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# *Peripherally inserted central catheters and upper extremity deep vein thrombosis*

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## SUMMARY

The purpose of the study was to determine the incidence and risk factors for venous thrombosis in patients with a peripherally inserted central catheter (PICC). A retrospective study of all upper extremity venous duplex scans was carried out in the Vascular Medicine department from year 2000 to 2002 inclusive. A chart review of positive scans was undertaken to identify possible thrombotic risk factors. Of 317 upper extremity venous duplex scans carried out, 115, or 32%, were positive for upper extremity deep vein thrombosis. Three main risk factors were identified – presence of a central line, malignancy and administration of chemotherapy. PICC were the most common central line present. Symptomatic thrombosis occurred in 7% of PICC inserted for chemotherapy compared with 1% of PICC inserted for other reasons. Ten per cent of the patients receiving chemotherapy through a PICC developed a thrombosis. The post-thrombotic syndrome was infrequent following upper extremity deep vein thrombosis. Patients receiving chemotherapy through a PICC are at increased risk of thrombosis. There may be a role for prophylactic low-dose anticoagulation in these high-risk patients.

**Key words:** *deep vein thrombosis; peripherally inserted central catheter.*

## INTRODUCTION

Upper extremity deep vein thrombosis (UEDVT) is a major complication of standard central venous and tunnelled central catheters such as Hickman and Portacaths.[1,2] This is in part because of their widespread use in hospital wards, intensive care units and also improved diagnostic testing with duplex ultrasound.[2] These catheters may also be complicated by infection, occlusion, fibrin sheath formation, pulmonary embolism and septicaemia.[2] Peripherally inserted central catheters (PICC) have emerged as a convenient, safe and a cost-effective alternative, being relatively simple to insert.[3–5] PICC can be inserted on the ward or in the radiology suite, where ultrasound and fluoroscopy guidance can be used. Administration of drugs or fluids can occur in the outpatient or home setting, enabling early discharge from hospital. All central venous catheters, including PICC, have been implicated in UEDVT. However, there have been few studies examining thrombosis related to PICC. The incidence of thrombosis in PICC was reported in a single series at approximately 4%.[3]

The Princess Alexandra Hospital is a tertiary institution with a large oncology and haematology service. The purpose of the study was to review cases of UEDVT related to PICC and to identify possible risk factors for thrombosis.

## PATIENTS AND METHODS

All upper extremity venous duplex scans carried out in the Department of Vascular Medicine over a 3-year period from 1 January 2000 to 31 December 2002 were reviewed. A chart review of patients with positive scans was then undertaken. Details of patient characteristics, the diagnosis, the type of central venous catheter if present, treatment and chemotherapy data were collected.

Venous duplex scans were carried out using either a Phillips ATL HDI3000 (Phillips, Bothell, WA, USA) or a GE Diasonics

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Gateway fx (General Electric, Santa Clara, CA, USA) ultrasound machine. A linear 7–4 MHz array transducer was used. Duplex criteria for diagnosis of thrombosis were absence of flow on Doppler scanning for axillo-subclavian vessels and non-compressibility of peripheral vessels.

All PICC were inserted under ultrasound and fluoroscopic guidance in the radiology suite. The radiologist accessed a vein in the mid-to-distal upper arm, using needle, guidewire and peel-away sheath. The position was routinely confirmed by fluoroscopy, the preferred position being junction of the superior vena cava (SVC) and right atrium. The total number of PICC inserted during the study period and the indication for insertion was recorded.

## RESULTS

Three hundred and seventeen venous duplex scans of the upper extremity were carried out. Only symptomatic patients were scanned, the most common indications being pain, swelling and erythema of the arm. There were 115 cases of UEDVT. A PICC was present in 76 patients (66%), other type of central line in 13 (11%) and no catheter present in 26 patients (23%).

Of the 76 patients with PICC thrombosis, 53 were men and the left upper extremity was involved in 46. The patient age ranged from 18 to 85 years with mean of 57 years.

During the study period, 2882 PICC were inserted, with 76 patients developing PICC-associated thrombosis, giving a symptomatic thrombosis rate of 2.6%. Sixty-one of the 76 patients (80%) had malignancy and the PICC was primarily for infusion of chemotherapy in 55 of these 61 patients (90%). The remaining 15 patients (20%) with no history of malignancy had a PICC for antibiotics or total parenteral nutrition.

As described, 55 of the 76 patients (72%) with a PICC-associated thrombosis were receiving chemotherapy through the PICC. During the study period, there were 739 PICC inserted for chemotherapy, giving a symptomatic thrombosis rate of 7%. This compares with 2143 PICC inserted for non-chemotherapy purposes and a symptomatic thrombosis rate of 1%.

Some of the chemotherapy patients received multiple PICC because of various complications, including occlusion, thrombosis, infection and fracture of the line. There were 739 PICC inserted in 548 patients. Therefore, 10% (55 of 548) of patients receiving chemotherapy through a PICC developed a symptomatic thrombosis.

Analysis of the time elapsed from insertion of PICC to the date of positive duplex scan showed that 58 of the 76 cases (78%) occurred within the first 20 days following insertion (Fig. 1). The mean number of days elapsed was 15 days, median 9 days and range 1–84 days.

The position of the tip of PICC was reviewed, but in 18 of the 76 cases, this was not recorded or could not be determined from subsequent imaging. These cases occurred early in the study before implementation of routine archiving of PICC position images onto the hospital Picture Archiving and Communications Systems (PACS). In 57 of the remaining 58 cases, the PICC was confirmed at the optimal position at the junction of SVC and right atrium. In one case, the tip of the PICC was located in the mid-SVC.

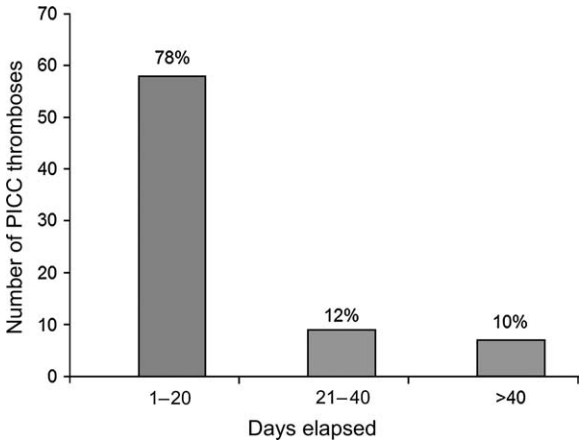


**Fig. 1.** Days elapsed from time of insertion to date of thrombosis. Seventy-eight percent of PICC-associated thrombosis occurred within 20 days of insertion of the peripherally inserted central catheter (PICC).

Thirty-two patients with PICC-related thrombosis were receiving treatment, most commonly chemotherapy, for which continuation of therapy was considered highly important. These patients had the PICC removed and commenced anticoagulation with therapeutic doses of unfractionated heparin or low-molecular-weight heparin (enoxaparin). A replacement PICC was inserted, usually in a contralateral arm vein. Twenty-nine of the 32 patients required a replacement PICC because of mid-cycle chemotherapy. The 32 patients with a second PICC line following anticoagulation for a recent UEDVT were assessed for occurrence of a second thrombosis. Only one patient was reported as having a second UEDVT. This diagnosis was not conclusive as the second PICC was inserted into the same vein as the first PICC because this was the only suitable upper extremity vein.

The follow up of patients with PICC-associated thrombosis was by phone to assess for symptoms of the post-thrombotic syndrome. Follow up was carried out at between 6 and 24 months. Twenty-one patients (28%) died, most commonly because of malignancy. Eleven patients (14%) were lost to follow up. There were 44 patients assessed for the presence of arm pain, swelling and loss of function. Thirty-one patients (70%) reported no pain. Twelve patients were experiencing pain at the time of follow up and were asked to rate the severity of the discomfort. Eleven patients (25%) had mild pain and one patient (2%) had moderate pain. None rated the pain as severe. Seven patients (15%) reported swelling of the affected arm at the time of follow up.

During the study period, there were 63 cases of superficial thrombophlebitis. In 33 of the patients (52%), a PICC was

present, compared with the 76 PICC in 115 cases (66%) of UEDVT. Malignancy was present in 17 of the 33 cases (51%), which compares with 61 of 76 cases (80%) of PICC-associated UEDVT ($P < 0.0005$). Sixteen of the 17 patients were receiving chemotherapy through the PICC.

## DISCUSSION

The true incidence of UEDVT complicating central venous catheters is difficult to assess. The measured incidence depends on the group studied (general vs cancer patients), the type of catheter in place, whether all or only symptomatic patients are assessed and investigation used (duplex ultrasound or contrast venography).[2,6–8] As expected, reported thrombosis rates were less when only symptomatic patients were evaluated. Balestreri *et al.*, using contrast venography, reported clinically silent complete thrombosis in 10% of oncology patients with a subclavian central line.[6] Varying degrees of partial thrombosis were seen in another 45%.[6] Luciani *et al.* monitored chemotherapy patients with portacaths and found a thrombosis rate of 11%, more than half of which were asymptomatic.[2] At present, there are no studies where patients with PICC were screened for thrombosis. Grove and Pevec reported a thrombosis rate of 3.9% for PICC, where duplex ultrasound was used to evaluate symptomatic patients.[3] Our study found a similar rate of 2.6%. Certainly, both studies would underestimate the true rate as there was no screening of asymptomatic patients. Furthermore, neither the clinical significance of asymptomatic thrombosis nor the role of anticoagulation therapy in such patients has been clearly defined.[4]

The pathogenesis of thrombosis related to PICC is considered multifactorial,[3,5] probably correlating with those of other central catheters. The PICC is an intravascular foreign body which may cause direct endothelial trauma, thereby predisposing to thrombosis.[9] Bacterial colonization of the catheter tip is common, although its consequences are unclear. Other mechanisms include the hypercoaguable state of malignancy and irritant effects of chemotherapeutic agents.[10] Poor position of the tip has also been implicated, with preferred placement being in the lower SVC or right atrium.[11,12] Position did not appear to be a contributing factor in our study with 57 of 58 PICC being confirmed in an optimal position on routine postinsertion fluoroscopy.

Upper extremity deep vein thrombosis has been reported to occur more frequently in patients with malignancy, especially those receiving chemotherapy.[4,10,11,13] Our study supports these findings as 61 of 76 patients (80%) with a PICC-associated thrombosis had malignancy. Fifty-five of these 61 patients (90%) were receiving chemotherapy. We found a symptomatic thrombosis rate of 7.4% in PICC used for chemotherapy and a very low rate of 1.2% in PICC for other purposes.

There have been no randomized trials of prophylactic unfractionated or low-molecular-weight heparin on PICC. A meta-analysis of heparin used for central venous and pulmonary artery catheters in randomized controlled trials found a reduction in thrombosis rates.[12] However, several i.v., s.c. and low or therapeutic doses of unfractionated and low-molecular-weight heparins were used. A subsequent single study by Monreal *et al.* found dalteparin (low-molecular-weight heparin) was effective in reducing thrombosis without haemorrhagic complications.[14] Three separate studies have trialled mini-dose warfarin in patients with central venous lines or tunnelled catheters.[15–17] A mini dose was defined as 1–2 mg without prolonging prothrombin time. There was reduction in rates of thrombosis with no haemorrhagic complications. Boraks *et al.* found mini-dose warfarin was safe in patients with haematological malignancies.[16] Our finding of symptomatic UEDVT occurring in 7.4% of PICC used for chemotherapy shows the need for a randomized study evaluating venous thrombosis prophylaxis in this group of patients. PICC in patients without malignancy had a low rate of thrombosis in our study and probably do not need prophylactic measures. In the subgroup of patients requiring placement of a second PICC line, therapeutic doses of unfractionated or low-molecular-weight heparin were very effective in preventing a second thrombosis.

Upper extremity deep vein thrombosis was compared with superficial thrombophlebitis in our study. Malignancy was present in 71% of patients with UEDVT compared with 51% of patients with superficial thrombophlebitis ($P = 0.0005$). This suggests that patients with malignancy may develop more extensive thrombosis. However, malignancy and chemotherapy administration remained a major risk factor for superficial venous thrombosis in our study.

The post-thrombotic syndrome is characterized by venous hypertension, arm swelling and pain. Prandoni and Bernardi found one-third of patients with UEDVT had mild arm pain. In this study, follow up of 44 patients with PICC-related DVT was carried out, with 11 experiencing mild pain and one moderate pain. No patient reported severe pain. Hill and Berry proposed that post-thrombotic sequelae are less common in catheter-related DVT compared with those patients with an underlying anatomic basis for UEDVT.[18] Our study supports the finding that functionally significant post-thrombotic symptoms are uncommon following PICC-associated thrombosis.

## CONCLUSION

Thrombosis related to PICC is a complication more likely to occur in patients with malignancy, especially those receiving chemotherapy. The true rate of thrombosis is probably underestimated in this and other studies. Randomized studies of venous thrombosis prophylaxis are required in patients with malignancy with a PICC, especially those receiving chemotherapy. The rate of symptomatic UEDVT is low in patients without malignancy with a PICC.

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