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Comparative analysis of patient outcomes in pulmonary embolism with chronic inflammatory diseases

Marlon V. Gatuz [a], Rami Abu-Fanne [a], Dmitry Abramov [b], Mamas A. Mamas [c,d], Ariel Roguin [a,1], Ofer Kobo [a,c,1,*]

[a] Department of Cardiology, Hillel Yaffe Medical Center, Hadera, Israel
[b] Department of Cardiology, Linda Loma University Health, Linda Loma, USA
[c] Keele Cardiovascular Research Group, Keele University, UK
[d] National Institute for Health and Care Research (NIHR) Birmingham Biomedical Research Centre, UK

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ABSTRACT

Background: Pulmonary embolism (PE) is a critical condition with significant morbidity and mortality, particularly among patients with chronic inflammatory diseases (CID) such as rheumatoid arthritis and systemic lupus erythematosus that are linked to a heightened risk of thromboembolic events.

Method: This retrospective analysis examined 725,725 adult patients hospitalized with a primary diagnosis of PE using the National Inpatient Sample database from 2016 to 2019. Patients were stratified by CID status. The study assessed in-hospital outcomes including all-cause mortality, major adverse cardiovascular and cerebrovascular events (MACCE), major bleeding, intracranial hemorrhage, length of stay, and total hospital charges. Multivariable logistic regression models were used to examine the association between CID and in-hospital outcomes, adjusting for baseline differences.

Results: Of the study population, 33,775 (4.6 %) had CID. Patients with CID were younger (62.07 vs 62.85 years, $p < 0.001$) and more likely to be female (69.9 % vs 51.0 %, $p < 0.001$). After adjustment, patients with CID showed an 8 % decreased mortality risk (aOR 0.92, 95 % CI: 0.86–0.98, $p = 0.015$) but a 15 % higher risk of major bleeding (aOR 1.15, 95 % CI: 1.08–1.23, $p < 0.001$). Additionally, there was a small but significant increase in the odds of MACCE for patients with CID (aOR 1.07, 95 % CI: 1.01–1.13, $p = 0.014$).

Conclusion: The findings indicate that while patients with CID experience lower in-hospital mortality rates, they are at a greater risk for major bleeding. This underscores the necessity for tailored treatment approaches that consider individual patient factors, such as age and comorbidities, to optimize outcomes in this vulnerable population.

1. Introduction

Pulmonary embolism (PE) is a potentially life-threatening condition with high rates of morbidity and mortality. The annual incidence of PE is about 1.15 per 1,000 people and causes 100,000 deaths annually in the United States [1,2]. Short-term mortality rates for massive PE range from 20.9 % to 37 % for in-hospital mortality and from 22.3 % to 39.6 % for 30-day mortality [3].

Chronic inflammatory diseases (CID), such as rheumatoid arthritis (RA), inflammatory bowel disease (IBD), and systemic lupus erythematosus (SLE), have been associated with increased risk of thromboembolic events, including pulmonary embolism [4,5]. These diseases are characterized by chronic inflammation, which can lead to a prothrombotic state enhancing thrombus formation [6]. The relationship between chronic inflammatory diseases and PE is complex and multifactorial, involving interactions between inflammation, coagulation, and endothelial function.

The impact of chronic inflammatory diseases on the outcomes of PE is understudied, highlighting a critical gap in current research. Understanding this relationship is crucial for several reasons. First, it can optimize patient care by identifying how CID affects PE outcomes, allowing clinicians to develop more tailored and effective treatment

* Corresponding author at: Department of Cardiology, Hillel Yaffe Hospital, Hadera, Israel.
E-mail address: oferk@hymc.gov.il (O. Kobo).
[1] Equally contributed.

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strategies for this high-risk population. Second, improved knowledge can enhance risk stratification, refining prognosis and management decisions. Third, addressing the unique needs of CID patients with PE can guide healthcare systems in efficient resource allocation, potentially reducing costs and improving care quality. Lastly, studying these outcomes can help address health disparities faced by CID patients. Therefore, the objective of the study is to assess the in hospital management and outcomes of patients with CID hospitalized with acute PE, seeking to improve management strategies and patient outcomes in this high-risk population.

2. Methods

2.1. Data source

The National Inpatient Sample (NIS), which has been available since 1988, is one of the largest publicly available all-payer inpatient healthcare databases in the United States. It contains data from around 7 million hospital stays each year, which approximates a 20-percent stratified sample of all discharges from U.S. community hospitals, excluding rehabilitation and long-term acute care hospitals. The NIS is part of the Healthcare Cost and Utilization Project (HCUP) and it intends to produce U.S. regional and national estimates of inpatient utilization, access, cost, quality, and outcomes [7].

2.2. Study design and population

In this retrospective study, we conducted a comprehensive analysis of adult patients (aged ≥ 18 years) hospitalized with a primary discharge diagnosis of PE stratified from 2016 – 2019 by known CID status. These patients were chosen based on the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes that were implemented in 2016 which provided more granular data as opposed to the previous ICD-9 coding. Table S1 provided the ICD–10 codes of the patient and procedural characteristics. Patient demographics were recorded for each hospital discharge including age, gender, race, admission day (weekday or weekend), expected primary payer and median household income according to ZIP code.

Missing data on age, gender, elective, admission type and day, mortality were excluded from the analysis. (Fig. 1 for study flow diagram). Each discharge record contained data on up to 30 diagnoses.

CID were combined into a single variable for this study. This category includes Crohn's disease, ulcerative colitis, RA, SLE, Sjögren's syndrome, systemic sclerosis, mixed connective tissue disease, and psoriasis. These conditions were selected based on their association with chronic inflammation and increased risk of thromboembolic events, as reported in various studies [6,8]. In this study, a "high-risk PE" was defined as PE with cardiogenic shock, mechanical ventilation, mechanical circulatory support (MCS), or vasopressors [9,10]. A full list of ICD-10-CM codes used to identify PE is provided in Supplementary Table S1. ICD-10-CM codes were also used to classify procedural information during hospitalization including systemic thrombolysis, catheter-directed thrombolysis, ultrasound-facilitated catheter-directed thrombolysis, catheter-directed embolectomy, surgical embolectomy/thrombectomy and inferior vena cava (IVC) filter placement.

2.3. Outcomes

The primary outcome of interest was the difference in all-cause in-hospital mortality between patients without CID and those with CID. The study also evaluated secondary outcomes, including in-hospital adverse events such as major adverse cardiovascular and cerebrovascular events (MACCE), all-cause mortality, major bleeding, intracranial hemorrhage (ICH), non-ICH bleeding events, length of stay and cost. MACCE was characterized as a composite of all-cause mortality, acute ischemic CVA or transient ischemic attack and cardiac complications. Major bleeding was defined as a composite of gastrointestinal, retroperitoneal, intracranial, and intracerebral hemorrhage, periprocedural hemorrhage, unspecified hemorrhage, or needing blood transfusion. Additionally, the participants' receipt of invasive management procedures such as systemic thrombolysis, catheter-directed thrombolysis, ultrasound-facilitated catheter-directed thrombolysis, catheter-directed embolectomy, surgical embolectomy/thrombectomy and inferior vena cava (IVC) filter placement were also measured.

2.4. Statistical analysis

Statistical analysis was performed on IBM SPSS version 25. Continuous variables were presented as mean, median and interquartile range,

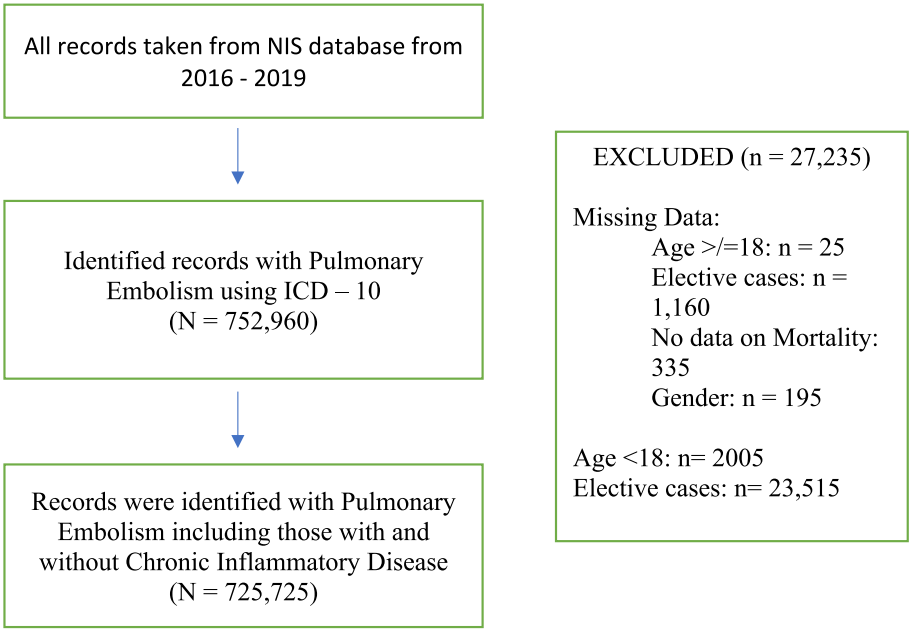

Fig. 1. Flow diagram.

due to skewed data, and categorical data were presented as frequencies and percentages. Categorical variables were compared using Pearson's chi-square test, while continuous variables were compared using the Mann-Whitney *U* test due to the non-normal distribution of the data. Sampling weights were used to calculate the estimated total discharges as specified by AHRQ. Multivariable logistic regression models were used to examine the association between in-hospital outcomes and number as well as site of diseased vascular bed, expressed as odds ratios (OR) with corresponding 95 % confidence intervals (CI). All models were adjusted for baseline differences between the groups, controlling for the following covariates: age, gender, weekend admission, hospital bed size, region and location/teaching status, previous acute myocardial infarction (AMI), previous cerebrovascular accident (CVA), atrial fibrillation (AF), heart failure (HF), hypertension, valvular heart disease, dyslipidemia, smoking status, chronic lung disease, chronic kidney disease, diabetes mellitus, solid malignancy, metastatic malignancy systemic thrombolysis, catheter-directed thrombolysis, ultrasound-facilitated catheter-directed thrombolysis, catheter-directed embolectomy, surgical embolectomy/thrombectomy and inferior vena cava (IVC) filter placement.

3. Results

In the study, records of 725,725 patients with a primary diagnosis of acute pulmonary embolism were identified. Among the patients studied, 33,775 (4.6 %) had CID. Baseline characteristics of patients, stratified by CID status are shown in Table 1. Patients with CID were less likely to be admitted with cardiogenic shock (1.1 % vs. 1.4 %, $p < 0.001$), saddle PE (7.3 % vs. 8.8 %, $p < 0.001$), and acute cor pulmonale (6.7 % vs. 7.7 %, $p < 0.001$). However, they were younger (62.1 vs 62.8 years, $p < 0.001$), and were more likely to be females (51.0 % vs 69.9 %, $p < 0.001$). Those with CID had a higher burden of key comorbidities, including chronic lung disease (32.0 % vs. 25.4 %, $p < 0.001$), anemia (30.5 % vs. 23.0 %, $p < 0.001$), and chronic kidney disease (15.0 % vs. 12.7 %, $p < 0.001$). Interestingly, CID patients had lower rates of diabetes mellitus (21.1 % vs. 23.4 %, $p < 0.001$) and dyslipidemia (34.7 % vs. 36.0 %, $p < 0.001$). For a comprehensive list of comorbidities and their prevalence, please refer to Table 1.

3.1. In-Hospital procedures and outcomes

3.1.1. Crude rates

Patients without CID were more likely to have undergone invasive treatment including systemic thrombolysis (3.2 % vs. 2.7 %, $p < 0.001$), catheter-directed thrombolysis (3.6 % vs. 2.9 %, $p < 0.001$), ultrasound-facilitated directed thrombolysis (0.9 % vs. 0.7 %, $p < 0.001$), catheter-directed embolectomy (0.9 % vs. 0.7 %, $p < 0.001$), and surgical embolectomy/thrombectomy (0.2 % vs. 0.1 %, $p < 0.001$), while the use of IVC filters was similar between the two groups (6.0 % vs. 5.8 %, $p = 0.141$).

Regarding circulatory and ventilatory support, the use of vasopressors was equal in both groups (0.8 %, $p = 0.709$), while mechanical ventilation was more common in patients without CID (3.3 % vs. 2.5 %, $p < 0.001$). ECMO utilization was rare and less frequent in patients with CID (0.1 % vs. 0.2 %, $p = 0.002$).

In terms of clinical outcomes, all-cause mortality was higher in patients without CID (3.1 % vs. 2.6 %, $p < 0.001$), while major bleeding was more common in those with CID (3.0 % vs. 2.4 %, $p < 0.001$). Incidences of intracranial hemorrhage were lower in patients with CID (0.3 % vs. 0.5 %, $p < 0.001$).

The average length of hospital stay was longer for patients with CID (4.6 days vs. 4.3 days, $p < 0.001$). Additionally, the mean total hospital charge was higher for patients with CID at $49,325 compared to $48,392 for patients without CID ($p = 0.015$) (see Table 2).

Patients with CID were more likely to have been discharged to intermediate care facilities (13.8 % vs. 12.8 %, $p < 0.001$) and to have

Table 1
Baseline characteristics of patients with pulmonary embolism, stratified by presence of chronic inflammatory disease.

	No Chronic Inflammatory Disease	With Chronic Inflammatory Disease	P-value
NIS discharge weight	691,950	33,775	<0.001
Mean Age	62.85	62.07	<0.001
Female, %	51.0	69.9	<0.001
Weekend admission, %	23.6	23.7	0.468
Ethnicity,%			<0.001
White	71.5	71.7	
Black	19.2	18.4	
Hispanic	5.8	6.2	
Asian	1.0	1.2	
Native	0.4	0.5	
Other	2.1	2.0	
Hospital Region,%			<0.001
Northeast	18.5	17.9	
Midwest or North Central	24.9	26.2	
South	38.7	38.1	
West	18.0	17.8	
Hospital Bed Size,%			0.006
Small	20.8	20.2	
Medium	29.8	29.8	
Large	49.4	50.1	
Hospital Location/ Teaching Status,%			<0.001
Rural	9.1	8.1	
Urban non-teaching	22.8	21.2	
Teaching	68.1	70.6	
Median ZIP income			<0.001
1st Quartile	28.4	27.9	
2nd Quartile	26.4	25.6	
3rd Quartile	25.0	25.0	
4th Quartile	20.2	21.5	
Primary Expected Payer, %			<0.001
Medicare	51.7	57.2	
Medicaid	12.2	10.7	
Private Insurance	29.1	27.9	
Self-pay	4.1	2.1	
No charge	0.3	0.2	
Other	2.6	1.9	
Record Characteristics, %			
High Risk Pulmonary Embolism	5.0	4.1	<0.001
Ventricular Fibrillation	0.2	0.1	0.001
Ventricular Tachycardia	1.3	1.2	0.013
Cardiogenic Shock	1.4	1.1	<0.001
Saddle PE	8.8	7.3	<0.001
Acute cor pulmonale	7.7	6.7	<0.001
Comorbidities,%			
Heart Failure	16.5	18.5	<0.001
Valvular Heart Disease	6.3	7.3	<0.001
Hypertension	61.9	63.8	<0.001
Diabetes Mellitus	23.4	21.1	<0.001
Dyslipidemia	36.0	34.7	<0.001
Atrial Fibrillation/ Flutter	10.9	11.3	0.022
Smoking	39.9	40.4	0.060
Dementia	6.0	4.2	<0.001
Chronic Kidney Disease	12.7	15.0	<0.001
Chronic Lung Disease	25.4	32.0	<0.001
Obesity	25.5	26.5	<0.001
Anemia	23.0	30.5	<0.001
Thrombocytopenia	5.6	5.4	0.073
Coagulopathy	6.2	9.4	<0.001
Chronic Liver Disease	0.7	1.0	<0.001
Peripheral Vascular Disease	3.3	5.5	<0.001
Previous Acute Myocardial Infarction	5.2	5.6	<0.001
Previous PCI	5.0	4.9	0.574

(*continued on next page*)

Table 1 (*continued*)

	No Chronic Inflammatory Disease	With Chronic Inflammatory Disease	P-value
Previous CABG	7.2	6.6	<0.001
Previous CVA	5.6	6.1	<0.001
Hematologic malignancy	2.3	2.0	<0.001
Solid malignancy	12.2	7.8	<0.001
Metastatic malignancy	7.8	4.3	<0.001

Table 2
In-hospital management and clinical outcomes, Stratified by Presence of Chronic Inflammatory Disease.

	No Chronic Inflammatory Disease	Chronic Inflammatory Disease	P-value
NIS discharge weight	691,950	33,775	<0.001
High Risk Pulmonary Embolism	5.0	4.1	<0.001
Management, %			
Systemic thrombolysis	3.2	2.7	<0.001
Catheter-directed thrombolysis	3.6	2.9	<0.001
Ultrasound-facilitated catheter-directed thrombolysis	0.9	0.7	<0.001
Catheter-directed embolectomy	0.9	0.7	<0.001
Surgical embolectomy / thrombectomy	0.2	0.1	<0.001
IVC filter	6.0	5.8	0.141
Circulatory and Ventilatory support			
Vasopressors	0.8	0.8	0.709
Mechanical Ventilation	3.3	2.5	<0.001
ECMO	0.2	0.1	0.002
Clinical outcomes, %			
All-cause mortality	3.1	2.6	<0.001
MACCE	4.6	4.7	0.246
Major bleeding	2.4	3.0	<0.001
ICH	0.5	0.3	<0.001
Non-ICH			
Retroperitoneal	0.2	0.1	0.001
Gastrointestinal	1.7	2.6	<0.001
Procedure related	0.1	0.1	0.187
Length of Stay, days, mean	4.32	4.61	<0.001
Total charge, $, mean	48,392.81	49,325.63	0.015

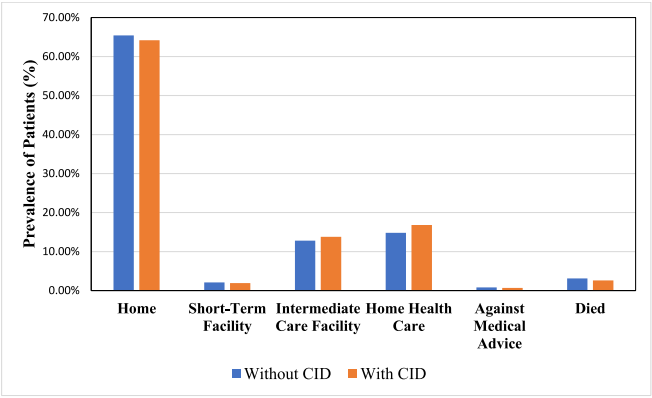

Fig. 2. Disposition of patients.

received home health services (16.8 % vs. 14.8 %, p < 0.001) (see Fig. 2).

3.1.2. Adjusted analysis

Following adjustment for baseline demographics and comorbidities, the multivariate analysis in Table 3 revealed several significant findings. Patients with CID had lower odds of receiving invasive treatments including systemic thrombolysis (aOR 0.82, 95 % CI: 0.77–0.88, p < 0.001), catheter-directed thrombolysis (aOR 0.77, 95 % CI: 0.72–0.82, p = 0.001), ultrasound-facilitated directed thrombolysis (aOR 0.77, 95 % CI: 0.68–0.88, p < 0.001), catheter-directed embolectomy aOR 0.70 (95 % CI: 0.61–0.80, p < 0.001) and surgical embolectomy/thrombectomy, aOR 0.36 (95 % CI: 0.26–0.51, p < 0.001). The use of an IVC filter showed a trend towards reduced likelihood, but this was not statistically significant (aOR 0.97, 95 % CI: 0.92–1.01, p = 0.161).

In terms of in-hospital complications, the analysis shows that patients with CID had lower odds of in hospital mortality aOR 0.92 (95 % CI: 0.86–0.98, p = 0.015), with increased odds of major bleeding aOR 1.15 (95 % CI: 1.08–1.23, p < 0.001). There was also a small but statistically significant increase in the odds of MACCE for patients with CID (aOR 1.07, 95 % CI: 1.01–1.13, p = 0.014).

4. Discussion

The study analyzed records of 725,725 patients with PE, of which 33,775 (4.6 %) had CID. This large-scale analysis provides a comprehensive overview of CID among patients hospitalized for PE, offering valuable insights into the management and outcomes of these patients. The main findings of our study are as follows: First, patients with CID were generally younger and had a higher proportion of females compared to patients without CID. Second, the patients with CID exhibited a higher burden of comorbidities. Third, the patients with CID experienced longer hospital stays, and incurred higher total hospital charges. Fourth, when adjusted to baseline demographics and co morbidities, patients with CID were less likely to undergo invasive procedures such as systemic thrombolysis, catheter-directed thrombolysis, ultrasound-facilitated directed thrombolysis, catheter-directed embolectomy, and surgical embolectomy/thrombectomy. Finally, after adjustments, patients with CID showed lower in-hospital mortality rates but higher risks of major bleeding. These findings highlights the

Table 3
Multivariate Analysis showing adjusted OR for in-hospital procedures and complications in patients with pulmonary embolism complicated by chronic inflammatory disease.

Outcome	aOR (95 % CI)	P value
In-Hospital Procedures		
Systemic thrombolysis	0.82 (0.77–0.88)	<0.001
Catheter-directed thrombolysis	0.77 (0.72–0.82)	<0.001
Ultrasound-facilitated catheter-directed thrombolysis	0.77 (0.68–0.88)	<0.001
Catheter-directed embolectomy	0.70 (0.61–0.80)	<0.001
Surgical embolectomy/thrombectomy	0.36 (0.26–0.51)	<0.001
IVC filter	0.97 (0.92–1.01)	0.161
In-Hospital Complications		
MACCE	1.07 (1.01–1.13)	0.014
Mortality	0.92 (0.86–0.98)	0.015
Major Bleeding	1.15 (1.08–1.23)	<0.001
ICH	0.68 (0.56–0.84)	<0.001

Reference: no chronic inflammatory disease; adjusted for age, gender, weekend admission, hospital bed size, region and location/teaching status, previous acute myocardial infarction (AMI), previous cerebrovascular accident (CVA), atrial fibrillation (AF), heart failure (HF), hypertension, valvular heart disease, dyslipidemia, smoking status, chronic lung disease, chronic kidney disease, diabetes mellitus, solid malignancy, metastatic malignancy, systemic thrombolysis, catheter-directed thrombolysis, ultrasound-facilitated catheter-directed thrombolysis, catheter-directed embolectomy, surgical embolectomy/thrombectomy and inferior vena cava (IVC) filter placement.

complex interplay between CID and PE for in-hospital management and outcomes.

Our findings of younger age and higher percentage of females in patients with CID align with several previous studies [8,11,12]. Aviña-Zubieta et al. reported that 86 % of systemic lupus erythematosus patients were female, with a mean age of 48.9 years [10]. Zöller et al. found that 67 % of patients with autoimmune disorders who developed subsequent pulmonary embolism were women [8]. Similarly, Grainge et al. noted that 53 % of inflammatory bowel disease patients who developed venous thromboembolism were female, and these patients tended to develop VTE at a much younger age compared to the general population [12]. These demographic patterns may be attributed to hormonal influences and the higher prevalence of autoimmune diseases in women. Estrogen has been shown to increase procoagulant factors and decrease anticoagulant proteins, potentially contributing to a hypercoagulable state [13,14]. Additionally, many CID, such as systemic lupus erythematosus and rheumatoid arthritis, disproportionately affect women and often manifest at younger ages.

In addition, patients with CID in our study exhibited a higher prevalence of comorbidities. This is consistent with previous findings that demonstrated an increased risk of comorbidities in patients with inflammatory bowel diseases and rheumatoid arthritis [15,16]. A large nationwide French cohort study found that patients with inflammatory bowel disease had a significantly increased overall risk of acute arterial events compared to the general population [15]. Similarly, a cross-sectional international study of over 3,900 patients with rheumatoid arthritis confirmed a high prevalence of comorbidities, including cardiovascular disease, infections, and certain cancers [16].

The high prevalence of comorbidities in patients with CID can be attributed to several interrelated factors, including chronic systemic inflammation affecting multiple organ systems and endothelial dysfunction resulting from persistent inflammation [17].

Our findings align with previous research on treatment patterns in patients with other high-risk conditions such as cancer. Mai et al. found that cancer patients who had a thromboembolism were less likely to receive systemic thrombolysis, catheter-directed therapy, and surgical thrombectomy/embolectomy compared to patients without cancer [18]. Similarly, Sedhom et al. found that patients with malignancy were less likely to receive systemic thrombolysis (11.3 % vs 19 %, $P < 0.001$), surgical embolectomy (1.2 % vs 3.2 %, $P < 0.001$), catheter-directed thrombolysis (6.1 % vs 8.7 %, $P < 0.001$), and catheter-directed embolectomy (3.9 % vs 5.1 %, $P = 0.02$) compared to patients without malignancy [19]. The parallel suggests that patients with chronic conditions that increase thrombosis risk, whether cancer or CID, may face similar barriers or considerations in receiving invasive treatments for pulmonary embolism.

Lastly, after adjusting for confounding factors, patients with CID showed lower in-hospital mortality rates but higher risks of major bleeding compared to those without CID. These results suggest a complex relationship between CID and PE outcomes. The lower mortality rates in patients with CID may be attributed to their younger age and potentially less severe presentations. Our data showed that patients with CID were less likely to be admitted with cardiogenic shock, saddle PE, and acute cor pulmonale, suggesting they may have presented with less severe PE, which contributed to their lower mortality rates. The paradox of lower mortality despite higher comorbidities in CID patients requires further investigation. While frequent medical encounters due to their chronic condition may lead to earlier PE detection, this hypothesis needs to be substantiated through additional research, as our study cannot establish a causal relationship between these factors and mortality outcomes. The increased risk of major bleeding in CID patients is concerning and may be due to the higher prevalence of comorbidities, including anemia and coagulopathy, chronic inflammation's impact on vascular integrity and coagulation pathways, and potential interactions between CID medications and anticoagulation therapy. This finding is consistent with the study by Kobo et al.[20], which analyzed outcomes of percutaneous coronary intervention (PCI) in patients with Crohn's disease and ulcerative colitis. The study found that while these patients had reduced or similar odds of major adverse cardiovascular and cerebrovascular events compared to those without inflammatory bowel disease, they exhibited a significantly higher risk of major bleeding. This parallel highlights the need for careful management of bleeding risks in CID patients undergoing various medical interventions.

The findings of our study regarding sex differences in patients with CID and PE align with recent research on sex disparities in outcomes for PE patients undergoing percutaneous pulmonary artery thrombectomy. Agarwal et al.'s [21] study of 5,160 patients undergoing percutaneous pulmonary artery thrombectomy for PE revealed significant sex-based differences. Women experienced higher rates of procedural bleeding (16.9 % vs 11.2 %), more blood transfusions (11.9 % vs 5.7 %), and increased vascular complications (5.0 % vs 1.5 %) compared to men. Women also had higher in-hospital mortality (16.9 % vs 9.3 %; adjusted OR, 1.9; 95 % CI, 1.2–3.0) and were less likely to be discharged home after hospitalization (47.9 % vs 60.3 %; adjusted OR, 0.7; 95 % CI, 0.50–0.99). These findings align with our observations in CID patients, emphasizing the need for tailored management strategies that consider sex-specific factors and the impact of chronic inflammation on coagulation and vascular integrity in PE treatment.

Our study have significant clinical implications for the management of pulmonary embolism in patients with CID. The lower mortality rates but higher risks of major bleeding highlights the need for a tailored approach to treatment. Clinicians should consider the patient's age, comorbidities, and potential medication interactions when developing treatment plans. The reduced likelihood of invasive procedures suggests that healthcare providers may be more cautious in their approach, possibly due to the increased bleeding risk. However, this conservative approach should be balanced against the potential benefits of these interventions in high-risk cases. Additionally, the longer hospital stays and higher costs associated with CID patients underscore the importance of efficient, evidence-based management strategies to optimize outcomes and resource utilization.

Several limitations of the study should have been noted when considering the results of this analysis. First, the study data was derived from the NIS which may have had coding errors and did not include detailed clinical data such as lab results and imaging studies. The use of ICD-10-CM codes for PE diagnosis and severity classification has inherent limitations, potentially affecting the accuracy of patient identification and risk stratification. Additionally, there is a potential for undercoding of CID in the dataset, which could affect our results, although we believe this impact is likely minimal due to our comprehensive list of ICD-10 codes used to identify CID patients and the consistency of our CID prevalence with previous literature. Second, the specific types and severity of CID were not differentiated, which may have masked important variations in outcomes among different CID subgroups. Our definition of major bleeding was broad and may not have captured the nuanced differences in bleeding risk among CID patients. The lack of data on specific medication use, such as corticosteroids, methotrexate, NSAIDs, and biologics, is another limitation that prevents a comprehensive analysis of how these medications might influence bleeding outcomes in CID patients with PE. This study only captures patients hospitalized with PE, which may introduce selection bias. It's possible that patients with CID with more severe PE might die in the community before reaching the hospital, resulting in only lower-risk cases being included in our analysis. Another limitation is the absence of long-term outcome data. Without follow-up data, we cannot assess important long-term outcomes such as recurrence rates, chronic complications, or long-term mortality. Despite these limitations, the study had notable strengths, including its large sample size, which enhanced statistical power and generalizability. The use of a nationwide database provided a comprehensive view of real-world clinical practices and outcomes across diverse healthcare settings. Additionally, the adjustment for multiple confounding factors in the analysis

strengthened the validity of the findings. Future prospective studies with more detailed clinical data, including specific laboratory and imaging results, and longer follow-up periods would be valuable in further elucidating the complex relationship between CID and PE outcomes. Such studies could more accurately assess PE incidence and severity in CID patients, addressing the limitations of the current retrospective design and providing a more nuanced understanding of this patient population.

5. Conclusion

In conclusion, our study revealed significant insights into the management and outcomes of PE in patients with CID. While patients with CID exhibited lower in-hospital mortality rates, they faced an increased risk of major bleeding, highlighting the need for tailored treatment approaches. The reduced likelihood of invasive procedures suggests that patients with CID may be managed with a more cautious treatment strategy, which should be balanced against potential benefits in high-risk cases. These findings underscore the importance of personalized care for PE patients with CID, considering factors such as age, comorbidities, and potential medication interactions to optimize outcomes and resource utilization.

CRediT authorship contribution statement

Marlon V. Gatuz: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Investigation, Formal analysis, Data curation. **Rami Abu-Fanne:** Writing – review & editing, Supervision. **Dmitry Abramov:** Writing – review & editing, Validation, Resources, Conceptualization. **Mamas A. Mamas:** Writing – review & editing, Validation, Resources, Conceptualization. **Ariel Roguin:** Writing – review & editing, Validation, Supervision, Conceptualization. **Ofer Kobo:** Writing – review & editing, Visualization, Validation, Supervision, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2025.101637.

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