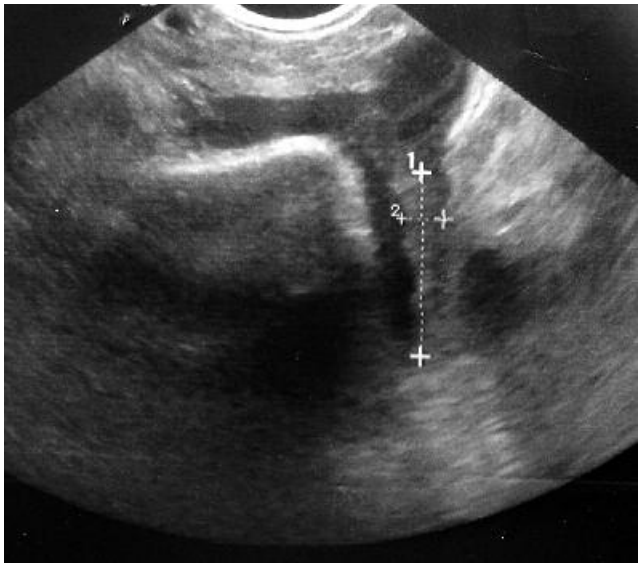

Figure 1 - Venous thrombosis in subclavian vein spreads through inferior vena cava.

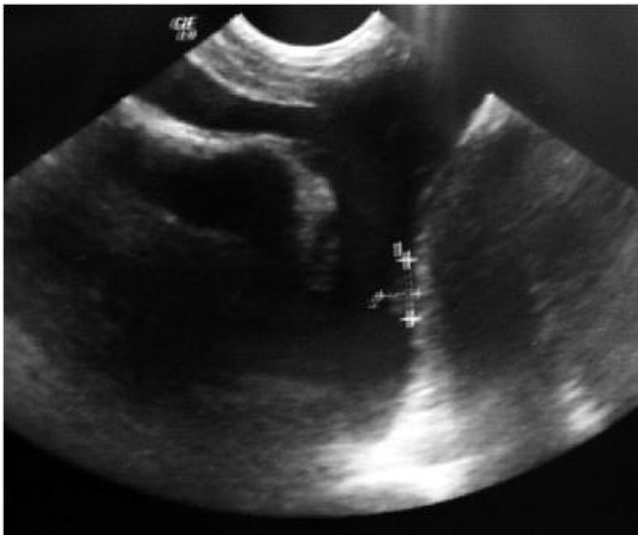

Figure 2 - Total thrombosis in internal jugular vein.

the administration of contrast media[1,6]. Color Doppler is now the diagnostic tool of choice, with a 95% accuracy rate for clots in the internal jugular and subclavian veins. The reliability falls with pathology in the deeper innominate veins and the superior vena cava[1,5,9].

The patients with CVC-related thrombosis had a longer duration of the CVC, although the difference did not reach statistical significance in our study. The correlation between duration of catheterization and incidence of thrombosis has been demonstrated in some studies[7,10] but others failed to confirm such a correlation[11]. It is important to note that our study included postoperative patients with a relatively shorter duration of CVC placement than long-term CVC used in cancer patients.

The size of the thrombi in our study was relatively small, and they were mostly located superficially. This could simply be a natural healing reaction to the sudden appearance of a hole in a major vein as a result of removing the CVC from a traumatized entry and then exit site. However, we detected in some patients multiple thrombi, thrombi in major veins and even total thrombosis. None of our patients experienced clinical signs of pulmonary embolism or paradoxical systemic embolism, although silent embolisms might have been missed. One-third or less of the catheter-associated thrombi showed clinical signs in previous reports[6,12,13]. The literature reports varied rates of clot extension, ranging from 6% to 50%, in individuals with upper extremity deep VT resulting in pulmonary embolism[1,6,7,12].

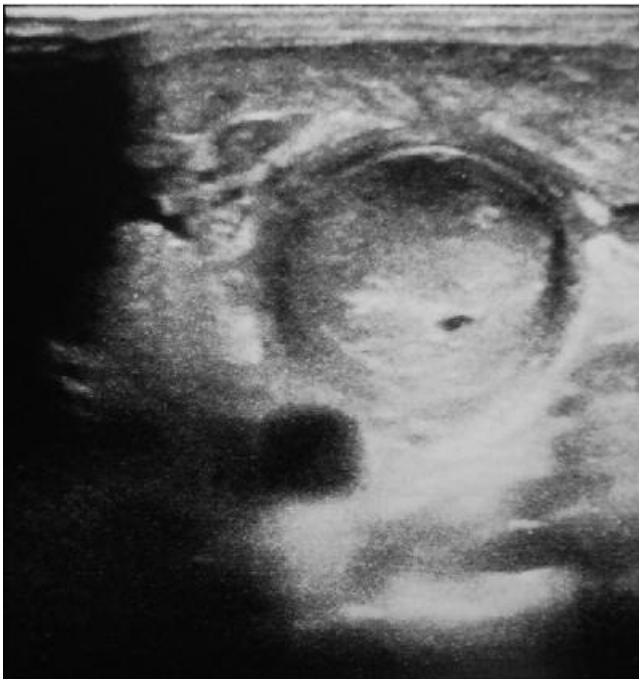

Figure 3 - Venous thrombosis in internal jugular-subclavian veins.

Figure 4 - Thrombosis in superior vena cava.

Many studies have shown links between the presence of thrombosis and fibrin sheaths and persistent catheter-related bloodstream infection, with the clot acting as a nidus for infection[6,14-16]. Although our study did not reveal thrombosis-related embolisms, infection or sepsis, our findings still reaffirm the importance of common clinical practice of promptly removing a CVC as soon as it is no longer needed perioperatively.

Cancer patients with CVC considering anticoagulation should consider the possible benefit of reduced incidence of thromboembolic complications with the burden and harms of anticoagulation[17]. Current evidence does not support routine use of thromboprophylaxis for CVC or a specific anticoagulant for perioperative thromboprophylaxis. Anticoagulants may improve survival, but more data will be useful in deciding which subgroups benefit most[18]. The balance of benefits and downsides of thromboprophylaxis in cancer patients with CVC are uncertain. Clinicians together with their patients should weigh these factors carefully when making decisions regarding thromboprophylaxis[19]. CDS is a rapid and noninvasive technique and it is accurate in the diagnosis of VT. Early detection of VT is important to prevent the systemic and fatal complication of the thrombosis.

In conclusion, cancer patients have a high CVC-related thrombosis risk despite prophylactic anticoagulation. CDS is a rapid and noninvasive technique and it is accurate in the diagnosis of VT. Early detection of VT is important to prevent the systemic and fatal complication of the thrombosis.

References

1. Verso M, Agnelli G: Venous thromboembolism associated with long-term use of central venous catheters in cancer patients. J Clin Oncol, 21: 3665-3675, 2003.
2. Young AM, Billingham LJ, Begum G, Kerr DJ, Hughes AI, Rea DW, Shepherd S,Stanley A, Sweeney A, Wilde J, Wheatley K: WARP Collaborative Group, UK. Warfarin thromboprophylaxis in cancer patients with central venous catheters (WARP): an open-label randomised trial. Lancet, 373: 567-574, 2009.
3. Prandoni P: Prophylaxis of catheter-related thrombosis in cancer patients. Lancet, 373: 523-524, 2009.
4. Wu X, Studer W, Skarvan K, Seeberger MD: High incidence of intravenous thrombi after short-term central venous catheterization of the internal jugular vein. J Clin Anesthesia, 11: 482-485, 1999.
5. Karnik R, Valentin A, Winkler WB, Donath P, Slany J: Duplex sonographic detection of internal jugular venous thrombosis after removal of central venous catheters. Clin Cardiol, 16: 26-29, 1993.
6. Yacopetti N: Central venous catheter-related thrombosis: a systematic review. J Infus Nurs, 31: 241-248, 2008.
7. Monreal M, Devant E: Thrombotic complications of central venous catheters in cancer patients. Acta Haematol, 106: 69-72, 2001.
8. Karthaus M, Kretzschmar A, Kröning H, Biakhov M, Irwin D, Marschner N, Slabber C, Fountzilas G, Garin A, Abecasis NG, Baronius W, Steger GG, Südhoff T, Giorgetti C, Reichardt P: Dalteparin for prevention of catheter-related complications in cancer patients with central venous catheters: final results of a double-blind, placebo-controlled phase III trial. Ann Oncol, 17: 289-296, 2006.
9. Gaitini D, Beck-Razi N, Haim N, Brenner B: Prevalence of upper extremity deep venous thrombosis diagnosed by color Doppler duplex sonography in cancer patients with central venous catheters. J Ultrasound Med, 25: 1297-1303, 2006.

10. Brismar B, Hardstedt C, Jacobson S, Kager L, Malmborg AS: Reduction of catheter associated thrombosis in parenteral nutrition by intravenous heparin therapy. Arch Surg, 117: 1196-1199, 1982.
11. Balestreri L, De Cicco M, Matovic M, Coran F, Morassut S: Central venous catheter-related thrombosis in clinically asymptomatic oncologic patients: a phlebographic study. Eur J Radiol, 20: 108-111, 1995.
12. Agnelli G, Verso M: Therapy insight: venous-catheter-related thrombosis in cancer patients. Nat Clin Pract Oncol, 3: 214-222, 2006.
13. Verso M, Agnelli G, Bertoglio S, Di Somma FC, Paoletti F, Ageno W, Bazzan M, Parise P, Quintavalla R, Naglieri E, Santoro A, Imberti D, Sorarù M, Mosca S: Enoxaparin for the prevention of venous thromboembolism associated with central vein catheter: a double-blind, placebo-controlled, randomized study in cancer patients. J Clin Oncol, 23: 4057-4062, 2005.
14. Kuter D: Thrombotic complications of central venous catheters in cancer patients. Oncologist, 9: 207–216, 2004.
15. Timsit J, Farkas J, Boyer J, Martin JB, Misset B, Renaud B, Carlet J: Central vein catheter-related thrombosis in intensive care patients: incidence, risk factors, and relationship with catheter-related sepsis. Chest, 114: 207-213, 1998.
16. Mehall J, Saltzman DA, Jackson RJ, Smith SD: Fibrin sheath enhances central venous catheter infection. Crit Care Med, 30: 908-912, 2002.
17. Akl EA, Karmath G, Yousico V, Kim SY, Barba M, Sperati F, Cook DJ, Schünemann HJ: Anticoagulation for thrombosis prophylaxis in cancer patients with central venous catheters. Cochrane Database Syst Rev, 3: CD006468, 2007.
18. Ald EA, Muti P, Schünemann HJ: Anticoagulation in patients with cancer: an overview of reviews. Pol Arch Med Wewn, 118: 183-193, 2008.
19. Akl EA, Karmath G, Yousico V, Kim SY, Barba M, Sperati F, Cook DJ, Schünemann HJ: Thromboprophylaxis for patients with cancer and central venous catheters: a systematic review and a meta-analysis. Cancer, 112: 2483-2492, 2008.