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# Long-Term Outcomes in Two-Year Follow-Up after Primary Treatment in Patients with a Prior Venous Thromboembolic Event: A Prospective, Observational, Real-Life Study

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# Background

- Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and/or pulmonary embolism (PE), is a common and potentially serious disease that urgently requires active anticoagulant treatment.
- International guidelines unanimously recommend that all patients with acute VTE should receive full-dose anticoagulation for at least 3–6 months to complete the primary treatment.
- After this period, the decision on anticoagulation duration is influenced by many factors, such as the physician's experience, confidence in guidelines and recommendations, and patient characteristics and preferences.

# AIM of the study

To analyze the occurrence of complications during two years of follow-up in patients currently present in the START2-POST-VTE study who discontinued or prolonged anticoagulation.

# Methods

- The START2-Register (Survey on anticoagulated pAtients RegisTer, NCT02219984), which is promoted and funded by the “Arianna Anticoagulazione” Foundation based in Bologna, Italy, is an ongoing multicenter, prospective, observational study.
- START2 POST-VTE, a part of the START2-Register, includes patients with a recent VTE episode who have given their written informed consent.
- This study examined the complications occurring during two years of follow-up in patients with a first VTE who had discontinued or prolonged anticoagulation.

# Results (I)

- A total of 720 patients (53.5% male) were included in the study.
- After a single VTE event, all patients received anticoagulation therapy for initial and primary treatment for a mean duration of 8.7 months.
- After completing primary treatment, which consisted of anticoagulation with a DOAC in 81.5% of cases, patients discontinued (439 subjects, 61%) or extended (281, 39%) anticoagulation.
- Prolongation of anticoagulation was preferred in cases with proximal DVT (62.2%), whereas anticoagulation was definitively discontinued in most cases with isolated distal DVT (82.2%).

**Table 3.** Factors associated with the extension of anticoagulation in the univariate and multivariate analyses.

| Factors                        | Univariate Analysis |               |          | Multivariable Analysis |               |          |
|--------------------------------|---------------------|---------------|----------|------------------------|---------------|----------|
|                                | OR                  | 95% CI        | <i>p</i> | OR                     | 95% CI        | <i>p</i> |
| Age *                          | 1.0                 | 1.0–1.02      | 0.03     | 2.2                    | 0.85–5.9      | 0.1      |
| Thrombophilia abnormalities    | 2.2                 | 1.4–3.5       | 0.01     | 2.2                    | 1.5–3.8       | 0.01     |
| Unprovoked Event               | 1.8                 | 1.3–2.4       | 0.001    | 1.7                    | 1.2–1.8       | 0.001    |
| Proximal DVT                   | 2.2                 | 1.3–4.2       | 0.02     | 1.8                    | 1.1–3.9       | 0.03     |
| Distal DVT                     | 0.7                 | 0.58–<br>0.79 | 0.01     | 0.2                    | 0.72–<br>0.82 | 0.02     |
| Isolated PE                    | 2.1                 | 1.5–7.1       | 0.02     | 2.1                    | 0.91–7.8      | 0.06     |
| Charlson’s score (moderate) °  | 1.1                 | 0.7–1.9       | 0.7      | 1.1                    | 0.58–5.3      | 0.3      |
| High risk for VTE recurrence # | 2.3                 | 1.3–4.2       | 0.01     | 2.2                    | 1.1–4.6       | 0.02     |
| Antiplatelet therapy           | 0.8                 | 0.5–1.5       | 0.6      | 0.5                    | 0.4–1.6       | 0.6      |

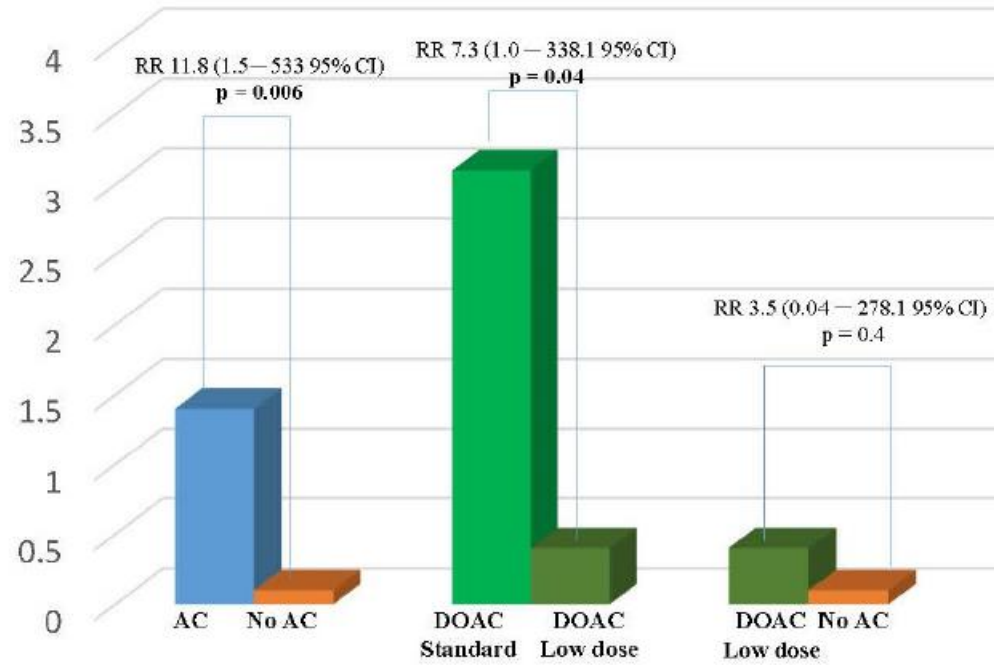
\* Age is considered as a continuous variable. ° Charlson’s score: mild class vs. moderate/high classes. # Individual thrombotic risk assessment of patients formulated by the treating physicians. DVT: deep venous thrombosis, PE: pulmonary embolism, VTE: venous thromboembolism.

## Results (II)

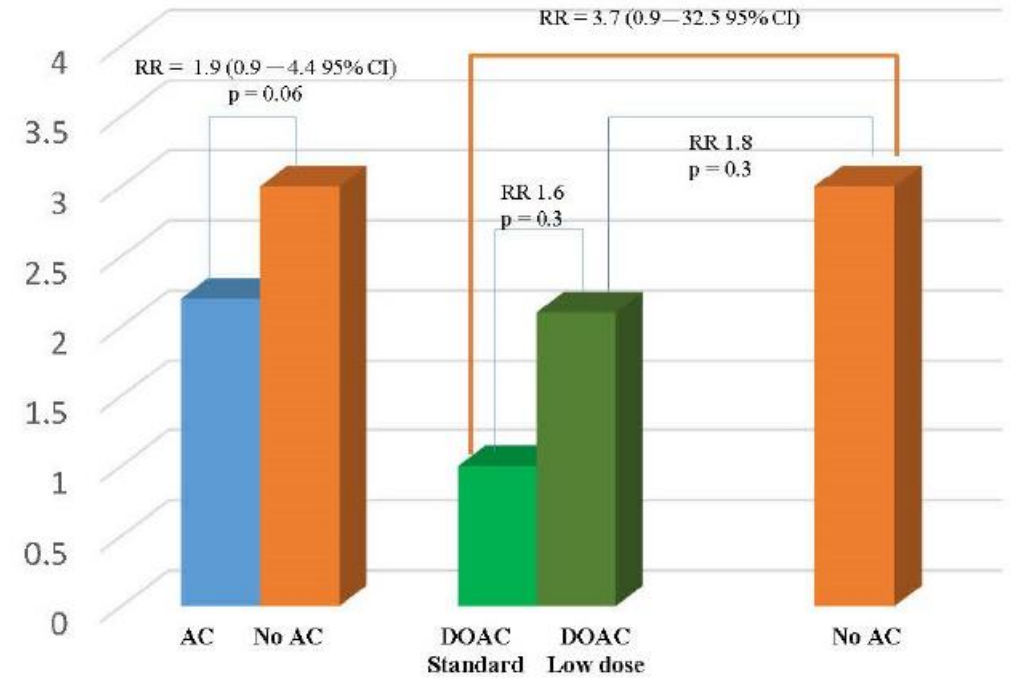
- The total follow-up duration was 1318 years.
- Most of the patients who continued anticoagulation (n = 281) were treated with a DOAC during follow-up at either the standard (45.5%) or a reduced dose (46.3%).
- Among the patients who discontinued anticoagulation (n = 439), 30 (4.5%) were prescribed aspirin (100 mg daily), while 89 (20.3%) were recommended cycles of sulodexide.
- More bleeding events occurred in patients who prolonged anticoagulation (1.6% pt/y) than in those who discontinued anticoagulation (0.1% pt/y, p = 0.001); bleeding was also more common in patients treated with a standard-dose DOAC (3.1% pt/y) than in those on reduced dose DOACs (0.4% pt/y, p = 0.028).
- The incidence of recurrent venous thrombotic events was not different between patients who prolonged anticoagulation (2.2%pt/y) and those who discontinued anticoagulation (3.0% pt/y, RR 0.56; 0.24–1.2 95% CI; p 0.1).

**A**

Bleeding Events (MB + CRNMB) during follow-up

**B**

Recurrent Events during follow-up





# Conclusions

- Physicians' decisions about AC duration were independent of the unprovoked/provoked nature of the index event.
- The bleeding rate was higher in patients who continued AC using standard-dose DOACs.
- Surprisingly, the rate of thrombotic recurrence was not different between those who continued or discontinued AC.
- Randomized studies comparing different procedures to decide on the duration of AC after a first VTE are needed.