Το παρόν και το μέλλον της επεμβατικής καρδιολογίας

Ιωάννης Ε. Καλλικάζαρος
Διευθυντής Καρδιολογικού Τμήματος
Γ.Ν.Α Ιπποκράτειο

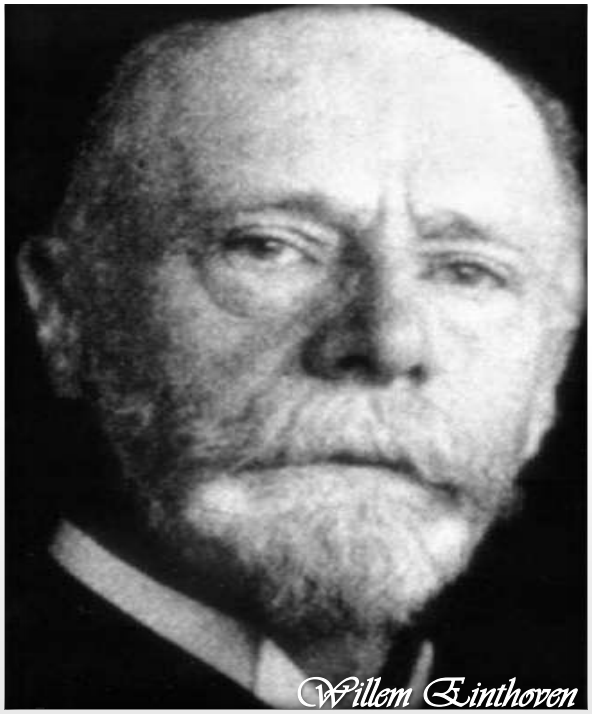
Renaissance…

"It has been shown by reason and experiment that by the beat of the ventricles blood flows through the lungs and it is pumped to the whole body. There it passes through pores in the flesh into the veins through which it returns from the periphery…finally coming to the vena cava and right auricle…It must then be concluded that the blood in the animal body moves around in a circle continuously, and that the action or function of the heart is to accomplish this by pumping. This is the only reason for the motion and beat of the heart"

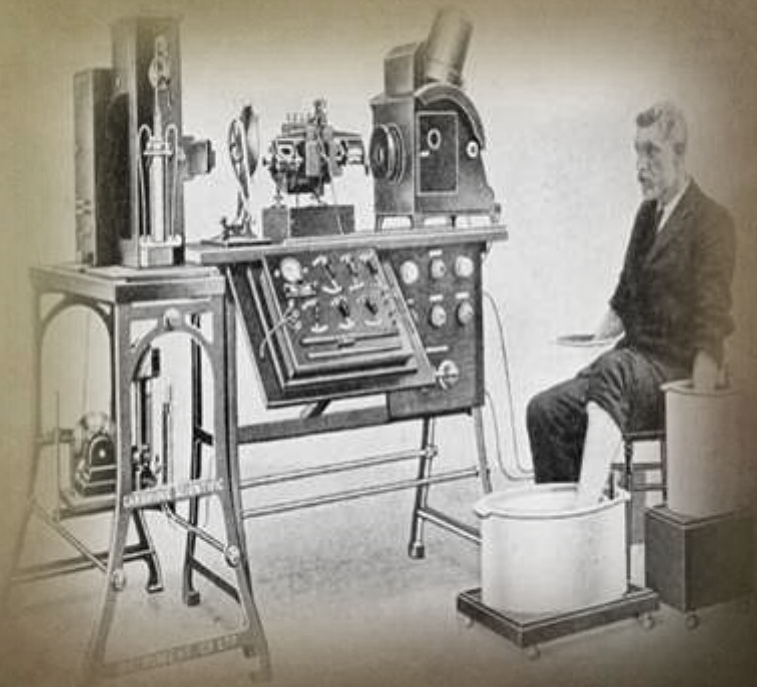
Harvey W. Exercitatio anatomica de motu cordis et sanyuinis in animalibus. London, 1628. Surrey, England: Barnes, 1847

Grand Achievements of the 20th Century

Electrocardiogram



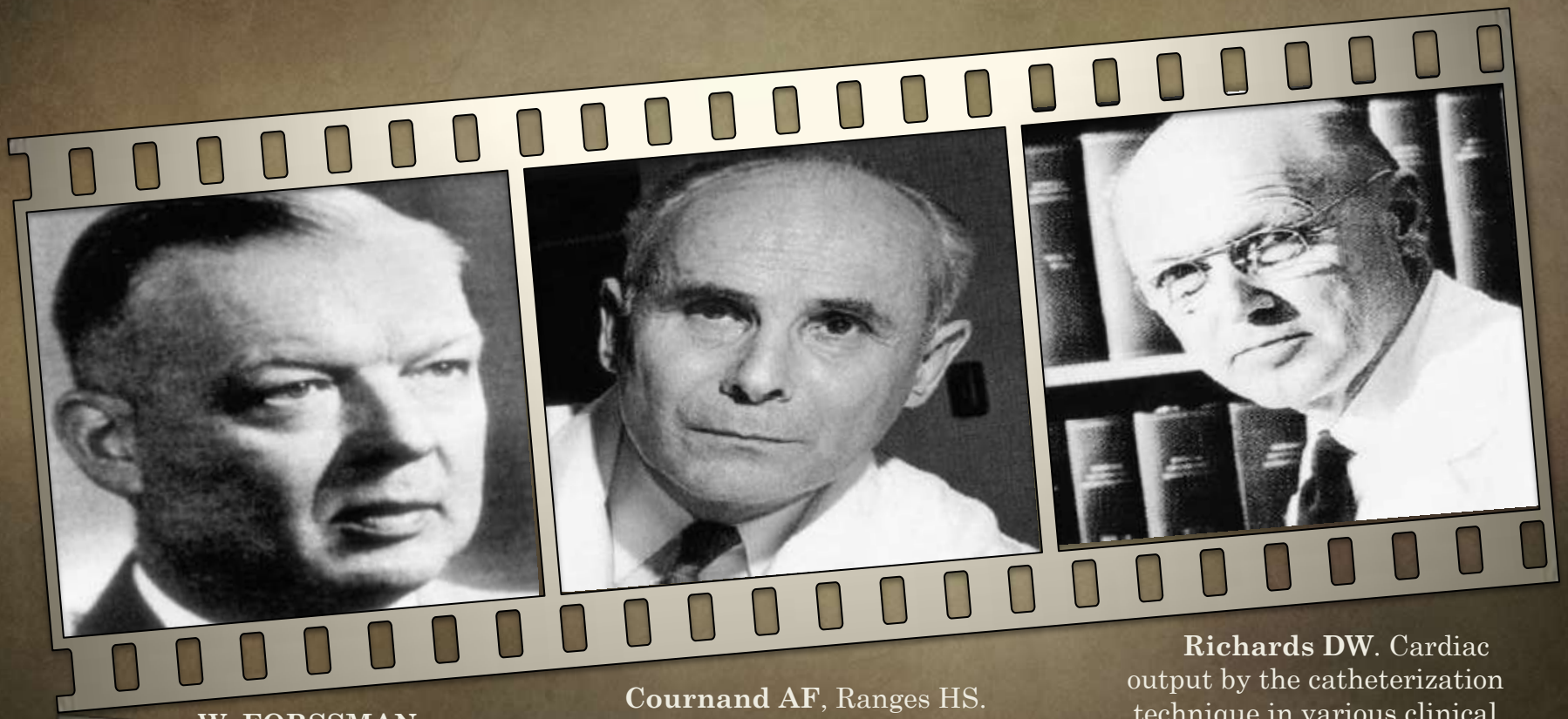
Semarang, May 21, 1860 –Leiden, September 29, 1927



Einthoven W. Die galvanometrische Registrirung des menschlichen Elektrokardiogramm. Pfluger's Arch f.d. Ges Physiol 1903;99:472–80

Grand Achievements of the 20th Century

Cardiac Catheterization



W. FORSSMAN
Die Sondierung des rechten Herzen
Klinishce Wochenschrift, vol. 8, pp. 2085-2087, 1929

Cournand AF, Ranges HS. Catheterization of the right auricle in man. Proc Soc Exp Biol Med 1941;46:462–6

Richards DW. Cardiac output by the catheterization technique in various clinical conditions. Fed Proc 1945;4:215–20

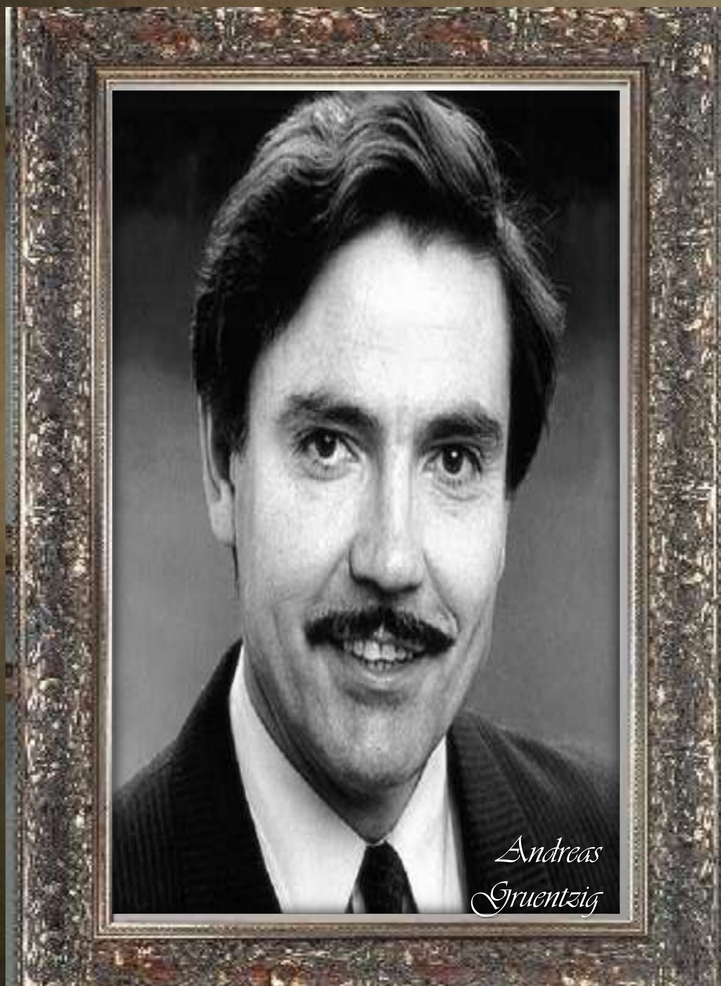
Grand Achievements of the 20th Century

Coronary angiography

Sones FM Jr.. Cine coronary arteriography. Mod Concepts Cardiovasc Dis 1962;31:735–8

Grand Achievements of the 20th Century

Interventional Cardiology



June 25, 1939–October 27, 1985

The New England
Journal of Medicine

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Volume 301 JULY 12, 1979 Number 2

NONOPERATIVE DILATATION OF CORONARY-ARTERY STENOSIS

Percutaneous Transluminal Coronary Angioplasty

Andreas R. Grüntzig, M.D., Åke Senning, M.D., and Walter E. Siegenthaler, M.D.

Abstract In percutaneous transluminal coronary angioplasty, a catheter system is introduced through a systemic artery under local anesthesia to dilate a stenotic artery by controlled inflation of a distensible balloon.

Over the past 18 months, we have used this technic in 50 patients. The technic was successful in 32 patients, reducing the stenosis from a mean of 84 to 34 per cent ($P<0.001$) and the coronary-pressure gradient from a mean of 58 to 19 mm Hg ($P<0.001$). Twenty-nine patients showed improvement in cardiac function during follow-up examination. Because of acute deterioration in clinical status, emergency bypass was later necessary in five patients; three showed electrocardiograpic evidence of infarcts.

Patients with single-vessel disease appear to be most suitable for the procedure, and a short history of pain indicates the presence of a soft (distensible) atheroma likely to respond to dilatation. We estimate that only about 10 to 15 per cent of candidates for bypass surgery have lesions suitable for this procedure. A prospective randomized trial will be necessary to evaluate its usefulness in comparison with surgical and medical management. (N Engl J Med 301:61-68, 1979)

In 1964, Dotter and Judkins[1] introduced the technic of transluminal angioplasty for the treatment of atherosclerotic obstruction of the femoral artery. Despite their enthusiasm, the technic has been largely ignored in the United States. In Europe, however, several physicians have used this technic to treat large numbers of patients.[2]

Because of the technical difficulties, complications and limited usefulness of transluminal angioplasty in the treatment of obstruction of the peripheral arteries, we sought to modify the original technic of Dotter and Judkins. A double-lumen dilatation catheter with a nonelastic balloon was developed.[3] Such catheters have been used since February, 1974, in patients with obstructions of the femoropopliteal and iliac arteries and have yielded low complication rates and no mortality.[4]

Recently, we modified this catheter to allow us to develop a technic for percutaneous dilatation of renal-artery[5] and coronary-artery stenosis.[6] This technic was used in human beings[7] after preliminary trials in dogs and cadavers.[8-10] We present here preliminary results obtained with the technic in the past 18 months.

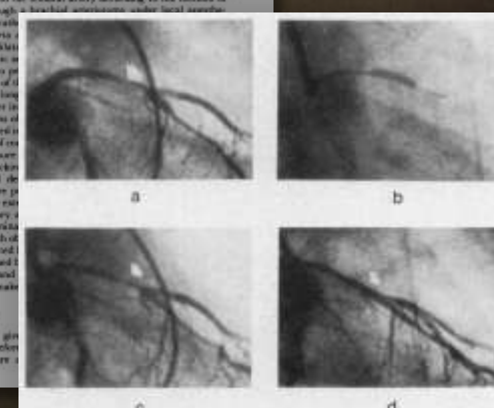
MATERIALS AND METHODS

Technic

Drug Treatment

From the Section of Cardiology, Medical Policlinic, Department of Medicine, and Surgical Clinic A, University Hospital, Zurich, Switzerland (address reprint requests to Dr. Grüntzig at Medical Policlinic, Department of Medicine, University Hospital, Rämistrasse 100, CH-8091 Zurich, Switzerland).

Supported by a grant from the Swiss National Science Foundation.



Gruentzig AR, Myler RK, Hanna ES, Turina MI. Coronary transluminal angioplasty. Circulation 1977;84:55–6

Grand Achievements of the 20th Century

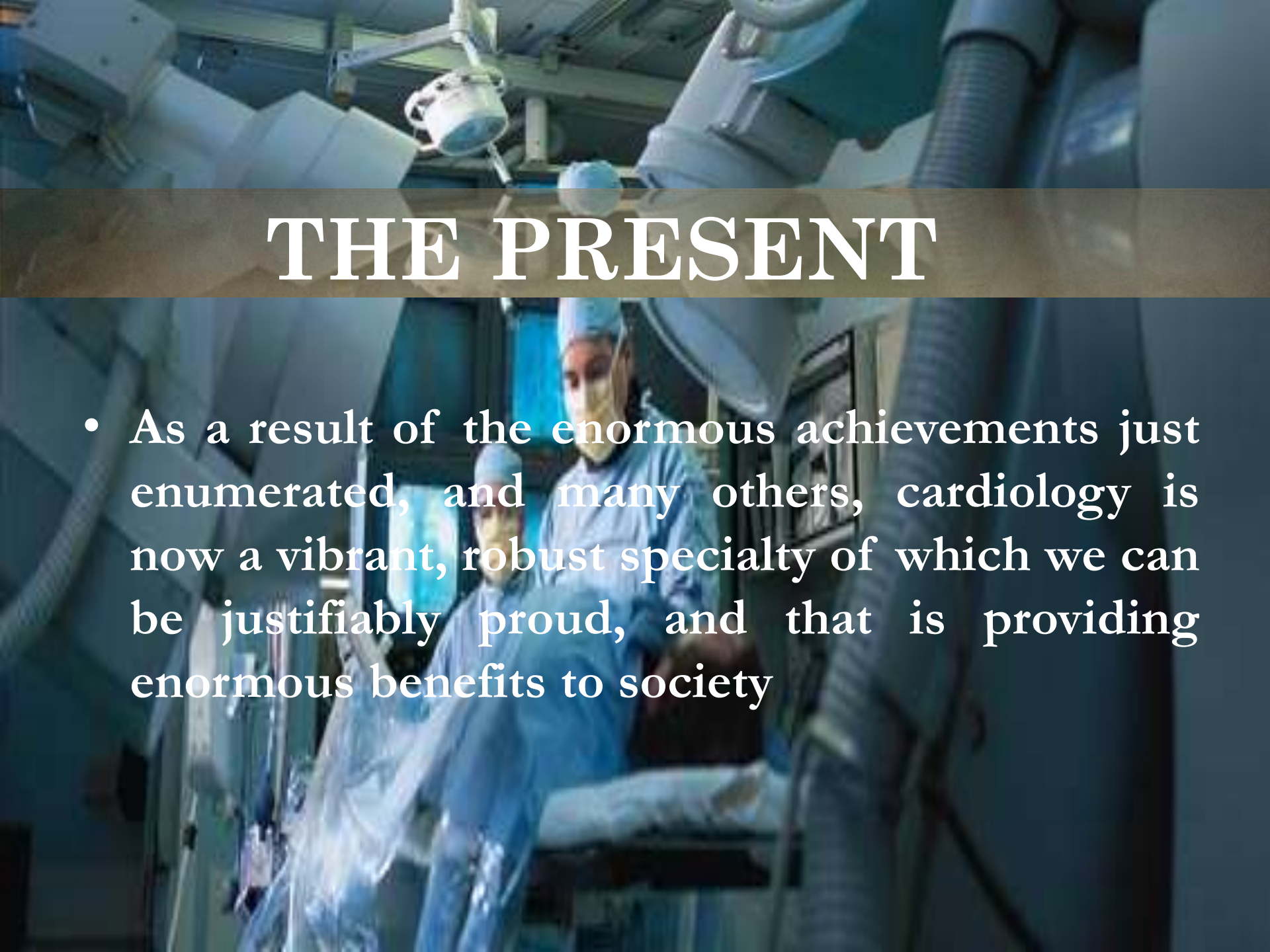
Pacemakers and ICDs

July 15, 1911 - January 5, 1999

October 14, 1924 – March 26, 1990

Zoll PM. Resuscitation of the heart by external electrical stimulation. N Engl J Med 1952;247:768–71

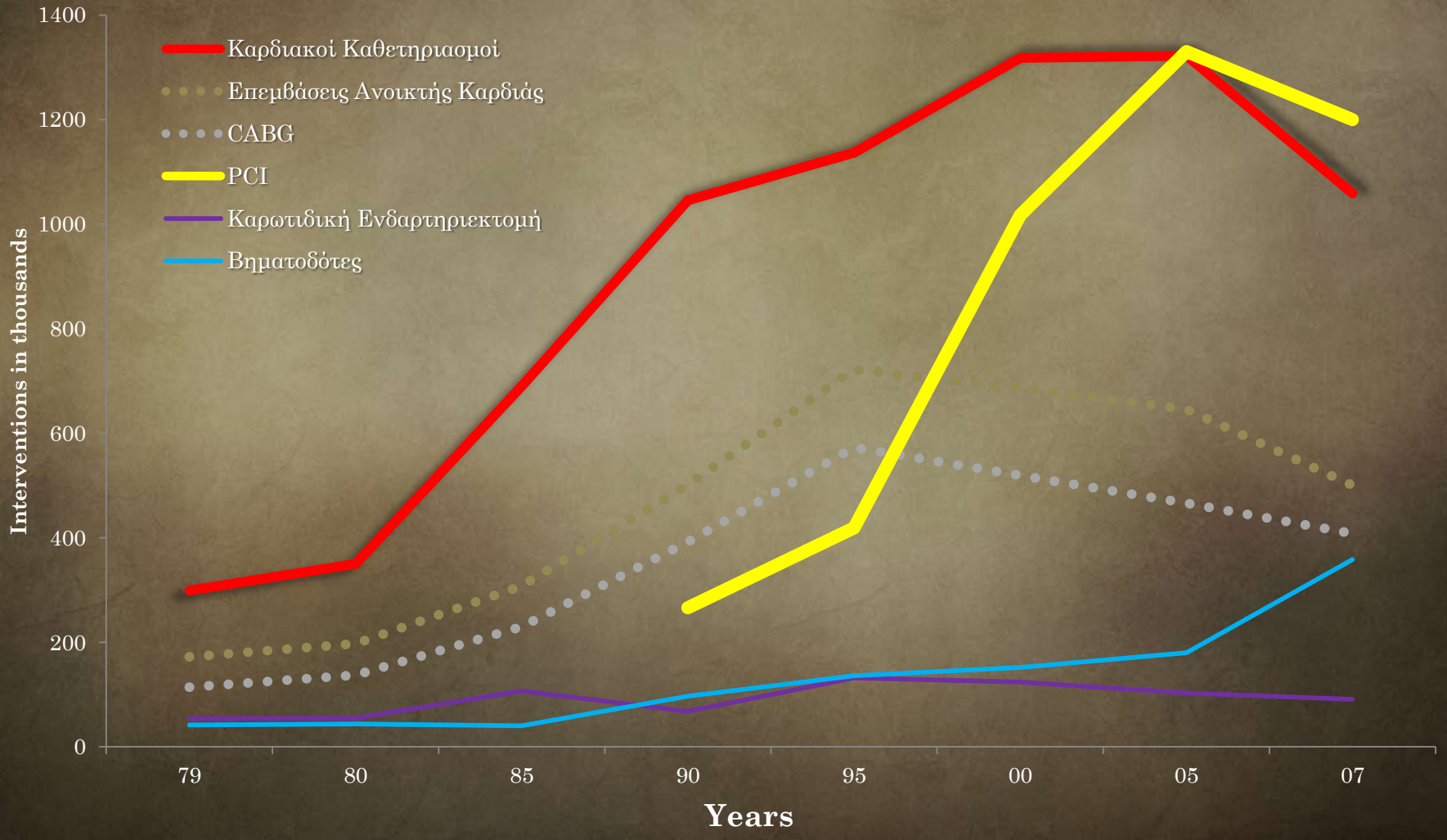
Mirowski M et al. An approach to prevention of sudden coronary death. Arch Intern Med 1970;126:158–61



THE PRESENT

- As a result of the enormous achievements just enumerated, and many others, cardiology is now a vibrant, robust specialty of which we can be justifiably proud, and that is providing enormous benefits to society

USA CV interventions 1979-2007



Heart Disease and Stroke Statistics-2011

Heart Failure

- 6 million people in the USA
- 15 million people in Europe
- CRT in appropriately selected patients has been shown to improve cardiac function, heart failure symptoms, and survival
- Treatment guidelines by AHA & ESC recommended CRT in patients with systolic heart failure, NYHA class 3 or 4 symptoms, and a QRS duration of ≥120 msec
- 1/3 to 1/2 of patients receiving CRT based on the guidelines did not respond to this treatment

Heart Disease and Stroke Statistics-2011

Tendera M. *Eur Heart J Suppl. 2005* (suppl J):J5-J9. doi:10.1093/eurheartj/sui056

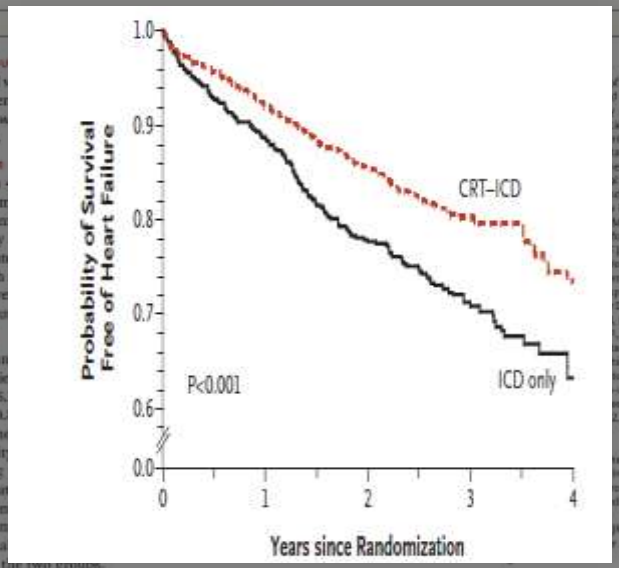
CRT

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 1, 2009 VOL. 361 NO. 14

Cardiac-Resynchronization Therapy for the Prevention of Heart-Failure Events

Arthur J. Moss, M.D., W. Jackson Hall, Ph.D., David S. Cannom, M.D., Helmut Klein, M.D., Mary W. Brown, M.S., James P. Daubert, M.D., N.A. Mark Estes III, M.D., Elyse Foster, M.D., Henry Greenberg, M.D., Steven L. Higgins, M.D., Marc A. Pfeffer, M.D., Ph.D., Scott D. Solomon, M.D., David Wilber, M.D., and Wojciech Zareba, M.D., Ph.D., for the MADIT-CRT Trial Investigators*



CONCLUSIONS

CRT combined with ICD decreased the risk of heart-failure events in relatively asymptomatic patients with a low ejection fraction and wide QRS complex. (ClinicalTrials.gov number, NCT00180271.)

N Engl J Med 2009;361:1329-38

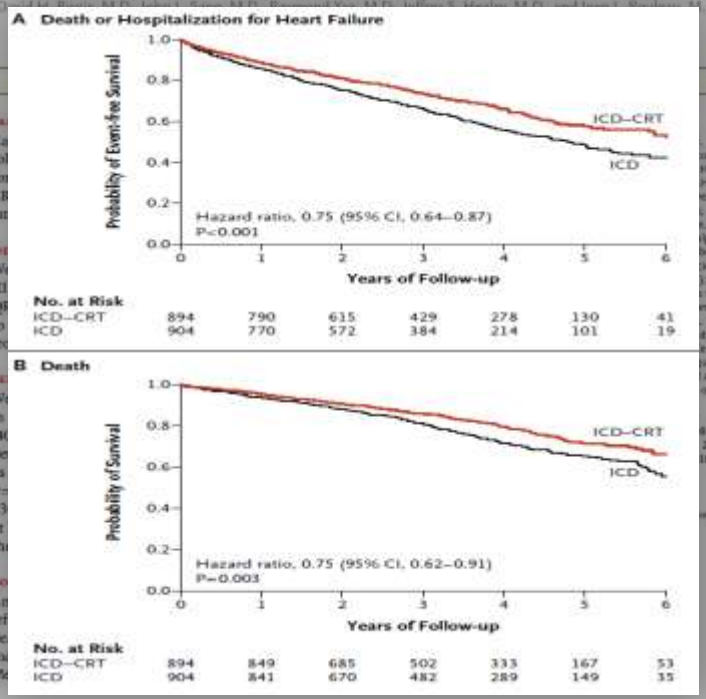
MADIT CRT Trial. N Engl J Med 2009;361:1329-38

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 16, 2010 VOL. 363 NO. 25

Cardiac-Resynchronization Therapy for Mild-to-Moderate Heart Failure

Anthony S.L. Tang, M.D., George A. Wells, Ph.D., Mario Talajic, M.D., Malcolm O. Arnold, M.D., Robert Sheldon, M.D., Stuart Connolly, M.D., Stefan H. Hohnloser, M.D., Graham Nichol, M.D.,



RAFT Trial. N Engl J Med 2010;363:2385-95

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®
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When Right May Not Be Right : Right Bundle-Branch Block and Response to Cardiac Resynchronization Therapy

Karoly Kaszala and Kenneth A. Ellenbogen

Table. Adverse Clinical Predictors in CRT

- Advanced age
- Male gender
- Ischemic cardiomyopathy
- Baseline non-left bundle-branch block
- QRS duration <150 ms
- Lack of mechanical dyssynchrony
- Significant left ventricular scar
- New York Heart Association class IV symptoms
- Severe noncardiac comorbidities (eg, pulmonary disease, pulmonary hypertension, renal dysfunction, diabetes mellitus)

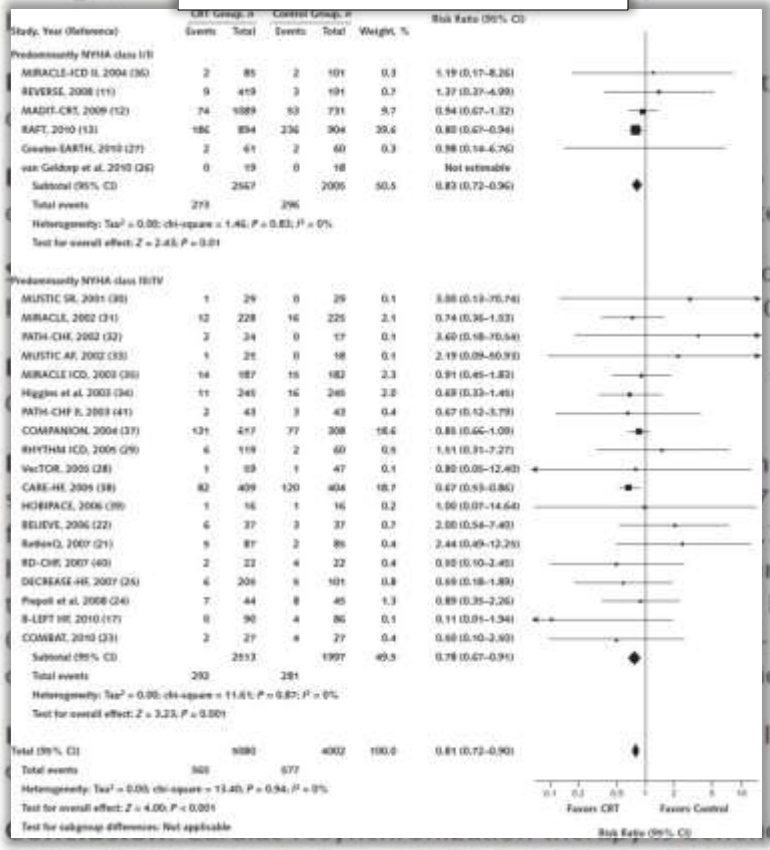
Annals of Internal Medicine
Established in 1927 by the American College of Physicians

Meta-analysis: Cardiac Resynchronization Therapy for Patients With Less Symptomatic Heart Failure

Nawaf S. Al–Majed, MBBS; Finlay A. McAlister, MD, MSc; Jeffrey A. Bakal, PhD; and Justin A. Ezekowitz, MBBCh, MSc

All cause mortality

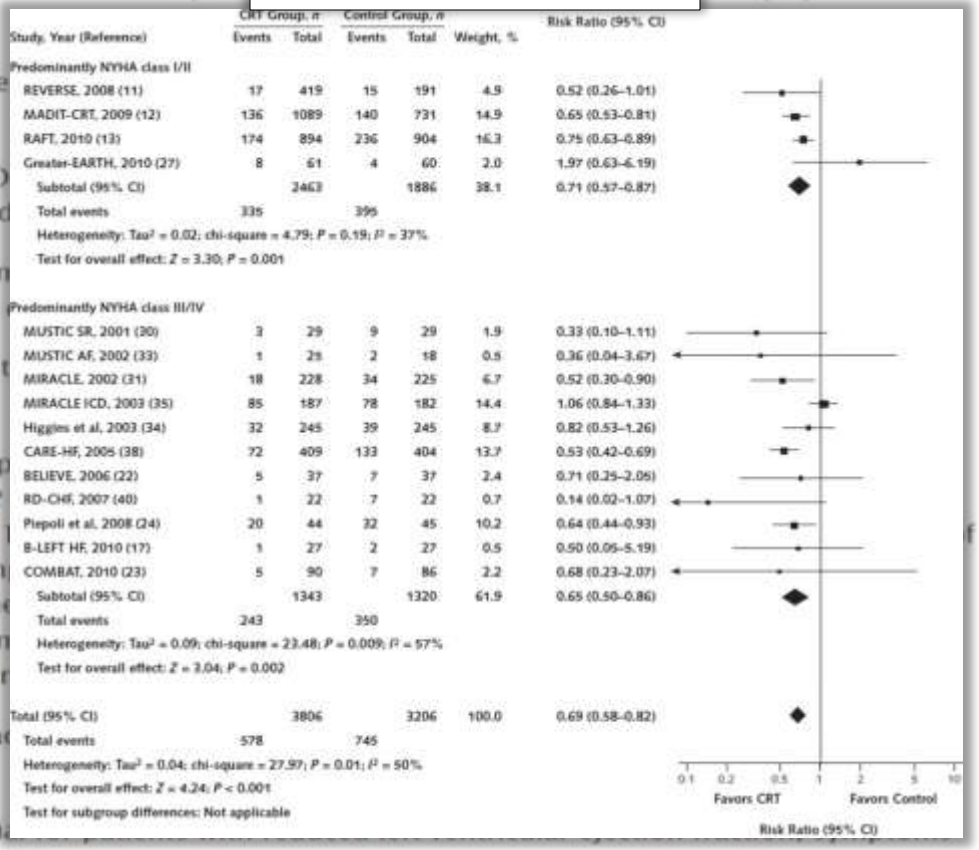
HF Hospitalizations



Study, Year (Reference)	CRT Group, # Events	CRT Group, # Total	Control Group, # Events	Control Group, # Total	Weight, %	Risk Ratio (95% CI)
Predominantly NYHA class I/II						
MIRACLE-ICD II, 2004 (36)	2	85	2	101	0.3	1.19 (0.17–8.26)
REVERSE, 2008 (11)	9	419	3	191	0.7	1.37 (0.37–4.99)
MADIT-CRT, 2009 (12)	74	1089	53	731	9.7	0.94 (0.67–1.32)
RAFT, 2010 (13)	186	894	236	904	39.6	0.80 (0.67–0.94)
Greater-EARTH, 2010 (27)	2	61	2	60	0.3	0.98 (0.14–6.76)
van Geldorp et al, 2010 (26)	0	19	0	18		Not estimable
Subtotal (95% CI)		2567		2005	50.5	0.83 (0.72–0.96)
Total events	273		296			
Heterogeneity: $Tau^2 = 0.00$; chi-square = 1.46, $P = 0.83$; $I^2 = 0\%$						
Test for overall effect: $Z = 2.43$, $P = 0.01$						
Predominantly NYHA class III/IV						
MUSTIC SR, 2001 (30)	1	29	0	29	0.1	3.00 (0.13–70.74)
MIRACLE, 2002 (31)	12	228	16	225	2.1	0.74 (0.36–1.53)
PATH-CHF, 2002 (32)	2	34	0	17	0.1	2.60 (0.18–70.54)
MUSTIC AF, 2002 (33)	1	21	0	18	0.1	2.19 (0.09–50.93)
MIRACLE ICD, 2003 (35)	14	187	15	182	2.3	0.91 (0.45–1.82)
Higgins et al, 2003 (34)	11	245	16	245	2.0	0.69 (0.33–1.45)
PATH-CHF II, 2003 (41)	2	43	3	43	0.4	0.67 (0.12–3.79)
COMPANION, 2004 (37)	131	417	77	308	18.6	0.88 (0.66–1.09)
RHYTHM ICD, 2005 (29)	6	119	2	60	0.5	1.51 (0.31–7.27)
VecTOR, 2005 (28)	1	69	1	47	0.1	0.80 (0.05–12.40)
CARE-HF, 2005 (38)	82	409	120	404	18.7	0.67 (0.53–0.86)
HOBIPACE, 2006 (39)	1	16	1	16	0.2	1.00 (0.07–14.64)
BELIEVE, 2006 (22)	6	37	3	37	0.7	2.00 (0.54–7.40)
ReSync, 2007 (21)	5	81	2	86	0.4	2.44 (0.49–12.26)
RD-CHF, 2007 (40)	2	22	4	22	0.4	0.50 (0.10–2.45)
DECREASE-HF, 2007 (26)	6	206	5	101	0.8	0.59 (0.18–1.89)
Piepoli et al, 2008 (24)	7	44	8	45	1.3	0.89 (0.35–2.26)
B-LEFT HF, 2010 (17)	0	90	4	86	0.1	0.11 (0.01–1.94)
COMBAT, 2010 (23)	2	27	4	27	0.4	0.50 (0.10–2.60)
Subtotal (95% CI)		2513		1997	49.5	0.78 (0.67–0.91)
Total events	293		281			
Heterogeneity: $Tau^2 = 0.00$; chi-square = 11.61, $P = 0.87$; $I^2 = 0\%$						
Test for overall effect: $Z = 3.23$, $P = 0.001$						
Total (95% CI)		5080		4002	100.0	0.81 (0.72–0.90)
Total events	568		577			
Heterogeneity: $Tau^2 = 0.00$; chi-square = 13.40, $P = 0.94$; $I^2 = 0\%$						
Test for overall effect: $Z = 4.00$, $P < 0.001$						
Test for subgroup differences: Not applicable						

Favors CRT | Favors Control

Risk Ratio (95% CI)



Study, Year (Reference)	CRT Group, # Events	CRT Group, # Total	Control Group, # Events	Control Group, # Total	Weight, %	Risk Ratio (95% CI)
Predominantly NYHA class I/II						
REVERSE, 2008 (11)	17	419	15	191	4.9	0.52 (0.26–1.01)
MADIT-CRT, 2009 (12)	136	1089	140	731	14.9	0.65 (0.53–0.81)
RAFT, 2010 (13)	174	894	236	904	16.3	0.75 (0.63–0.89)
Greater-EARTH, 2010 (27)	8	61	4	60	2.0	1.97 (0.63–6.19)
Subtotal (95% CI)		2463		1886	38.1	0.71 (0.57–0.87)
Total events	335		396			
Heterogeneity: $Tau^2 = 0.02$; chi-square = 4.79; $P = 0.19$; $I^2 = 37\%$						
Test for overall effect: $Z = 3.30$; $P = 0.001$						
Predominantly NYHA class III/IV						
MUSTIC SR, 2001 (30)	3	29	9	29	1.9	0.33 (0.10–1.11)
MUSTIC AF, 2002 (33)	1	21	2	18	0.5	0.36 (0.04–3.67)
MIRACLE, 2002 (31)	18	228	34	225	6.7	0.52 (0.30–0.90)
MIRACLE ICD, 2003 (35)	85	187	78	182	14.4	1.06 (0.84–1.33)
Higgins et al, 2003 (34)	32	245	39	245	8.7	0.82 (0.53–1.26)
CARE-HF, 2005 (38)	72	409	133	404	13.7	0.53 (0.42–0.69)
BELIEVE, 2006 (22)	5	37	7	37	2.4	0.71 (0.25–2.06)
RD-CHF, 2007 (40)	1	22	7	22	0.7	0.14 (0.02–1.07)
Piepoli et al, 2008 (24)	20	44	32	45	10.2	0.64 (0.44–0.93)
B-LEFT HF, 2010 (17)	1	27	2	27	0.5	0.50 (0.05–5.19)
COMBAT, 2010 (23)	5	90	7	86	2.2	0.68 (0.23–2.07)
Subtotal (95% CI)		1343		1320	61.9	0.65 (0.50–0.86)
Total events	243		350			
Heterogeneity: $Tau^2 = 0.09$; chi-square = 23.48; $P = 0.009$; $I^2 = 57\%$						
Test for overall effect: $Z = 3.04$; $P = 0.002$						
Total (95% CI)		3806		3206	100.0	0.69 (0.58–0.82)
Total events	578		745			
Heterogeneity: $Tau^2 = 0.04$; chi-square = 27.97; $P = 0.01$; $I^2 = 50\%$						
Test for overall effect: $Z = 4.24$; $P < 0.001$						
Test for subgroup differences: Not applicable						

0.1 0.2 0.5 1 2 5 10

Favors CRT | Favors Control

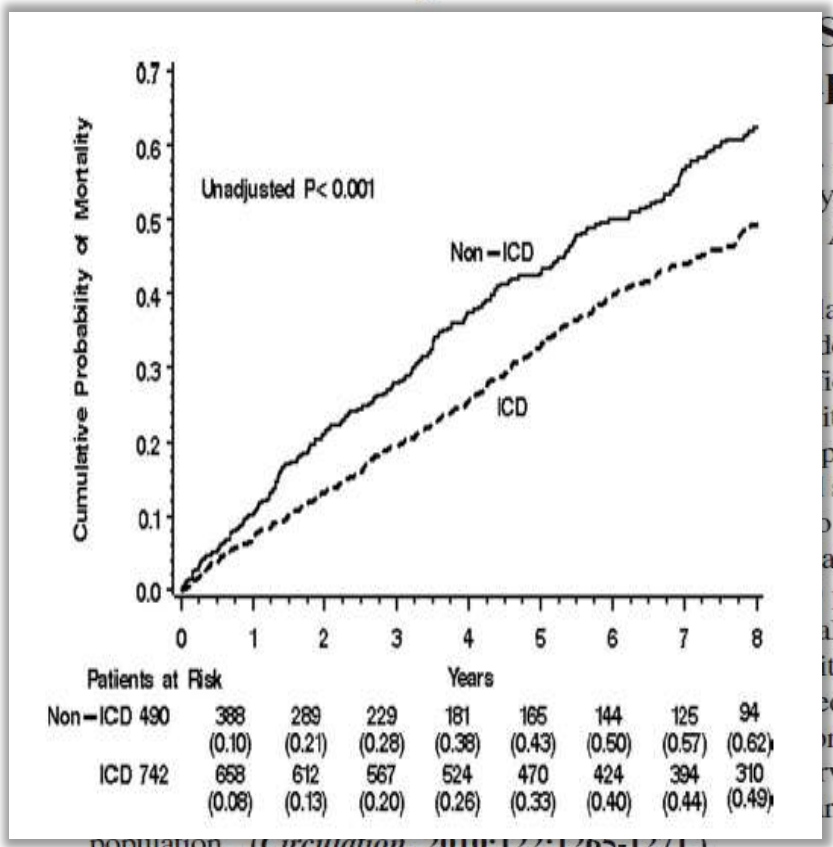
Risk Ratio (95% CI)

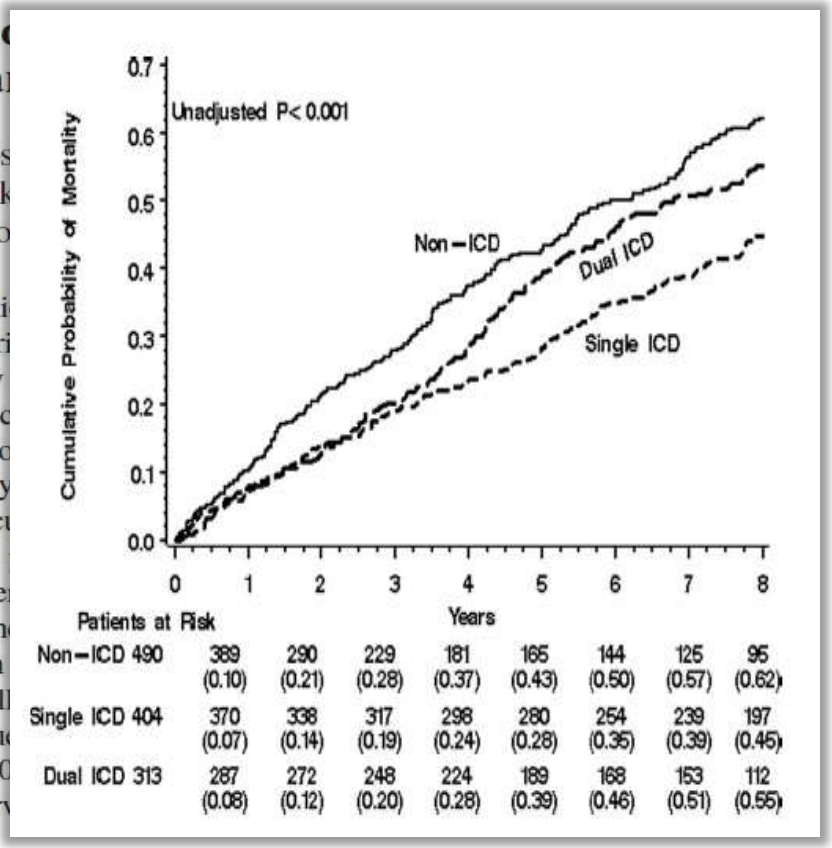
of heart failure, and prolonged QRS, regardless of NYHA class.

Al-Majed N S et al. Ann Intern Med doi:10.1059/0003-4819-154-6-201103150-00313

Implantable Cardioverter - Defibrillators

Long-Term Benefit of Primary Prevention With an Implantable Cardioverter-Defibrillator





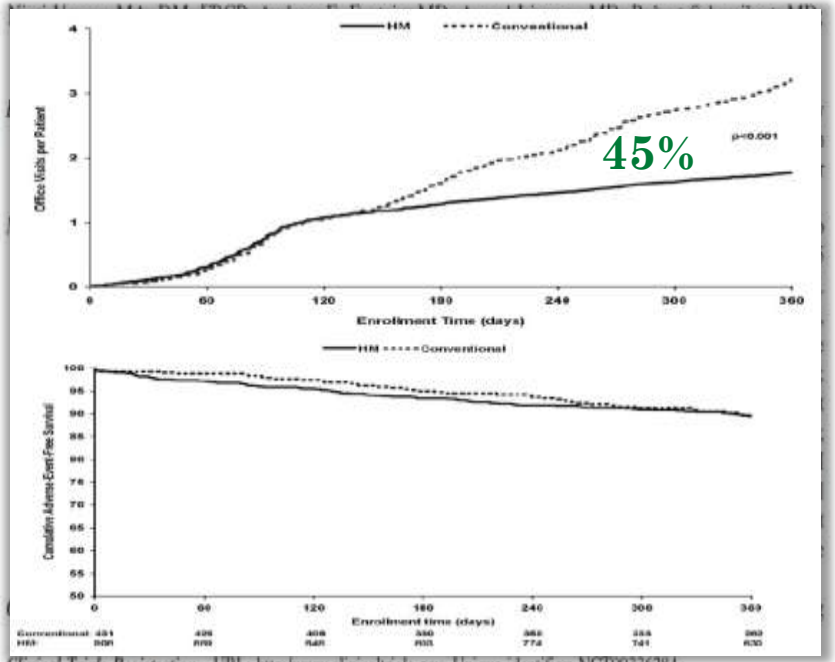
population. (*Circulation*. 2010;122:1265-1271.)

Remote Device Monitoring

Arrhythmia/Electrophysiology

Efficacy and Safety of Automatic Remote Monitoring for Implantable Cardioverter-Defibrillator Follow-Up

The Lumos-T Safely Reduces Routine Office Device Follow-Up (TRUST) Trial

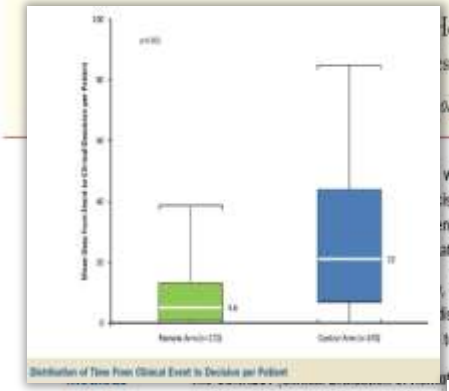


Clinical Trials Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00536284.
(*Circulation*. 2010;122:325-332.)

Clinical Trial

The CONNECT (Clinical Evaluation of Remote Notification to Reduce Time to Clinical Decision) Trial

The Value of Wireless Remote Monitoring With Automatic Clinician Alerts



Holly Vitense, PhD,‡ Yanping Chang, MS,§
stigators
olis, Minnesota; and Redwood City, California

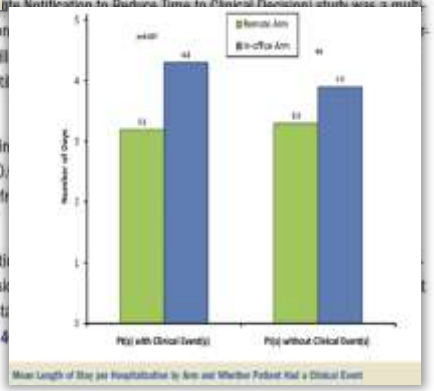
wireless remote monitoring with automatic clinician alerts reduces the
ision in response to arrhythmias, cardiovascular (CV) disease progres-
nts receiving standard in-office care. A secondary objective was to
ation between patients in the remote and in-office arms.

, implantable cardioverter-defibrillators collect advanced diagnostics
isease. Device technology has progressed to allow wireless remote
to replace some scheduled in-office visits.

center, prospective, randomized evaluation
tion of an implantable cardioverter-defibril
followed up for 15 months. Health care uti
partment visits, and clinic office visits.

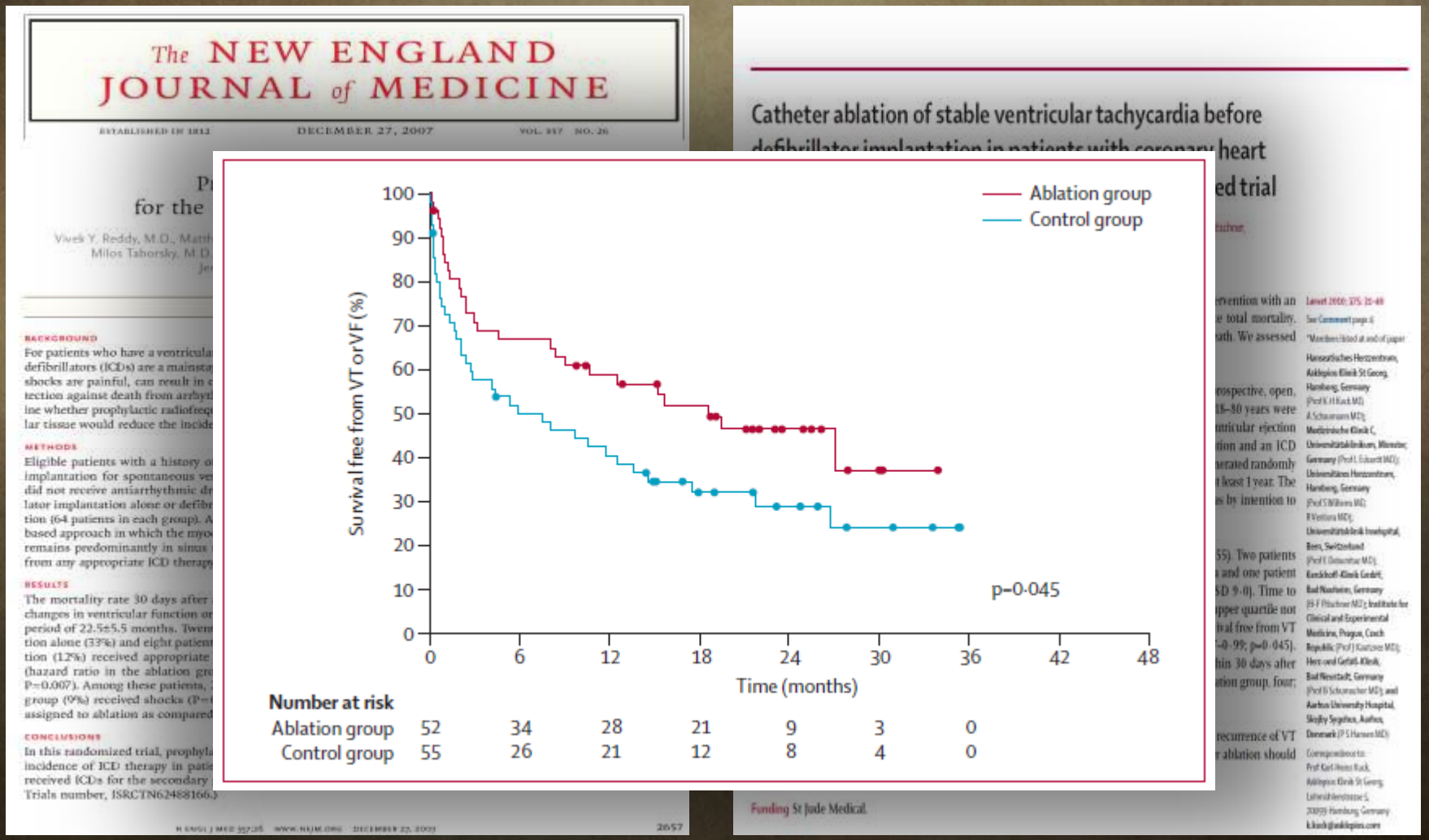
Results The median time from clinical event to clin
arm to 4.6 days in the remote arm ($p < 0.$
length of stay per CV hospitalization visit fr
($p = 0.002$).

Conclusions Wireless remote monitoring with automati
cantly reduced the time to a clinical decisi
reduction in mean length of CV hospital st
Clinical Decision [CONNECT]; NCT0040224
College of Cardiology Foundation



Crossley GH, Boyle A, Vitense H, Chang Y, Mead RH, for the CONNECT Investigators. JACC. 2011;57:1181–9

Catheter ablation of ventricular arrhythmias



Reddy V. et al. N Engl J Med 2007;357:2657-65

Kuck KH et al. VTACH trial. Lancet 2010;375:31–40

Atrial Fibrillation

- Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, estimated to afflict >5.5 million people in the United States alone today and to increase to >15 million by the year 2050. Of its various clinical consequences, the most devastating is thromboembolic stroke. In patients with significant risk factors for stroke, warfarin is the treatment of choice for stroke prevention

- However, because of the problems associated with long-term warfarin therapy, it is often not administered or tolerated

- Accordingly, there has been intense interest in developing alternative treatment strategies

Go AS et al. Prevalence of diagnosed AF in adults: ATRIA Study. JAMA. 2001;285:2370 –2375

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

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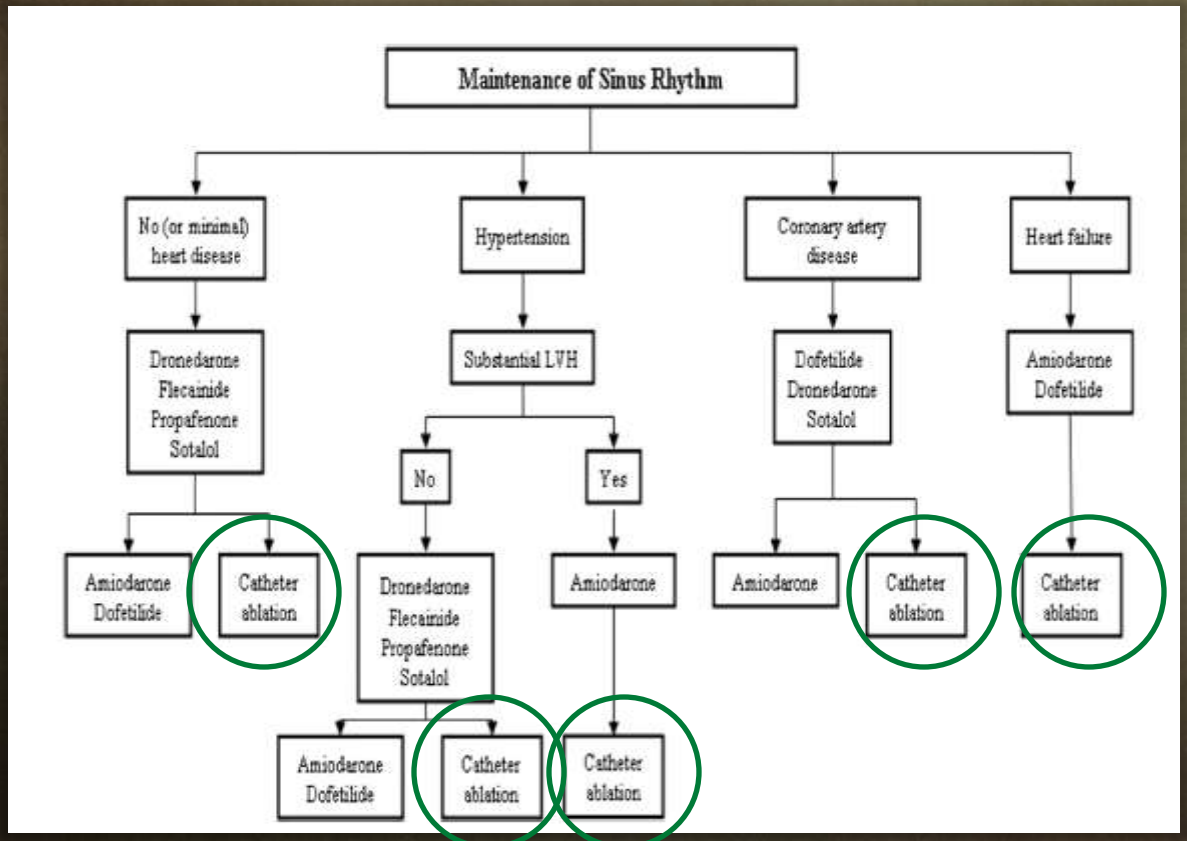
2011 ACCF/AHA/HRS Focused Update on the Management of Patients With Atrial Fibrillation (Updating the 2006 Guideline) : A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

2011 Writing Group Members, L. Samuel Wann, Anne B. Curtis, Craig T. January, Kenneth A. Ellenbogen, James E. Lowe, N.A. Mark Estes III, Richard L. Page, Michael D. Ezekowitz, David J. Slotwiner, Warren M. Jackman, William G. Stevenson and Cynthia M. Tracy



Class I

Catheter ablation performed in experienced centers* is useful in maintaining sinus rhythm in selected patients with significantly symptomatic, paroxysmal AF who have failed treatment with an antiarrhythmic drug and have normal or mildly dilated left atria, normal or mildly reduced LV function, and no severe pulmonary disease.[38–51] *(Level of Evidence: A)*

Class IIa

Catheter ablation is reasonable to treat symptomatic persistent AF.[38,48,55–64] *(Level of Evidence: A)*

Class IIb

1. Catheter ablation may be reasonable to treat symptomatic paroxysmal AF in patients with significant left atrial dilatation or with significant LV dysfunction.[38,48,55–64] *(Level of Evidence: A)*

Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation. JACC. 2011;57:223– 42

Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial

David R Holmes, Vivek Y Reddy, Zoltan G Turi, Shephal K Doshi, Horst Sievert, Maurice Buchbinder, Christopher M Mullin, Peter Sick, for the PROTECT AF Investigators*

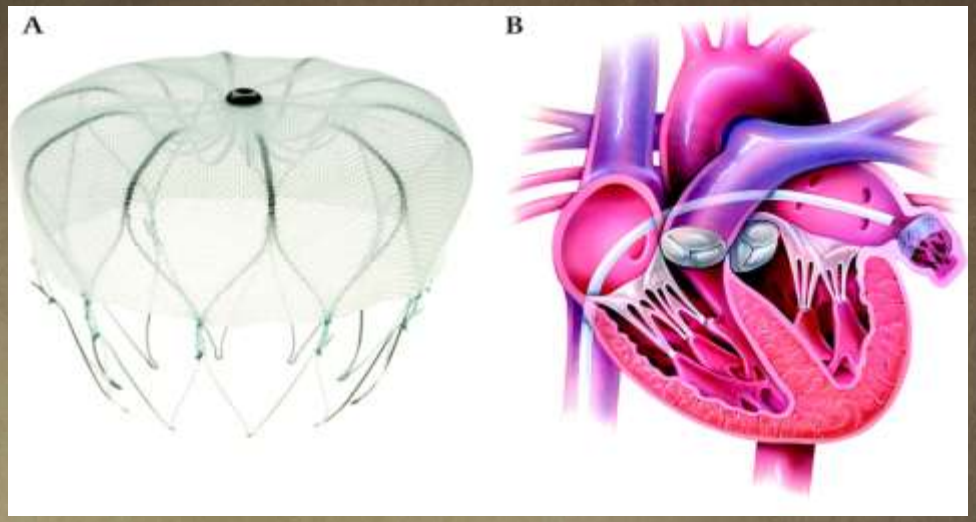
Summary

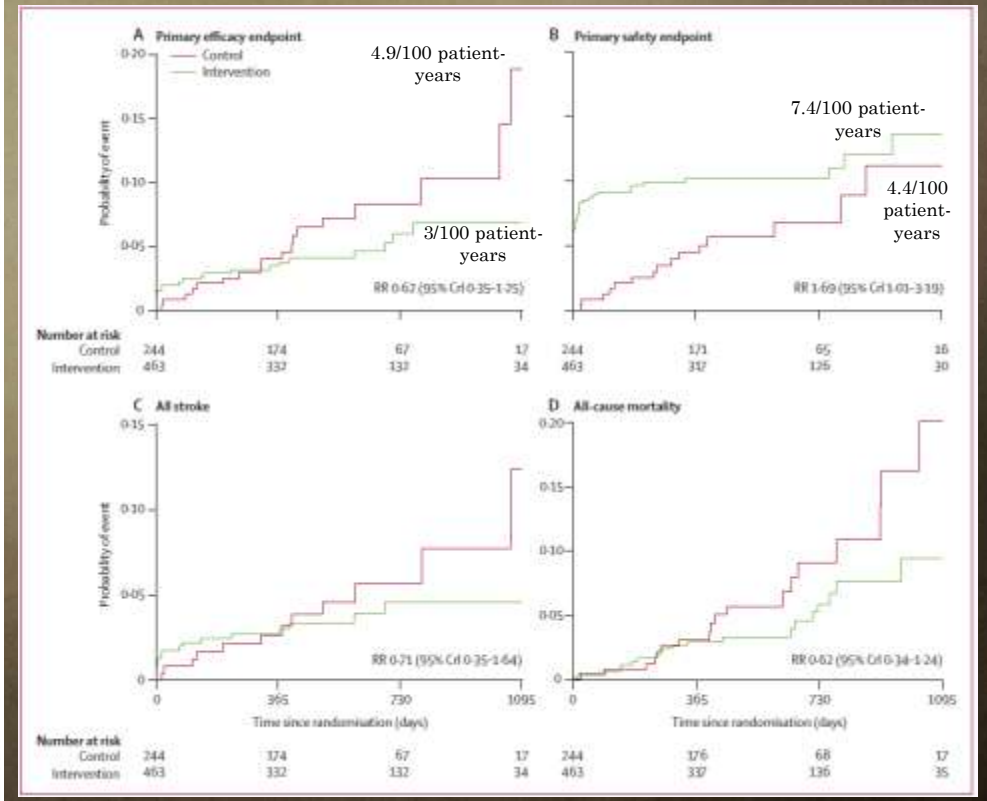
Background In patients with non-valvular atrial fibrillation, embolic stroke is thought to be associated with left atrial appendage (LAA) thrombi. We assessed the efficacy and safety of percutaneous closure of the LAA for prevention of stroke compared with warfarin treatment in patients with atrial fibrillation.

Methods Adult patients with non-valvular atrial fibrillation were eligible for inclusion in this multicentre, randomised non-inferiority trial if they had at least one of the following: previous stroke or transient ischaemic attack, congestive heart failure, diabetes, hypertension, or were 75 years or older. 707 eligible patients were randomly assigned in a 2:1 ratio by computer-generated randomisation sequence to percutaneous closure of the LAA and subsequent discontinuation of warfarin (intervention; n=463) or to warfarin treatment with a target international normalised ratio between 2·0 and 3·0 (control; n=244). Efficacy was assessed by a primary composite endpoint of stroke, cardiovascular death, and systemic embolism. We selected a one-sided probability criterion of non-inferiority for the intervention of at least 97·5%, by use of a two-fold non-inferiority margin. Serious adverse events that constituted the primary endpoint for safety included major bleeding, pericardial effusion, and device embolisation. Analysis was by intention to treat. This study is registered with Clinicaltrials.gov, number NCT00129545.

Findings At 1065 patient-years of follow-up, the primary efficacy event rate was 3·0 per 100 patient-years (95% credible interval [CrI] 1·9–4·5) in the intervention group and 4·9 per 100 patient-years (2·8–7·1) in the control group (rate ratio [RR] 0·62, 95% CrI 0·35–1·25). The probability of non-inferiority of the intervention was more than 99·9%. Primary safety events were more frequent in the intervention group than in the control group (7·4 per 100 patient-years, 95% CrI 5·5–9·7, *vs* 4·4 per 100 patient-years, 95% CrI 2·5–6·7; RR 1·69, 1·01–3·19).

Interpretation The efficacy of percutaneous closure of the LAA with this device was non-inferior to that of warfarin therapy. Although there was a higher rate of adverse safety events in the intervention group than in the control group, events in the intervention group were mainly a result of periprocedural complications. Closure of the LAA might provide an alternative strategy to chronic warfarin therapy for stroke prophylaxis in patients with non-valvular atrial fibrillation.

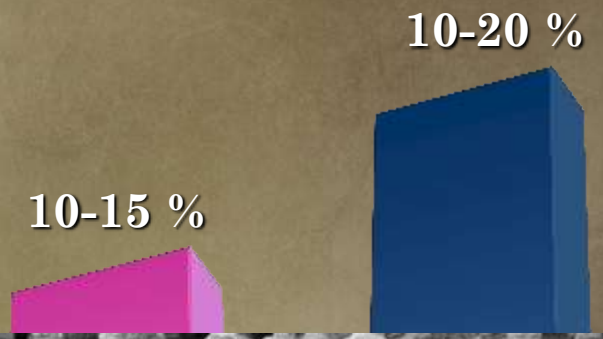


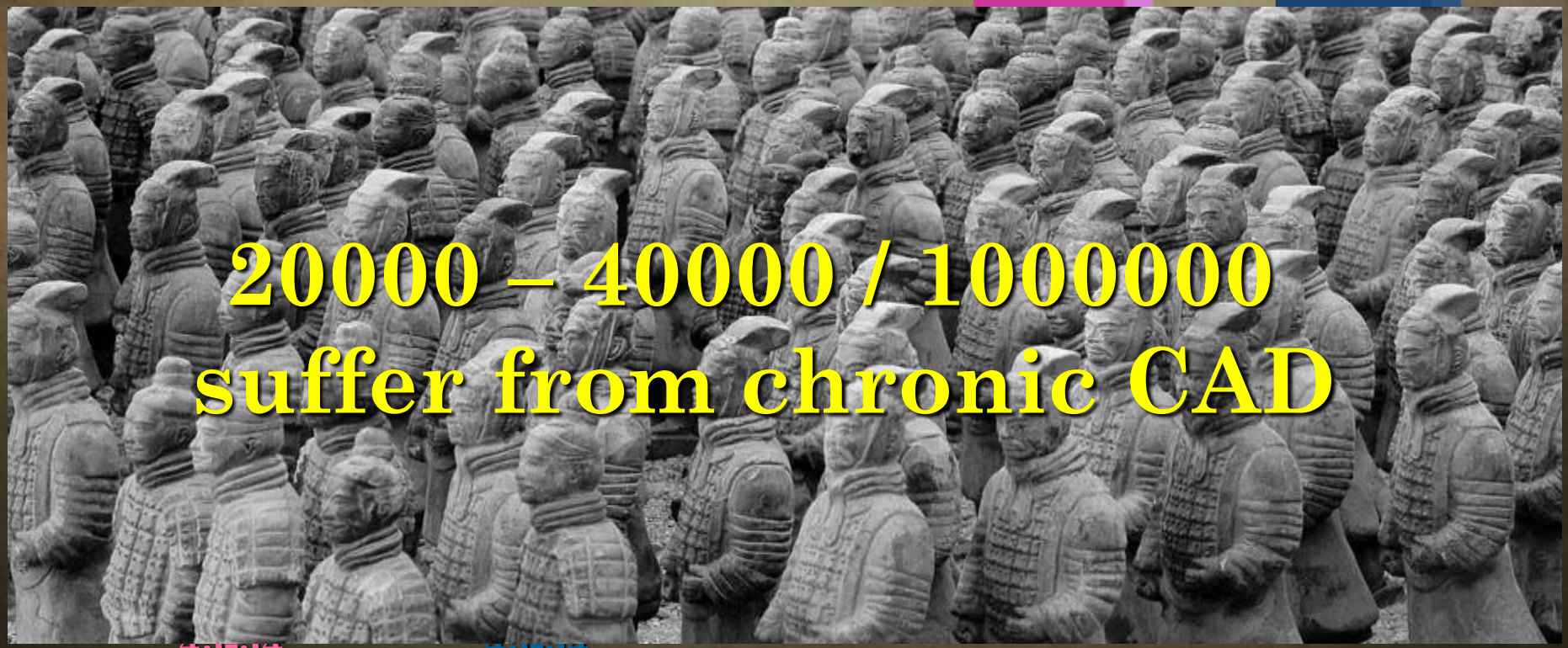


Lancet 2009; 374: 534–42

Chronic CAD

CAD incidence increases sharply with age in both genders

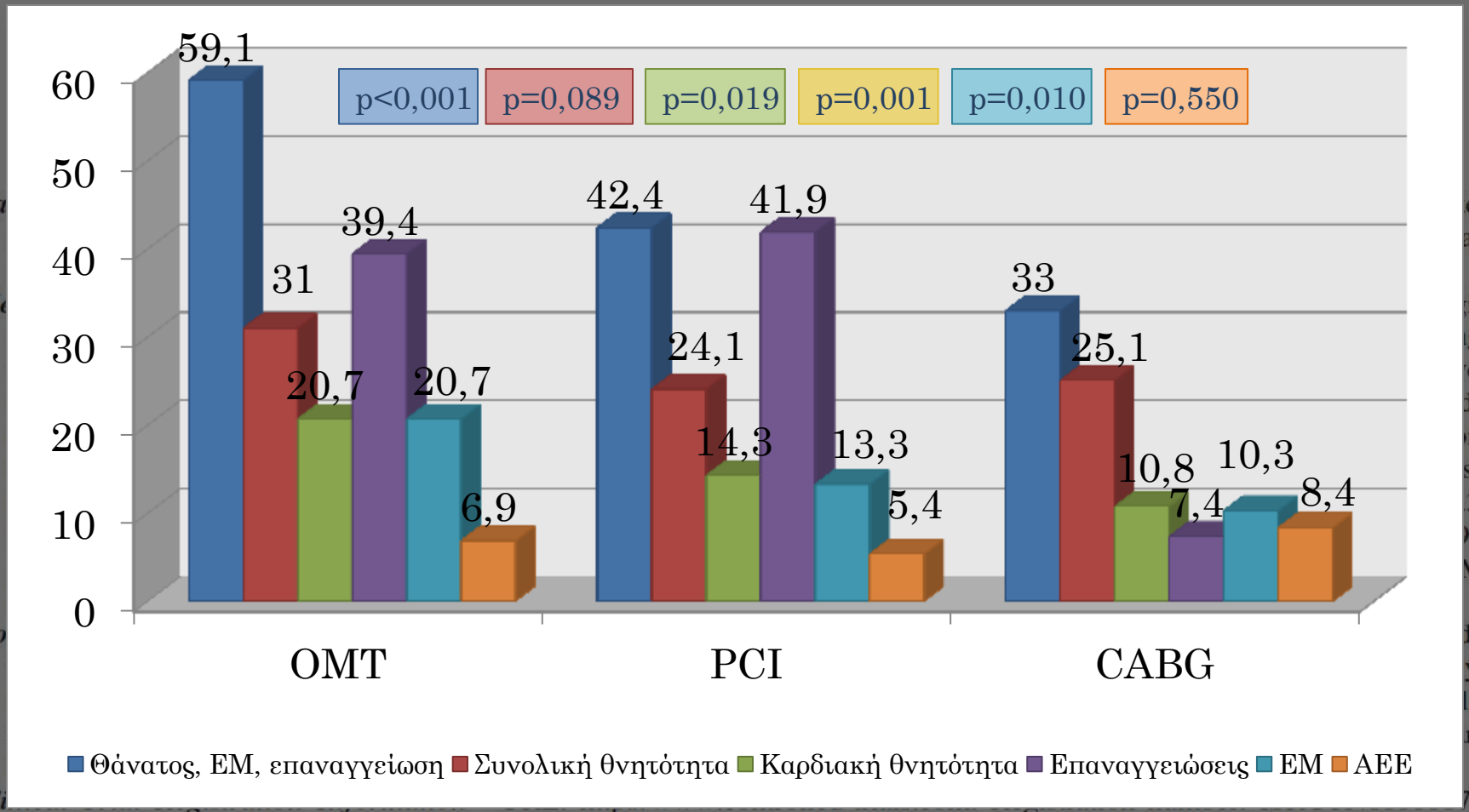




Kim Fox et al. Guidelines on the management of stable angina pectoris. The task force on the management of stable angina pectoris of the European society of cardiology. Eur heart j 2006 27:1341-1381

Ten-Year Follow-Up Survival of the Medicine, Angioplasty, or Surgery Study (MASS II)

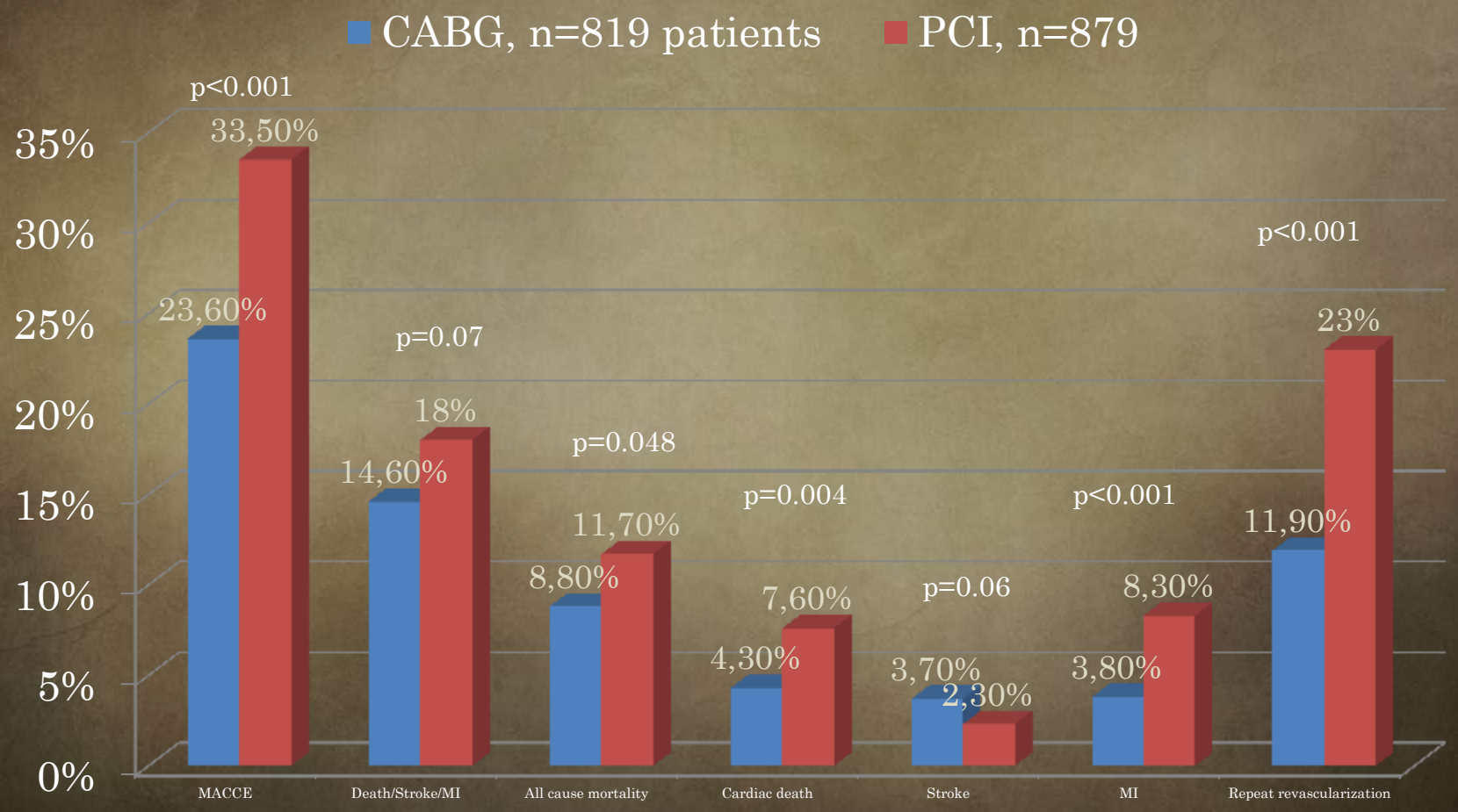
A Randomized Controlled Clinical Trial of 3 Therapeutic Strategies for Multivessel Coronary Artery Disease



(*Circulation*. 2010;122:949-957.)

Hueb W et al. Circulation. 2010;122:949–957

SYNTAX Trial: 4-Year Cumulative Results

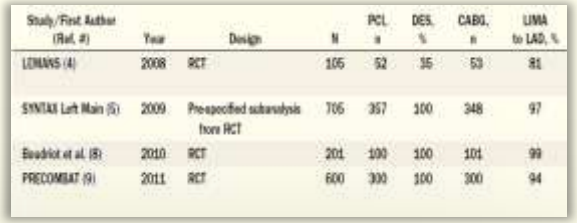


Sub analysis by SYNTAX Score

- No difference in MACCE between CABG and PCI in those with a SYNTAX score of 0 to 22 (26.1% vs. 28.6%; p=0.57)
- But for those with an intermediate SYNTAX score of 23 to 32, there was a highly significant difference" in MACCE rate (21.5% for CABG vs. 32% for PCI; p=0.006)
- For those with a high SYNTAX score ($\geq$33), "mortality is double in the PCI group compared with CABG (16.1% vs. 8.4%; p=0.04) and MI is two to three times higher with PCI than with CABG (9.3% vs. 3.9%; p=0.01)
- In this highest-risk group, even the end point of death/stroke/MI becomes significantly higher with PCI (22.7% vs. 14.6%; p=0.01), and MACCE were much higher (40.1% vs. 23.6%; p<0.001), driven in large part by a 17% higher rate of revascularization in this high-risk group at four years

Percutaneous Coronary Intervention Versus Coronary Artery Bypass Graft Surgery in Left Main Coronary Artery Disease

A Meta-Analysis of Randomized Clinical Data



Study/First Author (Ref. #)	Year	Design	N	PCI, n	DES, %	CABG, n	LIMA to LAD, %
LEMANS (4)	2008	RCT	105	52	35	53	81
SYNTAX Left Main (5)	2009	Pre-specified subanalysis from RCT	705	357	100	348	97
Boudriot et al. (8)	2010	RCT	201	100	100	101	99
PRECOMBAT (9)	2011	RCT	600	300	100	300	94

Davide Capodanno, MD,* Gregg W. Stone, MD,† Marie C. Morice, MD,‡ Theodore A. Bass, MD,§ Corrado Tamburino, MD, PhD*

Catania, Italy; New York, New York; Massy, France; and Jacksonville, Florida

Table 3 1-Year Outcomes in Left Main Patients Revascularized by PCI or CABG

Endpoint	PCI (n = 809)	CABG (n = 802)	Absolute Difference (95% CI)	Number Needed to Treat	Number Needed to Harm	p Value
MACCE	14.5 (117/807)	11.8 (93/790)	2.7 (−0.6 to 6.0)	—	37	0.11
Death/MI/CVA	5.3 (35/655)	6.8 (43/636)	−1.5 (−4.1 to 1.2)	67	—	0.26
Death	3.0 (24/807)	4.1 (32/790)	−1.1 (−3.0 to 0.8)	91	—	0.29
MI	2.8 (23/807)	2.9 (23/790)	−0.1 (−1.8 to 1.6)	1,000	—	0.95
CVA	0.1 (1/707)	1.7 (12/689)	−1.6 (−2.9 to −0.6)	63	—	0.013
TVR	11.4 (92/807)	5.4 (43/790)	6.0 (3.3 to 8.7)	—	17	<0.001

Obje …rvention …y (LMCA)

Bacl …tional

Met …ary end- …l as death,

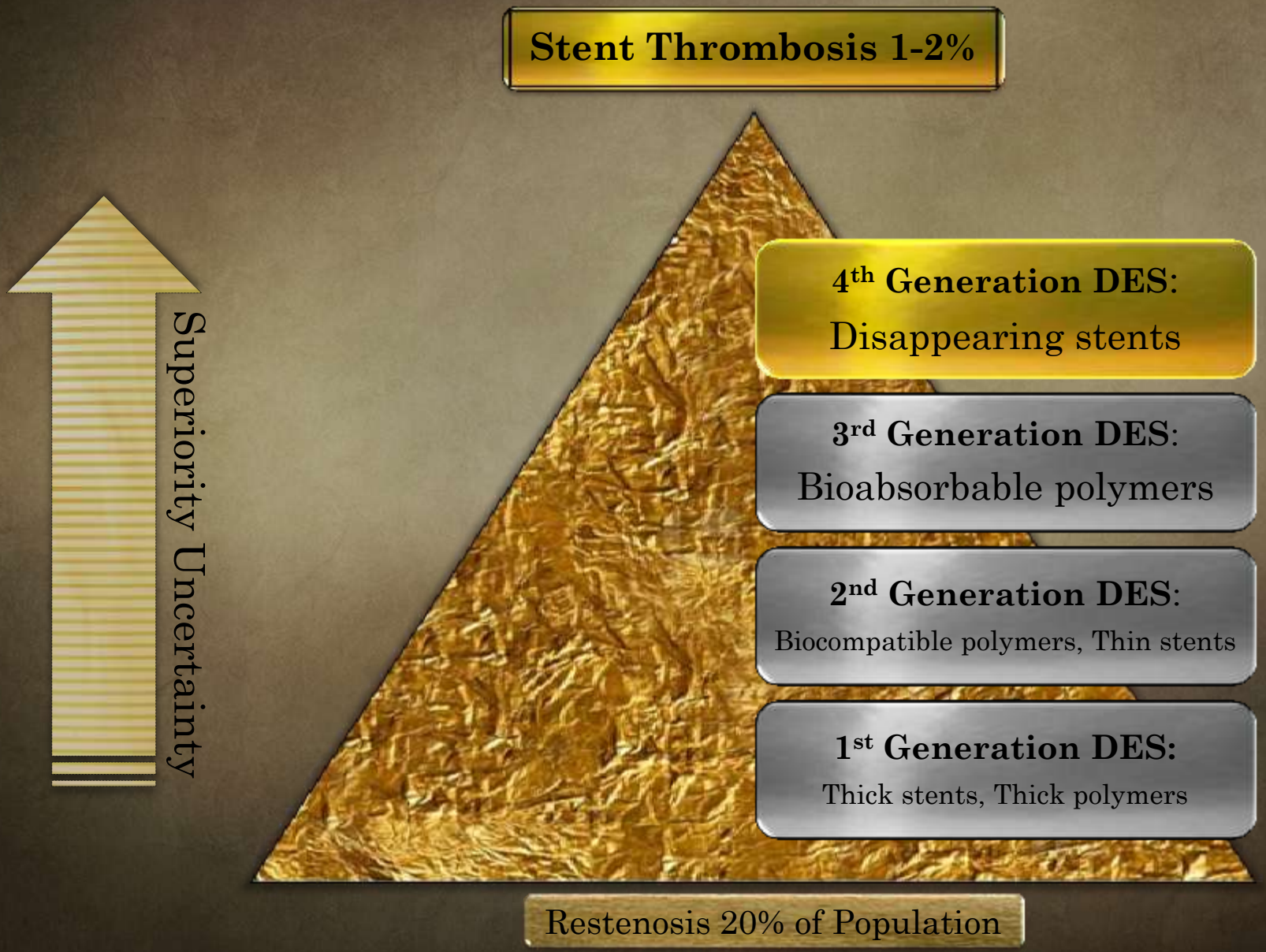
Resu …5% vs. …reased TVR …equently …ifferences

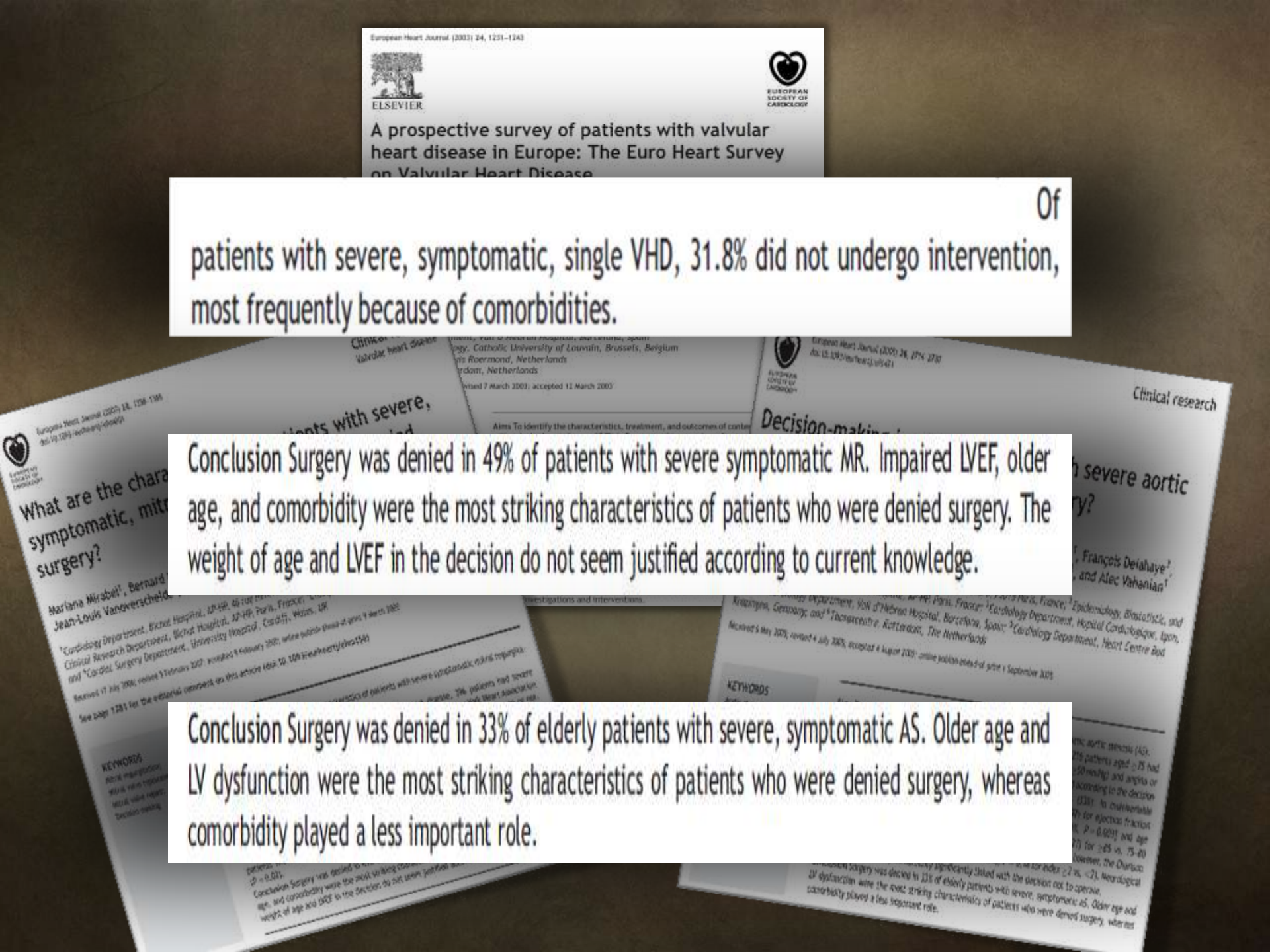
in death (3.0% vs. 4.1%; OR: 0.74; 95% CI: 0.43 to 1.29; p = 0.29) or MI (2.8% vs. 2.9%; OR: 0.98; 95% CI: 0.54 to 1.78; p = 0.95).

Conclusions In patients with LMCA disease, PCI was associated with nonsignificantly different 1-year rates of MACCE, death, and MI, a lower risk of stroke, and a higher risk of TVR compared with CABG. (J Am Coll Cardiol 2011;58: 1426–32) © 2011 by the American College of Cardiology Foundation

Davide Capodanno, Gregg W. Stone, Marie C. Morice, Theodore A. Bass, Corrado Tamburino. PCI Versus CABG in LMCAD. A Meta-Analysis of Randomized Clinical Data. JACC 2011;58:1426–32

The Development Pyramid for 4 Generations of DES




European Heart Journal (2003) 24, 1231–1243
ELSEVIER
A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease
Of
patients with severe, symptomatic, single VHD, 31.8% did not undergo intervention, most frequently because of comorbidities.
Conclusion Surgery was denied in 49% of patients with severe symptomatic MR. Impaired LVEF, older age, and comorbidity were the most striking characteristics of patients who were denied surgery. The weight of age and LVEF in the decision do not seem justified according to current knowledge.
Clinical research
Conclusion Surgery was denied in 33% of elderly patients with severe, symptomatic AS. Older age and LV dysfunction were the most striking characteristics of patients who were denied surgery, whereas comorbidity played a less important role.

Percutaneous Interventions

Goals

of transcatheter valve therapy

1. to provide a treatment modality that is less invasive,
2. associated with equal or greater efficacy compared with standard surgery, and
3. is potentially safer than more invasive procedures

Mitral Regurgitation

- MR remains one of the most common forms of valvular heart disease. It is estimated that 9.3% of the population age≥ 75 years, up to 20% of patients with heart failure and 12% of patients post–myocardial infarction have at least moderate MR
- Severe mitral regurgitation is associated with progressive left ventricular dysfunction and congestive heart failure
- Without intervention, symptomatic patients have an annual rate of death of 5% or more
- Medical management alleviates symptoms but does not alter the progression of the disease
- Current guidelines recommend surgical intervention for symptomatic severe MR or asymptomatic severe MR with left ventricular (LV) dysfunction or enlargement

Carabello BA. Curr Treat Options Cardiovasc Med 2009; 11:419-25

Percutaneous MV Repair And Replacement Technologies

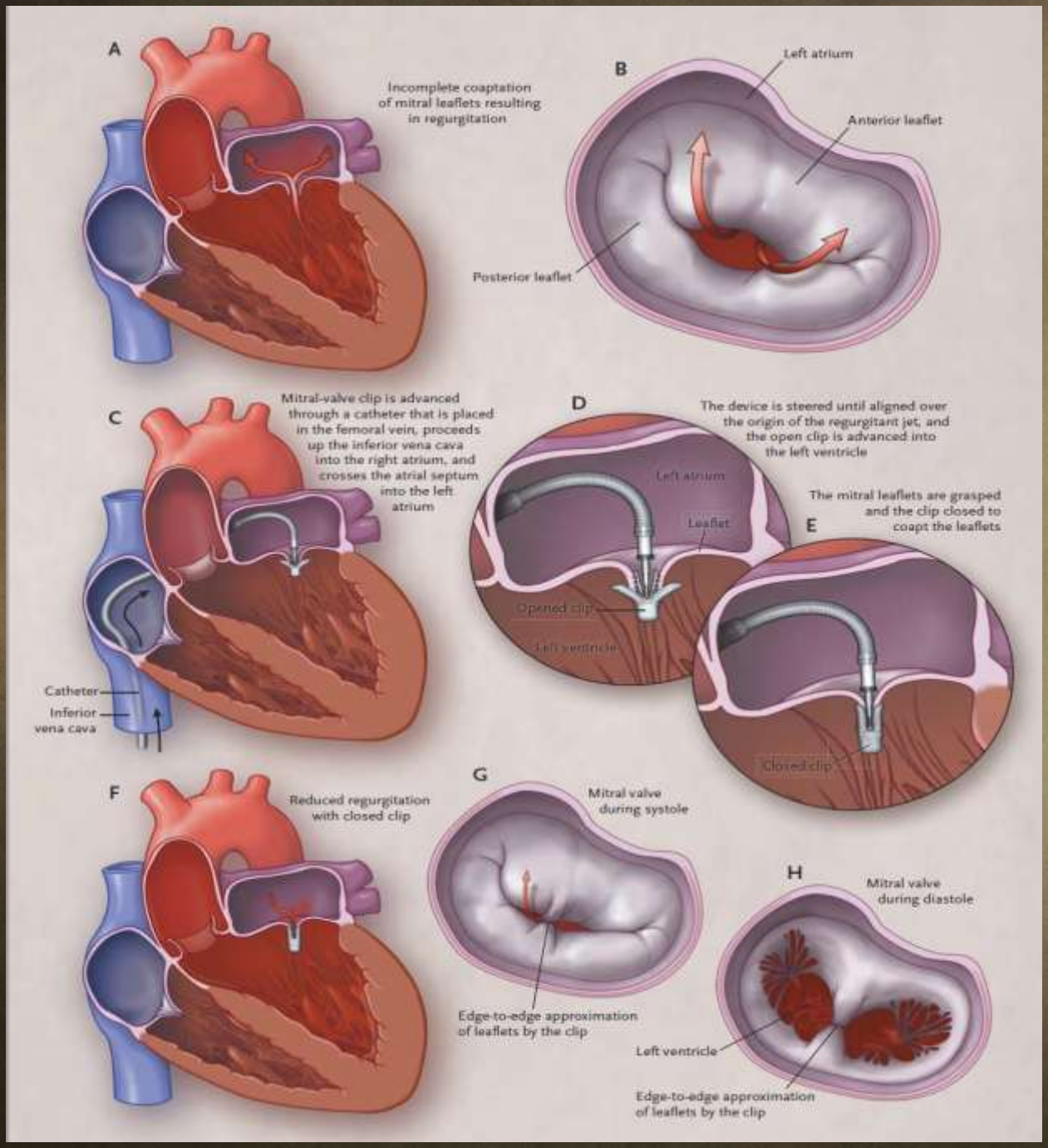
Site of Action	Mechanism of Action	Device	Status	Major Limitations
Percutaneous MV Repair Technologies				
Leaflets	Edge-to-edge (leaflet plication)	MitraClip	Randomized trial data presented	Results when performed alone may not be durable. Possibility of iatrogenic MS.
		MitraFlex	Pre-clinical development	As for MitraClip
	Space occupier (leaflet coaptation)	Percu-Pro	Phase 1 trial	Device thrombus formation. Residual MR or iatrogenic MS.
	Leaflet ablation	Thermocool	Animal models	Scarring not precise with residual MR. Leaflet/cardiac structure perforation.

Site of Action	Mechanism of Action	Device	Status	Major Limitations
Percutaneous MV Repair Technologies				
	Indirect annuloplasty			
Annulus	Coronary sinus approach (CS reshaping)	Monarc	FIM results. Feasibility study ongoing.	CS at a distance from MA. Possibility of coronary artery compression.
		Carillon	FIM results. Feasibility study complete.	As above
		Viacor	FIM results. Feasibility study ongoing.	As above
	Asymmetrical approach	St. Jude device	Animal models	CS at a distance from MA. Unequal tension on LA or MA. Device fracture or erosion, and thrombus formation.
		NIH-Cerclage technology	Animal models	CS at a distance from MA. Unequal tension on LA or MA.

Site of Action	Mechanism of Action	Device	Status	Major Limitations
Percutaneous MV Repair Technologies				
	Direct annuloplasty			
Annulus	Percutaneous mechanical cinching	Mitralign	FIM results	Only posterior MA cinching.
		Accucinch GDS	FIM results	As above
		Millipede ring system	Pre-clinical development	Feasibility and stability of fixation unknown
	Percutaneous energy-mediated cinching	QuantumCor	Animal models	Scarring not precise. Possible residual MR or iatrogenic MS. Risk of cardiac structure perforation.
		ReCor	Pre-clinical development	As above
	Hybrid	Mitral solutions	Pre-clinical development	Not true "percutaneous" technique
		MiCardia	Pre-clinical development	As above

Site of Action	Mechanism of Action	Device	Status	Major Limitations
Percutaneous MV Repair Technologies				
Chordal implants	Transapical			
	Artificial chord	Neochord, MitraFlex	Pre-clinical development	Residual leaflet prolapse or restriction with residual MR. Thrombus formation.
	Transapical-Transseptal			
	Artificial chord	Babic	Pre-clinical development	As above
LV	LV (and MA) remodeling	Mardil-BACE	Temporary human implant	Requires mini-thoracotomy. Long-term effects unknown.
Percutaneous MV Replacement Technologies				
Valve implants	Right mini-thoracotomy	Endovalve-Herrmann prosthesis	Animal models	Anchoring challenges. LV outflow obstruction. Paravalvular leaks.
	Transapical	Lutter prosthesis	Animal models	As above
	Transseptal	CardiaQ prosthesis	Pre-clinical development	As above

Paul T.L. Chiam, and Carlos E. Ruiz. JACC Intv. 2011;4;1-13


A
Incomplete coaptation of mitral leaflets resulting in regurgitation
B
Left atrium
Anterior leaflet
Posterior leaflet
C
Mitral-valve clip is advanced through a catheter that is placed in the femoral vein, proceeds up the inferior vena cava into the right atrium, and crosses the atrial septum into the left atrium
Catheter
Inferior vena cava
D
The device is steered until aligned over the origin of the regurgitant jet, and the open clip is advanced into the left ventricle
Left atrium
Leaflet
Opened clip
Left ventricle
E
The mitral leaflets are grasped and the clip closed to coapt the leaflets
Closed clip
F
Reduced regurgitation with closed clip
G
Mitral valve during systole
Edge-to-edge approximation of leaflets by the clip
H
Mitral valve during diastole
Left ventricle
Edge-to-edge approximation of leaflets by the clip

EVEREST II Randomized Controlled Trial

The NEW ENGLAND JOURNAL of MEDICINE

Study Design

279 Patients enrolled at 37 sites

Significant MR (3+-4+)

Specific Anatomical Criteria

Randomized 2:1

Device Group
MitraClip System
N=184

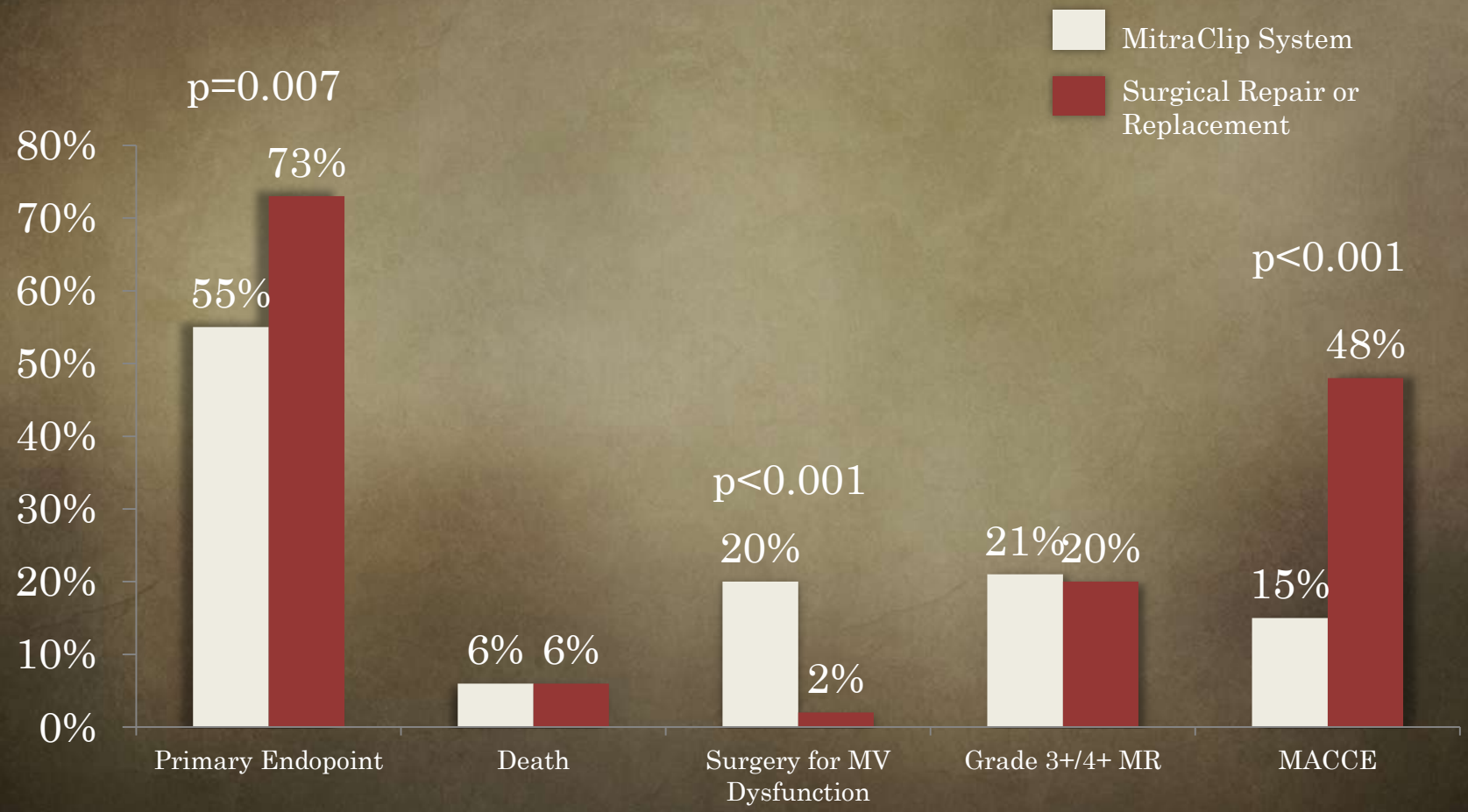
Control Group
Surgical Repair or Replacement
N=95

Primary efficacy composite end point: freedom from death, from surgery for mitral-valve dysfunction, and from grade 3+ or 4+ mitral regurgitation at 12 months

Primary safety composite end point: major adverse events within 30 days

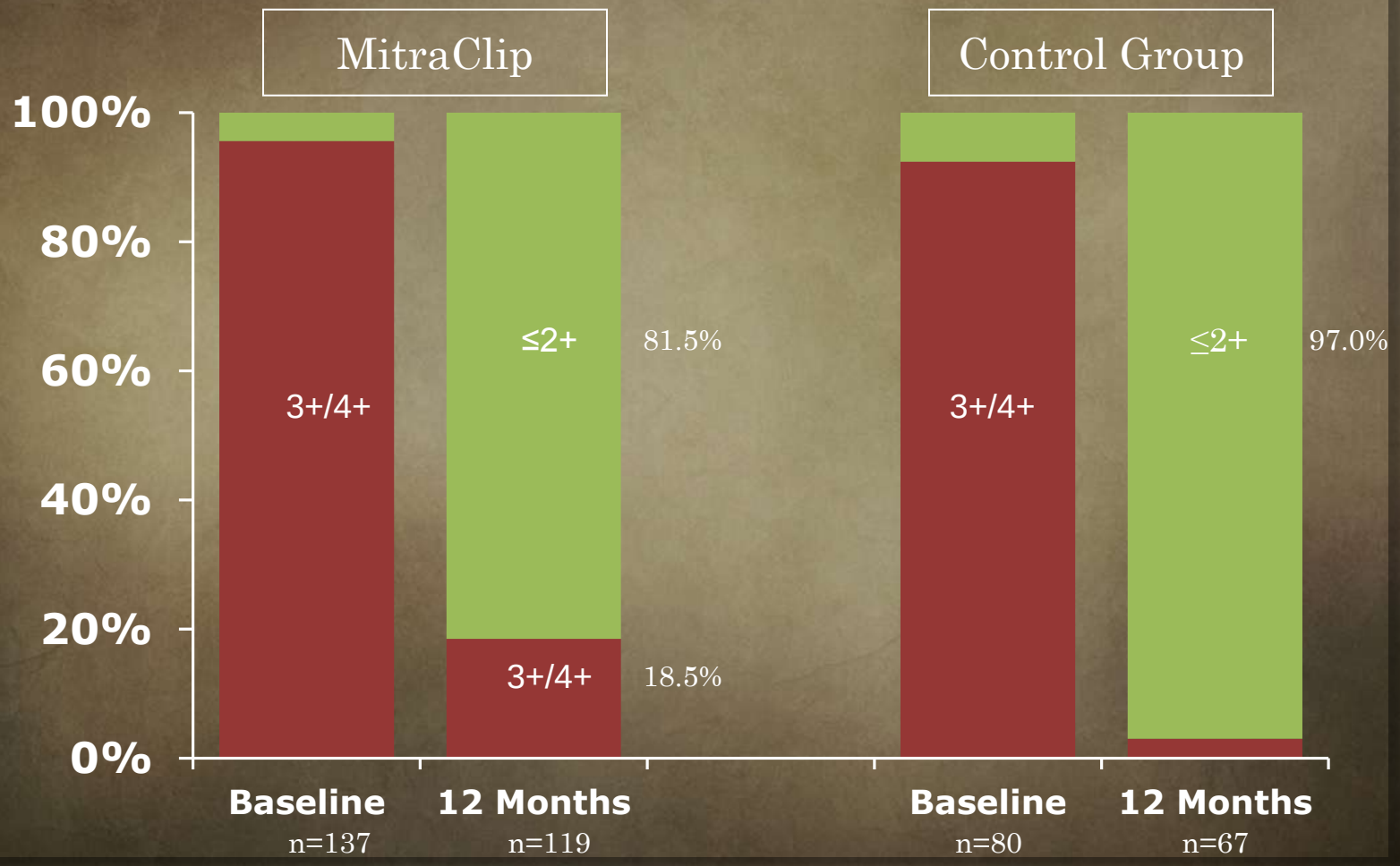
EVEREST II RCT

12 Month Efficacy and Safety Endpoints



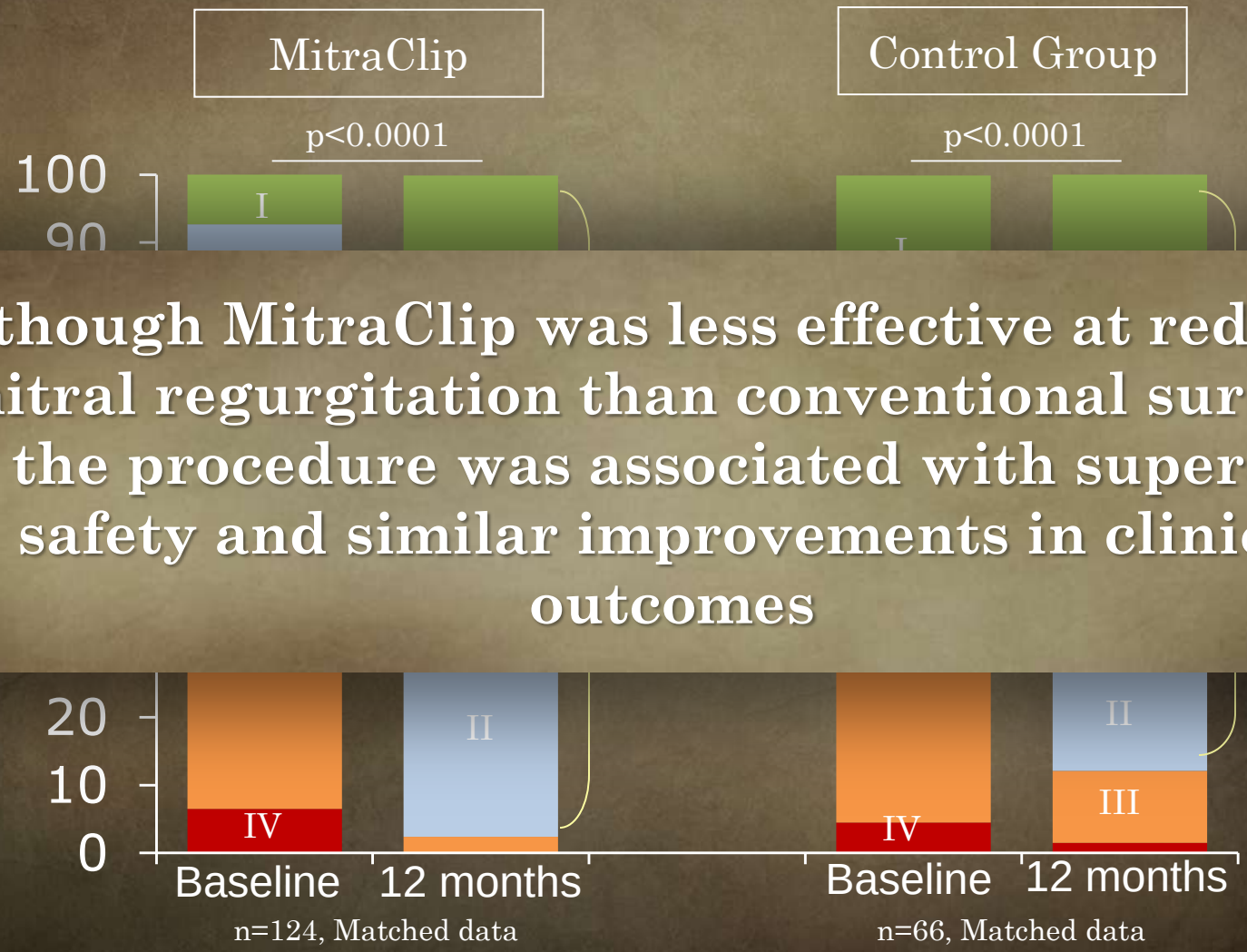
EVEREST II RCT

MR Reduction



EVEREST II RCT

NYHA Functional Class



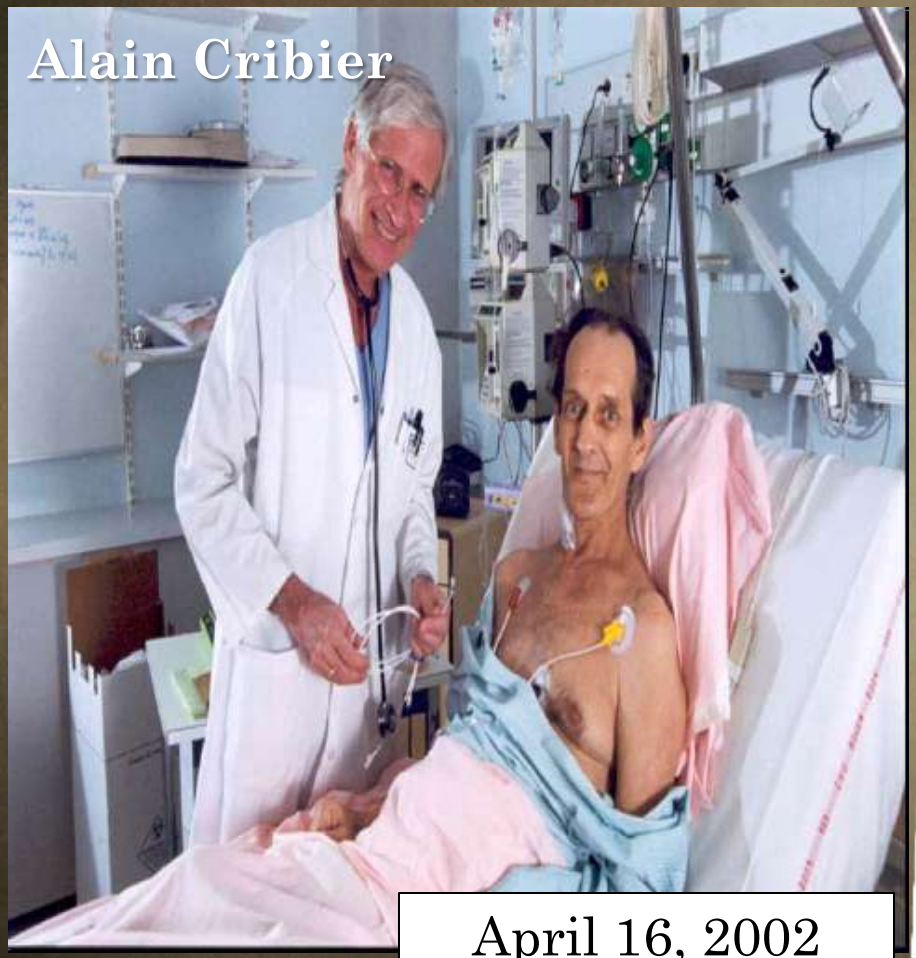
Although MitraClip was less effective at reducing mitral regurgitation than conventional surgery, the procedure was associated with superior safety and similar improvements in clinical outcomes

Aortic Stenosis

- Valvular aortic stenosis is the clinically most important valvular heart disease in the elderly
- It is associated with considerable morbidity and mortality if treated only medically (mean survival 2 years)
- Conventional open-heart aortic valve replacement (AVR) has been the only therapeutic option until transcatheter aortic valve implantation (TAVI) has been introduced in clinical practice as alternative treatment option for high-risk patients with severe, symptomatic aortic stenosis

Varadarajan P et al. Eur J Cardiothorac Surg. 2006 Nov;30(5):722-7

TAVI



April 16, 2002

8th postoperative day

Special Report

Percutaneous Transcatheter Implantation of an Aortic Valve Prosthesis for Calcific Aortic Stenosis

First Human Case Description

Alain Cribier, MD; Helene Eltchaninoff, MD; Assaf Bash, PhD; Nicolas Borenstein, MD; Christophe Tron, MD; Fabrice Bauer, MD; Genevieve Derumeaux, MD; Frederic Anselme, MD; François Laborde, MD; Martin B. Leon, MD

Background—The design of a percutaneous implantable prosthetic heart valve has become an important area for investigation. A percutaneously implanted heart valve (PHV) composed of 3 bovine pericardial leaflets mounted within a balloon-expandable stent was developed. After ex vivo testing and animal implantation studies, the first human implantation was performed in a 57-year-old man with calcific aortic stenosis, cardiogenic shock, subacute leg ischemia, and other associated noncardiac diseases. Valve replacement had been declined for this patient, and balloon valvuloplasty had been performed with nonsustained results.

Methods and Results—With the use of an anterograde transseptal approach, the PHV was successfully implanted within the diseased native aortic valve, with accurate and stable PHV positioning, no impairment of the coronary artery blood flow or of the mitral valve function, and a mild paravalvular aortic regurgitation. Immediately and at 48 hours after implantation, valve function was excellent, resulting in marked hemodynamic improvement. Over a follow-up period of 4 months, the valvular function remained satisfactory as assessed by sequential transesophageal echocardiography, and there was no recurrence of heart failure. However, severe noncardiac complications occurred, including a progressive worsening of the leg ischemia, leading to leg amputation with lack of healing, infection, and death 17 weeks after PHV implantation.

Conclusions—Nonsurgical implantation of a prosthetic heart valve can be successfully achieved with immediate and midterm hemodynamic and clinical improvement. After further device modifications, additional durability tests, and multicenter clinical implantations, PHV might become an important therapeutic alternative for the treatment of selected patients with nonsurgical aortic stenosis. (*Circulation*. 2002;106:3006-3008.)

Key Words: stenosis, aortic ■ valves, prosthetic ■ prosthesis ■ catheterization

Percutaneous catheter-based systems for the treatment of valvular heart disease have been designed and studied in animal models for several years.[1–4] Recently, Bonhoeffer et al,[5,6] using a bovine jugular vein valve mounted within a stent, performed the first in-human percutaneous implantation of artificial valves in children with right ventricle to pulmonary prosthetic conduits.

The goals of our research project were to develop a biological heart valve, mounted on a specially designed balloon-expandable stent, which could be delivered percutaneously via standard catheter-based techniques and implanted within a diseased aortic valve in calcific aortic stenosis. This concept was based on personal unpublished autopsy observations on calcific aortic stenosis showing that a stent could effectively open while strongly adhering within the native diseased valve without impairing the coronary ostia or the mitral valve.

An original percutaneous heart valve (PHV) was developed (Percutaneous Valve Technologies, Inc), which consisted of 3 bovine pericardial leaflets mounted within a tubular, slotted, stainless steel balloon-expandable stent, 14 mm in length, designed to achieve a diameter of 21 to 23 mm. PHV function and durability were first tested in ex vivo pulse duplicator models. Valve durability passed 100 million cycles (2 and a half years). In animal models, the PHV was accurately delivered by balloon inflation at various cardiac sites[7] in 60 sheep. Acute and short-term valve functions were satisfactory. Implantation in the subcoronary aortic valve position was technically difficult in this animal model (which varies considerably from humans) and was

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From the Department of Cardiology (A.C., H.E., C.T., F.B., G.D., F.A.), Charles Nicolle Hospital, University of Rouen, Rouen, France; the Centre d'Enseignement de Recherche Appliquée (CERA) (A.B.), Paris, France; the Cardiovascular Research Foundation (M.B.L.), Mount Sinai Hospital, New York, NY; and Percutaneous Valve Technologies, Inc (M.B.L.), Fort Lee, NJ (A.B.).

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DOI: 10.1161/01.CIR.0000047200.36165.B8

Cribier A. Circulation 2002;106:3006–8

Current Generation Transcatheter Aortic Valve Therapies

Edwards SAPIEN™ THV : Balloon expandable

- Stainless steel & recently nitinol support structure
- Bovine pericardial valve
- 20, 23, 26 & 29 mm diameter

CoreValve Revalving System™ : Self expandable

- Nitinol support structure
- Porcine pericardial valve
- 26 & 29 mm diameter

Indications for TAVI

Symptomatic patients with severe AS, who are considered:

- **High surgical risk**

Octogenarians with multiple co morbidities: COPD, DM, ↑Creatinine, PAD, ↓LVEF, prior cardiac surgery

- **STS score** >10%,
- Logistic **EuroSCORE** >30% (~15% perioperative risk of death @ 30 days)

- **Inoperable**

- **History of thoracic irradiation**
- **Severe thoracic deformity**
- **End stage COPD**
- **Porto pulmonary hypertension**
- **Porcelain aorta (confirmed with CT)**
- **Degenerative neurological disorders**
- **50% probability of death or hospital discharge**

PARTNER Trial

Symptomatic Severe Aortic Stenosis

ASSESSMENT: High-Risk AVR Candidate
3,105 Total Patients Screened

Total = 1,057 patients

2 Parallel Trials:
Individually Powered

High Risk — N = 699

ASSESSMENT: Transfemoral Access

- Yes → **Transfemoral (TF)**
  - **1:1 Randomization**
    - N = 244: **TF TAVR**
    - VS
    - N = 248: **AVR**
- No → **Transapical (TA)**
  - **1:1 Randomization**
    - N = 104: **TA TAVR**
    - VS
    - N = 103: **AVR**

Primary Endpoint: All-Cause Mortality at 1 yr (Non-inferiority)

Inoperable — N = 358

ASSESSMENT: Transfemoral Access

- Yes
  - **1:1 Randomization**
    - N = 179: **TF TAVR**
    - VS
    - N = 179: **Standard Therapy**
- No → **Not In Study**

Primary Endpoint: All-Cause Mortality Over Length of Trial (Superiority)
Co-Primary Endpoint: Composite of All-Cause Mortality and Repeat Hospitalization (Superiority)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 21, 2010 VOL. 363 NO. 17

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela S. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

ABSTRACT

BACKGROUND

Many patients with severe aortic stenosis and coexisting conditions are not candidates for surgical replacement of the aortic valve. Recently, transcatheter aortic-valve implantation (TAVI) has been suggested as a less invasive treatment for high-risk patients with aortic stenosis.

METHODS

We randomly assigned patients with severe aortic stenosis, whom surgeons considered not to be suitable candidates for surgery, to standard therapy (including balloon aortic valvuloplasty) or transfemoral transcatheter implantation of a balloon-expandable bovine pericardial valve. The primary end point was the rate of death from any cause.

RESULTS

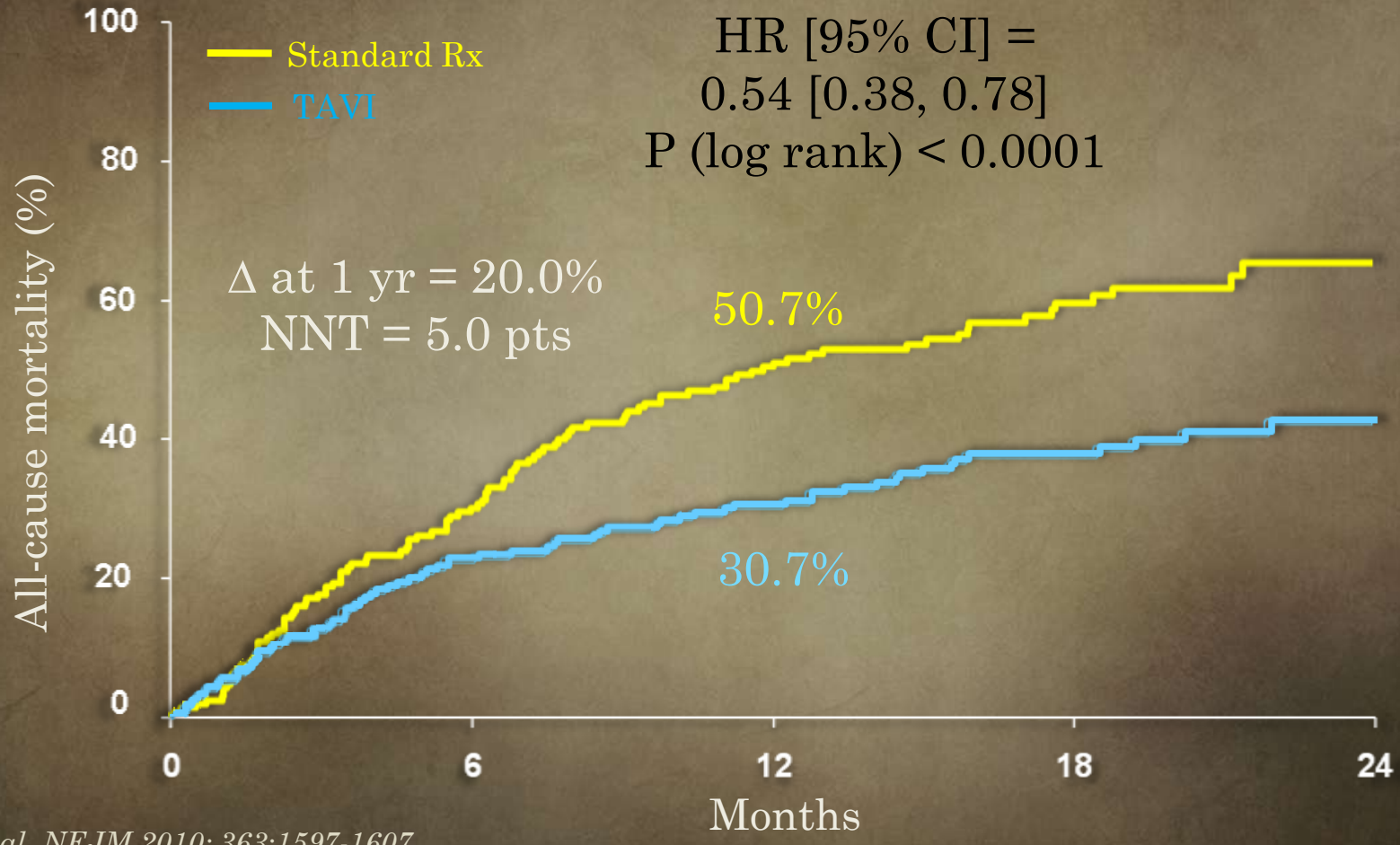
A total of 358 patients with aortic stenosis who were not considered to be suitable candidates for surgery underwent randomization at 21 centers (17 in the United States). At 1 year, the rate of death from any cause (Kaplan–Meier analysis) was 30.7% with TAVI, as compared with 50.7% with standard therapy (hazard ratio with TAVI, 0.55; 95% confidence interval [CI], 0.40 to 0.74; P<0.001). The rate of the composite end point of death from any cause or repeat hospitalization was 42.5% with TAVI as compared with 71.6% with standard therapy (hazard ratio, 0.46; 95% CI, 0.35 to 0.59; P<0.001). Among survivors at 1 year, the rate of cardiac symptoms (New York Heart Association class III or IV) was lower among patients who had undergone TAVI than among those who had received standard therapy (25.2% vs. 58.0%, P<0.001). At 30 days, TAVI, as compared with standard therapy, was associated with a higher incidence of major strokes (5.0% vs. 1.1%, P=0.06) and major vascular complications (16.2% vs. 1.1%, P<0.001). In the year after TAVI, there was no deterioration in the functioning of the bioprosthetic valve, as assessed by evidence of stenosis or regurgitation on an echocardiogram.

CONCLUSIONS

In patients with severe aortic stenosis who were not suitable candidates for surgery, TAVI, as compared with standard therapy, significantly reduced the rates of death from any cause, the composite end point of death from any cause or repeat hospitalization, and cardiac symptoms, despite the higher incidence of major strokes and major vascular events. (Funded by Edwards Lifesciences; ClinicalTrials.gov number, NCT00530894.)

Cohort B Population Profile 1	
Mean age	83 y
NYHA Class III-IV	93%
COPD, O2 dependent	23%
PVD	28%
Porcelain aorta	15%
Chest wall deformity	7%
CAD	71%
Frail	23%

Inoperable PARTNER Cohort
Primary Endpoint: All-Cause Mortality



Leon et al, NEJM 2010; 363:1597-1607

Numbers at Risk					
TAVI	179	138	122	67	26
Standard Rx	179	121	83	41	12

Major Events at 1 Year - Inoperable

✓TAVI resulted in 45% reduction in all-cause mortality and 61% reduction in cardiovascular mortality at 1 year compared with standard therapy

✓Echocardiographic criteria such as aortic valve area and mean aortic valve gradients, and symptom criteria such as NYHA class, also demonstrated a significant improvement

✓Preliminary cost-effectiveness analyses indicate significantly increased life expectancy at an incremental cost per life-year gained

✓The procedure is complex and fraught with numerous complications

Primary Non-inferiority Endpoint:
All-Cause Mortality at 1 Year in Cohort A

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 9, 2011 VOL. 364 NO. 23

Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Babaliaros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*

ABSTRACT

BACKGROUND

The use of transcatheter aortic-valve replacement has been shown to reduce mortality among high-risk patients with aortic stenosis who are not candidates for surgical replacement. However, the two procedures have not been compared in a randomized trial involving high-risk patients who are still candidates for surgical replacement.

METHODS

At 25 centers, we randomly assigned 699 high-risk patients with severe aortic stenosis to undergo either transcatheter aortic-valve replacement with a balloon-expandable bovine pericardial valve (either a transfemoral or a transapical approach) or surgical replacement. The primary end point was death from any cause at 1 year. The primary hypothesis was that transcatheter replacement is not inferior to surgical replacement.

RESULTS

The rates of death from any cause were 3.4% in the transcatheter group and 6.5% in the surgical group at 30 days (P=0.07) and 24.2% and 26.8%, respectively, at 1 year (P=0.44), a reduction of 2.6 percentage points in the transcatheter group (upper limit of the 95% confidence interval, 3.0 percentage points; predefined margin, 7.5 percentage points; P=0.001 for noninferiority). The rates of major stroke were 3.8% in the transcatheter group and 2.1% in the surgical group at 30 days (P=0.20) and 5.1% and 2.4%, respectively, at 1 year (P=0.07). At 30 days, major vascular complications were significantly more frequent with transcatheter replacement (11.0% vs. 3.2%, P<0.001); adverse events that were more frequent after surgical replacement included major bleeding (9.3% vs. 19.5%, P<0.001) and new-onset atrial fibrillation (8.6% vs. 16.0%, P=0.006). More patients undergoing transcatheter replacement had an improvement in symptoms at 30 days, but by 1 year, there was not a significant between-group difference.

CONCLUSIONS

In high-risk patients with severe aortic stenosis, transcatheter and surgical procedures for aortic-valve replacement were associated with similar rates of survival at 1 year, although there were important differences in periprocedural risks. (Funded by Edwards Lifesciences; Clinical Trials.gov number, NCT00530894.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Smith at Columbia University Medical Center–New York Presbyterian Hospital, 177 Fort Washington Ave., Milstein Bldg. 7-435, New York, NY 10032, or at crs2@columbia.edu.

*The investigators, institutions, and research organizations participating in the Placement of Aortic Transcatheter Valves (PARTNER) trial are in the Supplementary Appendix, available at NEJM.org.

N Engl J Med 2011;364:2187-98.

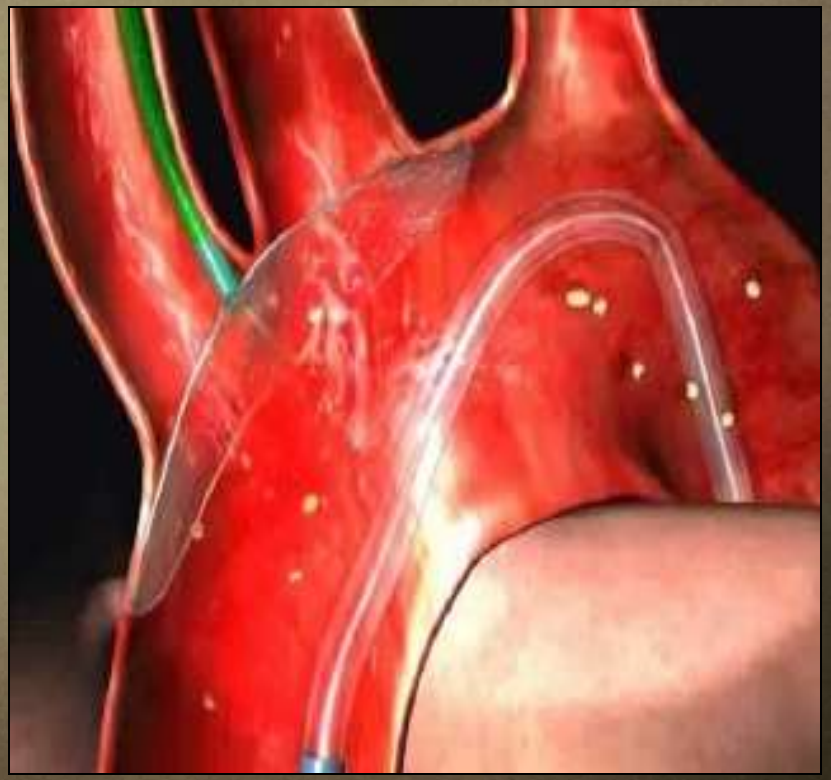
348	298	260	147	67
351	292	236	139	65

Both TAVR and AVR were associated with important but different periprocedural hazards

- Major strokes at 30 days (3.8 vs. 2.3%, p=0.20) and one year (4.8% vs. 2.6%, p=0.07) and major vascular complications were more frequent with TAVR (11.0% vs. 3.2%, p<0.001)

- Major bleeding (9.3% vs. 19.5%, p<0.001) and new onset atrial fibrillation (8.6% vs. 16.0%, p<0.001) were more frequent with AVR

Embrella Embolic Deflector System™



Weighted Meta – Analysis of Early and Late Clinical Outcomes after CoreValve TAVI in Seven National Registries

Registry	Pts	Procedural Succes, %	Vascular Compls, %	Stroke, %	PPM, %	30 Day Survival, %	1 Year Mortality, %
Italian[1]	663	98	2	1.2	16.6	94.1	15
Belgian[2]	141	98	-	5	23	91	21
French[3]	66	92.6	7.5	4.5	25.7	84.9	NR
Spanish[4]	108	98.1	5.6	0	35.2	92.6	17.7
UK[5]	460	-	4	4.3	26	94.5	18.4
German[6]	588	-	4	-	42.5	88.8	NR
Australia-NZ[7]	118	95.8	6.5	1.9	40	93.4	NR
Average	**2156**	**97.8**	**4.2**	**2.8**	**28.7**	**93.4**	**17.1**
95% CI		96.4-99.2	1.6-6.8	0.6-5	20.6-36.8		

Carlos E. Ruiz et al. PCR 2011

New TAVI Technologies

17 TAVI systems are in active development

7 have FIM implantation results

Direct Flow
Sadra
AorTx
Jena Valve
HLT
ABPS PercValve
EndoTech
Medtronic Engager
Symetis
etc…

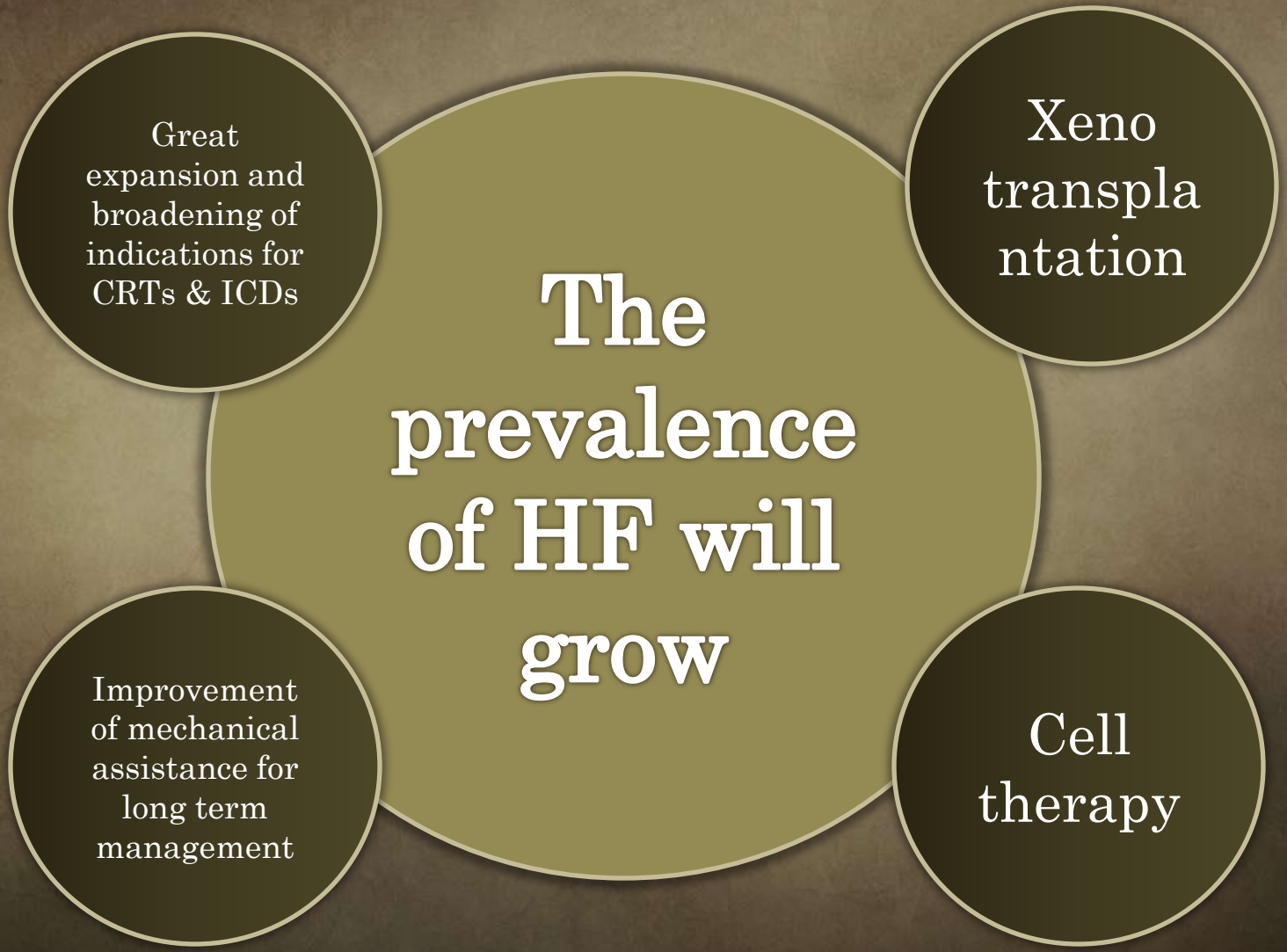
Recoverable / repositionable
Lower profile systems
No perivalvular leaks
More accurate positioning
Percutaneous access and closure

THE FUTURE

Continuing subspecialization in the pursuit of technical virtuosity & clinical excellence

Expansion of preventive measures and new phenotypic risk markers

THE FUTURE

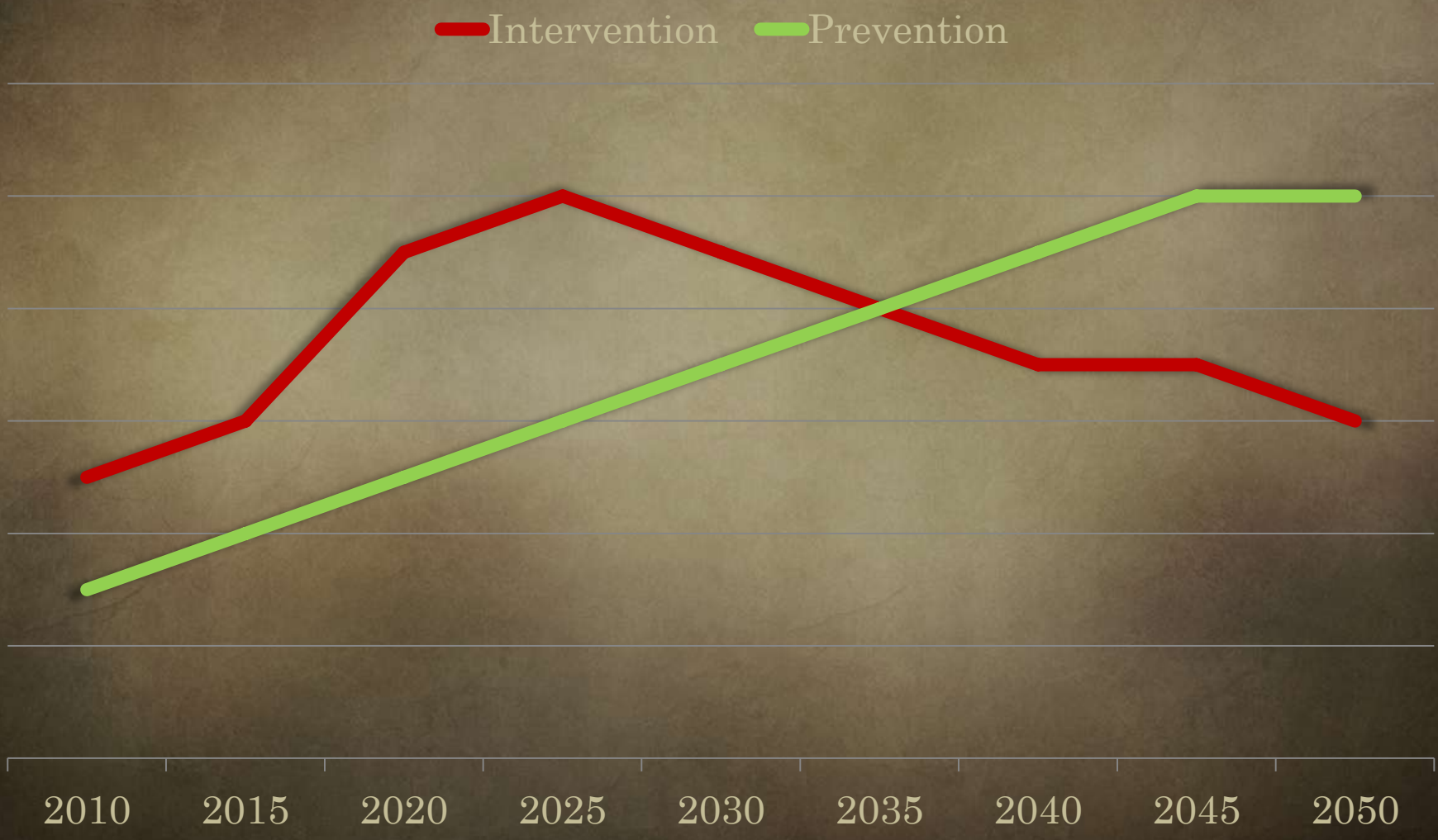

Great expansion and broadening of indications for CRTs & ICDs
Xeno transplantation
The prevalence of HF will grow
Improvement of mechanical assistance for long term management
Cell therapy

THE FUTURE

Increasing application of pharmacogenomics

Gene informed therapy

Future use and impact of interventional and preventive cardiology



CONCLUSIONS

- The principal role of the cardiologist will change from recognizing and managing established disease, as is the case today, to interpreting and applying genetic information in prevention and treatment in 2020 and beyond

- The grand goal, of course, is to eliminate cardiovascular disease as a major threat to long, productive life

- It is hoped this will be well underway by 2028, the 400th anniversary of William Harvey's discovery of the circulation and the 125th anniversary of Willem Einthoven's development of the string galvanometer

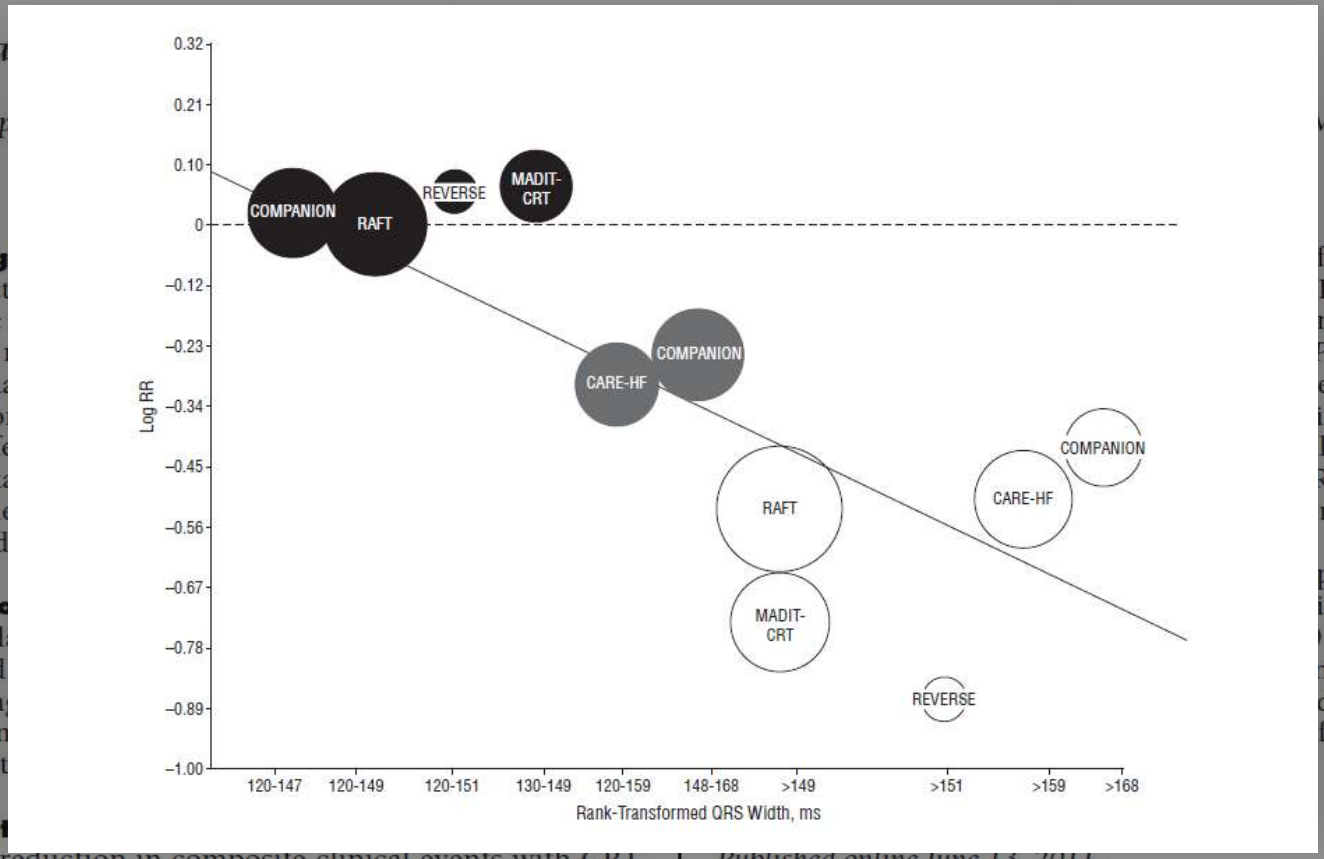
Thank you

ONLINE FIRST | LESS IS MORE

Impact of QRS Duration on Clinical Event Reduction With Cardiac Resynchronization Therapy

Meta

Ilke Sip *MD*



Backg fit of CRT
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failure nificantly
rogate P<.001).
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randon ds. These
patient f patients

Result
was a reduction in composite clinical events with CRT (risk ratio, 0.60; 95% confidence interval [CI], 0.53-

Published online June 13, 2011.
doi:10.1001/archinternmed.2011.247

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
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Radiofrequency Catheter Ablation of Atrial Fibrillation: A Cause of Silent Thromboembolism? : Magnetic Resonance Imaging Assessment of Cerebral Thromboembolism in Patients Undergoing Ablation of Atrial Fibrillation

Fiorenzo Gaita, Domenico Caponi, Martina Pianelli, Marco Scaglione, Elisabetta Toso, Federico Cesarani, Carlo Boffano, Giovanni Gandini, Maria Consuelo Valentini, Roberto De Ponti, Franck Halimi and Jean François Leclercq

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CLINICAL RESEARCH — Clinical Trials

Incidence of Asymptomatic Intracranial Embolic Events After Pulmonary Vein Isolation

Comparison of Different Atrial Fibrillation Ablation Technologies in a Multicenter Study

Claudia Herrera Siklódy, MD,* Thomas Deneke, MD,‡ Mélèze Hocini, MD,§ Heiko Lehmann, MD,* Dong-In Shin, MD,‖ Shinsuke Miyazaki, MD,§ Susanne Henschke, MD,† Peter Fiegel, MD,† Jochen Schiebeling-Römer, MD,* Paul M. Bansmann, MD,‡ Thomas Bourdias, MD,§ Vincent Douset, MD,§ Michel Haïssaguerre, MD,§ Thomas Arentz, MD*

Bad Krozingen and Köln, Germany; and Bordeaux-Pessac, France

Intracranial Emboli Associated With Catheter Ablation of Atrial Fibrillation: Has the Silence Finally Been Broken?

Jonathan S. Steinberg, and Suneet Mittal

J. Am. Coll. Cardiol. 2011;58;689-691
doi:10.1016/j.jacc.2011.05.014

Incidence of Silent Cerebral Thromboembolic Lesions After Atrial Fibrillation Ablation May Change According to Technology Used: Comparison of Irrigated Radiofrequency, Multipolar Nonirrigated Catheter and Cryoballoon

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Europace (2011) 13, 37–44
doi:10.1093/europace/euq303

CLINICAL RESEARCH
Ablation for Atrial Fibrillation

MEDAFI-Trial (Micro-embolization during ablation of atrial fibrillation): comparison of pulmonary vein isolation using cryoballoon technique vs. radiofrequency energy

Thomas Neumann[1]*, Malte Kuniss[1], Guido Conradi[1], Sebastien Janin[1], Alexander Berkowitsch[1], Maciej Wojcik[1], Johannes Rixe[1], Damir Erkapic[1], Sergey Zaltsberg[1], Andreas Rolf[1], Georg Bachmann[2], Thorsten Dill[1], Christian W. Hamm[1], and Heinz-Friedrich Pitschner[1]

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European Heart Journal (2010) 31, 943–957
doi:10.1093/eurheart/ehp492

CLINICAL RESEARCH
Coronary heart disease

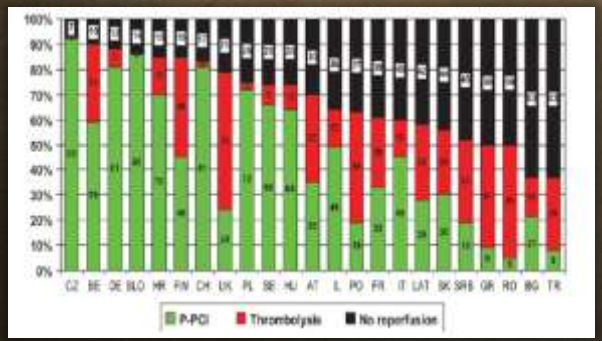
Reperfusion therapy for ST elevation acute myocardial infarction in Europe: description of the current situation in 30 countries

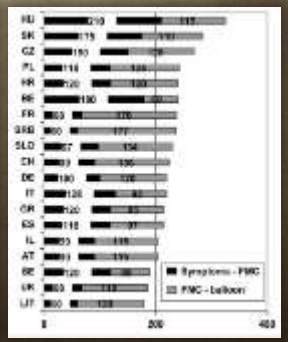
Petr Widimsky*, William Wijns, Jean Fajadet, Mark de Belder, Jiri Knot, Lars Aaberge, George Andrikopoulos, Jose Antonio Baz, Amadeo Betriu, Marc Claeys, Nicholas Danchin, Slaveyko Djambazov, Paul Erne, Juha Hartikainen, Kurt Huber, Petr Kala, Milka Klinčeva, Steen Dalby Kristensen, Peter Ludman, Josephina Mauri Ferre, Bela Merkely, Davor Miličić, Joao Morais, Marko Noč, Grzegorz Opolski, Miodrag Ostojić, Dragana Radovanović, Stefano De Servi, Ulf Stenestrand, Martin Studenčan, Marco Tubaro, Zorana Vasiljević, Franz Weidinger, Adam Witkowski, and Uwe Zeymer on behalf of the European Association for Percutaneous Cardiovascular Interventions†

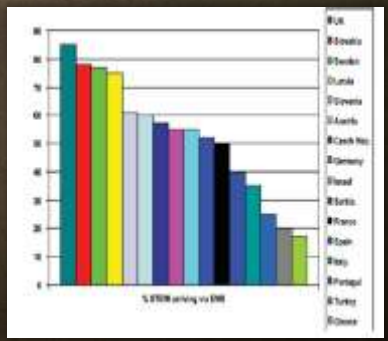
GREECE

ACS

- 40 PCI centers, 10 pPCI centers
- 20000 AMI hospitalizations
- 12000 STEMI hospitalizations
- STEMI:
  - 9% pPCI,
  - 41% Thrombolysis,
  - 50% none
- 20000 PCIs annually ➔ 5% pPCIs
- Symptoms –FMC time delay:120 min
- FMC-balloon time delay:95 min







European Heart Journal (2010) 31, 943–957

Vascular access

Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial

Sanjit S Jolly, Salim Yusuf, John Cairns, Kari Niemelä, Denis Xavier, Petr Widimsky, Andrzej Budaj, Matti Niemelä, Vicent Valentin, Basil S Lewis, Alvaro Avezum, Philippe Gabriel Steg, Sunil V Rao, Peggy Gao, Rizwan Afzal, Campbell D Joyner, Susan Cholakovicius, Shamir R Mehta, for the RIVAL trial group*

Summary

Background Small trials have suggested that radial access for percutaneous coronary intervention (PCI) reduces vascular complications and bleeding compared with femoral access. We aimed to assess whether radial access was superior to femoral access in patients with acute coronary syndromes (ACS) who were undergoing coronary angiography with possible intervention.

Methods The RadIal Vs femorAL access for coronary intervention (RIVAL) trial was a randomised, parallel group, multicentre trial. Patients with ACS were randomly assigned (1:1) by a 24 h computerised central automated voice response system to radial or femoral artery access. The primary outcome was a composite of death, myocardial infarction, stroke, or non-coronary artery bypass graft (non-CABG)-related major bleeding at 30 days. Key secondary outcomes were death, myocardial infarction, or stroke; and non-CABG-related major bleeding at 30 days. A masked central committee adjudicated the primary outcome, components of the primary outcome, and stent thrombosis. All other outcomes were as reported by the investigators. Patients and investigators were not masked to treatment allocation. Analyses were by intention to treat. This trial is registered with ClinicalTrials.gov, NCT01014273.

Findings Between June 6, 2006, and Nov 3, 2010, 7021 patients were enrolled from 158 hospitals in 32 countries. 3507 patients were randomly assigned to radial access and 3514 to femoral access. The primary outcome occurred in 128 (3·7%) of 3507 patients in the radial access group compared with 139 (4·0%) of 3514 in the femoral access group (hazard ratio [HR] 0·92, 95% CI 0·72–1·17; p=0·50). Of the six prespecified subgroups, there was a significant interaction for the primary outcome with benefit for radial access in highest tertile volume radial centres (HR 0·49, 95% CI 0·28–0·87; p=0·015) and in patients with ST-segment elevation myocardial infarction (0·60, 0·38–0·94; p=0·026). The rate of death, myocardial infarction, or stroke at 30 days was 112 (3·2%) of 3507 patients in the radial group compared with 114 (3·2%) of 3514 in the femoral group (HR 0·98, 95% CI 0·76–1·28; p=0·90). The rate of non-CABG-related major bleeding at 30 days was 24 (0·7%) of 3507 patients in the radial group compared with 33 (0·9%) of 3514 patients in the femoral group (HR 0·73, 95% CI 0·43–1·23; p=0·23). At 30 days, 42 of 3507 patients in the radial group had large haematoma compared with 106 of 3514 in the femoral group (HR 0·40, 95% CI 0·28–0·57; p<0·0001). Pseudoaneurysm needing closure occurred in seven of 3507 patients in the radial group compared with 23 of 3514 in the femoral group (HR 0·30, 95% CI 0·13–0·71; p=0·006).

Interpretation Radial and femoral approaches are both safe and effective for PCI. However, the lower rate of local vascular complications may be a reason to use the radial approach.

	Radial (n=3507)	Femoral (n=3514)	Hazard ratio (95% CI)	p value
Primary outcome				
Death, MI, stroke, or non-CABG bleeding at 30 days	128 (3·7%)	139 (4·0%)	0·92 (0·72–1·17)	0·50
Secondary outcomes at 30 days				
Death, MI, or stroke	112 (3·2%)	114 (3·2%)	0·98 (0·76–1·28)	0·90
Non-CABG major bleeding	24 (0·7%)	33 (0·9%)	0·73 (0·43–1·23)	0·23
Death	44 (1·3%)	51 (1·5%)	0·86 (0·58–1·29)	0·47
MI	60 (1·7%)	65 (1·9%)	0·92 (0·65–1·31)	0·65
Stroke	20 (0·6%)	14 (0·4%)	1·43 (0·72–2·83)	0·30
Secondary outcomes at 48 h				
Death, MI, stroke, or non-CABG bleeding	50 (1·4%)	65 (1·8%)	0·77 (0·53–1·11)	0·17
Non-CABG major bleeding	11 (0·3%)	18 (0·5%)	0·61 (0·29–1·30)	0·20
Death	9 (0·3%)	15 (0·4%)	0·60 (0·26–1·37)	0·23
MI	29 (0·8%)	31 (0·9%)	0·94 (0·56–1·56)	0·80
Stroke	7 (0·2%)	6 (0·2%)	1·17 (0·39–3·48)	0·78
Other secondary outcomes				
PCI success*	2204 (95·4%)	2235 (95·2%)	1·01 (0·95–1·07)	0·83
Access site crossover	265 (7·6%)	70 (2·0%)	3·82 (2·93–4·97)	<0·0001
Major vascular complications	49 (1·4%)	131 (3·7%)	0·37 (0·27–0·52)	<0·0001
Minor bleeding	100 (2·9%)	118 (3·4%)	0·84 (0·65–1·10)	0·21
Safety outcomes				
Non-CABG TIMI major bleeding	19 (0·5%)	19 (0·5%)	1·00 (0·53–1·89)	1·00
CABG-related bleeding	48 (1·4%)	48 (1·4%)	1·00 (0·67–1·49)	1·00
Non-CABG-related blood transfusions	39 (1·1%)	45 (1·3%)	0·87 (0·56–1·33)	0·51
All blood transfusions	99 (2·8%)	98 (2·8%)	1·01 (0·76–1·33)	0·95
Post-hoc exploratory outcomes				
ACUITY major bleeding†	66 (1·9%)	157 (4·5%)	0·43 (0·32–0·57)	<0·0001
Death, MI, or stroke, or ACUITY major bleed†	167 (4·8%)	256 (7·3%)	0·65 (0·53–0·78)	<0·0001
Non-CABG major bleeding and major vascular complications	67 (1·9%)	157 (4·5%)	0·43 (0·32–0·57)	<0·0001
Death, MI, stroke, non-CABG major bleeding, or major vascular complications	167 (4·8%)	260 (7·4%)	0·63 (0·52–0·77)	<0·0001

Data are number (%). MI=myocardial infarction. CABG=coronary artery bypass graft. PCI=percutaneous coronary intervention. TIMI=thrombolysis in myocardial infarction. ACUITY=Acute Catheterization and Urgent Intervention strategy. *As a proportion of patients who had PCI: n=2311 in the radial group and n=2349 in the femoral group. †Large haematomas diagnosed as per investigator's clinical decision.

Table 3: **Primary, secondary, safety, and exploratory outcomes**

Jolly SS, Yusuf S, Cairns J, et al; RIVAL Trial Group. Lancet 2011;377:1409–20

Stenting

Heparin plus a glycoprotein IIb/IIIa inhibitor versus bivalirudin monotherapy and paclitaxel-eluting stents versus bare-metal stents in acute myocardial infarction (HORIZONS-AMI): final 3-year results from a multicentre, randomised controlled trial

Gregg W Stone, Bernhard Witzenbichler, Giulio Guagliumi, Jon C Peruga, Bruce R Brodie, Dariusz Dudek, Ron Kornowski, Franz Hartmann, Bernard J Gersh, Stuart J Pocock, George Dangas, S Chiu Wong, Martin Fahy, Helen Parise, Roxana Mehran, on behalf of the HORIZONS-AMI Trial Investigators*

Summary

Background Primary results of the HORIZONS-AMI trial have been previously reported. In this final report, we aimed to assess 3-year outcomes.

Methods HORIZONS-AMI was a prospective, open-label, randomised trial undertaken at 123 institutions in 11 countries. Patients aged 18 years or older were eligible for enrolment if they had ST-segment elevation myocardial infarction (STEMI), presented within 12 h after onset of symptoms, and were undergoing primary percutaneous coronary intervention. By use of a computerised interactive voice response system, we randomly allocated patients 1:1 to receive bivalirudin or heparin plus a glycoprotein IIb/IIIa inhibitor (GPI; pharmacological randomisation; stratified by previous and expected drug use and study site) and, if eligible, randomly allocated 3:1 to receive a paclitaxel-eluting stent or a bare metal stent (stent randomisation; stratified by pharmacological group assignment, diabetes mellitus status, lesion length, and study site). We produced Kaplan-Meier estimates of major adverse cardiovascular events at 3 years by intention to treat. This study is registered with ClinicalTrials.gov, number NCT00433966.

Findings Compared with 1802 patients allocated to receive heparin plus a GPI, 1800 patients allocated to bivalirudin monotherapy had lower rates of all-cause mortality (5·9% *vs* 7·7%, difference −1·9% [−3·5 to −0·2], HR 0·75 [0·58–0·97]; p=0·03), cardiac mortality (2·9% *vs* 5·1%, −2·2% [−3·5 to −0·9], 0·56 [0·40–0·80]; p=0·001), reinfarction (6·2% *vs* 8·2%, −1·9% [−3·7 to −0·2], 0·76 [0·59–0·99]; p=0·04), and major bleeding not related to bypass graft surgery (6·9% *vs* 10·5%, −3·6% [−5·5 to −1·7], 0·64 [0·51–0·80]; p=0·0001) at 3 years, with no significant differences in ischaemia-driven target vessel revascularisation, stent thrombosis, or composite adverse events. Compared with 749 patients who received a bare-metal stent, 2257 patients who received a paclitaxel-eluting stent had lower rates of ischaemia-driven target lesion revascularisation (9·4% *vs* 15·1%, −5·7% [−8·6 to −2·7], 0·60 [0·48–0·76]; p<0·0001) after 3 years, with no significant differences in the rates of death, reinfarction, stroke or stent thrombosis. Stent thrombosis was high (≥4·5%) in both groups.

Interpretation The effectiveness and safety of bivalirudin monotherapy and paclitaxel-eluting stenting are sustained at 3 years for patients with STEMI undergoing primary percutaneous coronary intervention.

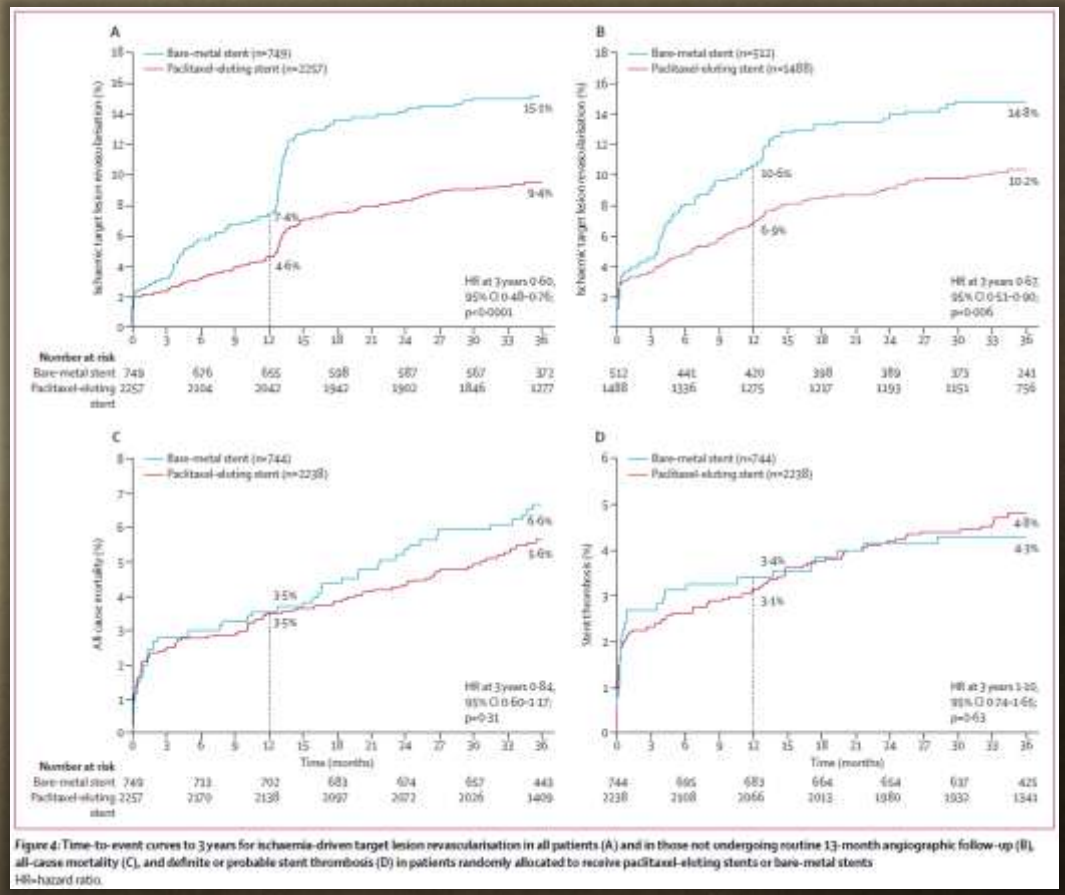


Figure 4: Time-to-event curves to 3 years for ischaemia-driven target lesion revascularisation in all patients (A) and in those not undergoing routine 13-month angiographic follow-up (B), all-cause mortality (C), and definite or probable stent thrombosis (D) in patients randomly allocated to receive paclitaxel-eluting stents or bare-metal stents
HR=hazard ratio.

Stone GW et al; HORIZONSAMI Trial Investigators. Lancet 2011;377:2193–204

Thrombectomy

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CLINICAL RESEARCH — Interventional Cardiology

Thrombus Aspiration During Primary Percutaneous Coronary Intervention Improves Myocardial Reperfusion and Reduces Infarct Size

The EXPIRA (Thrombectomy With Export Catheter in Infarct-Related Artery During Primary Percutaneous Coronary Intervention) Prospective, Randomized Trial

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Objectives The purpose of this study was to evaluate the impact on myocardial perfusion and infarct size as assessed by contrast-enhanced magnetic resonance imaging (CE-MRI) of a manual thrombectomy device, Export Medtronic (EM) (Medtronic Inc., Minneapolis, Minnesota), as adjunctive therapy in primary percutaneous coronary intervention (PPCI) in a subset of patients with anterior ST-segment elevation myocardial infarction (STEMI).

Background PPCI may cause thrombus dislodgment, leading to microvascular damage.

Methods One hundred seventy-five STEMI patients were randomly assigned to standard percutaneous coronary intervention (PCI) (n = 87) or EM-PCI (n = 88). The primary end points were the occurrence of myocardial blush grade ≥2 and the rate of 90-min ST-segment resolution >70%. The CE-MRI substudy was performed in 75 patients with anterior STEMI to assess microvascular obstruction and infarct size.

Results Myocardial blush grade ≥2 and ST-segment resolution occurred more frequently in the EM-PCI group (88% vs. 60%, p = 0.001; and 64% vs. 39%, p = 0.001). In the acute phase, microvascular obstruction extent was significantly lower in the EM-PCI group and at 3 months, infarct size was significantly reduced only in the EM-PCI group. A lower incidence of cardiac death in the EM-PCI group (4.6% vs. 0%, log-rank test p = 0.02) was observed at 9 months.

Conclusions Thrombectomy prevents thrombus embolization and preserves microvascular integrity reducing infarct size, and it therefore represents an useful adjunctive therapy in PPCI. (J Am Coll Cardiol 2009;53:309–15)

Thrombus aspiration in ST elevation myocardial infarction: comparative efficacy in patients treated early and late after onset of symptoms

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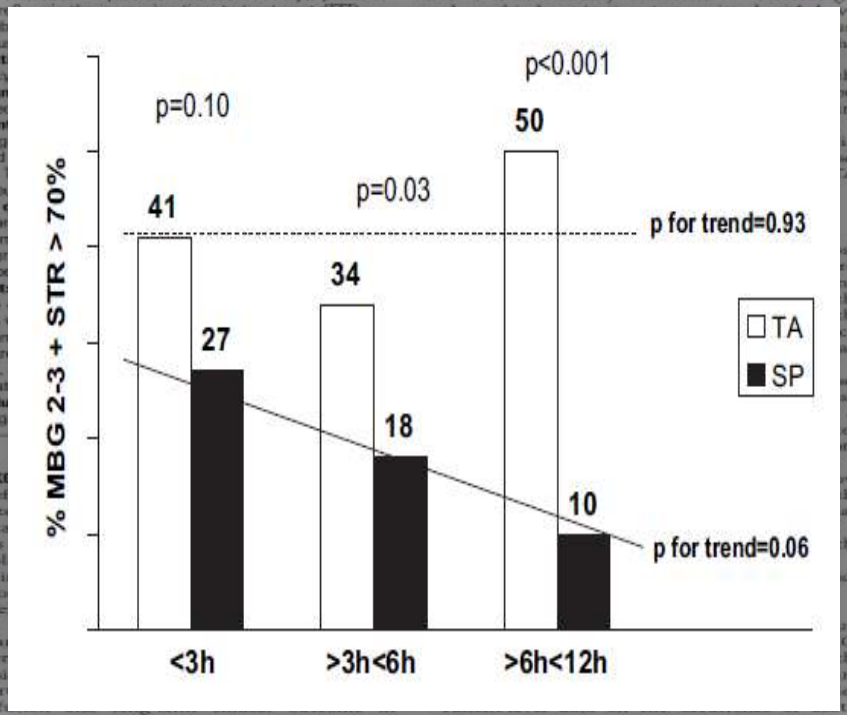
ABSTRACT

Background Restoration of myocardial perfusion is the goal of percutaneous coronary intervention (PCI) in patients with ST elevation myocardial infarction. A major predictor of no-

microvascular injury is strongly dependent on the duration of ischaemia, with reduced salvage of myocardium when reperfusion is accomplished after 3 h of coronary occlusion.[8–10] Accordingly,

patients with ST elevation myocardial infarction (STEMI) undergoing mechanical reperfusion is time to treatment (TTT). Indeed, experimental studies have shown that the extent of myocardial and

new myocardial infarction and target vessel revascularisation (early major adverse coronary events (MACE)) during hospitalisation were also obtained from the original studies.



De Vita M et al. Heart 2010;96:1287–90

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ORIGINAL ARTICLE

Coronary-Artery Bypass Surgery in Patients with Left Ventricular Dysfunction

ABSTRACT

BACKGROUND

The role of coronary-artery bypass grafting (CABG) in the treatment of patients with coronary [illegible] established.

METHODS

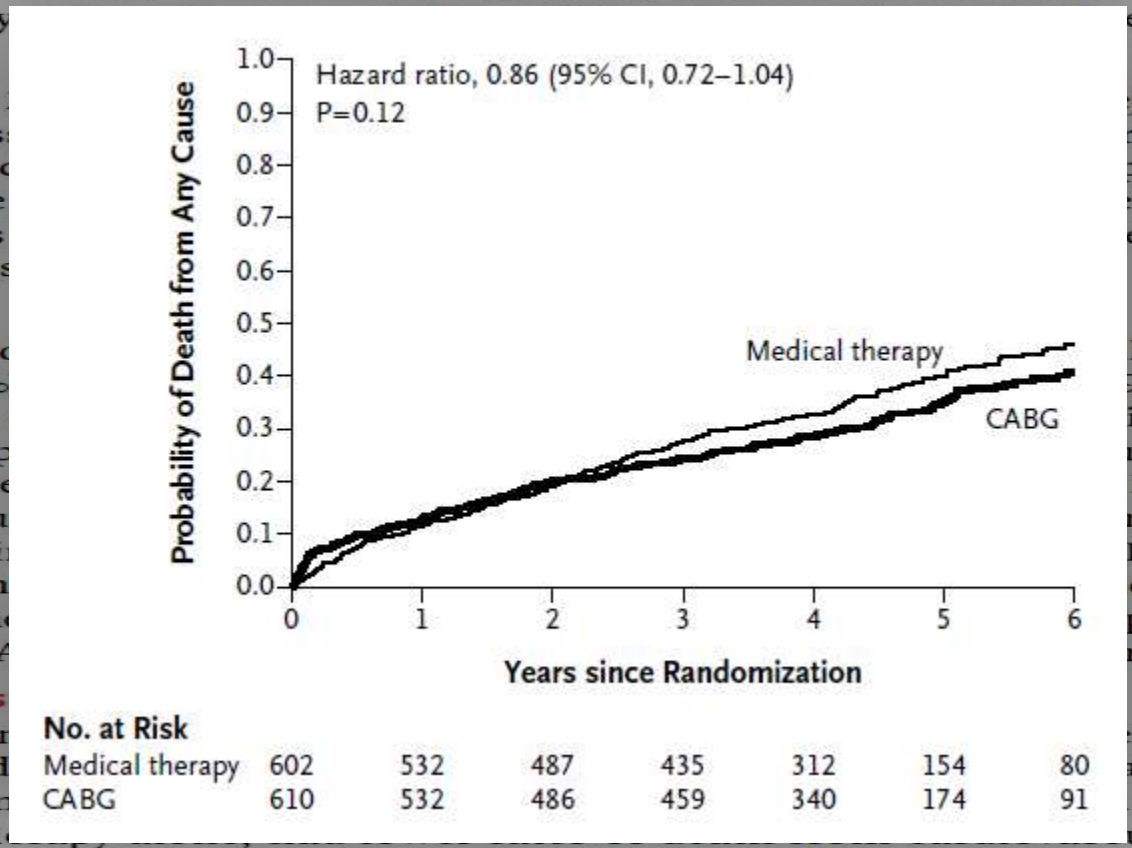
Between July [illegible] jection fraction of 35% or les[illegible] re randomly assigned to med[illegible] plus CABG (610 patients). The[illegible] . Major secondary outcomes [illegible] es and of death from any caus[illegible]

RESULTS

The primary [illegible] l-therapy group and 218 (36%[illegible] 95% confidence interval [CI], [illegible] in the medical-therapy group[illegible] dicated cardiovascular cause[illegible] P=0.05). Death from any cau[illegible] rred in 411 patients (68%) i[illegible] BG group (hazard ratio with[illegible] d of the follow-up period (m[illegible] py group (17%) underwent CA[illegible] rwent CABG.

CONCLUSIONS

In this randor[illegible] n medical therapy alone and[illegible] ary end point of death from an[illegible] those assigned to medical th[illegible] ular causes and of death from any cause or hospitalization for cardiovascular causes. (Funded by the National Heart, Lung, and Blood Institute and Abbott Laboratories; STICH ClinicalTrials.gov number, NCT00023595.)



Velazquez EJ, Lee KL, Deja MA, et al; STICH Investigators. Coronary-artery bypass surgery in patients with left ventricular dysfunction. N Engl J Med 2011;364:1607–16

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Safety of Percutaneous Left Atrial Appendage Closure : Results From the Watchman Left Atrial Appendage System for Embolic Protection in Patients With AF (PROTECT AF) Clinical Trial and the Continued Access Registry

Vivek Y. Reddy, David Holmes, Shephal K. Doshi, Petr Neuzil and Saibal Kar

Table 2. Safety Event Rates in PROTECT AF and CAP

		PROTECT AF		PROTECT AF					
	PROTECT AF	Early	Late	First 3 Patients	Other Patients	CAP	*P**	*P*†	*P*‡
Procedure time, mean±SD, min	62±34	67±36	58±33	82±40	55±29	50±21	<0.001	<0.001	<0.001
Implant success, n/total (%)	485/542 (89.5)	239/271 (88.2)	246/271 (90.8)	133/154 (86.4)	352/388 (90.7)	437/460 (95.0)	0.001	0.001	0.136
Procedure/device-related safety adverse event within 7 d, n/total (%)	42/542 (7.7)	27/271 (10.0)	15/271 (5.5)	19/154 (12.3)	23/388 (5.9)	17/460 (3.7)	0.007	0.006	0.012
Serious pericardial effusion within 7 d, n/total (%)	27/542 (5.0)	17/271 (6.3)	10/271 (3.7)	10/154 (6.5)	17/388 (4.4)	10/460 (2.2)	0.019	0.018	0.308
Procedure-related stroke, n/total (%)	5/542 (0.9)	3/271 (1.1)	2/271 (0.7)	1/154 (0.7)	4/388 (1.0)	0/460 (0)	0.039	0.039	0.675

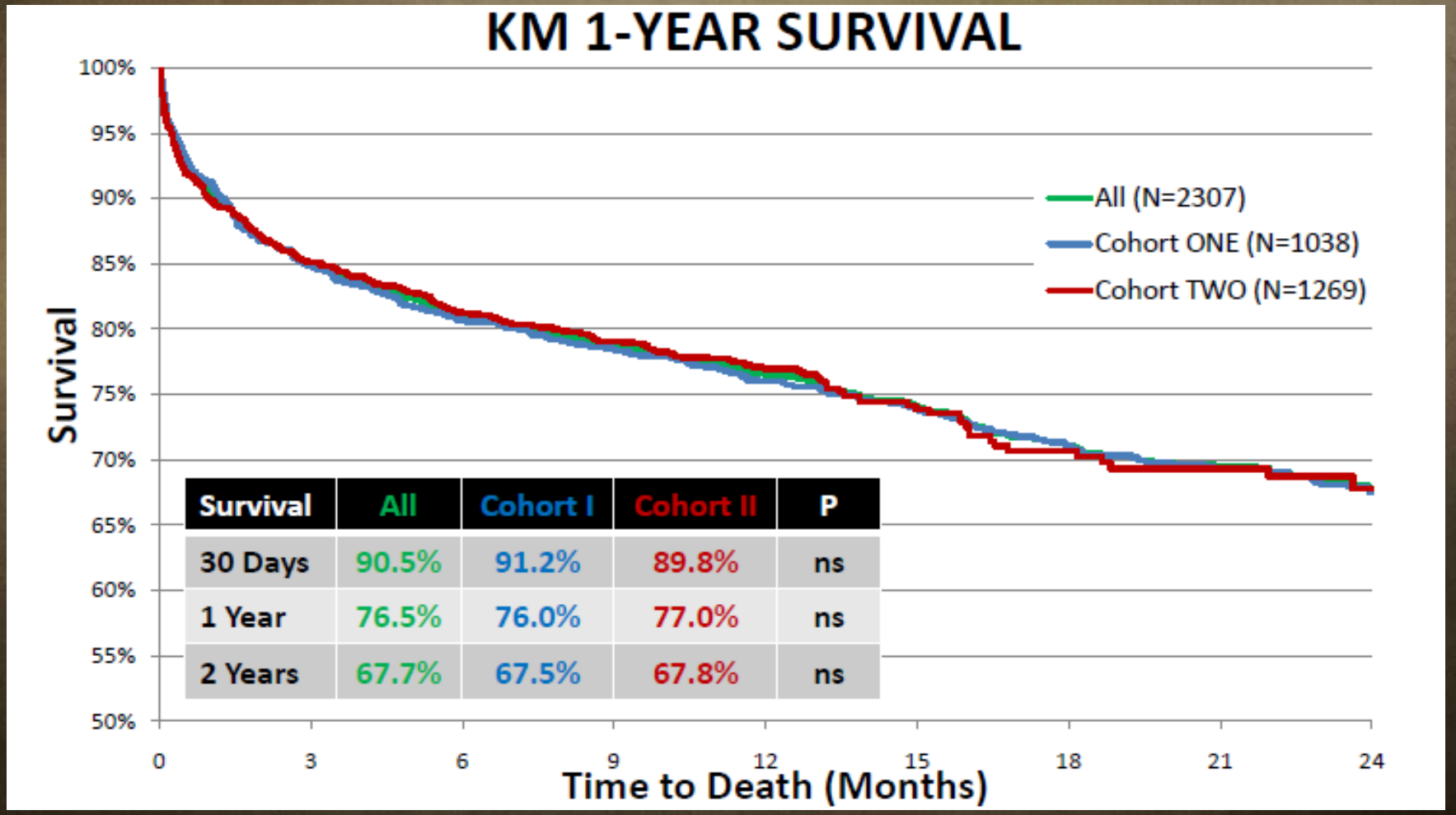
P values are from χ^2 tests or ANOVA tests as appropriate.

*From tests comparing the PROTECT AF cohort with the CAP cohort.

†From tests for differences across 3 groups (early PROTECT AF, late PROTECT AF, and CAP). By definition, early and late refer to the first half and second half of the entire cohort of patients enrolled in PROTECT AF.

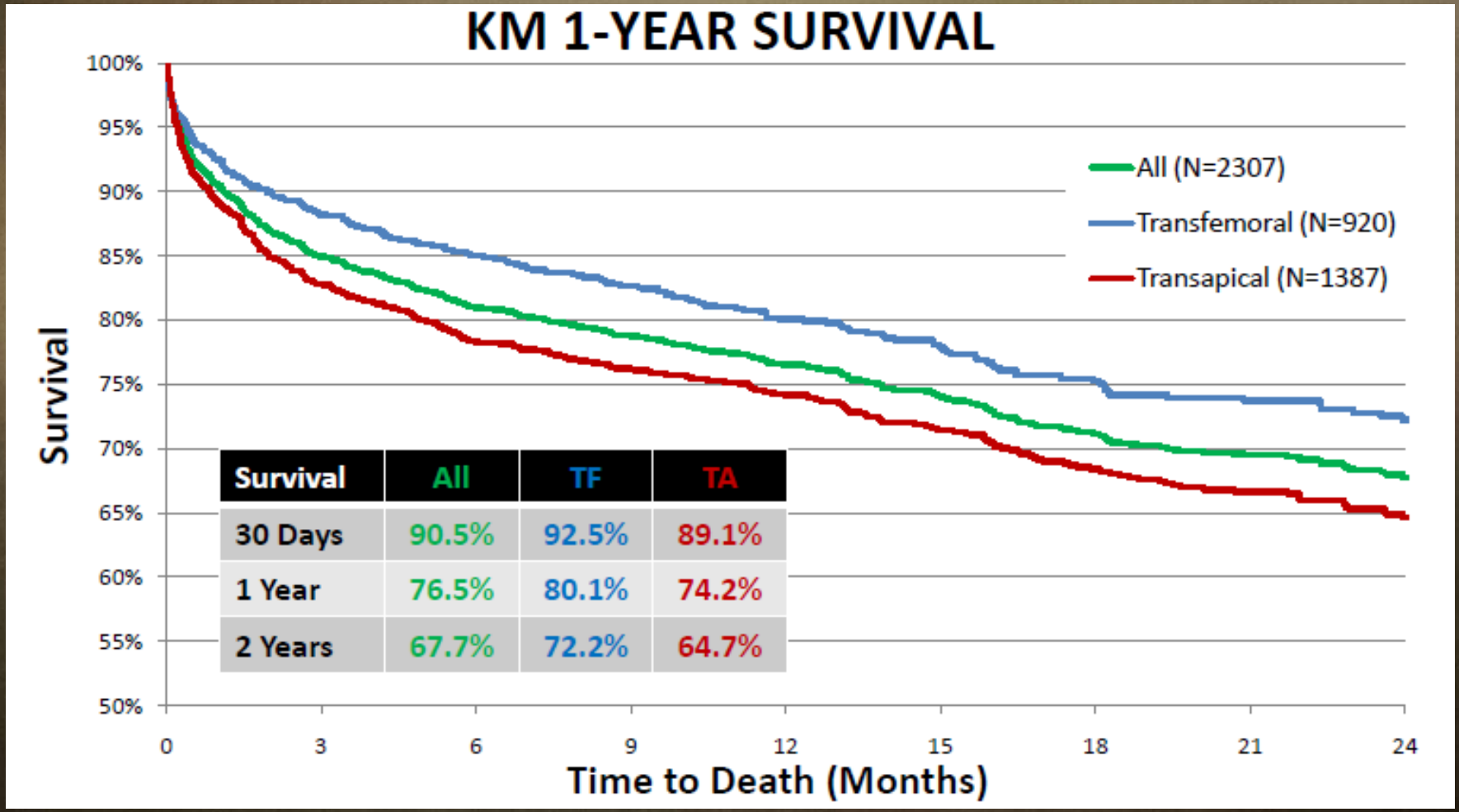
‡From tests for differences between the first 3 patients implanted at any given institution in PROTECT AF compared with all subsequent patients implanted at that institution.

1-Year Results from combined Cohort I and Cohort II of The SOURCE Registry for more than 2300 patients



Survival	All	Cohort I	Cohort II	P
30 Days	90.5%	91.2%	89.8%	ns
1 Year	76.5%	76.0%	77.0%	ns
2 Years	67.7%	67.5%	67.8%	ns

1-Year Results from combined Cohort I and Cohort II of The SOURCE Registry for more than 2300 patients



Survival	All	TF	TA
30 Days	90.5%	92.5%	89.1%
1 Year	76.5%	80.1%	74.2%
2 Years	67.7%	72.2%	64.7%

PREDICTORS FOR 1 YEAR MORTALITY

(Multivariable analysis)

TRANSFEMORAL

INCREASED MORTALITY	p	Hazard Ratio
Smoking	0.0001	1.94
Renal insufficiency / Failure	0.0003	1.77
Scaled LogEURO Score (/10)	0.004	1.15
Carotid endarterectomy / Carotid stent	0.01	2.81

DECREASED MORTALITY	p	Hazard Ratio
Carotid artery stenosis (over 50%)	0.006	0.29
Hyperlipidemia / Hypercholesterolemia	0.006	0.65

TRANSAPICAL

INCREASED MORTALITY	p	Hazard Ratio
Scaled LogEURO Score (/10)	<.0001	1.17
Renal insufficiency / Failure	0.0002	1.51
Liver disease	0.009	1.83

DECREASED MORTALITY	p	Hazard Ratio
Female	0.002	0.68
Hyperlipidemia / Hypercholesterolemia	0.003	0.73
Product valve size 26	0.002	0.68