



BRIEF COMMUNICATION

Cannula provoked upper extremity superficial vein thrombophlebitis: are we overtreating?

Hiu L. A. Yuen ^{1,2}, Wendy Fang ¹, Huyen Tran ^{1,2} and Sanjeev D. Chunilal ^{1,2}¹Monash Haematology, Monash Health, and ²Monash University, Melbourne, Victoria, Australia**Key words**

thrombophlebitis, cannula, venous thrombosis.

Correspondence

Hiu L. A. Yuen, Monash Haematology, Monash Health, 246 Clayton Road, Melbourne, Vic. 3168, Australia.

Email: hiulamagnes.yuen@monashhealth.org

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Abstract

Cannula provoked upper extremity superficial vein thrombophlebitis (UESVT) is common. Retrospective audit of 93 consecutive patients, 51% male, median age 57 years (range 20–91), with symptomatic UESVT revealed varied management including symptomatic management (37%), prophylactic (37%) and higher dose anticoagulation (27%). There was 2% (95% confidence interval (CI) 0–7.6) thrombus extension and 1% (95% CI 0–5.9) major bleeding, both limited to cancer. We argue anticoagulation is unnecessary in most UESVT patients.

Upper extremity superficial vein thrombophlebitis (UESVT) is relatively common, occurring in 15–32% of hospitalised patients with intravenous catheters.¹ UESVT management aims to resolve symptoms and decrease the risk of extension. The American College of Chest Physicians (ACCP) 2008 guidelines recommended oral non-steroidal anti-inflammatory drugs, topical diclofenac or heparin gel for up to 2 weeks over systemic anticoagulation,² but UESVT is not covered by the 2012 ACCP³ nor the 2018 American Society of Hematology guidelines.⁴ Locally, we noticed considerable variability in management, with some prescribing therapeutic anticoagulation and others recommending conservative management with topical measures or anti-inflammatories. We questioned whether anticoagulation was required given the bleeding risks and anecdotal evidence that UESVT is relatively innocuous. However, there is a lack of data on the rates of superficial or deep extension of UESVT. Hence, we conducted our audit.

We retrospectively reviewed consecutive adult patients with UESVT diagnosed from March 2015 to December 2017 who were identified from a radiology database at Monash Health, a tertiary hospital network in Melbourne, Australia. Only symptomatic,

radiologically confirmed UESVT while an intravenous catheter was *in situ* or up to 4 weeks post-intravenous catheter removal were included. UESVT was defined as cubital, cephalic or basilic vein thrombosis. The imaging criterion for UESVT was non-compressibility of a superficial venous segment of the upper extremity on ultrasound. Exclusion criteria were central venous catheter *in situ* within 30 days of UESVT, concurrent indication for more than a prophylactic dose of anticoagulants, current pregnancy or up to 8 weeks postpartum or diagnosis of upper limb concurrent deep vein thrombosis (internal jugular, axillosubclavian, brachial, radial or ulnar veins). If a patient had multiple UESVTs within the audit period, only the first episode was reviewed for inclusion. Information on patients' demographics, management and outcomes were obtained from medical records. Patients with incomplete data or lost to follow-up were removed from analysis. Follow-up period was defined as the period from UESVT diagnosis to the last clinical contact with the hospital network (e.g. outpatient review, discharge from hospital or emergency department).

The primary outcome was to describe UESVT management strategies and secondary outcomes included rates of International Society of Thrombosis and Haemostasis-defined bleeding and radiologically confirmed thrombus resolution or extension into superficial or deep systems. Screening for thrombus resolution or extension was not routinely undertaken. Superficial extension was defined as objective imaging demonstrating the involvement of a

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superficial vein not originally identified as involved, where deep extension was defined as radiologically confirmed involvement of the radial, ulnar, brachial or axillosubclavian veins.

A descriptive summary of baseline characteristics is provided. Management strategies were categorised into three groups as shown in Table 1 to facilitate comparison: group 1 for observation or symptomatic management such as anti-inflammatories or topical medication, group 2 for prophylactic dose of anticoagulation with/without symptomatic management and group 3 for intermediate to therapeutic dose of anticoagulation with/without symptomatic management. We used variables selected *a priori* to compare the three groups. Differences in proportions were tested using Fisher's test and differences in means of continuous variables using *t*-test. Significance was set at $P < 0.05$. Statistical analysis was performed using GraphPad Prism version 7.0e. This study was approved by the local ethics committee.

We identified 93 cases of UESVT, of whom 54 were male (51%) with median age 57 years (range 20–91) and 89% had follow-up period greater than 60 days. All UESVT were diagnosed via ultrasonography. Patient characteristics, management and outcomes are shown in Table 1. Most (69%) were inpatients at diagnosis. Median treatment duration was 8 (range 2–175) and 21 days (range 3–223) for groups 2 and 3 respectively. Inpatients had a numerically higher likelihood of receiving any anticoagulation (1.46 RR 95% confidence interval (CI) 0.97–2.2) with 30 of 34 patients in group 2 continuing on venous thromboembolism (VTE) prophylaxis with prophylactic dose anticoagulation.

UESVT risk factors identified included underlying cancer (25%) and infection (28%); 73% involved a single segment ≥ 5 cm, and 63% were proximal to the cubital fossa.

Twenty-eight cases (30%) had one to three repeat scans, requested as a routine repeat scan in the absence of persisting or recurrent VTE symptoms. Group 1 had no thrombus resolution, whereas groups 2 and 3 had low rates of thrombus resolution (25% and 36% respectively). Extension occurred in two out of 28 assessed patients, both being in group 3. These two patients who had extension had initial thrombi ≥ 5 cm in length and active malignancy on treatment and were asymptomatic at extension. Bleeding occurred only in group 3, again occurring in cancer only. There was one case of major bleeding with haemorrhage into brain metastases and no documented minor bleeding.

Discussion

Our study represents real-world management practices of UESVT in Australia. This is highly variable, with 64% receiving anticoagulation. Our overall rates of extension were low (2%), being confined to cancer. Intermediate/therapeutic dose of anticoagulation resulted in 4% bleeding, again limited to cancer. While we did not capture any minor bleeding, this may reflect the limitation of this audit as minor bleeding may not have been documented.

There are no previous studies on UESVT extension rates to compare with, but this low rate is concordant with anecdotal evidence that UESVT is relatively benign.

Table 1 Patient characteristics, management and outcomes

		Group 1 Observation or symptomatic relief $n = 34$	Group 2 Prophylactic dose anticoagulation [†] $n = 34$	Group 3 Intermediate or therapeutic dose anticoagulation [‡] $n = 25$
Patient	Median age (range, years)	63.8 (29.3–88)	60.8 (25.5–90.5)	48.9 (20.3–89)
	Male, n (%)	26 (74)	20 (59)	9 (36)
	Cancer, n (%)	11 (32)	4 (12)	8 (32)
	Infection, n (%)	4 (12)	15 (44)	7 (28)
	No cancer or infection, n (%)	19 (56)	15 (44)	10 (40)
Thrombus	Single segment ≥ 5 cm, n (%)	25 (74)	25 (74)	17 (68)
	Proximal to cubital fossa, n (%)	22 (65)	26 (76)	10 (40)
Treatment	Duration (weeks, median, range)	NA	1.07 (0.1–25)	3 (0.6–31.9)
Treatment outcomes	Thrombus resolution, n/n (post-treatment ultrasounds)	0/6	2/8	5/14
	Thrombus extension, n/n (post-treatment ultrasounds)	0/6	0/8	2/14
	Bleeding, n (%)	0	0	1 (4)

[†]Prophylactic dose = enoxaparin 40 mg daily or equivalent if dose reduction required due to body weight/renal function.

[‡]intermediate/therapeutic anticoagulation = greater than prophylactic dose, for example, enoxaparin 40 mg, up to enoxaparin 1 mg/kg BD.

NA, not applicable.

A systematic review of mainly non-radiologically confirmed UESVT found only low-quality evidence on management, with most studies focussing on symptomatic benefit rather than thrombus extension.⁵

In a prospective cohort of 57 patients with UESVT, 69% were provoked by factors such as cancer (35%), CVC *in situ* (15%) and peripheral venous cannula (40%).⁶ Similar to our population, anticoagulation was employed in 73% and mostly at therapeutic doses. Only one patient with cancer experienced recurrent VTE. In contrast, patients who were not prescribed anticoagulation did not develop recurrent VTE. This may rather reflect clinicians identifying individuals at thrombotic risk and employing aggressive anticoagulation. In our cohort, cancer conferred a numerically higher risk of extension (RR 14.6 95% CI 0.7–293), and both cases of extension were asymptomatic and detected on re-imaging.

The rates of re-imaging in our cohort were higher than anticipated. In venous thromboembolism, re-imaging is obtained in case of suspected recurrence. This is unlikely in UESVT unless recurrent cannulation or placement of a central venous catheter is being considered. Therefore, re-imaging should be limited to suspicion of deep extension or patients who are at high-risk of extension or bleeding (e.g. cancer).

Based on our cohort with the low rates of extension, it seems reasonable to reserve anticoagulation for active cancer where the bleeding risk is judged to be low. In other circumstances, the risk of bleeding conferred by anticoagulation does not seem justified. Currently, management practice varies greatly. A standardised conservative treatment approach would minimise potential over-treatment with anticoagulation, reduce costs and

improve quality of life. This type of treatment approach would benefit from prospective validation.

We acknowledge the limitations of our study given its retrospective, single-centre nature. We saw variable management and many radiological assessments being performed, reflecting real-world management. Our follow-up data were limited to data available within our hospital network, so we might have missed some events if patients presented to their general practitioner or other health networks. It is possible that the patients who received an interval ultrasound scan were different to those who did not. However, the group that received interval imaging could have been deemed to be at high risk for thrombotic complications by their treating specialists. The other strengths of our study include the adequacy of follow-up and clinical relevance of outcomes in a relatively common complication.

UESVT management is variable, with more frequent use of anticoagulant therapy and radiological follow-up than expected. Reassuringly, superficial and deep extension from UESVT is uncommon and only occurs in known associated active cancer. Most patients received a prophylactic dose of anticoagulation or conservative management, and none had extension. Therefore, whether anticoagulation is necessary for most UESVT cases without cancer should be challenged.

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