Fibrilace síní:
Uzávěr LAA nebo nic v prevenci CMP - Proti

P. Červinka
Krajská zdravotní a.s., Masarykova nemocnice v Ústí nad Labem o.z
a UJEP Ústí nad Labem

(XXVI sjezd ČKS, 6,-9.5. 2018, Brno)

➢ Uzávěr LAA…

Intervenční kardiolog

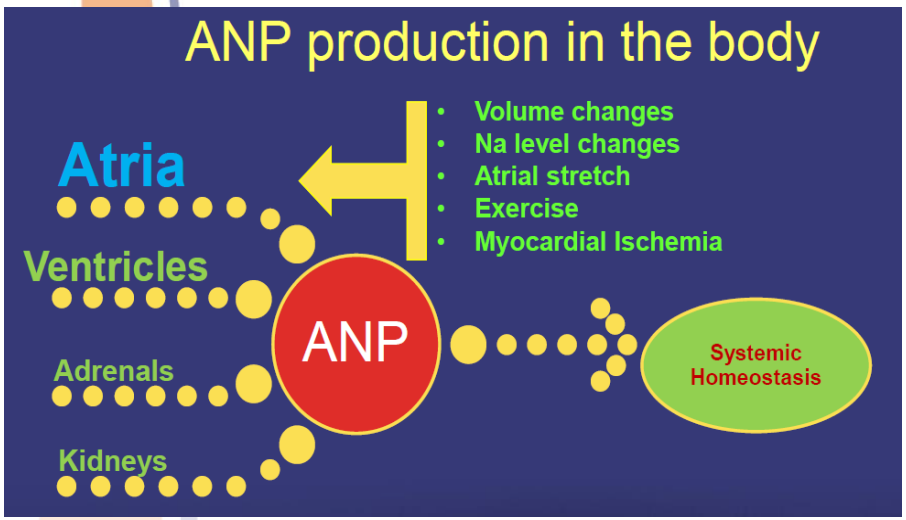
Go, hero, go!!

➢ Uzávěr LAA…

- **To, že něco umíme udělat neznamená, že to udělat máme!!!**

➢ Uzávěr LAA…

- ***Ouško levé síně : produkce ANP***



Variable	Pre LARIAT	Immediately Post-LARIAT	24 hr Post-LARIAT	3 months Post-LARIAT	p-value baseline vs 24 hours post LARIAT
NTp-ANP (pg/ml)	18.5±18.3	14.9±14.2	41.2±49.0	18.5±17.8	<0.001
NTp-BNP (pg/ml)	334.3±95.2	304.6±79.8	391.1±83.9	337.9±78.7	<0.001
Sodium (mm/L)	139.1±3.1	136.6±2.8	131.6±3.2	137.9±2.9	<0.001
Potassium (mm/L)	4.3±0.3	3.9±0.7	4.1±0.4	4.3±0.3	0.102
Magnesium (mg/dl)	1.8±0.2	1.8±0.2	1.9±0.1	1.9±0.6	0.842
Creatinine (mg/dl)	1.08±0.2	1.07±0.2	1.06±0.3	1.1±0.2	0.043

➢ Uzávěr LAA…

- ***Trombus není jen a pouze v oušku!***

Location of thrombi in non-rheumatic atrial fibrillation

Setting	Total no. thrombi found in LAA and atrium	Found LAA		Found in left atrium		Reference
		No.	%	No.	%	
TEE	67	66	99	1	1.5	Stoddard: JACC, '95
TEE	35	34	97	1	2.9	Manning: Circ. '94
Autopsy	47	35	74	12	25.5	Aberg: Acta Med Scan, '69
TEE	4	2	50	2	50.0	Tsai: JFMA, '90
TEE	13	12	92	1	7.7	Klein: Int J Card Imag. '93
TEE & operation	11	8	73	3	27.3	Manning: Circ, '94
SPAF III & TEE	20	19	95	1	5.0	Klein: Circ, '94
TEE	19	19	100	0	0.0	Leung: JACC, '94
TEE	6	6	100	0	0.0	Hart: Stroke, '94
Total	222	201	91	21	9.5	

Ann Thor Surg 61:755, 1996

➢ Uzávěr LAA…

Atrial Fibrillation and Mechanisms of Stroke

Time for a New Model

Hooman Kamel, MD; Peter M. Okin, MD; Mitchell S.V. Elkind, MD, MS; Costantino Iadecola, MD

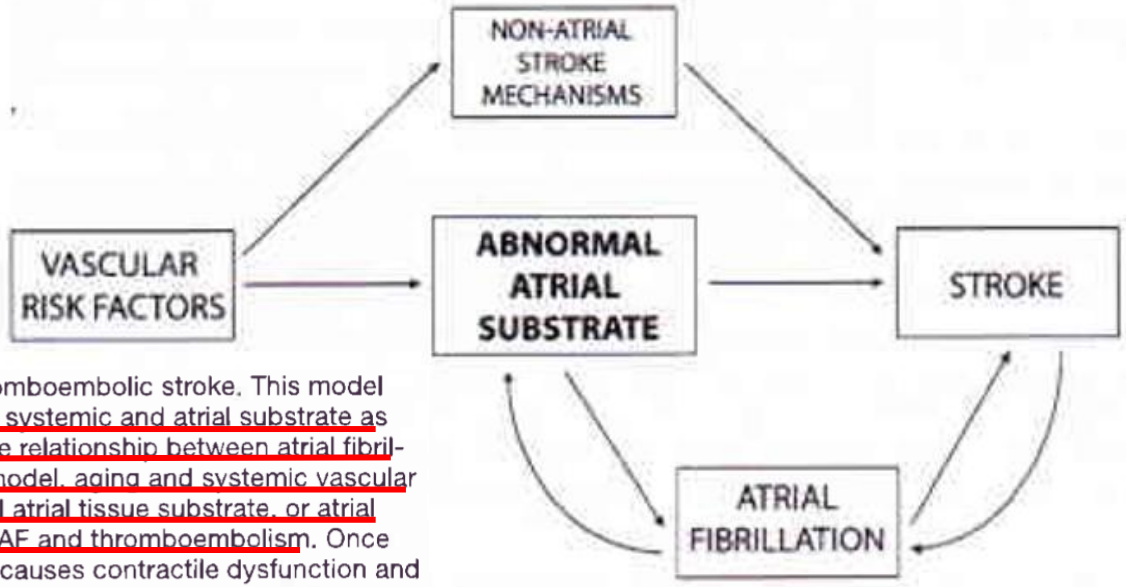


Figure. Updated model of thromboembolic stroke. This model emphasizes the importance of systemic and atrial substrate as well as rhythm in explaining the relationship between atrial fibrillation (AF) and stroke. In this model, aging and systemic vascular risk factors cause an abnormal atrial tissue substrate, or atrial cardiopathy, that can result in AF and thromboembolism. Once AF develops, the dysrhythmia causes contractile dysfunction and stasis, which further increases the risk of thromboembolism. In addition, over time, the dysrhythmia causes structural remodeling of the atrium, thereby worsening atrial cardiopathy and increasing the risk of thromboembolism even further. In parallel, systemic risk factors increase stroke risk via other mechanisms outside the atrium, such as large-artery atherosclerosis, ventricular systolic dysfunction, and in-situ cerebral small-vessel occlusion. Once stroke occurs, autonomic changes and post-stroke inflammation may transiently increase AF risk.

(*Stroke*. 2016;47:895-900. DOI: 10.1161/STROKEAHA.115.012004.)

➢ Uzávěr LAA: Proti

- ***Chirurgické odstranění ouška levé síně: prevence CMP?***

Circulation. 2017 Jan 24;135(4):366-378. doi: 10.1161/CIRCULATIONAHA.116.021952. Epub 2016 Nov 30.

Impact of Left Atrial Appendage Closure During Cardiac Surgery on the Occurrence of Early Postoperative Atrial Fibrillation, Stroke, and Mortality: A Propensity Score-Matched Analysis of 10 633 Patients.

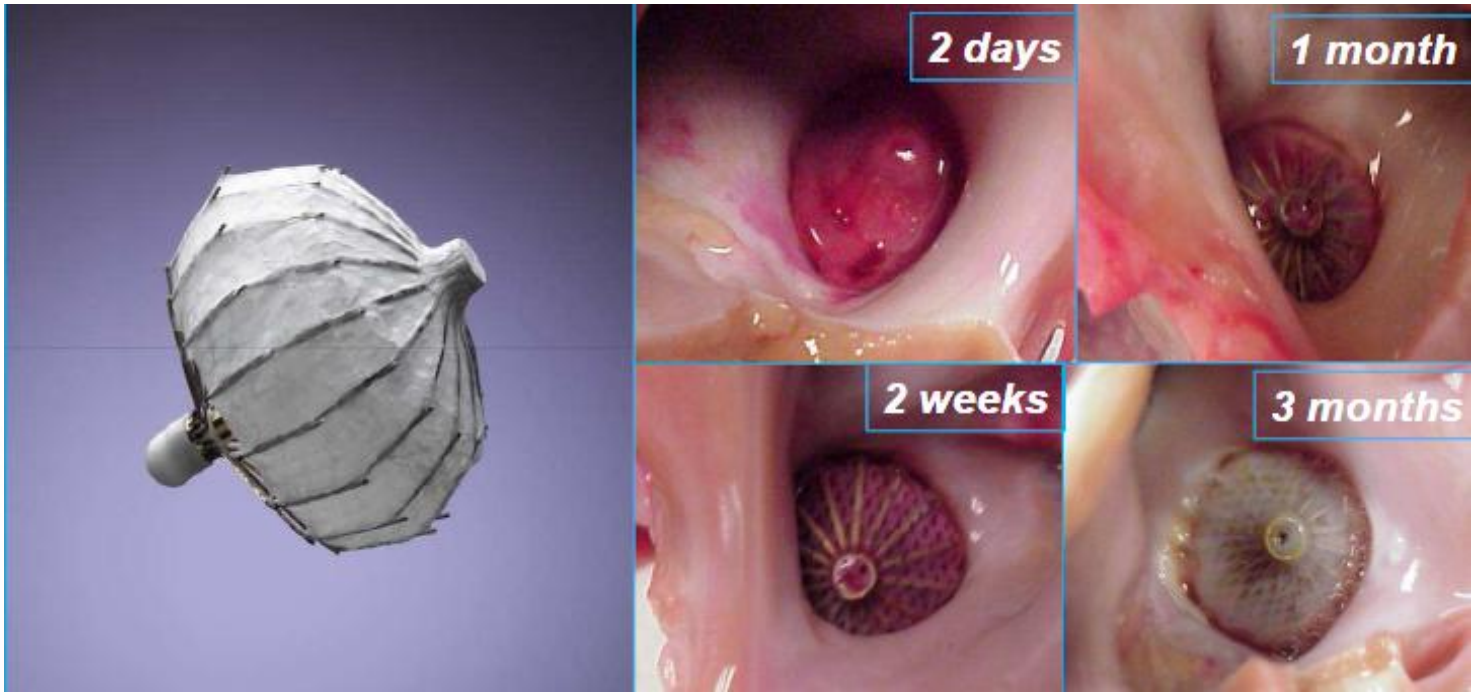
Melduni RM[1], Schaff HV[2], Lee HC[2], Gersh BJ[2], Noseworthy PA[2], Bailey KR[2], Ammash NM[2], Cha SS[2], Fatema K[2], Wysokinski WE[2], Seward JB[2], Packer DL[2], Rihal CS[2], Asirvatham SJ[2].

METHODS: Of 10 633 adults who underwent coronary artery bypass grafting and valve surgery between January 2000 and December 2005, 9792 patients with complete baseline characteristics, surgery procedure, and follow-up data were included in this analysis. A propensity score-matching analysis based on 28 pretreatment covariates was performed and 461 matching pairs were derived and analyzed to estimate the association of LAA closure with early postoperative atrial fibrillation (POAF) (atrial fibrillation ≤30 days of surgery), ischemic stroke, and mortality.

CONCLUSIONS: After adjustment for treatment allocation bias, LAA closure during routine cardiac surgery was significantly associated with an increased risk of early POAF, but it did not influence the risk of stroke or mortality. It remains uncertain whether prophylactic exclusion of the LAA is warranted for stroke prevention during non-atrial fibrillation-related cardiac surgery.

➢ Uzávěr LAA: Proti

➢ Cíl uzávěru ouška?



! Zabránit CMP a systémové embolizaci !
(„proof-of-concept“)

Je tomu tak??

➢ Uzávěr LAA: Proti

5-Year Outcomes After Left Atrial Appendage Closure

From the PREVAIL and PROTECT AF Trials

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 70, NO. 24, 2017

Vivek Y. Reddy, MD,[a,b] Shephal K. Doshi, MD,[c] Saibal Kar, MD,[d] Douglas N. Gibson, MD,[e] Matthew J. Price, MD,[e] Kenneth Huber, MD,[f] Rodney P. Horton, MD,[g] Maurice Buchbinder, MD,[h] Petr Neuzil, MD, PhD,[b] Nicole T. Gordon, BSEE,[i] David R. Holmes, Jr, MD,[j] on behalf of the PREVAIL and PROTECT AF Investigators

Characteristic	PROTECT AF N=463	PREVAIL N=269	P value
Age, years	71.7 ± 8.8 (463) (46.0, 95.0)	74.0 ± 7.4 (269) (50.0, 94.0)	<0.001
Gender (Male)	326/463 (70.4%)	182/269 (67.7%)	0.252
$CHADS_2$ Score (Continuous)	2.2 ± 1.2 (1.0, 6.0)	2.6 ± 1.0 (1.0, 6.0)	<0.001
$CHADS_2$ Risk Factors			
CHF	124/463 (26.8%)	63/269 (23.4%)	
Hypertension	415/463 (89.6%)	238/269 (88.5%)	
Age ≥ 75	190/463 (41.0%)	140/269 (52.0%)	
Diabetes	113/463 (24.4%)	91/269 (33.8%)	
Stroke/TIA	82/463 (17.7%)	74/269 (27.5%)	

➢ Uzávěr LAA: Proti

- ***PREVAIL publikována v r. 7/2014 v JACC:***

(pouze 28% nemocných 18-M FU – CMP/SE 2,5% vs 2%=non inferiorita /5 ischemických CMP/),

ALE !

10/2014 (TCT, FDA meeting) – dalších 8 CMP=13 vs. 1

Am J Cardiol. 2015 Feb 1;115(3):378-84. doi: 10.1016/j.amjcard.2014.11.011. Epub 2014 Nov 12.

Overview of the Food and Drug Administration circulatory system devices panel meetings on WATCHMAN left atrial appendage closure therapy.

Waksman R[1], Pendyala LK[2].

⊕ Author information

Abstract

The WATCHMAN left atrial appendage closure (LAAC) technology is a percutaneously delivered permanent cardiac implant placed in the LAA. This device is designed to reduce the risk of stroke and systemic embolism in warfarin-eligible patients with nonvalvular atrial fibrillation. The first circulatory system device panel reviewed the Embolic Protection in Patients With Atrial Fibrillation (PROTECT AF) study in 2009, and a "not approvable" letter was issued by the US Food and Drug Administration (FDA) based on safety concerns. Subsequently, the FDA, collaboratively with the sponsor, designed a new Prospective Randomized Evaluation of the WATCHMAN LAAC Device in Patients With Atrial Fibrillation Versus Long-Term Warfarin Therapy (PREVAIL) trial to address the earlier study limitations. A second panel was convened in December 2013 to review the results of PREVAIL and additional long-term follow-up data from PROTECT AF. The second panel voted favorably 13 to 1 that the benefits of the WATCHMAN LAAC therapy do outweigh the risks for use in patients who meet the criteria specified in the proposed indication. Subsequently, and during the premarket approval review, updated data from the PREVIAL study revealed more ischemic strokes in the WATCHMAN group, corresponding to a total of 13 ischemic strokes in the WATCHMAN group versus 1 in the control group. As a result of these strokes, the FDA called for a third panel to assess the benefit-risk profile of the WATCHMAN device. This summary aims to describe the discussions and recommendations made during the panel meetings.

➢ Uzávěr LAA: Proti

5-Year Outcomes After Left Atrial Appendage Closure

From the PREVAIL and PROTECT AF Trials

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 70, NO. 24, 2017

Vivek Y. Reddy, MD,[a,b] Shephal K. Doshi, MD,[c] Saibal Kar, MD,[d] Douglas N. Gibson, MD,[e] Matthew J. Price, MD,[e] Kenneth Huber, MD,[f] Rodney P. Horton, MD,[g] Maurice Buchbinder, MD,[h] Petr Neuzil, MD, PhD,[b] Nicole T. Gordon, BSEE,[i] David R. Holmes, Jr, MD,[j] on behalf of the PREVAIL and PROTECT AF Investigators

TABLE 3 Efficacy Rates at 5 Years (2:1 Randomization)

	PROTECT AF Subjects					PREVAIL-Only Subjects				
	Device Group (n = 463)		Control Group (n = 244)			Device Group (n = 269)		Control Group (n = 138)		
	No. of Events	Rate*	No. of Events	Rate*	p Value	No. of Events	Rate*	No. of Events	Rate*	p Value
Primary efficacy: stroke/SE/CV death	40/1,787.7	2.24	34/929.4	3.66	0.04	37/1,038.3	3.65%	15/530.4	2.94%	0.47
All stroke	26/1,781.7	1.46	20/929.4	2.15	0.23	19/1,042.4	1.97%	7/530.4	1.29%	0.32
Ischemic stroke	24/1,781.7	1.35	10/932.8	1.07	0.49	17/1,043.1	1.68%	4/533.3	0.73%	0.13
Hemorrhagic stroke	3/1,837.7	0.16	10/945.6	1.06	0.005	2/1,084.6	0.18%	3/538.0	0.54%	0.23
Systemic embolism	3/1,837.1	0.16	0	N/A	N/A	1/1,080.6	0.09%	0/540.9	N/A	N/A
CV/unexplained death	19/1,843.2	1.03	22/948.9	2.32	0.009	18/1,084.7	1.79%	10/540.9	1.98%	0.76

*Events are per 100 patient-yrs.

CV = cardiovascular; SE = systemic embolism; other abbreviations as in Table 1.

➢ *Statisticky významné non-inferiority nebylo dosaženo*

= uzávěr horší než standardní léčba (warfarin)

➢ Uzávěr LAA: Proti

5-Year Patient-Level Meta-Analysis of PROTECT AF and PREVAIL (2:1 Randomization)

	Device Group (n = 732)		Control Group (n = 382)			
	No. of Events	Rate (per 100 PY)	No. of Events	Rate (per 100 PY)	Hazard Ratio (95% Confidence Interval)	p Value
Efficacy: stroke/SE/CV death	79/2,856.0	2.8%	50/1,472.8	3.4%	0.82 (0.58–1.17)	0.27
All stroke or SE	49/2,849.4	1.7%	27/1,472.9	1.8%	0.96 (0.60–1.54)	0.87
Ischemic stroke or SE	45/2,850.2	1.6%	14/1,479.1	0.95%	1.71 (0.94–3.11)	0.08
Hemorrhagic stroke	5/2,954.8	0.17%	13/1,499.0	0.87%	0.20 (0.07–0.56)	0.0022
Ischemic stroke or SE >7 days	37/2,862.1	1.3%	14/1,479.1	0.95%	1.40 (0.76–2.59)	0.28
Disabling stroke	13/2,943.0	0.44%	15/1,493.8	1.0%	0.45 (0.21–0.94)	0.03
Nondisabling stroke	31/2,879.1	1.1%	12/1,484.3	0.81%	1.38 (0.71–2.68)	0.35
CV/unexplained death	39/2,960.5	1.3%	33/1,505.2	2.2%	0.59 (0.37–0.94)	0.027
All-cause death	106/2,961.6	3.6%	73/1,505.2	4.9%	0.73 (0.54–0.98)	0.035
Major bleeding, all	85/2,748.4	3.1%	50/1,414.7	3.5%	0.91 (0.64–1.29)	0.60
Major bleeding, non-procedure-related	48/2,853.6	1.7%	51/1,411.3	3.6%	0.48 (0.32–0.71)	0.0003

Two strokes in PREVAIL are excluded because the baseline MRS score was unavailable. Disabling stroke is defined as a stroke that increases the Modified Rankin Score by ≥2.

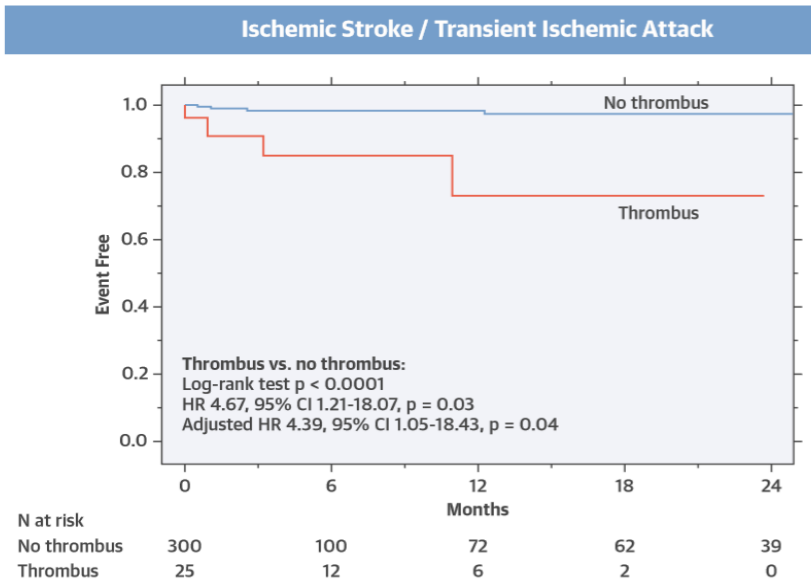
PY = patient-yrs. Other abbreviations as in Table 3.

➢ Uzávěr LAA: Proti

Device-Related Thrombosis After Percutaneous Left Atrial Appendage Occlusion for Atrial Fibrillation

Laurent Fauchier, MD,[a] Alexandre Cinaud, MD,[a] François Brigadeau, MD,[b] Antoine Lepillier, MD,[c] Bertrand Pierre, MD,[a] Selim Abbey, MD,[d] Marjaneh Fatemi, MD,[e] Frederic Franceschi, MD,[f] Paul Guedeney, MD,[g] Peggy Jacon, MD,[h] Olivier Paziaud, MD,[c] Sandrine Venier, MD,[h] Jean Claude Deharo, MD,[f] Daniel Gras, MD,[d] Didier Klug, MD,[b] Jacques Mansourati, MD,[e] Gilles Montalescot, MD,[g] Olivier Piot, MD,[c] Pascal Defaye, MD[h]

CENTRAL ILLUSTRATION Kaplan-Meier Cumulative Event-Free Curves of Ischemic Strokes and Transient Ischemic Attacks With and Without Thrombus on the Device



Fauchier, L. et al. J Am Coll Cardiol. 2018;71(14):1528-36.

The curves are representative of being event-free for ischemic strokes and transient ischemic attacks, with and without thrombus on the device, after left atrial appendage occlusion. Time zero is time at first post-procedure left atrial appendage imaging. The curves demonstrate a higher risk for ischemic strokes or transient ischemic attacks in the patients with a diagnosis of device-associated thrombus after left atrial appendage occlusion. The mean follow-up time was 13 ± 13 months. CI = confidence interval; HR = hazard ratio.

➢ Uzávěr LAA: Proti

Device-Related Thrombosis After Percutaneous Left Atrial Appendage Occlusion for Atrial Fibrillation

TABLE 2 Major Adverse Events (n = 98) in Patients Treated With LAA Occlusion Using the Nitinol Plug or Nitinol Cage Devices

	Overall (N = 469)	Nitinol Cage (n = 272)	Nitinol Plug (n = 197)	p Value (Nitinol Cage vs. Nitinol Plug)
Death	33 (6.9)	18 (6.7)	15 (7.1)	0.85
Ischemic stroke	19 (4.0)	10 (3.7)	9 (4.3)	0.86
TIA	2 (0.4)	2 (0.7)	0 (0)	—
Major hemorrhage	18 (3.8)	10 (3.7)	8 (3.8)	0.76
Thrombus on the device				
In the whole study group	26 (5.4)	13 (4.8)	13 (6.2)	0.36
In patients with LAA imaging	26 (7.2)	13 (5.5)	13 (11.0)	0.02
Antithrombotic therapy at discharge				
No OAC, no APT	4 (15.4)	14 (4.5)		0.02
Single APT	11 (42.3)	91 (29.1)		0.15
Dual APT	1 (3.8)	81 (25.9)		0.01
OAC, no APT	10 (38.5)	108 (34.5)		0.68
OAC plus APT	0 (0.0)	19 (6.1)		0.23

Values are n (yearly rate %).
LAA = left atrial appendage; TIA = transient ischemic attack.

8,2% s ACP (=100)

25% s Amulet (N=97)

TABLE 4 Multivariable Analysis (Cox Regression Model) for Predictors of Thrombus Formation on the Device and Predictors of Stroke and TIA*

	HR (95% CI)	p Value
Thrombus formation on the device		
Age (per 1-yr increase)	1.07 (1.01–1.14)	0.02
Previous ischemic stroke	3.68 (1.17–11.62)	0.03
CHA_2DS_2-VASc score	0.69 (0.44–1.06)	0.09
APT at discharge	0.35 (0.12–1.04)	0.06
Dual APT at discharge	0.10 (0.01–0.76)	0.03
OAC at discharge	0.26 (0.09–0.77)	0.02
Strokes or TIAs		
Vascular disease	5.03 (1.39–18.23)	0.01
Thrombus on the device	4.39 (1.05–18.43)	0.04
CHA_2DS_2-VASc score	0.71 (0.47–1.06)	0.09
APT at discharge	1.35 (0.20–9.06)	0.75
Dual APT at discharge	0.64 (0.15–2.69)	0.54
OAC at discharge	0.39 (0.06–2.61)	0.33

*Analysis restricted to patients with LAA imaging during follow-up. For prediction of thrombus formation on the device, time zero is time at discharge after LAA closure. For prediction of stroke or TIA, time zero is time at first post-procedure LAA imaging.
CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.

➢ Uzávěr LAA: Proti

- *Výskyt krvácivé mozkové příhody při OAC*

PROTECT-AF : MOZKOVÉ KRVÁCENÍ

Table 2. Intention-to-Treat Primary Efficacy and Safety Outcomes According to Treatment Group by Bayesian Model

Event	Device Group (n = 463) Events/Patient-Years	Device Group (n = 463) Observed Rate[a]	Warfarin Group (n = 244) Events/Patient-Years	Warfarin Group (n = 244) Observed Rate[a]	Device/Warfarin Rate Ratio (95% Credible Interval)
Primary efficacy end point[b]	39/1720.2	2.3 (1.7-3.2)	34/900.8	3.8 (2.5-4.9)	0.60 (0.41-1.05)
Stroke	26/1720.7	1.5 (1.0-2.2)	20/900.9	2.2 (1.3-3.1)	0.68 (0.42-1.37)
Ischemic	24/1720.8	1.4 (0.9-2.1)	10/904.2	1.1 (0.5-1.7)	1.26 (0.72-3.28)
Hemorrhagic	3/1774.2	0.2 (0.0-0.4)	10/916.2	1.1 (0.5-1.8)	0.15 (0.03-0.49)
Disabling[c]	8/1771.3	0.5 (0.2-0.8)	11/912.7	1.2 (0.6-1.9)	0.37 (0.15-1.00)
Nondisabling[c]	18/1723.7	1.0 (0.7-1.7)	9/907.7	1.0 (0.4-1.7)	1.05 (0.54-2.80)
Systemic embolization	3/1773.6	0.2 (0.0-0.4)	0/919.5	0	NA
Cardiovascular or unexplained death	17/1774.3	1.0 (0.6-1.5)	22/919.4	2.4 (1.4-3.4)	0.40 (0.23-0.82)
Primary safety end point[d]	60/1666.2	3.6 (2.8-4.6)	27/878.2	3.1 (2.0-4.3)	1.17 (0.78-1.95)

BAFTA : MOZKOVÉ KRVÁCENÍ

	Warfarin (n=488) n	Warfarin (n=488) Risk per year	Aspirin (n=485) n	Aspirin (n=485) Risk per year	Warfarin vs aspirin RR (95% CI)	Warfarin vs aspirin p
Stroke	21	1·6%	44	3·4%	0·46 (0·26–0·79)	0·003
By severity						
Fatal	13	1·0%	21	1·6%	0·59 (0·27–1·24)	0·14
Disabling non-fatal	8	0·6%	23	1·8%	0·33 (0·13–0·77)	0·005
Type of stroke*						
Ischaemic	10	0·8%	32	2·5%	0·30 (0·13–0·63)	0·0004
Haemorrhagic	6	0·5%	5	0·4%	1·15 (0·29–4·77)	0·83
Unknown	5	0·4%	7	0·5%	0·69 (0·17–2·51)	0·53
Other intracranial haemorrhage†	2	0·2%	1	0·1%	1·92 (0·10–113·3)	0·65
Systemic embolism‡	1	0·1%	3	0·2%	0·32 (0·01–3·99)	0·36
Total number of events	24	1·8%	48	3·8%	0·48 (0·28–0·80)	0·0027

➢ Uzávěr LAA: Proti

- ***AVERROES :*** ***je pro mozkové krvácení nebezpečnější aspirin nebo (N)OAC???***

	No previous stroke or TIA (n=4832)					Previous stroke or TIA (n=764)					p value*
	Aspirin (n=2415†)		Apixaban (n=2417)		HR with apixaban (95% CI)	Aspirin (n=374)		Apixaban (n=390)		HR with apixaban (95% CI)	
	Number of events‡	Kaplan-Meier cumulative hazard at 1 year (%, 95% CI§)	Number of events	Kaplan-Meier cumulative hazard at 1 year (%, 95% CI§)		Number of events	Kaplan-Meier cumulative hazard at 1 year (%, 95% CI§)	Number of events	Kaplan-Meier cumulative hazard at 1 year (%, 95% CI§)		
Efficacy endpoints											
Stroke or systemic embolism	80	3·06 (2·38–3·92)	41	1·68 (1·18–2·37)	0·51 (0·35–0·74)	33	9·16 (6·27–13·40)	10	2·39 (1·17–4·90)	0·29 (0·15–0·60)	0·17
Stroke	75	2·81 (2·17–3·64)	39	1·62 (1·13–2·30)	0·52 (0·35–0·76)	30	8·26 (5·53–12·35)	10	2·39 (1·17–4·90)	0·33 (0·16–0·67)	0·26
Ischaemic or unspecified stroke	70	2·67 (2·05–3·49)	34	1·42 (0·97–2·07)	0·48 (0·32–0·73)	27	7·46 (4·91–11·33)	9	2·12 (0·99–4·57)	0·33 (0·15–0·69)	0·36
Haemorrhagic stroke	5	0·14 (0·04–0·43)	5	0·19 (0·07–0·53)	1·00 (0·29–3·46)	4	1·07 (0·33–3·42)	1	0·27 (0·04–1·89)	0·25 (0·03–2·25)	0·25
Disabling or fatal stroke	49	1·75 (1·26–2·42)	24	0·97 (0·61–1·53)	0·49 (0·30–0·79)	23	6·27 (3·95–9·94)	7	1·86 (0·81–4·27)	0·30 (0·13–0·70)	0·32

Lancet Neurol 2012; 11: 225–31

➢ Uzávěr LAA: Proti

- *NOACs: nový silný kompetitor*

- ***Ekonomické náklady***

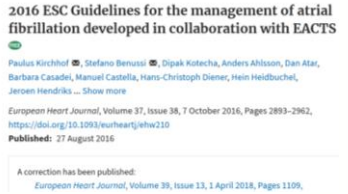
NOACs	*LAA closure*
cca 24 000 Kč/rok	*cca 120 000 Kč*

Published in final edited form as:
J Thromb Thrombolysis. 2013 August ; 36(2): 163–174. doi:10.1007/s11239-013-0956-2.

Clinical strategies for selecting oral anticoagulants in patients with atrial fibrillation

➢ Uzávěr LAA: Proti

- Co nám říkají guidelines?



2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

Paulus Kirchhof, Stefano Benussi, Dipak Kotecha, Anders Ahlsson, Dan Atar, Barbara Casadei, Manuel Castella, Hans-Christoph Diener, Hein Heidbuchel, Jeroen Hendriks ... Show more

European Heart Journal, Volume 37, Issue 38, 7 October 2016, Pages 2893–2962, https://doi.org/10.1093/eurheartj/ehw210

Published: 27 August 2016

A correction has been published:
European Heart Journal, Volume 39, Issue 13, 1 April 2018, Pages 1109,

Table 1

Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective; and in some cases may be harmful.	Is not recommended

Table 2

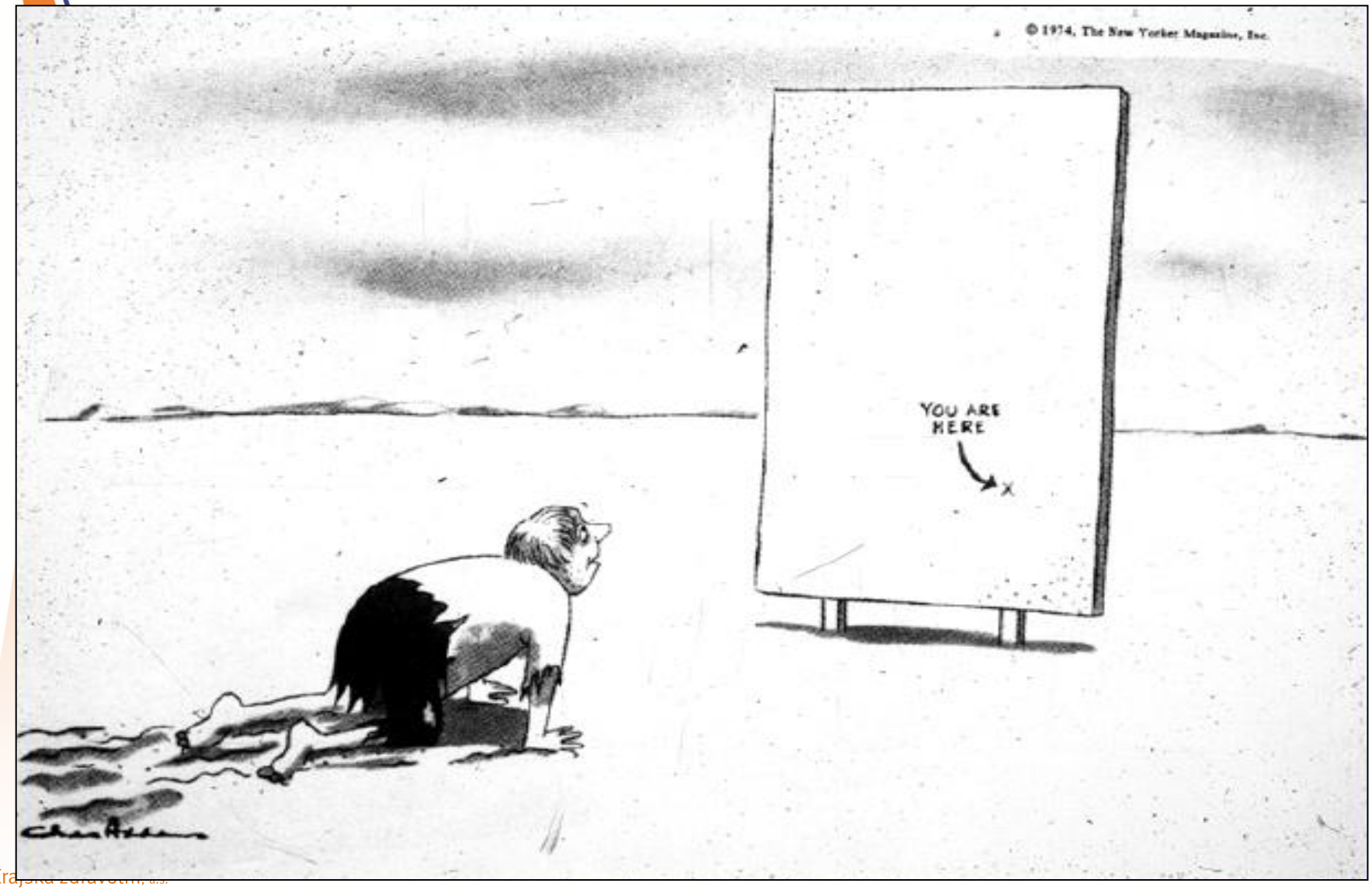
Levels of evidence

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Recommendations for occlusion or exclusion of the left atrial appendage

Recommendations	Class[a]	Level[b]	Ref[c]
After surgical occlusion or exclusion of the LAA, it is recommended to continue anticoagulation in at-risk patients with AF for stroke prevention.	I	B	461, 462
LAA occlusion may be considered for stroke prevention in patients with AF and contra-indications for long-term anticoagulant treatment (e.g. those with a previous life-threatening bleed without a reversible cause).	IIb	B	449, 453, 454
Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing cardiac surgery.	IIb	B	463
Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients undergoing thoracoscopic AF surgery.	IIb	B	468

➢ Uzávěr LAA: Proti




Děkuji za pozornost
B

➢ Uzávěr LAA: Proti

- Výskyt krvácivé mozkové příhody při OAC/APT

PROTECT-AF : MOZKOVÉ KRVÁCENÍ

Table 2. Intention-to-Treat Primary Efficacy and Safety Outcomes According to Treatment Group by Bayesian Model

Event	Device Group (n = 463)		Warfarin Group (n = 244)		Device/Warfarin Rate Ratio (95% Credible Interval)
	Events/Patient-Years	Observed Rate[a]	Events/Patient-Years	Observed Rate[a]	
Primary efficacy end point[b]	39/1720.2	2.3 (1.7-3.2)	34/900.8	3.8 (2.5-4.9)	0.60 (0.41-1.05)
Stroke	26/1720.7	1.5 (1.0-2.2)	20/900.9	2.2 (1.3-3.1)	0.68 (0.42-1.37)
Ischemic	24/1720.8	1.4 (0.9-2.1)	10/904.2	1.1 (0.5-1.7)	1.26 (0.72-3.28)
Hemorrhagic	3/1774.2	0.2 (0.0-0.4)	10/916.2	1.1 (0.5-1.8)	0.15 (0.03-0.49)
Disabling[c]	8/1771.3	0.5 (0.2-0.8)	11/912.7	1.2 (0.6-1.9)	0.37 (0.15-1.00)
Nondisabling[c]	18/1723.7	1.0 (0.7-1.7)	9/907.7	1.0 (0.4-1.7)	1.05 (0.54-2.80)
Systemic embolization	3/1773.6	0.2 (0.0-0.4)	0/919.5	0	NA
Cardiovascular or unexplained death	17/1774.3	1.0 (0.6-1.5)	22/919.4	2.4 (1.4-3.4)	0.40 (0.23-0.82)
Primary safety end point[d]	60/1666.2	3.6 (2.8-4.6)	27/878.2	3.1 (2.0-4.3)	1.17 (0.78-1.95)

PROTECT-AF : DEMOGRAFIE

	Device Group (n = 463)	Warfarin Group (n = 244)
Age, mean (SD) [range], y	71.7 (8.8) [46-95]	72.7 (9.2) [41-95]
Heart rate, mean (SD) [range], beats/min	73 (13) [37-120]	74 (13) [42-109]
Blood pressure, mean (SD) [range], mm Hg		
Systolic	135 (21) [90-229]	135 (19) [90-194]
Diastolic	77 (12) [32-117]	76 (12) [44-120]
Body mass index, mean (SD) [range][a]	31.6 (6.0) [14-54]	31.3 (6.2) [20-57]
Male sex, No. (%)	326 (70.4)	171 (70.1)
Race/ethnicity, No. (%)		
Asian	4 (0.9)	1 (0.4)
Black/African American	6 (1.3)	5 (2.0)
White	425 (91.8)	222 (91.0)
Hispanic/Latino	25 (5.4)	15 (6.1)
Hawaiian Pacific Islander	1 (0.2)	1 (0.4)
Other	2 (0.4)	0
$CHADS_2$ score[b]		
Mean (SD) [range]	2.2 (1.2) [1-6]	2.3 (1.2) [1-6]

➢ Uzávěr LAA: Proti

- Výskyt krvácivé mozkové příhody při OAC

BAFTA : KRVÁCENÍ

	Warfarin (n=488)		Aspirin (n=485)		Warfarin vs aspirin	
	n	Risk per year	n	Risk per year	RR (95% CI)	p
Stroke	21	1·6%	44	3·4%	0·46 (0·26–0·79)	0·003
By severity						
Fatal	13	1·0%	21	1·6%	0·59 (0·27–1·24)	0·14
Disabling non-fatal	8	0·6%	23	1·8%	0·33 (0·13–0·77)	0·005
Type of stroke*						
Ischaemic	10	0·8%	32	2·5%	0·30 (0·13–0·63)	0·0004
Haemorrhagic	6	0·5%	5	0·4%	1·15 (0·29–4·77)	0·83
Unknown	5	0·4%	7	0·5%	0·69 (0·17–2·51)	0·53
Other intracranial haemorrhage†	2	0·2%	1	0·1%	1·92 (0·10–113·3)	0·65
Systemic embolism‡	1	0·1%	3	0·2%	0·32 (0·01–3·99)	0·36
Total number of events	24	1·8%	48	3·8%	0·48 (0·28–0·80)	0·0027

BAFTA : DEMOGRAFIE

	Warfarin	Aspirin
Number of patients	488	485
Age (years)	81·5 (4·3)	81·5 (4·2)
Age group		
75–79	197 (40%)	200 (41%)
80–84	196 (40%)	190 (39%)
≥85	95 (19%)	95 (20%)
Male	267 (55%)	264 (54%)
Method of identification		
Practice register	342 (70%)	341 (70%)
Screening	146 (30%)	144 (30%)
CHADS2 score*		
1–2	349 (72%)	349 (72%)
3–6	139 (28%)	136 (28%)

Lancet 2007; 370: 493–503

➢ Uzávěr LAA: Proti

- Výskyt krvácivé mozkové příhody při OAC

ROCKET – AF: KRVÁCENÍ

Table 3. Rates of Bleeding Events.*

Variable	Rivaroxaban (N=7111) Events no. (%)	Rivaroxaban (N=7111) Event Rate no./100 patient-yr	Warfarin (N=7125) Events no. (%)	Warfarin (N=7125) Event Rate no./100 patient-yr	Hazard Ratio (95% CI)†
Principal safety end point: major and nonmajor clinically relevant bleeding§	1475 (20.7)	14.9	1449 (20.3)	14.5	1.03 (0.96–1.11)
Major bleeding					
Any	395 (5.6)	3.6	386 (5.4)	3.4	1.04 (0.90–1.20)
Decrease in hemoglobin ≥2 g/dl	305 (4.3)	2.8	254 (3.6)	2.3	1.22 (1.03–1.44)
Transfusion	183 (2.6)	1.6	149 (2.1)	1.3	1.25 (1.01–1.55)
Critical bleeding¶	91 (1.3)	0.8	133 (1.9)	1.2	0.69 (0.53–0.91)
Fatal bleeding	27 (0.4)	0.2	55 (0.8)	0.5	0.50 (0.31–0.79)
Intracranial hemorrhage	55 (0.8)	0.5	84 (1.2)	0.7	0.67 (0.47–0.93)
Nonmajor clinically relevant bleeding	1185 (16.7)	11.8	1151 (16.2)	11.4	1.04 (0.96–1.13)

ROCKET – AF: DEMOGRAFIE

Table 1. Characteristics of the Intention-to-Treat Population at Baseline.

Characteristic	Rivaroxaban (N=7131)	Warfarin (N=7133)
Age — yr		
Median	73	73
Interquartile range	65–78	65–78
Female sex — no. (%)	2831 (39.7)	2832 (39.7)
Body-mass index*		
Median	28.3	28.1
Interquartile range	25.2–32.1	25.1–31.8
Blood pressure — mm Hg		
Systolic		
Median	130	130
Interquartile range	120–140	120–140
Diastolic		
Median	80	80
Interquartile range	70–85	70–85
Type of atrial fibrillation — no. (%)		
Persistent	5786 (81.1)	5762 (80.8)
Paroxysmal	1245 (17.5)	1269 (17.8)
Newly diagnosed or new onset	100 (1.4)	102 (1.4)
Previous medication use — no. (%)		
Aspirin	2586 (36.3)	2619 (36.7)
Vitamin K antagonist	4443 (62.3)	4461 (62.5)
$CHADS_2$ risk of stroke†		
Mean score (±SD)	3.48±0.94	3.46±0.95

➢ Uzávěr LAA: Proti

- Výskyt krvácivé mozkové příhody při OAC

ARISTOTLE : KRVÁCENÍ

Table 2. Efficacy Outcomes.*

Outcome	Apixaban Group (N=9120)		Warfarin Group (N=9081)		Hazard Ratio (95% CI)	P Value
	Patients with Event	Event Rate	Patients with Event	Event Rate		
	no.	*%/yr*	*no.*	*%/yr*		
Primary outcome: stroke or systemic embolism	212	1.27	265	1.60	0.79 (0.66–0.95)	0.01
Stroke	199	1.19	250	1.51	0.79 (0.65–0.95)	0.01
Ischemic or uncertain type of stroke	162	0.97	175	1.05	0.92 (0.74–1.13)	0.42
Hemorrhagic stroke	40	0.24	78	0.47	0.51 (0.35–0.75)	<0.001
Systemic embolism	15	0.09	17	0.10	0.87 (0.44–1.75)	0.70
Key secondary efficacy outcome: death from any cause	603	3.52	669	3.94	0.89 (0.80–0.998)	0.047
Other secondary outcomes						
Stroke, systemic embolism, or death from any cause	752	4.49	837	5.04	0.89 (0.81–0.98)	0.02
Myocardial infarction	90	0.53	102	0.61	0.88 (0.66–1.17)	0.37
Stroke, systemic embolism, myocardial infarction, or death from any cause	810	4.85	906	5.49	0.88 (0.80–0.97)	0.01
Pulmonary embolism or deep-vein thrombosis	7	0.04	9	0.05	0.78 (0.29–2.10)	0.63

ARISTOTLE : DEMOGRAFIE

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Apixaban (N=9120)	Warfarin (N=9081)
Age — yr		
Median	70	70
Interquartile range	63–76	63–76
Female sex — no. (%)	3234 (35.5)	3182 (35.0)
Region — no. (%)		
North America	2249 (24.7)	2225 (24.5)
Latin America	1743 (19.1)	1725 (19.0)
Europe	3672 (40.3)	3671 (40.4)
Asian Pacific	1456 (16.0)	1460 (16.1)
Systolic blood pressure — mm Hg		
Median	130	130
Interquartile range	120–140	120–140
Weight — kg		
Median	82	82
Interquartile range	70–96	70–95
Prior myocardial infarction — no. (%)	1319 (14.5)	1266 (13.9)
Prior clinically relevant or spontaneous bleeding — no. (%)	1525 (16.7)	1515 (16.7)
History of fall within previous year — no. (%)	386 (4.2)	367 (4.0)
Type of atrial fibrillation — no. (%)		
Paroxysmal	1374 (15.1)	1412 (15.5)
Persistent or permanent	7744 (84.9)	7668 (84.4)
Prior use of vitamin K antagonist for >30 consecutive days — no. (%)	5208 (57.1)	5193 (57.2)
Qualifying risk factors		
Age ≥75 yr — no. (%)	2850 (31.2)	2828 (31.1)
Prior stroke, TIA, or systemic embolism — no. (%)	1748 (19.2)	1790 (19.7)
Heart failure or reduced left ventricular ejection fraction — no. (%)	3235 (35.5)	3216 (35.4)
Diabetes — no. (%)	2284 (25.0)	2263 (24.9)
Hypertension requiring treatment — no. (%)	7962 (87.3)	7954 (87.6)
$CHADS_2$ score		
Mean	2.1±1.1	2.1±1.1

Table 1

r stroke prevention in atrial fibrillation

	ROCKET-AF	ARISTOTLE	ENGAGE-AF-TIMI 48
e daily	Rivaroxaban 20 mg daily	Apixaban 5 mg twice daily	Edoxaban 60 mg daily
e daily	Rivaroxaban 15 mg daily (creatinine clearance 30–49 mL/min)	Apixaban 2.5 mg twice daily	Edoxaban 30 mg daily
)	Warfarin (INR goal 2–3)	Warfarin (INR goal 2–3)	Warfarin (INR goal 2–3)
	55.0 %	62.0 %	
	14,264	18,201	20,500 (estimated)
	Randomized, double-blind, double-dummy	Randomized, double-blind, double-dummy	
	3.5	2.1	
	0.0 %	34.0 %	
	13.0 %	35.8 %	
	87.0 %	30.2 %	
	54.8 %	19.4 %	
	62.5 %	35.4 %	
	40.0 %	25.0 %	
	90.5 %	87.5 %	
	17.3 %	14.2 %	
	73	70	
	39.7 %	35.2 %	
	36.5 %	30.9 %	
	62.4 %	57.2 %	
	80.9 %	84.7 %	
	17.7 %	15.3 %	
	1.4 %		
	0.0 %		
	20.8 %		
	79.2 %		
factor	Non-valvular		
odynamically relevant valve disease	Hemodynami repair, comm		
>12months	Event driven		
nic embolism	Composite: st		
al infarction	1		
y embolism			
zation			

Hazard ratios for NOACs compared with warfarin

	RE-LY	ROCKET-AF	ARISTOTLE
Stroke and systemic embolism	0.65 (0.52–0.81)	0.88 (0.75–1.03)	0.79 (0.66–0.95)
Ischemic or unspecified stroke	0.76 (0.60–0.98)	0.91 (0.73–1.13)	0.92 (0.74–1.13)
Hemorrhagic stroke	0.26 (0.14–0.49)	0.59 (0.37–0.93)	0.51 (0.35–0.75)
Myocardial infarction	1.27 (0.94–1.71)	0.81 (0.63–1.06)	0.88 (0.66–1.17)
All-cause mortality	0.88 (0.77–1.00)	0.85 (0.70–1.02)	0.89 (0.80–0.998)
Major bleeding	0.93 (0.81–1.07)	1.04 (0.90–1.20)	0.69 (0.60–0.80)
Gastrointestinal bleeding	1.50 (1.19–1.89)	1.47 (1.20–1.81)	0.89 (0.70–1.15)
Intracranial bleeding	0.40 (0.27–0.60)	0.67 (0.47–0.93)	0.42 (0.30–0.58)

e ≥ 2

is, mechanical valve

olism

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Clinical strategies for selecting oral anticoagulants in patients with atrial fibrillation

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➢ Uzávěr LAA: Proti

PROTECT – AF, 4-leté výsledky

Table 2. Intention-to-Treat Primary Efficacy and Safety Outcomes According to Treatment Group by Bayesian Model

Event	Device Group (n = 463)		Warfarin Group (n = 244)		Device/Warfarin Rate Ratio (95% Credible Interval)
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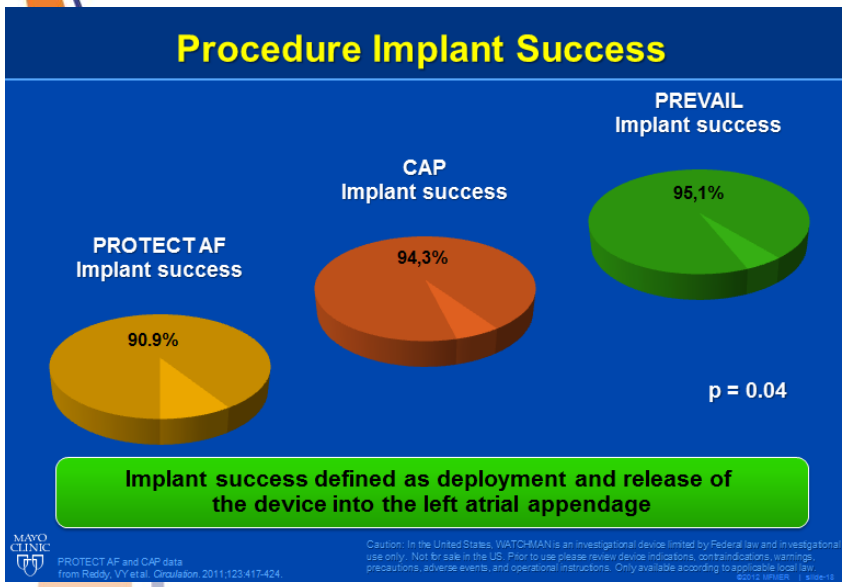
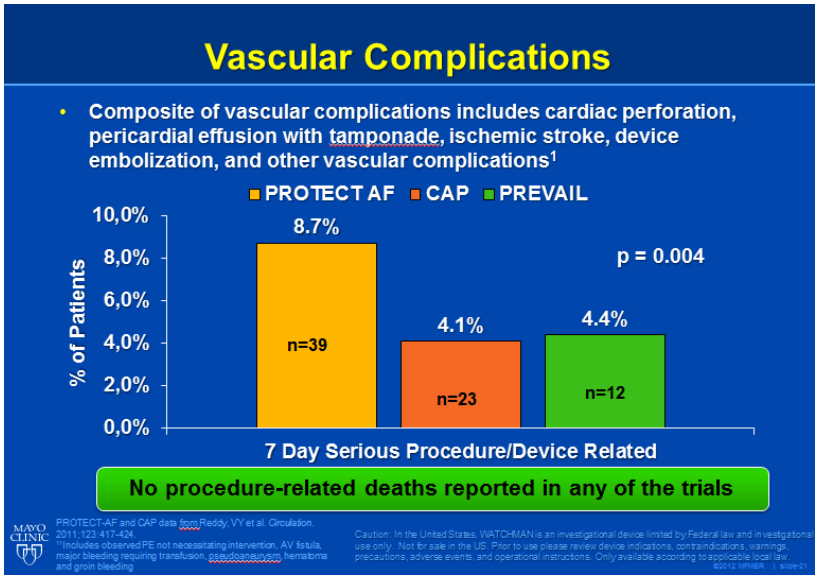
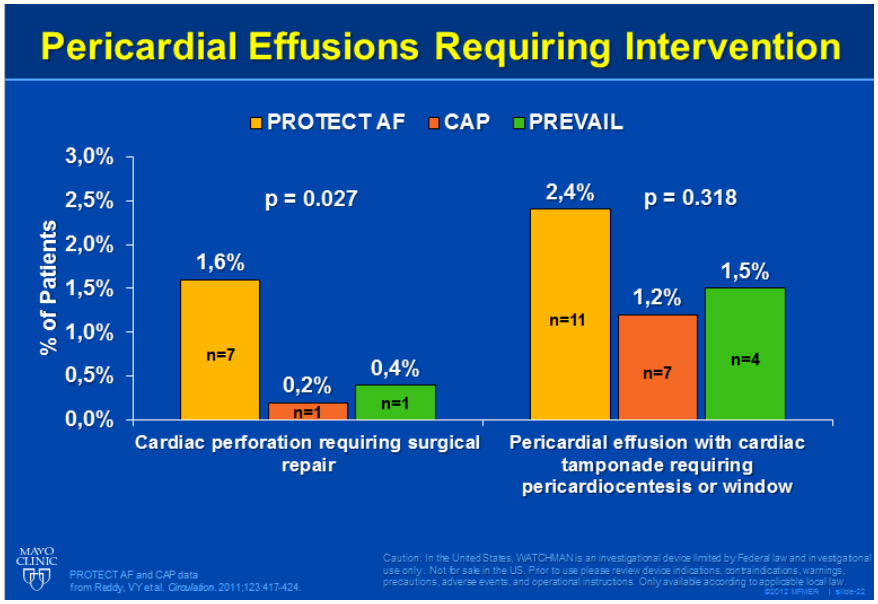
Stroke	26/1720.7	1.5 (1.0-2.2)	20/900.9	2.2 (1.3-3.1)	0.68 (0.42-1.37)
Ischemic	24/1720.8	1.4 (0.9-2.1)	10/904.2	1.1 (0.5-1.7)	1.26 (0.72-3.28)
Hemorrhagic	3/1774.2	0.2 (0.0-0.4)	10/916.2	1.1 (0.5-1.8)	0.15 (0.03-0.49)
Disabling[c]	8/1771.3	0.5 (0.2-0.8)	11/912.7	1.2 (0.6-1.9)	0.37 (0.15-1.00)
Nondisabling[c]	18/1723.7	1.0 (0.7-1.7)	9/907.7	1.0 (0.4-1.7)	1.05 (0.54-2.80)
Systemic embolization	3/1773.6	0.2 (0.0-0.4)	0/919.5	0	NA
Cardiovascular or unexplained death	17/1774.3	1.0 (0.6-1.5)	22/919.4	2.4 (1.4-3.4)	0.40 (0.23-0.82)
Primary safety end point[d]	60/1666.2	3.6 (2.8-4.6)	27/878.2	3.1 (2.0-4.3)	1.17 (0.78-1.95)

JAMA. 2014;312(19):1988-1998. doi:10.1001/jama.2014.15192

Proč uzavírat ouško levé síně?







➢ Proč uzavírat ouško levé síně?

PREVAIL
Control (Warfarin) Group Performance

- In spite of the high average $CHADS_2$ score of 2.6 in the control group, the observed rate of stroke in the PREVAIL Control group was lower than in other published warfarin studies
- PREVAIL control group rate = 0.7 (95% CI 0.1, 5.1)
  - Wide confidence bounds due to small number of patients with 18-months of follow-up

Trial	Control (Warfarin) Group Stroke, Systemic Embolism Rate (Per 100 PY)
PROTECT AF[1]	1.6
RE-LY (Dabigatran)[2]	1.7
ARISTOTLE (Apixaban)[3]	1.6
ROCKET AF (Rivaroxaban)[4]	2.2
PREVAIL	0.7

Results are preliminary; final validation not yet complete

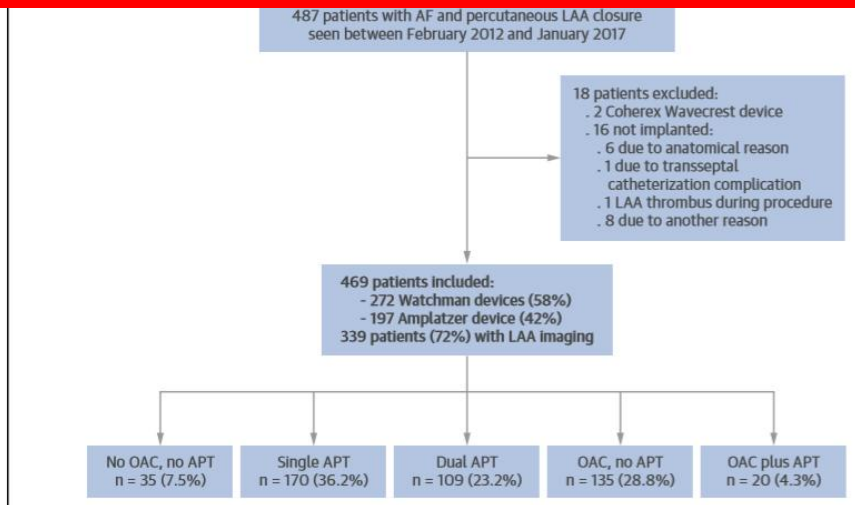
MAYO CLINIC

[1]Ischemic stroke rate from Holmes et al. *Lancet* 2009; 374:534-42
[2]Connolly et al. *N Engl J Med* 2009; 361:1139-51
[3]Granger et al. *N Engl J Med* 2011; 365:981-92
[4]Patel et al. *N Engl J Med* 2011; 365:883-91

➢ Uzávěr LAA: Proti

	All Patients (N = 487)	Nitinol Cage (n = 272)	Nitinol Plug (n = 197)	(Nitinol Cage vs. Nitinol Plug)
Age, yrs	74.9 ± 8.9	74.6 ± 9.2	75.6 ± 8.5	0.25
Men	299 (61.4)	169 (62.1)	112 (61.9)	0.99
Medical history				
Hypertension	328 (84.1)	217 (84.1)	102 (85.7)	0.69
Diabetes mellitus	119 (30.6)	76 (29.6)	39 (32.8)	0.53
Ischemic stroke	179 (41.1)	102 (38.6)	69 (44.2)	0.26
Vascular disease	141 (43.4)	85 (44.0)	50 (42.0)	0.73
Permanent AF	244 (51.2)	132 (49.6)	102 (52.0)	0.61
LV ejection fraction, %	55.9 ± 10.0	56.4 ± 9.3	55.4 ± 10.4	0.32
LAA maximum diameter, mm (n = 353)	21.9 ± 4.4	21.4 ± 4.1	22.6 ± 4.9	0.01
CHA_2DS_2-VASc score	4.5 ± 1.4	4.4 ± 1.5	4.7 ± 1.2	0.008
HAS-BLED score	3.7 ± 1.0	3.7 ± 1.0	3.8 ± 1.0	0.08
Indication				
Previous bleeding	426 (90.1)	237 (89.4)	174 (91.1)	0.55
Contraindication to OAC	345 (72.8)	199 (74.8)	136 (71.2)	0.40
Recurrent ischemic stroke	25 (5.3)	18 (6.8)	5 (2.6)	0.05
LAA closure device				
Nitinol cage	272 (55.9)	–	–	–
Nitinol plug	197 (40.5)	–	–	–
WaveCrest	2 (0.4)	–	–	–
Implantation failure	16 (3.3)	–	–	–
Antithrombotic therapy at discharge				
No OAC, no APT	37 (7.7)	9 (3.3)	26 (13.2)	<0.0001
Single APT	171 (35.8)	82 (30.1)	88 (44.7)	0.002
Dual APT	110 (23.0)	63 (23.2)	46 (23.4)	0.96
OAC, no APT	138 (28.9)	101 (37.1)	34 (17.3)	<0.0001
OAC plus APT	22 (4.6)	17 (6.3)	3 (1.5)	0.009
LAA imaging during follow-up*	340 (72.1)	238 (87.5)	101 (51.3)	<0.0001

Values are mean ± SD or n (%). Percentages calculated from available data. *In patients with implanted device.
AF = atrial fibrillation; APT = antiplatelet therapy; CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stoke or transient ischemic attack or thromboembolism, vascular disease, age 65 to 74 years, and female sex; HAS-BLED = hypertension, abnormal renal and liver function, stroke, bleeding, labile international normalized ratio, elderly (age <65 years), drug or alcohol use; LAA = left atrial appendage; LV = left ventricular; OAC = oral anticoagulation.



The study cohort from RELEXAO (REgistry on Real-Life EXperience With Left Atrial Appendage Occlusion: NCT03279406) between February 1, 2007 and January 31, 2017 is shown. The proportions of the different devices for left atrial appendage (LAA) closure and patients with left atrial appendage imaging are shown, as well as the different antithrombotic regimens at hospital discharge. AF = atrial fibrillation; APT = antiplatelet therapy; OAC = oral anticoagulation.

➢ Uzávěr LAA: Proti

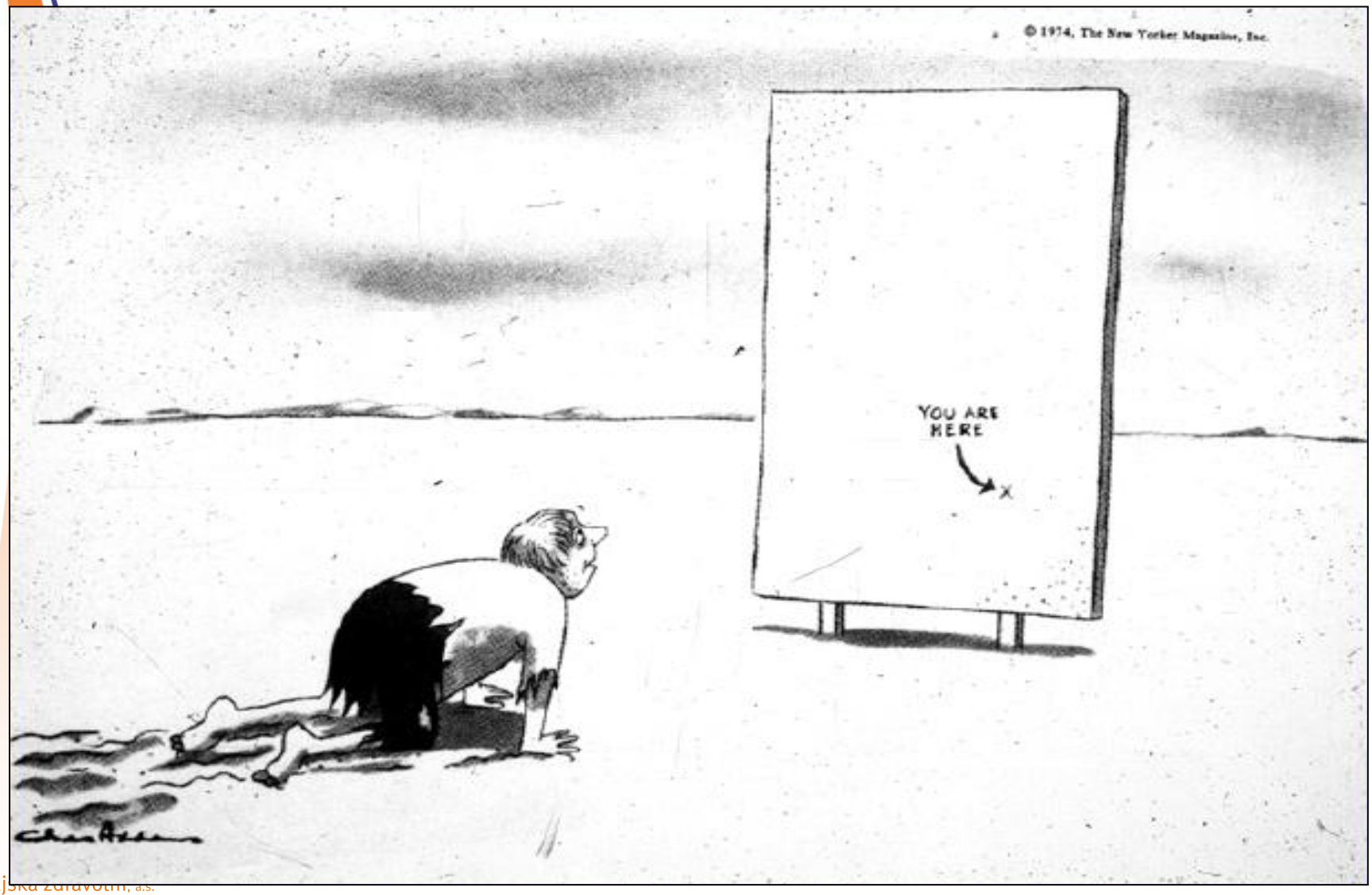
- "So far, there is no 'free lunch'.

Cena:

- ***66 (67) kč/den***
- ***24090 (24 455) kč/rok***

Eugene Braunwald

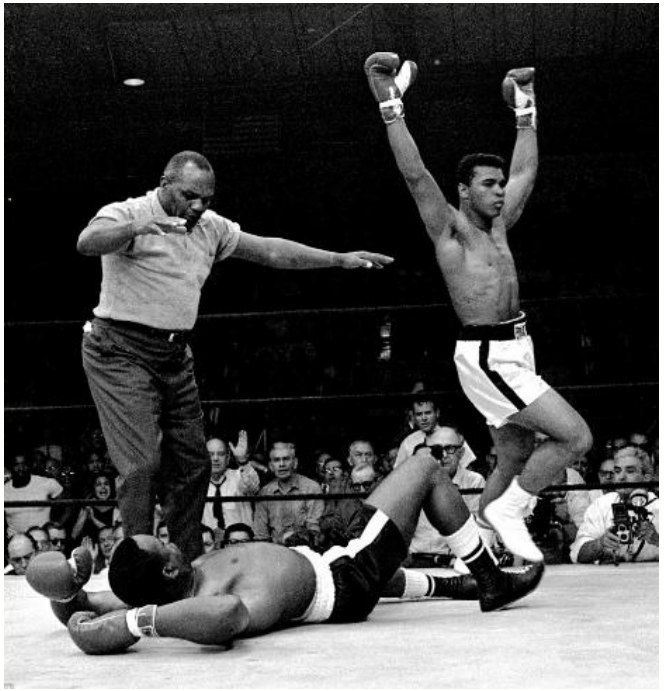
➢ Uzávěr LAA: Proti



Doporučené postupy ESC 2016

Recommendations for occlusion or exclusion of the left atrial appendage

Recommendations	Class[a]	Level[b]	Ref[c]
After surgical occlusion or exclusion of the LAA, it is recommended to continue anticoagulation in at-risk patients with AF for stroke prevention.	I	B	461, 462
LAA occlusion may be considered for stroke prevention in patients with AF and contra-indications for long-term anticoagulant treatment (e.g. those with a previous life-threatening bleed without a reversible cause).	IIb	B	449, 453, 454
Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing cardiac surgery.	IIb	B	463
Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients undergoing thoracoscopic AF surgery.	IIb	B	468



	(n = 26)	(n = 313)	p Value
Age, yrs	76.1 ± 8.9	74.2 ± 9.0	0.31
Men	16 (61.5)	185 (59.1)	0.81
Medical history			
Hypertension	19 (79.2)	259 (86.3)	0.33
Diabetes mellitus	6 (25.0)	88 (29.4)	0.65
Ischemic stroke	14 (58.3)	129 (41.9)	0.12
Permanent AF	11 (42.3)	155 (49.7)	0.47
Previous bleeding	23 (92.0)	276 (90.2)	0.77
CHA_2DS_2-VASc score	4.7 ± 1.7	4.5 ± 1.4	0.49
HAS-BLED score	3.5 ± 1.3	3.7 ± 1.0	0.26
LV ejection fraction, %	53.1 ± 12.2	56.7 ± 9.4	0.15
LAA maximum diameter, mm (n=353)	22.2 ± 4.9	21.4 ± 4.3	0.48
Nitinol plug device	13 (12.9)	88 (87.1)	0.02
Nitinol cage device	13 (5.5)	225 (94.5)	0.02
Antithrombotic therapy at discharge			
No OAC, no APT	4 (15.4)	14 (4.5)	0.02
Single APT	11 (42.3)	91 (29.1)	0.15
Dual APT	1 (3.8)	81 (25.9)	0.01
OAC, no APT	10 (38.5)	108 (34.5)	0.68
OAC plus APT	0 (0.0)	19 (6.1)	0.23
Leaks			
Peridevice leakage	1 (3.8)	50 (16.0)	0.10
Peridevice leakage >5 mm	0 (0.0)	17 (5.4)	0.22

Values are mean ± SD or n (%). *Analysis restricted to patients with LAA imaging during follow-up.
Abbreviations as in Table 1.

Proti

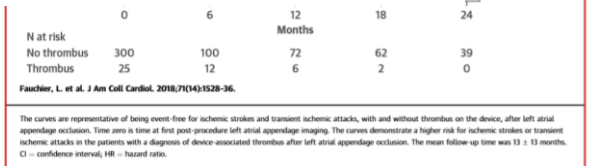
p Value

0.02
0.03
0.09
0.06
0.03
0.02

0.01
0.04
0.09
0.75
0.54
0.33

up. For prediction
charge after LAA
st post-procedure

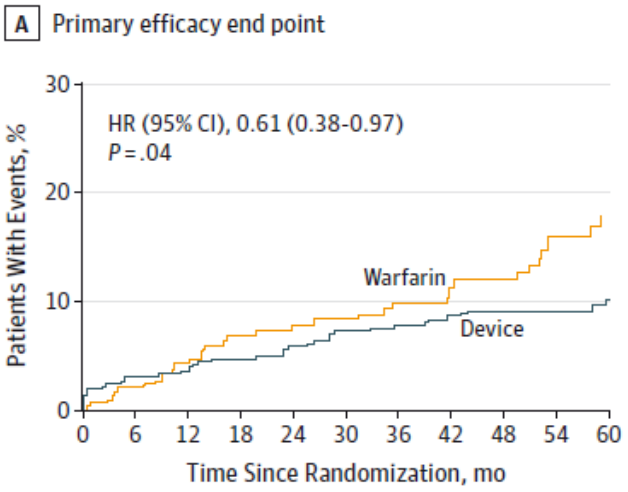
ons as in Table 1.



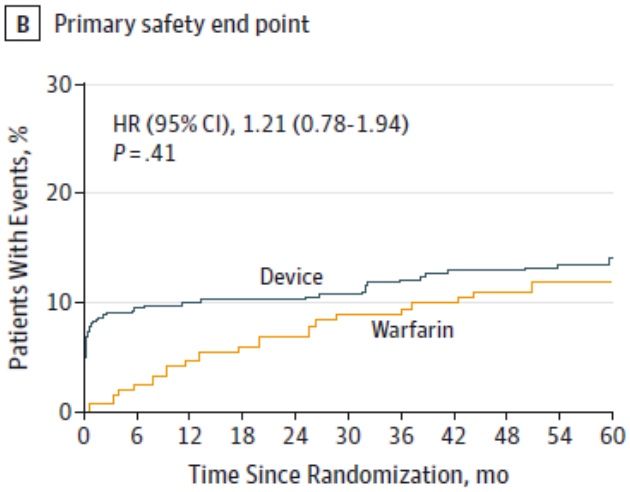
➢ Uzávěr LAA: Proti

▪ PROTECT AF/ PREVAIL

Primary efficacy endpoint:
CMP, SE, CVD



Primary safety endpoint:
Device related (CT,DE,CMP) + major bleeding



JAMA. 2014;312(19):1988-1998. doi:10.1001/jama.2014.15192

TABLE 3 Efficacy Rates at 5 Years (2:1 Randomization)

	PROTECT AF Subjects					PREVAIL-Only Subjects				
	Device Group (n = 463)		Control Group (n = 244)			Device Group (n = 269)		Control Group (n = 138)		
	No. of Events	Rate*	No. of Events	Rate*	p Value	No. of Events	Rate*	No. of Events	Rate*	p Value
Primary efficacy: stroke/SE/CV death	40/1,787.7	2.24	34/929.4	3.66	0.04	37/1,038.3	3.65%	15/530.4	2.94%	0.47
All stroke	26/1,781.7	1.46	20/929.4	2.15	0.23	19/1,042.4	1.97%	7/530.4	1.29%	0.32
Ischemic stroke	24/1,781.7	1.35	10/932.8	1.07	0.49	17/1,043.1	1.68%	4/533.3	0.73%	0.13
Hemorrhagic stroke	3/1,837.7	0.16	10/945.6	1.06	0.005	2/1,084.6	0.18%	3/538.0	0.54%	0.23
Systemic embolism	3/1,837.1	0.16	0	N/A	N/A	1/1,080.6	0.09%	0/540.9	N/A	N/A
CV/unexplained death	19/1,843.2	1.03	22/948.9	2.32	0.009	18/1,084.7	1.79%	10/540.9	1.98%	0.76

*Events are per 100 patient-yrs.

CV = cardiovascular; SE = systemic embolism; other abbreviations as in Table 1.

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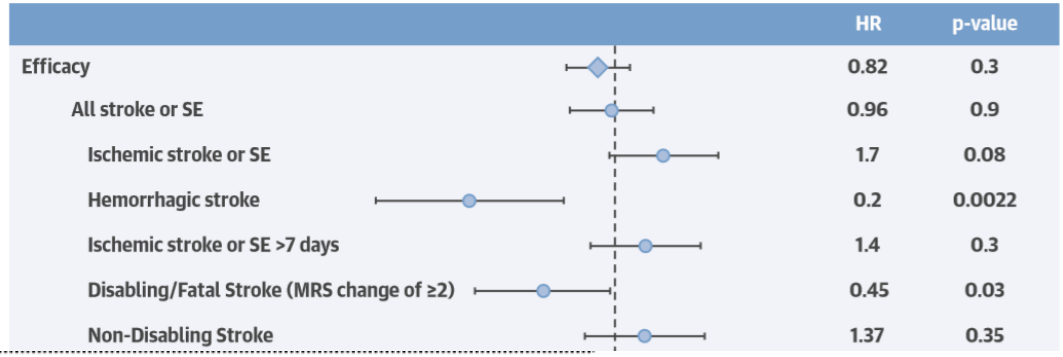
CENTRAL ILLUSTRATION Stroke Prevention in Nonvalvular Atrial Fibrillation With LAA Closure



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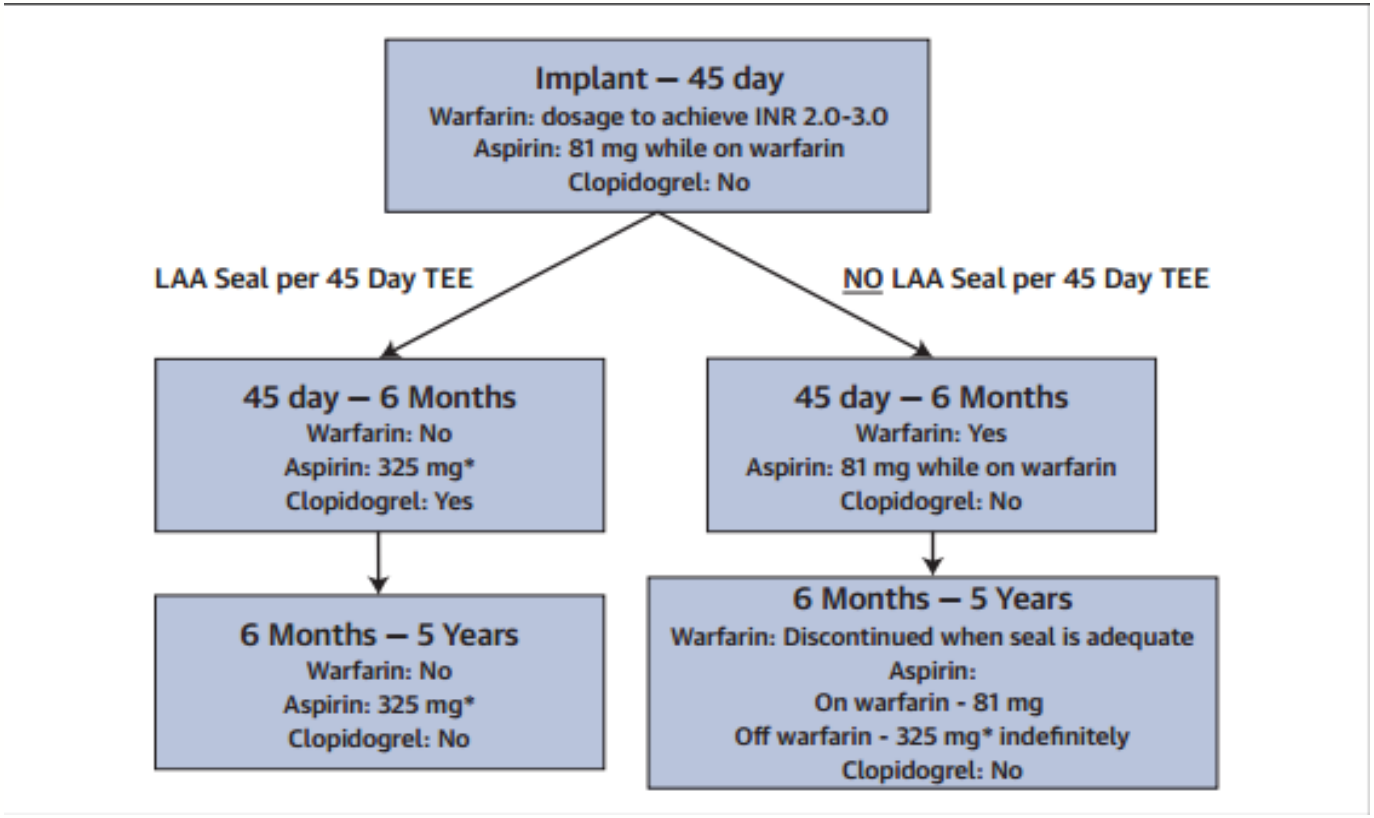
➢ Uzávěr LAA: Proti

PROTECT AF



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➢ Uzávěr LAA: Proti

PROTECT – AF, 2-leté výsledky

Table 2. Efficacy and Safety Results

	Device		Control		
	Events/ Patient-Years	Observed Rate: Events per 100 Patient-Years (95% CrI)	Events/Patient-Years	Observed Rate: Events per 100 Patient-Years (95% CrI)	Rate Ratio (Intervention/Control) (95% CrI)
Primary efficacy	31/1025.7	3.0 (2.1–4.3)	24/562.7	4.3 (2.6–5.9)	0.71 (0.44–1.30)
Ischemic stroke	19/1026.3	1.9 (1.1–2.9)	8/564.9	1.4 (0.6–2.4)	1.30 (0.66–3.60)
Cardiovascular/unexplained death	11/1050.4	1.0 (0.5–1.8)	16/573.2	2.8 (1.5–4.2)	0.38 (0.18–0.85)
Hemorrhagic stroke	3/1050.3	0.3 (0.1–0.7)	7/571.0	1.2 (0.5–2.3)	0.23 (0.04–0.79)
Systemic embolism	3/1049.8	0.3 (0.1–0.7)	0/573.2	0	…
All stroke	21/1026.3	2.0 (1.3–3.1)	15/562.7	2.7 (1.5–4.1)	0.77 (0.42–1.62)
All-cause mortality	34/1050.4	3.2 (2.3–4.5)	26/573.2	4.5 (2.8–6.2)	0.71 (0.46–1.28)
Primary safety	54/979.9	5.5 (4.2–7.1)	20/554.6	3.6 (2.2–5.3)	1.53 (0.95–2.70)

Clinical Trial Registration:—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00129545. **(*Circulation*. 2013;127:720-729.)**