The Treatment of Venous Thromboembolism in the Emergency Department in the DOACs Era

Ibrahim Osman MD[1], Alaa Atamna MD[2,3], and Avishay Elis MD[1,3]

[1]Department of Internal Medicine C and [2]Infectious Diseases Unit, Rabin Medical Center (Beilinson Campus), Petah Tikva, Israel
[3]Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

ABSTRACT **Background:** Low-risk venous thromboembolism (VTE) patients are advised to be discharged from the emergency department (ED) on direct oral anticoagulants (DOACs) treatment. No data are available on whether this recommendation is followed in Israel.

Objectives: To characterize newly diagnosed VTE patients who were discharged from the ED, their anticoagulation treatment at the ED, the recommended discharge protocol, and patient adherence.

Methods: We conducted a retrospective cohort study, which included all newly diagnosed VTE patients who were discharged from the ED. Collected data included demographic and clinical background, anticoagulation treatment at the ED, recommended discharge protocol, patient subsequent adherence, recommended hematological evaluation, and adverse events.

Results: The study group included 443 patients, 89% with deep vein thrombosis (DVT). Approximately three-quarters were treated with anticoagulants in the ED, 98% with enoxaparin. At discharge, anticoagulants were recommended for all; 49% continued enoxaparin, 47% DOACs, and 4% warfarin. After 4 weeks, 67% were treated with DOACs, 22% with enoxaparin, and 5% with warfarin. Approximately 6% discontinued all treatment. After 12 weeks, 90% of the patients who were taking DOACs adhered to the protocol, whereas only 70% and 50% among the enoxaparin and warfarin users, respectively, did. Only 56% were referred for hematological evaluation. The 12-week rate of adverse reactions was approximately 2%. The use of DOACs and the recommendation for further hematological evaluation increased over time.

Conclusions: Clinician training regarding discharge of VTE patients from the ED should continue.

IMAJ 2023; 25: 734–740

KEY WORDS: anticoagulation, direct oral anticoagulants (DOACs), emergency department (ED), enoxaparin, venous thromboembolism (VTE)

Venous thromboembolism (VTE), defined as deep vein thrombosis (DVT), pulmonary embolism (PE), or both, causes significant morbidity and mortality. It can occur in all races, at any age, and in both sexes. Related risk factors include advanced age, immobility, post-surgery, obesity, pregnancy, malignancy, and coagulations disorders [1].

Anticoagulation treatment for VTE is essential, both as a primary treatment and especially for secondary prevention. The standard treatment policy for most patients includes hospitalization and subsequent follow-up in an outpatient setting [2]. The anticoagulation treatment was based on vitamin K antagonists (VKA), mainly warfarin, after overlap with heparin, mainly the low molecular weight heparin (LMWH), enoxaparin. This policy required routine international normalized ratio (INR) monitoring, drug dose adjustments due to a narrow therapeutic index, and multiple drug and food interactions. An increased risk of massive bleeding was also noted [3,4].

Recently, direct oral anticoagulants (DOACs) have been introduced and have quickly become a superior and safe alternative in the treatment of VTE. DOACs have also been used for stroke prevention in patients with non-valvular atrial fibrillation [5]. These agents enable a fast and safe anticoagulation effect, which simplifies the management and facilitates an easy transition from hospital to community care. Furthermore, DOACs significantly reduce the risk of major bleeding (overall, fatal, intracranial, and clinically relevant non-major) [6-10].

In a previous study between 2014 and 2015, prior to DOACs usage, we found that all of the patients who were diagnosed with VTE were hospitalized [11]. Recently, the recommendations for the discharge of VTE patients from the emergency department (ED) have been expand-

ed. This policy is recommended for hemodynamically stable patients in whom the risk of bleeding is low, who do not experience impalement of kidney function, and especially for those who have appropriate environmental support [10]. It is recommended that these patients be treated with anticoagulants for at least 12 weeks and then be evaluated by a hematologist to verify their treatment policy [11,12].

As there are no data whether this policy is used in Israel, the aims of the current study were to explore the demographic and clinical characteristics of newly diagnosed VTE patients who were discharged from the ED, the anticoagulation treatment given, the recommended treatment at discharge, and the treatment that was suggested afterward. In addition, we assessed the recommendations for further evaluation by a hematologist.

PATIENTS AND METHODS

We conducted a retrospective cohort study at Rabin Medical Center (Beilinson Campus), Petah Tikva, Israel. The study was approved by the local Helsinki Committee.

The inclusion criteria included adults (age > 18 years) who were diagnosed with a new VTE (DVT or PE) in the ED and were discharged between 2017 and 2021. The exclusion criteria included previous diagnosis of VTE, thrombosis in upper limbs and/or internal organs, or VTE that was ruled out in post-discharge reevaluation.

The data retrieved from the hospital's computerized medical records included demographics (sex, age), co-morbidities according to previous diagnosis (ischemic heart disease, heart failure, renal failure, diabetes mellitus, previous stroke, chronic obstructive pulmonary disease, active malignant disease), final diagnosis (DVT/PE), and anticoagulation treatment in the ED. In addition, we reviewed the recommended treatment at discharge and the one suggested after 4 weeks and 12 weeks, the recommendation for follow-up by a hematologist, 12-week adherence to the anticoagulation treatment, and adverse reactions. The adherence to the anticoagulation treatment was evaluated only for Clalit Health Services patients due to limited access to the data by other healthcare providers. Full adherence was defined as medication dispensation in all treatment durations.

Adverse reactions to the anticoagulation treatment were defined as those requiring hospitalization. Active malignant disease was defined according to the clinical data, without the necessity of chemical, immunobiological, or radiation treatment.

STATISTICAL ANALYSES

Statistical analyses were performed using SAS 9.4 software (SAS Institute Inc., Cary, NC, USA). Continuous variables were expressed as mean ± standard deviation or median, which were compared according to the *t*-test. Categorical variables were presented by number and per-

Table 1. Demographic and clinical characteristics of the study group

Variable	Entire cohort, N=443	DVT, n=394 (89%)	PE, n=49 (11%)	*P*-value
Age, median (IQR)	61 (21–98)	61 (21–98)	60 (26–98)	NS
Male sex, n (%)	239 (54%)	219 (55%)	20 (41%)	NS
Co-morbidities				
Hypertension, n (%)	81 (18%)	71 (18%)	10 (20%)	NS
Malignancy, n (%)	65 (15%)	48 (12%)	17 (34%)	0.001
Diabetes, n (%)	58 (13%)	48 (12%)	10 (20%)	NS
Ischemic heart disease, n (%)	20 (5%)	18 (5%)	2 (4%)	NS
Previous stroke, n (%)	17 (4%)	16 (4%)	1 (2%)	NS
Chronic kidney disease, n (%)	10 (2.2%)	10 (2.5%)	0 (0%)	NS
Congestive heart failure, n (%)	6 (1.3%)	4 (1%)	2 (4%)	NS
Chronic obstructive pulmonary disease, n (%)	7 (1.58%)	4 (1%)	3 (6%)	0.032

DVT = deep vein thrombosis, PE = pulmonary embolism, IQR = interquartile range

Table 2. Anticoagulation treatment in the emergency department: recommendations at discharge and short-term adherence

Variable	Entire cohort, N=443	DVT, n=394 (89%)	PE, n=49 (11%)	*P*-value
Anticoagulation in the ED, n (%)	315 (71%)	277 (70%)	38 (78%)	NS
Enoxaparin, n (%)	310 (98%)	273 (98%)	37 (98%)	
Rivaroxaban, n (%)	3 (1%)	2 (1%)	1 (2%)	
Apixaban, n (%)	2 (1%)	2 (1%)	0 (0%)	
Dabigatran, n (%)	0 (0%)	0 (0%)	0 (0%)	
No anticoagulation, n (%)	128 (29%)	117 (30%)	11 (22%)	
Anticoagulation recommended at discharge, n (%)	443 (%100)	394 (100%)	49 (100%)	NS
Enoxaparin, n (%)	218 (49%)	192 (49%)	26 (53%)	
Warfarin, n (%)	17 (4%)	17 (4%)	0 (0%)	
DOACS, n (%)	208 (47%)	185 (47%)	23 (47%)	
Rivaroxaban, n (%)	92 (44%)	83 (45%)	9 (40%)	
Apixaban, n (%)	112 (54%)	98 (53%)	14 (60%)	
Dabigatran, n (%)	4 (2%)	4 (2%)	0 (0%)	
Anticoagulation treatment 4 weeks after discharge, n (%)	410 (94%)	363 (94%)	47 (98%)	NS
Enoxaparin, n (%)	92 (22%)	79 (22%)	13 (29%)	
Warfarin, n (%)	22 (5%)	20 (5%)	2 (4%)	
DOACS, n (%)	296 (67%)	264 (67%)	32 (65%)	
Rivaroxaban, n (%)	129 (43%)	115 (43%)	14 (44%)	
Apixaban, n (%)	164 (56%)	146 (56%)	18 (56%)	
Dabigatran, n (%)	3 (1%)	3 (1%)	0 (0%)	
No anticoagulation, n (%)	33 (6%)	31 (6%)	2 (2%)	
12-week anticoagulation compliance and adherence, n (%)	344 (78%)	302 (77%)	42 (86%)	NS
Enoxaparin, n (%)	65 (15%)	56 (14%)	9 (19%)	
Warfarin, n (%)	11 (3%)	10 (3%)	1 (2%)	
DOACS, n (%)	268 (60%)	236 (60%)	32 (65%)	
Rivaroxaban, n (%)	116 (43%)	102 (43%)	14 (44%)	
Apixaban, n (%)	149 (56%)	131 (56%)	18 (56%)	
Dabigatran, n (%)	3 (1%)	3 (1%)	0	
No anticoagulation n (%)	99 (22%)	92 (23%)	7 (14%)	
Recommendation for hematological evaluation, n (%)	250 (56%)	221 (56%)	29 (59%)	NS

NS = non-significant, *P*-value > 0.05
DOACs = direct oral anticoagulants, DVT = deep vein thrombosis, ED = emergency department, PE = pulmonary embolism

cent using the X test. All *P* values were two-sided. *P*-value < 0.05 was considered statistically significant.

RESULTS

During the research period, 2017–2021, 443 patients were diagnosed with VTE in the ED at Beilinson Hospital and were discharged.

Table 1 provides the clinical and demographic characteristics of the entire group according to diagnoses. In total, 394 patients (89%) were diagnosed with DVT and 49 (11%) with PE. Their median age was 61 years (range 21–98). There were no significant differences in the demographic and the co-morbidities between the DVT/PE groups, except for malignancy: 34% of the patients with PE compared to 12% in with DVT ($P = 0.001$).

Table 2 provides the anticoagulation treatment at ED, recommendations at discharge, and short-term adherence. Approximately three-quarters of the patients (71%) were treated at the ED with anticoagulants. The vast majority (98%) by enoxaparin with no difference in the diagnoses.

At the time of discharge, anticoagulants were recommended for all patients. For half (49%), enoxaparin continuation was recommended, while the others were advised to take DOACs (47%) and 4% warfarin. Of the 310 patients who were treated with enoxaparin in the ED, 70% were recommended to continue.

The comparison between the patients who were discharged with enoxaparin and those who were discharged with DOACs reviled no demographic or clinical differences except in patients with malignancy, where the vast majority were discharged with enoxaparin treatment [Table 3].

Among the DOACs agents, the distribution was almost equal between apixaban (54%) and rivaroxaban (44%), only 2% were recommended to be treated with dabigatran. After 4 weeks, most patients (67%) were treated with DOACs, an equal proportion of apixaban and rivaroxaban, 22% were treated with enoxaparin, 5% with warfarin, and 6% discontinued all treatment. After 12 weeks, 70% of the patients who were treated with enoxaparin adhered to the recommendations compared to 90% of the patients treated with DOACs and 50% who were treated with warfarin. Only 56% of the pa-

Table 3. Demographic and clinical characteristics of study group according discharge recommendation, DOACs, or enoxaparin

Variable	Entire cohort, N=446	Enoxaparin (n=218)	DOACs (n=208)	*P*-value
Age, median (IQR)	61 (21–98)	60 (22–98)	62 (21–94)	
Male sex, n (%)	224 (53%)	98 (45%)	126 (60%)	
DVT, n (%)	377 (88.5%)	192 (88%)	185 (89%)	
PE, n (%)	49 (11.5%)	26 (11.9%)	23 (11%)	
Co-morbidities				
Hypertension, n (%)	77 (18%)	32 (15%)	45 (22%)	NS
Malignancy, n (%)	64 (15%)	44 (20%)	20 (9.3%)	0.003
Diabetes, n (%)	56 (13%)	27 (12.3%)	29 (14%)	NS
Ischemic heart disease, n (%)	18 (4%)	10 (4.5%)	8 (3.8%)	NS
Previous stroke, n (%)	15 (3.5%)	9 (4%)	6 (3%)	NS
Chronic kidney disease, n (%)	10 (2.5%)	7 (3%)	3 (1.4%)	NS
Congestive heart failure, n (%)	6 (1.4%)	4 (2%)	2 (1%)	NS
Chronic obstructive pulmonary disease, n (%)	6 (1.4%)	3 (1.4%)	3 (1.4%)	NS
Enoxaparin in the ED, n (%)	297 (70%)	186 (85%)	111 (53%)	0.040

NS = non-significant, *P*-value > 0.05

DOACs = direct oral anticoagulants, DVT = deep vein thrombosis, ED = emergency department, IQR = interquartile range, PE = pulmonary embolism

tients were referred at ED discharge for hematological evaluation [Table 2].

The 12-week rate of adverse events was very low, about 2%, with no difference between the DVT and PE patients or between the agents (data not shown).

Table 4 summarizes the trends in discharge recommendations and anticoagulation treatment between 2017 and 2021. There was no significant difference in the number of DVT or PE patients over the years (data not shown). The number of recommendations of DOACs treatment at discharge was significantly increased, from 23% in 2017 to 55% in 2021 ($P < 0.001$). The number of patients who were treated with DOACs 4 weeks after discharge increased from 43% in 2017 to 76% in 2021 ($P < 0.001$). The rate of patients who were referred at ED discharge for further evaluation by hematologist also increased, from 48% in 2017 to 61% in 2021 ($P = 0.085$).

DISCUSSION

Our study results on newly diagnosed VTE patients who were discharged from the ED revealed that most of the VTEs were DVT, approximately 15% had an active malignancy. Enoxaparin was the most used anticoagulant in the ED. At discharge, anticoagulants were recommended to all patients, half were recommended DOACs. We found no demographic or clinical difference between those treated with DOACs and those treated with enoxaparin. Four weeks after discharge most patients were treated with DOACs. The rate of DOACs treatment at discharge and after 4 weeks has increased. A referral for follow-up with a hematologist was suggested to only half of the patients.

In a previous study from 2014 to 2015, before the DOACs era, we found that all VTE patients were hospital-

Table 4. Anticoagulation recommendation and treatment during years

	2017, n=65 (15%)	2018, n=89 (20%)	2019, n=85 (19%)	2020, n=97 (22%)	2021, n=107 (24%)
DVT, n (%)	54 (83%)	81 (83%)	76 (89%)	90 (93%)	93 (87%)
PE, n (%)	11 (17%)	8 (17%)	9 (11%)	7 (7%)	14 (13%)
Anticoagulation recommended at discharge n (%)					
Enoxaparin, n (%)	41 (63%)	44 (49%)	38 (45%)	52 (53%)	47 (44%)
Warfarin, n (%)	9 (14%)	5 (6%)	1 (1%)	2 (2%)	1 (1%)
DOACS, n (%)	15 (23%)	40 (45%)	46 (54%)	43 (45%)	59 (55%)
Rivaroxaban, n (%)	11 (73%)	14 (35%)	23 (50%)	23 (53%)	19 (32%)
Apixaban, n (%)	4 (27%)	25 (62.5%)	20 (43%)	20 (47%)	40 (68%)
Dabigatran, n (%)	0 (0%)	1 (2.5%)	3 (7%)	0 (0%)	0 (0%)
Anticoagulation treatment 4 weeks after discharge, n (%)					
Enoxaparin, n (%)	17 (26%)	24 (27%)	16 (19%)	13 (13%)	20 (19%)
Warfarin, n (%)	11 (17%)	3 (3%)	3 (3.5%)	1 (1%)	3 (3%)
DOACS, n (%)	**28 (43%)**	**58 (65%)**	**61 (72%)**	**77 (79%)**	**76 (71%)**
Rivaroxaban, n (%)	16 (57%)	21 (36%)	34 (56%)	40 (52%)	19 (25%)
Apixaban, n (%)	12 (43%)	37 (64%)	24 (39%)	37 (48%)	57 (75%)
Dabigatran, n (%)	0 (0%)	0 (0%)	3 (5%)	0 (0%)	0 (0%)
No anticoagulation, n (%)	9 (14%)	4 (5%)	5 (5.5%)	6 (7%)	8 (7%)
Referral for hematological evaluation, n (%)	30 (46%)	50 (54%)	48 (56%)	56 (57%)	66 (61%)

DOACs = direct oral anticoagulants, DVT = deep vein thrombosis, ED = emergency department, PE = pulmonary embolism

ized [11]. However, the current recommendation is that hemodynamically stable patients, in whom the risk of bleeding impalement of kidney functions is low and especially those who have appropriate environmental support, should be discharged from the ED [10]. A retrospective study of patients diagnosed with acute DVT in 2019 in the United States showed that only 41.9% of eligible patients were discharge from the ED for treatment in the community [13]. From our clinical experience, with the expanding use of DOACs, the discharge rate of hemodynamically stable VTE patients from the ED will increase.

In our study, 89% VTE patients were diagnosed with DVT, compared to approximately two-thirds, as was described previously [14].

Approximately 15% of our study group had an active malignant disease, similar to what was previously reported (20–25%) [15]. Most of these patients were discharged with enoxaparin, as per the guidelines at that time [12,16,17]. Recently it has been found that DOACs are effective and safe also for cancer-associated VTE [18-20]. It can be assumed that their use for this indication will expand.

During the stay in the ED, most of the patients were treated with enoxaparin. At the time of discharge, anticoagulation treatment was recommended to all patients, half of them DOACs. A study in the United States in 2019 found that 89.7% of the patients were discharged with oral direct anticoagulants [13].

The use of DOACs after discharge has increased. These findings are like those from the United Kingdom, where approximately 62% were given DOACs in 2019 compared to 16% in 2005 [21].

The 12-week compliance with anticoagulants in our study was 78%, while the adherence to DOACs was about 90% compared to 50% for warfarin. In a study from Germany, which assessed anticoagulation therapy in patients with atrial fibrillation, it was found that 223 of 2600 patients (18.5%) discontinued rivaroxaban during a mean follow-up period of 544 days, with a mean discontinuation rate of 13.6 (95% confidence interval 11.8–15.4) per 100 patient-years (15% in the first year and very low thereafter). Overall adherence to rivaroxaban treatment was much higher than reported for warfarin in all age groups, with the most common reason for discontinuation bleeding complications (30% of all discontinuations) [22]. These results are consistent with the findings of other studies, like a large German observational study on atrial fibrillation patients [23]. During follow-up, estimated treatment persistence was significantly greater for patients receiving rivaroxaban than for patients receiving warfarin, both after 180 days and after 360 days. Among the factors that influence treatment compliance with DOACs compared to warfarin are the fixed dose, fewer interactions with food or drugs, and no need for INR monitoring [22,24,25].

From our clinical experience, most of the efforts of physicians are in the diagnosis of the VTE, whereas the initial treatment and the instructions regarding the duration of anticoagulation treatment as well as the need for hematological follow-up are less noted. Our results support this finding, as only half of the patients were referred for further follow-up with a hematologist. Nevertheless, the analysis indicates a learning curve, both in the use of DOACs and in the referral rates for hematological consultation.

The rates of reported side effects after 12 weeks were very low, with no difference between the DVT and PE patients or between the agents. These findings contrast the results of a similar American study from 2019, in which the risk of bleeding was recorded in 6.9% of patients discharged from the ED [13]. However, we defined adverse events of the anticoagulation therapy as those that required hospitalization.

The advantage of our study is its size, 443 patients, and that it represented real life at the ED and after discharge in Israel. The study's limitations include being a single center and lack of comparison and data of the patients who were hospitalized. Nevertheless, we believe that our findings reflect the policy in other centers and areas around the country.

CONCLUSIONS

Training regarding the discharge of VTE patients from the ED on DOACs treatment, including hematological follow-up, should be continued.

Correspondence

Dr. A. Elis
Dept. of Medicine C, Rabin Medical Center (Beilinson Campus), Petah Tikva 4941492, Israel
Phone: (972-3) 937-6301
Fax: (972-3) 937-6311
Email: avishayel@clalit.org.il

References

1. Maynard G, Stein J. Preventing hospital-acquired venous thromboembolism: a guide for effective quality improvement. (AHRQ Publication No. 16-0001) Agency for Healthcare Research and Quality, Rockville MD August 2016. [Available from https://www.ahrq.gov/sites/default/files/publications/files/vteguide.pdf].

2. Cohen AT, Agnelli G, Anderson FA, et al. VTE Impact Assessment Group in Europe (VITAE). Venous thromboembolism (VTE) in Europe. The number of VTE events and associated morbidity and mortality. *Thromb Haemost* 2007; 98 (4): 756-64.
3. Ageno W, Gallus AS, Wittkowsky A, Crowther M, Hylek EM, Palareti G. Oral anticoagulant therapy: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2012; 141 (2 suppl): e44S-e88S.
4. Hutten BA, Prins MH. Duration of treatment with vitamin K antagonists in symptomatic venous thromboembolism. *Cochrane Database Syst Rev* 2000; (3): CD001367.
5. Gunawardena T. Direct Oral Anticoagulants: A review for the non-specialist. *Hematol Rep* 2021; 13 (4): 9239.
6. Nakamura M, Yamada N, Ito M. Novel anticoagulant therapy of venous thromboembolism: current status and future directions. *Ann Vasc Dis* 2017; 10 (2): 92-8.
7. Pradaxa® (dabigatran etexilate) summary of product characteristics. Ingelheim am Rhein: Boehringer Ingelheim International GmbH; 2015. [Available from https://www.ema.europa.eu/en/documents/product-information/pradaxa-epar-product-information_en.pdf].
8. Xarelto® (rivaroxaban) summary of product characteristics. Berlin: Bayer Pharma AG; 2015. [Available from https://www.ema.europa.eu/en/documents/product-information/xarelto-epar-product-information_en.pdf].
9. Eliquis® (apixaban) summary of product characteristics. Uxbridge: Bristol-Myers Squibb, Pfizer; 2015. [Available from https://www.ema.europa.eu/en/documents/product-information/eliquis-epar-product-information_en.pdf].
10. Chai-Adisaksopha C, Crowther M, Isayama T, Lim W. The impact of bleeding complications in patients receiving target-specific oral anticoagulants: a systemic review and meta-analysis. *Blood* 124 (15): 2450-8.
11. Amor S, Menndel Y, Atamna A, Elis A. The management of venous thromboembolism in a tertiary hospital-- the pre direct oral anticoagulants (DOAC) era. *Harefuah* 2019; 158 (8): 409-502.
12. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; 141 (2 Sppl): e419S-e496S.
13. Snipes G, Becker T, Kelkar AH, et al. Improving value in emergency department management of deep vein thrombosis. *Blood* 2021; 138 (Suppl 1): 1905.
14. Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. *Circulation* 2003; 107 (23 Suppl 1): I9-16.
15. Timp JF, Brakkan SK, Versteeg HH, Cannegieter SC. Epidemiology of cancer-associated venous thrombosis. *Blood* 2013; 122; 1712-23.
16. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease; anti-thrombotic therapy for VTE Disease CHEST guidelines and Expert Panel Report. *Chest* 2016; 149; 315-52.
17. Lyman GH, Khorana AA, Kuderer NM, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer; American society of Clinical oncology clinical practice guideline update. *Clin Oncol* 2013; 31: 2189-204.
18. Mantha S, Laube E, Miao Y, et al. Safe and effective use of rivaroxaban for treatment of cancer-associated venous thromboembolic disease; a prospective cohort study. *Thromb Thrombolysis* 2017; 43: 166-71.
19. Raskob GE, van Es N, Verhamme P, et al. Edoxaban for the treatment of cancer-associated venous thromboembolism. *N Engl J Med* 2018; 378: 615-24.
20. Xiang E, Ahuja T, Raco V, Cirrone F, Green D, Papadopoulos J. Anticoagulation prescribing patterns in patients with cancer. *J Thromb Thrombolysis* 2018; 45; 89-98.
21. Afzal S, Zaidi STR, Merchant HA, Babar ZU, Hasan SS. Prescribing trends of oral anticoagulants in England over the last decade: a focus on new and old drugs and adverse events reporting. *J Thromb Thrombolysis* 2021; 52 (2): 646-53.
22. Beyer-Westendorf J, Förster K, Ebertz F, et al. Drug persistence with rivaroxaban therapy in atrial fibrillation patients-results from the Dresden non-interventional oral anticoagulation registry. *Europace* 2015; 17 (4): 530-8.
23. Beyer-Westendorf J, Ebertz F, Thomas E. Real-world persistence and adherence to oral anticoagulation for stroke risk reduction in patients with atrial fibrillation. *Europace*. 2016; 18: 1150-7.
24. Ho MH, Ho CW, Cheung E, et al. Continuation of dabigatran therapy in "real-world" practice in Hong Kong. *PLoS One* 2014; 9: e101245.
25. Beyer-Westendorf J, Ebertz F, Förster K, et al. Effectiveness and safety of dabigatran therapy in daily-care patients with atrial fibrillation. Results from the Dresden NOAC registry. *Thromb Haemost* 2015; 113: 1247-57.

Every great advance in science has issued from a new audacity of imagination.

John Dewey (1859–1952), American philosopher, psychologist, and educational reformer

Capsule

Exhausted T cells turn off transposable elements

Transposable elements (TEs) are non-protein-coding DNA sequences capable of moving throughout the genome and composing nearly 50% of genomic DNA, but their function in T cells remains unclear. By analyzing bulk and single-cell transcriptomics, **Bonté** and colleagues explored the expression and regulation of TEs during the establishment of T cell exhaustion. In mouse tumor and chronic viral infection models, TEs belonging to the VL30 family were highly repressed in terminally exhausted, tumor-infiltrating T cells and were controlled by the transcription factor Fli1. In human tumors, TE expression patterns were associated with the state of T cell exhaustion and reprogrammed by anti-PD-1 immunotherapy. These findings demonstrated that TE expression is tightly regulated during the progression of T cell exhaustion, which could improve the accuracy of T cell gene signatures.

Sci Immunol 2023; 8 (88): eadf8838

Eitan Israeli