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Dual Anti Platelet Therapy and COUMADIN After PCI

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Internist and Cardiologist
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Introduction

- AF is the most common arrhythmia associated with stroke and thromboembolism
- In high-risk patients with nonvalvular AF, anticoagulation with coumarins is recommended
- Dual antiplatelet therapy with aspirin plus clopidogrel is advised following ACS or stenting

Introduction

- The recommended duration of dual antiplatelet therapy varies, ranging from 4 weeks to at least 6 to 12 months

- A management problem arises when a patient in whom long-term anticoagulation is recommended because AF subsequently presents with ACS and/or undergoes PCI.

Introduction

- Coumarin monotherapy is a poor therapeutic choice in post-stent patients, with a high rate of adverse cardiac complications.

- The use of “aspirin plus coumarins” or “triple therapy” is associated with more bleeding.

The New England
Journal of Medicine

VOLUME 347 SEPTEMBER 26, 2002 NUMBER 13

WARFARIN, ASPIRIN, OR BOTH AFTER MYOCARDIAL INFARCTION

METTE HURLEN, M.D., MICHAEL ABDELNOOR, M.P.H., PH.D., PÅL SMITH, M.D., PH.D., JAN ERIKSSEN, M.D., PH.D., AND HARALD ARNESEN, M.D., PH.D.*

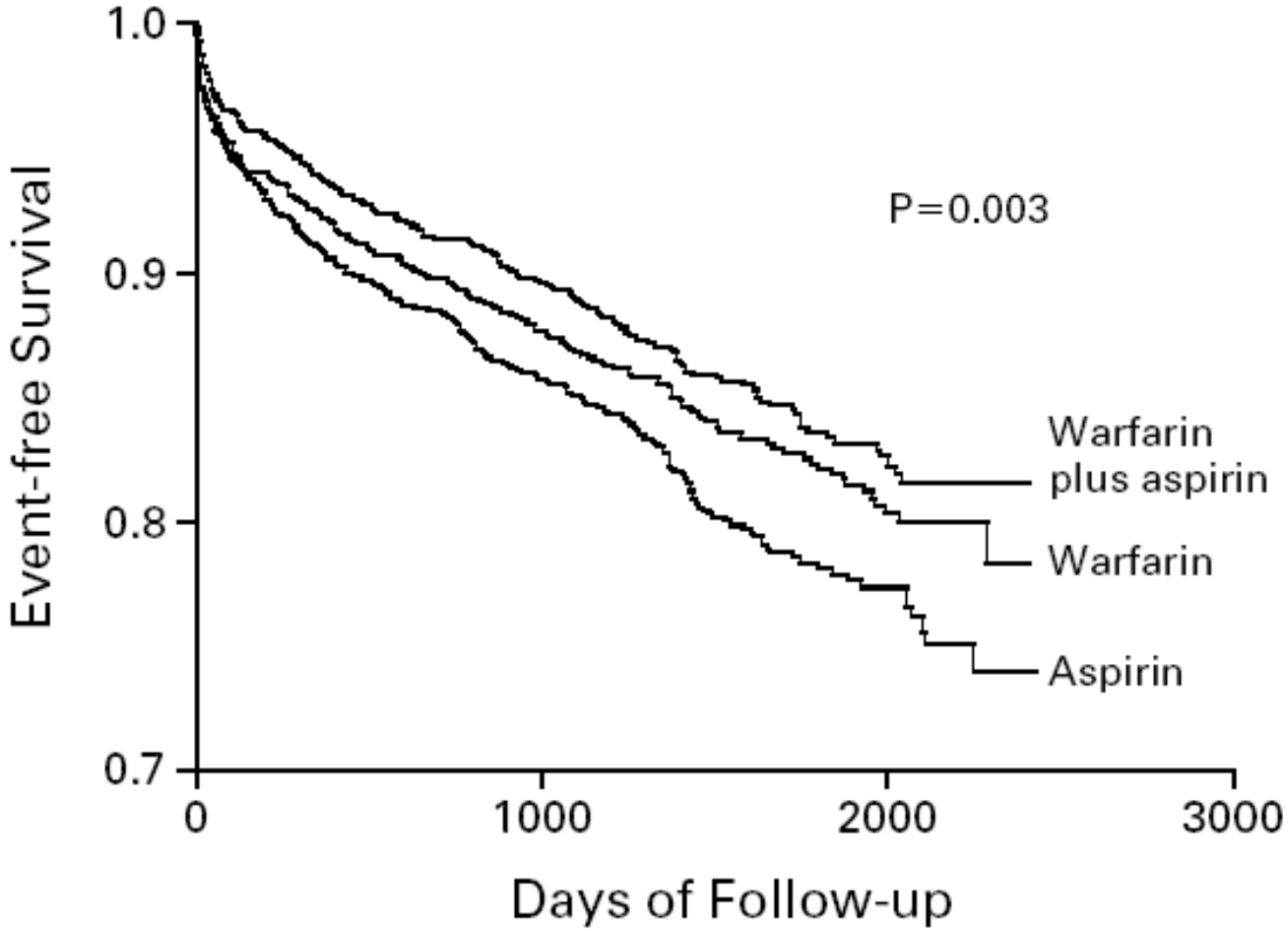


Figure 1. Event-free Survival Curves for the Composite End Point of Death, Nonfatal Reinfarction, and Thromboembolic Stroke.

The P value refers to the overall difference among the curves (Tarone–Ware method).

Anticoagulation with coumarins in CAD subjects may provide a similar degree of “vascular protection” to antiplatelet therapy, at least in the post-ACS setting.

Annals of Internal Medicine

2005;143:241-250. ARTICLE

Warfarin plus Aspirin after Myocardial Infarction or the Acute Coronary Syndrome: Meta-Analysis with Estimates of Risk and Benefit

Michael B. Rothberg, MD, MPH; Carmel Celestin, MD; Louis D. Fiore, MD, MPH; Elizabeth Lawler, MPH; and James R. Cook, MD, MPH

- 10 trials involving a total of 5,938 patients

Figure 1. Forest plot showing rate ratios of myocardial infarction for warfarin plus aspirin compared with aspirin alone.

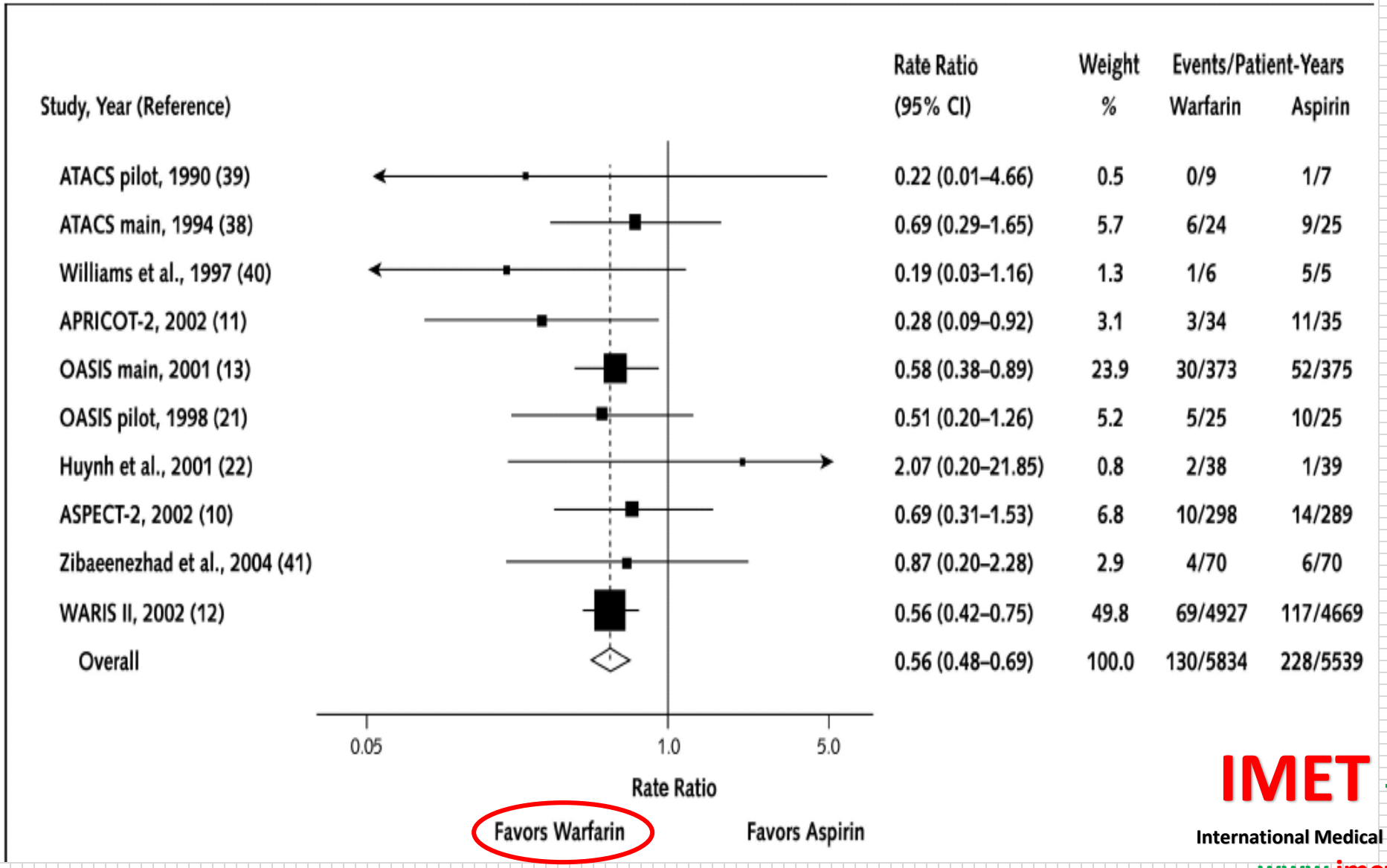


Figure 2. Forest plot showing rate ratios of ischemic stroke for warfarin plus aspirin compared with aspirin alone.

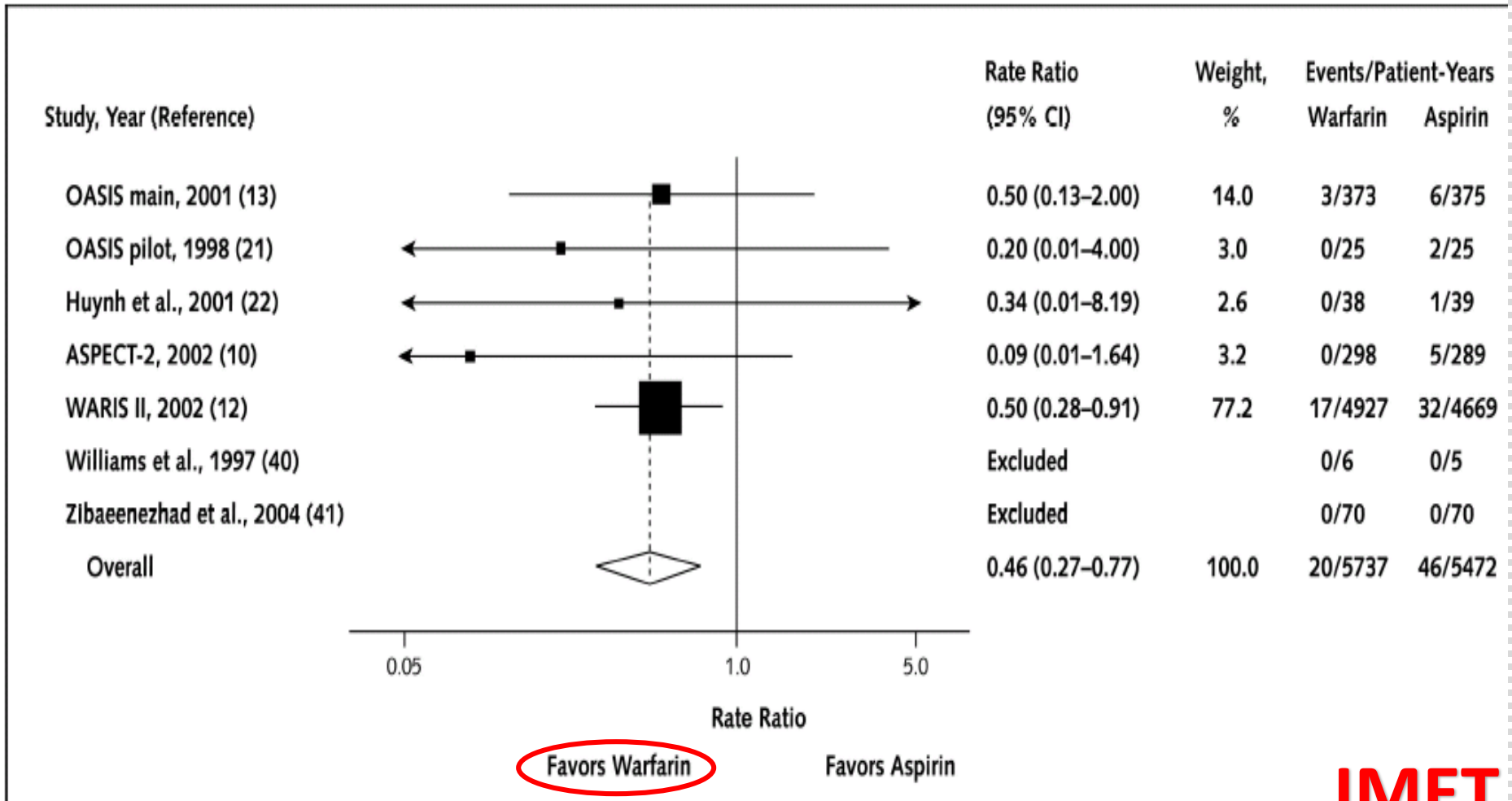


Figure 3. Forest plot showing rate ratios of death for warfarin plus aspirin compared with aspirin alone.

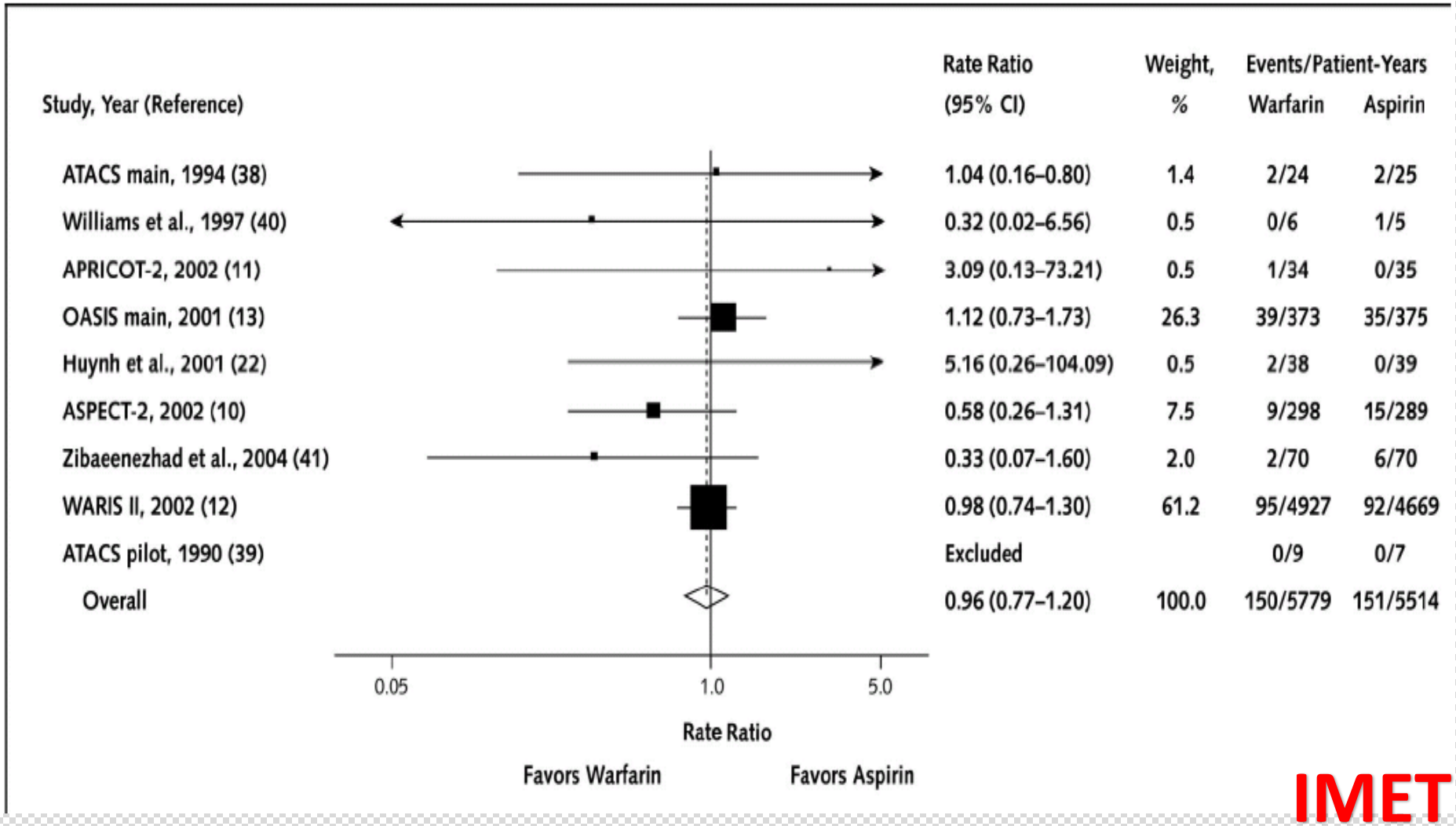


Figure 4. Forest plot showing rate ratios of major bleeding for warfarin plus aspirin compared with aspirin alone.

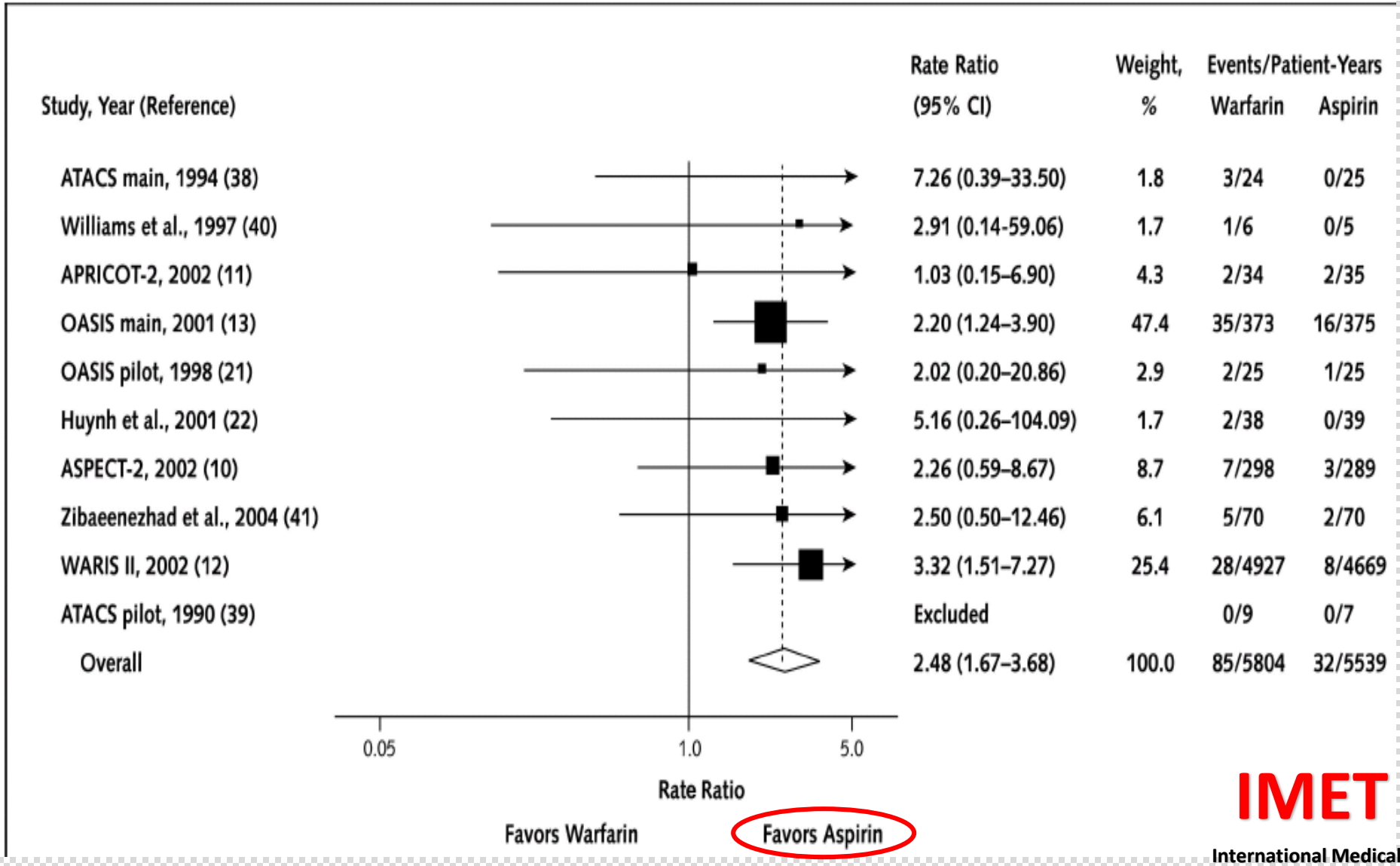
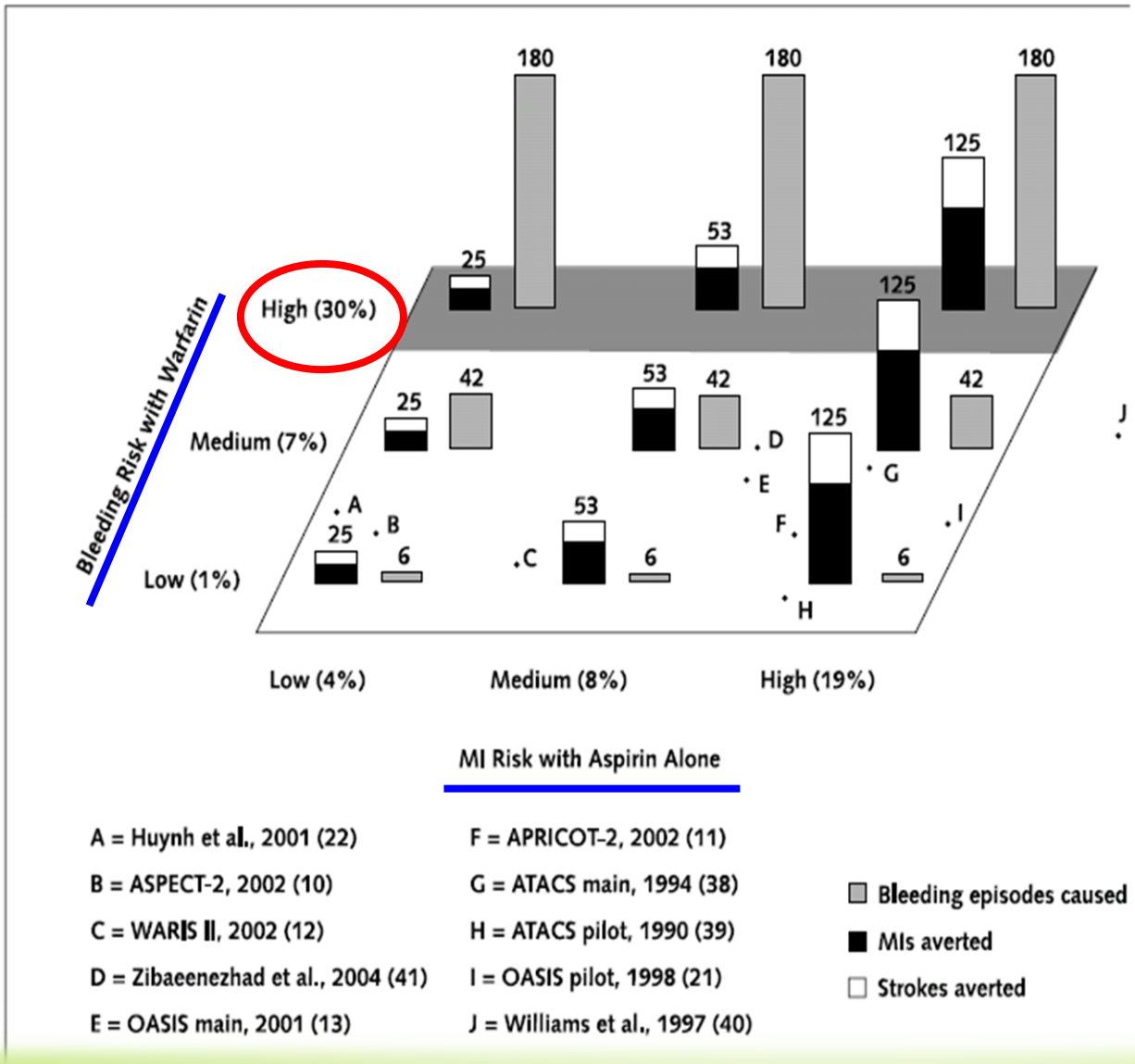


Figure 5. Predicted myocardial infarctions (*MIs*) and thrombotic strokes averted and excess bleeding episodes caused in 1000 patients as a result of adding warfarin to aspirin for 1 year, stratified by bleeding and MI risk.



Conclusion

Patients who are at low or intermediate risk for , the cardiovascular benefits of coumarins outweigh the bleeding risks

- *There is a lack of published evidence on the optimal antithrombotic management strategy in anticoagulated AF patients who present with an ACS and/or undergo PCI.*

Guidelines

- The 2006 ACC/AHA/ESC guidelines on AF management acknowledge that no adequate studies specifically address this issue

- These guidelines suggest that the maintenance regimen should be a combination of clopidogrel and coumarins for 9 to 12 months, after which warfarin may be continued as monotherapy in the absence of a subsequent coronary event.

Guidelines

- Other authorities* have suggested an antithrombotic management schema based on ACS presentation, perceived bleeding risk, and the type of stent used.

- *None of these strategies have been tested in prospective randomized trials.*

* Lip GYH. Chest 2006;130:1823-7

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FOCUS ISSUE: ATRIAL FIBRILLATION

Anticoagulant and Antiplatelet Therapy Use in 426 Patients With Atrial Fibrillation Undergoing Percutaneous Coronary Intervention and Stent Implantation

Implications for Bleeding Risk and Prognosis

Juan M. Ruiz-Nodar, MD, PHD,* Francisco Marín, MD, PHD,†‡ José Antonio Hurtado, MD,†‡ José Valencia, MD, PHD,* Eduardo Pinar, MD, PHD,†‡ Javier Pineda, MD, PHD,* Juan Ramón Gimeno, MD, PHD,†‡ Francisco Sogorb, MD, PHD,* Mariano Valdés, MD, PHD,† Gregory Y. H. Lip, MD, FACC, FESC§

Alicante, Murcia, and Madrid, Spain; and Birmingham, United Kingdom

Objective of the trial

- To present a case series of 426 patients with AF undergoing PCI from registry data
- Particular attention to:
  - *Clinical characteristics*
  - *Demographic characteristics*
  - *Stroke risk factors* by the CHADS2
  - *Antithrombotics before PCI and at discharge*
  - *Bleeding at follow-up*
  - *Thromboembolism at follow-up*
  - *MACE at follow-up*

Methods

- Retrospective 2-center registry of PCI database of patients with AF that underwent PCI over a 5-year period (2001 to 2006)

- Patients with a preexisting diagnosis of AF and those who developed new onset AF during their current admission were included.

Methods

- The type of stent implanted was recorded. Since May 2002, DES were routinely available for use.
- Individual patient management decisions were decided by the interventional cardiologist and/or responsible cardiologist.
- The regimen of oral anticoagulation and/or antiplatelet drugs at discharge was again decided by the responsible clinical cardiologist.

Methods

- Patients were followed up as part of the usual routine.
- Telephone follow-up was also performed to confirm the antithrombotic therapy regimen followed, and to ascertain any episodes of bleeding, stroke/thromboembolism, MACE.
- Medical records and/or outpatient clinic interviews were also reviewed.

End point definitions

- The primary end point:
  - MACE:
    - Death
    - MI
    - TVR
- The secondary safety end point:
  - MAE:
    - Any MACE
    - Major bleeding complications
    - Stroke

Major bleeding was defined as

- Decrease in the blood Hb level of more than 5.0 g/dl (including the period around the PCI)
- The need for the transfusion of ≥ 2 units of blood
- The need for corrective surgery
- The occurrence of an intracranial or retroperitoneal hemorrhage
- Any combination of these events

Results

Results

Table 1 Baseline Characteristics of the Study Population

	Whole Cohort n = 426	Chronic n = 256 (60.1%)	Paroxysmal n = 170 (39.9%)	p Value
Men, n (%)	70.9	69.0	73.7	0.31
Age (yrs)	71.5 ± 8.5	72.3 ± 8.5	70.0 ± 8.5	<0.01
Medical history				
Diabetes (%)	40.2	41.5	38.2	0.49
Hypertension (%)	74.5	75.4	73	0.58
Previous heart failure (%)	26.7	32.4	17.4	<0.01
Previous stroke or thromboembolism (%)	15.9	18	12.4	0.14
Renal failure	14.9	12.8	21.4	0.39
Number of embolic factors	2.5 ± 1.1	2.7 ± 1	1.9 ± 1.1	<0.01
Any embolic factor	95.8	96.9	92.3	0.21
$CHADS_2$ risk score	2 (1-3)	2 (2-3)	2 (1-2)	<0.01
Previous ischemic events (%)	43.7	45.1	40.3	0.29

Results

Table 1 Baseline Characteristics of the Study Population (Cont.)

	Whole Cohort n = 426	Chronic n = 256 (60.1%)	Paroxysmal n = 170 (39.9%)	p Value
Treatment on admission (%)				
Previous aspirin	36.2	31.5	43.6	0.01
Previous clopidogrel	13.8	13.4	14.5	0.77
Previous oral anticoagulation	50.1	69.2	16.0	<0.01
Indication of the catheterization procedure (%)				0.22
Acute STEMI	20.1	16.4	25.7	
Acute NSTEMI	63.8	66.1	60.5	
Stable angina and/or ischemia	16.1	17.5	13.8	

Results

Table 2 Procedural Characteristics

	Whole Cohort n = 426	Chronic n = 256	Paroxysmal n = 170	p Value
Left ventricular ejection fraction <45%	31.2%	31.3%	30.8%	1.0
Stent diameter used (mm)	2.9 ± 0.5	2.9 ± 0.5	2.9 ± 0.5	0.61
Total stent length (mm)	29.7 ± 21.9	27.6 ± 17.0	32.9 ± 27.2	0.03
No. of total stents	1.8 ± 1.2	1.7 ± 0.9	2.1 ± 1.5	<0.01
Patients with DES (%)	40.1	40.7	39.2	0.75
No. of total DES in patients with DES	1.9 ± 1.2	1.6 ± 0.9	2.3 ± 1.5	<0.01
Complete revascularization	60.2	56.3	66.7	0.04
Glycoprotein IIb/IIIa inhibitor	25.7	20.4	34.3	<0.01

Results

Table 3 Antithrombotic Regimen Adopted in AF Patients at Discharge

	Whole Cohort n = 426	Chronic n = 256	Paroxysmal n = 170	p Value
Coumarin + aspirin + clopidogrel (%)	213 (50)	143 (55.8)	70 (41.3)	
Aspirin + clopidogrel (%)	174 (40.8)	90 (35.2)	84 (49.5)	
Coumarin + aspirin (%)	8 (1.9)	6 (2.3)	2 (1.2)	
Coumarin + clopidogrel (%)	16 (3.7)	13 (5.1)	3 (1.7)	
Coumarin monotherapy (%)	5 (1.2)	2 (0.8)	3 (1.7)	
Aspirin monotherapy (%)	5 (1.2)	0	5 (2.9)	
Clopidogrel monotherapy (%)	5 (1.2)	2 (0.8)	3 (1.7)	
				<0.01

Antithrombotic drugs at discharge

- There was wide variability in the antithrombotic therapy regimen and duration of treatment.

- Patients discharged with triple therapy, there was no consistency in the duration of treatment, with either coumarins or 1 antiplatelet agent

Table 4 Differences Between the AF Patients Undergoing PCI/Stenting, Treated at Discharge With Anticoagulation Compared to Those Not Treated With Anticoagulation

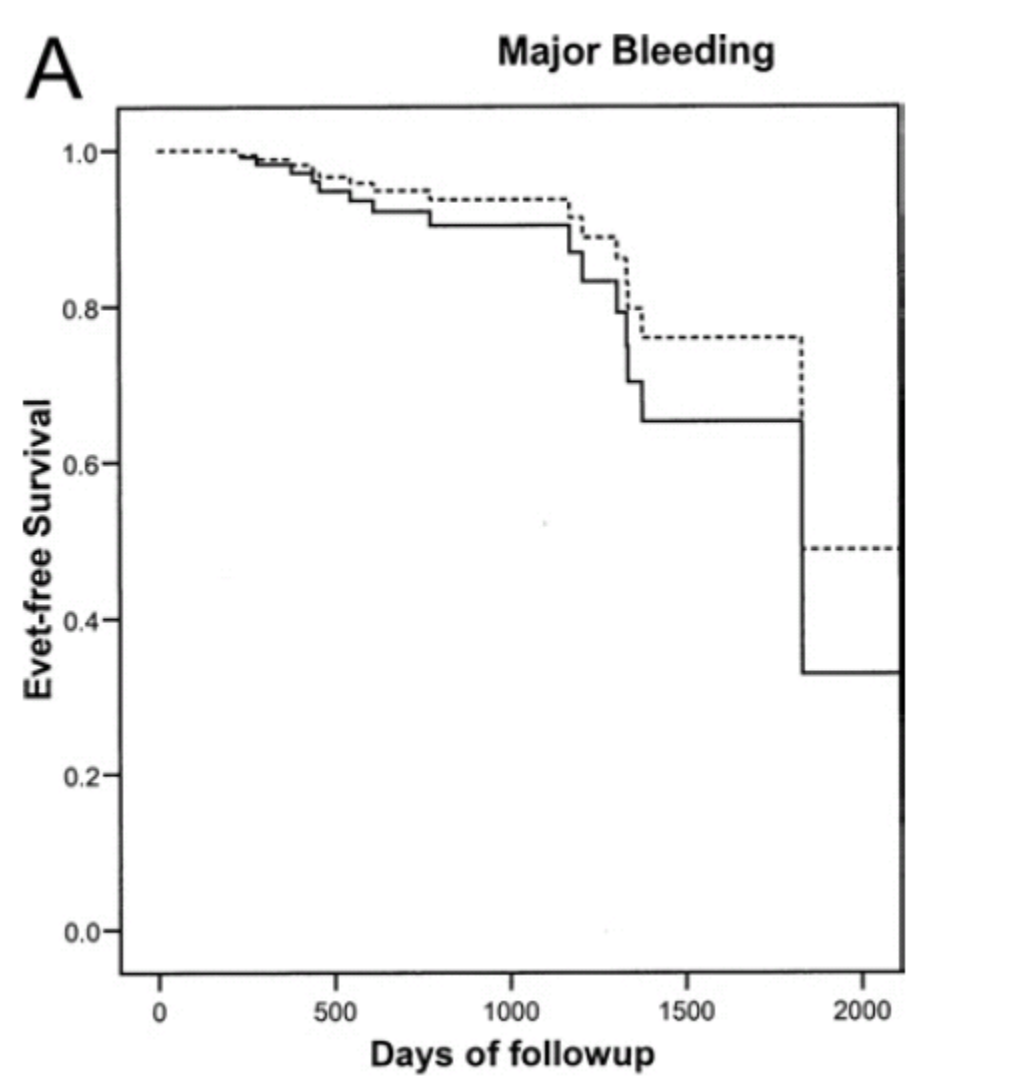
	Whole Cohort n = 426	Anticoagulated n = 242	Not Anticoagulated n = 184	p Value
Men (%)	70.5	70.7	70.4	0.93
Age (yrs)	71.5 ± 8.5	71.6 ± 8.7	71.2 ± 8.5	0.74
Diabetes (%)	40.2	42.5	41.8	0.91
Hypertension (%)	74.5	81.6	72.1	0.04
Previous heart failure (%)	26.7	29.2	22.8	0.18
Previous stroke (%)	15.9	19.6	11.1	0.04
Renal failure	14.9	10.9	22.9	0.09
No. of embolic factors	2.5 ± 1.1	2.8 ± 1.0	2.2 ± 1.1	<0.01
Any embolic factor	95.8	98.8	90.6	0.04
$CHADS_2$ risk score, median (IQR)	2 (1–3)	2 (1–3)	2 (1–3)	0.02
Previous ischemic events (%)	43.7	43.2	44	0.99
Treatment on admission (%)				
Previous aspirin	36.2	30.3	40.9	0.05
Previous clopidogrel	13.8	11.0	17.8	0.11
Previous oral anticoagulation	50.1	69.2	27.7	<0.01
Indication of the catheterization procedure (%)				0.20
Acute STEMI	20.1	16.0	23.1	
Acute NSTEMI	63.8	66.0	61.3	
Stable angina and/or ischemia	16.1	18.6	15.6	

Table 5 Events During Follow-Up

	Whole Cohort n = 373	Anticoagulated n = 195	Not Anticoagulated n = 178	p Value
Major bleeding (%)	12.3	14.9	9.0	0.19
Minor bleeding (%)	11.0	12.6	9.0	0.32
Embolism (%)	4.2	1.7	6.9	0.02
Death (%)	22.6	17.8	27.8	0.02
Acute myocardial infarction (%)	8.4	6.5	10.4	0.14
Target vessel revascularization (%)	7.7	7.1	8.4	0.3
Target vessel failure (%)	9.2	9.2	16.7	<0.01
Revascularization of other lesions (%)	7.1	5.9	8.5	0.25
Subacute or late thrombosis (%)	1.2	1.2	1.3	0.65
MACE (%)	32.3	26.5	38.7	0.01
MAE (%)	36.6	31.8	41.9	0.03

Complete follow-up was achieved in 88% of the cohort (median 595 days; range 0 to 2,190 days).

Kaplan-Meier Survival Curves in Relation to Anticoagulation Use at Discharge

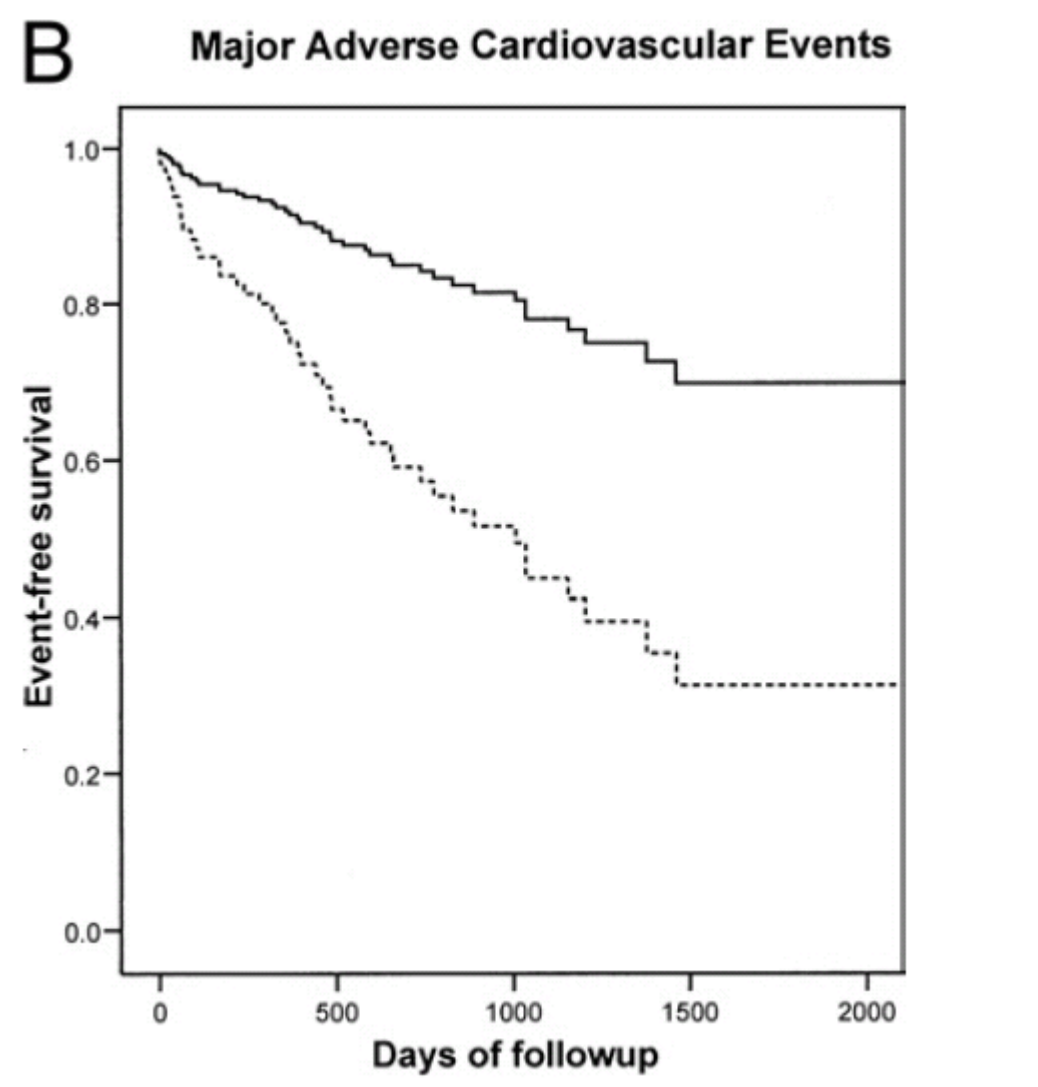


Anticoagulation

No Anticoagulation

$p = 0.6$

Kaplan-Meier Survival Curves in Relation to Anticoagulation Use at Discharge

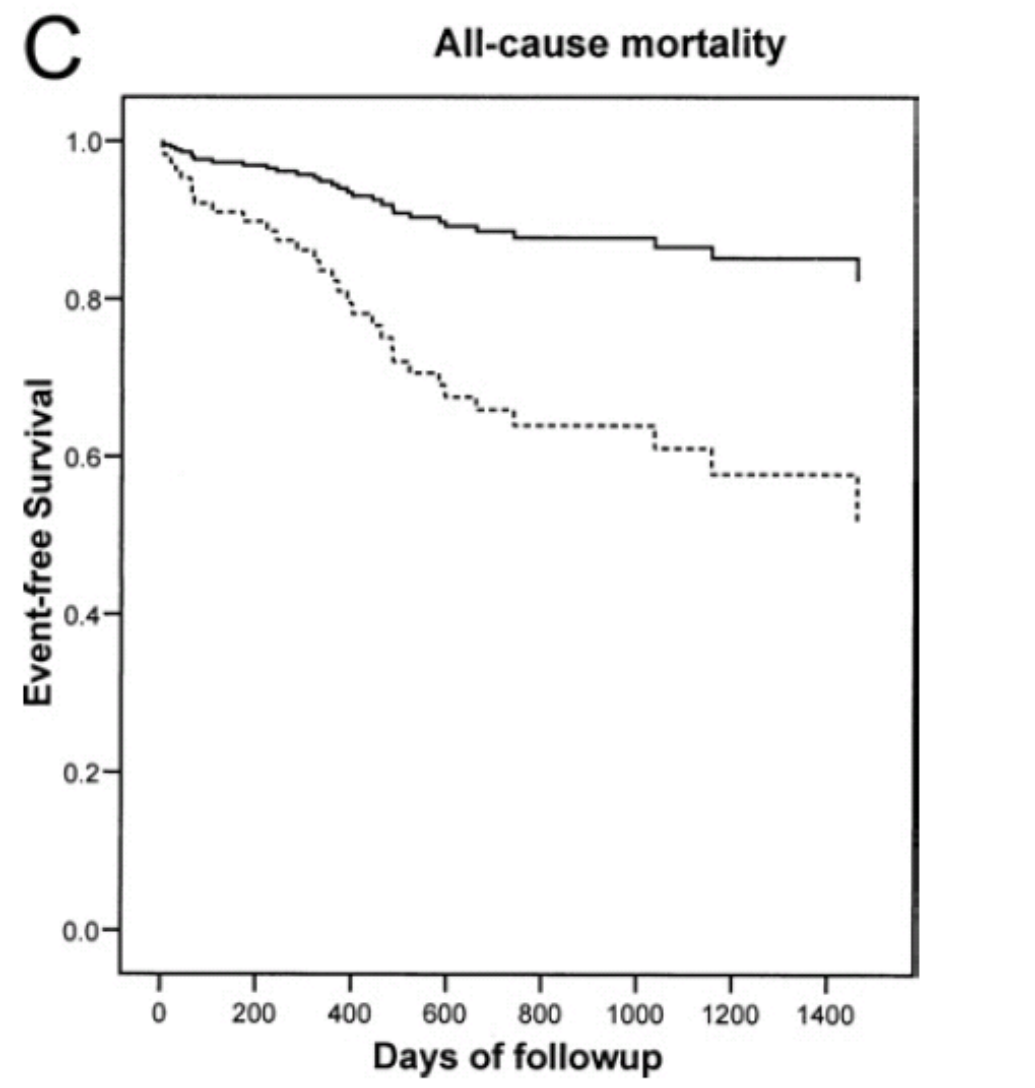


Anticoagulation

No Anticoagulation

$p = 0.02$

Kaplan-Meier Survival Curves in Relation to Anticoagulation Use at Discharge



Anticoagulation

No Anticoagulation

$p = 0.03$

Table 6 Cox Regression for the Analysis of Major Adverse Cardiovascular Events

Variables	β	SE	p Value	HR	95% CI
Age	0.06	0.02	0.02	1.07	1.01–1.12
Type of AF	0.41	0.53	0.44	1.51	0.53–4.31
Hypertension	−0.36	0.43	0.40	0.69	0.30–1.61
Diabetes	−0.23	0.35	0.51	0.80	0.40–1.58
Congestive heart failure or low LVEF	−0.15	0.35	0.67	0.86	0.43–1.71
Renal failure	−0.89	0.66	0.18	0.41	0.11–1.50
Previous stroke	0.22	0.49	0.65	1.24	0.48–3.25
Previous aspirin	0.23	0.41	0.58	1.25	0.57–2.78
Previous clopidogrel	−0.13	0.41	0.75	0.88	0.40–1.95
Previous oral anticoagulation	−0.76	0.50	0.12	0.47	0.18–1.23
Use of DES	−0.35	0.33	0.29	0.70	0.36–1.35
Nonanticoagulation at discharge	1.59	0.42	<0.01	4.9	2.17–11.09
Complete revascularization	−0.68	0.33	0.07	0.51	0.27–1.17

Table 7 Cox Regression Analysis for Major Adverse Events

Varlables	β	SE	p Value	HR	95% CI
Age	0.06	0.03	0.02	1.06	1.01–1.12
Type of AF	0.47	0.53	0.38	1.60	0.56–4.54
Hypertension	−0.29	0.41	0.48	0.75	0.33–1.68
Diabetes	−0.23	0.34	0.50	0.79	0.41–1.54
Congestive heart failure or low LVEF	−0.13	0.34	0.71	0.88	0.45–1.73
Renal failure	−0.87	0.65	0.18	0.42	0.12–1.51
Previous stroke	0.28	0.49	0.56	1.33	0.51–3.43
Previous aspirin	0.12	0.39	0.76	1.13	0.53–2.41
Previous clopidogrel	−0.08	0.40	0.84	0.92	0.42–2.02
Previous oral anticoagulation	−0.78	0.49	0.11	0.46	0.18–1.19
Use of DES	−0.39	0.33	0.23	0.68	0.36–1.29
Nonanticoagulation at discharge	1.47	0.40	<0.01	4.33	1.96–9.59
Complete revascularization	−0.56	0.32	0.08	0.57	0.31–1.07

Discussion

- This is the largest dataset of AF patients undergoing PCI where antithrombotic therapy management strategies have been related to clinical outcomes.

- These patients represent a high-risk population owing to:
  - Age
  - Comorbidities
  - The presence of stroke risk factors
  - High incidence of ACS as the indication for PCI

Discussion

- This data confirm *the protective effect of the coumarins in patients with AF treated with PCI by decreasing the incidence of MACE.*

- The beneficial effect of coumarins is confirmed in the multiple regression analysis as an independent predictors of MACE.

Discussion

- The present study illustrates that various antithrombotic drug combinations are used in everyday practice.

- Such variability is due to the lack of available guidelines.

- The combination of Coumarins plus Aspirin after PCI has previously been shown to be less effective compared to Ticlopidine plus Aspirin in preventing stent thrombosis.

- There is clear superiority of oral anticoagulation over dual antiplatelet therapy with Aspirin plus Clopidogrel in stroke prevention in AF *

* The ACTIVE Writing Group. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the ACTIVE trial. Lancet 2006;367:1903-12.

Discussion

- Although *the combination of aspirin and clopidogrel* (40.7%) or *triple therapy* (50.0%) accounted for the majority of patients, the duration of their use still varied widely among patients.

- This variability was due essentially to the use of DES

European Heart Journal (2007) 28, 726–732
doi:10.1093/eurheartj/ehl488

EUROPEAN SOCIETY OF CARDIOLOGY®

Clinical research
Interventional cardiology

Safety and efficacy of combined antiplatelet-warfarin therapy after coronary stenting

Pasi P. Karjalainen[1]*, Pekka Porela[2], Antti Ylitalo[1], Saila Vikman[3], Kai Nyman[4], Mari-Anne Vaittinen[5], Tuukka J. Airaksinen[6], Matti Niemelä[6], Tero Vahlberg[7], and K.E. Juhani Airaksinen[2]

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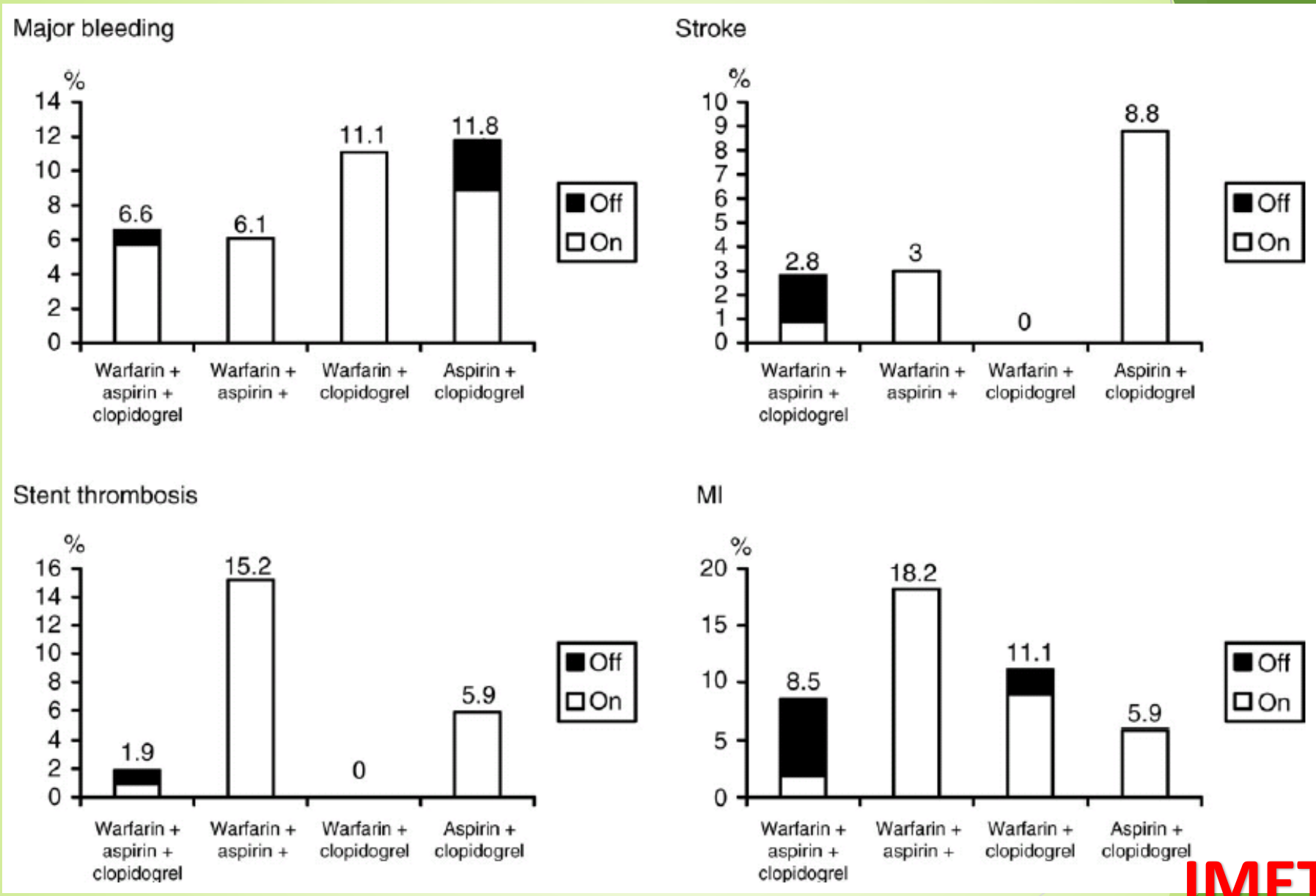
Such therapy cessation exposes these patients to stent thrombosis or stroke/thromboembolism

Triple therapy is currently the best option for the majority of the patients, although this predisposes to an increased risk of bleeding, which may require stopping anticoagulation and/or antiplatelet therapy.



Complications during 12-month follow-up with various drug regimens

The long-term prognosis of warfarin treated patients is unsatisfactory irrespective of the drug combinations used.

DES subgroup

- 174 patients (40.1%) were treated with ≥ 1 DES.
- A higher prevalence of diabetes was observed in these patients (46% vs. 35%: p 0.03), but no other differences
- The characters of the implanted stents:
  - *Number of stents higher (2.17 vs. 1.59; p 0.01)*
  - *Smaller (2.78 mm vs. 2.99 mm; p 0.01)*
  - *Longer (39 mm vs. 35 mm; p 0.01)*

DES subgroup

- In a univariate analysis, a lower incidence of MACE was observed in the DES group (29.0% vs. 40.5%; p 0.032)
- This difference did not persist in a multivariate analysis.
- Patients treated with DES had a higher rate of stent thrombosis (2.8% vs. 0%; p 0.034)

Incidence, Predictors, and Outcome of Thrombosis After Successful Implantation of Drug-Eluting Stents

Ioannis Iakovou, MD
Thomas Schmidt, MD
Erminio Bonizzoni, PhD
Lei Ge, MD
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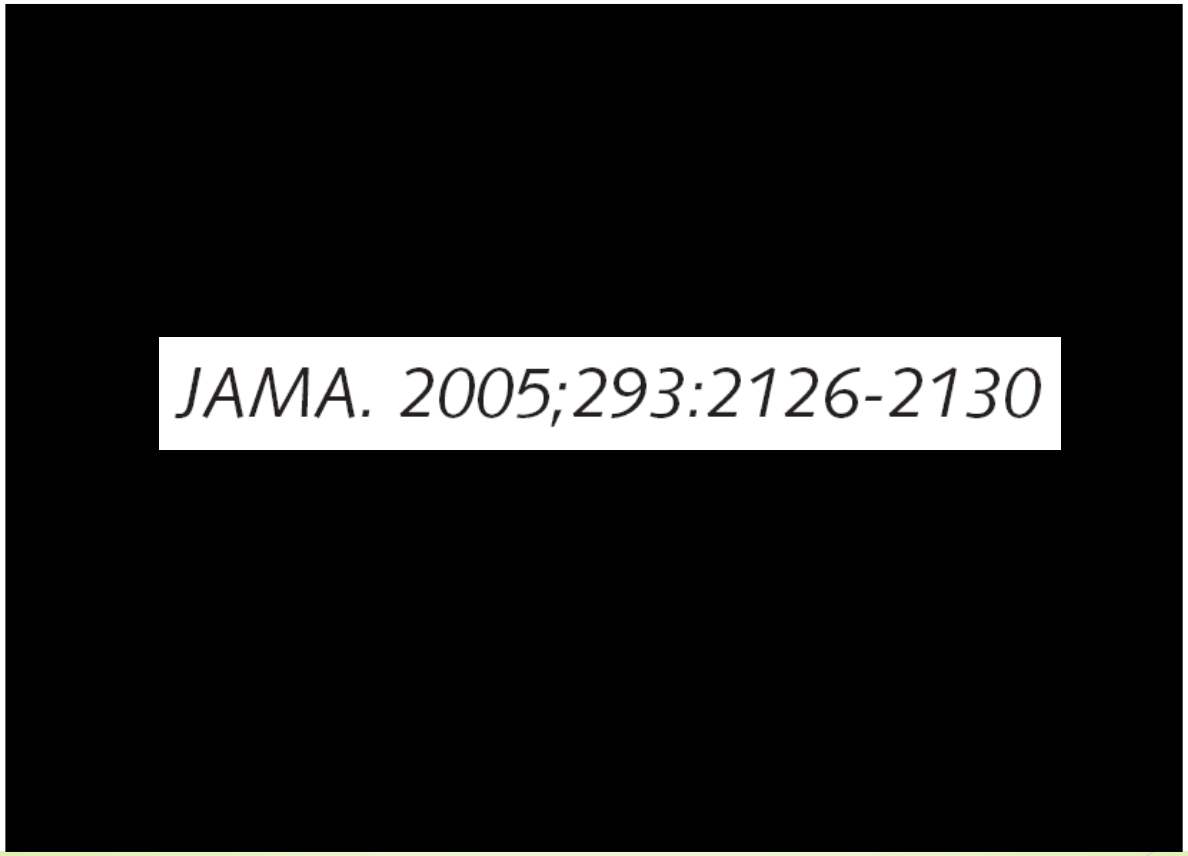
Iassen Michev, MD
Nicola Corvaja, MD
Carlo Briguori, MD
Ulrich Gerckens, MD
Eberhard Grube, MD
Antonio Colombo, MD



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Review

Antithrombotic treatment for patients on oral anticoagulation undergoing coronary stenting
A review of the available evidence and practical suggestions for the clinician

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Available online 16 April 2007

The implantation of DES should probably be discouraged in anticoagulated AF patients due to the need for prolonged dual antiplatelet administration.

Limitation of the Study

- This large study is limited by its registry design.
- Many confounders/biases are possible, although they have tried to address most in a multivariate analysis.
- The changes of antithrombotic regiment in these patients during the follow-up period, sometimes in relation to the presence of thrombotic or hemorrhagic complications.

Conclusion

- Treatment with coumarins at discharge shows a beneficial effect on prognosis by reducing the incidence of death and MACE
- Such benefits do not appear to be associated with a substantial increase in major bleeding events.
- Patients with low risk of bleeding complications, a triple-therapy regimen should be used
- Further large studies are required

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FOCUS ISSUE: ATRIAL FIBRILLATION

Editorial Comment

"Triple Therapy" or Triple Threat?

Balancing the Risks of Antithrombotic Therapy for Patients With Atrial Fibrillation and Coronary Stents*

Steven Francescone, MD, Jonathan L. Halperin, MD, FACC

New York, New York

Editorial Comment

- Consider the imperative of preventing ischemic stroke in patients with AF.
- Warfarin reduces thromboembolism by about one-half while increasing major bleeding to 1% to 2% per year.
- For the highest-risk AF patients, the benefit of anticoagulation outweighs the bleeding risk.

Editorial Comment

- Although Aspirin is the prophylactic antiplatelet drug of choice, it reduces the risk of recurrent stroke, MI, and vascular death by only 13%.

- Clopidogrel was 8% better than aspirin and associated with fewer GI bleeding.

* CAPRIE Steering Committee. Lancet 1996;348:1329 -39.

Characteristics and Outcomes of Patients Taking Warfarin Prior to Percutaneous Coronary Intervention

- Atul Aggarwal,[1] David Dai,[2] John S. Rumsfeld,[3]
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- on behalf of the American College of Cardiology –
- National Cardiovascular Data Registry (NCDR)

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Methods

- Patients undergoing PCI in American College of Cardiology – National Cardiovascular Data Registry from January 1st, 2004 till March 30, 2006 were evaluated (n=307,443)

Data collection

- Patients taking warfarin at home prior to PCI and compared with those not taking
- Patients stratified according to the urgency of the procedure
  - Urgent PCI defined as cardiogenic shock at admission, STEMI with onset of symptoms within 24 hours of performance of PCI, or primary, rescue or facilitated PCI
  - Elective All other PCI procedures categorized as

Primary outcome

- Mortality
- Composite bleeding complications

Clinical Characteristics

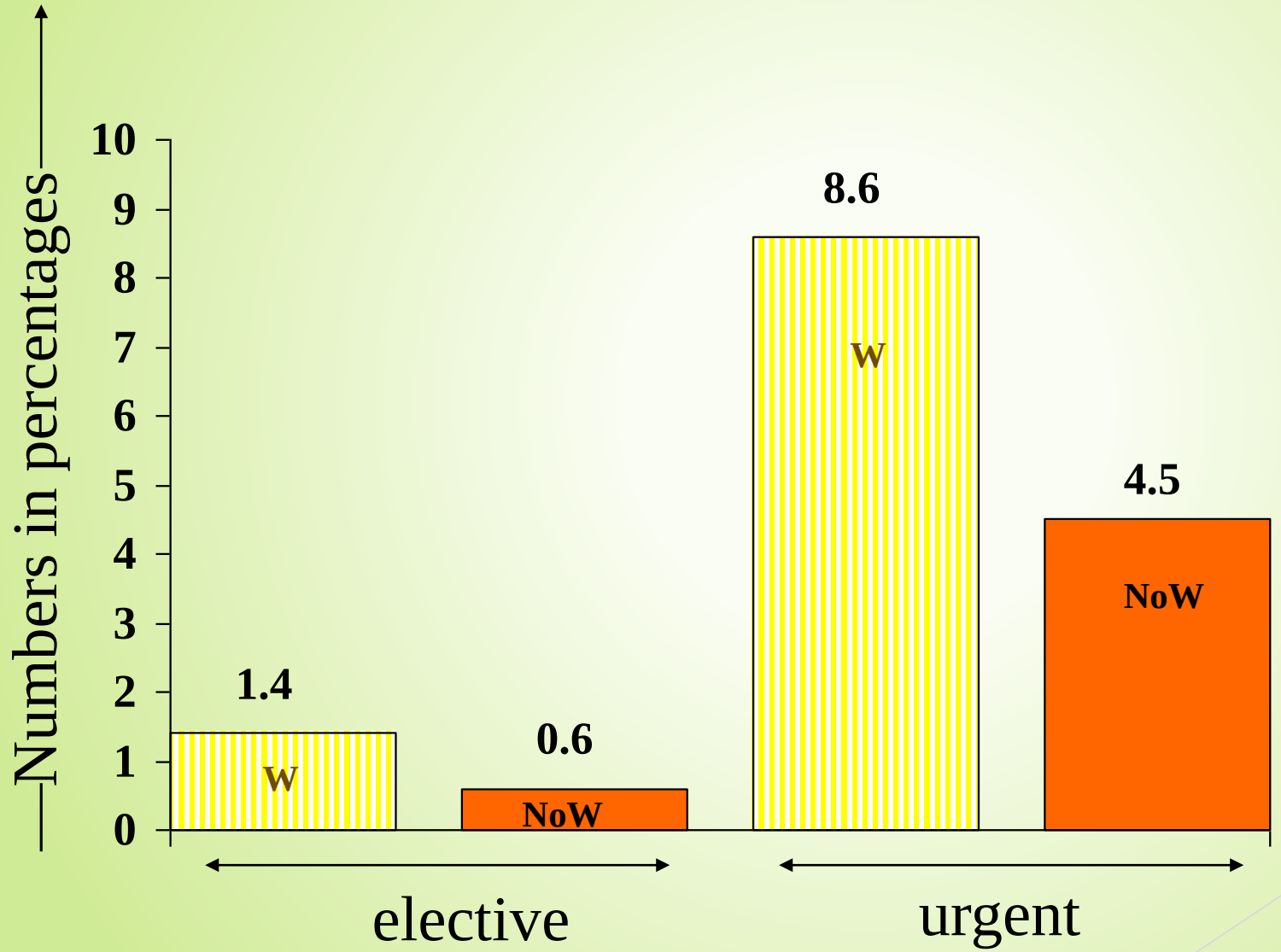
- Of the 307,443 patients who underwent PCI, 11,173 (3.6%) were receiving warfarin before PCI, and 44,443 patients (15%) underwent urgent PCI

	Elective PCI (n=263,000)			Urgent PCI (n=44,443)		
	Warfarin (n=10002)	No Warfarin (n=252998)	P-value	Warfarin (n=1171)	No Warfarin (n=43272)	P-value
Demographics						
Age (years)	70±10.8	64.4±11.9	<0.0001	67.1±13.2	60.5±13.0	<0.0001
Male sex	66.1	65.6	0.26	65.9	70.9	0.0002
Risk factors for Coronary Artery Disease						
Diabetes mellitus (%)	38.8	33.3	<0.0001	31.0	21.0	<0.0001
Hypertension (%)	82.1	77.7	<0.0001	71.0	59.0	<0.0001
Tobacco abuse (%)	57.9	61.8	<0.0001	59.0	67.5	<0.0001
Family history (%)	25.6	29.3	<0.0001	20.8	26.7	<0.0001
Dyslipidemia (%)	73.4	76.4	<0.0001	58.7	56.4	0.12
Medical History						
Old MI >7 days (%)	37.5	30.8	<0.0001	29.4	17.7	<0.0001
History of CHF (%)	28.7	10.6	<0.0001	17.0	4.4	<0.0001
Previous PCI (%)	38.4	37.9	0.33	26.9	17.1	<0.0001
Previous CABG (%)	32.2	20.4	<0.0001	12.6	6.2	<0.0001
Prior valve surgery (%)	8.5	0.8	<0.0001	5.2	0.4	<0.0001
Cerebrovascular disease (%)	23.9	11.5	<0.0001	21.3	6.3	<0.0001
Cardiogenic shock (%)	1.2	0.8	<0.0001	13.6	8.9	<0.0001

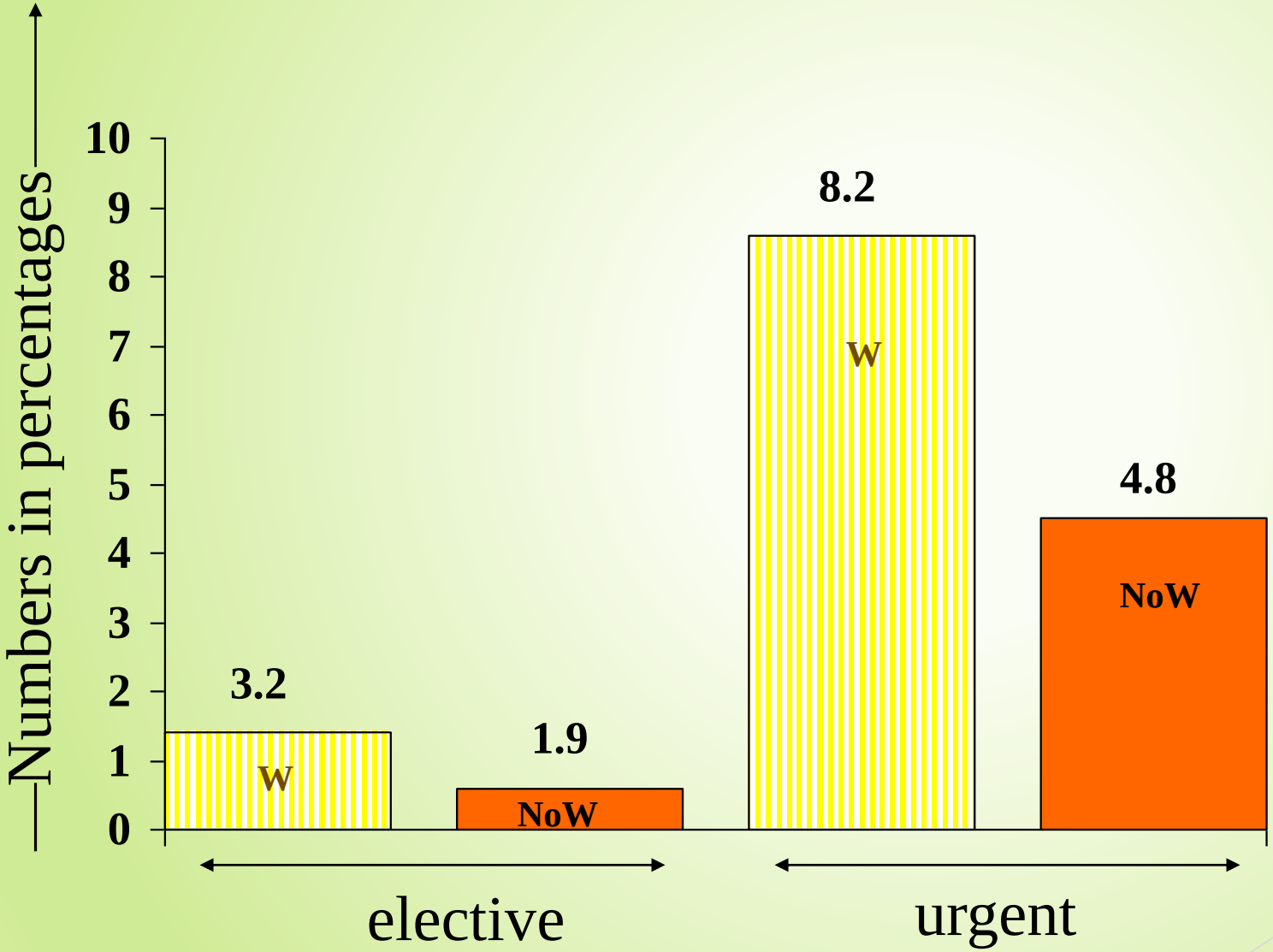
Procedural Characteristics

	Elective PCI (n=263000)			Urgent PCI (n=44443)		
	Warfarin	No Warfarin	P-value	Warfarin	No Warfarin	P-value
Ejection fraction (%)	48.1±15	53.8±12	<0.0001	41.5±14	46.6±13	<0.0001
IABP use (%)	1.3	1.0	0.01	14.3	9.6	<0.0001
Multi-vessel (%)	66.4	65.5	0.07	57.6	64.1	<0.0001
High risk (type C, %)	39.4	38.2	0.01	61.7	58.0	0.01
Vein graft lesion (%)	11.2	7.2	<0.0001	5.9	3.3	<0.001
Stents per procedure	1.5±0.9	1.5±0.9	0.01	1.4±0.9	1.4±0.9	0.05
DES use (%)	81.3	85.5	<0.0001	71.3	77.5	<0.0001
Post procedure TIMI 3 flow (%)	95.5	96.5	0.002	91.2	93.5	0.08
No-reflow (%)	1.4	1.1	0.02	4.4	3.1	0.02

Unadjusted In-Hospital Mortality



Unadjusted In-Hospital Bleeding



Unadjusted Clinical Outcomes

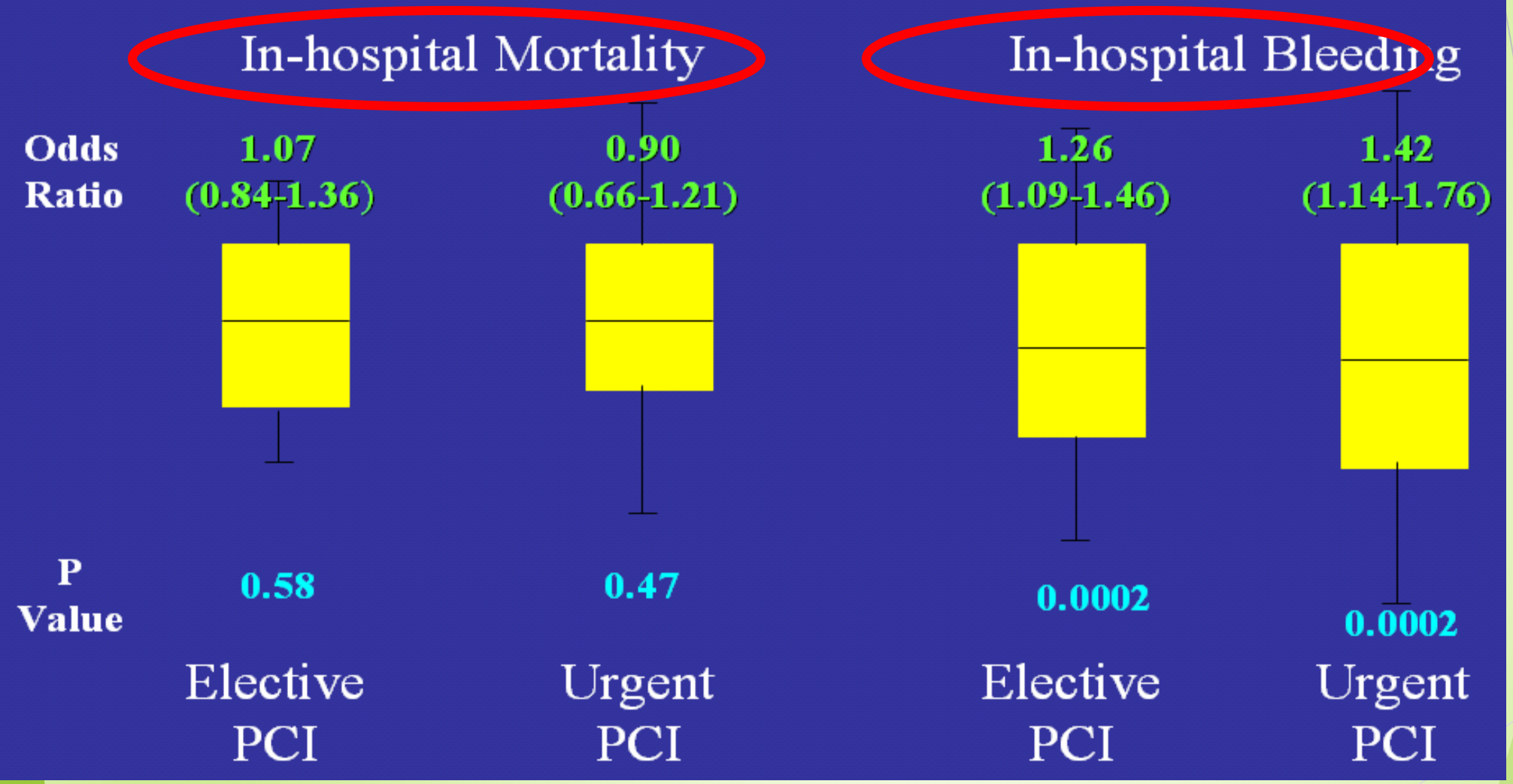
	Elective PCI			Urgent PCI		
	Warfarin	No Warfarin	P-value	Warfarin	No Warfarin	P-value
In-hospital Mortality (%)	1.4	0.6	<0.0001	8.6	4.5	<0.0001
Periprocedural MI (%)	1.7	1.5	0.05	1.7	1.1	0.03
Cardiogenic shock (%)	1.1	0.7	<0.0001	4.2	2.9	0.01
CHF (%)	1.6	0.7	<0.0001	5.9	2.9	<0.0001
Stroke (%)	0.8	0.5	<0.0001	1.2	0.6	0.02
Renal failure (%)	1.0	0.5	<0.0001	2.7	1.4	0.0004

Patients who died on the same day as PCI are excluded (n=786)

Unadjusted Clinical Bleeding Outcomes

	Elective PCI (85%)			Urgent PCI (15%)		
	Warfarin	No Warfarin	P-value	Warfarin	No Warfarin	P-value
Bleeding, composite (%)	3.2	1.9	<0.0001	8.2	4.8	<0.0001
Bleeding at access site (%)	1.3	0.8	<0.0001	2.8	1.9	0.04
Retroperitoneal bleeding (%)	0.3	0.3	0.64	0.4	0.7	0.35
Gastrointestinal bleeding (%)	0.8	0.4	<0.0001	2.3	1.2	0.0004
Genitourinary bleeding (%)	0.3	0.1	<0.0001	0.7	0.2	0.003
Bleeding site not classified (%)	0.8	0.4	<0.0001	2.6	1.2	<0.0001
Cardiac tamponade (%)	0.6	0.4	0.0001	0.9	0.4	0.01

Adjusted Clinical Outcomes



Conclusions

- Patients taking warfarin prior to elective and urgent PCI were at *increased risk of bleeding complications*
- *No association was observed between warfarin use and risk-adjusted in-hospital mortality*
- *Warfarin use is largely a marker for co-morbidities*

The Incidence and Outcomes of Patients Receiving Triple Therapy with Aspirin, Warfarin and a Thienopyridine vs. Dual Therapy with Aspirin and a Thienopyridine for Acute Coronary Syndrome – Data from The ACSIS Surveys 2000-2004.

Yuval Konstantino[1], Zaza Iakobishvili[1], Avital Porter[1], Amir Sandach[2], Doron Zahger[2], Hanoch Hod[2], Haim Hammerman[2], Jonathan Leor[2], Shmuel Gottlieb[2], Solomon Behar[2], and David Hasdai[1].

Results: In-hospital bleeding complications

	DT (n=2661)	TT (n=76)	P
Major bleeding (%)	**0.6**	**2.6**	**0.03**

Results: Outcomes - Unadjusted and adjusted mortality rates

	DT n=2661	TT n=76	P
7-Days (%)	0.2	0.0	0.68
30-Days (%)	1.1	4.0	0.02
6-months (%)	3.1	8.1	0.02
1-Year (%)	4.0	9.1	0.1

Adjusted* 30d Mortality - O.R: 2.27, CI:0.53-7.14

Adjusted* 6m Mortality – O.R: 1.6, CI:0.56-3.85

- * Age, Gender, H/O CAD, Heart failure, 1° PCI, Log CK, Renal failure

Conclusions

- **The TT group was a small group characterized by:**
  - Worse baseline risks features
  - Higher rate of invasive procedures, cardiovascular complications and in-hospital major bleeding
- **Hemorrhagic complications in the TT group were uncommon (2.6%)**
- **Adjusted mortality rates were similar in both groups**
- **Thus, TT is feasible in ACS pts with a clear indication for warfarin treatment**

Recommendations

- Re-consider the need for PCI
- Re-consider the indication for warfarin

Recommendations

- *If both warfarin and stenting necessary:*
  - Avoid DES as much as possible
  - Triple anticoagulation probably the best
  - Give low dose (75-80 mg/d) aspirin
  - Give clopidogrel for 3 months only
  - Carefully monitor the INR
  - If bleeding risk is high, warfarin + clopidogrel may be considered.
  - Carefully educate the patient

Some attention and luck may save your patient

Thank You

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