JOBNAME: JRSM PAGE: 1 SESS: 10 OUTPUT: Mon Apr 28 14:09:53 2008
/hling/journals/rsm/200/070366

RESEARCH

A case–control study of seated immobility at work as a risk factor for venous thromboembolism

Jill West[1] • Kyle Perrin[2] • Sarah Aldington[2] • Mark Weatherall[3] • Richard Beasley[1,2,4]

[1] Capital & Coast District Health Board, Wellington, New Zealand
[2] Medical Research Institute of New Zealand, Wellington, New Zealand
[3] University of Otago Wellington, Wellington, New Zealand
[4] University of Southampton, Southampton, United Kingdom

Correspondence to: Professor Richard Beasley. E-mail: Richard.Beasley@mrinz.ac.nz

DECLARATIONS

Competing interests
None declared

Funding
None

Ethical approval
The study was approved by the Central Regional Ethics Committee (CEN/05/08/054) and all cases and controls gave written informed consent

Guarantor
RB

Contributorship
All authors contributed equally

Acknowledgements
None

Summary

Objective To determine the relative risk of prolonged seated immobility at work in patients with a deep vein thrombosis (DVT) or pulmonary embolism (PE).

Design A case–control study: cases and controls completed an interviewer-administered questionnaire to obtain information on risk factors for venous thromboembolism (VTE), including prolonged seated immobility at work. Univariate and multivariate logistic regression was used to determine the association between predicted variables and the probability of being a case or control.

Participants Cases were patients <65 years old attending the Wellington Hospital Outpatient VTE Clinic following hospital discharge for DVT and/or PE. Controls were patients <65 years old admitted to the Coronary Care Unit at Wellington Hospital.

Setting The Wellington Hospital Outpatient VTE Clinic and Coronary Care Unit.

Main outcome measures Odds ratio of VTE for prolonged seated immobility.

Results There were 97 cases (53 DVT, 29 PE, 15 DVT and PE), and 106 controls. In the multivariate analysis the odds ratio of VTE for prolonged seated immobility at work was 1.8 (95% CI 0.71–4.8). The maximum number of hours seated at work was associated with VTE, with the risk increasing by 10% per hour longer seated (odds ratio 1.1, 95% CI 1.0–1.2). The maximum number of hours seated at work without getting up was associated with VTE, with the risk increasing by 20% per hour longer seated (odds ratio 1.2, 95% CI 0.96–1.6).

Conclusions This study provides preliminary evidence that prolonged seated immobility at work may represent a risk factor for VTE.

Introduction

The history of prolonged seated immobility as a risk factor for venous thromboembolism (VTE) is intriguing. It was first recognized during the London Blitz in World War II, when the coroner's pathologist reported a six-fold increase in the incidence of fatal pulmonary embolism (PE)

occurring in people who sat for prolonged periods in air raid shelters.[1] This was thought to be due to the common practice of sitting in deck chairs for the duration of the air raid; when they were replaced by bunks, the incidence of fatal PE fell dramatically. The next report was not until 1954, when Homans published evidence that VTE may occur in other situations associated with prolonged cramped sitting, such as air travel, car trips and attendance at the theatre.[2] Since this report, attention has focused mainly on VTE associated with air travel, initially with case series,[3–7] then with prospective studies,[8] epidemiological studies of risk factors[9–11] and randomized controlled trials of preventive measures.[12–14] As a result of these studies, the public health importance of air travel-related VTE is now widely recognized.[15]

In contrast, the association between VTE and sitting at work or with recreation has received little attention. Information has been limited to the publication of a number of case reports[16–20] of the occurrence of major VTE events in young individuals without recognized risk factors, but who had sat for prolonged periods at work or recreation prior to the presentation of their VTE event. Recently we undertook a case series which suggested that prolonged seated immobility may represent a common risk factor for VTE leading to hospital admission.[21] This case series was limited by the lack of a control group, however, which meant that it was not possible to determine the relative risk of VTE associated with prolonged seated immobility. As a result, we have now undertaken a case–control study to investigate the relative risk of seated immobility at work amongst subjects admitted to hospital with VTE.

Methods

Consecutive patients attending the Wellington Hospital VTE outpatient clinic between October 2005 and December 2006 were included as cases. Attendees were approached to take part if they had a hospital discharge diagnosis of deep-vein thrombosis (DVT) and/or PE within the previous 12 months, were <65 years old (standard retirement age in New Zealand) and had the ability to complete the interviewer-administered questionnaire.

We excluded patients who had superficial thrombophlebitis but no extension into the deep venous system, and those with arterial thrombosis or embolism. The clinical diagnosis of DVT or PE required radiological confirmation by one of the following: positive compression Doppler ultrasound, high or intermediate probability V/Q scan or positive helical CT with pulmonary angiography.

Controls were obtained from the Wellington Hospital Coronary Care Unit (CCU). Patients were approached to take part if they were <65 years old, had been admitted acutely to the CCU and had the ability to complete the questionnaire.

The study was approved by the Central Regional Ethics Committee (CEN/05/08/054) and all cases and controls gave written informed consent.

Questionnaire

Cases and controls completed the interviewer-administered questionnaire that collected demographic data, clinical details of the presenting VTE event or CCU admission and detailed information on VTE risk factors. The VTE risk factors were grouped into eight categories, as defined in Table 1.

Prolonged seated immobility was defined in accordance with the maximum number of hours seated in a 24-hour period and the maximum time spent seated on any occasion without getting up, as follows:

- Seated at least eight hours a day *and* at least three hours at a time without getting up
- Seated at least 10 hours a day *and* at least two hours at a time without getting up
- Seated at least 12 hours a day *and* at least one hour at a time without getting up.

Patients had to meet these criteria at least once in the four weeks prior to the onset of the symptoms that led to their VTE diagnosis or admission to the CCU. Seated immobility at work was defined by the time seated at work in a 24-hour period; seated immobility total was defined by the time seated at work, seated during travel to and from work, and seated at a computer at home in a 24-hour period.

Statistical methods

The main risk factor of interest was prolonged seated immobility at work. Other risk factors of interest, related to the main risk factor, were total seated immobility, maximum hours seated in a 24-hour period, both at work and total, and the maximum hours seated without getting up in a 24-hour period, both at work and total.

Univariate and multivariate logistic regression was used to describe the association between

Table 1
Risk factors for venous thromboembolism

Age	• Decades older
Family history	• Confirmed VTE in parents or siblings
Past medical history	• Confirmed previous VTE >6 months prior to this event
Medical risk factors	• Relevant chronic disease (e.g. ulcerative colitis, arthritis) • Cancer (active) • General immobility (including bed-rest >2 days, overdose with reduced level of consciousness, or wheelchair use in the 4 weeks preceding the event) • Hormone therapy (hormonal contraceptive or hormone replacement therapy) • Pregnancy
Surgery or trauma	• Surgery (requiring general anaesthetic or spinal/epidural anaesthesia in the 4 weeks preceding the event) • Trauma (requiring medical attention) • Cast immobility (orthopaedic limb/foot cast in the 4 weeks preceding the event)
Prolonged travel	• Car travel (≥8 hour trip in the 4 weeks preceding the event) • Air travel (≥8 hour trip in the 4 weeks preceding the event)
Prolonged seated immobility at work in the 4 weeks preceding the event	• Seated at least 8 hours in a 24-hour period and at least 3 hours at a time without getting up • Seated at least 10 hours in a 24-hour period and at least 2 hours at a time without getting up • Seated at least 12 hours in a 24-hour period and at least 1 hour at a time without getting up
Prolonged seated immobility total* in the 4 weeks preceding the event	• Seated at least 8 hours in a 24-hour period and at least 3 hours at a time without getting up • Seated at least 10 hours in a 24-hour period and at least 2 hours at a time without getting up • Seated at least 12 hours in a 24-hour period and at least 1 hour at a time without getting up

* Including duration seated at work, in travel to and from work, and at home seated at a computer

possible predictor variables and the probability of being a case or control. For the multivariate logistic regression, the predictor variables of seated immobility at work, seated immobility total, maximum hours seated (at work and total), and maximum hours seated without getting up (at work and total), were all adjusted for other confounding variables, described in Table 1. In the event, surgery/trauma was omitted from the multivariate models, as there was only one control subject with this risk factor and inclusion resulted in unstable estimates of risk for the other risk factors.

Power calculation

Based on a case series of VTE patients[21] which demonstrated the occurrence of prolonged seated immobility at work, 35% of in-patients aged <65 years admitted to hospital with a VTE event, a sample size of 100 in each group had 80% power to detect an odds ratio for risk of 2.3 with a type I error rate of 5%.

Results

A total of 97 cases and 106 controls participated in the study. The mean age of the cases was 44.9 years (standard deviation [SD] 13.1) and of the controls 52.4 years (SD 9.7); difference 7.6 years (95% CI 4.4–10.7, $p<0.001$). 57 of 97 cases (58.8%) were male compared to 72 of 106 controls (54.6%). Amongst cases, there were 53 patients with a DVT, 29 patients with a PE and 15 patients with both a DVT and a PE. Amongst the cases, 65 were admitted to hospital and 32 presented to the emergency department, where the initial investigations and management were undertaken prior to their discharge. Amongst the controls, the most common disorders resulting in a CCU admission were ischaemic heart disease, arrhythmias, congestive heart failure and pericardial disease, occurring in 71 (67%), 12 (11%), seven (7%) and six (6%) patients, respectively. The number of cases and controls who were unemployed, retired or on a benefit were 6 of 97 (6%) and 17 of 106 (16%), respectively.

The univariate analysis of the risk factors for VTE is shown in Table 2. Both prolonged seated immobility at work and total were significantly associated with a VTE event. The adjusted multivariate analyses for prolonged seated immobility at work and total are shown in Table 3. Although the association with prolonged seated immobility either at work or total was still present after adjustment, it was weaker and in neither case was the association statistically significant.

The analysis of risk by hours seated is shown in Table 4. The adjusted analyses were for the same variables shown in Table 3. There was a consistent

Table 2
Univariate odds ratios (95% CI) for association with VTE

Risk factor	*Case*		*Control*		*Odds ratio (95% CI)*
	n	*(%)*	n	*(%)*	
Age*					0.56 (0.43 to 0.73)
Family history	32	(33.0)	13	(12.3)	3.5 (1.7 to 7.2)
Medical risk factors	50	(51.6)	27	(25.5)	3.1 (1.7 to 5.6)
Personal history of VTE	28	(28.9)	7	(6.6)	5.7 (2.4 to 13.9)
Surgery or trauma	39	(40.2)	1	(1.0)	70.6 (9.5 to 527)
Prolonged travel	25	(25.8)	10	(9.4)	3.3 (1.5 to 7.4)
Prolonged seated immobility (work)	20	(20.6)	11	(10.4)	2.2 (1.0 to 5.0)
Prolonged seated immobility (total)	27	(27.8)	13	(12.3)	2.8 (1.3 to 5.7)

* Per decade older

association between the number of hours seated, by the various definitions, and VTE.

Discussion

This case–control study provides preliminary evidence that prolonged seated immobility at work may represent a risk factor for VTE requiring hospital admission. Both the maximum time seated at work during a 24-hour period and the maximum time seated without getting up were associated with an increased risk of VTE. A better understanding of the potential role of prolonged seated immobility at work requires further studies of sufficient size to allow proper adjustment for confounding variables.

There are some important methodological issues relevant to the interpretation of this study. First, the controls were selected from patients presenting to the CCU at the same hospital with an acute medical illness, predominantly due to thrombosis in the arterial system, rather than thrombosis in the venous system as in the cases. This method of selection was based on that used in the large case–control study on travellers' thrombosis.[22] The use of patients admitted to CCUs, however, might lead to biased estimates of association, as they are more likely to have pre-existing cardiovascular disease that may restrict activity and result in a more sedentary lifestyle and work. In addition, such patients are more likely to be receiving background combination antithrombotic or anticoagulation therapy which may also modify their risk of VTE.

While the criteria for prolonged seated immobility were somewhat arbitrary, they were designed to recognize that both total duration of being seated and the duration seated at any particular time may both contribute to the risk of VTE associated with air travel. The criteria were based on the evidence that the risk of PE increases

Table 3
Multivariate odds ratios (95% CI) for association with VTE

	Work		*Total*	
Predictor variable	*Odds ratio*	*(95% CI)*	*Odds ratio*	*(95% CI)*
Age*	0.55	(0.40–0.75)	0.56	(0.41–0.76)
Family history of VTE	3.8	(1.6–8.9)	3.6	(1.5–8.5)
Medical risk factors	2.8	(1.3–5.8)	2.8	(1.3–5.7)
Personal history of VTE	9.9	(3.6–27.6)	10.4	(3.7–29.0)
Prolonged travel	5.0	(2.0–12.6)	4.9	(1.9–12.5)
Prolonged seated immobility	1.8	(0.71–4.8)	2.2	(0.95–5.3)

* Per decade older

JOBNAME: JRSM PAGE: 5 SESS: 10 OUTPUT: Mon Apr 28 14:09:53 2008
/hling/journals/rsm/200/070366

Table 4
Odds ratios (95% CI) for association with VTE event by hours seated*

Predictor variables	*Case*		*Control*		*Univariate Association*†		*Multivariate Association*†	
	Mean	*(SD)*	*Mean*	*(SD)*	*Odds Ratio*	*(95% CI)*	*Odds Ratio*	*(95% CI)*
Maximum hours seated at work	5.1	(4.4)	3.3	(3.3)	1.1	(1.0–1.2)	1.1	(1.0–1.2)
Maximum hours seated total	6.3	(5.2)	4.4	(3.5)	1.1	(1.0–1.2)	1.1	(1.0–1.2)
Maximum hours seated at work without getting up	1.4	(1.5)	1.0	(1.1)	1.3	(1.0–1.6)	1.2	(1.0–1.6)
Maximum hours seated total without getting up	1.8	(1.7)	1.2	(1.1)	1.4	(1.1–1.7)	1.3	(1.0–1.7)

* Maximum number of hours seated in a 24-hour period in the 4 weeks prior to VTE event
† Per hour longer seated

markedly in flights longer than eight hours duration, with the risk increasing further in flights more than 12 hours duration.[5,11,23] Consistent with these studies, it has also been reported that the risk of VTE with any form of travel (plane, car, bus or train) is increased with duration $\geq$10 hours.[10] With regard to the role of duration of seating without getting up, this has been suggested by the observation that subjects with VTE secondary to air travel seldom get up during their flights.[5] We focused on the period of four weeks prior to the onset of symptoms due to reports that VTE may develop at any time during this period following air travel.[3,4,22,23] For the cases the questionnaire was administered up to 12 months after the VTE event, and as a result it is likely that recall bias may have influenced some of the cases' responses.

Two important difficulties with interpretation of this study are the lower-than-anticipated power to detect differences in the proportion of cases and controls with prolonged seated immobility at work and the small proportion of controls with surgery/trauma. The planned sample size of 100 cases and 100 controls was based on a previous case series where the proportion of subjects with prolonged seated immobility at work was 34%.[21] This contrasts with the 21% observed in this case–control study, perhaps reflecting the current broader referral base for the clinic, in particular from the Orthopaedic Service. Thus although the point estimates for risk suggested seated immobility at work was a risk factor for VTE, the confidence intervals were wide. We were also unable to properly control for surgery/trauma in the multivariate analyses, with only one subject in the control group with this risk factor.

This is the first case–control study which has investigated the potential role of seated immobility at work and risk of VTE. In the univariate analyses, prolonged seated immobility at work, the maximum length of time seated in a 24-hour period and the maximum time seated without getting up were all associated with a VTE event. In the multivariate analyses, the 1.8-fold risk of VTE associated with seated immobility at work was not statistically significant. However, when seated immobility was expressed as a continuous rather than categorical variable, the maximum number of hours seated at work was significantly associated with VTE, with the risk increasing by 10% per hour longer seated. Similarly, the maximum time seated without getting up was also associated with VTE, with the risk increasing by 20% per hour longer seated.

In addition to assessing the relative risk of seated immobility at work, the association with seated immobility throughout a 24-hour period was also investigated. This predictor variable comprised the sum of the time spent seated at work, while travelling to and from work, and at a computer at home. This variable did not include time seated in other circumstances at home, such as watching TV, as this was considered not to represent a sufficiently cramped environment (i.e. it is not similar to the cramped position occurring with air travel). With total seated immobility, there was

a significant 2.8-fold increased risk observed with the univariate analysis, although the 2.2-fold risk with the multivariate analysis was not significant. Utilizing continuous variables, the association between the maximum time seated in a 24-hour period and the maximum time seated without getting up and VTE was significant, with odds ratios of a similar magnitude as that for seated immobility at work.

That the risk of VTE was increased by both the maximum number of hours seated at work and the number of hours seated at work without getting up suggests that measures to reduce both these factors may be important from an occupational health perspective. It has been recommended that reminder systems are implemented to encourage workers to get up from their desks or computers every 30–60 minutes as part of general work hygiene.[24,25] It is possible that such strategies may reduce the risk of VTE associated with prolonged seating at work; however, this was not assessed in our study.

The potential mechanisms of venous thrombosis with prolonged sitting were likewise not investigated in our study, although the three components of Virchow's triad[26] – venous stasis, vessel-wall injury and hypercoagulability – are all likely to contribute. Probably the most important factor is the two-thirds reduction of lower limb venous blood flow that occurs while sitting.[27] Venous stasis may also be increased by pressure on the lower limb veins from sitting with legs crossed or from the edge of the seat. This latter mechanism was proposed to account for the increased risk of fatal PE in people who sat for prolonged periods in deck-chairs while taking refuge in air-raid shelters.[1] These factors may be exacerbated by sitting in cramped conditions, or if intense prolonged concentration results in reduced muscle activity.

In conclusion, this case–control study suggests that prolonged seated immobility at work represents a risk factor for VTE. Further studies with greater power are now required to understand this association. In addition, studies of workplace environment and the potential effect of office chair design on lower limb blood flow would contribute to the understanding of the mechanisms involved.

References

1 Simpson K. Shelter deaths from pulmonary embolism. *Lancet* 1940;**ii**:744
2 Homans J. Thrombosis of the deep leg veins due to prolonged sitting. *NEJM* 1954;**250**:148–9
3 Kesteven PJL, Robinson BJ. Clinical risk factors for venous thrombosis associated with air travel. *Aviat Space Environ Med* 2001;**72**:125–8
4 Mercer A, Brown JD. Venous thromboembolism associated with air travel: a report of 33 patients. *Aviat Space Environ Med* 1998;**69**:154–7
5 Lapostolle F, Surget V, Borron SW, *et al.* Severe pulmonary embolism associated with air travel. *NEJM* 2001;**345**:779–83
6 Barker WF, Hickman EB, Harper JA, Lungren J. Venous interruption for pulmonary embolism: the illustrative case of Richard M Nixon. *Ann Vasc Surg* 1997;**11**:387–90
7 Symington IS, Stack BHR. Pulmonary thromboembolism after travel. *Br J Dis Chest* 1977;**71**:138–40
8 Hughes R, Hopkins RJ, Hill S, *et al.* Frequency of venous thromboembolism in low to moderate risk long distance air travellers: the New Zealand Air Traveller's Thrombosis (NZATT) Study. *Lancet* 2003;**362**:2039–44
9 Paganin F, Bourdé A, Yvin J-L, *et al.* Venous thromboembolism in passengers following a 12-h flight: a case–control study. *Aviat Space Environ Med* 2003;**74**:1277–80
10 ten Wolde M, Kraaijenhagen RA, Schiereck J, *et al.* Travel and the risk of symptomatic venous thromboembolism. *Thromb Haemost* 2003;**89**:499–505
11 Schwarz T, Siegert G, Oettler W, *et al.* Venous thrombosis after long-haul flights. *Arch Intern Med* 2003;**163**:2759–64
12 Scurr JH, Machin SJ, Bailey-King S, *et al.* Frequency and prevention of symptomless deep-vein thrombosis in long-haul flights: a randomised trial. *Lancet* 2001;**357**:1485–9
13 Belcaro G, Geroulakos G, Nicolaides AN, *et al.* Venous thromboembolism from air travel: the LONFLIT study. *Angiology* 2001;**52**:369–74
14 Cesarone MR, Belcaro G, Nicolaides AN, *et al.* Venous thrombosis from air travel: the LONFLIT3 study – prevention with aspirin vs low molecular weight heparin (LMWH) in high-risk subjects: a randomized trial. *Angiology* 2002;**53**:1–6
15 Mendis S, Yack D, Alwan A. Air travel and venous thromboembolism. *Bull World Health Org* 2002;**80**:403–6
16 Beasley R, Raymond N, Hill S, *et al.* eThrombosis: the 21st century variant of thrombosis associated with immobility. *Eur Respir J* 2003;**21**:374–6
17 Beasley R, Heuser P, Masoli M. One name to rule them all: on name to find them: Lord of the Rings and 'seated immobility thromboembolism (SIT) syndrome'. *NZ Med J* 2003;**116**:U498
18 Beasley R, Heuser P, Raymond N. SIT (seated immobility thromboembolism) syndrome: a 21st century lifestyle hazard. *NZ Med J* 2005;**118**:U1376
19 Ng SM, Khurana RM, Aw Yeang HW, *et al.* Is prolonged use of computer games a risk factor for deep venous thrombosis in children? *Clin Med* 2003;**3**:593–4
20 Koullias GJ, Elefteriades JA, Wu I, *et al.* Massive paradoxical embolism: caught in the act. *Circulation* 2004;**109**:3056–7
21 Aldington S, Pritchard A, Perrin K, *et al.* Prolonged seated immobility at work is a common risk factor for venous thromboembolism leading to hospital admission. *Int Med J* 2008;**38**:133–5
22 Ferrari E, Chevallier T, Chapelier A, Baudouy M. Travel as a risk factor for venous thromboembolic disease: a case–control study. *Chest* 1999;**115**:440–4
23 Perez-Rodriguez E, Jimenez D, Diaz G, *et al.* Incidence of air travel-related pulmonary embolism at the Madrid-Barajas Airport. *Arch Intern Med* 2003;**163**:2766–70
24 US Deprtment of Labor, Occupational Safety & Health Administration. *Computer Workstations: Good Working Positions* Available at: http://www.osha.gov/SLTC/etools/computerworkstations/positions.html (accessed October 2007)

25 Yale University Ergonomics web homepage. *Computer Workstations: Anatomy and ergonomic interactions with the human body* Available at: http://www.yale.edu/ergo/legs.htm (accessed October 2007)
26 Virchow R. *Gesammelte Abhandlungen zur Wissenschaftlichen Medizin.* Frankfurt: Meidinger; 1856
27 Wright HP, Osborn SB. Effects of posture on venous velocity, measured with ^{24}NaCl. *Br Heart J* 1952;**14**:325–30