

Arterial Thrombosis in Patients with Primary Immune Thrombocytopenia: A Nationwide Study

Primer İmmün Trombositopenisi Olan Hastalarda Arteriyel Tromboz: Ülke Geneline Yapılan Bir Çalışma

Demirci U. et al.: Arterial Thrombosis in Immune Thrombocytopenia

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No artificial intelligence-supported technology was used in our study.

Abstract

Introduction: Primary immune thrombocytopenia (pITP) is an acquired bleeding disorder related with mainly decreased number of platelets due to destruction or impaired production of platelets. Clinical presentation of pITP can be multifaceted, and thrombotic events may rarely manifest. Thrombosis can develop with treatment or during the untreated period.

Aim: The primary objective of the study was to examine the frequency of arterial thromboembolism (ATE) in patients with pITP. We also aimed to evaluate the risk factors in these patients and the effect of ITP treatments on ATE.

Materials and Methods: The study was designed as a retrospective, multicenter, conducted under the Turkish Society of Hematology's Scientific Subcommittee on Hemostasis-Thrombosis. Patients over the age of 18 with pITP and who subsequently developed ATE while undergoing follow-up for pITP were evaluated.

Results: A total of 2,178 patients with pITP were screened, and 37 patients (1.7%) were observed to have ATE. The mean age was 62 years. Fifteen (40.5%) of the patients who developed ATE were not receiving pITP treatment at the time of thromboembolism. The patients receiving pITP treatment at the time of ATE, 9 patients (24.3%) were receiving eltrombopag and 10 patients (27%) were receiving corticosteroids. Compared to patients who did not develop ATE, multivariate analysis revealed that presence of hypertension, comorbidity, and the history of venous thromboembolism statistically significantly increased the risk of developing ATE (p : 0.008, 0.018, 0.038).

Discussion: It should be noted that the risk of ATE may increase in pITP patients both during and without treatment. It is important to inquire thoroughly about the presence of comorbidities, atherosclerotic risk factors, hypertension and history of thrombosis in patients at the initiation of treatment. Correctable risk factors should be addressed to minimize the number of risk factors present. The treatment of pITP shall be individualized and incorporate age-related disorders.

Keywords: Arterial Thrombosis, Immune Thrombocytopenia, Atherosclerosis

Özet

Giriş: Primer immün trombositopeni (pITP), trombosit yıkımı veya trombosit üretiminin bozulması nedeniyle trombosit sayısının azalmasıyla ilişkili edinilmiş bir kanama bozukluğudur. pITP'nin klinik sunumu çok yönlü olabilir ve trombotik olaylar nadiren ortaya çıkabilir. Tromboz, tedavi ile veya tedavi edilmeyen dönemde gelişebilir.

Amaç: Çalışmanın birincil amacı, pITP'li hastalarda arteriyel tromboembolizm (ATE) sıklığını incelemektir. Ayrıca bu hastalardaki risk faktörlerini ve ITP tedavilerinin ATE üzerindeki etkisini değerlendirmeyi amaçladık.

Materyaller ve Yöntemler: Çalışma, Türk Hematoloji Derneği Hemostaz-Tromboz Bilimsel Alt Komitesi altında yürütülen retrospektif, çok merkezli bir çalışma olarak tasarlandı. pITP tanısı almış ve daha sonra pITP takibi sırasında ATE geliştiren 18 yaş üstü hastalar çalışmaya dahil edildi.

Sonuçlar: pITP'li toplam 2.178 hasta tarandı ve 37 hastada (%1,7) ATE olduğu görüldü. Ortalama yaş 62 idi. ATE gelişen hastaların 15'i (%40,5) tromboembolizm sırasında pITP tedavisi almıyordu. ATE sırasında pITP tedavisi alan hastalardan 9'u (%24,3) eltrombopag, 10'u (%27) ise kortikosteroid alıyordu. ATE gelişmeyen hastalar ile karşılaştırıldığında, çoklu risk faktörleri birlikte değerlendirildiğinde, hipertansiyon, komorbidite ve venöz tromboz öyküsünün ATE gelişme riskini istatistiksel olarak belirgin artırdığı saptandı (p : 0.008, 0.018, 0.038).

Tartışma: pITP hastalarında ATE riskinin hem tedavi sırasında hem de tedavi olmadan artabileceği unutulmamalıdır. Tedavi başlangıcında hastalarda komorbiditelerin, aterosklerotik risk faktörlerinin, hipertansiyon varlığının ve potansiyel trombotik risk faktörlerinin varlığının kapsamlı bir şekilde değerlendirilmesi önemlidir. Mevcut risk faktörlerinin sayısını en aza indirmek için düzeltilebilir risk faktörleri

ele alınmalıdır. pITP tedavisi, morbidite ve mortaliteyi önlemek için kişiye özel olmalı ve yaşa bağlı bozuklukları kapsamalıdır.

Anahtar Sözcükler: Arteriyel Tromboz, İmmün Trombositopeni, Ateroskleroz

Introduction

Primary immune thrombocytopenia (pITP) is an acquired bleeding disorder related with mainly decreased number of platelets due to destruction or impaired production of platelets. While it may develop in all age groups, population-based studies revealed a rather two age peaks (1-5 years and over 60 years) [1,2]. Majority of the symptoms are related with bleeding due to thrombocytopenia though recently both venous and arterial thrombosis have been recognized and reported. From this perspective, a paradox tendency towards thrombosis have been implicated and clinical trials on the treatment of pITP have included the survey of thromboembolic events as secondary endpoints [3,4,5].

Thrombotic events in pITP are multifactorial and depend mainly on factors related to the patient itself and its comorbidities, the treatment offered to the patient and factors related to the own ITP disease. Based on the universally embraced triad of Virchow as the three pillars of coagulation may be compromised, vessel wall, blood components and blood flow, many hypotheses have been proposed including increased vonWillebrand factor (vWF) levels as a result of endothelial damage induced with autoimmune activity, and increased amounts of microparticles of phosphatidylserine and tissue factor released from the damaged tissue on the surface membranes. It has been stated that large, young, and reactive platelets in circulation may play a role in the pathophysiology of thrombosis [5,6]. Also, there are studies in the literature showing that platelet microparticles formed by the platelet membrane, which cannot be detected in the platelet count, increase the risk of inflammation, atherosclerosis, and thrombosis in ITP [7]. Additionally to disease-related factors, pITP treatments and patient-related factors have been suggested as probable contributing risk factors. Arterial thrombosis can be a significant cause of mortality and morbidity in these patients. Management of ITP patients due to thrombocytopenia is also difficult. In our study, we planned to retrospectively screen arterial thromboembolic events (ATE) including myocardial infarcts, ischemic stroke and peripheral arterial disease (PAD) in adult patients who have been diagnosed with pITP, and to determine contributing risk factors such as known atherosclerotic risks as well as pITP treatments.

Materials and Methods

The study was planned as a retrospective, multicenter study under the Turkish Society of Hematology, Hemostasis-Thrombosis Scientific Subcommittee and 14 centers participated. Patients diagnosed with pITP aged 18 years and older were screened. Patients diagnosed with pITP who developed arterial thrombosis during follow-up were included in the study (Group- 1). The patients' demographic data, diagnosis time, follow-up period, atherosclerotic risk factors, thrombosis history, cardiovascular disease history, ITP treatments, comorbidities and laboratory findings, and splenectomy history were scanned. Additionally, a control group was formed from a single center consisting of patients diagnosed with pITP without a history of arterial thrombosis and retrospectively screened in a similar manner (Group-2). This study was approved by XXX University Faculty of Medicine Ethical Committee (XXX-GOBAEK 2023/503) with consent letters from the participants' own centers.

ATE included documentation of a confirmed diagnosis of cerebrovascular events (CVE), acute coronary events (ACE), and peripheral arterial disease. Details of thrombosis were characterized with attention to demographic features, time since diagnosis, previous ITP therapies, current ITP therapies, cardiac risk factors, thrombotic risk factors, platelet count, maximum platelet value before thrombosis and the subsequent management of the event. Type 2 diabetes, smoking, hypertension, hypercholesterolemia, family history, and/or prior acute myocardial infarction/CVE were evaluated as cardiac risk factors [8].

Statistics

Kolmogorov-Smirnov test was used to assess the normality assumption. The continuous variables that do not have normal distribution were expressed as median (minimum-maximum). Categorical variables were summarized as counts (percentages). For continuous variables, Mann-Whitney U Test was used to compare independent groups. Categorical variables were examined using the Pearson/Fisher Exact Test.

Univariate logistic regression analysis was used to analyze the risk factors of ATE. A two-sided p value <0.05 was considered as statistically significant. Multivariable logistic regression analysis was used to predict potential risk factors of ATE. The variables which had a significance level of $p<0.25$ from the univariate analysis were identified as candidate variables for multivariable model.

Results

In total, 2178 pITP patients were screened. During the follow-up of the patients, ATE was observed in thirty-seven patients (1.7%). The incidence rate was 1.95 cases / 1000 people-year. The mean age was 62 (26-84) years and 21 patients were male (57%). Most patients (83.7%) had at least one comorbidity (Table-1).

Twelve of the 37 patients had a history of thrombosis (ATE in 8 patients and venous thromboembolism in 4 patients). It was observed that 22 patients had ACE, 10 patients had CVE, and 5 patients had PAD (Table- 2). Twenty-one patients were aged 65 years and older (57%). Of these patients, it was observed that 16 had ACE, 4 had CVE, and 1 had PAD (Figure- 1). At the time of the ATE, it was determined that 3 patients were already using acetylsalicylic acid, 1 patient was using DOAC, 1 patient was using warfarin, 1 patient was using clopidogrel, and 1 patient was using low molecular weight heparin.

Fifteen (40.5%) patients who developed ATE were not receiving treatment for pITP at the time of thromboembolism. Nine (24.3%) patients were receiving eltrombopag, 10 (27%) patients were receiving corticosteroids, and 2 patients were receiving combined treatment. ATE was detected in 1 patient at the time of diagnosis (Table- 3).

The average period between diagnosis and manifestation of ATE was 65.07 months (range 0-486 months). In patients receiving eltrombopag, ATE occurred after an average of 30.13 months (1-108 months) of treatment. Furthermore, in patients undergoing corticosteroid treatment, ATE was observed an average of 2.05 months (8 days to 6 months) after the commencement of corticosteroid therapy. In all splenectomized patients, ATE was observed to develop at least 2 years after splenectomy.

At the time of ATE, the mean platelet value was $142 \times 10^9/L$, MPV 10.3, and leukocyte count was $12 \times 10^9/L$. Twenty patients had platelet counts above $100 \times 10^9/L$ and 5 patients had platelet values below $30 \times 10^9/L$ (Table- 4). The average of the maximum platelet value before the arterial event was $252 \times 10^9/L$. Lupus anticoagulant and anticardiolipin antibodies were found to be positive in 1 patient, and no tests were performed in 7 patients. However, it was found to be low titer in the positive patient and not clinically significant.

In the Group-2, complete data of 128 pITP patients with no history of arterial thrombosis were evaluated. The mean age was 52 (20-85) years and 51 patients (40%) were male. Almost half of patients (41.4%) had at least one comorbidity. Coronary artery risk factors and hypertension history were observed less than the Group- 1. The mean follow-up in Group-2 was 62.9 months (2-297 months). It was observed that 65.6% of the patients were followed up without treatment (Table- 5).

In pITP patients with ATE, the distribution of male patients ($p: 0.068$), and the mean age ($p:0.002$) were higher. Again, in patients who developed ATE, the presence of hypertension, and at least one comorbidity and one cardiovascular risk factor were more common and statistically significant ($p<0.01$) (Table- 1). Multivariate analysis showed that the presence of hypertension, comorbidities and history of venous thrombosis increased the risk of ATE ($p: 0.008, 0.018, 0.038$; adjusted OR: 3.6/2.8/5.4) (Table- 6).

Discussion

In patients with pITP, both co-morbidities, ITP-related factors and the treatments may increase the risk of thrombosis. In our study, the male patient population and mean age were higher in patients with ATE ($p:0.07, p:0.03$). The literature consistently highlights both age and male gender as significant risk factors for atherosclerotic endpoints. Once more, an analysis of Group-1 revealed that 56.7% of the patient population were in the geriatric age group. In the study by Zhang et al., most ITP patients developing ATE were of advanced age and 80% had one or more thrombosis risk factors [9]. Population-based Scandinavian and Danish studies also highlight the importance of advanced age and the presence of comorbidities for the risk of ATE in ITP [5,10]. Consistent with the findings in the extant literature, multivariate analysis revealed that hypertension and comorbidity were significantly associated with an elevated risk of ATE. Both the accompanying comorbidities and ITP-related thromboembolic risk and the treatments given to the patients due to ITP may increase the risk of thrombosis. Also, patient-related arterial thromboembolic risk factors should not be forgotten. The development

of ATE in half of the cases during the period when they were not receiving treatment suggests that the comorbidities of the cases and multi-hit hypothesis are important in the development of thromboembolism. It may also be assumed that an ongoing (albeit untreated) pITP process may also be a risk factor.

In a population-based study, the cumulative incidence of venous and arterial thromboembolism in patients with pITP was reported to be increased compared to healthy population (2.9-1.9% and 4.1-3%). This was regarded as independent of the comorbidities and treatments [11]. The risk of developing ATE in pITP may be considered as mildly or moderately increased with an annual incidence of 0.96-1.15 [12]. In our study, similar to the literature, the incidence of arterial thromboembolism, which are the endpoints of atherosclerotic events, was determined to be 1.7 % in pITP and incidence rate was 1.95 cases / 1000 people-year. Additionally, the incidence of stroke in Turkey has been reported as 1.54 cases per 1,000 person-years, and mean age of patients with ACE is 62 years [13,14]. In our cohort, we observed a slightly higher rate of atherosclerotic events among patients of comparable age, which may be attributable to pITP (encompassing both the disease itself and its treatments) as a potential risk factor for atherosclerotic endpoints.

The increase in the risk of thromboembolism after the global use of TPO-RAs is also a controversial issue. There are studies demonstrating a minimal increase in the risk for both eltrombopag and romiplostim, especially in the first year of treatment, as well as studies with significant number of patients reporting no increase in the long term follow up after these treatments. Individual risk factors have been emphasized as the major factors that lead to any thromboembolic event and should be recognized and addressed [10,15,16]. It was observed that ATE developed in 9 (24.3%) patients while receiving eltrombopag. However, all patients had at least one additional cardiovascular risk factor. The mean time to development of ATE in patients receiving eltrombopag was 30.13 months. However, this period was found to be considerably shorter for corticosteroids. The negative effects of corticosteroid on endothelial damage and vascular remodeling may be the main mechanism of the increase the development of ATE in the early period [17]. Likewise, the use of corticosteroids as a rescue treatment in ITP cases and during the active disease period may accelerate the development of atherosclerotic plaques and contribute to the development of any thromboembolic event. Again, rapid platelet increase after steroids and the release of active, reactive young platelets may increase the risk. In such cases, novel treatment models may prove crucial in ensuring the safety of patients, particularly regarding the potential for adverse effects, including the risk of thromboembolism associated with the use of corticosteroids and TPO-RAs. In the follow-up period of Fostamatinib, a spleen tyrosine kinase inhibitor, mild transient ischemic attack was detected in only one of 146 patients (87% had at least one thrombosis risk), and it was not considered treatment related. Consequently, access to novel treatment modalities that mitigate thrombosis risk emerges as a pivotal consideration for patients within advanced age groups and/or those exhibiting multiple thrombosis risk factors [18]. Given the unavailability of Fostamatinib in our country, this medication represents a notable deficit in the therapeutic options available to this population.

The impact of splenectomy on the risk of ATE in patients with pITP remains to be elucidated. The study by Ruggeri et al. showed that the ATE rates were increased after splenectomy in pITP patients [19]. However, in population-based studies, myocardial infarction (1.13% - 1.30%) and stroke (2.09% - 2.56%) rates were similar in pITP compared to patients without splenectomy [20]. It was observed that ATE developed in the late period (median 136 months) in splenectomised patients. Furthermore, no statistically significant difference was identified in splenectomy rates between the two groups.

As Saldanha et al. posit, there exists a correlation between the number of platelets and the development of thromboembolic events [21]. We did not observe such a relation and only 20 of the patients had a platelet count above $100 \times 10^9/L$ at the time of thrombosis and 8 of these not receiving any treatment for pITP. The platelet counts were below $30 \times 10^9/L$ in only 5 (13.5%) patients. The finding that the platelet count was below $100 \times 10^9/L$ in 46% of the patients suggests that low platelet counts may not offer protection against ATE. In the same aforementioned study, age >60, atrial fibrillation, cancer, chronic kidney damage, hypertension, cardiovascular disease, obesity, history of thrombosis, being male, smoking and aPL positivity were determined as significant risk factors for thrombosis with multivariate analysis [21]. Again, Diz-Küçükkaya et al. study, it was reported that 5-year thrombosis-free survival was found to be lower in pITP patients with aPL positive patients [22].

However, in our study, we found that only one out of 30 patients had anticardiolipin IgM, while seven patients were not evaluated for aPL. Limitations of this study were that it was a multicenter study, the number of patients was small, and aPL was not examined in all patients.

Conclusion

As atherosclerosis develops from early adulthood and accelerates with age, inflammation as well as lifestyle and medications, all adult patients with pITP should be monitored at their age-appropriate atherosclerotic risk factors. In pITP patients, thrombocytopenia is predominantly associated with bleeding; however, ATE may occur even in cases of low platelet counts. In long-term follow-ups, cases should be evaluated not only in terms of platelet values but also in terms of risk factors that increase the risk of thrombosis, even in the untreated

period. The occurrence of ATE, especially during the thrombocytopenic period, poses significant challenges in terms of treatment and management, often resulting in substantial morbidity. Furthermore, it is crucial to acknowledge that the arterial thrombosis risk of pITP may escalate both in the absence of treatment and during the treatment period. In order to reduce the risk of thrombosis, the use of treatment options with minimal thrombosis side effects may be a safe management method in patients who are elderly, have comorbidities, and history of venous thrombosis. However, the limited availability of drugs with minimal thrombosis risk, such as Fostamatinib, poses a significant challenge. Consequently, all pITP guidelines recommend, the treatment of pITP shall be individualized and incorporate age related disorders to prevent morbidity and mortality.

Author contribution

UD, EGÜ, MB: researched literature and conceived the study; SS: involved in protocol development; UD, BD, MC, RÇ, DÖ, MCA, SG, ÖS, TG, ZTG, AY, SY, FA, VK, YI, GY, SS, MB, MCU, IEP: patient recruitment and data analysis; EGÜ, AMD: Supervising and interpretation of data; UD, EGÜ, MB: wrote the first draft of the manuscript. All authors approved the final version of the manuscript.

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Risk factors for ATE	Univariate logistic regression analysis			Multivariable logistic regression analysis		
	Crude OR	95% CI	<i>p</i> value	Adjusted OR	95% CI	<i>p</i> value
Gender (reference female)	1.982	0.945-4.155	0.070	-	-	-
mAge	1.035	1.012-1.059	0.003	-	-	-
mAge at diagnosis	1.026	1.005-1.047	0.016	-	-	-
Hyperlipidemia	0.911	0.401-2.068	0.824	-	-	-
AF	1.794	0.426-7.550	0.425	-	-	-
Smoking	1.071	0.497-2.308	0.862	-	-	-
Type 2 Diabetes Mellitus	1.736	0.713-4.226	0.224	-	-	-
Hypertension	6.324	2.852-14.020	< 0.001	3.640	1.403-9.444	0.008
Overweight and Obesity	1.958	0.892-4.299	0.094	-	-	-
Comorbidity	7.311	2.850 - 18.759	< 0.001	3.770	1.259-11.289	0.018
Family history of coronary artery disease (Reference no)	-	-	-	-	-	-
Yes	1.223	0.527-2.841	0.640	-	-	-
Unknown	1.896	0.442-8.139	0.390	-	-	-
Risk factor of coronary artery disease	5.155	2.288 - 11.611	< 0.001	-	-	-
Splenectomy	1.426	0.545-3.731	0.470	-	-	-
Venous thrombosis history	3.758	0.892-15.829	0.071	5.429	1.097-26.869	0.038

The variables which had a significance level of $p < 0.25$ from the univariate analysis were identified as candidate variables for multivariable model.

Abbreviations: ATE: Arterial thromboembolic event, mAGE: mean AGE, AF: Atrial fibrillation

Table- 5: Treatment history of Group-2 patients		
	No.	%
Follow up without treatment	84	65.6
TPO-RAs*	41	32.1
Eltrombopag	39	30.5
Romiplostim	2	1.6
Combined treatment	3	2.3
(TPO-RAs, Azathioprine, Mycophenolate mofetil, corticosteroid)		
Immunosuppressive treatment history	18	14
(Rituximab, Azathioprine, Mycophenolate mofetil, Vincristine)		
Splenectomy history	18	14

Abbreviations: TPO-RAs: Thrombopoietin receptor agonists

Table- 4: Platelet values at the time of arterial thromboembolic events

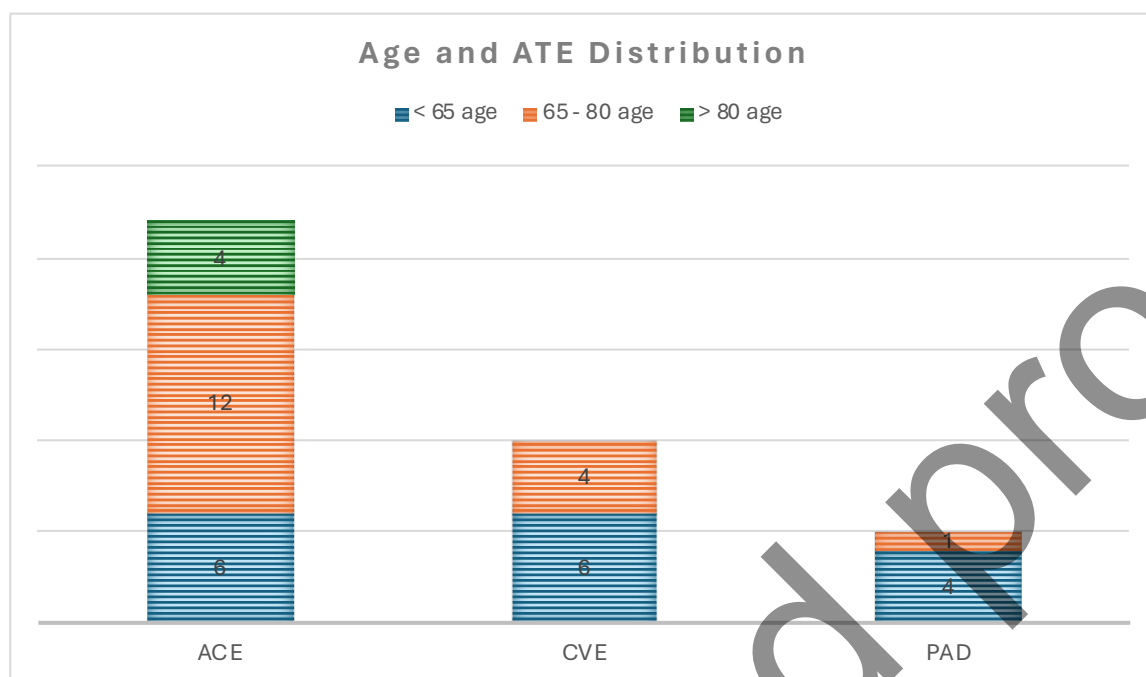
Table- 4: Platelet values at the time of arterial thromboembolic events		
	Platelet values	No/%
Arterial thromboembolic events	> 100 x 10 ⁹ /L	20 / 54 %
	50-100 x 10 ⁹ /L	8 / 22 %
	30-50 x 10 ⁹ /L	4 / 11 %
	< 30 x 10 ⁹ /L	5 / 13 %

Table- 3: Characteristics of pITP Patients Complicated with Thrombosis

No	Sex	Age	Thrombotic event	PLT Count at the Time of ATE (10 ⁹ /L)	ITP treatment at the time of ATE	Splenectomy history	Time between ITP treatment and ATE development (months)
1	F	51	ACE	240	Eltrombopag	-	40
2	F	59	ACE	92	without treatment	-	
3	F	52	PAD	175	Eltrombopag	+	1
4	F	74	ACE	72	GC	-	2
5	F	67	ACE	191	Eltrombopag	-	1
6	M	84	ACE	154	without treatment	-	
7	M	74	ACE	278	GC	-	3
8	F	58	CVE	148	without treatment	-	
9	M	51	ACE	19	at the diagnosis	-	
10	M	74	ACE	134	without treatment	-	
11	F	72	ACE	313	Eltrombopag	-	108
12	F	30	CVE	225	GC	-	5
13	M	80	ACE	191	Eltrombopag	-	72
14	F	38	CVE	220	GC	+	6
15	M	70	ACE	93	Eltrombopag	-	6
16	M	34	PAD	105	without treatment	-	
17	F	34	CVE	77	without treatment	-	
18	M	59	PAD	96	without treatment	-	
19	M	73	ACE	97	Eltrombopag		9
20	M	80	ACE	36	Combined treatment	-	8
21	M	59	ACE	19	GC	+	0,3
22	F	75	CVE	141	GC	-	0,5
23	M	84	ACE	34	without treatment	-	
24	M	75	CVE	14	without treatment	-	
25	M	69	ACE	26	without treatment	-	
26	M	64	PAD	31	without treatment	-	
27	M	26	CVE	20	Combined treatment	+	0,5
28	F	27	CVE	249	without treatment	-	
29	M	75	CVE	222	without treatment	+	
30	F	68	CVE	278	without treatment	-	
31	M	61	ACE	194	without treatment	-	
32	F	59	ACE	530	Eltrombopag	+	5
33	M	69	ACE	82	GC	-	0,5
34	F	66	ACE	58	GC	-	1
35	M	67	ACE	40	GC	-	1
36	M	76	ACE	225	GC	-	1
37	F	65	PAD	690	Eltrombopag	+	30

Abbreviations: ITP, immune thrombocytopenia; PLT, platelet; ACE, Acute coronary events; PAD, Peripheral arterial disease; CVE, Cerebrovascular events; GC, glucocorticoids; CVrf: Cardiovascular risk factors; ATE, Arterial thromboembolic events; F, Female; M, Male

Figure- 1: Distribution of ATE in older age patients



Abbreviations: ACE, Acute coronary events; PAD, Peripheral arterial disease; CVE, Cerebrovascular events; ATE, Arterial thromboembolic events

Table- 2: pITP treatments and cardiovascular risk factors in patients with arterial thromboembolic events

Table- 2: pITP treatments and cardiovascular risk factors in patients with arterial thromboembolic events				
ATE	No/%	Treatment No/%	CVrf ≥ 1 No/%	CVrf ≥ 3 No/%
Acute coronary events	22 / 59%	Eltrombopag 7 / 19% Without treatment* 7 / 19% Corticosteroid 7 / 19% Combine treatment 1 / 2%	10 / 27%	11 / 30%
Cerebrovascular events	10 / 27%	Eltrombopag - / - Without treatment 6 / 17% Corticosteroid 3 / 9% Combine treatment 1 / 2%	3 / 8%	4 / 11%
Peripheral arterial disease	5 / 14 %	Eltrombopag 4 / 11% Without treatment 1 / 2% Corticosteroid - / -	3 / 8%	1 / 2%

* 1 patient is at the time of diagnosis

Abbreviations: ATE: Arterial thromboembolic events, CVrf: Cardiovascular risk factors

Table- 1: Characteristic features of pITP patients with or without arterial thromboembolism				
		pITP - arterial thromboembolism Group- 1	pITP - no arterial thromboembolism Group- 2	P value
Patients No.		37	128	
Age	mean	62 (26-84)	52 (20-85)	0.002
Age at diagnosis	mean	53 (18-82)	44 (19-79)	0.017
Gender		Male 21 – 57% Female 16 – 43%	Male 51 – 40% Female 77 – 60%	0.068
Comorbidity ≥1		31 - 83.7%	53 – 41.4%	<0.001
Coronary arterial disease		12 - 32.4%	-	-
Family history of coronary artery disease		10 - 27%	31 – 24.4%	0.539
Risk factor of coronary artery disease	Number-%	27 - 73%	44 – 34.3%	<0.001
Atrial fibrillation		3 - 8.3%	6 – 4.7%	0.421
Smoking		13 - 35%	43 – 33.5%	0.847
Hyperlipidemia		10 - 27%	37 – 29%	0.823
Tip 2 Diabetes		9 - 24%	20 – 15.6%	0.227
Hypertension		21 – 57%	22 – 17.1%	<0.001
BMI		Overweight and Obesity 26 - 70.2%	Overweight and Obesity 70 – 54.6%	0.129
Splenectomy		7 – 18.9%	18 – 14%	0.468
History of thrombosis		Venous 4 – 10.8% Arterial 8 – 21.6%	Venous 4 – 3.1% Arterial -	0.076 -

Abbreviations: pITP: Primary immune thrombocytopenia