“Anticoagulación en intervencionismo estructural: pacientes sometidos a implante de TAVI y papel del cierre percutáneo de orejuela.”

Roberto Martín-Reyes, MD, PhD.

quirónsalud
La salud persona a persona

Indicaciones de TAVI: Flujo de pacientes

>75 años

75% Sintomática

40% No Qx

Tto. Médico

40%

TAVI

60% Sí Qx

5%

80%

TAVI

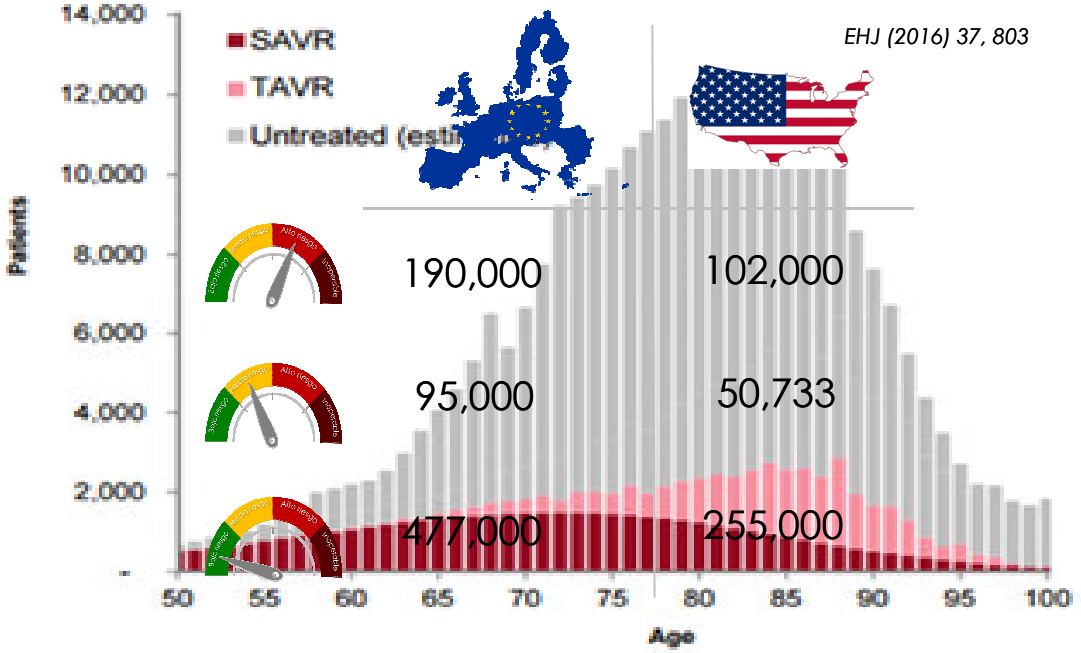
15%

80%

RVAO

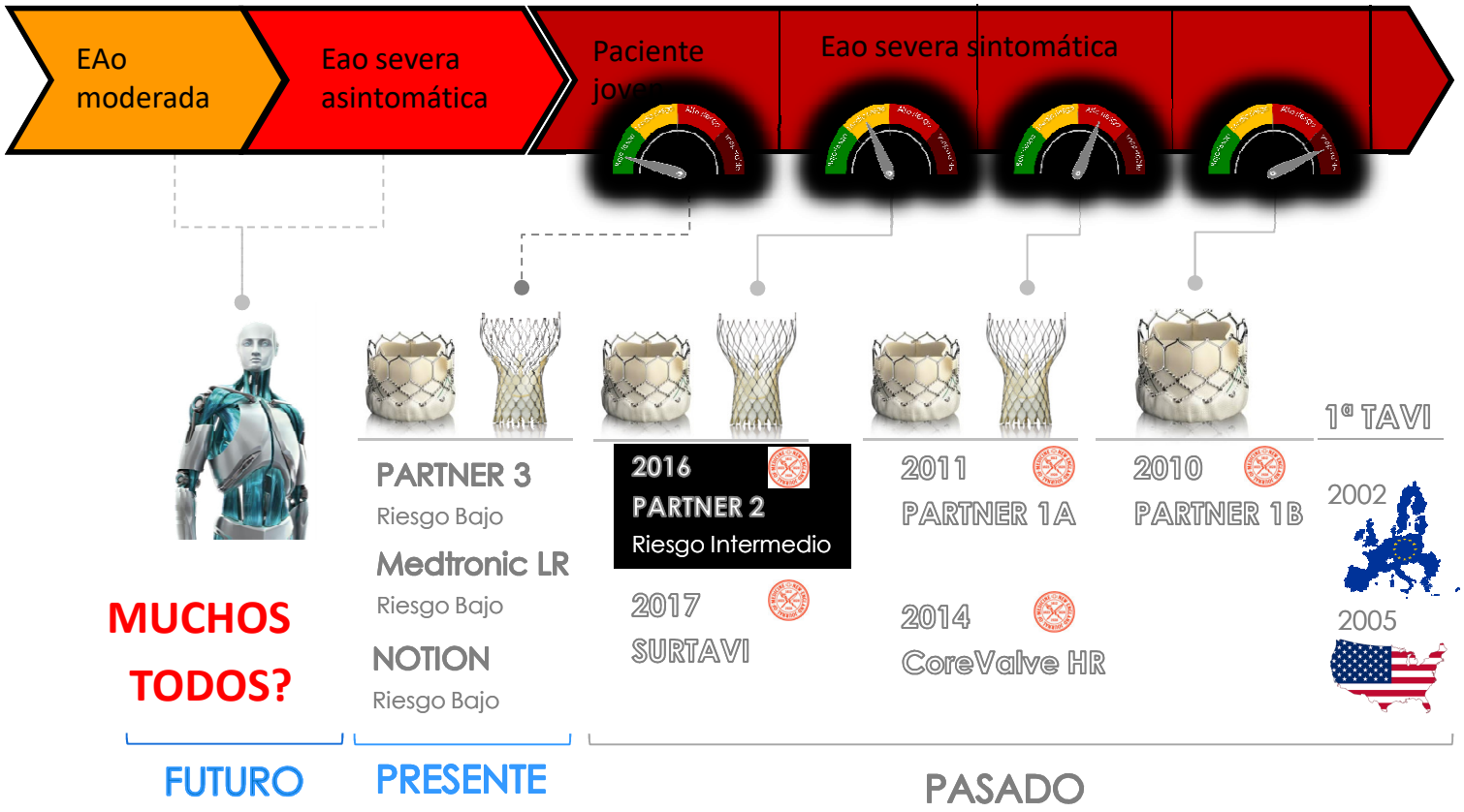
Pasado y Futuro

Estimación pacientes con EAo severa sintomática



EHJ (2016) 37, 803

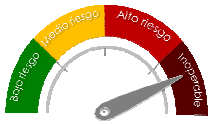
Expansión de las indicaciones



Evolución de las indicaciones

AMERICAN COLLEGE of CARDIOLOGY

AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

EAo severa + riesgo PROHIBITIVO		I B	I A
EAo severa + ALTO riesgo		IIa B	I A

¿Cómo ha evolucionado el STS de los pacientes incluidos en estudios TAVI?

ATT after TAVI/SAVR: 2017 ESC/EACT guidelines

SAVR

Oral anticoagulation is recommended lifelong for patients with surgical or transcatheter implanted bioprostheses who have other indications for anticoagulation.[c]	I	C
Low-dose aspirin (75 - 100 mg/day) should be considered for the first 3 months after surgical implantation of an aortic bioprosthesis or valve-sparing aortic surgery.	IIa	C
Oral anticoagulation may be considered for the first 3 months after surgical implantation of an aortic bioprosthesis.	IIb	C

TAVR

Oral anticoagulation is recommended lifelong for patients with surgical or transcatheter implanted bioprostheses who have other indications for anticoagulation.[c]	I	C
Dual antiplatelet therapy should be considered for the first 3–6 months after TAVI, followed by lifelong single antiplatelet therapy in patients who do not need oral anticoagulation for other reasons.	IIa	C
Single antiplatelet therapy may be considered after TAVI in the case of high bleeding risk.	IIb	C

NOACs should be considered as an alternative to VKAs after the third month of implantation in patients who have atrial fibrillation associated with a surgical or transcatheter aortic valve bioprosthesis.	IIa	C

Baumgartner H, et al. *Eur Heart J* 2017;38:2739-2791.

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Baumgartner H, et al. *Eur Heart J* 2017;38:2739-2791.

Current recommendations for ATT after TAVI

(All expert opinion- level of evidence C)

2/3 **Sinus rythm: Aspirin + Clopidogrel for 3-6 mo.**

- As other aortic biological valves, no anti-coagulation is recommended.
- Based on coronary stents experience, DAPT was initially prescribed.
- SAPT (AAS) in high bleeding risk patients.

1/3 **Atrial fibrillation: oral anticoagulation.**

- Low-dose aspirin in association with anticoagulation.
- No other anti-platelet therapy.
- Triple therapy discouraged.
- New oral anticoagulants: consider after 3 months. NO EVIDENCE.

Holmes DR. *JACC* 2012;59:1200-54. Nishimura RA. *JACC* 2014;63:e57-185. Webb J. *Can J Cardiol* 2012;28;52-8. Baumgartner H. *EHJ* 2017;38:2739-91.

Rationale for DAPT after TAVI

- Thromboemboli from the bioprosthesis before endothelialization completes.
- Neointimal tissue growth & endothelialization of the valve stent occur in ≈ 3 months.
- Aggregation of platelet and fibrin has been known to occur on valve leaflet within a few hours after implantation.
- Expression of tissue factor in aortic valve stenosis.
- Initial procedures with extra-corporeal bypass induced severe thrombocitopenia when not on clopidogrel.

Breyne J, et al. Atherosclerosis 2010;213:369-76
Grube E, et al. Circulation 2006;114:1616-24.
Noble S, et al. EuroIntervention 2009;5:78–85.
Whitlock RP, et al. *Chest* 2012;141(2 Suppl):e576S-600S.
Marechaux S, et al. Cardiovasc Pathol 2009;18:67-76.
Mérie C, et al. JAMA 2012;308:2118–25.
Tay J, et al. JACC Cardiovasc Interv 2011;4:1290-7.

1. TAVI thrombosis: how important is it?

4,266 TAVI patients in 12 centers

THV dysfunction secondary to thrombosis diagnosed based on:

- Response to anticoagulation therapy, imaging modality or histopathology findings,
- or mobile mass detected on THV suspicious of thrombus, irrespective of dysfunction and in absence of infection.

Thrombosis: 26/4.266 (0.61%).

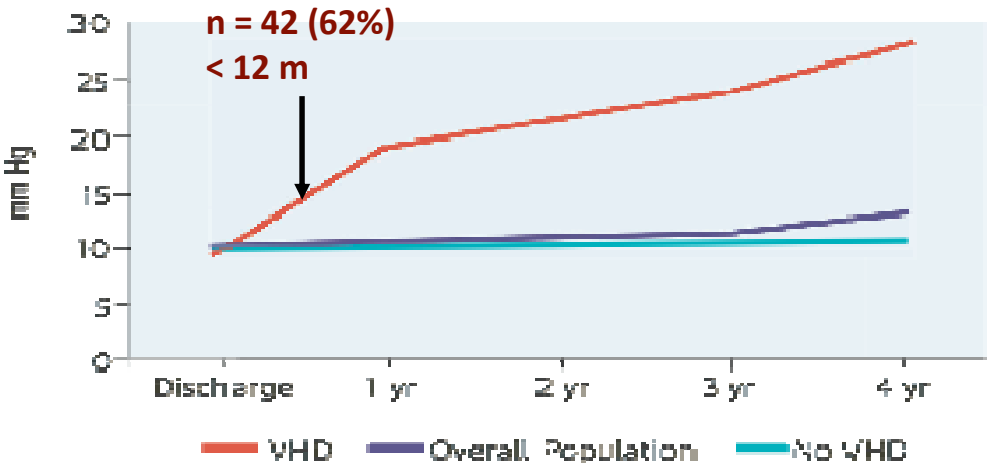
- Mean time after TAVI: 181 days.
- Most frequent symptom: effort dyspnea (n=17; 65%).
    - … although 8 (31%) asymptomatic.
- Echo: increased mean gradient (40.5±14.0 mm Hg), thickening and/or thrombus (n= 20, 77%).
- In 23 (88%), anti-coagulation significantly reduced gradients in 2 mo.

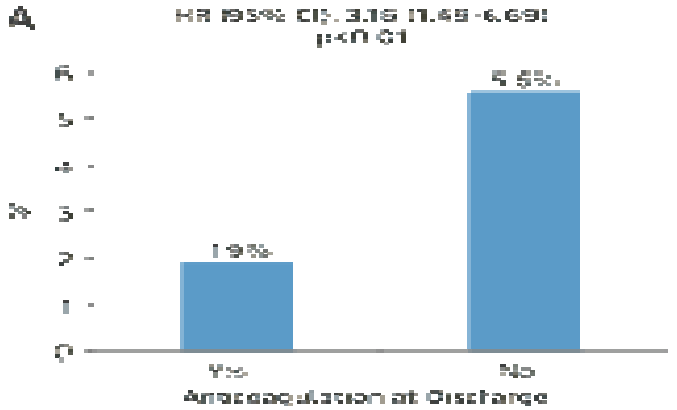
We could be underestimating the problem

Incidence, Timing, and Predictors of Valve Hemodynamic Deterioration After Transcatheter Aortic Valve Replacement

- Multicenter registry (n = 1,521).
- Echo: 6 m, 12 m and anually.
- Mean FU 20±13 m (min 6 m).

VHD: increase in mean gradient ≥ 10 mmHg vs discharge: n = 68 (4,5%).





JACC 2016;67:644-655.

2. Prevalence of atrial fibrillation in patients undergoing TAVI

TAVR: most important randomized trials.

Study	Design	n	% AF
PARTNER 1B	RCT vs OMT	179 / 358	33%
PARTNER 1A	RCT vs SAVR	348 / 699	41%
PARTNER 2	RCT vs SAVR	1,011 / 2,033	31%
Corevalve US	RCT vs SAVR	394 / 795	41%
SURTAVI	RCT vs SAVR	879 / 1746	28%
CHOICE	RCT HTH	241	29%
REPRISE III	RCT HTH	912	34%
SOLVE-TAVI	RCT HTH	438	45%

RCT: randomized clinical trial; OMT: optimal medical treatment; SAVR: surgical aortic valve replacement; HTH: head-to-head (trials comparing 2 different types of valves).

Periprocedural stroke in TAVI

- 30-day rates 1.5-7.0% (average 3-4%).
- Similar to SAVR.
- 3/4 show new silent cerebral lesions detected by MRI (could be related with potential neurological impairment??).
- Peri-operative stroke increases mortality x 4.

Am J Card 2016;118:1031-1045. Eur Heart J 2013;34:1894-1905. JACC 2012;60:1614-1616. N Engl J Med 2016;374:1609-1620.

New onset atrial fibrillation after TAVI

Thoracic Surgeons/ACC TVT (Transcatheter Valve Therapy) Registry

13,556 patients w/o previous AF and w/o OAC undergoing TAVR from 2011 to 2015

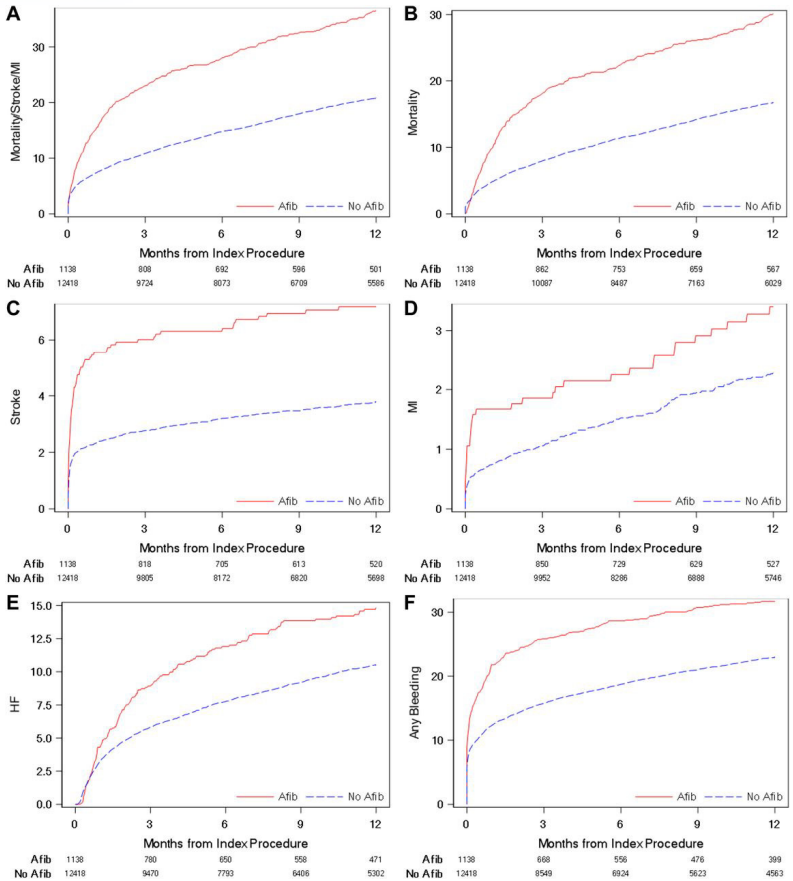
- NOAF: n = 1,138 (8.4%): 4.4% TF-TAVI vs 16.5% non-TF-TAVR.
- Median CHA2DS2-VASc: 5.
- … but only 28.9% of patients with new AF were discharged on OAC.

TABLE 3 One-Year Outcomes for Patients With Atrial Fibrillation Treated Without Versus With Oral Anticoagulation

	Unadjusted Cumulative Incidence (%)				
	AF Without OAC (n = 319)	AF With OAC (n = 819)	p Value	Adjusted HR (95% CI)	p Value
Composite endpoint (mortality/stroke/MI)	39.7	28.4	<0.01	1.72 (1.35-2.22)	<0.01
Mortality	33.8	20.7	<0.01	2.08 (1.56-2.78)	<0.01
Rehospitalization for stroke	7.5	6.3	<0.01	1.12 (0.67-1.89)	0.66
Rehospitalization for MI	3.5	3.1	0.82	1.14 (0.49-2.63)	0.77
Rehospitalization for heart failure	13.0	19.6	<0.01	0.60 (0.41-0.88)	0.01
Rehospitalization for major bleeding	30.1	35.7	<0.01	0.77 (0.61-0.98)	0.03

Vora AN, et al. J Am Coll Cardiol Intv 2018;11:1746–56.

Fibrilación Auricular en pacientes TAVI



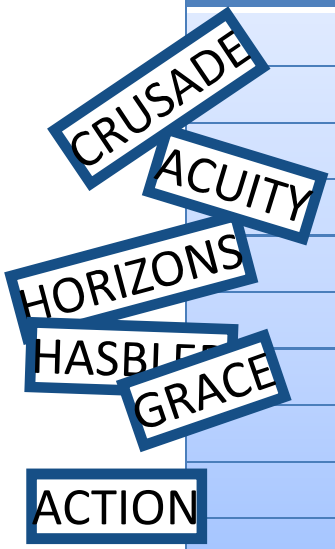
One-Year Outcomes Following Transcatheter Aortic Valve Replacement

13,556 patients (8.4%) who developed new onset AF.

CHA_2DS_2-VASc score of 5 (25th and 75th percentile: 5 to 6), only 28.9% of patients with new AF were discharged on oral anticoagulation

JACC Cardiovasc Interv. 2018 Sep 10;11(17):1746-1756.

Candidates for TAVI are at very high risk of bleeding

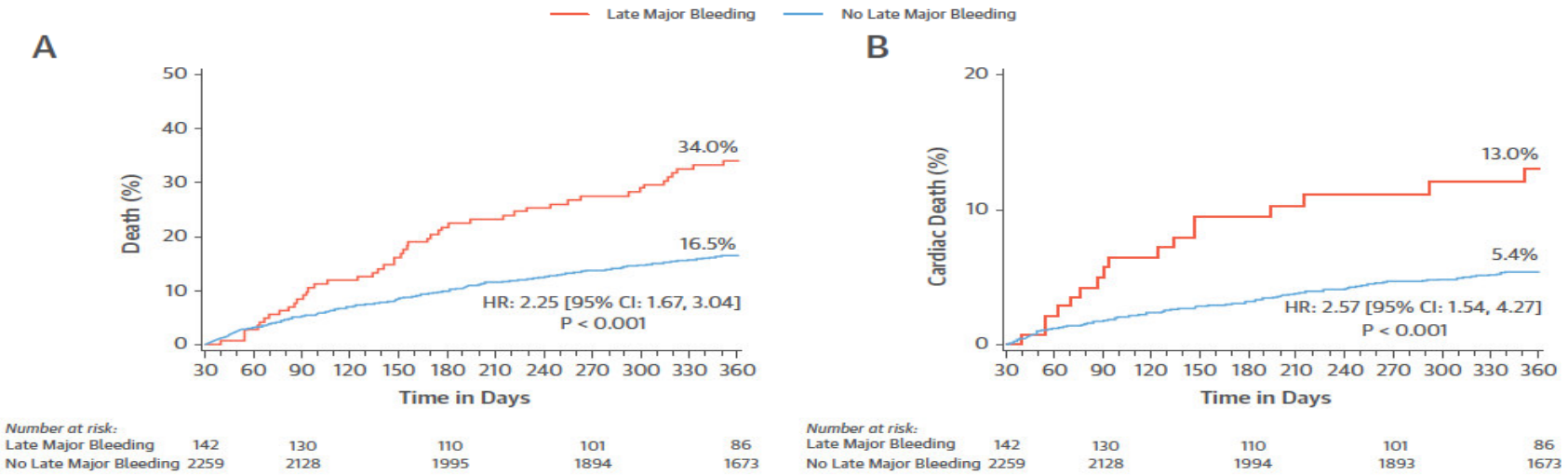


Risk factors for bleeding	TAVI patients
Age	mean age > 80
Female	≈ 50%
Heart Failure	≈ 80%
Renal failure	Creatinine > 2 mg/dl in ≈ 10%
Diabetes	35-40%
Prior stroke/TIA	≈15%
Vascular disease	30-40%
Anemia	≈ 30% Hb < 11 g/dl; ≈ 50% anemia
Hypertension	75-80%
Atrial fibrillation	≈ 40%

J Am Coll Cardiol 2015;66:2813–23. Circ Cardiovasc Interv. 2013;6:625-34.

Late bleeding is a predictor of death after TAVI

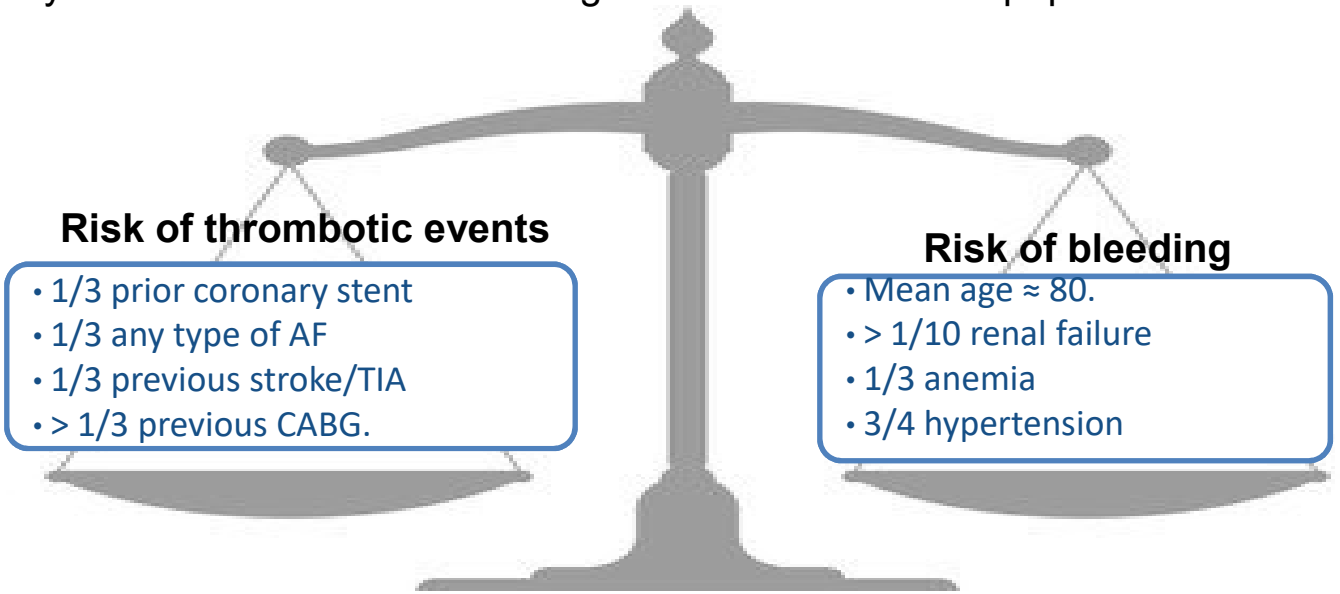
- Randomized cohorts and continued access registries in the PARTNER trial alive at 30 days (n=2,401).
- Late major bleeding (> 30 days): 142 patients (5.9%).
- They were an independent predictor of mortality between 30 days and 1 year.



Genereux P, et al. *J Am Coll Cardiol* 2014;64:2605–15

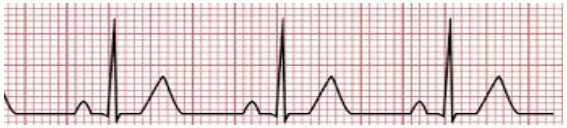
TAVR: a trade-off between bleeding & thrombotic complications

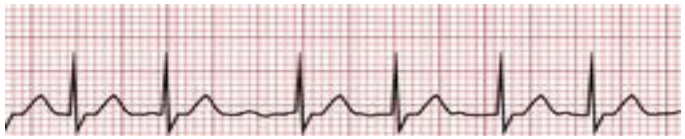
- Elderly and co-morbidities increase the risk of both type of events.
- Secondary effects of anti-thrombotic drugs are increased in this population.

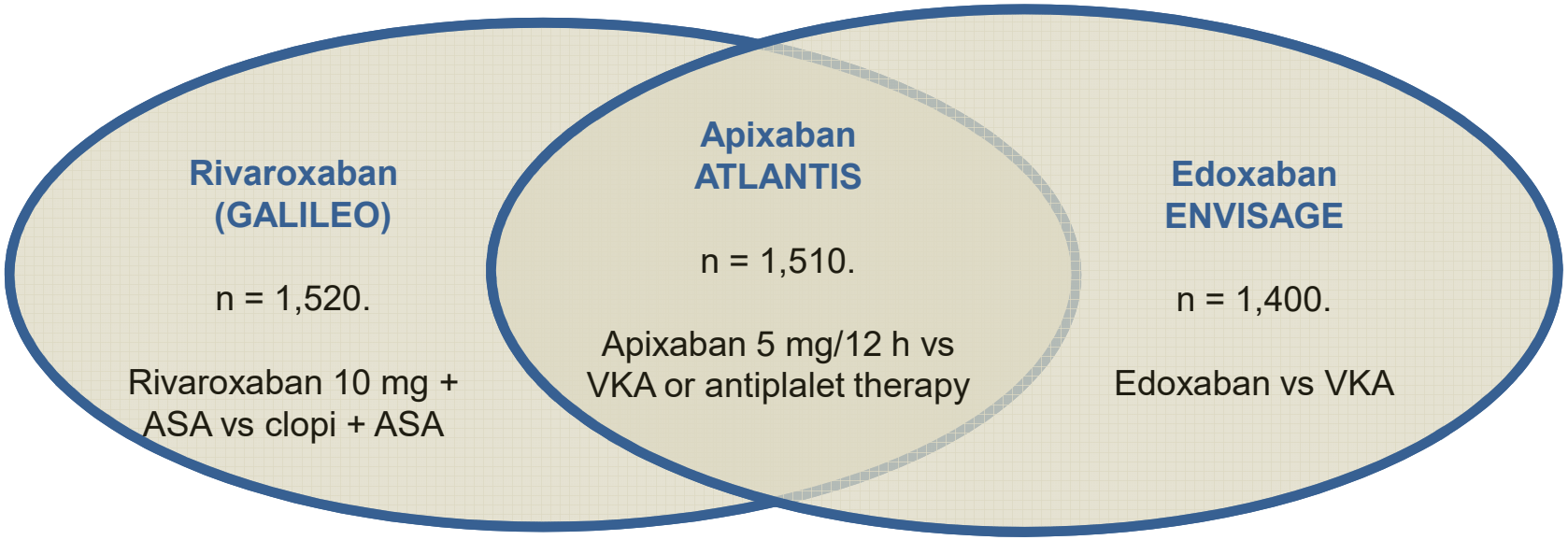


Genereaux P, et al. JACC 2012;59:2317-1607. Pagnesi M, et al. Inj J Cardiol 2016;221:97-106. Rodes-Cabau J, et al. JACC 2013;62:2349-2359.

NOACs & TAVI: Randomized Controlled Trials

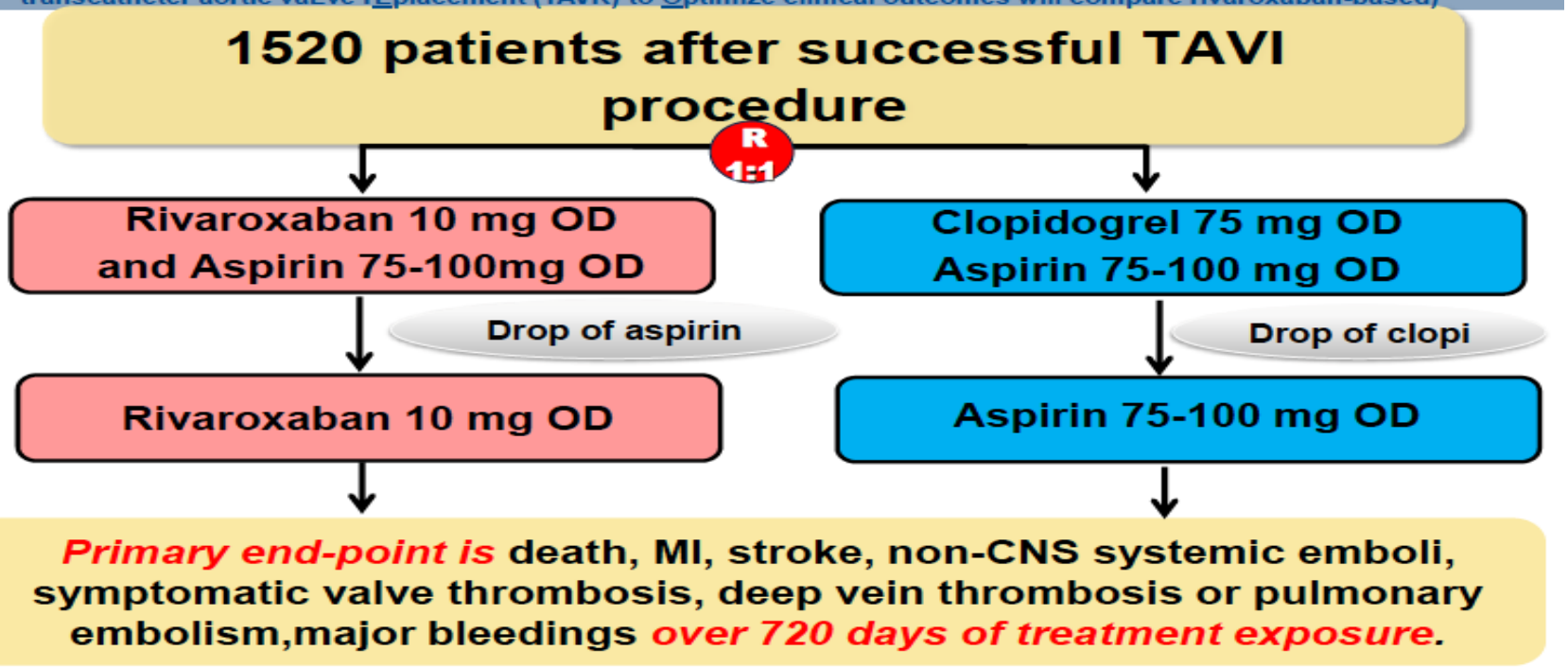
SR 

AF 



GALILEO

(Global multicenter, open-label, randomized, event-driven, active-controlled study comparing a rivAroxaban-based antithrombotic strategy to an antipLatelet-based strategy after transcatheter aortic vaLve rEplacement (TAVR) to Optimize clinical outcomes will compare rivaroxaban-based)



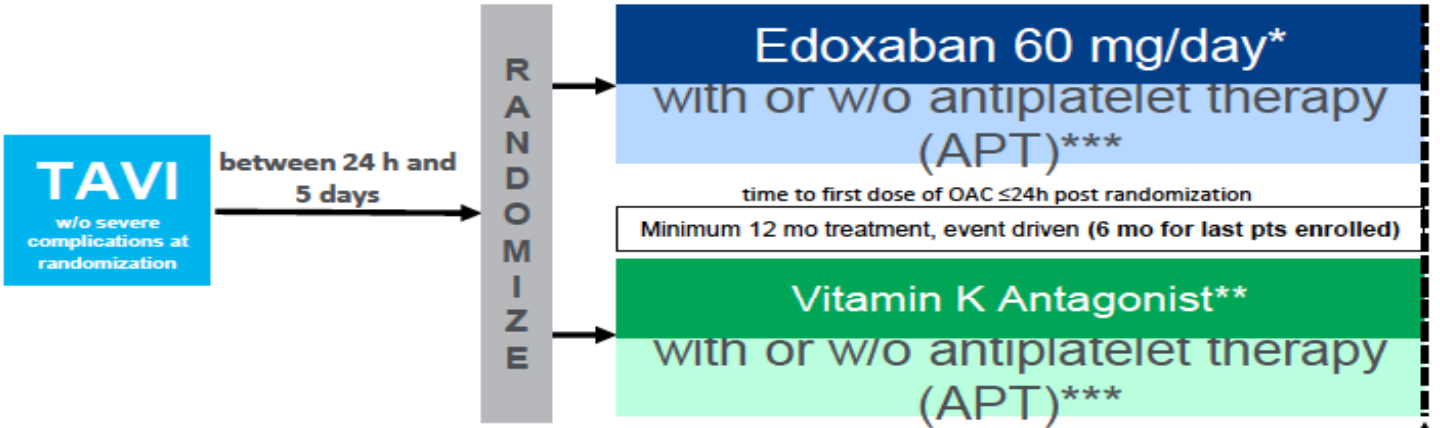
GALILEO

	Rivaroxaban 10 mg	DAPT
Death	6.8	3.3
Severe bleeding	4.2	2.4
Death or embolic events	8.6	3.3

The phase 3 GALILEO trial was terminated early after a preliminary analysis showed that rivaroxaban was associated with an increase in all-cause death, thromboembolic events, and bleeding when given following successful transcatheter aortic valve replacement.

ENVISAGE-TAVI AF

PROBE design: prospective, randomized, open label, blinded evaluation Edoxaban based regimen vs VKA based regimen in N ≈1,400 AF patients (≈ 2500 patient-years)



* Edoxaban dose reduction to 30 mg if
- CrCL≤50 ml/min
- BW≤60 kg
- certain P-gp inhibitors

** **VKA as approved in countries,** target INR 2-3

*** Clopidogrel 75mg OD or ASA 75 – 100 mg OD, pre-declare AP type and duration before R
- Stratification by stenting and dose reduction
- Without stenting: no APT at all or either ASA for 3 months only or Clopidogrel for 3 months only (other $P2Y_{12}$ are permissible)
- With stenting for atherosclerotic disease: SAPT with ASA or Clopidogrel up to 12 months, DAPT allowed for 1 month post stenting in select cases

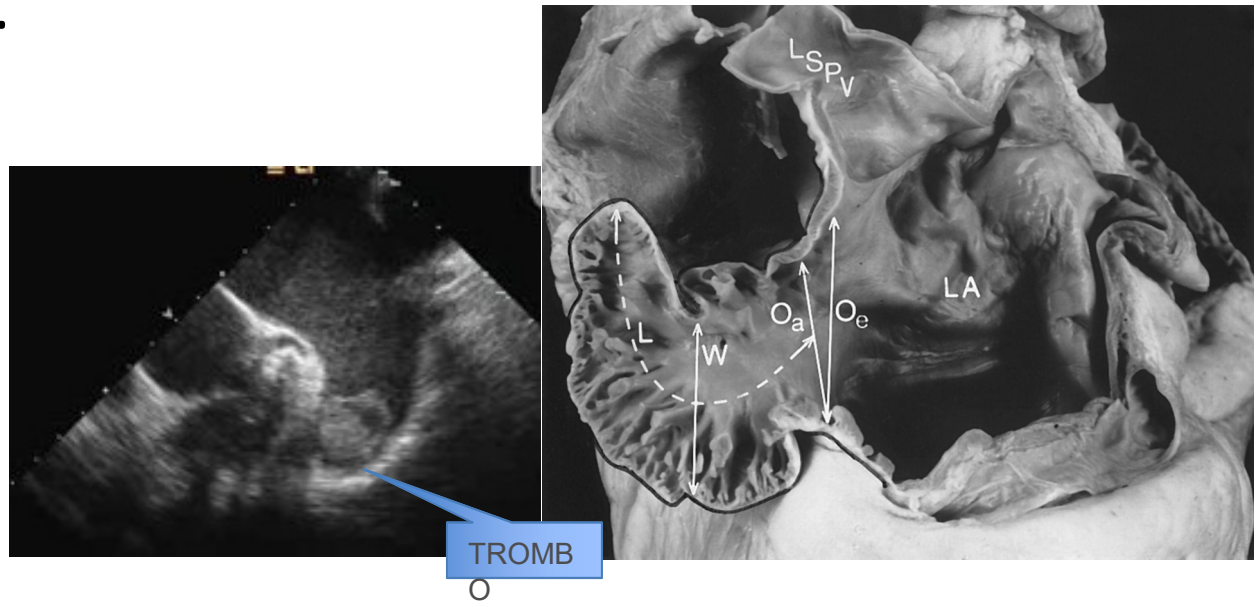
Primary end-point: composite of all-cause death, myocardial infarction (MI), ischemic stroke, systemic thromboembolism (SEE), valve thrombosis, and major bleeding

Y si no podemos anticoagular, qué opciones tenemos?

Orejuela Izquierda: Fuente de embolias

La <u>orejuela izquierda</u> es la fuente principal de embolia (> 90%) en la FA no valvular.

Diagnóstico por medio de ETE:



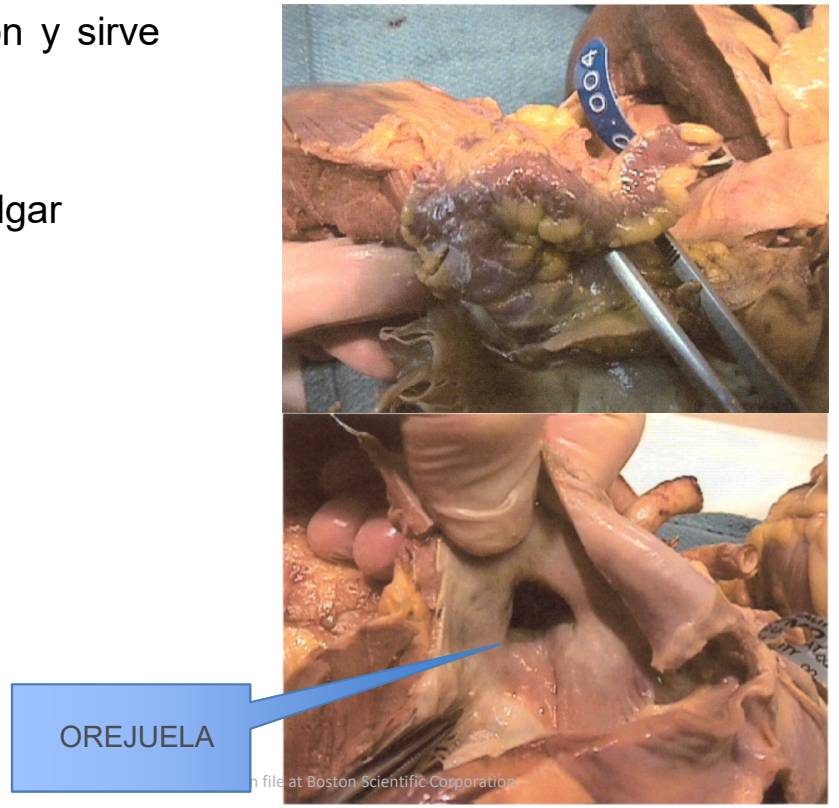
Watson T, Shantsila E, Lip GY. Mechanisms of thrombogenesis in atrial fibrillation: Virchow's triad revisited. Lancet 2009;373:155–66.30

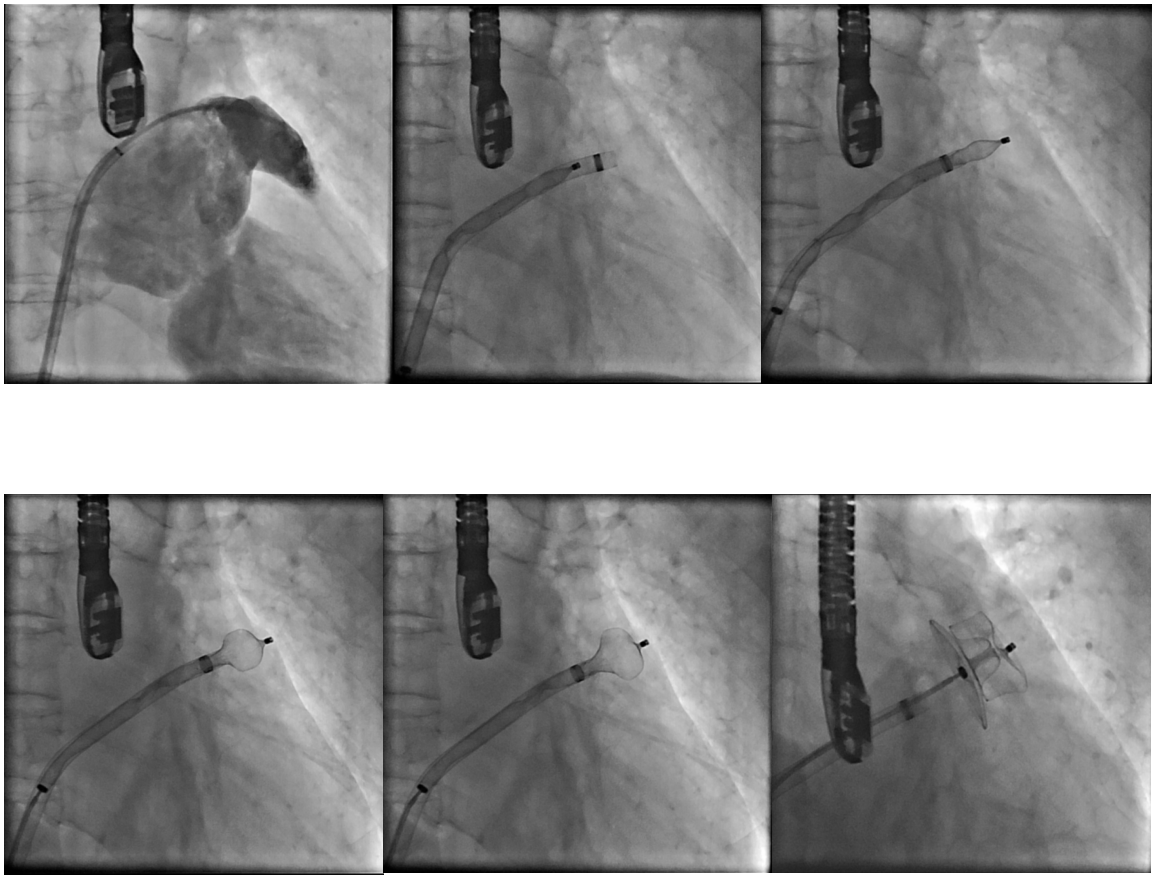
Se forma durante la tercera semana de gestación y sirve de aurícula izquierda del feto

Su tamaño es en general similar al de un dedo pulgar

Su ostium varía entre 10mm - 40mm

Su estructura es muy variable:
- Puede ser de paredes finas o gruesas
- Puede tener curvas
- Puede tener multiples lóbulos

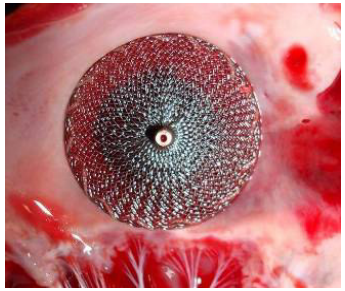




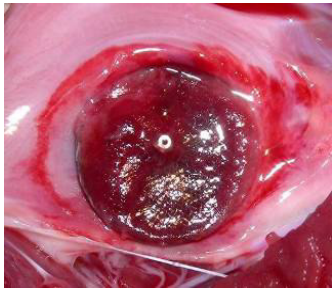
WATCHMAN™
LAA Closure Device

AMPLATZER™
Left Atrial Appendage Occluders

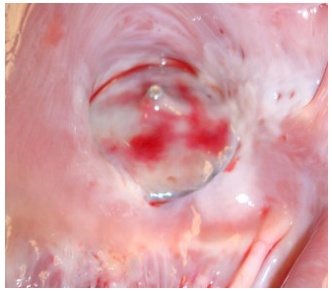
INMEDIATO



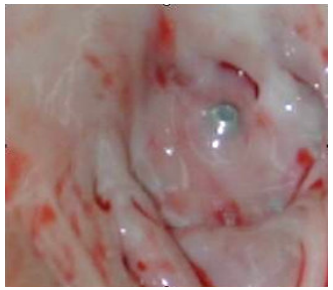
2 DIAS



1 MES



9 MESES

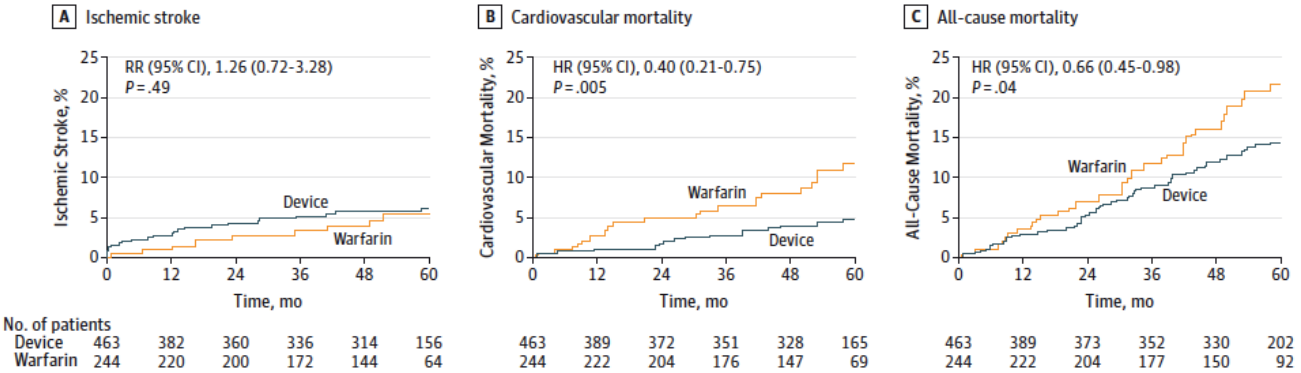


Protocolo:

- Doble antiagregación (AAS y Clopidogrel) durante 3 meses
- AAS 3 meses adicionales y posteriormente se suspende.

PROTECT-AF:

- First randomized trial comparing LAA occlusion to warfarin
- 707 subjects with nonvalvular AF and $CHADS_2$ score > 1
  - 59 centers in the US. Follow-up with TEE at 45 days, six months and one year
  - 87% were able to stop warfarin therapy at 45-day follow-up
- Primary Efficacy Endpoint
  - All stroke (ischemic and hemorrhagic), CV or unexplained death, systemic embolism
- Primary Safety Endpoint
  - Device embolization requiring retrieval, Pericardial effusion requiring drainage, Cranial, GI or other significant bleed



EWOLUTION:

- 1021 subjects.
- CHADS2 score: 2.8 + 1.3
- CHA2DS2-VASc: 4.5 + 1.6
- HAS-BLED score: 2.3 + 1.2

CONCLUSION: LAA closure with the WATCHMAN device has a high implant and sealing success. This method of stroke risk reduction appears to be safe and effective with an ischemic stroke rate as low as 1.1%, even though 73% of patients had a contraindication to and were not using oral anticoagulation.

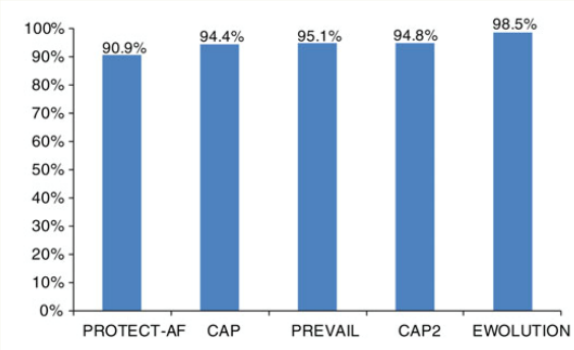


Figure 1 Implant success in EWOLUTION when compared with prior WATCHMAN studies.

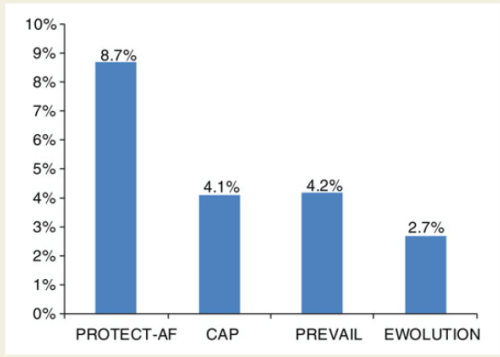
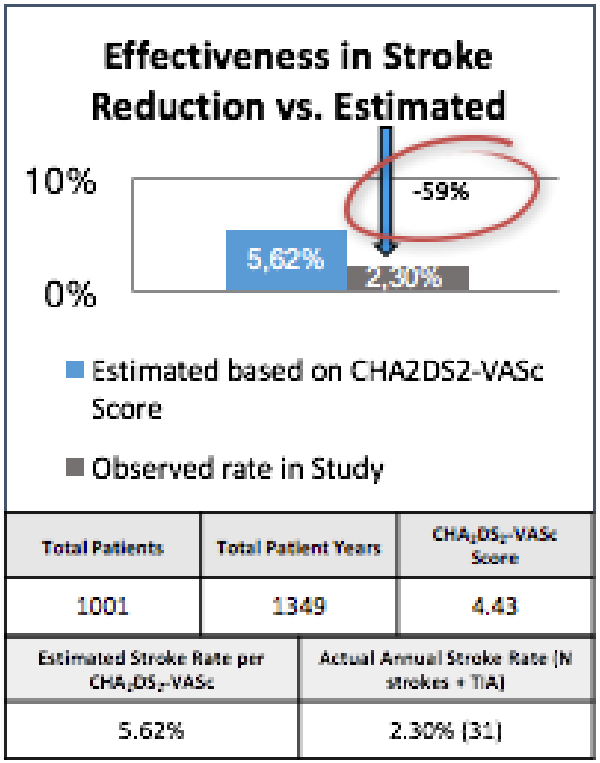


Figure 2 Serious procedure-/device-related events through 7 days in EWOLUTION when compared with prior WATCHMAN studies.

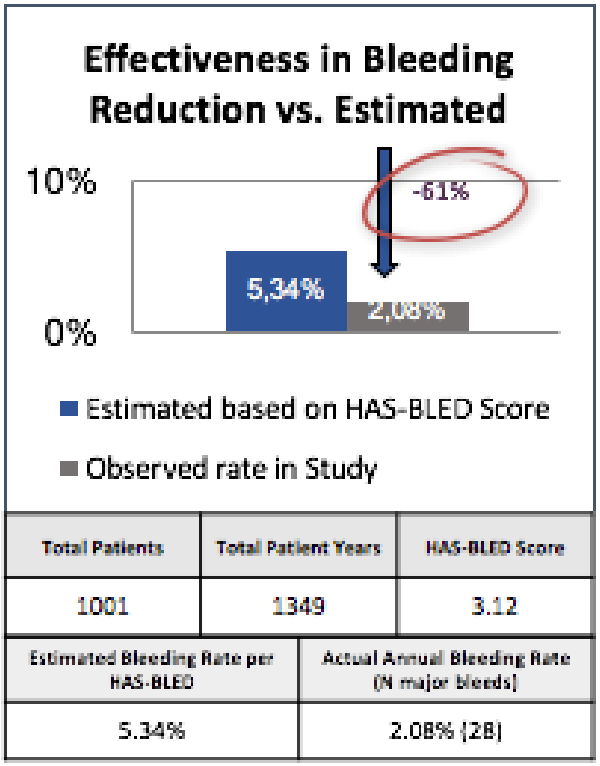
Seguimiento 1 año

Eur Heart J. 2016 Aug;37(31):2465-74.



Total Patients	Total Patient Years	CHA_2DS_2-VASc Score
1001	1349	4.43

Estimated Stroke Rate per CHA_2DS_2-VASc	Actual Annual Stroke Rate (N strokes + TIA)
5.62%	2.30% (31)



Total Patients	Total Patient Years	HAS-BLED Score
1001	1349	3.12

Estimated Bleeding Rate per HAS-BLED	Actual Annual Bleeding Rate (N major bleeds)
5.34%	2.08% (28)

Source: Tzikas, et al. (2014, May). *Multicenter experience with the Amplatzer Cardiac Plug (ACP).* Presented at EuroPCR 2014, Paris. Slides available at http://www.pcronline.com/Lectures/2014/Left-atrial-appendage-occlusion-for-stroke-prevention-in-atrial-fibrillation-multicentre-experience-with-the-Amplatzer-cardiac-plug

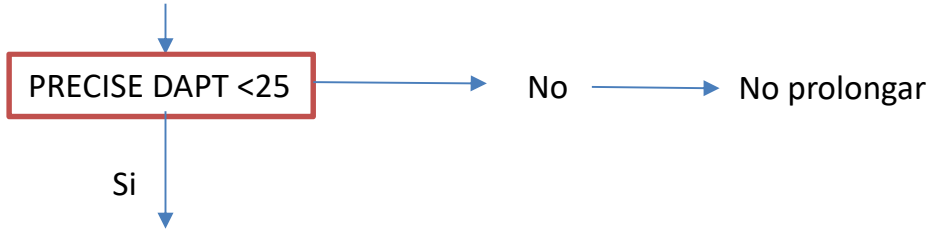
Gracias

Hospital La Luz
Grupo quirónsalud

Hospital quirónsalud
Sur

Protocolo de Prolongación de la doble antiagregación:

- Se inicia 1 año tras el SCA.
- Se continúa con Ticagrelor 60 mg 1 cp cada 12 h y AAS 100mg 1 cp al día.



Criterios Clínicos (indicación en consulta)	Criterios Angiográficos (indi
SCA recurrente	>60 mm de stent o uso >3 st