Management and Outcomes of Isolated Distal Deep Vein Thromboses: A Questionable Trend toward Long-Lasting Anticoagulation Treatment. Results from the START-Register

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Background

- Isolated distal deep vein thrombosis (IDDVT) is a frequent finding in patients with suspected DVT; however, its prevalence in suspected patients varies greatly.

- IDDVT optimal treatment has still not been adequately standardized: anticoagulant of choice, appropriate dosing, and duration of treatment are still a matter of discussion.

- This state of affairs, in large part, can be put down to a general lack of interest by researchers in the disease, as witness the literature which has been persistently much less than that on proximal DVT or pulmonary embolism.

AIM of the study

- To analyze the therapeutic approach of Italian clinicians to patients diagnosed with acute IDDVT, as first venous thrombotic episode, who were included in the prospective, observational, multicenter START-VTE-Registry.

- Their baseline characteristics, type of management, and clinical results were analyzed and compared with those recorded in patients included in the registry for a first event that was proximal DVT of a lower limb, without PE.

Methods

- The START-Register is an observational, multicenter, dynamic cohort study of adults starting anticoagulation therapy, whatever the indication for treatment and drug/dosage used.

- The present study focused on patients included in the START-Register for October 2010 up to June 2018 for a first episode of IDDVT or of PDVT of a lower limb.

Results (I)

- 412 patients with IDDVT were analyzed and compared with 1173 patients with PDVT.

- At baseline, patients with IDDVT versus PDVT were significantly younger, had a generally better renal function, and a lower prevalence of so-called fragile conditions.

- The unprovoked or provoked nature of thrombotic events was equally distributed across the two groups of patients; however, major risk factors were more frequently transient in IDDVT (p <0.0001) and permanent in PDVT (p<0.0001).

Results (II)

- Parenteral anticoagulation drugs (including LMWH or fondaparinux) were used in a small and similar proportion in IDDVT and PDVT patients.

- Warfarin and DOACs were prescribed in equal measure in IDDVT patients, whereas DOAC use was markedly higher and warfarin lower in PDVT patients (61.3 and 32.5%, respectively).

- Among DOACs, rivaroxaban was the most frequently used drug, given it was the first in the category to be available for this indication (since 2014) and reimbursed by the Italian National Healthcare System.

Table 1

| n		IDDVT (n = 412)	PDVT (n = 1,173)	n	p
	Fondaparinux n	9	31		
	Duration (mo) Median (IQR)	2.8 (0.9–6.5)[a]	6.9 (3.1–12.8)		
	• Warfarin n (%)	185 (44.9)	381 (32.5)		<0.0001
	Duration (mo) Median (IQR)	9.6 (4.3–23.1)	14.5 (6.8–26.3)		
	• DOACs n (%)	201 (48.8)	719 (61.3)		<0.0001
	Duration (mo) Median (IQR)	5.6 (3.1–9.7)[b]	8.7 (4.7–15.9)		
	Apixaban n (n. low dose)	38 (6)	157 (33)		
	Dabigatran n (n. low dose)	28 (3)	72 (10)		
	Edoxaban n (n. low dose)	15 (1)	55 (17)		
	Rivaroxaban n (n. low dose)	120 (0)	435 (24)		

Results (III)

- Less than one-fourth (22.3%) of IDDVT patients received anticoagulation treatment up to 90 days, and more than half (52.7%) were treated for >180 days.

- About 29% of PDVT patients were treated for up to 180 days, whereas the large majority (>70%) received anticoagulation for >180 days.

- In a sub-analysis comparing IDDVT patients included before or after 2014, the VKAs use dropped from 77.4% to 11.3% ($p<0.0001$), whereas DOACs increased from 20.7% to 78% ($p<0.0001$); at the same time, the median duration of treatment lowered from 8.7 months to 4.9 months.

- Similar results were found in patients with PDVT.

Results (IV)

- During treatment, bleeding occurred in 5.6% and 2.8% patient-years in IDDVT and PDVT, respectively (p=0.0082).

- Bleeding was more frequent in IDDVT than PDVT patients treated with warfarin (6.8 vs. 3.2 patient-years, p=0.0228, respectively).

- Thrombotic complications occurred in 1.1% and 2.4% patient-years in IDDVT and PDVT patients, respectively (not significant).

- Analyzing together the two groups, 66.1% of bleeds and 86.1% thrombotic complications occurred after 90 days anticoagulation treatment.
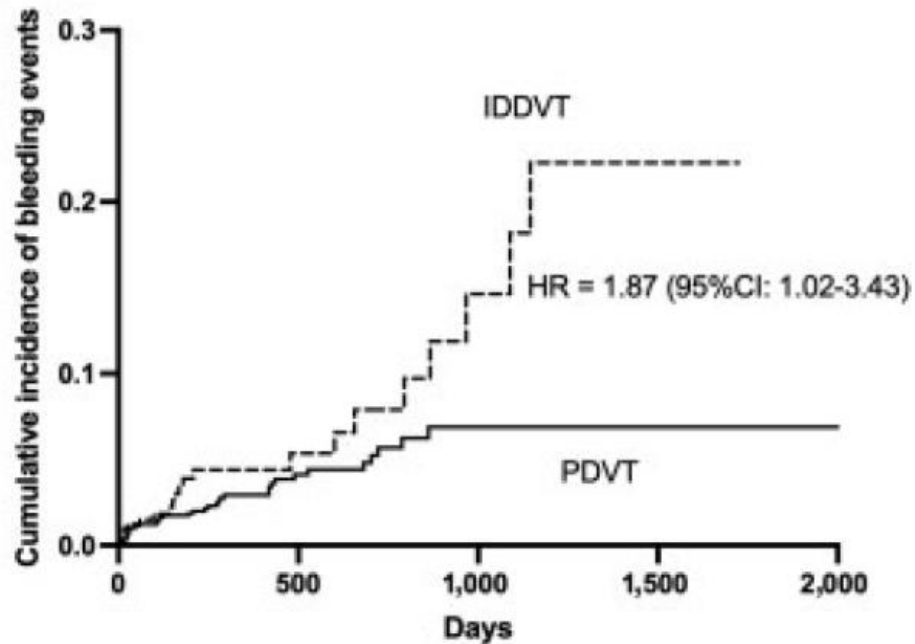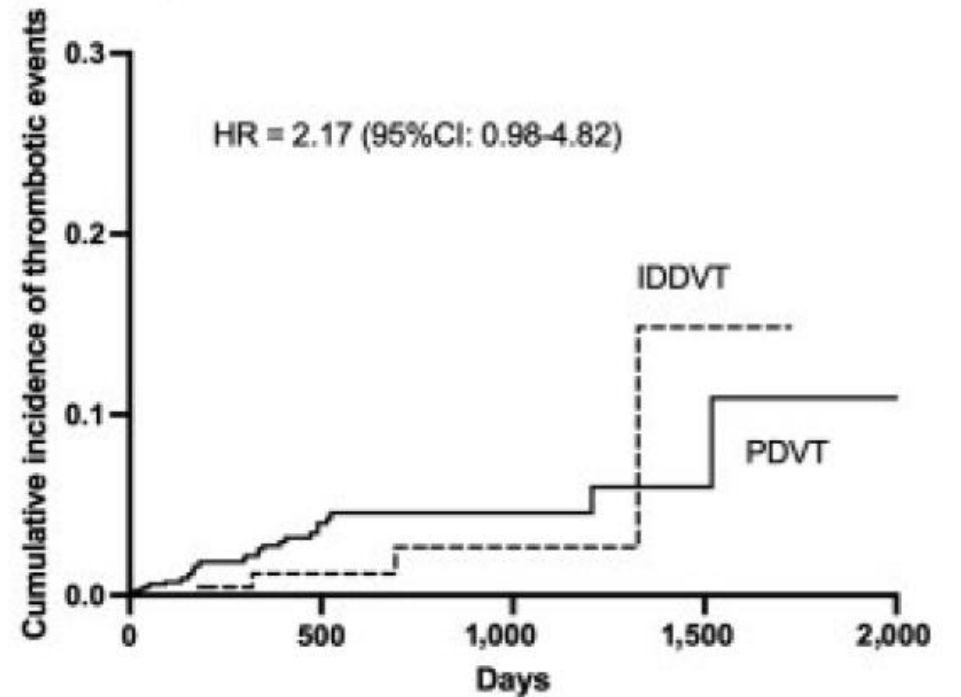
Cumulative occurrence of bleeding (Panel A) and thrombotic (Panel B) events in patients with IDDVT or PDVT.

CI, confidence interval; HR, hazard ratio.

Conclusions

- The large majority of IDDVT patients received anticoagulation for more than 3 months.

- Most bleeding and thrombotic complications occurred after the first 90 days of anticoagulation therapy.

- These results indicate that an extended anticoagulation beyond 90 days in IDDVT patients is associated with increased risk of complications.

- Whether an extended treatment may lower recurrences after anticoagulation withdrawal should be assessed by specifically designed studies.