Left Atrial Appendage Closure: Neurological events

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Disclosures

- Speaker/Consultant/Board member
  - BSC
  - Abbott
  - Micardia
  - STENTYS
  - Endocross
  - Cardiodex
  - MValve

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The PROTECT AF trial demonstrated the WATCHMAN Device's non-inferiority to warfarin in 707 randomized patients

- PROTECT AF is the first prospective, randomized, multi-center trial comparing the WATCHMAN device to warfarin for thromboembolic prophylaxis
- 707 patients were randomized (2:1 device to medical therapy including warfarin)
- Primary efficacy endpoint (non-inferiority)
  - All stroke: ischemic or hemorrhagic
  - Systemic embolisms
  - Cardiovascular and unexplained death
- Patients who received the WATCHMAN device had 45 days of post operative warfarin therapy to ensure endothelialization
- Transesophogeal echocardiography was performed at 45 days, 6 months and 1 year to verify device placement left atrial appendage flow and presence of thrombus .

Baseline Risk Factors

$CHADS_2$	WATCHMAN	warfarin
1	33.9%	27%
2	34.1%	36.1%
3	19%	20.9%
4	8%	9.8%
5	4.1%	4.1%
6	0.9%	2%

Average age for WATCHMAN was 71.7 years +/- 8.8 years

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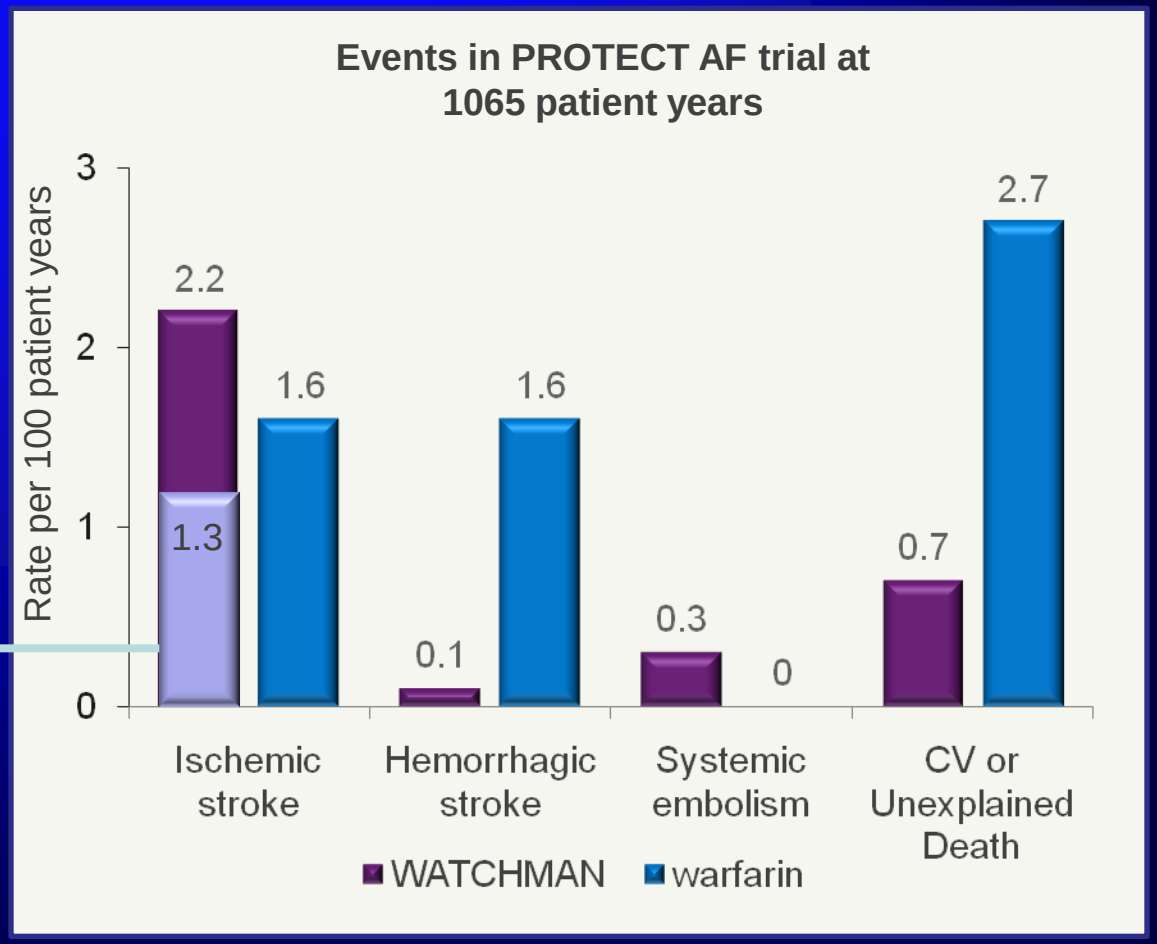
At 1065 patient years, the WATCHMAN® Device was non-inferior to warfarin

- Following successful device implantation, rates of ischemic strokes with the WATCHMAN Device were 1.3 per 100 patient years vs. 1.6 with warfarin .

Rate of ischemic stroke is lower than warfarin following periprocedural period



Holmes DR et al. *Lancet* 2009; 374: 534–42

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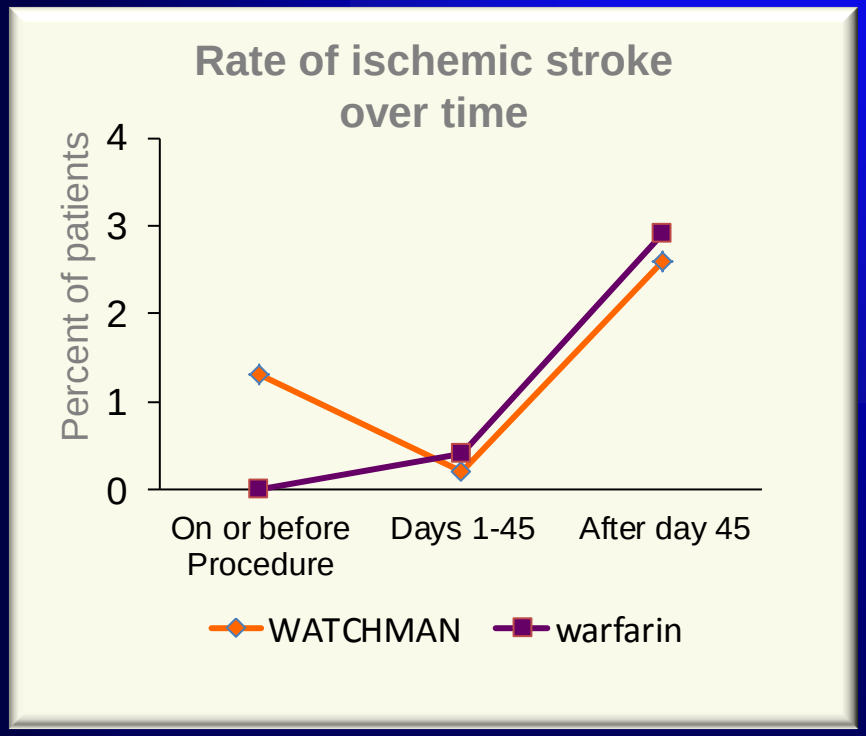
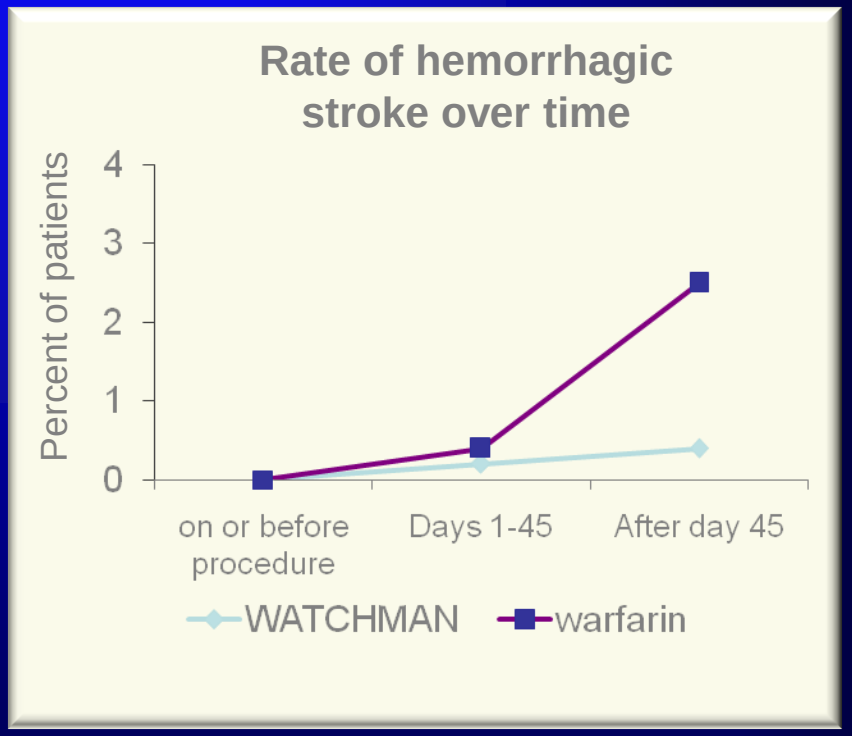
After procedure, rates of ischemic and hemorrhagic stroke were lower with the WATCHMAN® Device

After day 1, rates of hemorrhagic stroke increased sharply with warfarin, compared to a slight increase with the WATCHMAN Device





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In addition to efficacy, PROTECT AF demonstrated the long-term safety of the WATCHMAN® device

Subjects with Primary Safety Endpoints within 7 days of Procedure

Event Description	WATCHMAN (% of 463)	Warfarin (% of 244)
Pericardial effusion	4.8%	NA
Ischemic stroke	**1.1%**	**NA**
Device embolization	0.4%	NA
Major bleeding	1.1%	NA
Other	0.4%	NA

- Both the WATCHMAN Device and warfarin patients experienced adverse events
- The WATCHMAN Device events were concentrated around procedure
- Warfarin events occurred at any time

Subject with Primary Safety Endpoints >7 days after Procedure

Event Description	WATCHMAN (% of 463)	Warfarin (% of 244)
Pericardial effusion	0.2%	NA
Device embolization	0.2%	NA
Hemorrhagic stroke	0.6%	2.9%
Major bleeding	3.0%	5.3%
Total	**4.1%**	**8.2%**

Higher rates of adverse events seen post procedure with warfarin group

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Procedure Related Stroke

- Stroke = 5 patients
- Air embolism during the procedure
- Outcomes :
- Extended hospital stay by 9 days (5-9)
- Three recovered with no long term effects
  - Two experienced significant/permanent neurological deficits

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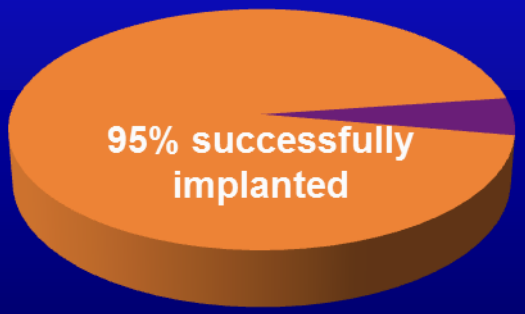
A continued access registry demonstrated ongoing improvement in the WATCHMAN® Device procedure safety

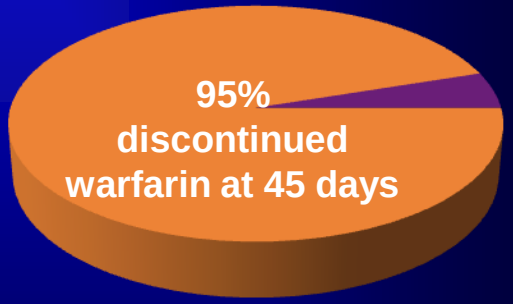
- A continued access registry (CAP) implanted an additional 460 patients at 26 centers that participated in PROTECT AF .
- Primary safety endpoint:
  - Pericardial effusion/tamponade
  - Procedure related stroke
  - Device embolization and bleeding events

	PROTECT AF	CAP
Mean Age	72	74
Mean $CHADS_2$	2.2	2.4

Implantation Success



Warfarin Discontinuation



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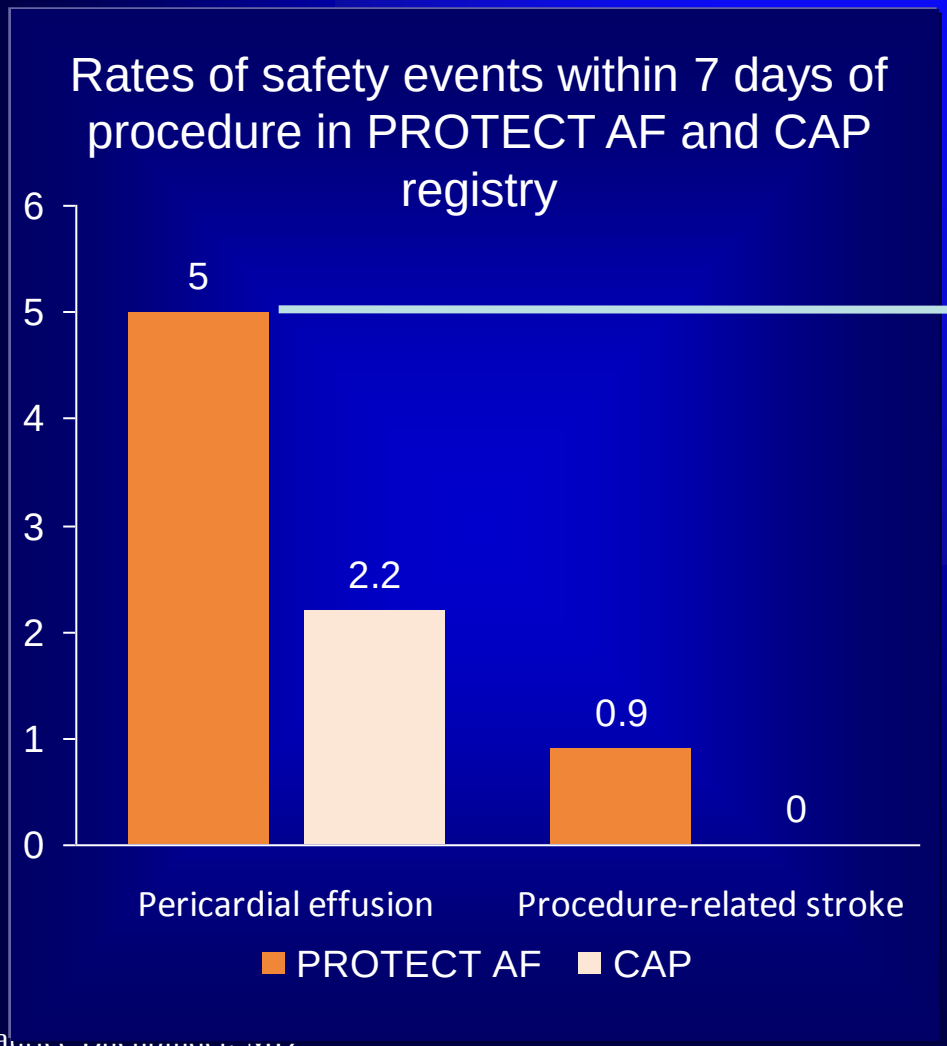
Reddy VY et al. *Circulation*. 2011;123:417-424

Procedure related safety events declined as implant experience grew



- 56% reduction in pericardial effusion rates between studies
- Procedure-related stroke reduced to 0

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Reddy VY et al. *Circulation*. 2011;123:417-424

Conclusion

- Rates of ischemic strokes with device in place are lower than with warfarin following peri procedural period.
  - 1.3 per 100 patient years .
- Peri procedural ischemic strokes were primarily caused by inadvertent introduction of air through large bore catheters leading to cerebral events
- Risk of neurological adverse events with device implantation decreases dramatically with experience
  - Procedure related strokes reduced to zero in CAP

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