TITLE:

Venous thromboembolism management in Northeast Melbourne – How does it compare to international guidelines and data?

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INTRODUCTION

Venous thromboembolism (VTE) affects 0.83 per 1000 residents in Australia and is estimated to cost AUD 117,000 per person, accounting for 0.15% of the Australian GDP.^{1,2} Prior to the listing of direct oral anticoagulants (DOAC) on the Pharmaceutical Benefits Scheme (PBS) for the treatment of VTE in December 2012, the majority of VTE patients would have been treated with bridging enoxaparin, while being initiated on warfarin. However, the introduction and maintenance of patients on warfarin can be challenging as it has multiple drug interactions and may require frequent monitoring, as opposed to DOAC, which has more predictable pharmacokinetics.³

While there have been significant developments in oral anticoagulation with DOAC,^{3,4} there remain many unanswered questions, including predicting the risk of recurrence and the appropriate duration of anticoagulation for different types of VTE. This has led to the advent of numerous international guidelines and VTE clinical risk assessment models with differing recommendations.⁵⁻⁸ For instance, the recommended duration of anticoagulation for isolated distal deep vein thrombosis (IDDVT) can range from no anticoagulation (with serial ultrasound monitoring) to 3 months of anticoagulation.^{5,6} The categorisation of provoked VTE in the literature is also inconsistent, in particular the types and intensity of provoking events.^{5,6}

By evaluating how physicians manage VTE during the warfarin era, we are poised to further understand how the introduction of DOAC has changed clinical practice, allowing us to work towards developing national VTE management guidelines. Moreover, rationalising resources and unnecessary testing will reduce the economic

impact of VTE. Hence, we aim to review the overall VTE experience in our hospitals to provide a “real-world” warfarin era evaluation, which will provide insight into how our local practice compares to current international recommendations.

METHODS

We performed a retrospective review of consecutive VTE presentations at two major teaching hospitals in Melbourne, Austin Health and Northern Health, from July 2011 to December 2012. Both institutions are the only tertiary hospitals serving Northeast Melbourne with an estimated population of over 1.5 million, and constitute the main referral centres. Cases were identified through medical records using the relevant International Classification of Diseases (10th revision, ICD-10) codes.⁹ Clinical information, pathology and radiology results were obtained from computerised medical records and each individual was assessed for demographics, event description, risk factors, anticoagulation, bleeding and thrombotic complications as well as mortality data. The results of this audit were compared to recommendations from international guidelines that are widely used in Australia (i.e. CHEST and NICE guidelines)^{5,8} as well as other published audits and “real-world” warfarin era data retrieved via the MEDLINE database.¹⁰⁻¹³

Specifically, IDVT was defined as deep vein thrombosis (DVT) below the level of popliteal vein; major VTE as above-knee DVT, from popliteal vein onwards, and/or pulmonary embolism (PE). An event was considered provoked if an identifiable provoking factor (i.e. surgery, immobility, travel, oestrogen-related) was present within 8 weeks of the VTE presentation. Antiphospholipid syndrome was defined as per the Sydney Classification Criteria (2006).¹⁴ Long-term anticoagulation was

defined as ongoing therapy without a finite duration. Recurrent thrombosis was the recurrence in the same area after a minimum of 30 days of treatment, in which clot resolution has previously been documented or in a new site following an index event. Bleeding complications were evaluated based on the International Society on Thrombosis and Haemostasis (ISTH-SSC) bleeding assessment tool with events scoring 3 or more points being considered clinically significant.¹⁵

All patients were followed-up for a minimum of 24 months, with a median of 27 (range 1-48) months post cessation of anticoagulation. Patients who did not re-present to either hospital, or have subsequent documentation of VTE in our medical records, were further tracked through medical records of two major private haematology medical practices in this catchment area. If no further data were available, these patients were considered not to have had recurrence or clinically significant bleeding, given that most patients in the warfarin era would require administration of subcutaneous low molecular weight heparin (LMWH) either as an inpatient or through a hospital-based outpatient program.

Statistical analysis

Descriptive statistics were provided as appropriate to summarise patient characteristics and outcomes. Differences in categorical variables were evaluated using the Chi-squared test, or Fisher's Exact test. For the continuous variables, which were non-normally distributed, the Mann-Whitney (rank-sum) test was applied. Time-to-event analysis was conducted with two end-points: recurrent thrombosis and clinically significant bleeding, with mortality treated as a competing risk. Patients who were alive or lost to follow-up before recurrent thrombosis, clinically significant

bleeding or death were censored at the date of last follow-up (31 December 2015). Univariate and multivariate Cox proportional hazards competing risk regression analyses were used to identify and quantify associations between recurrent thrombosis and clinical variables, with VTE groups (Major vs IDVT) treated as the primary exposure variable. Manual backwards step-wise regression techniques were employed to identify those variables independently associated with recurrent thrombosis or clinically significant bleeding, with results presented as Hazard Ratios with associated 95% confidence intervals.

A two-tailed P-value of less than 0.05 was considered to indicate statistical significance. STATA statistical analysis software (version 12.1) was used (StataCorp, College Station, TX, USA). Ethics approval was obtained from the Austin and Northern Human Research Ethics Committee (LHR/14/Austin/660 and ALR 10.2015).

RESULTS

A total of 1002 patients (519 males (51.8%); 483 females) presented with 1024 VTE episodes (Figure 1) during the study period, of which 28.6% (293/1024) were diagnosed as complications of inpatient hospitalisations. Of the emergency department presentations, 30.5% (223/731) were treated via the hospital-in-the-home program and 4.7% (34/731) as outpatients. Initially, all VTE episodes were reviewed and for the purposes of this analysis, cancer patients, superficial VTE, cerebral sinus thrombosis, upper limb DVT and portal vein thrombosis (n=260) were excluded. Only the remaining 742 non-cancer patients were analysed.

Demographics and VTE presentation

There were 752 episodes involving 742 non-cancer patients (367 males, 375 females), with median age of 64 years (range 16-97). Most were symptomatic at presentation (96.0%) and females were more likely to present with PE compared to males (59.1% (224/379) vs 50.6% (189/373); $p=0.02$). A previous history of VTE was reported by 22.5% (167/742) of patients and 7.5% (56/742) of patients reported first-degree family history of VTE with 2.4% (18/742) reporting both. Bilateral PE occurred in 59.3% (245/413) of PE cases and was more common in patients with concurrent DVT (67.5% (77/114) vs 56.2% (168/299), $p=0.02$).

Thrombophilia screen

A thrombophilia screen was performed in 40.8% (303/742) of patients (Table 1), of which 61.7% (187/303) were performed in those over 50 years of age and 27.6% (124/449) in those with transient provoking factors. Antiphospholipid antibodies (APA) were tested in 36.4% (270/742) of patients including 152 patients with unprovoked events; although only 31.5% (85/270) of them had all 3 components performed (lupus anticoagulant, anticardiolipin antibody (IgG), beta-2 glycoprotein 1 antibody). Whilst 14 patients had positivity in one or more of the APA, only 5 were subsequently confirmed to have antiphospholipid syndrome. The presence of inheritable thrombophilia did not predict for VTE recurrence (Table 2; $p=0.74$).

VTE diagnosis

Compression doppler ultrasonography was the primary diagnostic modality for DVT while computed tomography pulmonary angiogram (CTPA) (65.1%; 263/404) was more commonly used to diagnose PE compared to ventilation-perfusion (VQ) scan

(28.7%; 116/404). Twenty-five patients (6.2%) had both VQ and CTPA due to diagnostic uncertainty with the initial investigation.

Provoking factors

Excluding 5 patients with myeloproliferative neoplasm, 60.1% (449/747) of events were associated with one or more transient provoking factors, occurring within 8 weeks of the index VTE event: surgery-associated (40.5%; 182/449), travel (12.7%; 57/449), other non-surgical causes of immobility or injury (39.6%; 178/449), and oestrogen exposure (7.1%; 32/449). Unprovoked events were more common in men (45.8% (167/364) vs 34.0% (127/373), $p<0.001$) and patients with major VTE (42.2% (246/583) vs 31.5% (52/165), $p=0.01$).¹⁶

VTE management

Most patients (84.8%; 638/752) received LMWH initially, followed by warfarin (90.1%; 678/752), reflecting the Australian standard of care prior to the availability of DOAC. Of those with known finite duration, the median duration of anticoagulation was 3.5 (range 0.5-24) and 6 (range 0.5-26) months for IDVT and major VTE respectively.¹⁷

More than half the patients (54.3%; 209/393) had at least 3 months of anticoagulation for their first provoked VTE, and 34.4% (65/189) had more than 6 months for their first unprovoked VTE. Eighteen percent of (133/742) patients received long-term anticoagulation: recurrent VTE (n=65), chronic VTE (n=8), positive thrombophilia screen (n=14), extensive VTE (n=17), other VTE-related causes (n=7) and non-VTE related reasons (n=22).

Inferior vena caval (IVC) filters & thrombolysis

Thirty-five patients required acute interventions including IVC filter insertion (n=22), thrombolysis (n=6), both (n=7) or extracorporeal membrane oxygenation (n=2). The indications for IVC filter were bleeding/high risk bleeding (n=12), pre-operative anticoagulation cessation (n=4), clot progression (n=2) and high clot burden (n=11). All but six IVC filters were removed - 3 patients were lost to follow-up and the remaining 3 were not removed due to incidental finding of dilated ascending aorta, extensive residual clot and death prior to removal respectively. Of those thrombolysed, two experienced clinically significant bleeding (both muscle haematomas) in the immediate period and four (30%) died following cardiac arrests from presumed massive PE.

Complications

Further thrombosis

Fifty-seven patients (7.5%; 3.23/100 person-years) had recurrent thrombosis within the follow-up period with a recurrence rate of 4.4% (33/752) in the first year. The median time to recurrence was 7 (range 0.5-27) months after stopping anticoagulation. Four recurrences occurred despite therapeutic anticoagulation. There were 41 cases of VTE recurrence in the major VTE group of 586 cases (3.02/100 person-years), compared to a recurrence rate of 3.94/100 person-years in the IDVT group (16 cases). The cumulative incidence of recurrent thrombosis did not differ between major VTE and IDVT patients (HR 1.41, 95% CI: 0.79-2.50) (Figure 2).¹⁷ Table 2 shows the univariate analysis of the risk factors assessed for recurrent thrombosis. Upon multivariate analysis, the only identifiable risk factor for recurrence

during the follow-up period was unprovoked VTE at presentation (HR 2.06, 95% CI: 1.21-3.49; $p=0.01$). Furthermore, patients with recurrence were more likely to be diagnosed with subsequent malignancy (8.8% (5/57) vs 1.3% (9/685), relative risk (RR) 6.68; $p<0.001$).

Risk of Bleeding

Forty-two patients (5.6%; 2.37/100 person-years) reported clinically significant bleeding in the setting of anticoagulation, including five mortalities. Two-thirds of these episodes (66.7%; 28/42) occurred within the first month of anticoagulation. The cumulative incidence of clinically significant bleeding was higher for major VTE patients when compared to IDVT patients (2.82 vs 0.93/100 person-years, HR 5.03, 95% CI: 1.21-20.96) (Figure 3). Table 3 shows the risk factors assessed for clinically significant bleeding.

Subsequent malignancy

Fourteen patients (1.9%) were subsequently diagnosed with malignancies (5 local, 9 metastatic) in the 12 months following initial VTE diagnosis. Eight patients initially presented with unprovoked VTE (2.7% vs 1.4% of the provoked group, $p=0.19$). The types of prospective malignancies were gastrointestinal ($n=7$), unknown primary ($n=2$), urothelial ($n=1$), lung ($n=1$), ovarian ($n=1$), thyroid ($n=1$) and glioblastoma ($n=1$).

Mortality

There were 25 thrombosis-related deaths (25/742), of which 24 occurred within 30 days of initial presentation or clot recurrence (median 7 days, range 0-490). The acute

PE mortality rate was 5.8% (24/413). The all-cause mortality rate was 14.8% (110/742) with a 30-day and 1-year mortality of 3.4% and 9.1% respectively.

Comparison of current local practice to international guidelines

Table 4 provides the comparison between local VTE management and current guidelines. The median duration of anticoagulation in the IDVT population was 3.5 months, which was longer than the international recommendations.¹² The majority of the patients with provoked VTE (87.2%) had greater than 3 months of anticoagulation even though the current recommendation is 3 months⁴ while 35.5% of those with unprovoked VTE received more than 6 months of anticoagulation.

Although current international recommendations do not advise performing thrombophilia screen in patients with provoked events or those age older than 50 years, 61.7% of the thrombophilia screens in this audit were done in those over 50 years of age and 27.6% in the of patients with provoked events. Overall, this represented 22.0% of all patients at a cost of approximately AUD 29,000 (Table 1).

Our audit reported an IVC filter retrieval rate of 79.3%. This was better than the reported retrieval rate of 34% in a recent published systematic review.¹⁸

DISCUSSION

The total health system cost of VTE in 2008 was estimated as AUD 148 million, including the total hospital inpatient expenditure of AUD 81.2 million and these figures are likely to escalate over time.² However, few studies provide a holistic

overview of “real-world” VTE experience including how the local practice correlates with international guidelines and our study aims to fill this gap.

Despite current guidelines discouraging routine inherited thrombophilia testing due to its limited role in clinical management or predicting recurrence,^{11,12,19} unnecessary testing was performed in 22.0% of patients. This represented 73.2% of tests performed, amounting to approximately AUD 29,000 (Table 1). Major heritable thrombophilia (factor V Leiden homozygosity, protein C deficiency, compound heterozygotes) were detected in only four patients (0.5%). Consistent with other population studies, minor thrombophilias, including factor V Leiden and prothrombin gene heterozygosity, were detected in 11-14% of patients and did not predict for recurrence or longer periods of anticoagulation.¹⁹⁻²¹ This reaffirms the need for further education about the judicious use of thrombophilia testing, given the substantial costs involved, potential overtreatment and unnecessary anxiety generated for the patient and family members.

While there are numerous published guidelines regarding the duration of treatment, the recommended duration for specific VTE types remains unclear. Recently, it has been suggested that 3 months of anticoagulation is sufficient for most patients with first unprovoked VTE, with no additional advantage offered by longer periods except perhaps in a subgroup with high D-dimer after cessation of anticoagulation.^{4,5,13,22-24} Nonetheless, most clinicians in Australia treat provoked VTE for 3 months and first unprovoked VTE for between 3-6 months. In this audit, 54.3% of patients with provoked VTE had greater than 3 months of anticoagulation and 34.4% of patients with unprovoked VTE received more than 6 months of anticoagulation. While there

may be individual variation, it suggests that our clinicians tended to treat patients for longer than international recommendations (Table 4). However, despite this, our bleeding and recurrence rate was not significantly different from other published “real-world” data.²⁵⁻²⁶

Despite an overall 5.7% clinically significant bleeding rate, the rate beyond 3 months of anticoagulation was relatively low (0.6%/annum) with most (66.7%) occurring within the first month. This is consistent with previous findings of relatively low long-term bleeding rate.²⁷⁻²⁸ However, we note our acute “real-world” major bleeding rate in the first 12 months, was higher than reported in the warfarin arms of recent DOAC studies (1.6-2.0%),⁷ suggesting that “real-world” bleeding may be higher than reported as supported by the findings of another recent study (5.2/100 person-years).²⁵ Similarly, our recurrence rate (7.5%) was higher compared to the large DOAC studies (2.2-3.5%) but comparable to “real-world” data (7.6%).²⁶ Of note, thrombosis recurrence was associated with increased detection of subsequent malignancy (RR of 6.68; $p < 0.001$), suggesting that we should be more vigilant in screening for malignancy in these higher-risk individuals.

We acknowledge the potential limitations of the retrospective nature of this study, which is subject to the associated biases and confounders including treatment selection biases, quality of medical records and the possibility that some individuals may not re-present to our hospitals with complications, suggesting that the rate of thrombotic recurrence could be underreported. The listing of DOAC on PBS has led to a resultant fall in warfarin prescriptions.³ As this is within our follow-up period and

given the convenience of outpatient management with DOAC, recurrences managed with DOAC may have been missed.

In addition, there is significant heterogeneity in the investigations and management of VTE at our centres, subject to physician preference and individual variability, hence, analysis of these aspects cannot be fully elucidated. A recent survey involving haematologists and respiratory physicians across Australia also demonstrated significant variability in VTE management, highlighting the need for national guidelines.²⁹ Our “real-world” data provide a realistic overview of VTE in Melbourne compared to the typical clinical trial population, and could serve as the basis of comparison for future prospective observational studies in the era of DOAC.

This study has raised some new challenges for the future. Specifically, 16.1% of the patients were lost to follow-up in this retrospective study as they are subsequently managed by their general practitioners. Two-thirds of our patients were not managed by Haematology or Respiratory Medicine, the thrombosis specialists in our institutions, highlighting the need for wider dissemination of VTE guidelines beyond physicians with a thrombosis interest. It also supports the need for a prospective VTE registry to allow for increased transparency in the reporting of the results, in order to improve the quality and comprehensiveness of our management policies. The prospective registry will guide policymakers in identifying areas of need, directing appropriate resource allocation and reducing unnecessary testing. Moreover, the added convenience and lower spontaneous bleeding risk of DOAC could lead to a paradigm shift in risk-benefit ratio of VTE management, including increased acceptance of longer term anticoagulation in medium to high risk patients. Hence, it is

vital to be able to accurately capture the “real-world” cohort of VTE patients managed on DOAC.

CONCLUSION

This study provides a “real-world” analysis of various aspects of VTE management in the warfarin era. In comparison to international guidelines, hereditary thrombophilia screen, particularly in individuals with clear provoking factors, appears to be overutilised at substantial financial costs. Similarly, the duration of anticoagulation appears to be longer than international guidelines, suggesting that our physicians adopt a more conservative approach, although our complication rates were comparable to other “real-world” studies. Given the majority of VTE may not be managed by thrombosis specialists, further education is required to translate international and national thrombosis guidelines into clinical practice and this audit can serve as a basis of comparison for future studies in the DOAC era. A prospective study is being designed to enable a better capture of the “real-world” data of patients managed on DOAC.

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FIGURE LEGENDS

Figure 1 Breakdown of the major types of VTE presentations

Figure 2 – Cumulative incidence curves of thrombosis recurrence: IDDVT vs major VTE

Figure 3 – Cumulative incidence curves of clinically significant bleeding: Major VTE vs IDDVT

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Table 1 Cost of thrombophilia screen performed in the non-cancer cohort, including costs for unwarranted heritable thrombophilia screen

	Medicare Benefits Schedule (MBS) code – cost in AUD³⁰	Total performed	No. of positive tests	Total costs (AUD)
Factor V Leiden	73308 - \$36.45	226	Heterozygous: 31 (13.7%) Homozygous: 2 (0.9%)	\$8237.70
Prothrombin gene mutation	73308 - \$36.45	170	Heterozygous: 18 (10.6%) Compound heterozygote: 1	\$6196.50
Antithrombin III, protein C, protein S, lupus anticoagulant, activated protein C resistance (APCR)	65175 - \$25.35 each; or if in combination:	43	45/228 patients reported to have low protein C and/or S levels but 41/45 were tested during concurrent anticoagulation, making the results difficult to interpret	\$1090.05
	2 tests (65176): \$48.65	19		\$924.35
	3 tests (65177): \$71.95	23		\$1654.85
	4 tests (65178): \$95.20	57		\$5426.40
	5 tests (65179): \$118.50	140		\$16950.00
Anti-cardiolipin IgG +/- IgM, beta- 2-glycoprotein-1	71180 - \$34.55; or if in combination:	4		\$138.20
	2 tests (71183): \$47.45	86		\$4080.70
	3 tests (71186): \$60.30	88		\$5306.40
Total costs of all thrombophilia screen performed				\$50005.15
Heritable thrombophilia done in age >50 years and/or provoked VTE				
Factor V Leiden		140		\$5103.00
Prothrombin gene mutation		106		\$3863.70

Antithrombin III, protein C, protein S, APCR

1 test	21	\$532.35
2 tests	16	\$778.40
3 tests	67	\$4820.65
4 tests	146	\$13899.20
Total costs of heritable thrombophilia screen done in age >50 +/- provoked events		\$28997.30

Table 2 Risk factors assessed for recurrent thrombosis

Variable	HR	95% CI	p-value
VTE Type			
Major VTE	1	-	-
IDDTV	1.41	0.79 - 2.50	0.25
Male	1.65	0.97 - 2.80	0.07
Age category			
<50	1	-	-
50 - 64	1.83	0.89 - 3.75	0.10
65 - 74	0.93	0.38 - 2.28	0.88
≥ 75	1.40	0.68 - 2.91	0.36
Prior history of VTE	1.65	0.94 - 2.87	0.08
First-degree relative with VTE	1.86	0.85 - 4.06	0.12
Smoking Status			
Active Smoker	1.33	0.66 - 2.67	0.43
Ex-Smoker	0.83	0.43 - 1.83	0.75
Never Smoker	1	-	-
Unknown	0.94	0.46 - 1.90	0.86
Provoked [†]	0.49	0.29 - 0.83	0.01
Duration of anti-coagulation [‡]			
≤ 6 months	1	-	-
> 6 months	1.00	0.58 - 1.70	0.99
Thrombophilia Screen			
Not performed	1	-	-
Performed and negative	1.76	1.03 - 3.01	0.04
Thrombophilia screen positive	1.19	0.42 - 3.40	0.74

[†] n=747 cases only

[‡] n=563 cases only

Abbreviations: HR (hazard ratio); 95% CI (95% Confidence Interval); VTE (venous thromboembolism); IDDVT (isolated distal deep vein thrombosis)

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Table 3 Risk factors assessed for clinically significant bleeding

Variable	HR	95% CI	p-value
VTE Type			
IDDVT	1	-	-
Major VTE	5.03	1.21 - 20.96	0.03
Male	0.98	0.51 - 1.86	0.95
Age $\geq$ 75	1.82	0.95 - 3.47	0.07
Prior history of VTE	0.42	0.15 - 1.18	0.10
First-degree relative with VTE	0.33	0.05 - 2.41	0.28
Smoking Status			
Active Smoker	1.01	0.35 - 2.86	0.99
Ex-Smoker	1.51	0.65 - 3.49	0.33
Never Smoker	1	-	-
Unknown	1.45	0.63 - 3.34	0.38
Provoked [†]	0.99	0.51 - 1.90	0.97
Duration of anti-coagulation [‡]			
$\leq$ 6 months	1	-	-
> 6 months	1.35	0.60 - 3.06	0.47

[†] n=747 cases only[‡] n=563 cases only

Abbreviations: HR (hazard ratio); 95% CI (95% Confidence Interval); VTE (venous thromboembolism); IDDVT (isolated distal deep vein thrombosis)

Table 4 Our local practice in comparison to current international guidelines

	Guidelines/current recommendations	Our practice (median duration; range)	% not in accordance to current recommendations
Duration of treatment of IDVT (n=130*)	No anticoagulation (monitoring with serial ultrasound) – 3 months ^{5,8,12,13}	3.5 months ¹⁷ (0.5-24)	% < 6 weeks: 6.1% (8/130) % > 3 months: 40.0% (52/130)
Duration of treatment of provoked proximal DVT and PE (n=203*)	3 months ^{5,8}	6 months (range 0.25-25)	% <3 months: 5.4% (11/203) % >3m: 87.2% (177/203)
Duration of treatment of unprovoked proximal DVT and PE (n=104*)	At least 3 months ^{5,8} (with consideration for longer term therapy in high risk patients)	6 months (range 0.5-26)	% <3 months: 4.8% (5/104) % 3-6 months: 59.6% (62/104) % >6 months: 35.5% (37/104)
Thrombophilia screen in provoked events	Not recommended ^{11,12}		27.6% of provoked patients (124/449)
Thrombophilia screen in patients > 50 years	Not recommended ^{11,12}		61.7% (187/303)
Removal of IVC Filter	Recommended in all		Not removed in 20.7% (6/29)
D-dimer post completion of anticoagulation	Positive D-dimer at time of warfarin discontinuation helps to identify patients at higher risk of recurrence ^{13,24}		Not performed in 83% (624/752)

*Excluded patients without a known finite duration of anticoagulation, on long term anticoagulation, not commenced on anticoagulation or deceased prior to completion of intended duration of anticoagulation.

Abbreviations: IDDVT (isolated distal deep vein thrombosis); DVT (deep vein thrombosis); PE (pulmonary embolism); IVC (inferior vena cava)

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ABSTRACT

BACKGROUND: Venous thromboembolism (VTE) is a major cause of morbidity and mortality with significant heterogeneity in its management, both within our local practice and international guidelines.

AIMS: To provide a holistic evaluation of “real-world” Australian experience in the warfarin era, including how we compare to international guidelines.

METHODS: Retrospective evaluation of VTE from July 2011 to December 2012 at two major hospitals in Melbourne, Australia. These results were compared to recommendations in the international guidelines.

RESULTS: A total of 752 episodes involving 742 patients were identified. Contrary to international guidelines, unwarranted heritable thrombophilia screen was performed in 22.0% of patients, amounting to a cost of AUD 29,000. The duration of anticoagulation was longer compared to international recommendations although the overall recurrence (3.2/100-person years) and clinically significant bleeding rates (2.4/100-person years) were comparable to “real-world” data. Unprovoked VTE (HR 2.06; $p=0.01$) was a risk factor for recurrence and there was no difference in recurrence between major VTE (proximal deep vein thrombosis (DVT) and/or pulmonary embolism) and isolated distal DVT (3.02 vs 3.94/100-person years; $p=0.25$). Fourteen patients were subsequently diagnosed with malignancy and patients with recurrent VTE had increased risk of prospective cancer diagnosis (RR 6.68; $p<0.001$).

CONCLUSIONS: While our “real-world” VTE experience during the warfarin era largely correlates with international guidelines, there remains heterogeneity in the management strategies including excessive thrombophilia screening and longer duration of anticoagulation. This audit highlights the need for national VTE guidelines, as well as prospective auditing of VTE management in the DOAC era for future comparison.

KEYWORDS: venous thromboembolism, thrombophilia, economics, recurrence, haemorrhage

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