

Rates of venous thromboembolism associated with acute psychiatric admission: A retrospective cohort study

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Abstract. The present study aimed to identify rates of venous thromboembolism (VTE) amongst patients treated in inpatient mental health units using linked primary care and mental health care records. Patients resident in the London Borough of Lambeth admitted to mental health units in Southeast London between January 2008 and March 2019 were included, as well as a control group of patients being treated in the community for mental illness. The primary outcome measure was a diagnosis of VTE being recorded in GP records during or within 3 months of an admission to a mental health unit. For 7,198 psychiatric inpatient admissions, 11 episodes of VTE (1.5/1,000 admissions) were identified, with no VTE cases identified in 4,561 patients being treated in the community for mental illness during an equivalent window. This finding indicates that VTE rates following psychiatric inpatient admission might be similar to those following unselected acute medical admission. Larger scale studies are required to confirm the estimated incidence of VTE in patients with mental health conditions and the contribution of acute psychiatry hospitalisation to VTE risk.

Introduction

Venous thromboembolism (VTE) is a serious condition encompassing deep vein thrombosis and pulmonary embolism which has long been recognised as a significant cause of morbidity and mortality in hospitalised patients (1). Amongst general medical inpatients, estimates of VTE incidence range from 1.4/1,000 admissions (2) to 10-20% of inpatients developing asymptomatic DVT when not given prophylaxis (3). In

England, a national VTE prevention programme was launched in 2010 incorporating mandatory risk assessment for VTE on admission to acute hospitals for all adults, with guidance on the use of mechanical and anticoagulant thromboprophylaxis for patients at high risk (2). Updated NICE guidance issued in 2018 also recommends VTE risk assessment of all patients admitted to acute psychiatry wards, despite limited supporting evidence (4). Ellis *et al* (5) used the Department of Health screening tool and found 30.6% of psychiatric inpatients had risk-factors for VTE, however, this tool is designed for medical inpatients and establishing the salience of these risk-factors in psychiatric inpatients requires further research.

There is reason to believe that inpatients on mental health wards are at an increased risk of VTE, as there are numerous international studies which show an increased incidence of VTE in this group (6-8). Possible reasons for any increased risk in VTE include poor mobility-particularly in patients with catatonia (9) or in patients undergoing sedation (10), poor hydration status in some patients (11), and the use of mechanical restraint (12,13).

Antipsychotic use has been associated with an increased risk of VTE, although there is no clear evidence of causation and any biological mechanisms posited are putative. Effects of antipsychotic medications that may predispose to VTE include sedation and obesity leading to reduced mobility and stasis of blood in lower extremities; dyslipidaemia as part of metabolic syndrome and potentially via elevated circulating levels of anti-cardiolipin and lupus anticoagulant antibodies which have been found in patient taking antipsychotics (14).

Despite this, there have been few epidemiological studies focussing on VTE diagnosis in psychiatric inpatients in the UK. We present a study examining VTE rates amongst psychiatric inpatients in the London Borough of Lambeth.

Patients and methods

Study type. We performed a retrospective cohort study looking at VTE incidence in patients exposed to admission to a psychiatric ward compared to community mental health patients.

Data source. Lambeth DataNet (LDN) is a primary care database aggregating all GP records for patients in the

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London borough of Lambeth and is linked to the Clinical Record Interactive Search (CRIS) (15). CRIS is data resource of the South London and Maudsley (SLaM) mental health trust, containing secondary mental healthcare records from Lambeth since 2007 (16). CRIS, including linkage to Lambeth DataNet, has received ethical approval as an anonymized data resource (Oxford Research Ethics Committee C, reference 23/SC/0257).

Cohort generation. We used CRIS data to identify people who were registered with a Lambeth GP and also admitted to a mental health unit between January 2008 and March 2019. A control cohort consisted of patients receiving community mental health care from SLaM between January 2012 and December 2016, but no psychiatric inpatient admission. The shorter duration of those treated in the community was due to data completeness outside this date range.

Ascertainment of the VTE outcome and co-variates. For the admitted cohort, a period starting from the date of admission and ending 3 months following discharge was defined. For the control cohort, a window period of the average length of the admitted window was defined during which the patient was being treated in the community. VTE was identified by the presence in the primary care notes of a VTE Read or Systematized Nomenclature of Medicine Clinical Terms (SNOMED CT) code (see Table SI for a list of Read and SNOMED codes used) during the window period.

Coded data was also taken from primary care data to identify the presence of co-morbidities and risk factors associated with VTE.

Data analysis. The data was analysed using the python pandas, pyplot, statsmodels and scipy applications.

Results

Cohort. Overall, 7,899 patients were included in the study, whereby 3,338 had at least one psychiatric inpatient admission and 4,561 were controls receiving community mental health care.

Cohort characteristics. Characteristics of admitted and community control group are presented in Table I. The admitted group was younger (mean age 41.7 vs. 52.8 years) and had a higher proportion of male patients (54.6% vs. 43.3%). The admitted group was also more likely to be of Black ethnicity and to be taking antipsychotic medication. There were differences in the diagnoses of both groups, whereby the admitted group had higher rates of psychotic disorders (ICD-10 codes: F20-29), disorders due to alcohol/substance use (ICD-10 codes: F10-19), and neurotic or stress-related disorders (ICD-10: F40-48). The control group had higher rates of affective disorders (ICD-10 codes: F30-39).

Rate of VTE. The 3,338 patients in the admitted cohort had in total 7,198 admissions to psychiatric inpatient units. A VTE in the window period was recorded in 11 of the 7,198 admissions, giving a rate of 1.5/1,000 admissions (95% confidence interval: 0.6/1,000-2.4/1,000). All 11 VTEs occurred in

different patients (rather than the same patient with multiple admissions). Compared to patients without VTE during or after a psychiatric admission, those who had VTE were older (mean age 64 years), more frequently female (64%), of Black ethnicity (55%), taking antipsychotics (91%), more often had a diagnosis of affective disorder (55%), and a longer admission (mean length of stay of 120 days). The level of deprivation as measured by the index of multiple deprivations (IMD) score was similar in patients with a diagnosed VTE (29.8) to the entire cohort of admitted patients (32.6). 10 of the 11 VTEs were diagnosed between June 2010 and March 2019, with only one identified between January 2008 and June 2010, increasing the rate of diagnosis following the introduction of the VTE prevention programme by three times.

Among the patients, the 11 mental health inpatients with VTE had the following VTE co-morbidities/risk factors: Previous stroke (36%), heart failure (27%), diabetes mellitus (18%), previous renal failure (18%), and HIV (18%). None of the 11 patients had cancer, previous myocardial infarction, respiratory illness, peripheral artery disease, or severe liver disease on their primary care record.

In the community controls, no VTE was identified within the window period.

Discussion

We present a retrospective cohort study looking at VTE incidence in patients admitted to a psychiatric unit compared to community controls. The incidence of VTE within 3 months of admission to a psychiatric ward was 1.5 per 1,000 admissions. Although the study was not powered to find a statistically significant difference, it was striking that there were 11 cases amongst admitted patients with none in the control group of community mental health patients. Patients with VTE were more likely to be older, female, of Black ethnicity, suffer from an affective disorder and be taking antipsychotics compared to those admitted, but without VTE. The VTE rate of 1.5 per 1,000 admissions is similar to reports in medical inpatients but higher than the incidence seen in our community sample and previous estimates of community incidence of VTE (17). From the limited data, it may be that there was an increased incidence of VTE diagnosis following the introduction of the VTE prevention programme in 2010, which may represent greater awareness of VTE. Notably, there was a higher proportion patients of Black ethnic minority background in the group of psychiatric inpatients, as well as in the group having a VTE recorded.

Takeshima *et al* (7) found an incidence of asymptomatic VTE of 8.5% amongst 94 psychiatric inpatients with depression using D-dimer and contrast-enhanced CT. An incidence of 2.3% (97.4% asymptomatic) was found in unselected psychiatric inpatients at the same unit (8) screening 'at-risk' or symptomatic patients using D-dimer followed by CT. Delluc *et al* (6) assessed 458 patients for signs of VTE at day 10 and 90 following psychiatric admission, with all patients undergoing lower limb ultrasound at day 10. They found a 3.5% incidence during this period although, again, the clinical significance of asymptomatic DVT is unclear. Compared with these studies, the incidence found in our population is much lower. This could be explained by a lack of screening for VTE

Table I. Characteristics of the admitted and community control cohort.

Characteristic	Admitted cohort (n=3,338)	Community control cohort (n=4,561)
Mean age, years (SD)	41.7 (14.8)	52.8 (20.9)
Mean length of stay, days (SD)	46.2 (73.8)	-
Male sex, %	55.1%	43.2%
Ethnicity, %		
White	43.7%	42.3%
Black	40.2%	27.4%
Asian	5.4%	6.1%
Other ethnic group or unknown	10.7%	24.2%
Taking an antipsychotic, %	76.1%	30.0%
Diagnosis, %		
Disorder due to alcohol/substance use (F10-19)	7.5%	0.5%
Psychotic disorder (F20-29)	39.1%	23.5%
Affective disorder (F30-39)	27.2%	48.9%
Neurotic, stress-related and somatoform disorder (F40-F48)	3.4%	1.4%
Other diagnosis	22.8%	25.7%

in our cohort or differences between health care systems, for example mental health wards in the UK make less use of physical restraint. Gaertner *et al* (18) found an incidence of 3.3 symptomatic VTE per 1,000 patients hospitalised in a single centre retrospective study, aligning more closely with our findings.

The strength of this study is the inclusion of all psychiatric admissions over more than 10 years, with known local follow-up (as registered with a local primary care clinician) and consequently comparatively large patient numbers. This should minimise the risk of bias and provide a robust incidence. The outcome of clinically diagnosed VTE recorded in the primary care notes (rather than screening for asymptomatic events) ensures we are capturing events requiring treatment and of importance to patients. The use of primary care records for VTE diagnosis has previously been shown to capture more events than other data sources (19) (e.g. hospital records). While all coded data relies on correct coding by clinical coders, primary care coding has shown a high degree of accuracy (20). The main limitation is the low numbers of VTE, meaning that potential VTE risk factors described above cannot be used to infer any causal relationship with VTE. It is possible that VTE risk was under-estimated in our study as psychiatric patients with VTE may not present to health care services for diagnosis. The small numbers of VTE detected also do not allow us to describe patients with VTE in detail (e.g. in a table) due to data governance restrictions. Further, we were unable to ascertain contextual factors as the specific antipsychotics prescribed or overall burden of sedative medication. This should be examined in larger, potentially multi-centre, data sets of psychiatric inpatients.

Overall, our study suggests VTE rates following psychiatric admission are similar to those following unselected acute medical admission. Larger studies are required to confirm the estimated incidence of VTE in patients with mental health

conditions, the contribution of acute psychiatry hospitalisation to VTE risk and VTE risk factors in this patient group. This is particularly important to inform an appropriate VTE risk assessment strategy for patients admitted to psychiatric hospitals.

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Availability of data and materials

The data generated in the present study are not publicly available as individual-level data are restricted in accordance with

the strict patient-led governance framework established at South London and The Maudsley NHS Foundation Trust, but may be requested from the corresponding author upon reasonable request.

Authors' contributions

DC, CM and LR conceived the study. DC and CM acquired the data and DC analysed the data. DC, CM, JP, RS, RA and LR interpreted the data. DC, CM and LR drafted the manuscript. JP, RS and RA critically reviewed the manuscript for important intellectual content. DC and CM confirm the authenticity of all the raw data. All authors read and approved the final manuscript, and agree to be accountable for all aspects of the work.

Ethics approval and consent to participate

The Clinical Record Interactive Search (CRIS) system, including linkage to Lambeth DataNet, has received ethical approval as an anonymized data resource (Oxford Research Ethics Committee C, reference 23/SC/0257). This project was approved by the CRIS oversight committee (Project ID: 19-089) and the CRIS/LDN linkage is conducted by the CRIS data-linkage service.

Patient consent for publication

Not applicable.

Competing interests

RS declares research support received in the last 36 months from Janssen, GSK and Takeda. DC, CM, JP, RA, and LR declare no conflict of interest.

References

1. Khalafallah AA, Kirkby BE, Wong S, Foong YC, Ranjan N, Luttrell J, Mathew R, Chilvers CM, Mauldon E, Sharp C and Hannan T: Venous thromboembolism in medical patients during hospitalisation and 3 months after hospitalisation: A prospective observational study. *BMJ Open* 6: e012346, 2016.
2. Roberts LN, Porter G, Barker RD, Yorke R, Bonner L, Patel RK and Arya R: Comprehensive VTE prevention program incorporating mandatory risk assessment reduces the incidence of hospital-associated thrombosis. *Chest* 144: 1276-1281, 2013.
3. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR and Colwell CW: Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 133 (Suppl 6): 381S-453S, 2008.
4. National Institute for Health and Care Excellence: Venous thromboembolism in over 16s: Reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism. [NICE Guideline No. 89], 2018.
5. Ellis N, Grubb CM, Mustoe S, Watkins E, Codling D, Fitch S, Stirland L, Quraishy M, Jenkinson J and Harrison J: Venous thromboembolism risk in psychiatric in-patients: A multicentre cross-sectional study. *BJPsych Bull*: May 17, 2019 (Epub ahead of print). doi: 10.1192/bjb.2019.25.
6. Delluc A, Montavon S, Canceil O, Carpentier M, Nowak E, Mercier B, Bressollette L, Etienne S, Walter M, Mottier D and Lacut K: Incidence of venous thromboembolism in psychiatric units. *Thromb Res* 130: e283-288, 2012.
7. Takeshima M, Ishikawa H, Umetsu Y, Kudoh M, Umakoshi A, Yoshizawa K, Ito Y, Hosoya T, Tsutsui K, Ohta H and Mishima K: Prevalence of asymptomatic venous thromboembolism in depressive inpatients. *Neuropsychiatr Dis Treat* 16: 579-587, 2020.
8. Takeshima M, Ishikawa H, Shimizu K, Kanbayashi T and Shimizu T: Incidence of venous thromboembolism in psychiatric inpatients: A chart review. *Neuropsychiatr Dis Treat* 14: 1363-1370, 2018.
9. McCall WV, Mann SC, Shelp FE and Caroff SN: Fatal pulmonary embolism in the catatonic syndrome: two case reports and a literature review. *J Clin Psychiatry* 56: 21-25, 1995.
10. Croxford A, Clare A and McCurdy K: Introduction of a venous thromboembolism prophylaxis protocol for older adult psychiatric patients. *BMJ Qual Improv Rep* 4: u205852.w3226, 2015.
11. Beasley R, Raymond N, Hill S, Nowitz M and Hughes R: eThrombosis: The 21st century variant of venous thromboembolism associated with immobility. *Eur Respir J* 21: 374-376, 2003.
12. Hem E, Steen O and Opjordsmoen S: Thrombosis associated with physical restraints. *Acta Psychiatr Scand* 103: 73-76, 2001.
13. Funayama M and Takata T: Psychiatric inpatients subjected to physical restraint have a higher risk of deep vein thrombosis and aspiration pneumonia. *Gen Hosp Psychiatry* 62: 1-5, 2020.
14. Hagg S and Spigset O: Antipsychotic-induced venous thromboembolism: A review of the evidence. *CNS Drugs* 16: 765-776, 2002.
15. Davis KAS, Mueller C, Ashworth M, Broadbent M, Jewel A, Molokhia M, Perera G and Stewart RJ: What gets recorded, counts: Dementia recording in primary care compared with a specialist database. *Age Ageing* 50: 2206-2213, 2021.
16. Perera G, Broadbent M, Callard F, Chang CK, Downs J, Dutta R, Fernandes A, Hayes RD, Henderson M, Jackson R, *et al*: Cohort profile of the South London and Maudsley NHS Foundation Trust Biomedical Research Centre (SLaM BRC) Case Register: Current status and recent enhancement of an Electronic Mental Health Record-derived data resource. *BMJ Open* 6: e008721, 2016.
17. Heit JA: Epidemiology of venous thromboembolism. *Nat Rev Cardiol* 12: 464-474, 2015.
18. Gaertner S, Piemont A, Faller A, Bertschy G, Hallouche N, Mirea C, Le Ray I, Cordeanu EM and Stephan D: Incidence and risk factors of venous thromboembolism: Peculiarities in psychiatric institutions. *Int J Cardiol* 248: 336-341, 2017.
19. Abdul Sultan A, Tata LJ, Grainge MJ and West J: The incidence of first venous thromboembolism in and around pregnancy using linked primary and secondary care data: A population based cohort study from England and comparative meta-analysis. *PLoS One* 8: e70310, 2013.
20. Zghebi SS, Reeves D, Grigoroglou C, McMillan B, Ashcroft DM, Parisi R and Kontopantelis E: Clinical code usage in UK general practice: A cohort study exploring 18 conditions over 14 years. *BMJ Open* 12: e051456, 2022.



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