Outcomes in patients with atrial fibrillation after TAVI analysed by age: ENVISAGE-TAVI AF results

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Potential conflicts of interest

Speaker's name: Christian Hengstenberg

☑ Clinical proctor for Boston Scientific and Edwards Lifesciences, and reports payment for speaker bureaus, support for attending meetings, and advisory board participation from Daiichi Sankyo as well as institutional funding from Abbott Vascular, Amgen, Biosensors, Biotronik, Boehringer Ingelheim, Boston Scientific, Daiichi Sankyo, Edwards Lifesciences, Ferrer, Medtronic, Novartis, Philips, Siemens, and Terumo

Why this study?

- In patients with AF after TAVI, increasing age may be associated with increased clinical event rates, including any stroke and all-cause mortality[1–3]
- OAC therapy post-TAVI in patients with AF aged ≥75 years can be complicated by concerns about bleeding complications and comorbidities[4]
- The ENVISAGE-TAVI AF trial (NCT02943785) demonstrated noninferiority for NACE with edoxaban vs VKAs in patients with prevalent or incident AF after successful TAVI, but major bleeding events occurred more often[5]
- Clinical events associated with increasing age in these patients are currently unknown

AF, atrial fibrillation; NACE, net adverse clinical events; OAC, oral anticoagulant; TAVI, transcatheter aortic valve implantation; VKA, vitamin K antagonist.

1. Yamamoto M, et al. *Am J Cardiol.* 2023;207:150-58. 2. Attinger-Toller A, et al. *JACC: Cardiovasc Interv.* 2021;14:952-60. 3. Vlastra W, et al. *Circ Cardiovasc Interv.* 2019;12:e007546. 4. Karamichalakis N, et al. *Vasc Health Risk Manag.* 2015;11:555-62. 5. Van Mieghem NM, et al. *N Engl J Med*. 2021;385:2150-60.

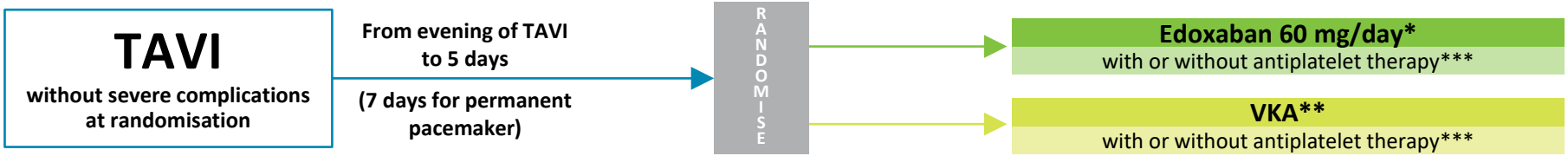
What did we study?

Objective

- To evaluate the differential clinical outcomes associated with increasing age in patients with AF receiving edoxaban or VKAs after successful TAVI

ENVISAGE-TAVI AF trial design

Prospective, randomised trial comparing the efficacy and safety of edoxaban vs VKA in patients with prevalent or incident AF and indication for chronic oral anticoagulation therapy after successful TAVI (NCT02943785)[1,2]



*Edoxaban dose reduction to 30 mg in patients with AF, if:
- CrCl 15–50 ml/min
- Body weight ≤60 kg†
- Concomitant P-glycoprotein inhibitors per local label†

†No dose reduction criteria in the US for AF

**VKA patient target international normalised ratio 2–3
In Japan, patients ≥70 years 1.6–2.6

***Stratification variable: Specified use of antiplatelet therapy for coronary stenting
Antiplatelet therapy was allowed per the treating physician's discretion, including:
- DAPT up to 3 months, or
- Single antiplatelet therapy indefinitely

AF, atrial fibrillation; CrCl, creatinine clearance; DAPT, dual antiplatelet therapy; TAVI, transcatheter aortic valve implantation; VKA, vitamin K antagonist.

1. Van Mieghem NM, et al. *Am Heart J*. 2018;205:63-9. 2. Van Mieghem NM, et al. *N Engl J Med*. 2021;385:2150-60.

How was the study executed?

Methods

- This pre-specified subanalysis of the ENVISAGE-TAVI AF intention-to-treat population (N = 1426) assessed baseline patient characteristics and clinical outcomes across 3 age subgroups (<75 years, ≥75 and <85 years, and ≥85 years), using age as a continuous variable with HRs and 95% CIs calculated per 2-year increase in age

Outcomes

- NACE, stroke (ischaemic, haemorrhagic, undetermined), ischaemic stroke, myocardial infarction, major bleeding, major GI bleeding, MACE, MACCE, all-cause death, and CV death

CI, confidence interval; CV, cardiovascular; GI, gastrointestinal; HR, hazard ratio; MACCE, major adverse cardiovascular and cerebrovascular events; MACE, major adverse cardiovascular events; NACE, net adverse clinical events.

What are the essential results?

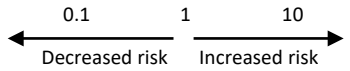
Parameter	<75 years n = 118	≥75 and <85 years n = 840	≥85 years n = 468	*P*-value*
Age, yrs, mean ± SD	70.4 ± 3.7	80.7 ± 2.6	87.6 ± 2.4	**<0.0001**
Sex, male	71 (60.2)	460 (54.8)	217 (46.4)	**0.003**
Race, White	101 (85.6)	714 (85.0)	372 (79.5)	**0.03**
BMI, kg/m^2, mean ± SD	32.4 ± 7.3	27.9 ± 5.2	26.1 ± 4.7	**<0.0001**
CrCl†, mL/min, mean ± SD	85.4 ± 33.7	60.9 ± 22.1	46.5 ± 16.6	**<0.0001**
≤50	15 (12.7)	273 (32.5)	282 (60.3)	**<0.0001**
HAS-BLED score, mean ± SD	1.4 ± 0.7	1.6 ± 0.8	1.5 ± 0.7	**0.003**
CHA_2DS_2-VASc score, mean ± SD	3.7 ± 1.4	4.6 ± 1.3	4.5 ± 1.2	**<0.0001**
Diabetes	73 (61.9)	323 (38.5)	131 (28.0)	**<0.0001**
COPD	33 (28.0)	123 (14.6)	50 (10.7)	**<0.0001**
Hypercholesterolaemia	91 (77.1)	597 (71.1)	311 (66.5)	**0.047**
Myocardial infarction	27 (22.9)	116 (13.8)	55 (11.8)	**0.01**
Coronary artery disease	69 (58.5)	455 (54.2)	243 (51.9)	0.4
Hypertension	106 (89.8)	776 (92.4)	422 (90.2)	0.3

Data presented as n (%) unless otherwise noted. *Statistically significant *P*-values are bolded and indicate a significant effect of age on the parameter. †Cockcroft–Gault formula. BMI, body mass index; CHA_2DS_2-VASc, Congestive heart failure, Hypertension, Age ≥75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65–74, Sex category (female); COPD, chronic obstructive pulmonary disease; CrCl, creatinine clearance; HAS-BLED, Hypertension, Abnormal liver/renal function, Stroke, Bleeding history or predisposition; SD, standard deviation; TIA, transient ischaemic attack.

What are the essential results?

- Within each age subgroup, there was not an increased risk of NACE, ischaemic stroke, any stroke, or myocardial infarction per 2-year increase in age
- Only patients aged ≥85 years had increased risk of all-cause death, CV death, MACE, and MACCE per 2-year increase in age

Endpoint	Hazard ratio (95% CI)	*P*-value
NACE		
<75 years	1.00 (0.81, 1.23)	1.0
≥75 and <85 years	1.10 (0.99, 1.23)	0.08
≥85 years	1.11 (0.97, 1.28)	0.1
Ischaemic stroke		
<75 years	1.08 (0.50, 2.33)	0.8
≥75 and <85 years	0.97 (0.76, 1.24)	0.8
≥85 years	0.69 (0.38, 1.25)	0.2
Any stroke		
<75 years	0.97 (0.63, 1.50)	0.9
≥75 and <85 years	1.00 (0.81, 1.23)	1.0
≥85 years	0.84 (0.56, 1.25)	0.4
MACE		
<75 years	0.97 (0.72, 1.31)	0.8
≥75 and <85 years	1.03 (0.84, 1.26)	0.8
≥85 years	1.34 (1.11, 1.62)	**0.003**
MACCE		
<75 years	0.97 (0.75, 1.27)	0.8
≥75 and <85 years	0.99 (0.86, 1.16)	1.0
≥85 years	1.21 (1.01, 1.45)	**0.04**
Myocardial infarction		
<75 years	0.93 (0.52, 1.67)	0.8
≥75 and <85 years	0.95 (0.58, 1.55)	0.8
≥85 years	1.37 (0.71, 2.63)	0.4
All-cause death		
<75 years	0.91 (0.69, 1.20)	0.5
≥75 and <85 years	1.16 (0.99, 1.36)	0.06
≥85 years	1.19 (1.01, 1.39)	**0.04**
CV death		
<75 years	0.98 (0.70, 1.39)	0.9
≥75 and <85 years	1.11 (0.89, 1.39)	0.4
≥85 years	1.35 (1.11, 1.65)	**0.003**

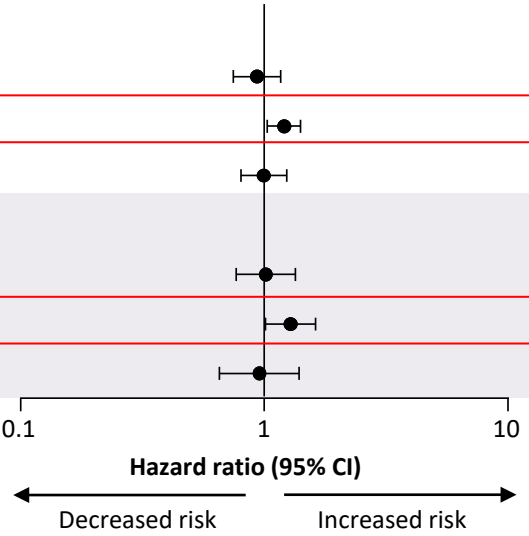


Statistically significant *P*-values are bolded.
CI, confidence interval; CV, cardiovascular; MACCE, major adverse cardiovascular and cerebrovascular events; MACE, major adverse cardiovascular events; NACE, net adverse clinical events.

What are the essential results?

- There was an increased risk of major bleeding and major GI bleeding with every 2-year increase in age among patients aged ≥75 and <85 years, but not among those aged <75 years or ≥85 years

Endpoint	Hazard ratio (95% CI)	*P*-value
Major bleeding*		
<75 years	0.93 (0.75, 1.17)	0.5
≥75 and <85 years	1.20 (1.03, 1.41)	**0.02**
≥85 years	1.00 (0.80, 1.24)	1.0
Major GI bleeding		
<75 years	1.02 (0.77, 1.34)	0.9
≥75 and <85 years	1.28 (1.01, 1.63)	**0.04**
≥85 years	0.95 (0.65, 1.39)	0.8



*ISTH definition. Statistically significant *P*-values are bolded.
CI, confidence interval; GI, gastrointestinal; ISTH, International Society on Thrombosis and Haemostasis.

Why is this important?

- In patients with AF treated with edoxaban or VKAs after successful TAVI, increasing age was associated with select clinical events, which varied across age subgroups
- Physicians should consider patient age when deciding on a treatment for patients with AF undergoing TAVI to reduce the risk of clinical events and optimise outcomes

AF, atrial fibrillation; TAVI, transcatheter aortic valve implantation; VKA, vitamin K antagonist.

The essentials to remember

- In this ENVISAGE-TAVI AF analysis, there was not an increased risk of NACE or ischaemic stroke per 2-year increase in age, in any age subgroup
- An increased risk of major bleeding and major GI bleeding were associated with increasing age among patients aged ≥75 and <85 years only, whereas the risk of all-cause and CV mortality, MACE, and MACCE increased with age among the ≥85-year subgroup only
- Among patients with prevalent or incident AF receiving edoxaban or VKAs after successful TAVI, increasing age had a limited event- and age group–specific association with increased risk of clinical events

AF, atrial fibrillation; CV, cardiovascular; GI, gastrointestinal; MACCE, major adverse cardiovascular and cerebrovascular events; MACE, major adverse cardiovascular events; NACE, net adverse clinical events; TAVI, transcatheter aortic valve implantation; VKA, vitamin K antagonist.

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