Der Vorhofohr-Okkluder zur Schlaganfallprävention bei Vorhofflimmern: Der Niereninsuffiziente im Fokus

Berliner Dialyse Seminare, 8.12.2018

HERZ IM ZENTRUM
HANNOVER
KARDIOLOGIE | RHYTHMOLOGIE
ELEKTROPHYSIOLOGIE

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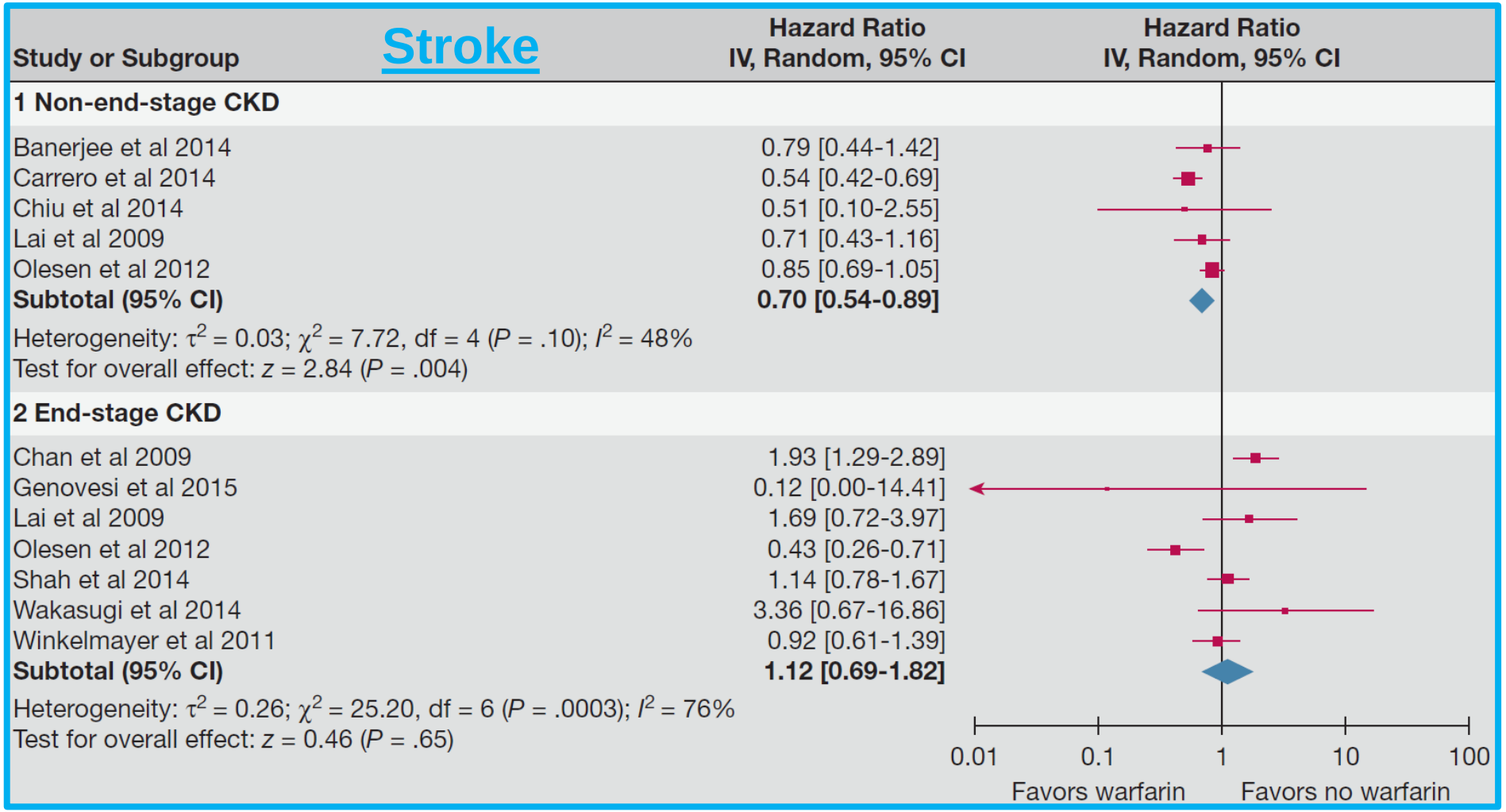
Disclosures

Vortragstätigkeiten: Amgen, Bayer Healthcare, Berlin-Chemie, Boehringer-Ingelheim, BMS, Boston, Medtronic, Novartis, Pfizer, Sanofi, St. Jude Medical

Beratertätigkeit: Boston, Novartis

Orale Antikoagulation (VKA) bei Vorhofflimmern und Niereninsuffizienz

Dahal et al., Chest 2016; 149: 951



48500 Patienten, davon 41767 mit Niereinsuffizienz und 6767 mit Nierenersatztherapie, 1,6 Jahre bis 15 Jahren Nachbeobachtung, >11600 Patienten mit Warfarin.

Orale Antikoagulation (VKA) bei Vorhofflimmern und Niereninsuffizienz

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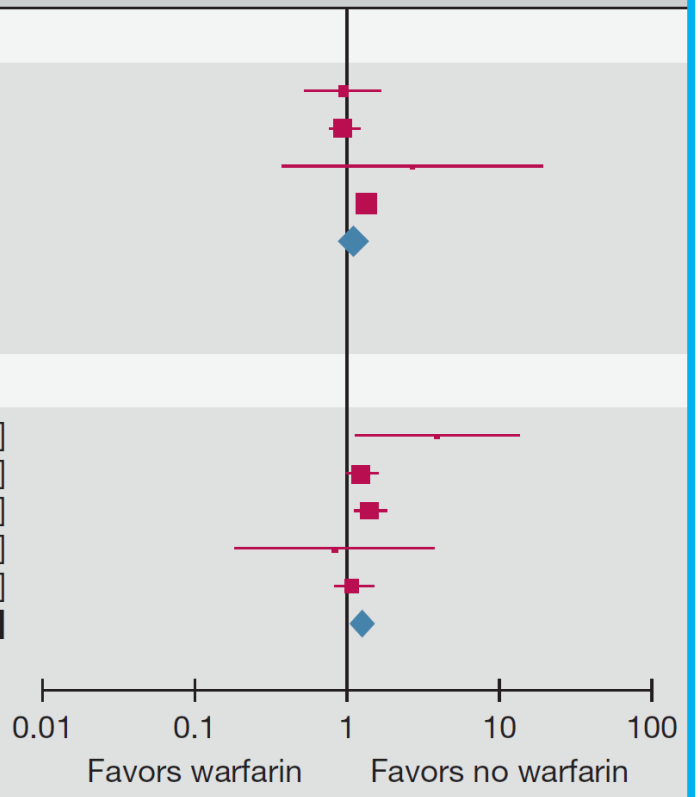
Majorblutung

Study or Subgroup	Hazard Ratio IV, Random, 95% CI
1 Non-end-stage CKD	
Banerjee et al 2014	0.96 [0.55-1.67]
Carrero et al 2014	0.97 [0.78-1.21]
Chiu et al 2014	2.72 [0.38-19.30]
Olesen et al 2012	1.36 [1.17-1.58]
Subtotal (95% CI)	**1.15 [0.88-1.49]**
Heterogeneity: $\tau^2 = 0.04$; $\chi^2 = 7.55$, df = 3 ($P = .06$); $I^2 = 60\%$	
Test for overall effect: $z = 1.00$ ($P = .31$)	
2 End-stage CKD	
Genovesi et al 2015	3.96 [1.15-13.64]
Olesen et al 2012	1.27 [1.01-1.60]
Shah et al 2014	1.44 [1.13-1.84]
Wakasugi et al 2014	0.85 [0.19-3.80]
Winkelmayer et al 2011	1.11 [0.83-1.48]
Subtotal (95% CI)	**1.30 [1.08-1.56]**
Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 5.29$, df = 4 ($P = .26$); $I^2 = 24\%$	
Test for overall effect: $z = 2.84$ ($P = .005$)	



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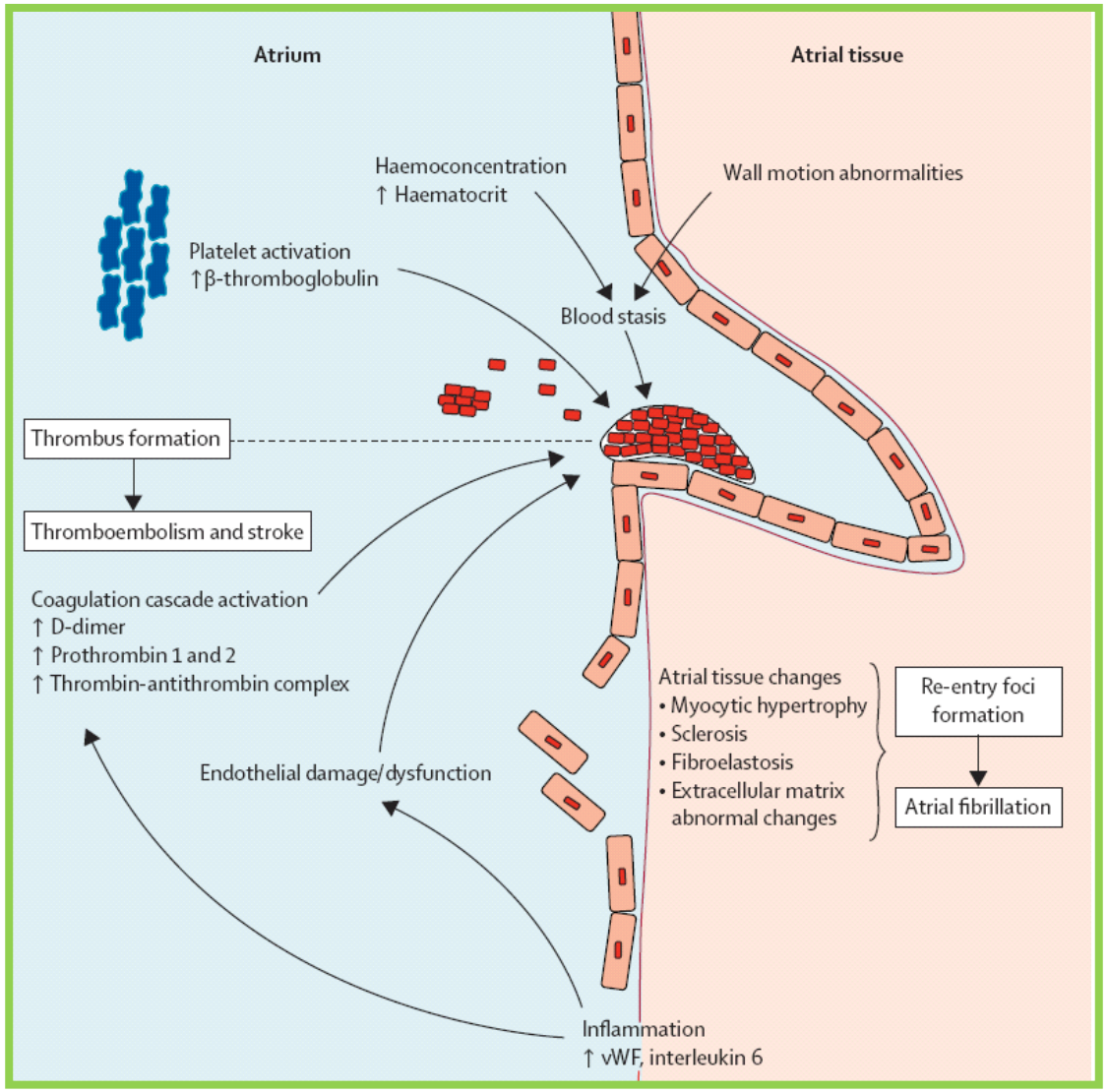
ESC-Leitlinie 2016: Vorhofflimmern und Niereninsuffizienz

Kirchhof et al., Eur. Heart J 2016

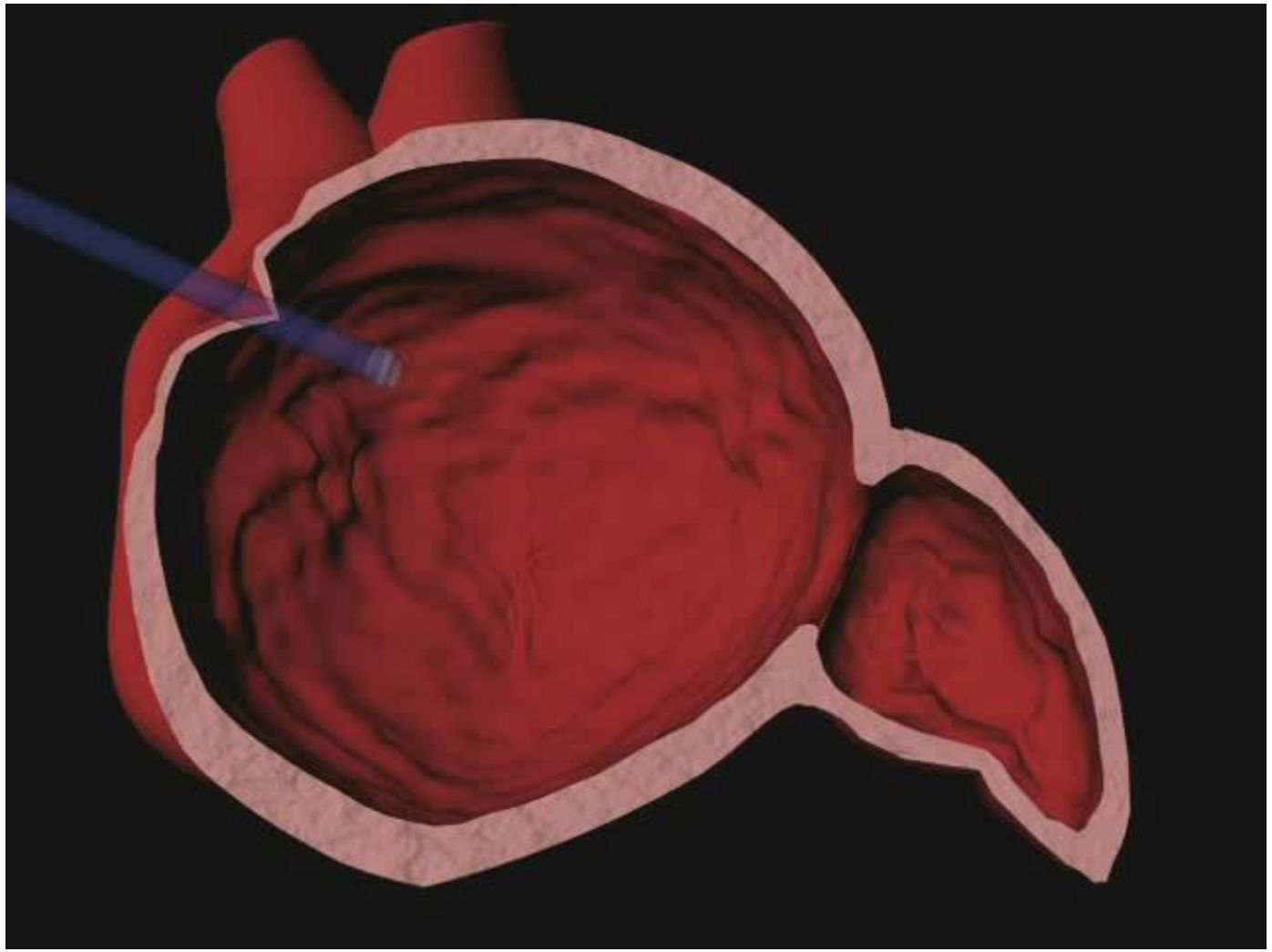
„**There are no randomized trials assessing OAC in haemodialysis patients, and no controlled trials of NOACs in patients with severe CKD** (CrCl ,25–30 mL/min). **Warfarin use** was associated either with **a neutral or increased risk of stroke** in database analyses of patients on dialysis, including a population-based analysis in Canada (adjusted HR for stroke 1.14; 95% CI 0.78–1.67, adjusted HR for bleeding 1.44; 95% CI 1.13–1.85). In contrast, data from Denmark suggest a benefit of OAC in patients on renal replacement therapy (423) **Hence, controlled studies of anticoagulants (both VKAs and NOACs) in AF patients on dialysis are needed.**“

Der Vorhofohrverschluß: Das Konzept

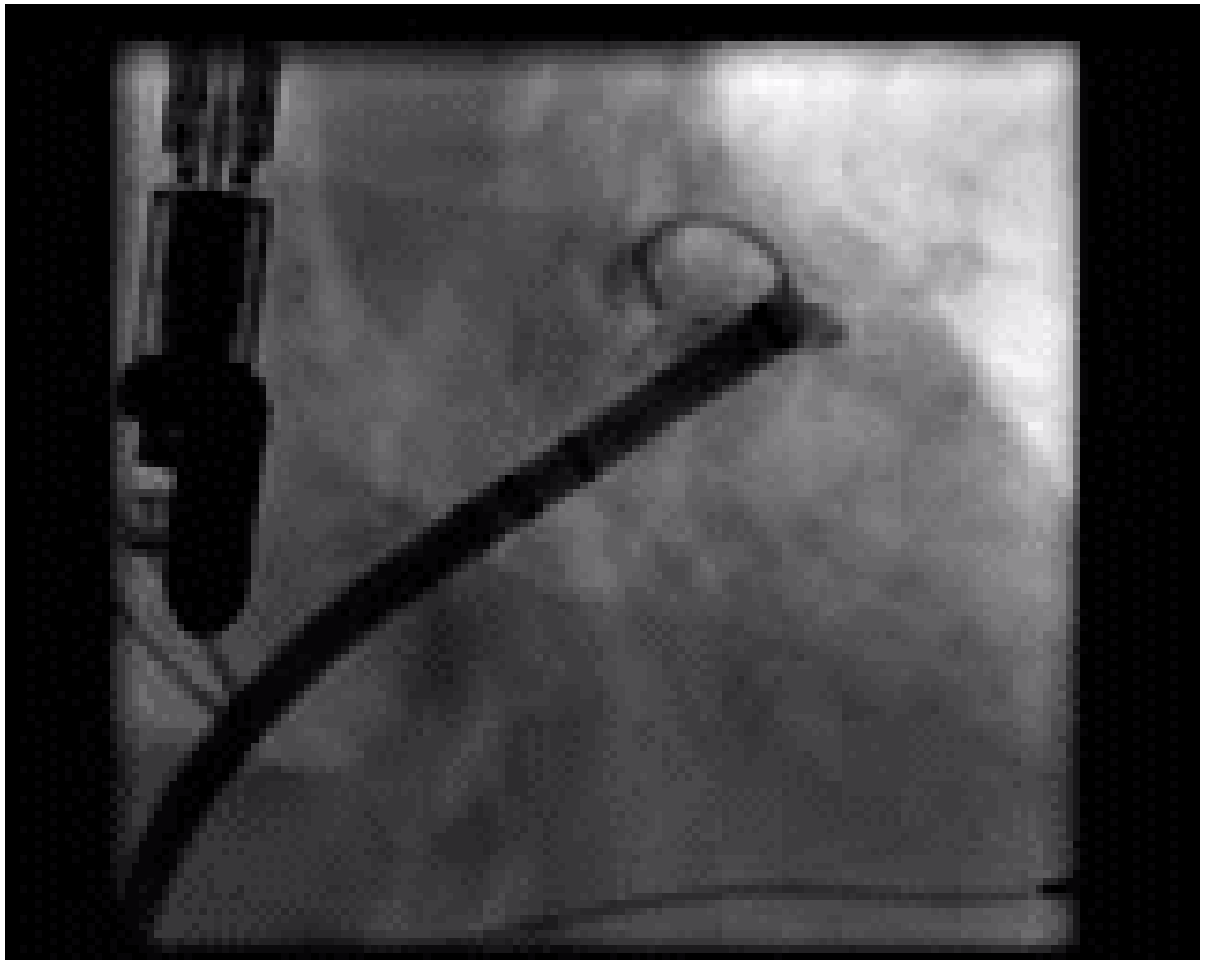
Watson et al., Lancet 2009; 373:155



Der Vohofohrverschluß: Das Konzept



Der Vohofohrverschluß: Ein Beispiel



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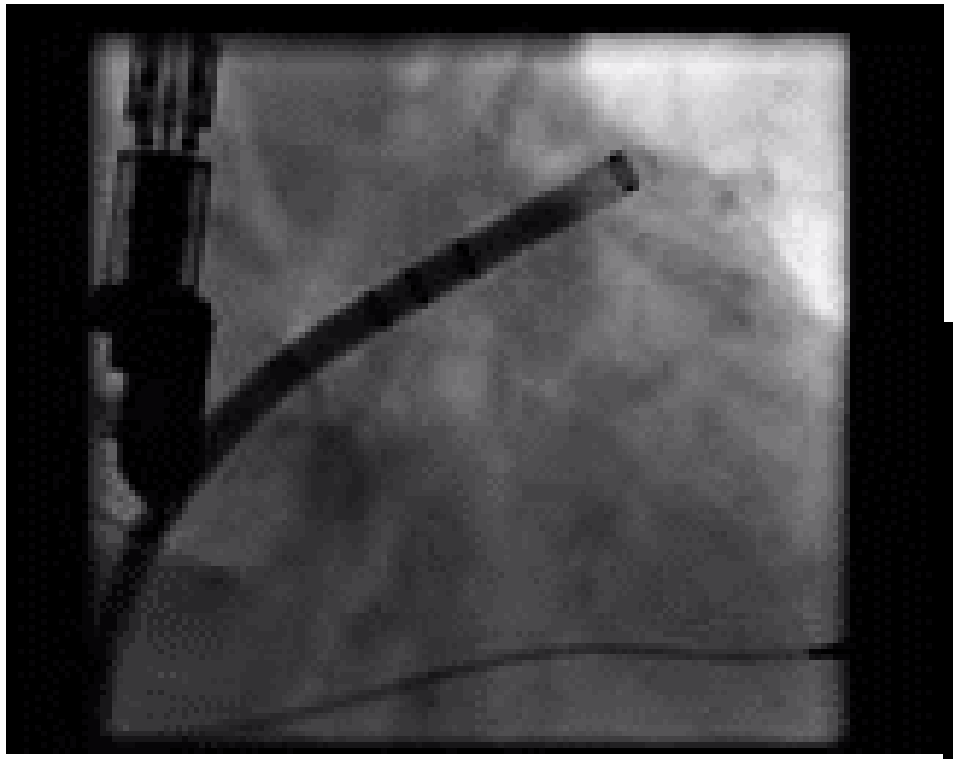

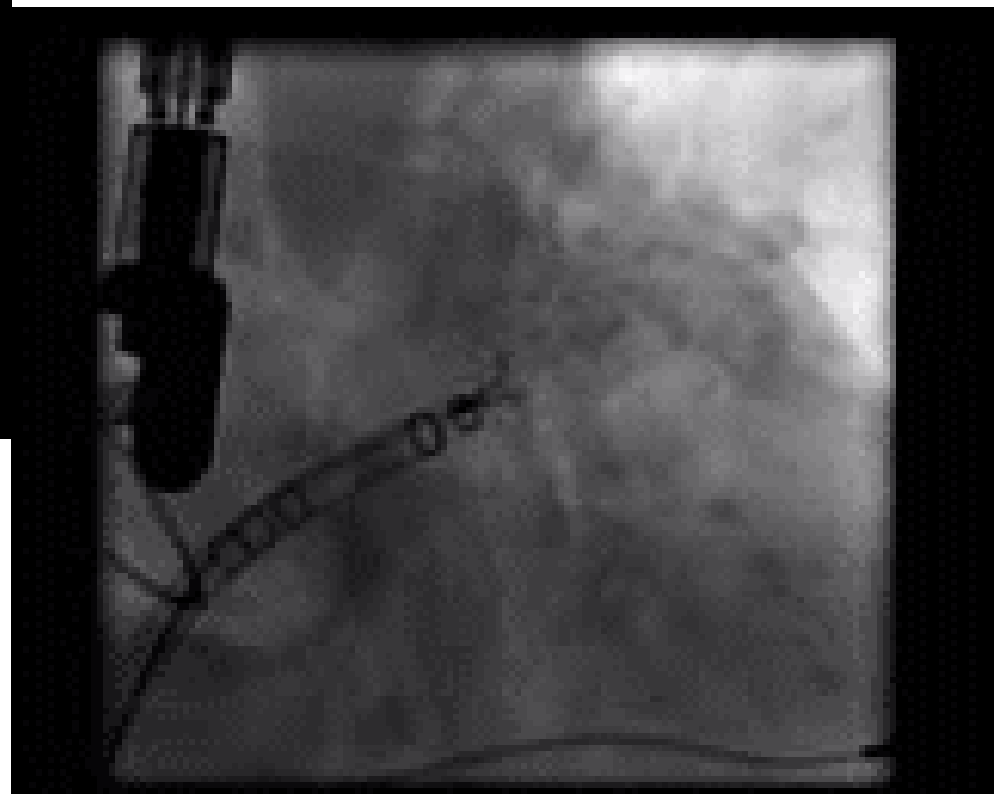

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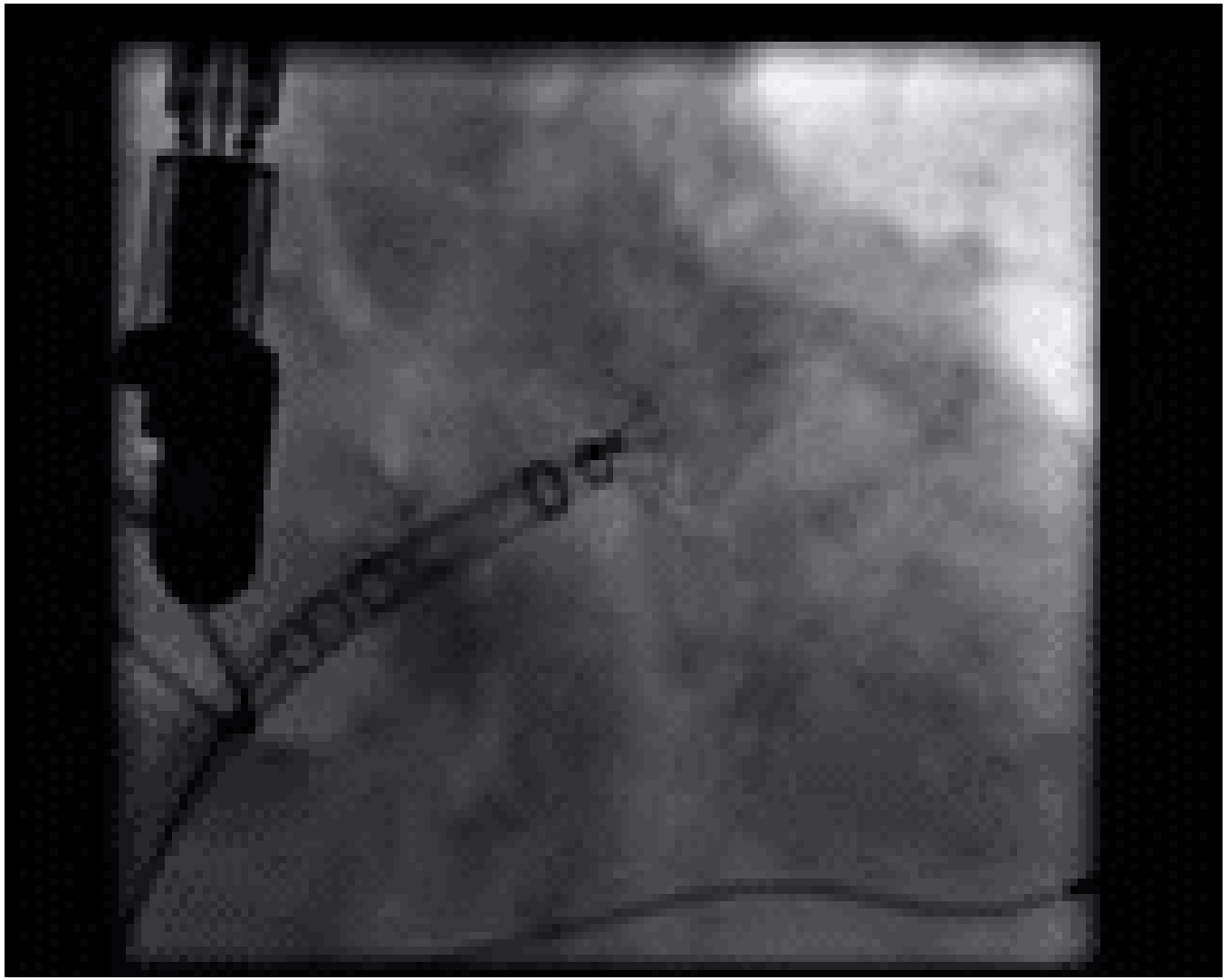
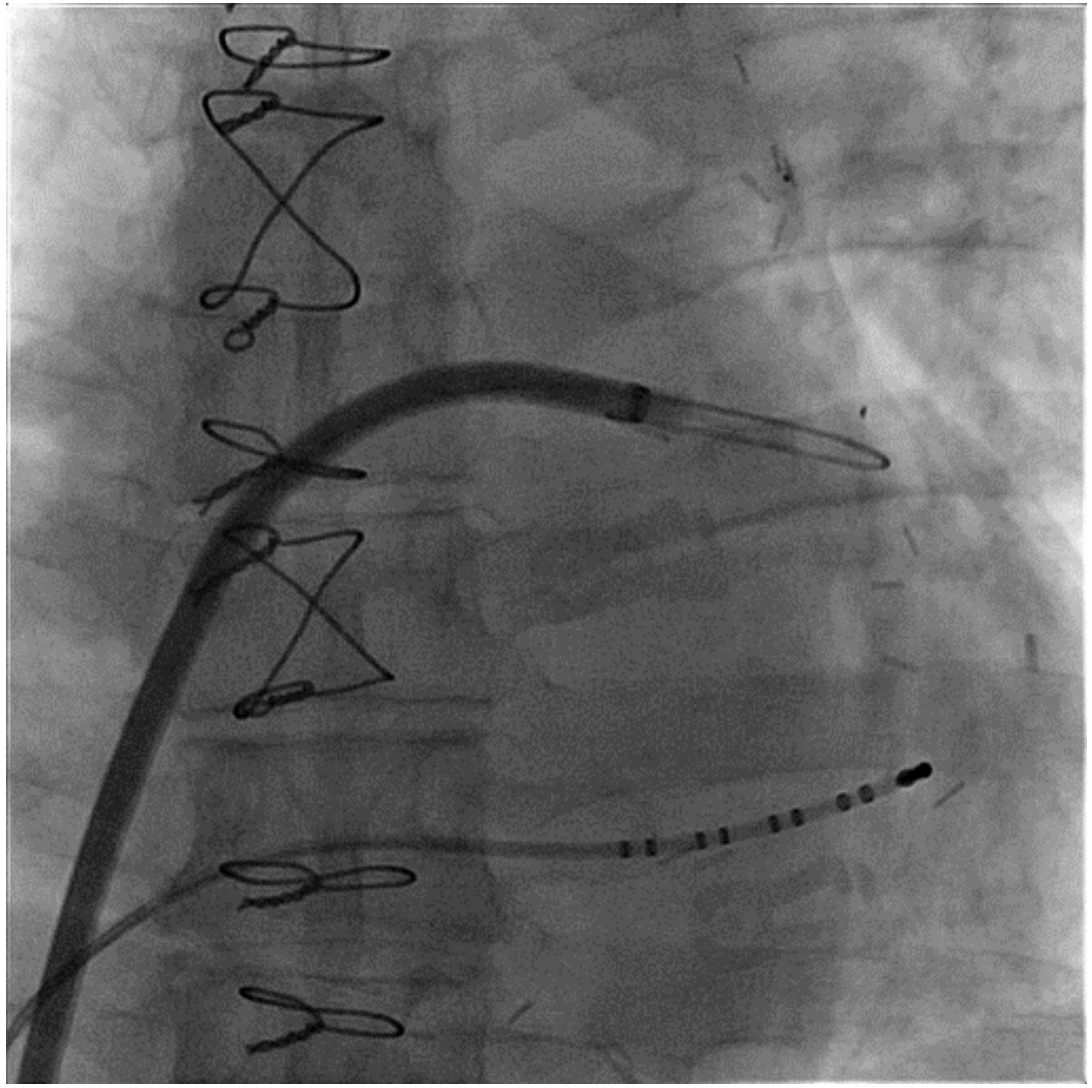
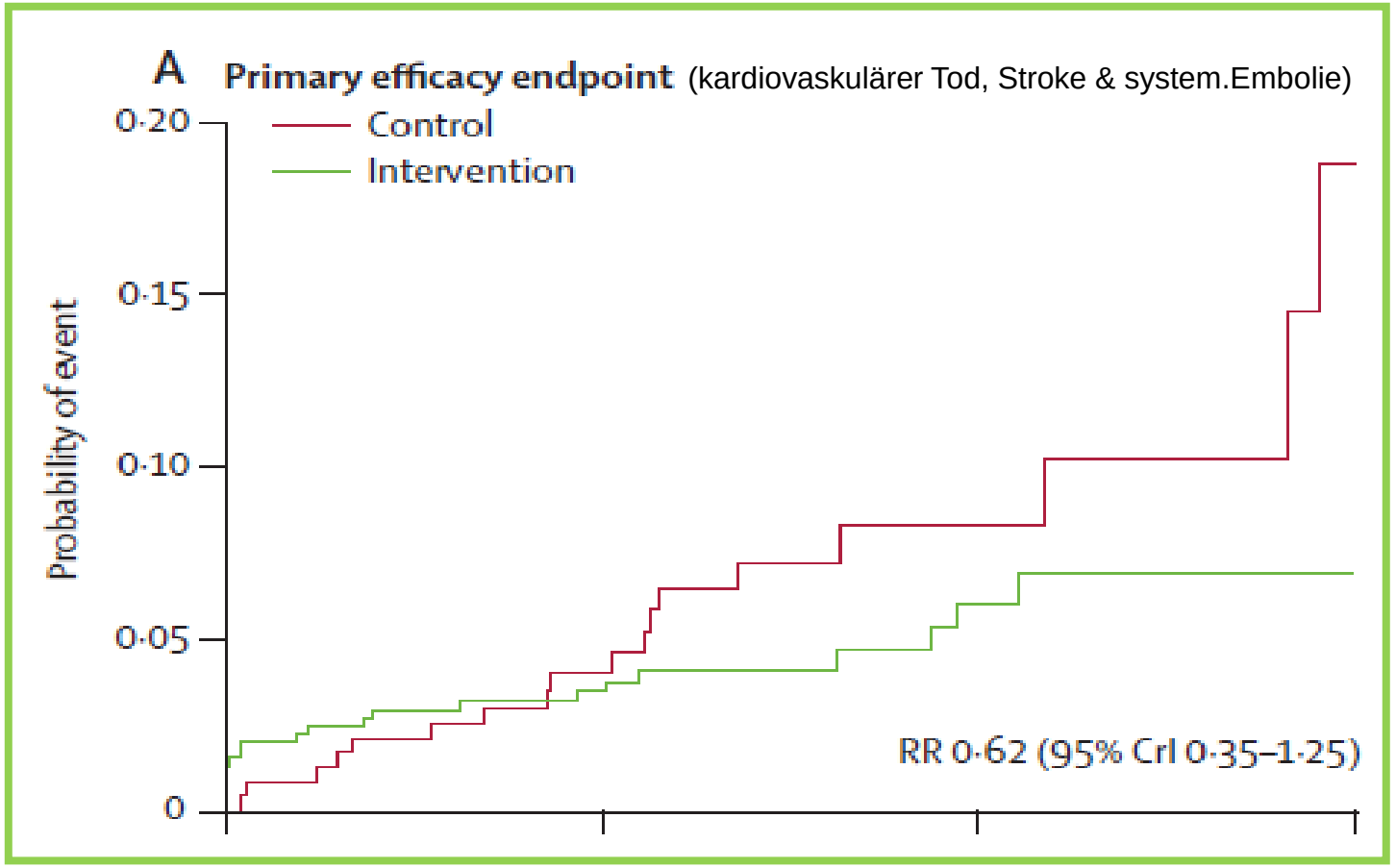


Der Vohofohrverschluß durch den Chirurg



Vorhofohrverschluß: Die Studie(n)

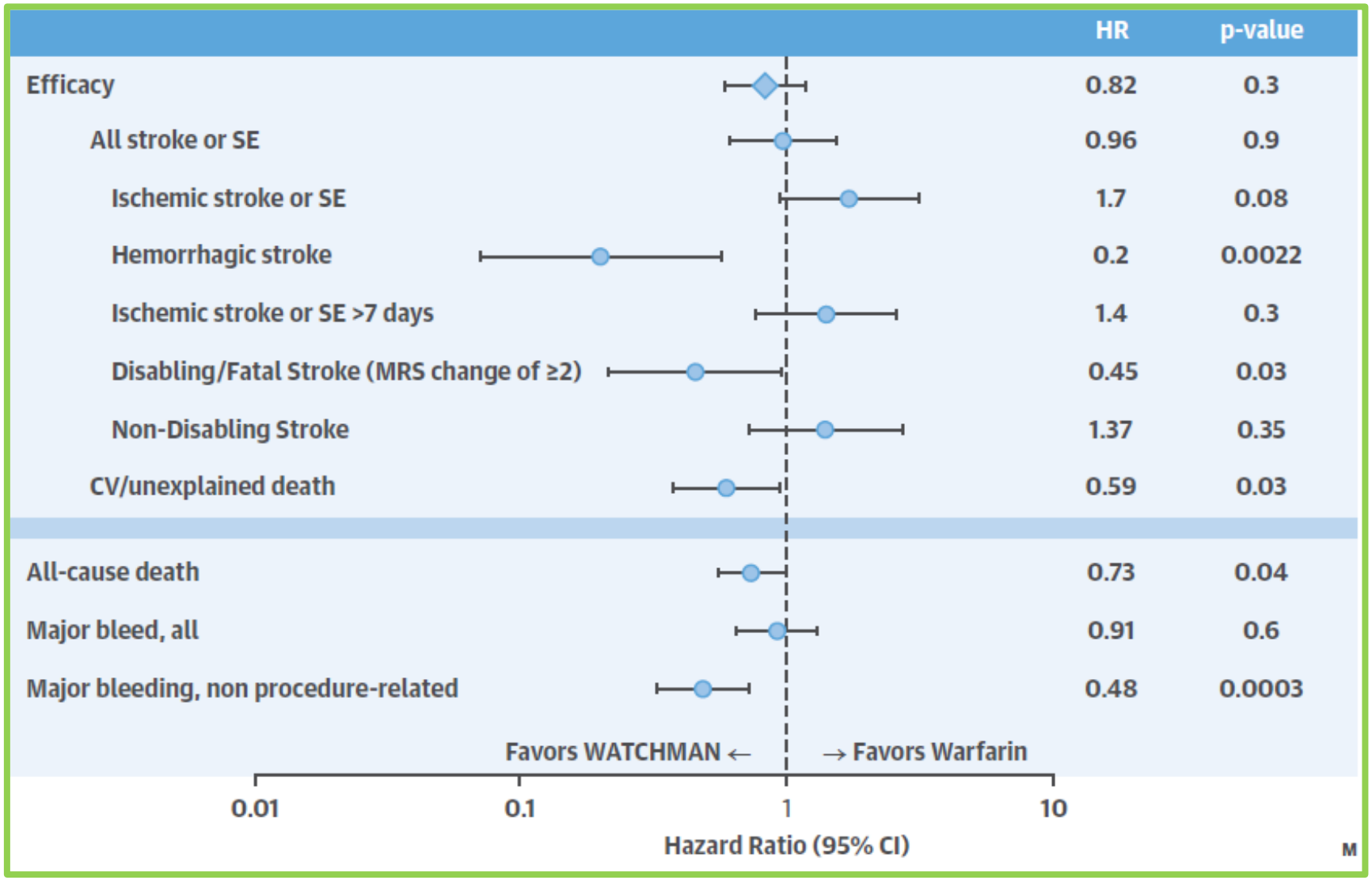
Holmes D. et al., LANCET 2009; 374: 534



463 Patienten mit LAA-Okklusion únd 244 Warfarin: 72 bzw. 73Jahre alt, 70% Männer, >60% CHADS2-Score ≥ 2 , 18 bzw. 20% Hx stroke, ~40% > 1 Jahr Warfarin, 40% paroxysmal, 35% permanent AF, EF 57%. 91% erfolgreiche Implantation, 91% nach 6 Monaten frei von leaks und Warfarin

Vorhofohrverschluß: Die Studien/Metaanalyse

Reddy et al., JACC 2017; 70: 2964



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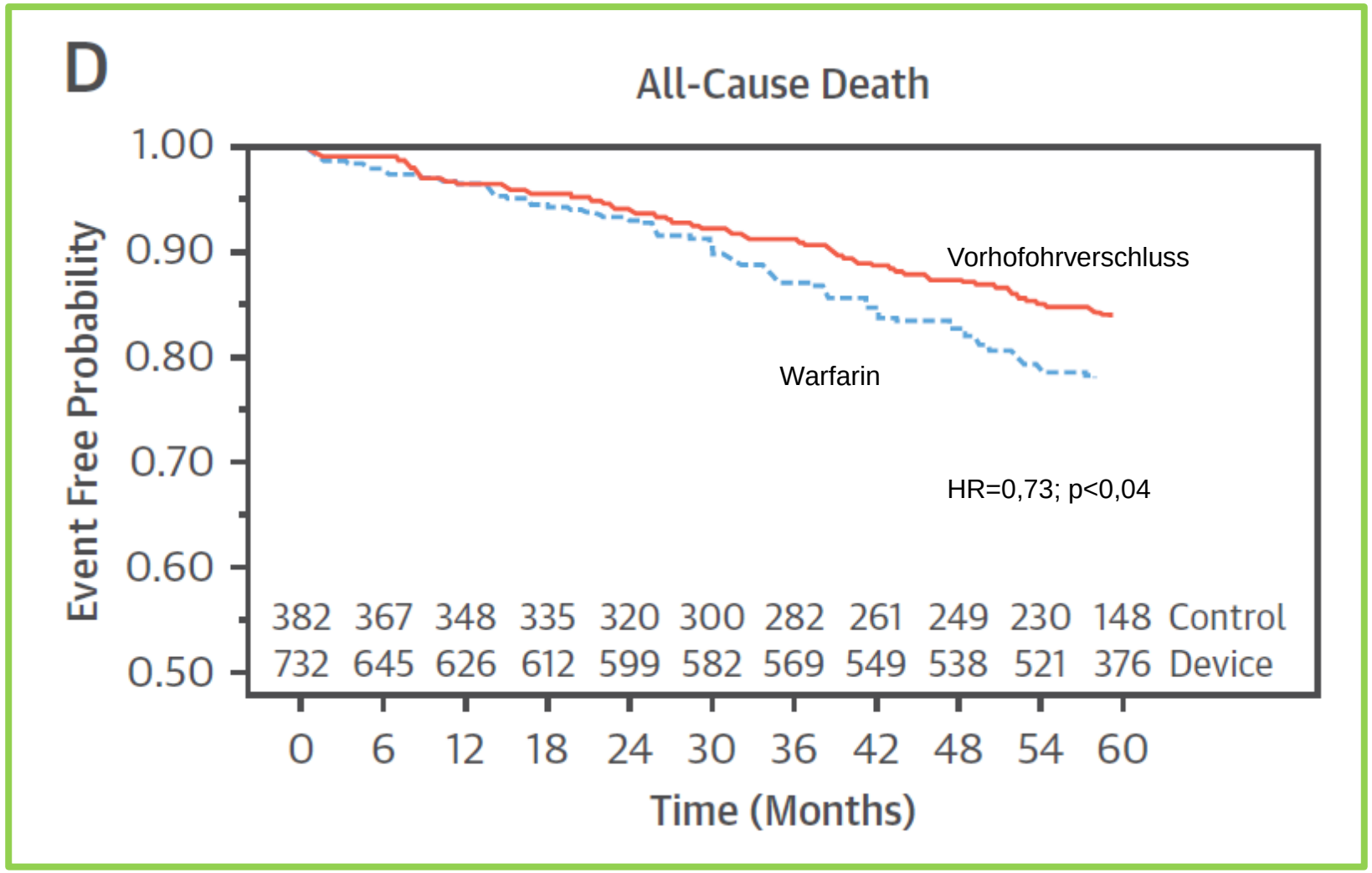
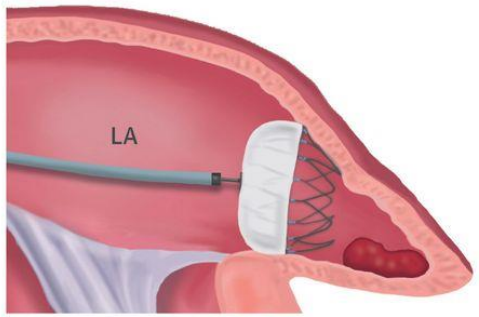


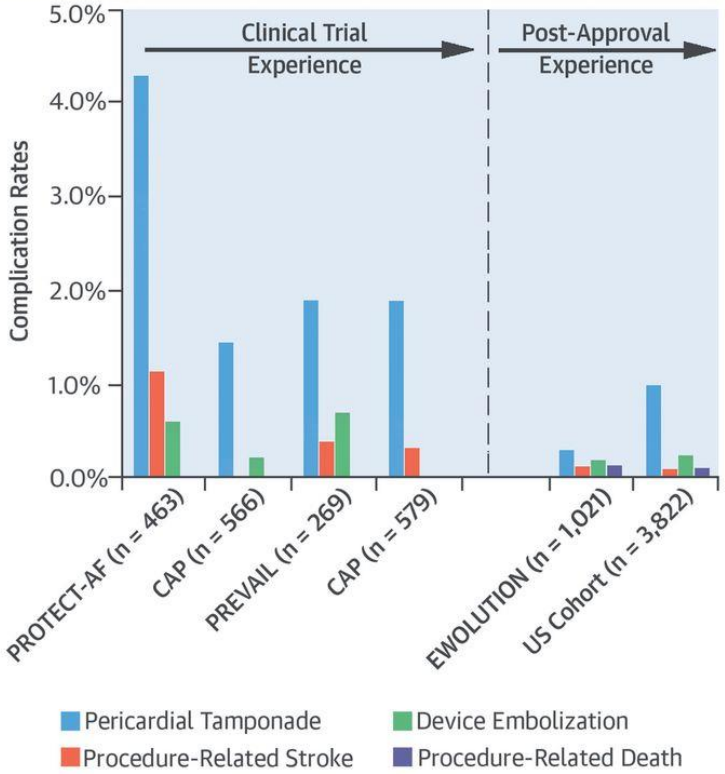
Vorhofohrverschluß: Sicherheitsdaten im Verlauf der Studien/Register

CENTRAL ILLUSTRATION: Major Complication Rates Across Watchman Clinical Studies

Major Complication Rates Across Watchman Clinical Studies



Procedural Parameters	Aggregate Clinical Data
Number of Procedures	6,720
Implantation Success, %	94.9%
Complication Rates	
Pericardial Tamponade	1.24%
Procedure-Related Stroke	0.18%
Device Embolization	0.25%
Procedure-Related Death	0.06%



Reddy, V.Y. et al. J Am Coll Cardiol. 2017;69(3):253–61.

LAA-Okklusion bei Niereninsuffizienz: Effektivität und Sicherheit

Kefer et al. Int. J. Cardiol. 2016; 207: 335

Characteristics		All	No CKD					CKD	p value
			Stage 1 + 2	Stage 3a	Stage 3b	Stage 4	Stage 5	Stage 3 + 4 + 5	
		N = 1014	N = 639	N = 176	N = 119	N = 61	N = 19	N = 375	
Age (yrs)	mean ± sd	74.9 ± 8.4	73.1 ± 8.4	77.8 ± 7.1	79.2 ± 7.2	76.3 ± 8.3	76.9 ± 6.6	77.9 ± 7.3	<0.0001
Gender	M/F	630/384	425/215	95/79	67/51	31/30	11/8	205/169	0.0003
BMI	mean ± sd	27.3 ± 4.8	27.1 ± 4.9	27.5 ± 4.8	27.6 ± 4.4	27.2 ± 5	27.6 ± 5	27.5 ± 4.7	0.21
Congestive heart failure	n (%)	259 (25)	124 (19)	54 (31)	40 (34)	34 (56)	7 (36)	135 (36)	<0.0001
Hypertension	n (%)	860 (85)	536 (84)	157 (90)	110 (93)	54 (88)	13 (68)	324 (87)	0.23
Diabetes	n (%)	299 (29)	152 (24)	58 (33)	49 (41)	28 (46)	8 (42)	147 (39)	<0.0001
Coronary artery disease	n (%)	354 (35)	183 (28)	74 (42)	62 (52)	26 (43)	9 (47)	171 (46)	<0.0001
Carotid disease	n (%)	83 (8)	50 (8)	6 (3)	15 (13)	9 (15)	3 (16)	33 (9)	0.63
Previous stroke/TIA	n (%)	384 (38)	264 (41)	55 (31)	40 (34)	16 (26)	9 (47)	120 (32)	0.003
Thromboembolism on anticoagulant	n (%)	162 (16)	99 (15)	36 (20)	0	4 (6)	3 (16)	62 (16)	0.65
Previous major bleeding	n (%)	466 (46)	282 (44)	84 (48)	58 (49)	26 (43)	13 (68)	184 (49)	0.11
Permanent AF	n (%)	573 (56)	361 (56)	96 (55)	71 (60)	31 (50)	14 (74)	212 (57)	0.94
Paroxysmal/persistent AF	n (%)	439 (43)	278 (43)	78 (45)	47 (40)	30 (50)	5 (26)	161 (43)	0.94
eGFR MDRD (ml/kg/1.73 m2)	mean ± sd	69.7 ± 27.5	86 ± 19	53.1 ± 4.4	38.4 ± 4.5	24.6 ± 3.8	9.9 ± 3.1	41.7 ± 13.7	<0.0001
eGFR CKD-EPI (ml/kg/1.73 m2)	mean ± sd	66.8 ± 23.7	81.8 ± 12.5	52.6 ± 4.4	37.3 ± 4.6	23.7 ± 3.8	9.1 ± 2.7	40.9 ± 13.9	<0.0001
Serum creatinine (mg/dl)	mean ± sd	1.1 ± 0.8	0.8 ± 0.1	1.2 ± 0.1	1.6 ± 0.2	2.3 ± 0.4	5.4 ± 1.6	1.7 ± 1	<0.0001
Dialysis	n (%)	14 (1)	0	0	0	2 (3)	12 (63)	14 (3)	0.0001
Renal transplant	n (%)	3 (0.3)	0	1 (0.5)	1 (0.8)	1 (1)	0	3 (0.8)	0.05
CHADS2 score		2.8 ± 1.3	2.6 ± 1.3	3 ± 1.2	3.2 ± 1.3	3.1 ± 1.5	3 ± 1.7	3 ± 1.4	<0.0001
CHA2DS2-VASc score		4.4 ± 1.6	4.2 ± 1.6	4.7 ± 1.5	5.1 ± 1.4	5.1 ± 1.7	4.7 ± 1.7	4.9 ± 1.5	<0.0001
HASBLED score		3.1 ± 1.2	2.9 ± 1.1	3.1 ± 1.1	3.5 ± 1.3	3.7 ± 1.3	4.3 ± 1.3	3.4 ± 1.3	<0.0001

LAA-Okklusion bei Niereninsuffizienz: Effektivität und Sicherheit

Kefer et al. Int. J. Cardiol. 2016; 207: 335

	All	Stage 1 + 2 + 3	Stage 4 + 5	p value
	N = 967	N = 895	N = 72	
Stroke	9 (0.9)	9 (1.0)	0	1.00
TIA	9 (0.9)	8 (0.9)	1 (1.3)	0.50
Major bleeding	15 (1.5)	14 (1.5)	1 (1.3)	1.00
Death	61 (6.3)	51 (5.6)	10 (14)	0.01
Cardiac death	18 (1.8)	13 (1.4)	5 (6.9)	0.007

LAA-Okklusion bei Niereninsuffizienz: Effektivität und Sicherheit

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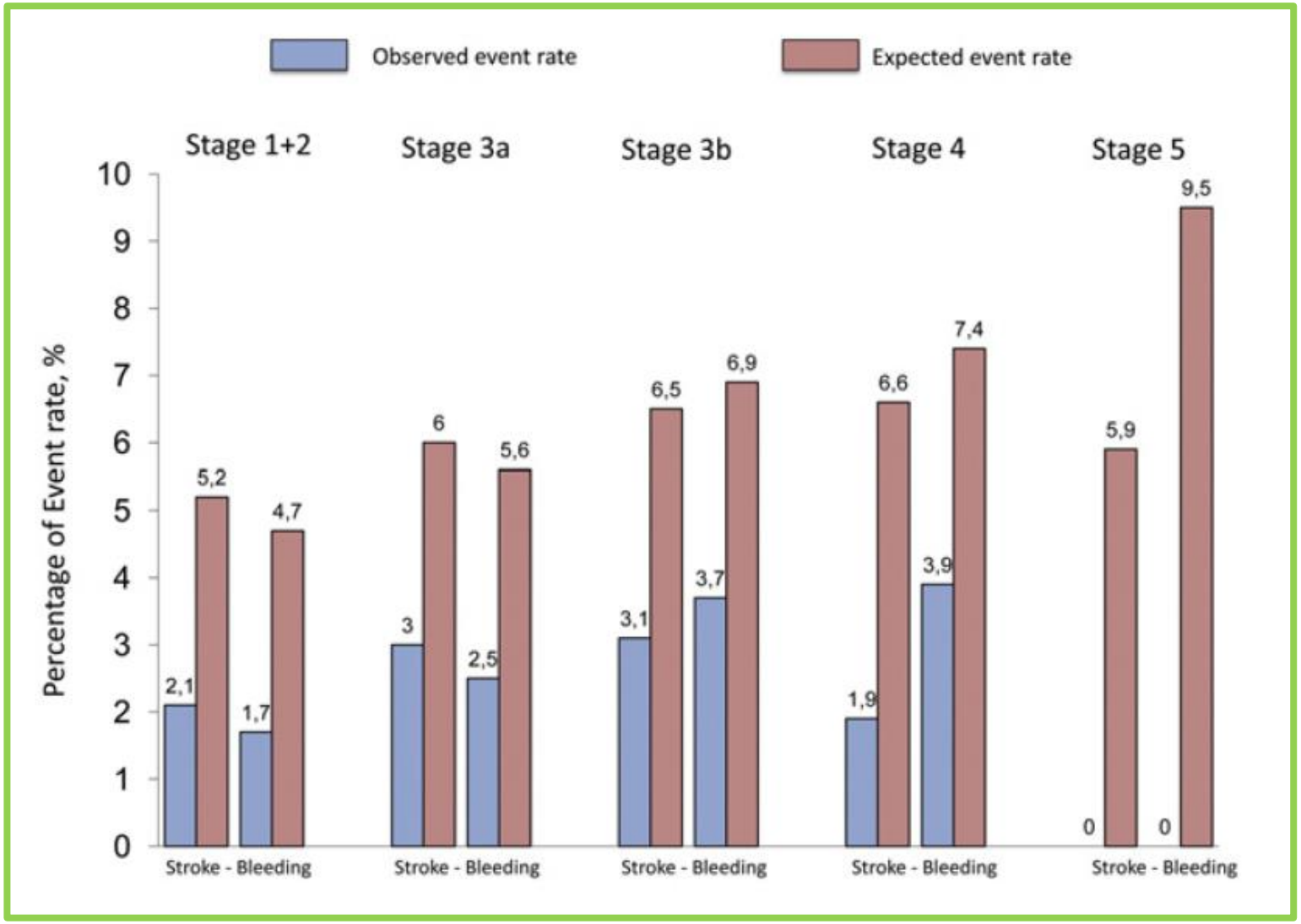
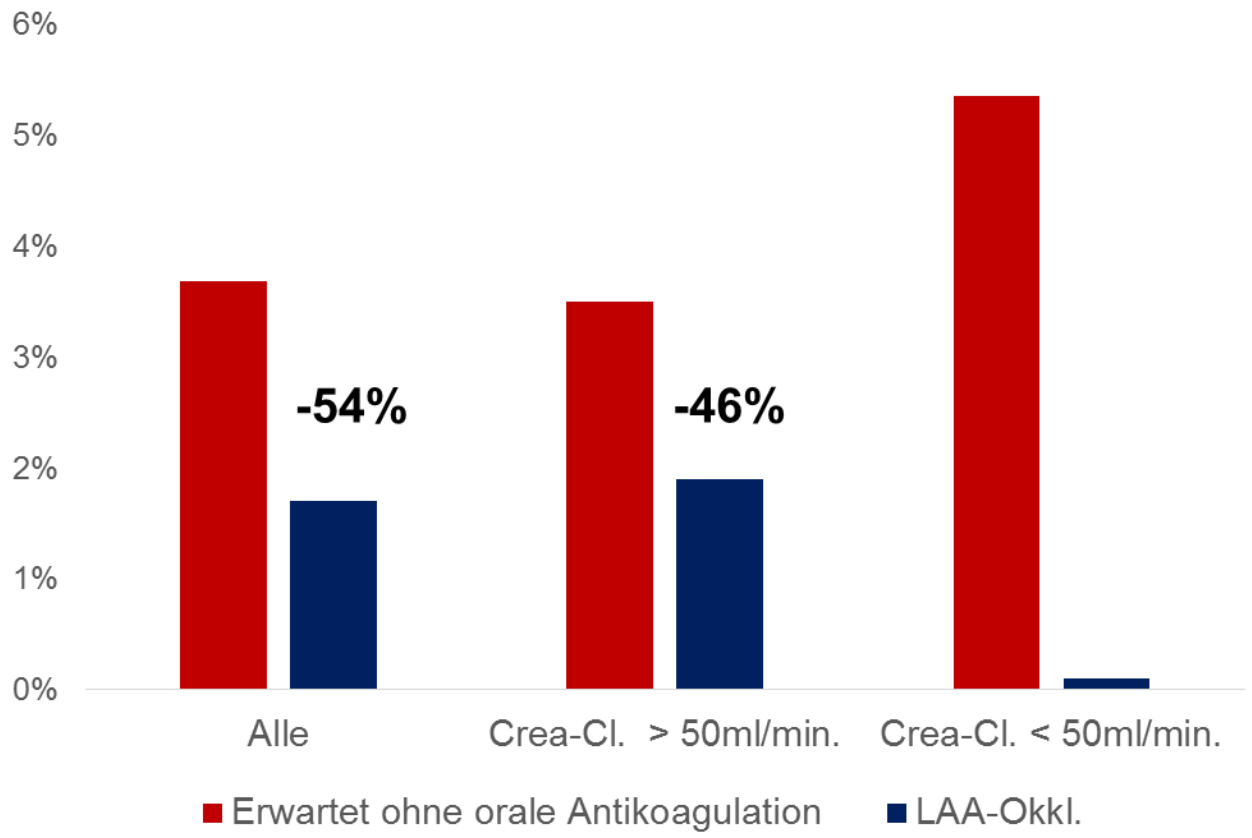
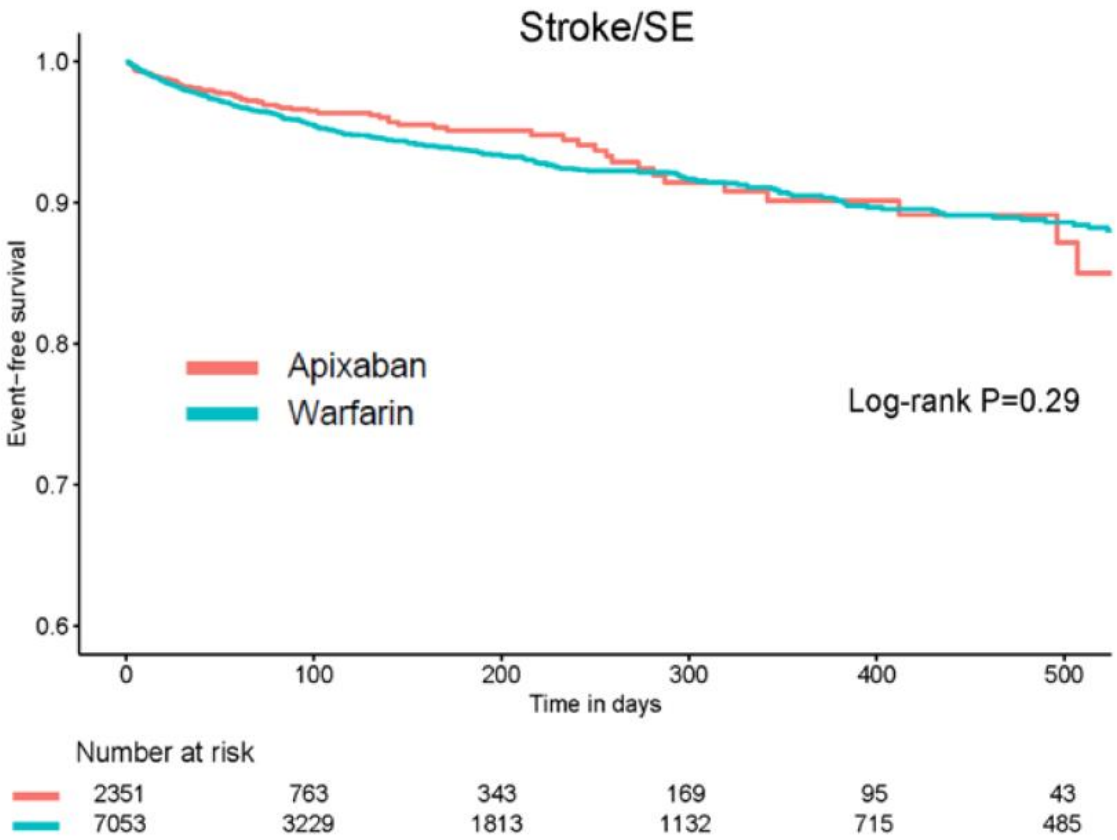


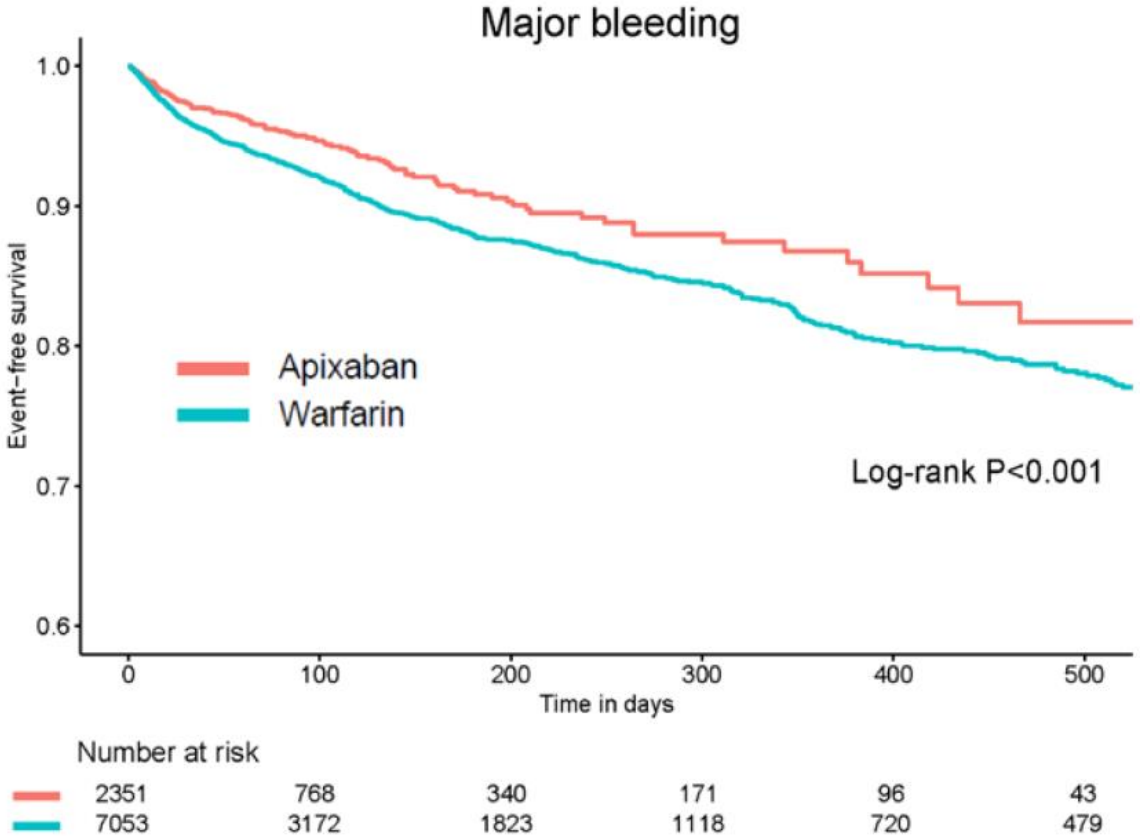
Eigene Patienten: Watchman bei Patienten mit und ohne schwere Niereninsuffizienz



NOACS bei terminaler Niereninsuffizienz

Siontis et al., Circulation 2018; 138: 1519





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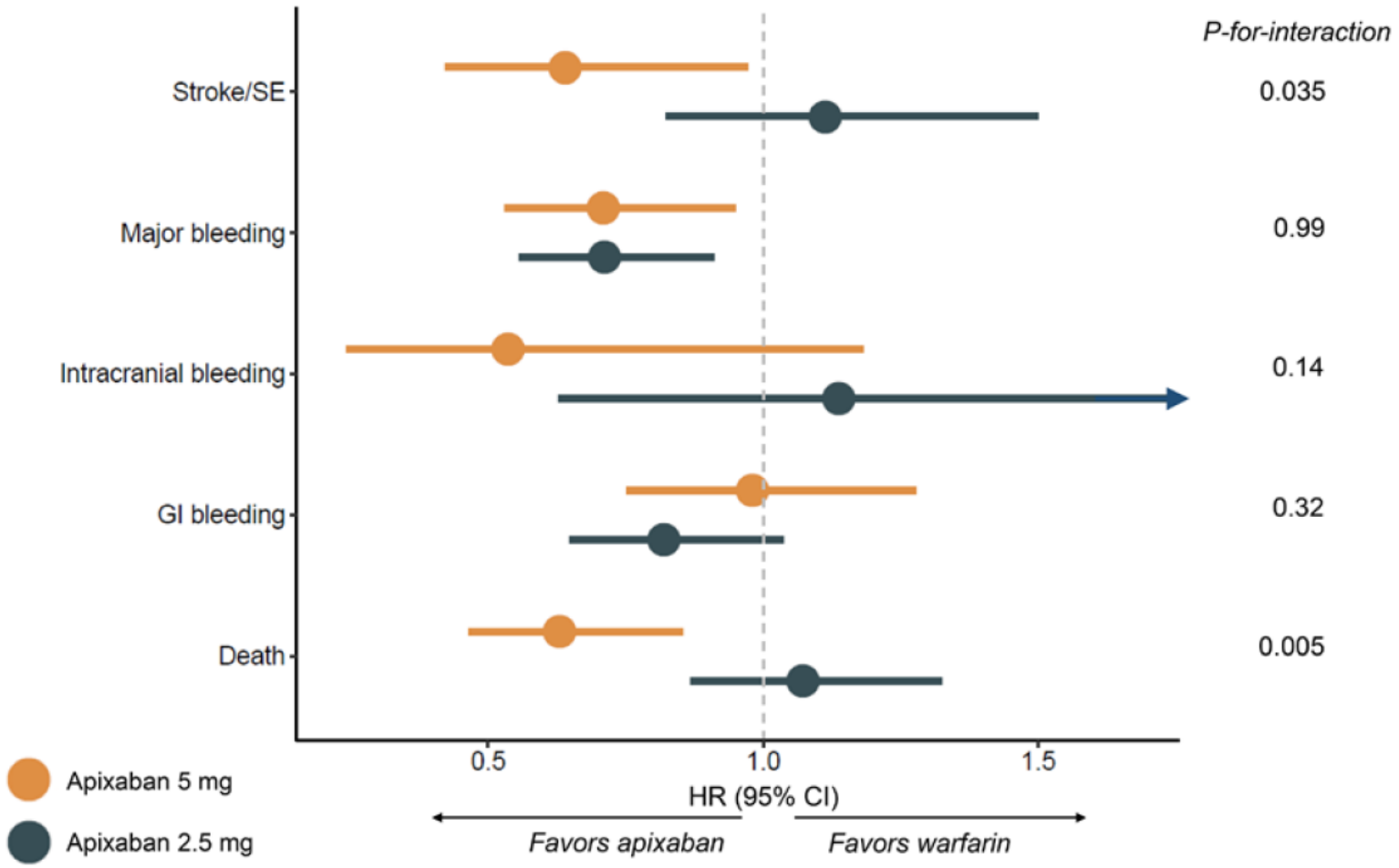


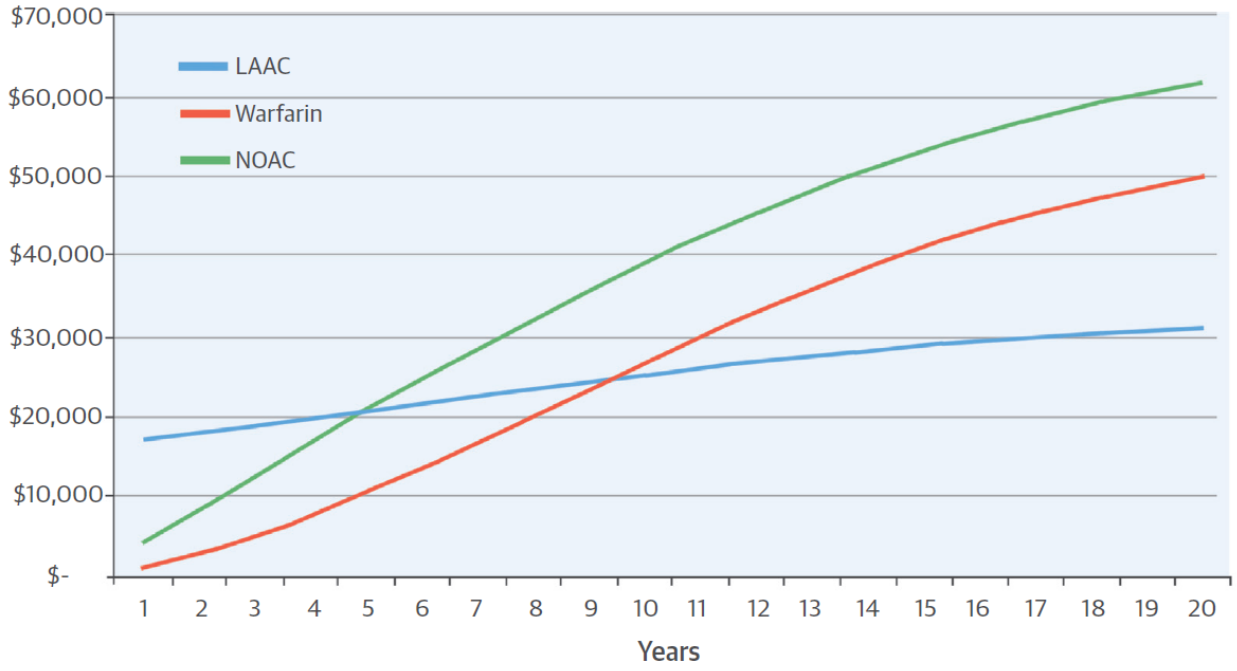
Therapiekontiuität bleibt dauerhaft ein Problem

Drug Discontinuation	Warfarin	NOAC
RE-LY (%)	10	16/15
ROCKET-AF (%)	22	24
ENGAGE AF (%)	34	34
ARISTOTLE (%)	27	25

„Jeder 3.-6. Patient unterbricht dauerhaft die NOAC/Warfarin-Therapie im Nachbeobachtungszeitraum von 2 Jahren innerhalb einer Studie!

Daten aus PROTECT-AF zeigt Kosteneffktivität des LAA-Okkuder verglichen mit Warfarin/NOAC

Reddy et al., JACC 2015; 68: 2728



	Time to Clinical Effectiveness (Incremental QALYs)	Time to Cost-Effectiveness (Cost per QALY)	Time to Dominance (More Effective, Less Costly)
LAAC vs. warfarin	Year 3 (0.015)	Year 7 ($42,994/QALY)	Year 10
NOACs vs. warfarin	Year 1 (0.008)	Year 16 ($48,446/QALY)	N/A
LAAC vs. NOACs	Year 5 (0.007)	Year 5 (Dominant)	Year 5

LAA-Okkluder: Für wen?

- **Patienten mit stattgehabter Blutung unter oraler Antikoagulation**
- **Patienten mit hohem Blutungsrisiko**
  - **HAS-BLED ≥ 3**
  - **Rez. GI-Blutungen**
  - **Urologische Blutungen**
  - **Rez. Schwere Epistaxis**
  - **Opthalmologische Blutungen**
- **Amyloidangiopathie (CAA)**
- **Schwere Nierensuffizienz/Dialyse**
- **Sturzgefährdung bzw. häufige Stürze**
- **Epilepsie**

Der Vorhofohr-Okkluder zur Schlaganfallprävention bei Vorhofflimmern: Der Niereninsuffiziente im Fokus

Berliner Dialyse Seminare, 8.12.2018

HERZ IM ZENTRUM HANNOVER

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