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Bologna 5-7 Ottobre 2017

**Dal primo studio ISCOAT ad oggi:
gli ultimi 20 anni di terapia anticoagulante
in Italia**

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START-Register

SURVEY ON ANTICOAGULATED PATIENTS – REGISTER

Registro computerizzato per la raccolta dei dati di pazienti trattati cronicamente con anticoagulanti



THE LANCET

1996

Articles

Bleeding complications of oral anticoagulant treatment: an inception-cohort, prospective collaborative study (ISCOAT)

Gualtiero Palareti, Nicoletta Leali, Sergio Coccheri, Mario Poggi, Cesare Manotti, Armando D'Angelo, ~~Vittorio Pengo~~, Nicoletta Erba, Marco Moia, Nicola Ciavarella, Gianluigi Devoto, Mauro Berrettini, Serena Musolesi, on behalf of the Italian Study on Complications of Oral Anticoagulant Therapy*

Intern Emerg Med
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IM - ORIGINAL

2017

Vitamin K antagonist therapy: changes in the treated populations and in management results in Italian anticoagulation clinics compared with those recorded 20 years ago

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print

The FCSA-START Registry

The ISCOAT 2016

- 27 FCSA Centers
- Participated in the FCSA-START-Registry
- 5707 naive patients were included
- From January 2012 and December 2015

	<i>N</i> (%)	Person-years of follow-up
All patients	5707	8906
Males	3029 (53)	4744
Age, mean (\pm SD) years	73.0 (19.0)	
Age <i>n</i> (%) < 70	2069 (36.2)	2930
\geq 70	3638 (63.8)	6321
>80	1605 (28.1)	2585
Indication for anticoagulation		
Atrial fibrillation	3516 (61.6)	5907
Venous thromboembolism	1593 (28.0)	2223
Heart-valve prosthesis	219 (3.8)	229
Other	379 (6.6)	150

ISCOAT 2016; Palareti et al., Intern Emerg Med 2017

Medical history

No comorbidity	1071 (18.8)
Hypertension	3945 (69.1)
Coronary artery disease	927 (16.2)
Diabetes	893 (15.6)
Previous stroke/TIA	674 (14.8)
Heart failure	654 (11.5)
Other	1478 (25.8)
Renal function (CrCl)	
>60 ml/min	3436 (60.2)
30–60	1940 (34.0)
<30	331 (5.8)

ISCOAT 2016; Intern Emerg Med 2017

Co-mediations

None	1360 (23.8)
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Number of associated drugs (*n*)

1–3	2262 (39.6)
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4–5	1334 (23.4)
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>5	751 (13.2)
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Patients who stopped anticoagulant treatment	1758 (30.8)
Died	351 (6.1)
Lost to follow-up	66 (1.2)
Quality of anticoagulation control	
Median (IQR) percent time spent in relation to the therapeutic range (2.0–3.0 INR)	
Below	21.0 (12.0–33.0)
Within (TTR)	66.0 (53.0–77.0)
Above	9.0 (3.0–16.0)

ISCOAT 2016; Intern Emerg Med 2017

Events <i>n</i> (rate % annually, CI)	Bleeding complications
Major events	123 (1.38; 1.1–1.6)
Fatal	10 (0.11; 0.06–1.2)
	Intracranial 38 (0.43; 7 fatal)
	Digestive 29 (0.33; 3 fatal)
	Hematuria 7 (0.08)
	Hemarthrosis 3 (0.03)
	Other 45 (0.50)

NMCRB *n* (% annually) 144 (1.62; 1.4–1.9)

Events <i>n</i> (rate % annually, CI)	Bleeding complications
Sex	
Males	71 (1.48; 1.1–1.8)
Females	52 (1.24; 0.9–1.6)
Age	
<70	30 (1.0; 0.7–1.4)
≥70	93 (1.55; 1.2–1.8)
RR	1.50 (1.0–2.4) <i>p</i> = 0.04
Indication	
VTE	23 (1.0; 0.7–1.5)
AF	86 (1.4; 1.1–1.8)
All Others	14 (1.8; 1.0–3.0)
Timing of events (days)	
≤90 <i>n</i> (% annually; CI)	28 (2.1; 1.5–3.2)
>90	95 (1.26; 1.0–1.5)
RR	1.68 (1.1–2.6) <i>p</i> = 0.02

ISCOAT 2016; Palareti et al., Intern Emerg Med 2017

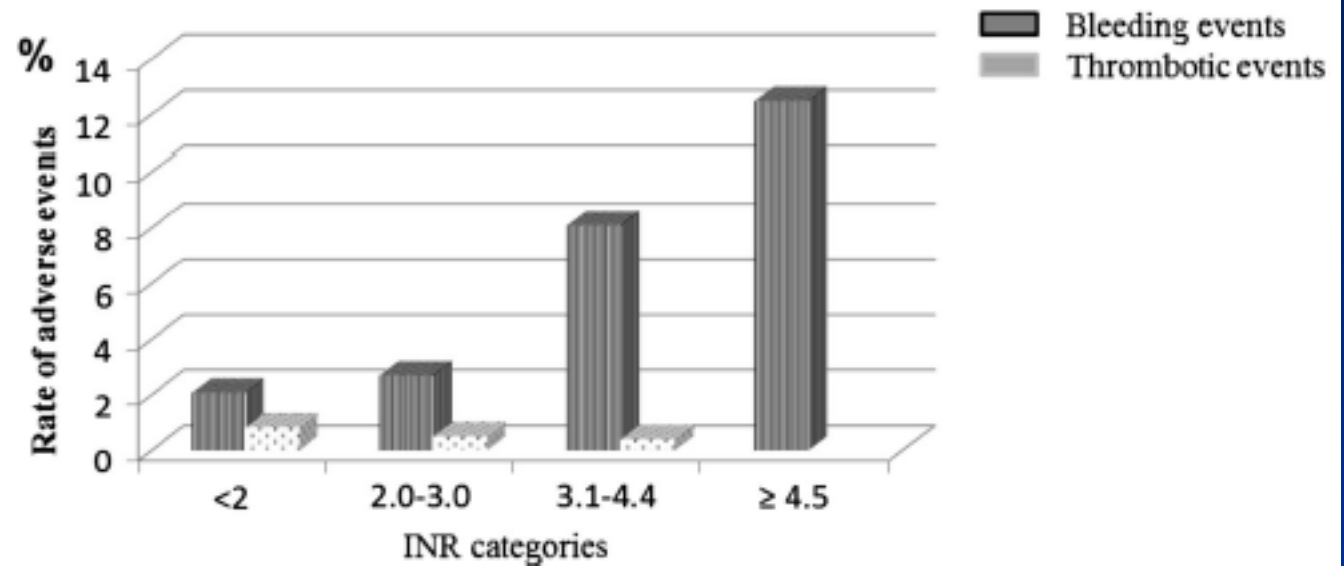
Events <i>n</i> (rate % annually, CI)	Thrombotic complications
Major events	47 (0.53; 0.4–0.7)
Fatal	4 (0.04; 0.02–0.1)
	Stroke 12 (0.13; 4 fatal)
	TIA 12
	AMI 9 (0.10)
	Recurrent VTE 7
	SVT 5
	Arterial embolism 2

Events <i>n</i> (rate % annually, CI)	Thrombotic complications
Sex	
Males	22 (0.46; 0.3–0.7)
Females	25 (0.60; 0.09–1.6)
Age	
<70	17 (0.58; 0.4–0.9)
≥70	30 (0.50; 0.3–0.7)
RR	
Indication	
VTE	15 (0.67; 0.4–1.0)
AF	27 (0.46; 0.3–0.7)
All Others	5 (0.64; 0.3–1.5)
Timing of events (days)	
≤90 <i>n</i> (% annually; CI)	10 (0.8)
>90	37 (0.48)

ISCOAT 2016;
Intern Emerg Med 2017

Bleeding/Thrombotic rates and time-related INR values

Fig. 1 Rates of bleeding and thrombotic events in relation to the total time spent in categories of increasing INR levels



ISCOAT 2016; Intern Emerg Med 2017

Relative risks

INR categories	
Bleeding events	
RR > 3.0 vs ≤3.0 INR (95% CI)	3.68 (2.66–5.01) <i>p</i> < 0.0001
RR ≥ 4.5 vs <4.5 INR (95% CI)	4.23 (1.53–9.75) <i>p</i> < 0.01

INR categories	
Thrombotic events	
RR < 2.0 vs ≥2.0 (95% CI)	1.61 (0.73–3.30) <i>p</i> < 0.01

ISCOAT 2016; Intern Emerg Med 2017

Comments on results 2016

- Very few patients lost (1.2%)
- High prevalence of elderly (>80 y) patients (28%)
- High prevalence of comorbidities and comedications
- Very low incidence of complications (pt/y)
 - MB: 1.38%; fatal 0.11%; NMCRB 1.62; ICH 0.43%
 - Thromb.: 0.53%; fatal 0.04%; stroke 0.13%
- Increased risk of bleeds if INR > 3
- “ “ thrombosis “ < 2

Comparison with ISCOAT 1996

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1996

Thromb Haemost 1997; 78: 1438-43

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Thrombotic Events during Oral Anticoagulant Treatment: Results of the Inception-cohort, Prospective, Collaborative ISCOAT Study

Gualtiero Palareti, Cesare Manotti, Armando D'Angelo, Vittorio Pengo, Nicoletta Erba, Marco Moia, Nicola Ciavarella, Gianluigi Devoto, Mauro Berrettini, Nicoletta Leali, Mario Poggi, Cristina Legnani, Serena Musolesi, Sergio Coccheri, on behalf of the ISCOAT Study Group (Italian Study on Complications of Oral Anticoagulant Therapy)*

1997





At that time ISCOAT was a new, important study

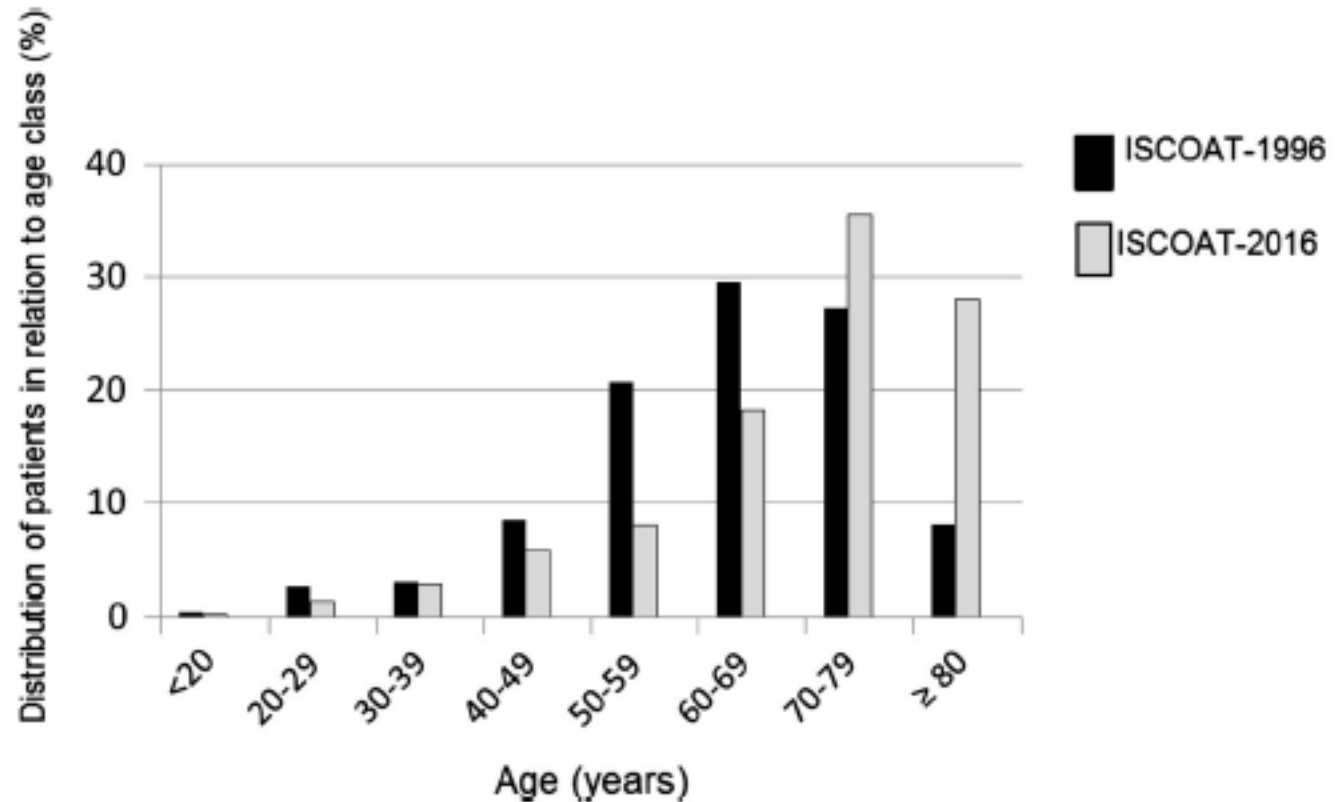
- Probably the first inception cohort (naive patients),
- Prospective, multicenter
- Both bleeding and thrombotic complications
- INR based,
- With INR-temporally related results
- TTR



	ISCOAT 2016, patients <i>n</i> 5707	ISCOAT 1996/7, patients <i>n</i> 2745	<i>p</i>
Age, mean (SD) years	73.0 (19.0)	63.6 (8.9)	0.01
Age			
<70	36.2	64.8	0.01
≥70	63.7	35.2	0.01
>80	28.1	8.0	0.01
Primary indication for anticoagulation %			
Venous Thromboembolism	28.0	32.5	0.01
Atrial fibrillation	61.6	16.8	0.01
Ischaemic heart disease	NA	14.7	
Arterial vascular disease	NA	10.2	
Heart-valve prosthesis/disease	6.2	17.5	0.01
Other	4.2	8.3	0.01



Fig. 2 Distribution of patients in the current study and in the ISCOAT 1996/7 in relation to age



ISCOAT 2016; Palareti et al., Int Emerg Med 2017



	ISCOAT 2016, patients <i>n</i> 5707	ISCOAT 1996/7, patients <i>n</i> 2745	<i>p</i>
Quality of anticoagulation control			
Median percent time spent in relation to the intended therapeutic range:			
Below	21.0	26.1	
Within (TTR)	66.0	68.0	
Above	9.0	5.9	
Major bleeding <i>n</i> . (% annually) [fatal]	123 (1.38)	28 (1.39)	
Fatal	10 (0.11)	5 (0.25)	
ICH	38 (0.43) [7]	9 (0.45) [5]	
Gastrointestinal	29 (0.33) [3]	7 (0.35) [1]	
Other	56 (0.63) [1]	12 (0.60) [1]	
Major + NMCRB events occurring during the first 90 days of treatment <i>n/N</i> (%)*	78/267 (29.2)	62/153 (40.5)	0.02
Thrombotic events <i>n</i> . (% annually)	47 (0.53)	70 (3.5)	0.01 RR = 6.5 (CI 4.5-9.7) <0.01
Fatal <i>n</i> (% annually)	4 (0.04)	20 (1.0)	0.01
In pts with VTE indication	17 (0.8)	27 (4.8)	0.01
Events occurring during the first 90 days of therapy <i>n/N</i> (%)	10/47 (21.3)	36/70 (51.4)	0.01
Died during follow-up <i>n</i> (%)	351 (6.1%)	102 (3.7%)	0.01



	ISCOAT 2016	ISCOAT 1996/7
Bleeding events		
Sex (females vs men)	0.57 (0.32–1.0; $p = 0.05$)	1.21 (0.86–1.70)
Age (≥ 70 vs < 70 years)	2.01 (1.08–3.73; $p = 0.03$)	1.69 (1.21–2.37; $p < 0.01$)
Indication (arterial disease vs others)	NA	1.72(1.17–2.54; $p < 0.01$)
Actual INR (≥ 4.5 vs < 4.5)	1.27 (0.18–8.63; $p = 0.2$)	5.96 (3.68–9.67; $p < 0.01$)
Timing of events (≤ 90 vs > 90 days)	11.85 (3.83–36.65; $p = 0.01$)	2.5 (1.4–3.3; $p < 0.01$)

Multivariate analysis for bleeding events



	ISCOAT 2016	ISCOAT 1996/7
Thrombotic events		
Sex (females vs men)	0.6 (0.3–1.1; $p = 0.11$)	0.71 (0.43–1.17; $p = 0.18$)
Age (≥ 70 vs < 70 years)	0.56 (0.29–1.1; $p = 0.60$)	1.62 (1.0–2.61) $p = 0.04$
Indication (arterial disease vs others)	NA	1.84 (1.01–3.36; $p = 0.04$)
Actual INR (< 2.0)	0.9 (0.42–1.73; $p = 0.86$)	1.88 (1.16–3.07; $p = 0.01$)
Timing of events (≤ 90 vs > 90 days)	2.1 (1.05–4.2; $p = 0.04$)	20.6 (12.7–33.5; $p < 0.01$)

Multivariate analysis for thrombotic events



Comparison 2016 vs 1996

- Much higher prevalence of elderly patients (28% vs 8%)
- Most treated for AF (62%) and VTE (28%)
- No longer treatment for CHD or arterial dis.
- The same TTR (66% vs 68%)
- The same very low MB rate (1.38% vs 1.39%)
- Much lower thrombosis rate (0.53% vs 3.5%; $p < 0.01$)
- The same initial high risk period (the first 90 d of therapy)

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Thank you