

Is There a Critical Value of Daily Atrial Tachyarrhythmia Burden from Device Diagnostics that Raises Stroke Risk? The TRENDS Study

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Disclosures

<i>Author</i>	<i>Activity</i>	<i>Company</i>	<i>Level</i>
T. Glotzer	Consulting	Medtronic	Modest
	Speaker	Medtronic, St. Jude, Boston Scientific	Modest
E. Daoud	Consulting	Medtronic, BARD, Biosense-Webster	Modest
	Speaker	Medtronic, St. Jude, Boston Scientific	Modest
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	Speaker	Astellas	Modest
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M. Ezekowitz	Consulting	Medtronic, ARYx Therapeutics, Bristol Myers, Wyeth, Johnson & Johnson	Modest
	Speaker	Pfizer	Modest
	Research Grant	Boehringer Ingelheim, ARYx Therapeutics	Significant
C. Hilker	Employee	Medtronic	Significant
C. Miller	Employee	Medtronic	Significant
D. Qi	Employee	Medtronic	Significant
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Background

- Atrial fibrillation increases the risk of stroke
- Currently PAF is thought to have the same stroke risk as sustained AF
- Risk posed by very short durations of AF is unknown
- Modern implantable devices are capable of recording and storing long term, accurate AT/AF burden data



Study Aims

- To assess the relationship between device-detected AT/AF and risk of Thromboembolic Events (TEs)
- To determine if there is a threshold value of AT/AF burden which increases TE risk



Methods

Patient Selection

- Class I/II indication for implantation of a dual chamber pacemaker, ICD, or CRT device
- ≥ 1 stroke risk factor:
 - Diabetes
 - HTN
 - CHF
 - Prior stroke/TIA
 - Age ≥ 65



Methods

Follow Up & Outcome

- Device diagnostics downloaded at 3 month intervals
- Clinical evaluation at 6 month intervals
- Antithrombotic therapy was directed by patients' MDs
- TEs were adjudicated by 3 neurologists
- **Primary outcome: Thromboembolic event (TE)**
 - Ischemic stroke
 - TIA
 - Systemic embolism



Methods

AT/AF Detection

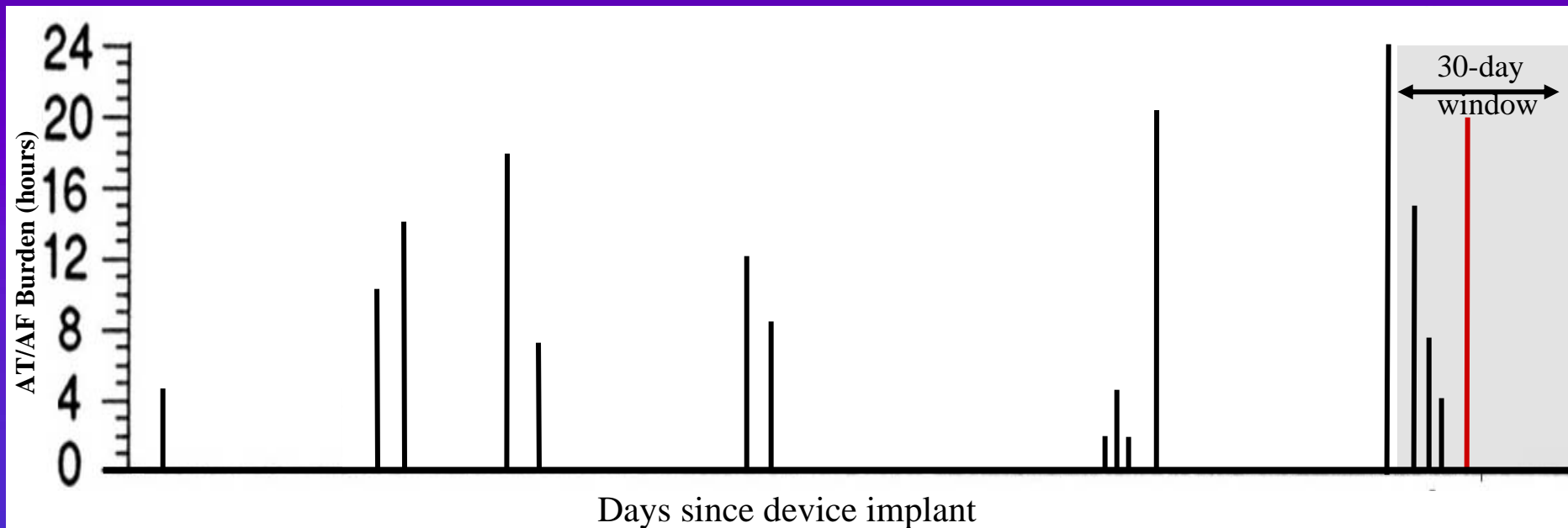
- All devices were programmed to dual chamber operation with active mode switching
- Threshold for AT/AF episode detection was:
 - Atrial rate >175 beats per minute
 - Lasting at least 20 seconds



Methods

AT/AF Burden

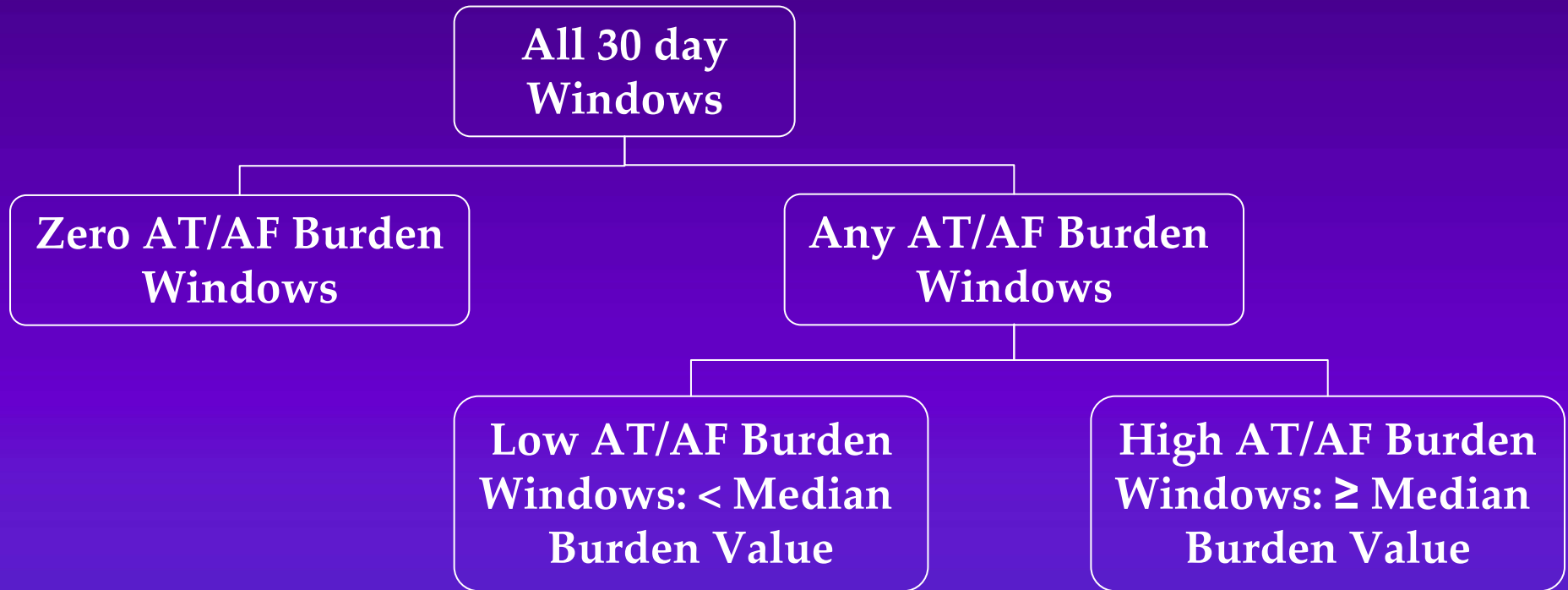
- AT/AF burden was defined as the longest total duration of AT/AF in hours (h) on any given day during a 30-day rolling window



- Window is “rolled” in 1-day increments



Methods Analysis

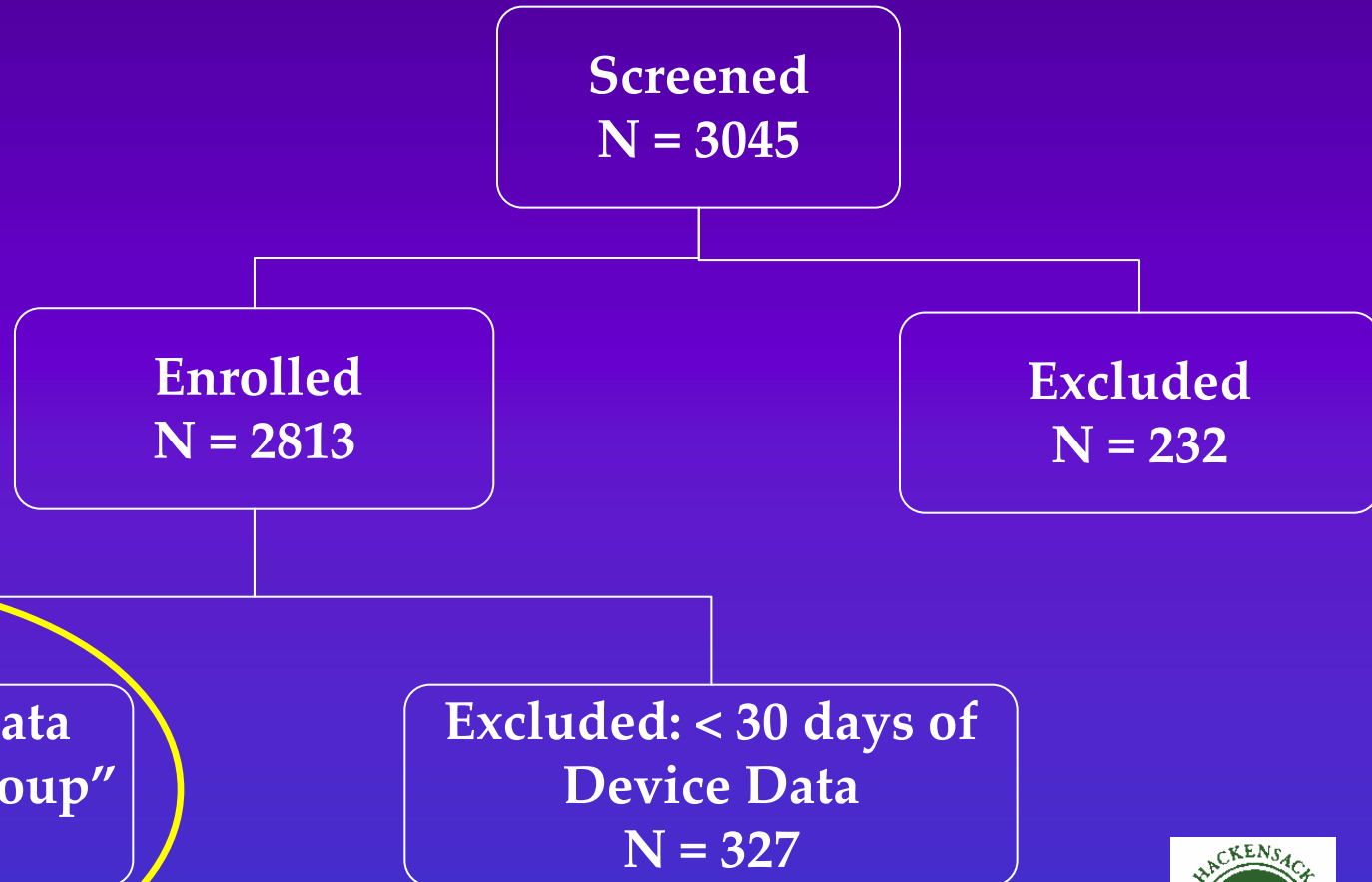


- A Cox proportional hazard model was used to relate time-dependent AT/AF burden to the risk of TE
- Stroke risk factors and time-dependent warfarin/aspirin use were included in the model



Results

Assembly of the Cohort



Results

Baseline Clinical Features - 1

<u>Variable</u>	<u>Value</u>
Age	70.9 ± 11.1 yrs
Male	66% (n=1650)
CHADS ₂	2.2 ± 1.2
CHF	60% (n=1479)
Hypertension	76% (n=1887)
Diabetes	32% (n=783)
Prior Stroke/TIA	13 % (n=333)
Systolic BP	133.3 ± 22.5 mmHg



Results

Baseline Clinical Features - 2

<u>Variable</u>	<u>Value</u>
IPG	50% (n=1234)
ICD	31% (n=781)
CRT	19% (n=471)
Warfarin	21% (n=517)
Aspirin	62% (n=1547)
Documented AT/AF History	20% (n=498)



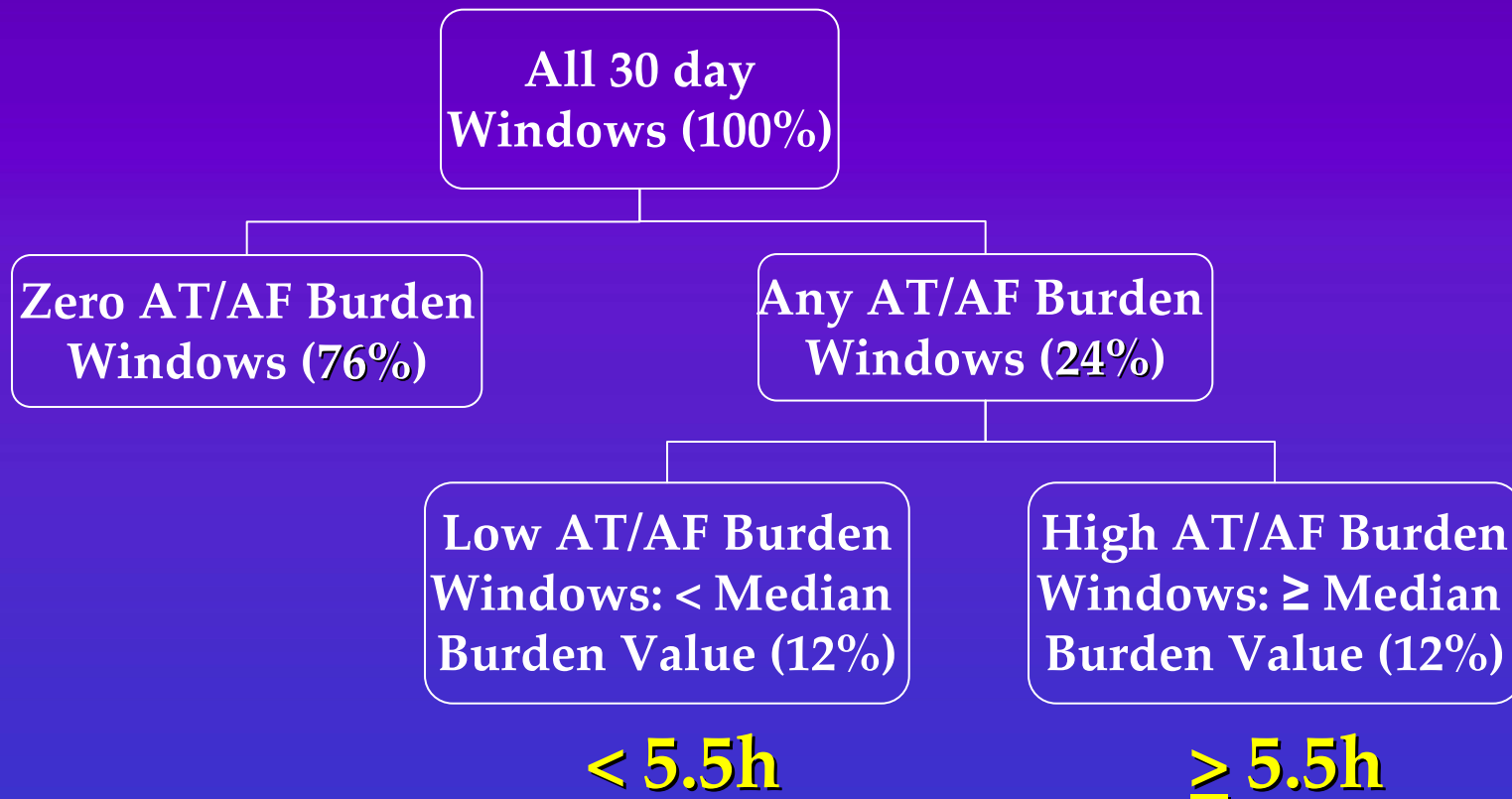
Results

- Average follow-up was 1.4 years (3382 patient-years)
- 40 TE events
 - 20 ischemic strokes
 - 17 TIAs
 - 3 systemic emboli
- Annualized TE event rate: **1.2% [0.8, 1.6%]**



Results

The median value for maximum daily burden in all 30-day windows with non-zero AT/AF was **5.5h**



Results

Annualized TE Event Rates

	<u>Annualized Rate</u>	<u>Annualized Rate (Excluding TIAs)</u>
Zero Burden	1.1%/Year	0.5%/Year
Low Burden < 5.5 hours	1.1%/Year	1.1%/Year
High Burden ≥ 5.5 hours	2.4%/Year	1.8%/Year



Results

Cox proportional hazard model adjusting for baseline stroke risk factors & time dependent AT/AF burden & antithrombotic therapy

<u>Variable</u>	<u>Hazard Ratio*</u>	<u>95% Confidence Interval</u>	<u>p-value</u>
Low Burden < 5.5 hours	0.98	0.34 to 2.82	0.97
High Burden ≥ 5.5 hours	2.20	0.96 to 5.05	0.06

**compared to no AT/AF burden*



Summary

- The observed stroke rate in this study was very low compared to prior studies of AF patients with similar risk profiles
- Our results suggest that device-detected AT/AF burden ≥ 5.5 h on any day during the preceding 30 days doubles the risk for TE, independent of known risk factors and antithrombotic therapy



Strengths/Limitations

Strengths

- Large cohort with devices that provide comprehensive recording capability
- Adjudicated outcomes

Limitations

- Retrospective analysis
- Unanticipated low number of events resulting in broad confidence intervals for hazard ratio estimates



Conclusions

- Our results suggest device-detected AT/AF burden may be used to stratify TE risk
- Further studies are needed to precisely identify an AT/AF burden threshold that merits medical intervention



Initial Study Design

- To study only patients NOT receiving warfarin
- To study only patients who had a either a hx of AF or new AF (zero AT/AF were excluded)

Event rate (1.3%) vs. the expected event rate (4%) was too low to permit meaningful analysis.



Stroke Rate Compared to Similar Studies

Study Name	Treatment Group	Sample Size	Event Rate	Event Types	CHADS ₂	AF Type
ACTIVE W	Clopidogrel+ASA	3335 pts	2.4%	Ischemic Stroke		
AFASAK	ASA or Placebo	672 pts	5.5%	TE complications		100% Chronic
AFASAK II	ASA	169 pts	3.6%	Stroke or SE		100% Chronic
BAATAF	ASA or nothing	477 pt-yrs	2.7%	Stroke		69% Permanent 13% Persistent 18% PAF
BAFTA	ASA	485 pts	4.9%	Stroke	72% 1-2 28% 3-6	80% Sustained
CAFA	Placebo	191 pts	5.2%	Stroke or SE		93% Chronic 7% PAF
MOST Substudy	Not specified	312 pts	1.4%	Stroke		
AT500	Not specified	725 pts	1.2%	Arterial embolism	1.2	70% PAF 14% Persistent



