The Risk of Venous Thromboembolism Events Resulting in Hospitalization following Exposure to Antipsychotic Medication in Pre-Disposed Adult Patients

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Abstract
Introduction: The primary objective of this study was to compare the incidence of antipsychotic use in those with venous thromboembolism (VTE) resulting in hospital admission. This study expands upon current knowledge regarding VTE risk and antipsychotic use and investigates potential risk factors and lab values that may precede antipsychotic-induced coagulopathy. *Methods:* This retrospective, case-control, chart review investigated patients admitted to an acute care hospital with either a VTE or non-VTE diagnosis. Primary outcome analysis compared the presence of an antipsychotic medication in patients who had a VTE versus those who did not. Secondary analysis included: 1) the duration, class, dose, frequency, and route of antipsychotic and 2) coagulation parameters, patient characteristics, and VTE risk factors. *Results:* Analysis included 400 participants with 200 participants in each group (VTE and non-VTE). Of the 51 patients who received an antipsychotic, 29 (56.9%) developed or presented with a VTE. However, there was no significant difference in VTE development between groups when controlled for antipsychotic use (OR 1.37, 95% CI 0.76-2.50, P-value=0.30). *Conclusion:* While primary study findings were not statistically significant, results support a weak association of exposure to antipsychotic(s) in VTE groups compared to control (non-VTE). Obesity significantly increased the odds of VTE whereas a history of type 2 diabetes significantly decreased the odds of VTE.

Keywords: venous thromboembolism, deep vein thrombosis, antipsychotic agents

INTRODUCTION

Venous Thromboembolism (VTE) events commonly result in hospital admission. According to the Centers for Disease Control and Prevention, up to 2/1000 people in the United States are diagnosed with a VTE each year with ~33% experiencing a re-occurrence in the subsequent year.[1,2] Given the additional mortality risk factors associated with comorbidities linked to VTEs, such as type 2 diabetes, further research into predictable causal factors is needed.

Some published risk factors for VTE include age $\geq$ 40 years, obesity, cancer, history of VTE, and estrogen treatment.[3] Recent literature suggests that antipsychotics may increase VTE risk. This is problematic as 1.6% of Americans take an antipsychotic and 9% of hospitalized patients receive at least 1 antipsychotic during admission, including both medical and psychiatric admissions.[4,5] The extent and exact mechanism of antipsychotic-induced VTE and risk associated with antipsychotics, especially in hospitalized patients, remains unclear. Adverse effects of antipsychotics relating to metabolic syndrome and similar effects have been hypothesized, but not yet proven to be the sole link between these agents and VTE risk.[6,7,8]

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Recent studies have investigated the association between VTEs and antipsychotic use in the outpatient setting. In a meta-analysis by Barbui et al, 17 studies produced an odds ratio (OR) of 1.54, confirming an increased risk of VTEs with antipsychotic use.[9] This was consistent with an ambulatory-based study by Rarrick et al, which found an increased risk of VTE with antipsychotic use (OR 1.48).[10] A meta-analysis by Dai et al assessing specific antipsychotics demonstrated evidence of increased VTE risk (OR 1.66) as well, supporting the hypothesis of an increased risk of VTEs with the use of antipsychotics in the outpatient setting.[12]

The risk of antipsychotic use and development of VTE has also been studied in the inpatient setting. One study, by Hernandez et. al, showed statistically significant differences in length of stay, and ninety-day care costs following total knee arthroplasty between those taking antipsychotics. This study also highlighted the increased risk of VTEs seen, specifically in patients receiving an antipsychotic.[11] Additionally, Jönsson et al proposed a VTE risk factor screening tool that included antipsychotic use as a factor that could assist in recognizing at-risk individuals during hospital stays.[6] To support the idea of antipsychotics being on risk factor tools/assessments, another study by Masestri et al highlighted specific antipsychotic characteristics that correlated to the highest risk of VTEs, including features such as atypical antipsychotics, high dosages, and recent initiation (prior 3 months) with two geriatric patients on an inpatient psychiatric stay.[13] Data on certain risk factors varies and further exploration is needed to identify key criteria to include on risk factor tools moving forward.

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The primary objective of this study was to examine antipsychotic exposure in patients who experienced a VTE resulting in hospital admission. Secondary objectives included: 1) assessing laboratory values that may predict an impending coagulation event, and 2) identifying risk factors anticipated to influence the VTE-antipsychotic relationship.

METHODS

Study Design and Setting

This retrospective, case-control study, compared the case (VTE) group and the control (no VTE) group. The case and control participants were further subdivided into four groups (A-D) for simplification/clarification in reporting, as shown in **Figure 1**, with the case group (VTE), composed of individuals diagnosed with a VTE, compared to a control group (no VTE). Group A was the case (VTE) group exposed to an antipsychotic, group B was the control (no VTE) group exposed to an antipsychotic, group C was the case (VTE) group not exposed to an antipsychotic, and group D was the control (no VTE) group not exposed to an antipsychotic. Statistical analysis and results were not impacted by this subdivision of participants. A VTE was defined as a deep vein thrombosis (DVT), pulmonary embolism (PE), or cerebrovascular accident (CVA). While VTEs typically do not include CVAs, CVAs were included to investigate potential coagulopathies resulting from cardioembolic causes. Hypertension (HTN), hyperlipidemia (HLD), and type II diabetes (DM2) were included in each group to allow for similar representation of at-risk populations of a VTE event between the case and control groups. These disease states were included as part of the participants' demographic information.

All adult patients admitted with a VTE diagnosis to Mercy Health St. Rita's Medical Center between July 31, 2016, and July 31, 2021, were included, with each patient considered one unique endpoint. Antipsychotic exposure was considered if the antipsychotic was documented as given on the medication administration record. Antipsychotics continued from home or initiated during admission were included.

Study Population

Patients in Group A were those currently prescribed an antipsychotic, have an International Classification of Diseases (ICD)-10 diagnosis code for VTE, and at least one of the following: DM2, HTN, or HLD. Those in Group B met all of the Group A criteria except the ICD-10 code for VTE. Group C met all of Group A's inclusion criteria except for the use of an antipsychotic. Finally, group D met all inclusion criteria of Group B except for antipsychotic use. Exclusion criteria for all groups included patients <18 years old, pregnancy, cancer, a SARS-CoV-2 positive result, or inherited coagulation disorders defined based on ICD-10: Factor V Leiden, Protein C Deficiency**,** Protein S Deficiency, Prothrombin G20210A mutation, or Antiphospholipid syndrome. Given the risk of VTE development with pro-coagulant disorders, participants with these disease states were excluded. Because antipsychotics are known to cause metabolic syndrome and this consequence is an active hypothesis for the risk of developing VTEs, metabolic syndromes were not excluded.

Variables of Interest

The primary outcome compared exposure to an antipsychotic medication between patients with HTN, HLD, or DM2 with and without a VTE. HTN, HLD, and DM2 were part of the inclusion criteria for both the case and control group to compare similar at-risk populations. To be included, participants had to have one of these three chronic disease states. Secondary outcomes included antipsychotic duration (time from initiation of antipsychotic to VTE); antipsychotic generation (typical v. atypical), dosing frequency, and formulation; coagulation lab results at the time of VTE; risk factors such as increased Body Mass Index (BMI), age, smoking status, ethnicity, and gender; medications that increase clotting risk (i.e. estrogen and thyroid products); and Padua risk scores. Coagulation labs that were investigated included the international normalized ratio (INR), activated partial thromboplastin time (aPTT), platelets, and D-dimer. The INR and aPTT are blood tests that measure how quickly the blood clots compared to normal. The D-dimer test measures the amount of D-dimer in a patient's blood to determine if they have a blood clotting disorder. The Padua Prediction Score is an accepted scoring method for VTE risk assessment of non-surgical patients during hospitalization and immediately following it, that is based on the following 11 criteria, each getting a score if present: active cancer, previous VTE, reduced mobility, already known thrombophilia, recent trauma/surgery in the last month, age $\geq$ 70, heart/respiratory failure, acute myocardial infarction (MI) or ischemic stroke, acute infection/rheumatologic disorder, obesity (BMI $\geq$ 30 kg/m^2), and ongoing hormonal treatment. The accumulated score determines the level of risk. A score of 4 and above indicates higher risk and a recommendation for chemical prophylaxis.[16] Criteria encompassed in the Padua Prediction Score were thus gathered, unless excluded by the criteria listed above, to compare specific VTE risk factors between subgroups.

Study Analysis

This study was approved by the Mercy Health North Institutional Review Board (IRB) on October 12, 2021. All data were gathered via chart review including quantitative variables measured in units reported by Mercy Health St. Rita's Medical Center electronic medical record (EMR). All charts were reviewed by one analyst to ensure accuracy. Because ~10% of hospitalized patients receive at least 1 antipsychotic during hospital admission, and the risk of those hospitalized on an antipsychotic having a VTE (OR ~2.37), 80% power, 0.05 a priori significance level, and a one-to-one ratio of cases-to-controls, a sample size of 190 was estimated for both case and control groups.[4,5,15] A target of 200 patients for each was therefore set. Continuous variables were tested for normality with QQ-plots and the Shapiro-Wilk test. If variables failed the normality test,

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medians are presented with their interquartile ranges and are compared with Kruskal-Wallis test. Dunn test with Benjamini-Hochberg adjustment was used for multiple comparisons between subgroups if Kruskal-Wallis test indicated a significant difference. Categorical variables were analyzed with the Chi-square/Fisher's Exact test. Data for proportions were compared with a 4-sample test for equality of proportions followed by pairwise comparison with Bonferroni correction for multiple comparison. The odds ratio of the primary outcome was calculated from cases and controls. Multivariate logistic regression was performed to identify factors that increase the risk of VTE. R4.2.3 was used for all statistical analysis (R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Initially, 46,185 charts were identified and reviewed for inclusion (**Figure 1**). Enrollment was stopped once 400 eligible participants were identified (200 VTE cases and 200 non-VTE controls). Demographic characteristics of both groups are described in **Table 1**. Although propensity score matching was not performed, participants in the case and control groups were nearly balanced. There were significant differences in the medians of BMI (group C vs group D; p=0.03), Padua Score (group C vs group D, p=0.03) and the proportions of patients with type 2 diabetes (group A vs group D, p=0.025), HTN (group A vs group C, p=0.018; group A vs D, p=0.013), history of VTE (group A vs group D, p=0.038; group C vs group D, p=0.047) and reduced mobility (without significant differences in pairwise comparisons).

Of the 200 VTE cases, 29 participants received an antipsychotic (group A). Of the 200 non-VTE controls, 22 participants received an antipsychotic (group B). Of the 51 patients (12.8%) that received an antipsychotic(s) during the study period, regardless of control or case group, all antipsychotic medication(s) were continued from home. Twenty-nine of the 51 patients (56.9%) who received an antipsychotic(s) experienced a VTE (group A). Specifics of the antipsychotics used are reported in **Table 2**. There was no statistically significant difference in antipsychotic use between the groups. There was also no statistical difference between typical and atypical antipsychotics. Seven participants were taking 2 to 3 antipsychotic medications before admission that were continued during the admission. Of note, no acute orders for an antipsychotic (ex. "PRN", "once") were given in the hospital as a new medication before the VTE.

Table 3 shows the type of VTE events that were present in each group. All 200 VTE cases were admitted with the primary problem of PE, DVT, or CVA. There were 29 VTE events in the case group (group A) and 171 VTE events in the control group (group C). In group A, 23 participants were diagnosed with a PE, 2 with a DVT, and 4 with a CVA. In group C, 150 participants were diagnosed with PE, 16 with a DVT, and 5 with a CVA. There was no statistical difference in the incidence of PE or DVT in the case group compared with the control group. Although there was only one more incidence of CVA in the control group (5 participants) compared to the case group (4 participants), this was found to be statistically significant (p-value=0.027).

Subgroup analysis included demographic characteristics known to predispose to VTEs. When evaluating the primary outcome, 29 patients in the case group (Group A) were exposed to an antipsychotic before the VTE event resulting in an odds ratio of VTE development of 1.37 (95% CI 0.76 - 2.50, p-value = 0.30). A multivariate logistic regression analysis of factors that increase the risk of VTE events was performed and summarized in **Table 4**. An adjusted odds ratio of 1.27 (95% CI 0.67 - 2.44, p-value = 0.46) was calculated for antipsychotic use and VTE events after controlling for factors provided in Table 4. Regressors indicating statistical significance for VTE development in this model include BMI $\geq$ 30 kg/m^2 (OR 2.73, 95% CI 1.24-6.21 p-value =0.014) and Type 2 diabetes (OR 0.44, 95% CI 0.28-0.70, p-value= 0.0006). Obesity significantly increased the odds of VTE whereas a history of type 2 diabetes significantly decreased the odds of VTE.

An exploratory analysis of coagulation laboratory data (**Table 5**) revealed a significant difference in D-dimer values (p-value = 0.004). Further investigation showed only a significant difference in D-dimer between groups C and D (p-value = 0.0026).

CONCLUSION

Based on our results, the risk of VTEs while on an antipsychotic is present, however, the surveillance necessary remains unclear. For the primary outcome, the resulting adjusted OR of 1.27 indicates a higher frequency of exposure to antipsychotics in cases compared to controls, although not statistically significant. The OR is fairly consistent with previous studies reporting ORs of 1.48 and 1.54.[9,10] Statistical significance in these previously published studies may have resulted from larger sample sizes, making smaller differences detectable. The overall percentage of patients on an antipsychotic (51/400 or 12.8%) found in the current study is also consistent with previous literature (14%).[10] Yet, the small sample size of our study may have hindered the ability to show a true statistical difference despite the predisposition of this population to thrombosis. We conclude that the risk of developing a VTE while on an antipsychotic may be more of a concern with chronic use rather than one-time, acute administration in the inpatient setting. This is supported by the overall continuation of home antipsychotics, rather than new orders, in all 51 patients in this study who were given an antipsychotic(s). The exact time it takes for an antipsychotic(s) to increase VTE risk, however, remains unclear and requires additional research to elucidate possible acute administration risk on VTE risk. Another factor we considered in the relationship between antipsychotic use and VTE development is the actual antipsychotic agent being used by the patient. In a recent

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publication, results suggested a significantly higher risk of fatal PE in patients using antipsychotics compared to non-users (OR 6.68, 95% CI 1.43-31.11) with clozapine being the most incriminated drug.[17] However, this study did not find a statistically significant difference in antipsychotic use and type between the groups.

Previous studies propose the addition of antipsychotic medications to VTE risk screening tools.[15] However, no studies have clarified the level of significance between VTE risk and antipsychotic use combined with other medications known to increase VTE risk. Additionally, current literature is scant regarding VTE predictive measures in patients taking antipsychotics (ex. laboratory values). Our study analyzed these parameters in hopes of finding additional predictors, however no statistical evidence was found.

Patient compliance with antipsychotic medication therapy has been a documented limitation of previous studies in the ambulatory setting.[10] We hoped that our study would address this confounding variable by ensuring patient medication compliance through nursing-documented medication administration via the EMR for one-time, acute doses of antipsychotics. However, this was not true. Antipsychotic administration or compliance documented through the EMR was not significant because the charting was done after admission, or after the thrombotic event already occurred thereby unintentionally failing to capture medication administration leading up to the thrombotic event. Future studies could evaluate antipsychotic duration in patients who experienced a coagulation event(s) in the hospital setting. This was initially set as a secondary objective, but due to a lack of inpatient antipsychotic data, this could not be analyzed during this study. Other future areas of study may include identifying better ways to measure compliance with antipsychotics before the thrombotic event, addressing other confounders in a hospital setting that could lead to a VTE, and evaluating continued use of home antipsychotics on mortality outcomes associated with thrombotic events and whether it may be prudent to hold home antipsychotic medications until acute thrombotic events are resolved.

The regression analysis identified significant risk factors for VTE including obesity (BMI >30 kg/m^2) which parallels previous literature.[6-10] The inclusion of obesity within the Padua prediction score is further validated by our results. Due to certain elements of the Padua Risk Score being exclusion criteria (ex. cancer), the calculated Padua Scores in this study population may underrepresent the true risk of thrombosis.

Results from the secondary analysis evaluate disease state prevalence and coagulation lab values. For both DM2 and HTN, group A's overall disease incidence was lower than group D, despite published literature identifying these diagnoses as proatherogenic. Group D had a statistically significantly lower Padua score and lower D-dimer, which aligns with the categorization in the control group. Interestingly, this was not seen with group B. Group D had a significantly lower incidence of prior VTE. Of note, the mean age of Group D was 72 years, which is slightly greater than the cutoff seen with the current Padua score age grouping (≥70 years). Despite this potential extra score for age correlating to increased risk of VTE, Group D still showed a statistically significantly lower Padua Score. Group D's results confirm the validity of the Padua score.

Limitations for this study include a retrospective design requiring reliance on records intended for medical documentation and not research purposes, the timing of VTE compared to antipsychotic medication administration, and a lack of data regarding the duration of antipsychotic use before the VTE event. Additionally, enrollment was stopped after reaching the estimated minimum enrollment sufficient to achieve 80% power, which could result in a type II error where only weak associations were detected but a true strong difference may exist. Finally, while a lower baseline INR could correlate to an increased risk for VTE, data was not collected regarding any anticoagulants given. The authors acknowledge in hindsight that this data was not collected based on the assumption that most individuals who would have an indication for anticoagulation, such as a hypercoagulable state, would have failed to meet inclusion criteria. The authors acknowledge that the lack of data regarding this confounding variable could impact the utility of the INR when screening for VTE events and evaluating predisposition to VTE risk in the context of antipsychotic usage, and thus could be seen as a limitation to this study. Data indicated obesity significantly increased the odds of a VTE, whereas a history of type 2 diabetes significantly decreased the odds of a VTE. One possible explanation for this could be the use of antidiabetic medications leading to reduced chronic risk. Further investigation and a larger sample size could provide additional insight into the possible meaning or lack thereof of this finding.

In conclusion, this study identified a weak association between antipsychotic use and increased risk of VTE, with the direction of the effect suggesting similarities to previously published literature.[18,19] Providers should continue to screen for VTE risk factors using tools such as the Padua scale and minimize the use of medications that could increase clot burden. Antipsychotics should be considered as a drug class that could potentially increase the risk of VTEs. Healthcare providers for both acute and chronic care could include antipsychotics as part of an innovative VTE risk reduction approach.

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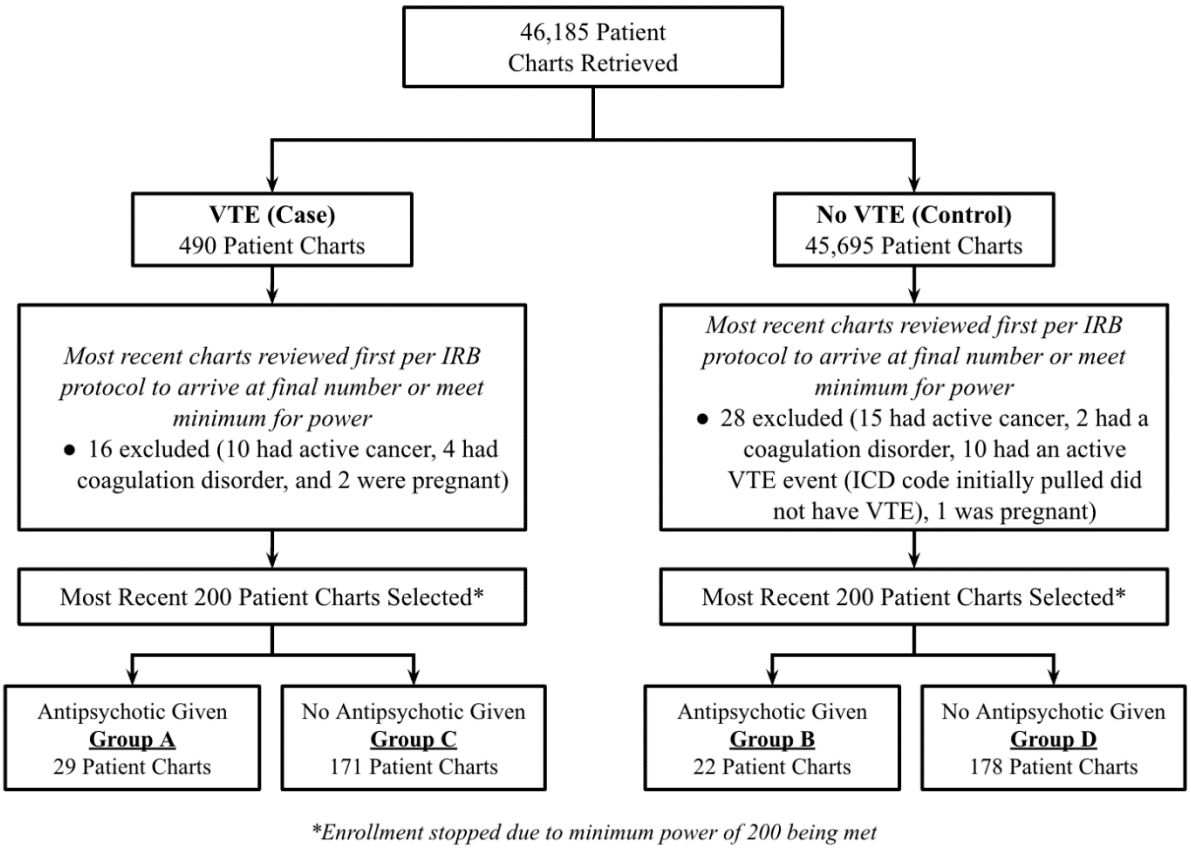
Figure 1: Schematic Flowchart of Enrollment, Inclusion Evaluation, and Group Allocation



Abbreviations: VTE, Venous Thromboembolism; IRB, Institutional Review Board

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Table 1. Baseline Demographics and Clinical Characteristics by Group[a]

Characteristic	Total (n=400)	Group A VTE, AP (n=29)	Group B No VTE, AP (n=22)	Group C VTE, No AP (n=171)	Group D No VTE, No AP (n=178)	P-Value
Age (years), median (IQR) [+]	69 (59-78.5)	72 (54-78)	70 (53-80)	66 (58.5-76)	72 (62-81)	0.06
BMI (kg/m2), median (IQR) [+]	29.3 (24.7-37.2)	28.7 (25.9-35.7)	25.9 (23.4-32.8)	31.9 (26.6-40.2)	28.2 (24.3-33.8)	0.003*
PADUA Score, median (IQR) [+]	5 (4-6)	5 (4-7)	4 (4-6)	5 (4-6)	4 (4-5)	0.03*
Male, n (%)	189 (47.3)	14 (48)	12 (55)	77 (45)	86 (48)	0.78
Caucasian, n (%)	361 (90.3)	27 (93)	21 (95)	154 (90)	159 (89)	0.77
Smoker, n (%)	77 (19.3)	8 (27.6)	5 (22.7)	28 (16.4)	36 (20.2)	0.46
Type 2 Diabetes, n (%)	147 (36.8)	4 (13.8)	9 (40.9)	56 (32.7)	78 (43.8)	0.001*
Hypertension, n (%)	357 (89.3)	20 (69.0)	20 (90.9)	155 (90.6)	162 (91.0)	0.002*
Hyperlipidemia, n (%)	281 (70.3)	23 (79.3)	14 (63.6)	116 (67.8)	128 (71.9)	0.58
History of prior VTE, n (%)	59 (14.8)	8 (27.6)	4 (18.2)	32 (18.7)	15 (8.4)	0.008*
Reduced mobility, n (%)	398 (99.5)	28 (96.6)	21 (95.5)	171 (100)	178 (100)	0.0028[b]
Acute infection or rheumatologic disorder, n (%)	89 (22.3)	7 (24.1)	6 (27.3)	39 (22.8)	37 (20.8)	0.85
Acute MI or ischemic Stroke, n (%)	12 (3)	0 (0.0)	1 (4.5)	2 (1.2)	9 (5.1)	0.13
Recent trauma or surgery (< 1 month), n (%)	32 (8)	1 (3.4)	3 (13.6)	17 (9.9)	11 (6.2)	0.30
Heart or respiratory failure, n (%)	54 (13.5)	4 (13.7)	4 (18.2)	25 (14.6)	21 (11.8)	0.76
On estrogen-containing Medication, n (%)	3 (0.8)	0 (0.0)	0 (0.0)	1 (0.6)	2 (1.1)	0.86
On thyroid-containing medication, n (%)	86 (21.5)	6 (20.7)	3 (13.6)	33 (19.3)	44 (24.7)	0.52

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Abbreviations: VTE, Venous Thromboembolism; AP, Antipsychotic; IQR, Inner Quartile Range; BMI, body mass index; MI, Myocardial infarction;

[a]At time of the event or most recent value if no thromboembolic event occurred

*indicates significant difference detected

[+] Kruskal-Wallis test and Dunn test for multiple comparisons.

- BMI group C vs group D; p-value=0.03
- Padua Score group C vs group D, p=value=0.03

4-sample test for equality of proportions followed by pairwise comparison with Bonferroni correction;

- Type 2 diabetes group A vs group D, p=0.025
- HTN group A vs group C, p=0.018; HTN A vs D, p=0.013
- H/o prior VTE group A vs group D, p=0.038; group C vs group D, p=0.047

[b]Pairwise comparison did not show any significant difference

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Table 2. Antipsychotic Medications Administered by Group

Antipsychotic medication, n		Group A VTE, AP (n=29)	Group B No VTE, AP (n=22)	P-Value[a]
First generation		4	7	0.17
Haloperidol		4	7	0.17
Second generation		25	19	1.00
Aripiprazole		6	4	1.00
Risperidone		2	4	0.38
Quetiapine		11	5	0.36
Clozapine		2	2	1.00
Ziprasidone		1	3	0.30
Lurasidone		2	1	1.00
Olanzapine		3	2	1.00
Total number of antipsychotic medications	1	27	17	<0.0001
	2-3	2	5	0.27

Abbreviations: VTE, Venous Thromboembolism; AP, Antipsychotic
[a]p-value from Fisher's Exact test.

- Seven patients were taking multiple antipsychotic medications.

Table 3. Venous Thromboembolism Type by Group

VTE type, n (%)	Group A VTE, AP (n=29)	Group C VTE, No AP (n=171)	P-Value[a]
PE	23 (79.3)	150 (87.7)	0.24
DVT	2 (6.9)	16 (9.4)	1
CVA	4 (13.8)	5 (2.9)	0.027*

Abbreviations: VTE, Venous Thromboembolism; AP, Antipsychotic; PE, Pulmonary Embolism, DVT, Deep Vein Thrombosis, CVA, Cerebral Vascular Accident
[a]p-value from Fisher's Exact test.
*indicates significant difference detected

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Table 4. Multivariable Logistic Regression Analysis of Factors that Increase Risk of VTE Events

Risk factor	Unadjusted			Adjusted		
	OR	95% CI	p-value	OR	95% CI	p-value
Antipsychotic use	1.37	0.76-2.50	0.30	1.27	0.67-2.44	0.46
Male sex				0.94	0.61-1.45	0.77
Age				1.00	0.97- 1.02	0.74
Caucasian race				1.20	0.57-2.50	0.63
Smoker				0.81	0.46-1.42	0.46
Hyperlipidemia				1.17	0.716-1.91	0.54
Hypertension				0.69	0.33-1.40	0.30
Type 2 diabetes				0.44	0.28-0.70	0.0006*
Thyroid-containing medication				0.82	0.47-1.39	0.45
BMI >30 kg/m^2[a]				2.73	1.24-6.21	0.014*
History of VTE[a]				3.73	0.45-33.18	0.23
Heart or respiratory failure[a]				1.67	0.67-4.22	0.27
Infection or rheumatologic disorder[a]				1.53	0.65-3.70	0.34
MI or stroke[a]				0.289	0.039-1.39	0.16
Estrogen-containing medication[a]				0.52	0.021-7.18	0.63
Recent trauma[a]				1.71	0.36-8.55	0.51
Padua Prediction Score				0.85	0.42-1.66	0.64

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; BMI, Body Mass Index; VTE, Venous Thromboembolism; MI, Myocardial Infarction

[a] indicates item in Padua Prediction Score\

*indicates significant difference detected

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Table 5. Coagulation Laboratory Exploratory Analysis [a]

Laboratory parameter	Group A VTE, AP (n=29)	Group B No VTE, AP (n=22)	Group C VTE, No AP (n=171)	Group D No VTE, No AP (n=178)	P-Value
INR, median (IQR)	1.1 (0.97-1.16)	1.07 (0.99-1.24)	1.04 (1.00-1.18)	1.10 (1.02-1.55)	0.088
aPTT (seconds), median (IQR)	31.30 (27.85-34.90)	33.50 (31.50-35.65)	31.10 (27.48-40.48)	32.55 (29.82-40.25)	0.53
Platelets (10^9/L), median (IQR)	256.0 (199.0-302.0)	205.0 (169.5-262.5)	238.0 (186.2-301.8)	214.0 (173.5-274.5)	0.052
D-Dimer (mg/L FEU), median (IQR)[+]	4118 (3441-5316)	2217 (1264-3312)	4505.5 (1126.0-7004.8)	613.5 (358.0-1287.0)	0.004*

Abbreviations: VTE, Venous Thromboembolism; AP, Antipsychotic; INR, International Normalized Ratio; IQR, Inner Quartile Range; aPTT, Activated Partial Thromboplastin Time; FEU, Fibrinogen Equivalent Unit

[a]At time of the event or most recent value if no thromboembolic event occurred;

*indicates significant difference detected

[+] Kruskal-Wallis test and Dunn test for multiple comparisons, adjusted with the Benjamini-Hochberg method

- D-Dimer group C vs group D, p=0.0026

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