Effect of Active Cancer on Clinical Outcomes in Elderly AF Patients

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Background

◆ Advances in screening and treatment for cancer have significantly improved the survival rates, and the number of cancer survivors continues to grow in the elderly as well.

◆ Although there are increasing opportunities to treat elderly AF patients with cancer in clinical settings, there may be hesitancy to start anticoagulation treatment in patients with cancer, particularly when receiving chemotherapy for active cancer, because anticoagulation treatment may increase the potential risk of bleeding.

◆ Therefore, it is an important issue to examine the optimal anticoagulation treatment for elderly AF patients with cancer.
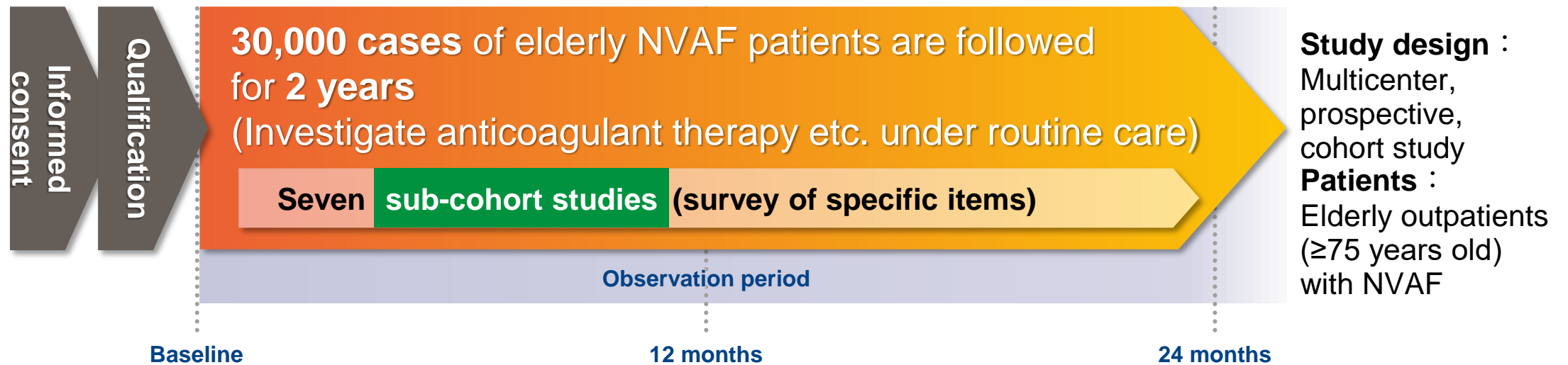
Objective

◆ This study examined the impact of active cancer complications on the incidence of thromboembolic and bleeding events in elderly AF patients, using the dataset of the ANAFIE (All Nippon AF In the Elderly) Registry, which was nation-widely performed in Japan.

Modified from "H. Inoue *et al., J. Cardiol.* 2018; 72: 300-6." and "T. Yamashita *et al., EHJ-QCCO.* 2021; doi:10.1093/ehjqcco/qcab025"

Methods

◆ A total of 32,275 patients, which is the data set of the ANAFIE registry, were divided into 2 groups according to whether they had active cancer. The cancer group was further divided into 2 groups: gastrointestinal (GI) cancer and non-gastrointestinal (non-GI) cancer groups.

◆ The incidences of stroke/systemic embolic events (SEE), major bleeding, intracranial hemorrhage (ICH), cardiovascular death, all-cause death, and net clinical outcomes* for two years were estimated by Kaplan-Meier analysis.

◆ The hazard ratio (HR) for each event was analyzed using the Cox proportional-hazards model between cancer and non-cancer groups, and between warfarin and direct oral anticoagulants [DOACs] groups.

*Net Clinical Outcome: Stroke/SEE, major bleeding and all-cause mortality
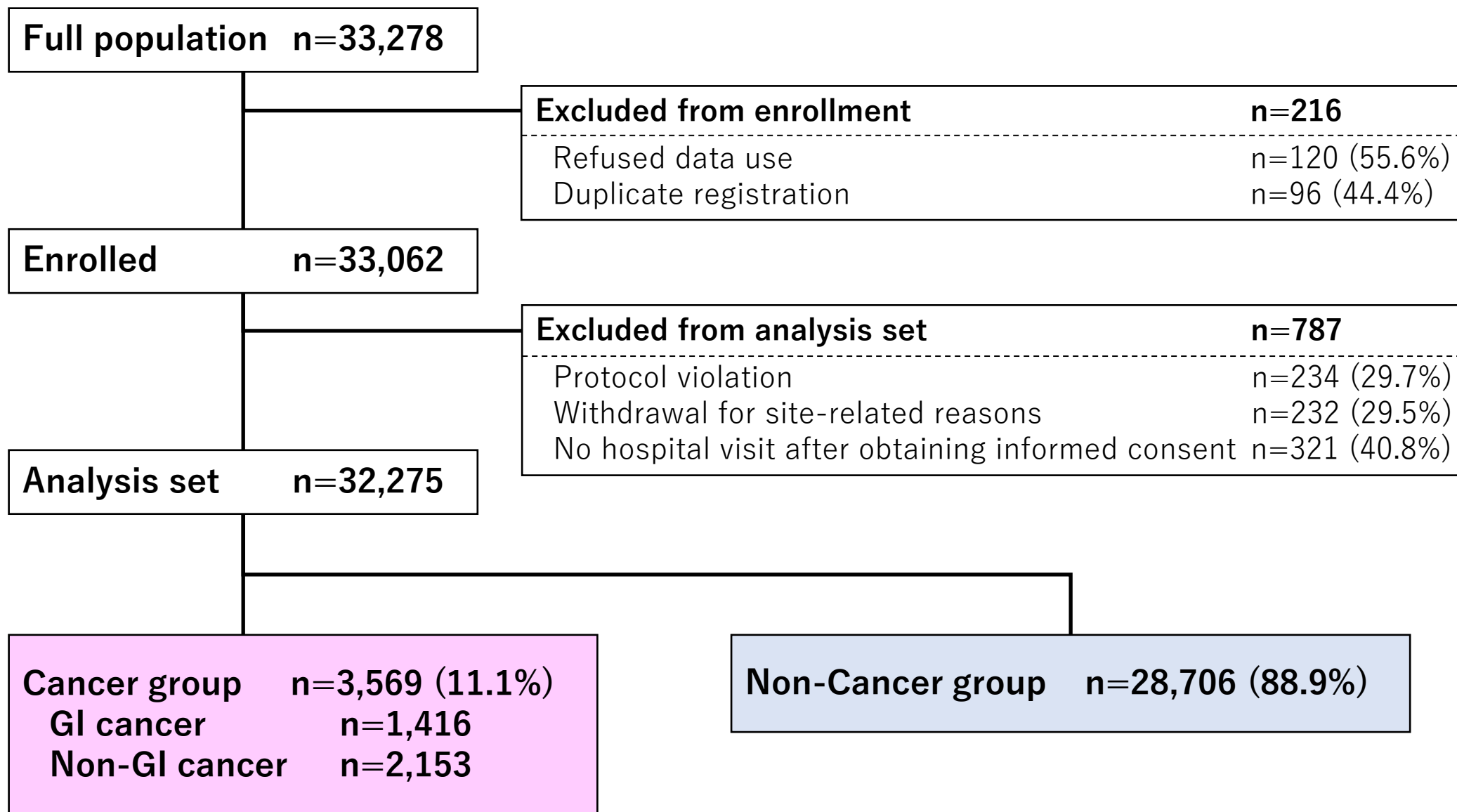
Types of Active Cancer

Cancer group	Total n=3,569
GI cancer	**1,416 (39.7)**
Gastric cancer	738 (20.7)
Colon cancer	736 (20.6)
Non-GI cancer	**2,153 (60.3)**
Lung cancer	364 (10.2)
Breast cancer	237 (6.6)
Gynecologic cancer	92 (2.6)
Pancreatic cancer	34 (1.0)
Other cancer	1,745 (48.9)

Data are n (%).

Patient Background by Absence or Presence of Cancer -1

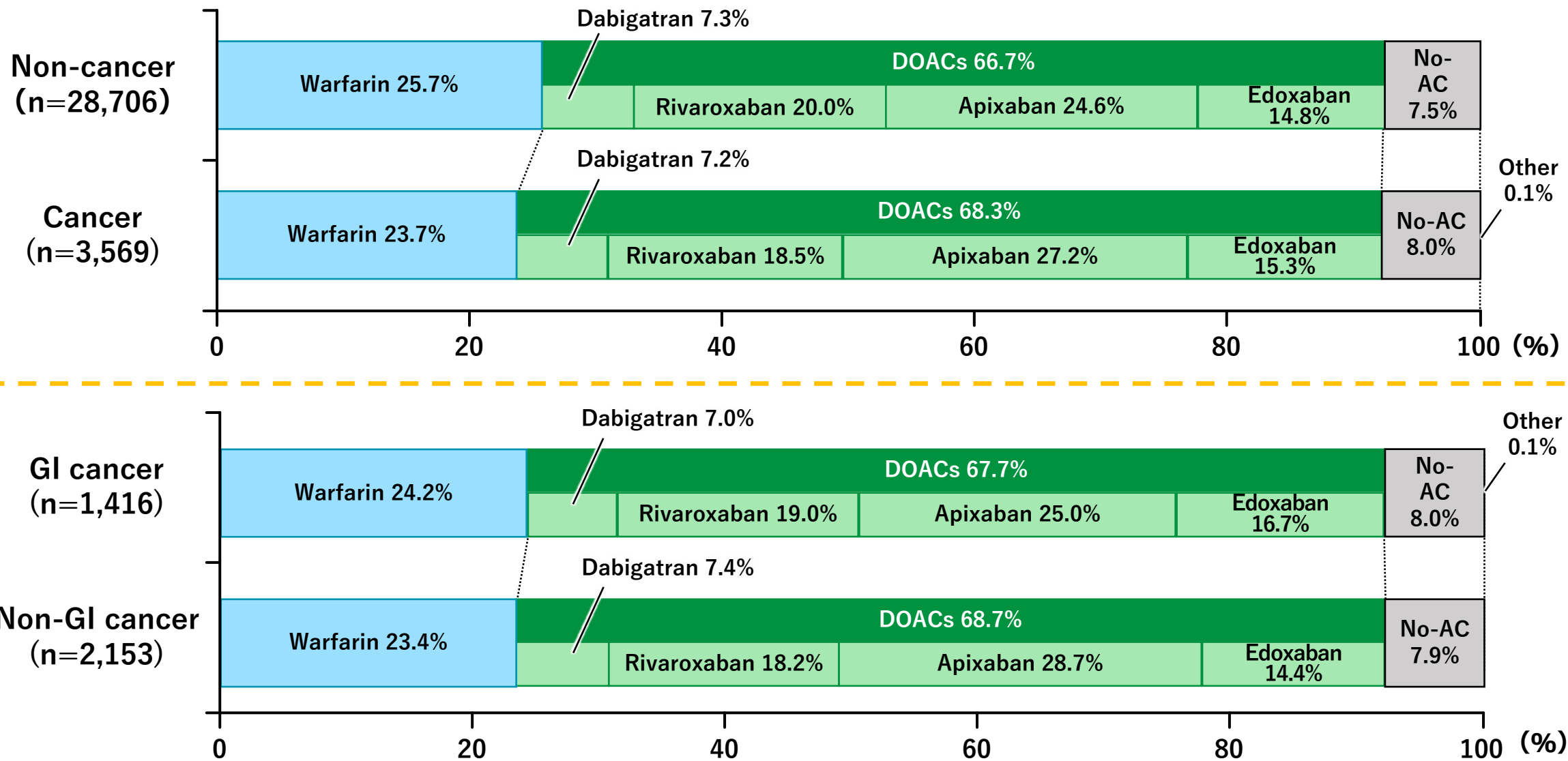|	Non-Cancer n=28,706	Cancer		
		All n=3,569	GI cancer n=1,416	Non-GI cancer n=2,153
Men	15,930 (55.5)	2,552 (71.5)*	1,054 (74.4)	1,498 (69.6)
Age, years	81.5±4.8	81.4±4.5	81.3±4.5	81.4±4.6
≥ 85	7,546 (26.3)	873 (24.5)	353 (24.9)	520 (24.2)
BMI, kg/m^2	23.4±3.6	23.1±3.6	22.7±3.6	23.4±3.5
SBP, mmHg	127.5±16.9	126.6±17.7	126.8±17.9	126.4±17.6
DBP, mmHg	70.7±11.6	70.2±11.8	70.3±12.3	70.1±11.5
Creatinine clearance, mL/min	48.4±18.4	48.0±17.1	47.6±16.4	48.3±17.5
CHADS$_2$ score	2.8±1.2	3.0±1.2*	3.0±1.2	2.9±1.2
CHA$_2$DS$_2$-VASc score	4.5±1.4	4.5±1.5	4.5±1.5	4.5±1.5
HAS-BLED score	1.8±0.8	2.1±0.9*	2.3±1.0	1.9±0.9
History of major bleeding	1,194 (4.2)	245 (6.9)*	101 (7.1)	144 (6.7)
AF type				
Paroxysmal	12,052 (42.0)	1,534 (43.0)	565 (39.9)	969 (45.0)
Persistent	4,781 (16.7)	555 (15.6)	228 (16.1)	327 (15.2)
Long-standing persistent/permanent	11,873 (41.4)	1,480 (41.5)	623 (44.0)	857 (39.8)

Data are n (%) or mean ± SD

Patient Background by Absence or Presence of Cancer -2

	Non-Cancer N=28,706	Cancer		
		All n=3,569	GI cancer n=1,416	Non-GI cancer n=2,153
History of non-pharmacological therapy for AF	4,982 (17.4)	695 (19.5)	239 (16.9)	456 (21.2)
Catheter ablation	2,598 (9.1)	372 (10.4)	115 (8.1)	257 (11.9)
Comorbidities	27,831 (97.0)	3,569 (100.0)	1,416 (100.0)	2,153 (100.0)
Hypertension	21,656 (75.4)	2,656 (74.4)	1,059 (74.8)	1,597 (74.2)
Diabetes mellitus	7,597 (26.5)	1,136 (31.8)*	493 (34.8)	643 (29.9)
Chronic kidney disease	5,905 (20.6)	800 (22.4)*	319 (22.5)	481 (22.3)
Myocardial infarction	1,576 (5.5)	275 (7.7)*	98 (6.9)	177 (8.2)
Heart failure	10,709 (37.3)	1,407 (39.4)*	586 (41.4)	821 (38.1)
History of Cerebrovascular disease	6,402 (22.3)	901 (25.2)*	374 (26.4)	527 (24.5)
Gastrointestinal diseases	7,945 (27.7)	1,522 (42.6)	820 (57.9)	702 (32.6)
Active cancer	0 (0.0)	3,569 (100.0)	1,416 (100.0)	2,153 (100.0)
Dementia	2,264 (7.9)	248 (6.9)	107 (7.6)	141 (6.5)
Fall within 1 year	2,070 (7.2)	277 (7.8)	126 (8.9)	151 (7.0)

ICD, implantable cardioverter defibrillator. Data are n (%) or mean ± SD.

Distribution of Anticoagulants

Non-cancer (n=28,706)
- Warfarin 25.7%
- DOACs 66.7%
  - Dabigatran 7.3%
  - Rivaroxaban 20.0%
  - Apixaban 24.6%
  - Edoxaban 14.8%
- No-AC 7.5%

Cancer (n=3,569)
- Warfarin 23.7%
- DOACs 68.3%
  - Dabigatran 7.2%
  - Rivaroxaban 18.5%
  - Apixaban 27.2%
  - Edoxaban 15.3%
- No-AC 8.0%
- Other 0.1%

GI cancer (n=1,416)
- Warfarin 24.2%
- DOACs 67.7%
  - Dabigatran 7.0%
  - Rivaroxaban 19.0%
  - Apixaban 25.0%
  - Edoxaban 16.7%
- No-AC 8.0%
- Other 0.1%

Non-GI cancer (n=2,153)
- Warfarin 23.4%
- DOACs 68.7%
  - Dabigatran 7.4%
  - Rivaroxaban 18.2%
  - Apixaban 28.7%
  - Edoxaban 14.4%
- No-AC 7.9%

No-AC: no use of anticoagulants

Adjusted HRs for Clinical Outcomes between Two Groups

Non-Cancer group vs Cancer group

Clinical events	HR (95%CI)	*P*-value
Stroke/SEE	1.00 (0.82, 1.22)	0.999
Stroke	1.00 (0.81, 1.22)	0.963
Ischemic stroke	0.95 (0.75, 1.20)	0.656
Hemorrhagic stroke	1.17 (0.78, 1.77)	0.439
SEE	0.96 (0.28, 3.28)	0.954
All bleeding*	1.32 (1.18, 1.48)	<0.001
Major bleeding*	1.34 (1.08, 1.68)	0.009
ICH	1.19 (0.90, 1.57)	0.222
GI bleeding	1.17 (0.99, 1.39)	0.065
All-cause death*	1.54 (1.38, 1.73)	<0.001
Cardiovascular death	0.86 (0.67, 1.12)	0.266
Net clinical outcomes*	1.41 (1.28, 1.55)	<0.001

Kaplan-Meier Event Curves for Each Clinical Outcome
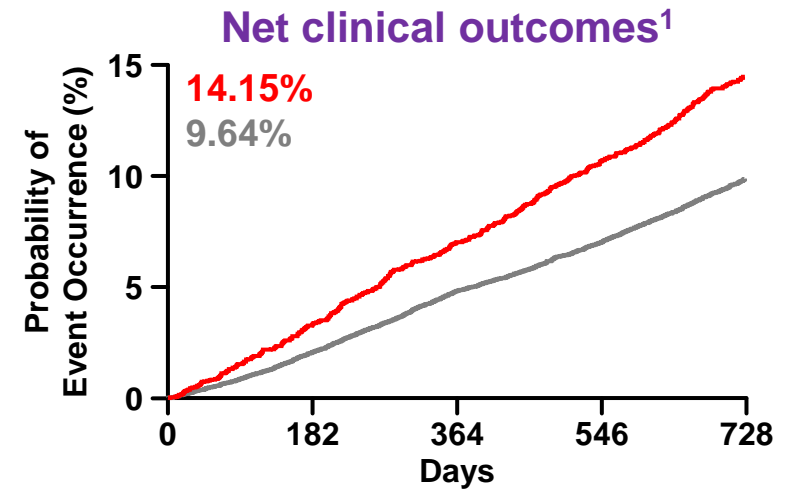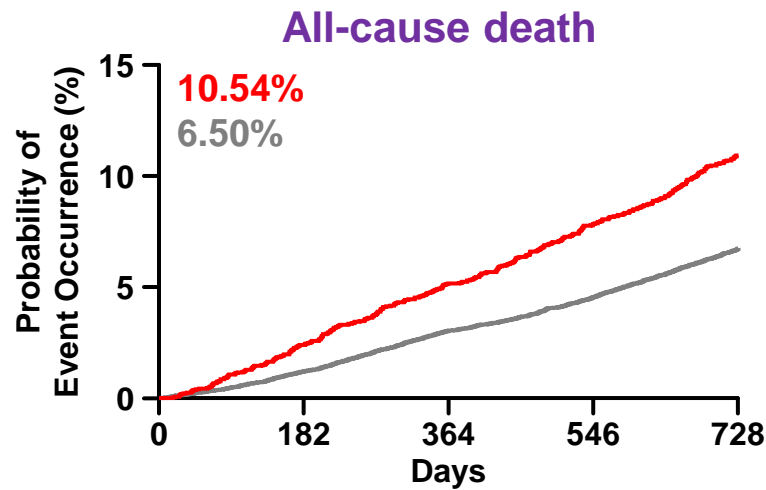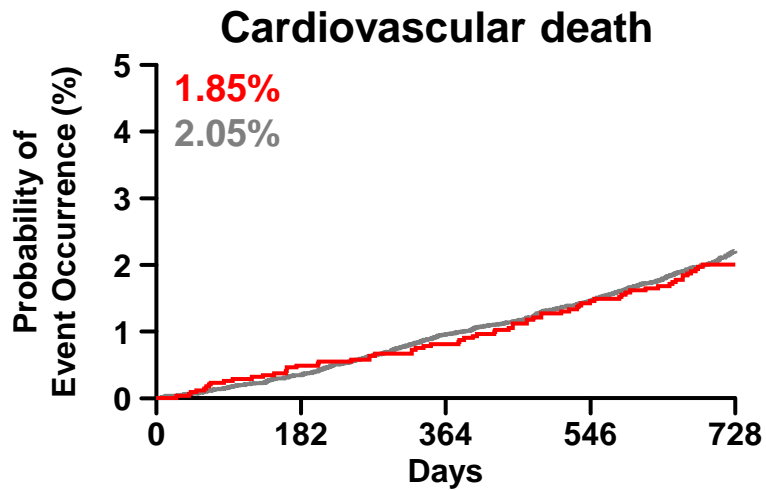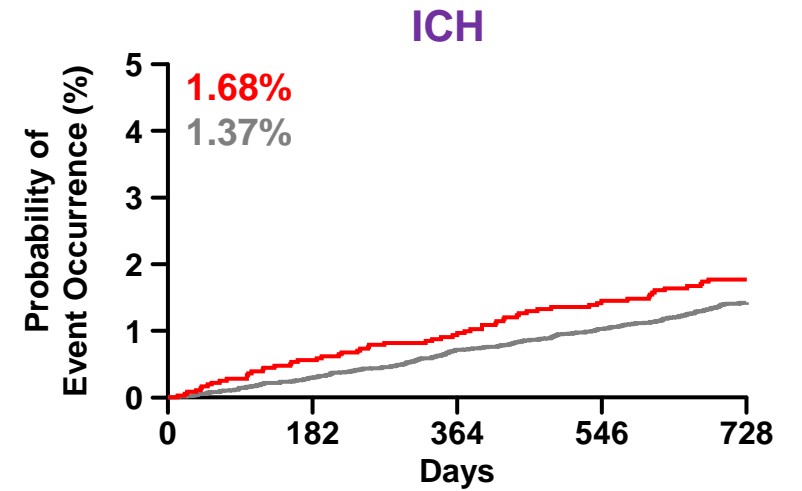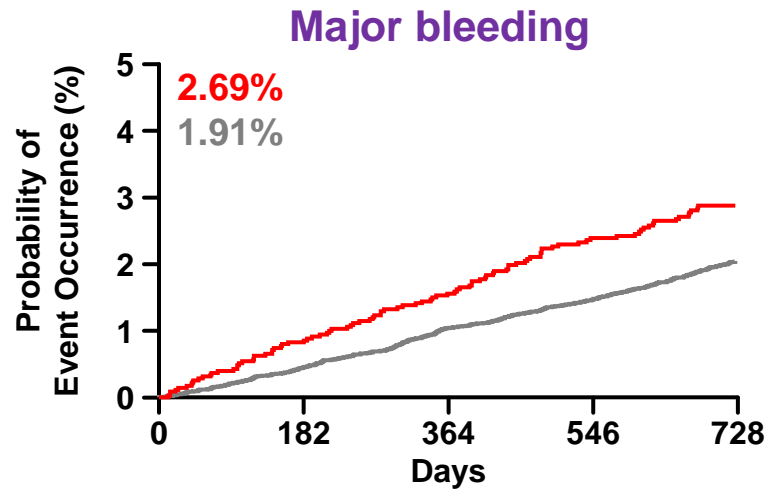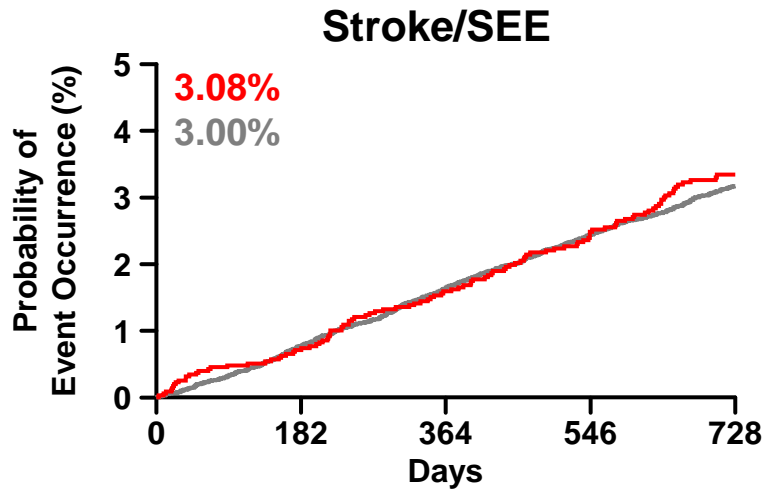
¹Net Clinical Outcome: Stroke/SEE, major bleeding and all-cause mortality

Adjusted HRs by Types of Cancer between Two Groups

Non-Cancer group vs GI Cancer group   Non-Cancer group vs Non-GI Cancer group

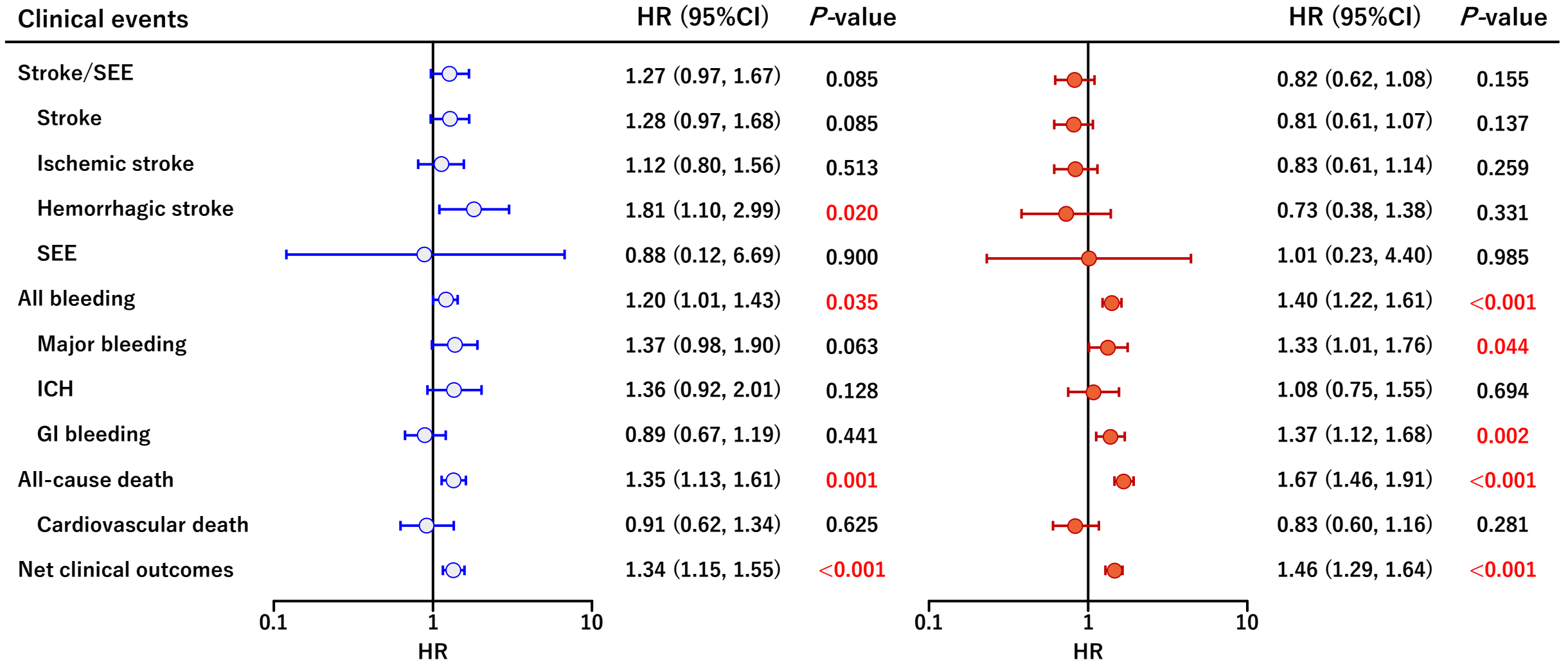| Clinical events	HR (95%CI)	P-value	HR (95%CI)	P-value
Stroke/SEE	1.27 (0.97, 1.67)	0.085	0.82 (0.62, 1.08)	0.155
Stroke	1.28 (0.97, 1.68)	0.085	0.81 (0.61, 1.07)	0.137
Ischemic stroke	1.12 (0.80, 1.56)	0.513	0.83 (0.61, 1.14)	0.259
Hemorrhagic stroke	1.81 (1.10, 2.99)	0.020	0.73 (0.38, 1.38)	0.331
SEE	0.88 (0.12, 6.69)	0.900	1.01 (0.23, 4.40)	0.985
All bleeding	1.20 (1.01, 1.43)	0.035	1.40 (1.22, 1.61)	<0.001
Major bleeding	1.37 (0.98, 1.90)	0.063	1.33 (1.01, 1.76)	0.044
ICH	1.36 (0.92, 2.01)	0.128	1.08 (0.75, 1.55)	0.694
GI bleeding	0.89 (0.67, 1.19)	0.441	1.37 (1.12, 1.68)	0.002
All-cause death	1.35 (1.13, 1.61)	0.001	1.67 (1.46, 1.91)	<0.001
Cardiovascular death	0.91 (0.62, 1.34)	0.625	0.83 (0.60, 1.16)	0.281
Net clinical outcomes	1.34 (1.15, 1.55)	<0.001	1.46 (1.29, 1.64)	<0.001

HR   HR

Comparison of Adjusted HRs by Anticoagulants in Each Group

Clinical events	Non-Cancer group DOACs vs Warfarin	HR (95%CI)	P-value	Cancer group DOACs vs Warfarin	HR (95%CI)	P-value
Stroke/SEE		0.78 (0.67, 0.91)	0.002		1.07 (0.67, 1.70)	0.777
Stroke		0.79 (0.68, 0.92)	0.003		1.09 (0.68, 1.75)	0.720
Ischemic stroke		0.79 (0.67, 0.94)	0.009		0.95 (0.55, 1.63)	0.855
Hemorrhagic stroke		0.79 (0.56, 1.10)	0.157		1.52 (0.55, 4.22)	0.423
SEE		0.48 (0.21, 1.11)	0.087		0.41 (0.00, −)	−
All bleeding		0.88 (0.80, 0.97)	0.011		1.19 (0.93, 1.54)	0.170
Major bleeding		0.69 (0.57, 0.83)	<0.001		1.08 (0.64, 1.80)	0.779
ICH		0.64 (0.51, 0.79)	<0.001		1.07 (0.57, 2.04)	0.827
GI bleeding		0.96 (0.83, 1.11)	0.597		1.29 (0.86, 1.93)	0.223
All-cause death		0.81 (0.73, 0.90)	<0.001		1.04 (0.81, 1.33)	0.746
Cardiovascular death		0.79 (0.66, 0.95)	0.010		0.83 (0.47, 1.44)	0.505
Net clinical outcome		0.81 (0.74, 0.88)	<0.001		1.06 (0.85, 1.31)	0.622

Summary

This study focusing on elderly AF patients revealed that

◆ The risk of safety events including major bleeding was higher in patients with cancer than without cancer, regardless of types of cancer.

◆ The benefit (efficacy and safety) of DOACs compared to warfarin as anticoagulation treatment was seen only in patients without cancer, but not in patients with cancer.