The incidence of venous thromboembolism: a prospective, community-based study in Perth, Western Australia

Wai Khoon Ho, Graeme J Hankey and John W Eikelboom

ABSTRACT

Objective: To determine the incidence of venous thromboembolism (VTE), comprising deep vein thrombosis (DVT) and pulmonary embolism (PE), in a well defined urban community broadly representative of the Australian population in terms of age, sex and ethnic distribution.

Design, setting and participants: A prospective, community-based study conducted over a 13-month period from 1 October 2003 to 31 October 2004. People in a population of 151 923 permanent residents of north-eastern metropolitan Perth, Western Australia, who developed VTE during the study period were identified prospectively and retrospectively through multiple overlapping sources.

Main outcome measure: Number of cases of symptomatic, objectively verified DVT and PE.

Results: 137 patients had 140 VTE events (87 DVT and 53 PE). The crude annual incidence per 1000 residents was 0.83 (95% CI, 0.69–0.97) for VTE, 0.52 (95% CI, 0.41–0.63) for DVT, and 0.31 (95% CI, 0.22–0.40) for PE. The annual incidence per 1000 residents after age adjustment to the World Health Organization World Standard Population was 0.57 (95% CI, 0.47–0.67) for VTE, 0.35 (95% CI, 0.26–0.44) for DVT, and 0.21 (95% CI, 0.14–0.28) for PE.

Conclusion: If the crude annual incidence of VTE in this area of metropolitan Perth is externally valid, then VTE affects about 17 000 Australians annually. Future studies of trends in VTE incidence will be needed to measure the effectiveness of VTE prevention strategies.

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For editorial comment, see page 134

In Western populations, venous thromboembolism (VTE), comprising deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common cause of morbidity and one of the most common preventable causes of inhospital deaths.[1]

As no community-based study has been performed in Australia, reliable data on the local incidence of VTE are lacking. International incidence figures may not be generalisable to the Australian population, as studies from other countries have shown regional variations. For example, VTE incidence in the Brest district of France was found to be almost twice that in north-eastern England,[2,3] and, in Sweden, the incidence of DVT in two districts in the 1970s was half that in the city of Malmö in 1987.[4,5]

To obtain reliable estimates of the incidence of symptomatic, objectively verified VTE in the Australian population, we conducted a prospective study in a well defined community in Perth, Western Australia.

METHODS

This was a prospective, community-based study with multiple overlapping sources of case ascertainment, similar to the Perth Community Stroke Study (PCSS) conducted in 1986.[6] We conducted this study from 1 October 2003 to 31 October 2004.

Study area and population

The study population comprised all residents of an area of about 94 km^2 in north-eastern metropolitan Perth (defined by 12 postcodes: 6000, 6003, 6004, 6006, 6050–6054, 6059, 6060 and 6062). This represented an expansion of the area covered by the PCSS, which included eight complete postcode districts and part of a ninth.[6] Royal Perth Hospital, a public tertiary referral centre, is located toward the southern apex of the study area, and another public tertiary centre, Sir Charles Gairdner Hospital, is situated just outside of the area to the west.

Data on resident population by sex and age were obtained from the Australian Bureau of Statistics 2001 national census. We defined residents as those who had lived, or intended to live, in the study area for ⩾ 6 months. Residents who experienced VTE while temporarily away from the area were included in the study, but visitors to Perth were excluded.

Case ascertainment

To ensure case ascertainment was as complete as possible, we searched for incident cases prospectively ("hot pursuit") during the study period and retrospectively ("cold pursuit") during and after the study period.

Prospectively, we identified cases of VTE in hospital patients from computerised inpatient and emergency department attendance registers, lists of patients undergoing radiological tests, and lists of patients attending the Royal Perth Hospital Thrombosis Clinic. Patients with VTE in the community were prospectively ascertained by inviting general practitioners and privately operated radiological services to refer patients to the study, and by reviewing lists of patients in domiciliary nursing programs. We also placed advertisements in community newspapers and the newsletter of a home nursing organisation so that potentially suitable patients could refer themselves to the study.

Retrospectively, hospital patients were identified by searching the hospital morbidity and mortality databases of the Western Australian Department of Health. All public and private hospitals in the Perth area are required to submit hospital discharge data to the Department of Health, where they are regularly collated. We retrieved data on VTE hospitalisations using ICD-10 (International classification of diseases, 10th revision) codes (Box 1).[7]

Sudden deaths in the community were ascertained through the Coroner's Court of Western Australia and its forensic pathology department. We also reviewed autopsy lists at Royal Perth Hospital and Sir Charles Gairdner Hospital, as they performed all postmortem examinations for inhospital deaths not subject to a coronial inquiry on behalf of community general hospitals in the study area.

We reviewed all patients' medical records and, wherever possible, interviewed the

patients to ensure that only symptomatic, objectively verified index events were included and that patients were residents of the study area.

Diagnostic criteria

To be counted as a case of VTE, symptomatic patients required objective confirmation of VTE by current standard diagnostic imaging or pathological confirmation of a clot removed during surgery or autopsy that was judged to have caused or contributed to the patient's symptoms (or death, in the case of PE). We accepted the diagnosis of VTE reported by radiologists or nuclear physicians; reports were not reviewed or adjudicated. We included all cases of thrombosis of the deep veins of the limbs (proximal and distal) and abdominal viscera, but excluded cases of thrombophlebitis of the superficial veins of the limbs without thrombus extension into the deep veins. Where objectively confirmed symptomatic embolism to the lung(s) coexisted with DVT, we considered the event to be PE.

VTE events were classified as "first ever" or recurrent, based primarily on results of previous radiological investigations. We considered DVT or PE in a patient with neither DVT nor PE previously confirmed as first ever, but coded first-ever DVT in a patient with previous objectively verified PE (and vice versa) as recurrent.

When previous medical records and radiology reports were unavailable, and there was no satisfactory clinical or diagnostic tool to confirm a previous diagnosis of VTE, we applied two sets of questions validated for use in epidemiological studies[8] to ascertain: (1) if patients thought they had ever had a VTE, if they had ever been hospitalised for a PE, or if a physician had ever diagnosed them with a VTE; and (2) if they had ever received anticoagulation therapy. We considered patients answering in the affirmative to both sets of questions to have had previous VTE, and the index event was then counted as a recurrence. This approach has a sensitivity of 37.1%, specificity of 99.4%, and positive and negative predictive values of 48.9% and 98.5%, respectively.[8]

1 ICD-10 codes used to retrospectively identify cases of venous thromboembolism

I26: Pulmonary embolism
I80.1: Phlebitis and thrombophlebitis of femoral vein
I80.2: Phlebitis and thrombophlebitis of other deep vessels of lower extremities
I80.3: Phlebitis and thrombophlebitis of lower extremities, unspecified
I80.8: Phlebitis and thrombophlebitis of other sites
I80.9: Phlebitis and thrombophlebitis of unspecified site
I82: Other venous embolism and thrombosis
O07.2: Failed medical abortion, complicated by embolism
O07.7: Other and unspecified failed attempted abortion, complicated by embolism
O08.2: Embolism following abortion and ectopic and molar pregnancy
O22.3: Deep phlebothrombosis in pregnancy
O22.8: Other venous complications in pregnancy
O22.9: Venous complication in pregnancy, unspecified
O87.1: Deep phlebothrombosis in the puerperium
O87.9: Venous complication in the puerperium, unspecified
O88.2: Obstetric blood-clot embolism
G08: Intracranial and intraspinal phlebitis and thrombophlebitis
K55.0: Acute vascular disorders of intestine
K55.9: Vascular disorders of intestine, unspecified
K75.1: Phlebitis of portal vein
N28.0: Ischaemia and infarction of kidney

ICD-10 = International classification of diseases, 10th revision.[7] ◆

Statistical analyses

The VTE event rate was the total number of symptomatic, objectively verified VTE events that occurred per 1000 residents in the study area per year. Individual patients could have multiple separate events during the study period (eg, recurrences).

Crude annual incidence of VTE was calculated as the number of patients with symptomatic, objectively verified VTE per 1000 residents in the study area per year.

Age-adjusted annual incidence of VTE was the number of patients with symptomatic, objectively verified VTE per 1000 residents in the study area per year adjusted (according to age) to the World Health Organization World Standard Population,[9] calculated by direct standardisation.[10]

We calculated 95% confidence intervals around estimates using exact limits.[11]

Ethics approval

We obtained ethics approval for the study from all five tertiary referral hospitals in metropolitan Perth, and community and private hospitals serving the north-eastern metropolitan area (see Acknowledgements).

RESULTS

According to the 2001 Australian census, 151 923 people resided permanently in the study area, of whom 1.4% were Indigenous Australians. By parental country of birth, 51.6% of residents were north-western European, 20.3% southern and eastern European, 11.3% Asian, and 1.2% North African or Middle Eastern. The remainder either described themselves as "Australian" or had parents born in other parts of the world.

Case ascertainment

During the study period, there were 140 VTE events among 137 patients (Box 2). Sixty-six patients with VTE (48.2%) were identified during hospital presentation or at the Royal Perth Hospital Thrombosis Clinic, and 22 (16.1%) were identified through review of radiology lists. Thirty-nine patients (28.5%) were ascertained from the hospital morbidity and mortality databases; four (2.9%) from domiciliary nursing programs; two (1.5%) by referral to the study by other nurses; two (1.5%) by referral from a private radiological service; one (0.7%) from the Coroner's Court; and one patient (0.7%) identified himself to the study after seeing a local advertisement.

VTE event rate and incidence

The 140 VTE events comprised 87 DVT events and 53 PE events. The annual VTE event rate was 0.85 (95% CI, 0.71–0.99) per 1000 residents.

The crude annual incidence per 1000 residents was 0.83 (95% CI, 0.69–0.97) for VTE (Box 2), 0.52 (95% CI, 0.41–0.63) for DVT, and 0.31 (95% CI, 0.22–0.40) for PE. The annual incidences per 1000 residents adjusted to the WHO World Standard Population were 0.57 (95% CI, 0.47–0.67), 0.35 (95% CI, 0.26–0.44) and 0.21 (95% CI, 0.14–0.28) for VTE, DVT and PE, respectively.

Of the 137 patients, 102 (74.5%) had their first-ever thrombosis event. The incidences of first-ever VTE, DVT and PE were 0.62 (95% CI, 0.50–0.74), 0.38 (95% CI, 0.29–0.47) and 0.24 (95% CI, 0.17–0.31) per 1000 residents per year, respectively.

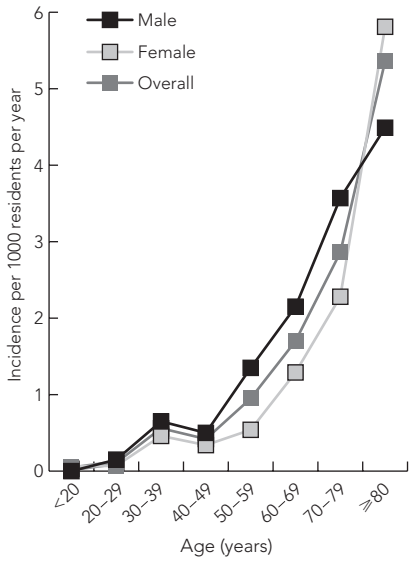
There was only one case of VTE among patients aged < 20 years; in this age group, the annual incidence was 0.03 (95% CI, 0–0.09) per 1000 residents. Among patients

2 Patients with venous thromboembolism in north-eastern Perth, by age and sex, 2003–2004

	Deep vein thrombosis		Pulmonary embolism		All venous thromboembolism			
Age (years)	Male	Female	Male	Female	Male	Female	Total	Incidence rate* (95% CI)
< 20	0	0	0	1	0	1	1	0.03 (0–0.09)
20–29	2	1	0	0	2	1	3	0.11 (0–0.23)
30–39	6	4	3	2	9	6	15	0.56 (0.28–0.84)
40–49	6	1	0	3	6	4	10	0.42 (0.16–0.68)
50–59	6	3	7	2	13	5	18	0.95 (0.51–1.39)
60–69	9	6	5	3	14	9	23	1.70 (1.01–2.39)
70–79	12	8	6	6	18	14	32	2.86 (1.87–3.85)
80–89	6	16	4	8	10	24	34	6.28 (4.17–8.39)
⩾ 90	0	0	0	1	0	1	1	0.90 (0–2.66)
Total	**47**	**39**	**25**	**26**	**72**	**65**	**137**	**0.83 (0.69–0.97)**
Incidence rate* (95% CI)	0.58 (0.41–0.75)	0.47 (0.32–0.62)	0.31 (0.19–0.43)	0.31 (0.19–0.43)	0.89 (0.68–1.10)	0.78 (0.59–0.97)		

* Incidence rate per 1000 residents per year. Data on resident population by sex and age were obtained from the 2001 census, Australian Bureau of Statistics. ◆

3 Incidence of venous thromboembolism in north-eastern Perth, by age and sex, 2003–2004



aged ⩾ 80 years, the annual incidence was 5.36 (95% CI, 3.59–7.13) per 1000 residents (Box 3).

Patient characteristics

The mean age of patients with VTE was 64.6 years (range, 19–90 years). Among patients with DVT, the mean age was 64.4 years, and for those with PE, 64.9 years. The mean age of patients with first-ever VTE was similar to those whose thrombosis was recurrent (64.7 and 64.4 years, respectively).

There was a male preponderance of VTE (1.14 : 1) due to a higher incidence of DVT in men; PE incidence was equal between the sexes. In patients with DVT, there were three cases of thrombosis of the mesenteric veins, one of the portal vein, four in the upper limbs, and the remaining 78 in the lower limbs.

DISCUSSION

This is the first population-based prospective study of the incidence of VTE in Australia, and it shows that in a region of metropolitan Perth in 2003–2004, the annual incidence of VTE was 0.83 (95% CI, 0.69–0.97) per 1000 residents.

The strengths of this study were its prospective design, community-based case ascertainment over more than 1 year, inclusion of only symptomatic and objectively verified cases, large population denominator, and appropriate statistical analysis. Furthermore, according to the 2001 census data, the study population was broadly representative of the national population.

This study has some limitations that may have resulted in underestimation of the number of cases of VTE. Quantifying the completeness of ascertainment is difficult, but it is unlikely that we identified every case of objectively verified, symptomatic VTE. PE can be difficult to diagnose antemortem, and fatal cases may have been missed due to very low autopsy rates. At Royal Perth Hospital and Sir Charles Gairdner Hospital, the autopsy rates during the study period were only 4.3% (41/955) and 3.4% (29/852), respectively, for all deaths that were not the subject of a coronial inquiry. Therefore, it is likely that our results underestimate the true burden of disease. The trend away from postmortem examinations appears to be a worldwide phenomenon.[2,3,12,13]

Symptomatic VTE can be misdiagnosed for other medical conditions. Cultural, financial, social and educational factors may also influence patients' perception and interpretation of symptoms and their willingness to seek medical attention. People with VTE who never sought medical help would have been missed by this study. However, with free universal medical care for Australian residents, there are likely to be very few people constrained by financial reasons from seeking attention.

Some symptomatic patients would have been excluded because their VTE was not objectively verified. Furthermore, the limited sensitivity of ultrasonography in detecting distal lower limb DVT[14] and the exclusion of all cases with "intermediate" or "low" probability for PE on ventilation/perfusion scanning mean that some true cases were not counted.[15]

Patients with DVT (especially those with distal limb thrombosis) managed in the community by GPs and not referred to this study could have been missed. It is unlikely that a significant number of patients with PE were managed in the community and missed by our study because home-based treatment was not recommended at the time,[16] although data have since accumulated to support safety and validation of outpatient management for selected cases of PE.[17,18]

Between the PCSS in 1986[6] and the census in 2001, north-eastern metropolitan Perth recorded an annual average population growth of 0.85%. Extrapolating the 2001 census data to 2003 gives an annual VTE incidence of 0.82 per 1000 residents.

We endeavoured to review relevant medical records and interview every potential subject to ascertain previous personal history of VTE. However, patients' recall of past events could be unreliable, and not all data from previous records were available. Thus, it is possible that index events were incorrectly classified as first ever or recurrent.

Comparing VTE incidence across studies is difficult due to differences in study methods (eg, non-verification of all symptomatic cases by objective means; inclusion of asymptomatic cases; inclusion of only cases of DVT and not PE) and changes in diagnostic methods over time. Current diagnostic tests are more convenient and less invasive than methods used in the past (eg, venography and pulmonary angiography) but have limited sensitivity in some instances. Further, the age structures of populations differ, so crude incidence data should be adjusted to a nominal standard (eg, the WHO World Standard Population[9]) for meaningful comparison across studies.

Consistent with other community-based incidence studies,[2,4,5] we found that VTE incidence increases with age. However, we were unable to confirm a previous report that the incidence of PE increases (as a proportion of VTE cases) with age,[2] as the mean age of patients with DVT in our cohort was similar to those with PE.

The crude annual incidence of VTE we found for a community in Perth is similar to that reported in north-eastern England (0.96 [95% CI, 0.91–1.01])[3] but lower than that reported in studies from Europe.[2,4,5,19] We believe the differences in incidence between Perth and parts of Europe may reflect differences in ethnicity (eg, the prevalence of the most common inherited thrombophilia, factor V Leiden, is only 2%–4% in Perth[20,21] compared with 15% in southern Sweden[22]) and cultural and environmental factors (eg, obesity, and clinical practices in regard to thromboprophylaxis and female hormonal manipulation).

An alternative explanation is that the lower incidence in our study is due to under-ascertainment of cases. We believe this is less likely, as case ascertainment was optimised by using multiple overlapping sources, prospectively and retrospectively. Another possible explanation for the lower VTE incidence in Perth is the low autopsy rate (particularly compared with Malmö, Sweden, where autopsies were performed in 79% of all deaths in 1987[5]), which predisposes to suboptimal detection of fatal PE. However, recent community-based studies in Europe[2] also had low autopsy rates and limited access to coronial data, yet found a higher VTE incidence than in Perth.

With an event rate of 0.85 per 1000 residents per year and a national population of around 20.5 million, an estimated 17 400 episodes of VTE would occur annually in Australia. Knowing the local incidence should allow Australian health planners to allocate clinical and social services accordingly and to perform appropriate pharmacoeconomic evaluations of management and preventive strategies. This study will serve as a baseline for future studies in the same area of metropolitan Perth, to allow measurement of time trends in the community incidence of VTE. In this way, the effectiveness of interventions can be gauged.

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COMPETING INTERESTS

None identified.

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