International Journal of General Medicine

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ORIGINAL RESEARCH

Systemic inflammatory response syndrome and platelet count ≥250×10^9 are associated with venous thromboembolic disease

This article was published in the following Dove Press journal:
International Journal of General Medicine
14 January 2015
Number of times this article has been viewed

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Introduction: Prior research has demonstrated that platelet count and inflammation are dominant contributors to hypercoagulability. Our objective is to determine whether elevated platelet count and systemic inflammatory response syndrome (SIRS) have an association with the development of venous thromboembolism (VTE) in hospitalized patients with a high clinical index of suspicion for thromboembolic disease.

Methods: We performed a retrospective medical record review of 844 medical and surgical patients with suspected VTE hospitalized from July 2012 to May 2013 who underwent screening by venous duplex and computed tomography pulmonary angiogram. For our purposes, thrombocytosis was arbitrarily defined as platelet count ≥250×10^9/L.

Results: Venous thromboembolic disease was detected in 229 patients (25.9%). Thrombocytosis was present in 389 patients (44%) and SIRS was present in 203 patients (23%) around the time of imaging. Thrombocytosis and SIRS were positively correlated with VTE ($P<0.001$). There was no correlation between thrombocytosis and SIRS. Multivariate analysis revealed that SIRS (odds ratio 1.91, 95% confidence interval 1.36–2.68, $P<0.001$) and thrombocytosis (odds ration 1.67, 95% confidence interval 1.23–2.26, $P=0.001$) were independently associated with VTE.

Conclusion: Patients at high risk for VTE should be routinely assessed for thrombocytosis (≥250×10^9/L) and SIRS; if either is present, consideration for empiric anticoagulation should be given while diagnostic imaging is undertaken.

Keywords: SIRS, thrombocytosis, VTE, platelet count

Introduction

In the United States, venous thromboembolism (VTE) affects approximately 900,000 people annually.[1] Roughly 300,000 cases are fatal; the 600,000 nonfatal cases result in multiple hospitalizations or extended inpatient stays costing $5.8–$7.8 billion.[1,2]

Virchow's triad states that the development of thrombosis can be attributed to the presence of one or more of the following: endothelial injury, stasis of blood flow, and hypercoagulability.[3] Multiple studies over the past century have lent credence to Virchow's theory and identified several modifiable and static risk factors for VTE.[4] Prior research demonstrated that platelet count and inflammation are dominant contributors to hypercoagulability.[5,6] Platelet count is strongly associated with clot strength and elevated platelet counts increase fibrin production and thrombus generation.[6]

Inflammatory states are highly prevalent amongst hospitalized patients. Systemic inflammatory response syndrome (SIRS) is present in one-third of the inpatient

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population and over 50% of all patients admitted to the intensive care unit.[7] Evidence regarding platelet count and systemic inflammation in relation to the development of VTE is sparse. Our objective was to determine whether elevated platelet count and SIRS have an association with the development of VTE in hospitalized patients with a high clinical index of suspicion for thromboembolic disease.

Methods

We performed a retrospective medical record review of all medical and surgical patients with clinically suspected VTE admitted to a 448-bed urban level-I trauma center over the course of July 2012 to May 2013 who underwent screening by both venous duplex and computed tomography pulmonary angiogram (CTPA). Institutional review board exemption was obtained prior to data collection and incomplete charts were excluded from analysis.

Data was collected on vital signs, hematology and coagulation profiles, and official imaging reports. The presence or absence of SIRS was determined by white blood cell count, heart rate, respiratory rate, and temperature collected as close to the time of venous duplex as possible. When duplicate imaging was ordered, the results of the first examination were used for data analysis. For our purposes, thrombocytosis was arbitrarily defined as platelet count greater than or equal to 250×10^9/L.

The sample was stratified by presence or absence of VTE as determined by official imaging reports. Statistical calculations were performed by chi-square analyses and Student's *t*-test for categorical and continuous variables, respectively. A bivariate model was also built to calculate odds ratios (OR) with 95% confidence intervals (CI) of thrombocytosis and presence of SIRS.

Table 1 Characteristics of patients with and without SIRS

	Overall sample (n=884)	SIRS present (n=203)	SIRS absent (n=681)	*P*-value
Mean platelet count ($\times10^9$)	254.6±8.1	278.7±21.6	247.4±8.2	0.001
Platelet count ≥250×10^9	44%	48.3%	42.7%	NS
VTE	23%	36.5%	22.8%	<0.001
Mean temperature (°F)	98.7±1.9	98.4±0.2	98.9±2.6	NS
Mean heart rate (bpm)	82.3±1.1	98.1±2.1	77.5±1.1	<0.001
Mean respiratory rate (bpm)	19.4±0.2	21.1±0.5	18.9±0.2	<0.001
Mean WBC count ($\times10^9$/L)	10.4±0.4	15.8±1.4	8.7±0.3	<0.001

Abbreviations: NS, not significant; SIRS, systemic inflammatory response syndrome; VTE, venous thromboembolism; WBC, white blood cell.

Results

Our final sample consisted of 884 patients. Venous thromboembolic disease was detected by duplex or CTPA in 229 patients (25.9%). Thrombocytosis was present in 389 patients (44%) and SIRS was present in 203 patients (23%) around the time of imaging.

Mean white blood cell count ($15.8\pm1.4\times10^9$/L versus $8.7\pm0.3\times10^9$/L), mean heart rate (98.1±2.1 versus 77.5±1.1 bpm), and mean respiratory rate (21.2±0.5 versus 18.9±0.2 bpm) were significantly higher in patients with SIRS ($P<0.001$, Table 1). Mean temperature was equivalent across the groups with and without SIRS. Mean platelet count was noted to be significantly higher in patients with SIRS ($278.7\pm21.6\times10^9$/L versus $247.4\pm8.2\times10^9$/L, $P=0.001$).

Of the entire population, 655 patients (74.1%) were found to be negative for VTE (Figure 1). Thrombocytosis was positively associated with venous thromboembolic disease ($P<0.001$, Table 2) and mean platelet count was significantly higher in patients with VTE ($291.5\pm18.8\times10^9$/L versus $241.7\pm8.5\times10^9$/L, $P<0.001$). The presence of SIRS was also positively associated with development of VTE ($P<0.001$).

Bivariate analysis revealed that SIRS (OR 1.91, 95% CI 1.36–2.68, $P<0.001$) and thrombocytosis (OR 1.67, 95% CI 1.23–2.26, $P=0.001$) were associated with venous thromboembolic disease.

Discussion

VTE is a major public health issue. While once considered a primarily postoperative or malignancy-related complication, multiple investigations into the pathophysiology, prevention, and treatment of VTE have led to increased clinical awareness over the past 2 decades.[1,4] Most health care institutions currently utilize protocol checklists to be completed on admission to ensure preventive measures for VTE. Recent recommendations by the American College of Chest Physicians state that patients hospitalized for acute medical illness, trauma, or major surgical procedures should receive VTE prophylaxis with low-molecular-weight heparin, low-dose unfractionated heparin, or fondaparinux.[8] There has been much debate regarding the appropriate timing, method, and dosage of pharmacoprophylaxis; however, it has been established that hospitalized patients are at significantly increased risk of VTE compared to the general population.[1]

SIRS is present in more than 30% of all hospitalized patients.[7] The association between SIRS/sepsis and disseminated intravascular coagulation has been extensively studied[5,9,10] yet there is little information on the link between systemic inflammation and VTE. A systematic review by Fox

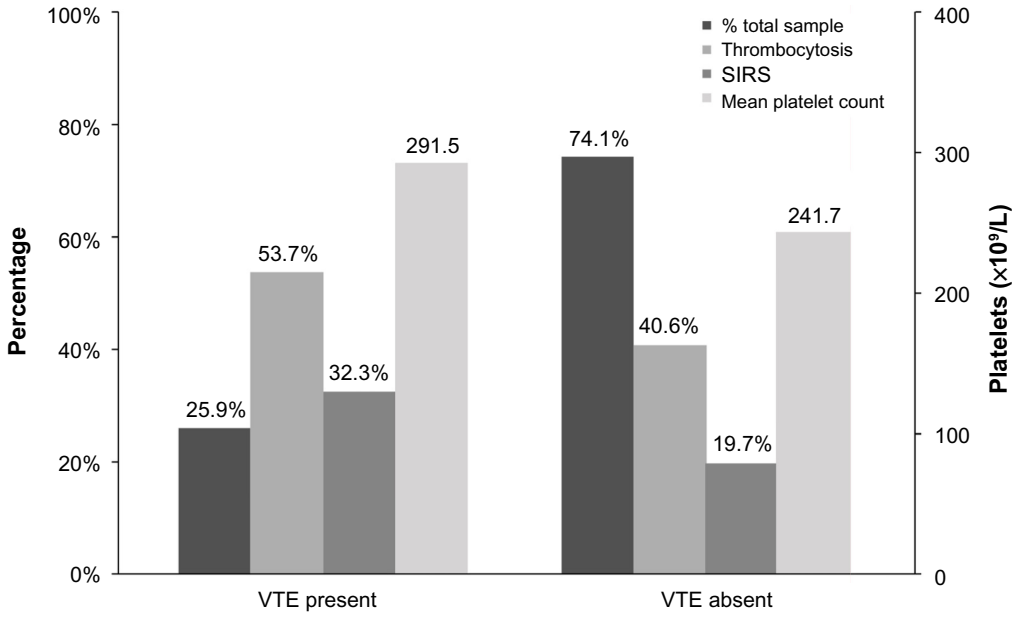

Figure 1 Comparison of subjects with and without VTE as determined by venous duplex and CTPA.
Note: Thrombocytosis (platelet count ≥250×10⁹/L) and SIRS were positively associated with VTE and mean platelet count was significantly higher in these patients ($P<0.001$).
Abbreviations: CTPA, computed tomography pulmonary angiogram; SIRS, systemic inflammatory response syndrome; VTE, venous thromboembolism.

and Kahn found no correlation between serum inflammatory markers and VTE.[11] It has been postulated that the relationship between inflammation and coagulation is bidirectional,[5] although there is no definitive evidence supporting a linear relationship suggesting inflammatory response is predictive of VTE. We hypothesize that systemic inflammation places patients at increased risk for VTE, the occurrence of which potentiates the inflammatory response.

Platelets are recognized as dominant contributors to overall clot strength. Serum platelet count and fibrinogen levels are important factors in the development of thrombosis.[12] Meta-analyses published within the past 20 years reported that antiplatelet therapy significantly reduces the occurrence of VTE; antiplatelet VTE prophylaxis with low-dose aspirin was studied in orthopedic patients and was found to proportionally reduce the incidence of pulmonary embolisms and symptomatic deep vein thrombosis by 43% and 29%, respectively.[13–15] Aspirin has also been found to reduce the incidence of recurrent VTE in patients with first-time unprovoked VTE without an apparent increase in the risk of major bleeding.[16]

Table 2 Characteristics of patients with and without VTE

	Overall sample (n=884)	VTE present (n=229)	VTE absent (n=655)	*P*-value
Mean platelet count (×10⁹)	254.6±8.1	291.5±18.8	241.7±8.5	<0.001
Platelet count ≥250×10⁹	44%	53.7%	40.6%	<0.001
SIRS	23%	32.3%	19.7%	<0.001
Mean temperature (°F)	98.7±1.9	101.3±7.6	97.9±0.1	NS
Mean heart rate (bpm)	82.3±1.1	83.8±2	81.8±1.3	NS
Mean respiratory rate (bpm)	19.4±0.2	19.7±0.4	19.3±0.2	NS
Mean WBC count (×10⁹/L)	10.4±0.4	10.6±0.8	10.3±0.5	NS

Abbreviations: NS, not significant; SIRS, systemic inflammatory response syndrome; VTE, venous thromboembolism; WBC, white blood cell.

This paper focused on examining the potential association between platelet count, systemic inflammation, and VTE in hospitalized patients already clinically suspected of suffering from VTE who were screened by both venous duplex and CTPA. We found that thrombocytosis (platelet count ≥250×10⁹/L) and SIRS were positively associated with imaging-confirmed VTE and mean platelet count was significantly higher in patients with VTE.

Treatment for VTE consists of rapid initial anticoagulation and long-term maintenance anticoagulation.[17] Rapid anticoagulation is initiated to prevent further extension of VTE and possibly fatal complications. Based on our findings, we believe that screening for thrombocytosis and SIRS while pending confirmatory imaging may help identify high-risk patients necessitating immediate anticoagulation.

Limitations

While this study has several strengths, the most prominent of which was our sample size, it also faced limitations

associated with its retrospective single-center design. Our primary focus was not on initial prophylaxis; we chose to evaluate patients clinically suspected of venous thromboembolic disease for the possible association between thrombocytosis, SIRS, and imaging-confirmed presence of VTE. Laboratory results and vital signs were collected as close to time of imaging as possible but there is no way to determine when the patient started manifesting symptoms. Our bivariate model did not include known risk factors for VTE such as age, sex, past medical history, and admission diagnosis since this data was not collected on initial review. However, our sample consisted of all hospitalized patients clinically suspected of having venous thromboembolic disease who had undergone screening by both venous duplex and CTPA; it is likely safe to assume the study population would be considered high-risk.

Our findings suggest that thrombocytosis and SIRS in patients clinically suspected of VTE are suggestive of VTE occurrence. Further large-scale prospective studies are necessary to determine whether our findings can be extrapolated to the inpatient population.

Conclusion

Patients at high risk for VTE should be assessed for thrombocytosis ($\geq 250\times10^9$/L) and SIRS; if either is present, diagnostic imaging should be undertaken in a timely fashion.

Disclosure

The authors report no conflicts of interest in this work.

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