

ADVANCES IN CARDIOVASCULAR ARRHYTHMIAS AND GREAT INNOVATIONS IN CARDIOLOGY

XXIV GIORNATE CARDIOLOGICHE TORINESI

Turin, October 20-22, 2011 – Centro Congressi Unione Industriale

TAVI: transaortic valve implantation in Italy and in Europe

Gian Paolo Ussia

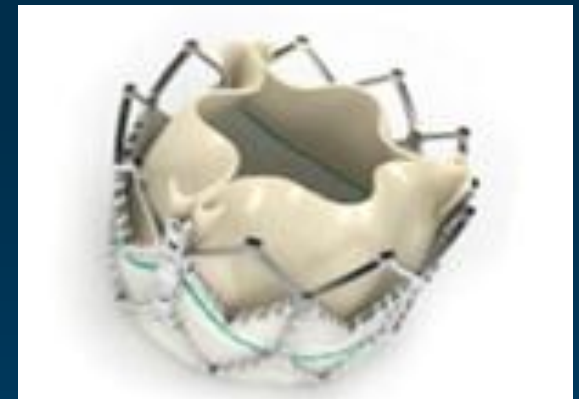
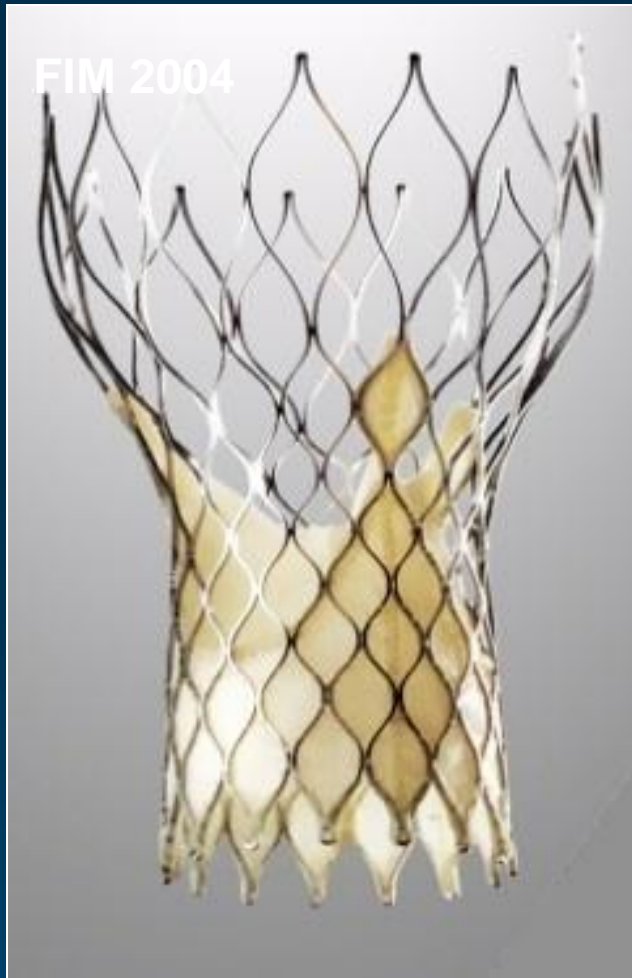
Divisione Clinicizzata di Cardiologia , Osp Ferrarotto, Catania, Italy



Ferrarotto Hospital
University of Catania



Valvole Transcatetere



Edward Sapien XT

CoreValve Revalving System

> 40.000 pazienti



Over 40.000 implants in 40 countries



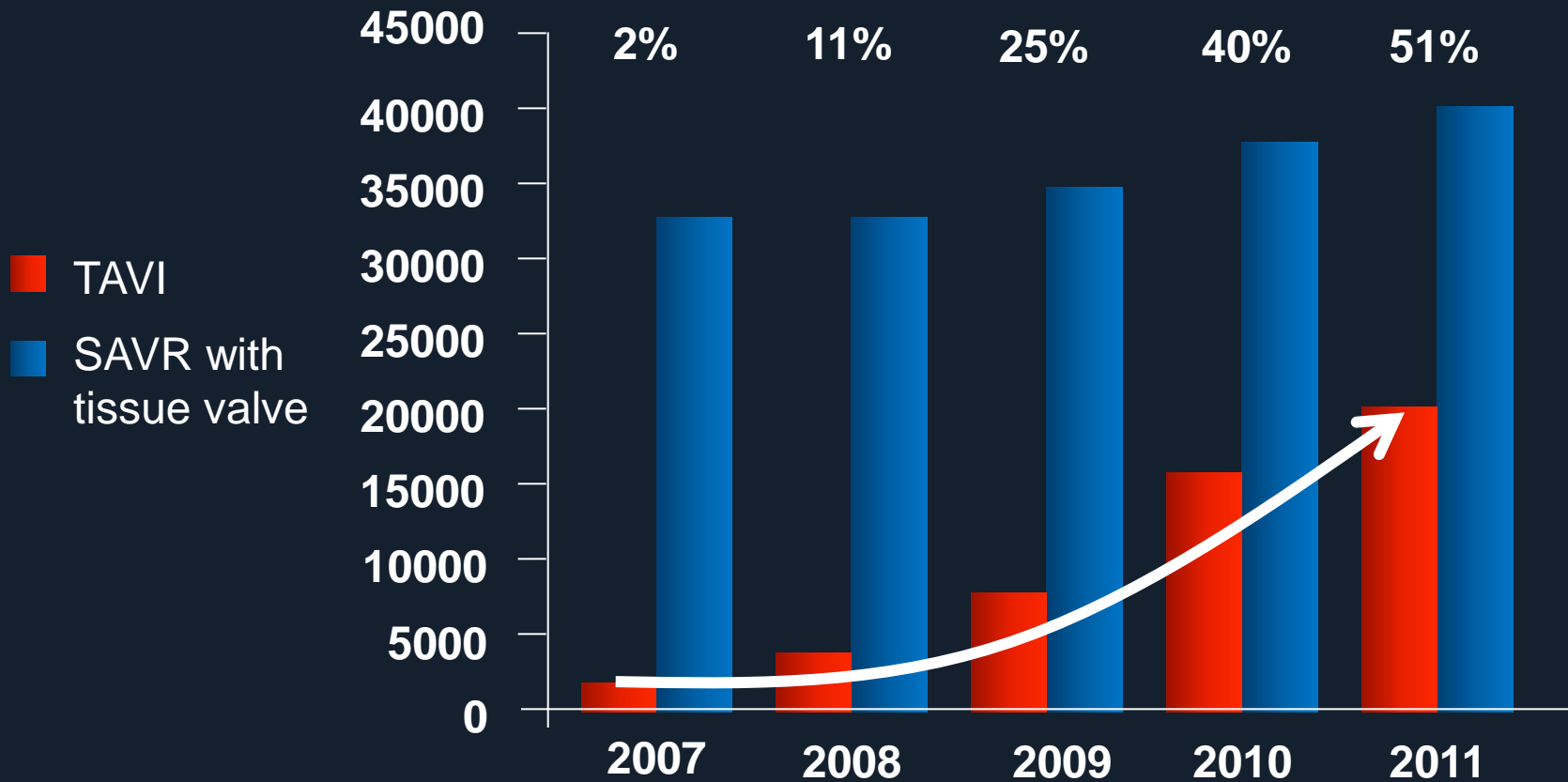
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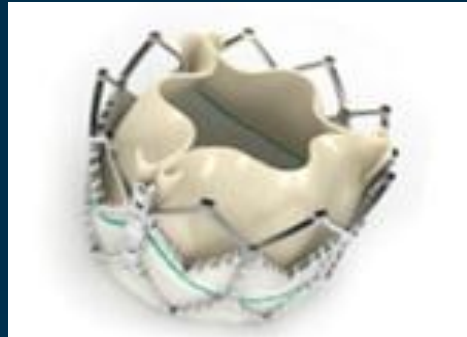
TAVR vs SAVR in EU Centers



- *More than 300 centers have active TAVI programs*
- *Almost 85 centers have > 50 TAVI /year implantation experience*



TAVI in Italia dal giugno 2007



> 4000 pazienti

indication

European Heart Journal Advance Access published May 12, 2008



European Heart Journal
doi:10.1093/eurheartj/ehn183

SPECIAL ARTICLE

Transcatheter valve implantation for patients with aortic stenosis: a position statement from the European Association of Cardio-Thoracic Surgery (EACTS) and the European Society of Cardiology (ESC), in collaboration with the European Association of Percutaneous Cardiovascular Interventions (EAPCI)

Alec Vahanian
Jeroen Bax
Gerard Forstner
Francesco Frascerra
José Luis Herrero
Ben van Helle

Essentially, indication for TAVI is:

- Symptomatic severe aortic stenosis and
- HIGH-RISK and/or CONTRAINDICATION for surgical aortic valve replacement

EACTS/ESC/EAPCI Position statement Eur Heart J 2008



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Which Patient?

Clinical Indication is the critical point

- **Heart-Valve Team decision**
- **High risk for cardiac surgery**
- **But how to assess this risk?**
 - **STS score/ Log EuroScore**
 - **Frailty index**
 - **Comorbidities: liver cirrhosis, porcelain aorta, cachexia, hostile thorax, pulmonary insufficiency ($FEV1 < 1$ liter), pulmonary hypertension ($PAPS > 60$ mmHg)**


Patient-related factors			Cardiac-related factors		
Age (years)	83	0	Unstable angina ⁶	No	0
Gender	Female	.3304052	LV function	Moderate	.4191643
Chronic pulmonary disease ¹	Yes	.4931341	Recent MI ⁷	No	0
Extracardiac arteriopathy ²	No	0	Pulmonary hypertension ⁸	No	0
Neurological dysfunction ³	No	0	Operation-related factors		
Previous Cardiac Surgery	No	0	Emergency ⁹	No	0
Creatinine > 200 µmol/ L	Yes	.6521653	Other than isolated CABG	Yes	.5420364
Active endocarditis ⁴	No	0	Surgery on thoracic aorta	No	0
Critical preoperative state ⁵	No	0	Post infarct septal rupture	No	0

Logistic **EuroSCORE** 33.47 %

Note: Logistic is now default calculator

Calculate Clear

> 20%


Online STS Risk Calculator
Dataset: 2.61
Definitions Support

Help [More about Risk Calculator](#) New Print

Today's Date 10/13/2009

Procedure

Coronary Artery Bypass ☐ Yes ☒ No ☐ Missing
Ventricular Assist Device ☐ Yes ☒ No ☐ Missing
Valve Surgery ☒ Yes ☐ No ☐ Missing
Aortic ☐ No ☒ Replacement ☐ Repair/Reconstruction ☐ Root Reconstruction with Valve Conduit ☐ Replacement + aortic graft conduit (not a valve conduit) ☐ Root Reconstruction with Valve Sparing

Calculations

Procedure Name	Isolated AVR/rep
Risk of Mortality	21.8%
Morbidity or Mortality	70.2%
Long Length of Stay	46.0%
Short Length of Stay	3.7%
Permanent Stroke	6.5%
Prolonged Ventilation	56.2%
DSW Infection	0.2%
Renal Failure	51.4%
Reoperation	20.2%

> 10%



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Clinical Results

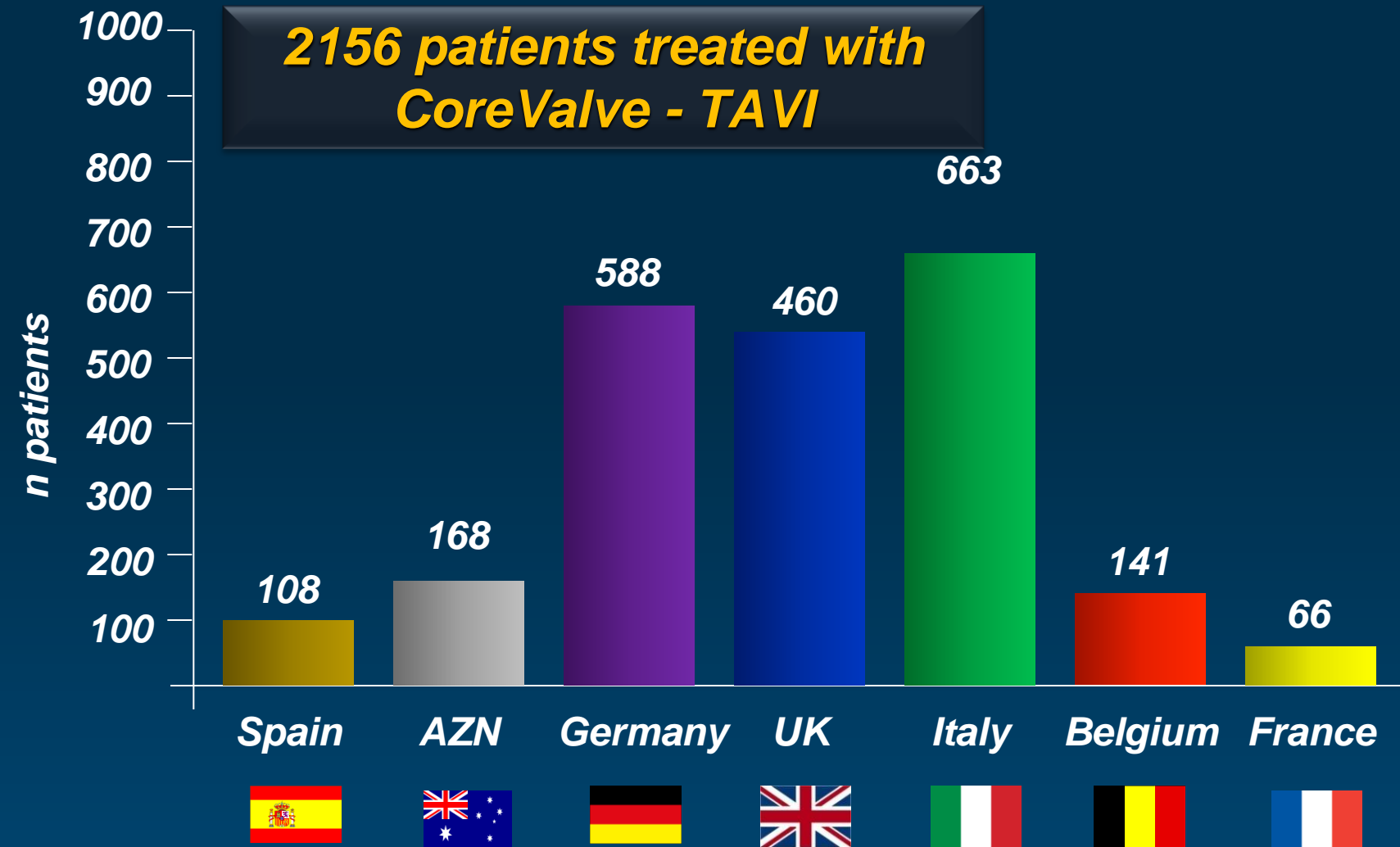
Specific issues

- **Procedural complications**
- **Predictors of mortality**
- **Short and long-term survival**
- **Quality of Life**

CRS Registries Results

Patient Enrollment

**2156 patients treated with
CoreValve - TAVI**



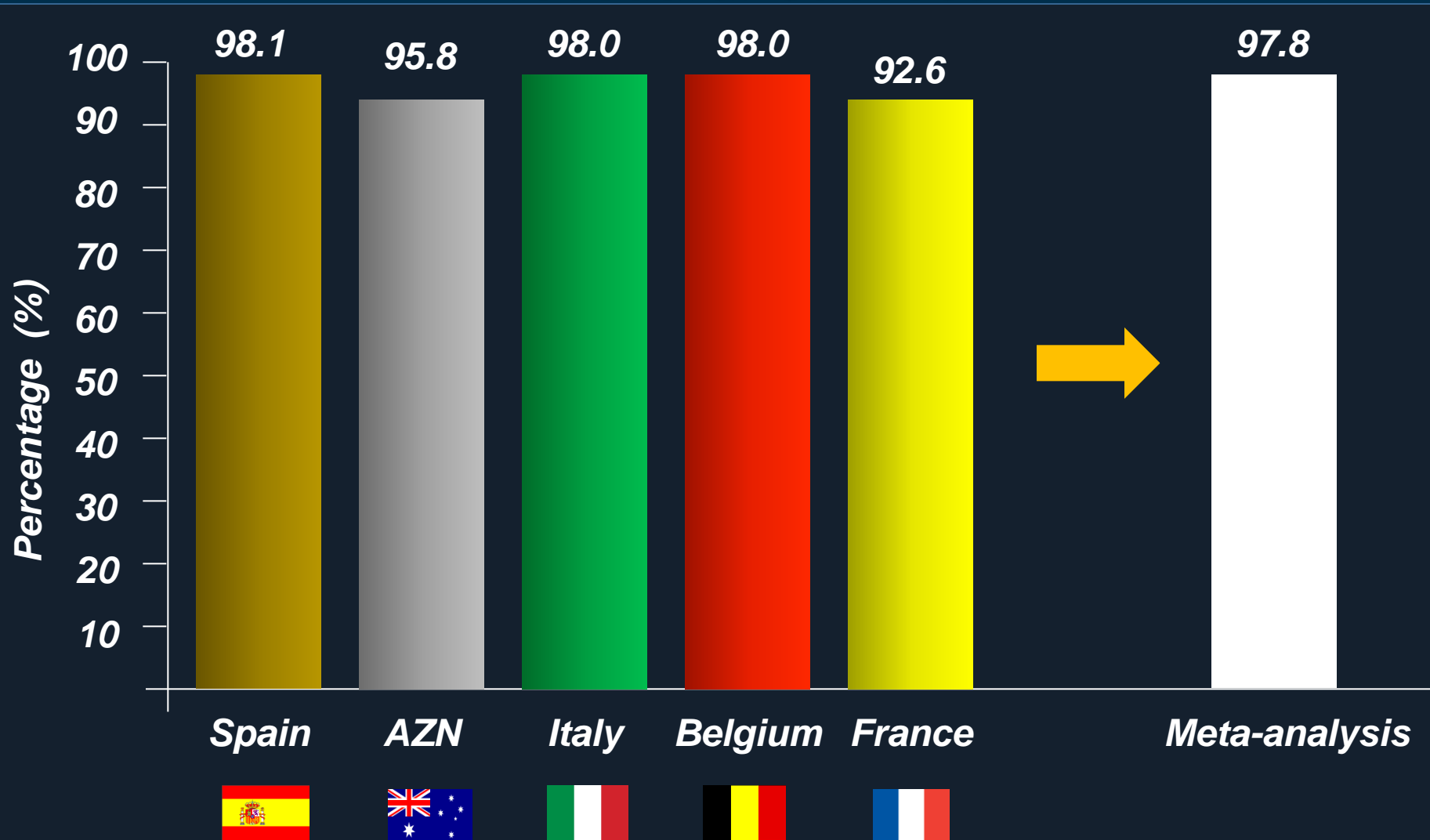
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C. Ruiz, EuroPCR 2011



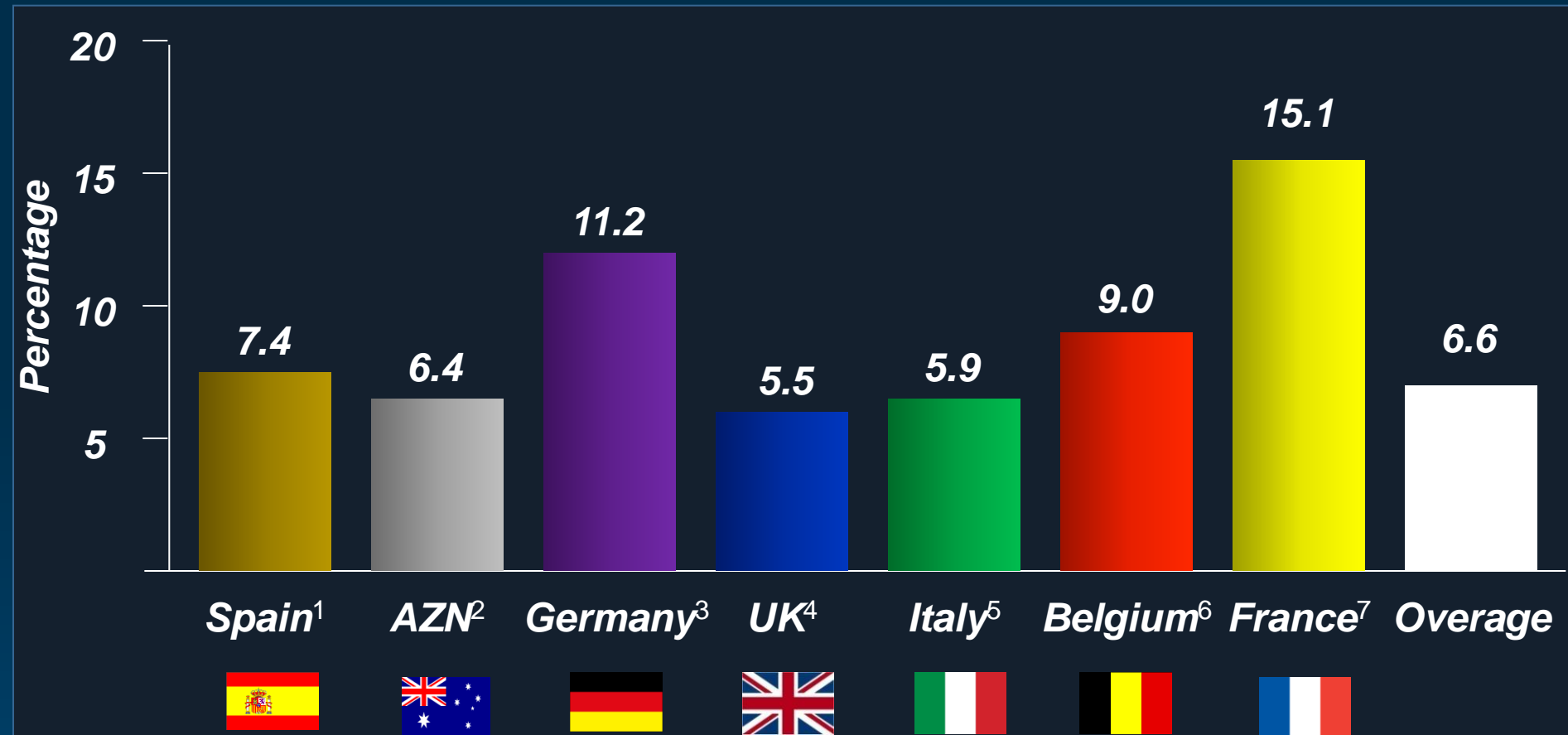
CRS Registries Results

Procedural Success



CRS Registries Results

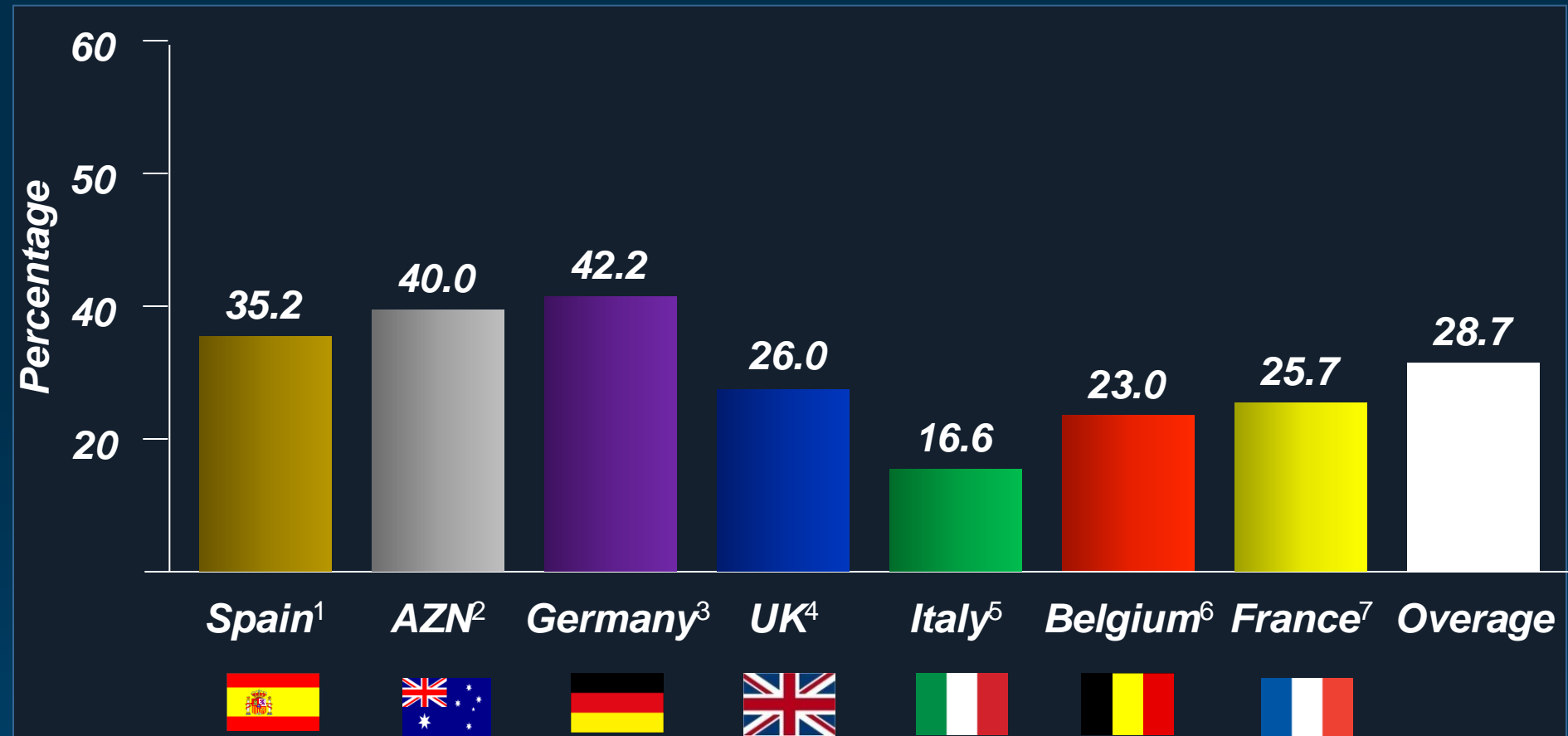
30-day mortality



¹Avanzas Rev Esp Cardiol 2010; ²Meredith TCT2010; ³Zahn EuroPCR 2010 ⁴Moat EuroPCR 2010; ⁵Tamburino Circulation 2011; ⁶Bosmans EuroPCR 2010; ⁷Eltchaninoff Eur Heart J 2010.

CRS Registries Results

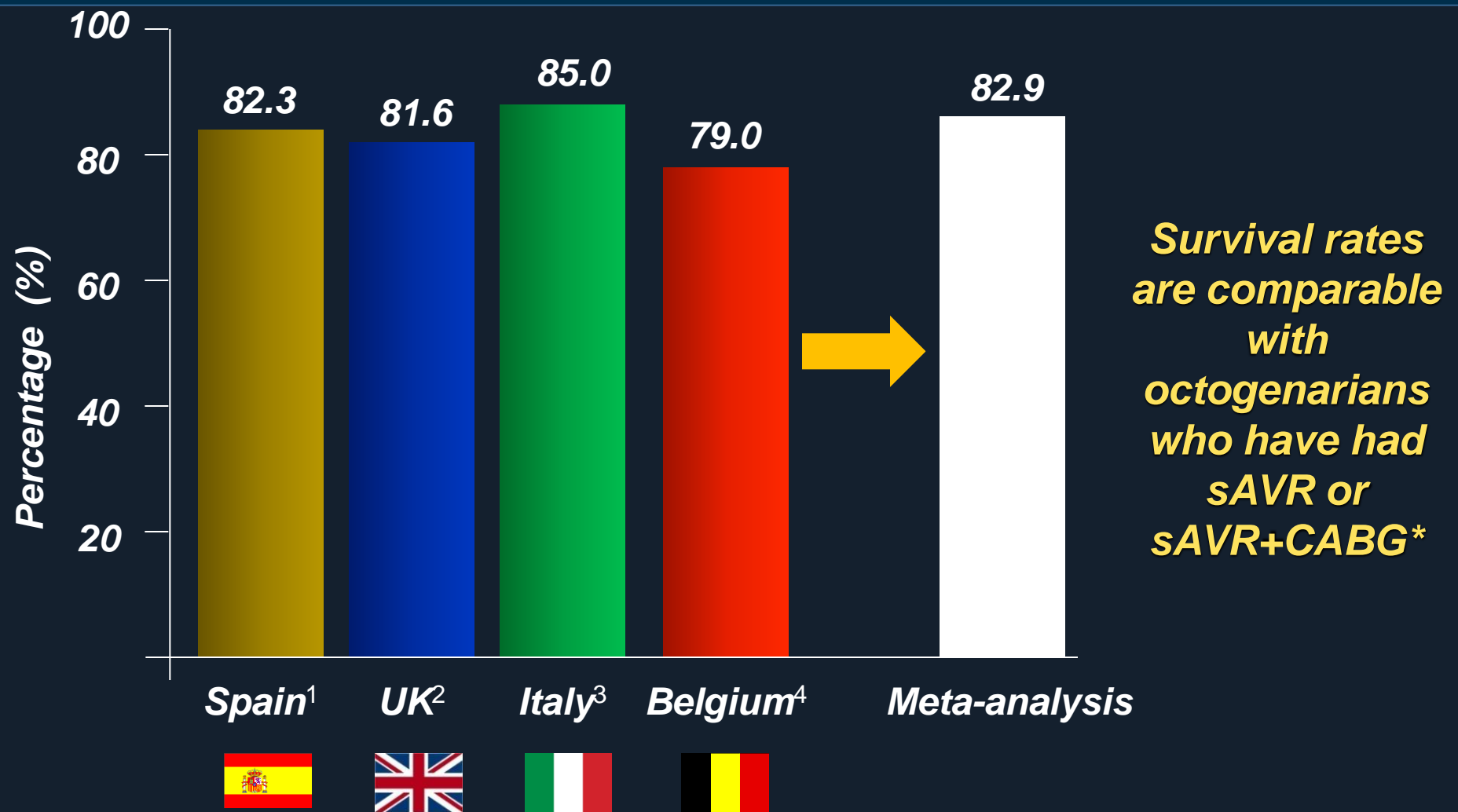
PM implantation



¹Avanzas Rev Esp Cardiol 2010; ²Meredith TCT2010; ³Zahn EuroPCR 2010 ⁴Moat EuroPCR 2010; ⁵Tamburino Circulation 2011; ⁶Bosmans EuroPCR 2010; ⁷Eltchaninoff Eur Heart J 2010.

CRS Registries Results

1-year Survival



¹Avanzas Rev Esp Cardiol 2010; ²Moat EuroPCR

2010; ³Tamburino Circulation 2011; ⁴Bosmans

Italian CoreValve *Registry*

First patient

Catania, University

Bari University

Valvular Heart Disease

Incidence and Predictors of Early and Late Mortality After Transcatheter Aortic Valve Implantation in 663 Patients With Severe Aortic Stenosis

Corrado Tamburino, MD, PhD; Davide Capodanno, MD; Angelo Ramondo, MD;
Anna Sonia Petronio, MD; Federica Etori, MD; Gennaro Santoro, MD; Silvio Klugmann, MD;
Francesco Bedogni, MD; Francesco Maisano, MD; Antonio Marzocchi, MD; Arnaldo Poli, MD;
David Antonucci, MD; Massimo Napodano, MD; Marco De Carlo, MD, PhD;
Claudia Fiorina, MD; Gian Paolo Ussia, MD

- Since June 2007 a web-based registry was started
- 14 participating sites

Firenze, Careggi

Bari, University

Mirano



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Italian CoreValve Registry

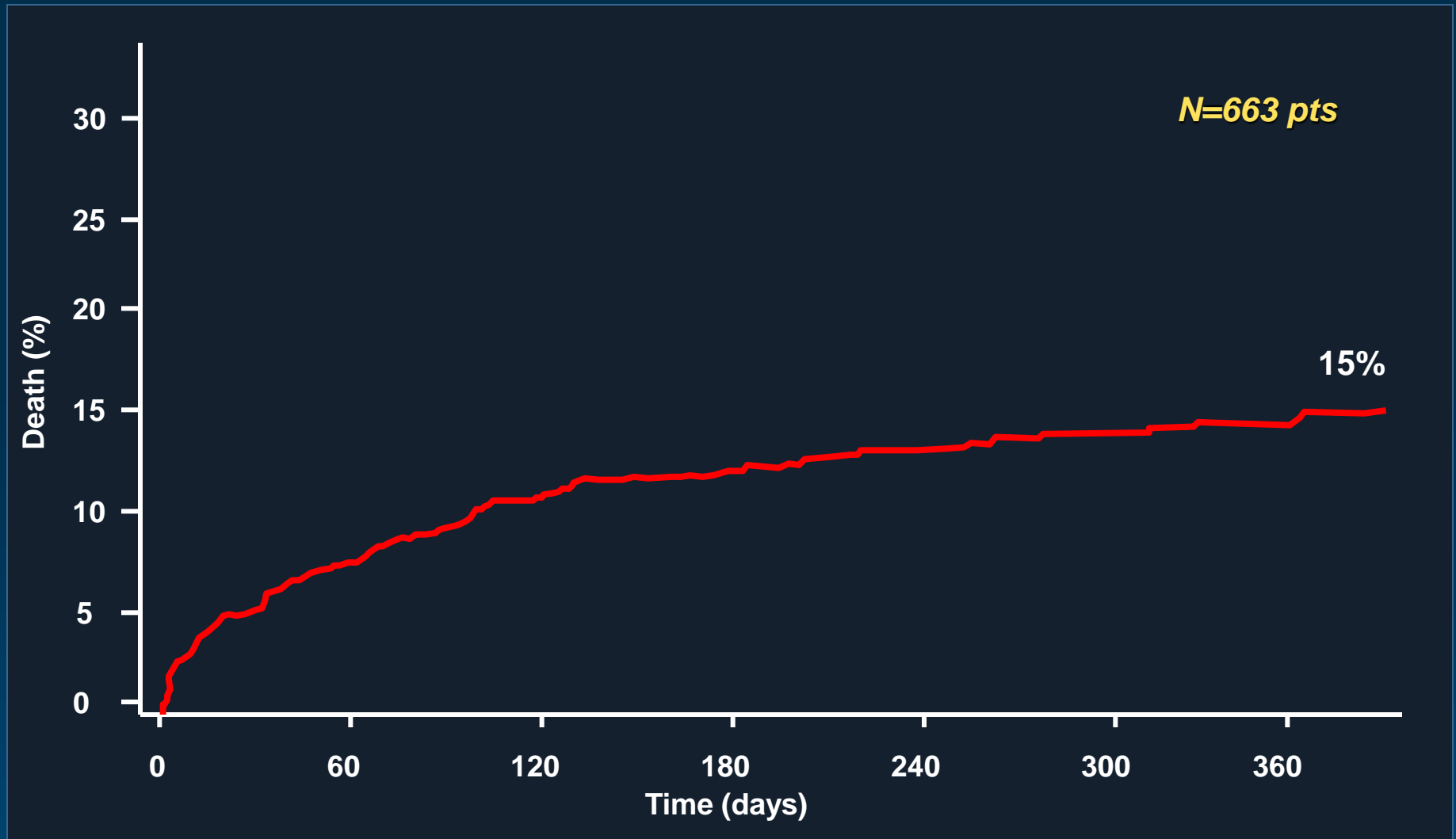
Procedural Outcomes 663 pts

	Overall population (n = 663)	Pts who died (n = 114)	Pts who Survived (n = 549)	p value
Death, n (%)	6 (0.9)	-	-	-
Myocardial infarction, n (%)	0 (0)	0 (0)	0 (0)	1.00
Stroke, n (%)	8 (1.2)	4 (3.5)	4 (0.7)	0.03*
Post-procedural paravalvular leak $\geq 2+$	139 (21.0)	33 (28.9)	106 (19.3)	0.11
Valve embolization, n (%)	4 (0.6)	1 (0.9)	3 (0.5)	0.53
Valve-in-valve implantation, n (%)	24 (3.6)	3 (2.6)	21 (3.8)	0.78
Conversion to open heart surgery, n (%)	5 (0.8)	4 (3.5)	1 (0.2)	0.004*
Major access site complications, n (%)	13 (2.0)	3 (2.6)	10 (1.8)	0.48
Life-threatening arrhythmias, n (%)	13 (2.0)	6 (5.3)	7 (1.3)	0.01*
Cardiac tamponade, n (%)	8 (1.2)	4 (3.5)	4 (0.7)	0.03*
Need for permanent pacemaker, n (%)	110 (16.6)	17 (14.9)	93 (16.9)	0.60



Italian CoreValve Registry

1-year Overall Mortality



Italian CoreValve Registry

One-year clinical results

Endpoint	Cumulative incidence
----------	----------------------

MACCE	16.6%
-------	-------

Death	15.0%
-------	-------

Myocardial infarction	1.2%
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Stroke	2.5%
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CHF requiring hospitalization	8.2%
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Major bleeding	3.2%
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Pacemaker implantation	19.1%
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Prosthesis dysfunction	0.2%
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Italian CoreValve Registry

Multivariate analysis

Overall mortality	Hazard ratio	95% LCL	95% UCL	p value
Intraprocedural stroke	15.76	3.27	75.90	0.001
Pre-procedural mitral regurgitation 3+ or 4+	4.62	1.66	12.87	0.003
Systolic pulmonary artery pressure > 60 mmHg	3.21	1.19	8.71	0.02
Prior acute pulmonary edema	2.75	1.32	5.72	0.007
Diabetes mellitus	2.45	1.19	5.07	0.02

Early mortality	Odds ratio	95% LCL	95% UCL	p value
Conversion to open heart surgery	38.68	2.86	522.59	0.006
Cardiac tamponade	10.97	1.59	75.61	0.02
Major access site complications	8.47	1.67	42.82	0.01
Left ventricular ejection fraction < 40%	3.51	1.62	7.62	0.002
Prior balloon aortic valvuloplasty	2.87	1.24	6.65	0.01
Diabetes mellitus	2.66	1.26	5.65	0.01

Late mortality	Hazard ratio	95% LCL	95% UCL	p value
Prior stroke	5.468	1.47	20.39	0.01
Post-procedural paravalvular leak $\geq 2+$	3.785	1.57	9.10	0.003
Prior acute pulmonary edema	2.696	1.09	6.68	0.03
Chronic kidney disease	2.532	1.01	6.35	0.048



TAVI Experience up to 2011

Valvular Heart Disease

Thirty-Day Results of the SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry

A European Registry of Transcatheter Aortic Valve Implantation Using the Edwards SAPIEN Valve

Martyn Thomas, MD; Gerhard Schymik, MD; Thomas Walther, MD; Dominique Himbert, MD;
Thierry Lefèvre, MD; Hendrik Treede, MD; Holger Eggebrecht, MD; Paolo Rubino, MD;
Iassen Michev, MD; Rüdiger Lange, MD; William N. Anderson, PhD; Olaf Wendler, MD

Background—Transcatheter aortic valve implantation was developed to mitigate the mortality and morbidity associated with high-risk traditional aortic valve replacement. The Edwards SAPIEN valve was approved for transcatheter aortic valve implantation transfemoral delivery in the European Union in November 2007 and for transapical delivery in January 2008.

Methods and Results—The SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry was designed to assess the initial clinical results of the Edwards SAPIEN valve in consecutive patients in Europe after commercialization. Cohort 1 consists of 1038 patients enrolled at 32 centers. Patients who were treated with the transapical approach (n=575) suffered more comorbidities than the transfemoral patients (n=463), resulting in a significantly higher logistic EuroSCORE (29.1% versus 25.7%; $P<0.001$). Therefore, these groups are considered different, and outcomes cannot be compared. Overall short-term procedural success was observed in 93.8%. The incidence of valve embolization was 0.3% (n=3), and coronary obstruction was reported for 0.6% (n=6 cases). Incidence of stroke was 2.5% and similar for both procedural approaches. Thirty-day mortality was 6.3% in transfemoral patients and 10.3% in transapical patients. The occurrence of vascular complications was not a predictor of <30-day mortality in the transfemoral population.

Conclusion—Technical proficiency can be learned and adapted readily as demonstrated by the short-term procedural success rate and low 30-day mortality rates reported in the SOURCE Registry. Specific complication management and refinement of patient selection are needed to further improve outcomes. (*Circulation*. 2010;122:62-69.)



SOURCE Registry

Procedure Complications <30 day

	TF (n=463)	TA (n=575)	Total (n=1038)
Acute procedure success	436/95.6% n=456	523/92.9% n=563	959/94.1% n=1019
Device Success*	428/92.4%	522/90.8%	950/91.5%
Conversion to sAVR	8/1.7%	20/3.5%	28/2.7%
AR >+2	15 (3.2%)	34 (5.9%)	49 (4.7%)
Valve Migration	0 (0.0%)	3(0.5%)	3(0.3%)
Valve Malposition	8 (1.7%)	8 (1.4%)	16(1.5%)
Coronary Obstruction	3 (0.7%)	3 (0.5%)	6 (0.6%)

**Device success is a composite including AR <2+ and only 1 valve*



SOURCE Registry

Preliminary data – Major Complications <30 day

	TF (n=463)	TA (n=575)	Total (n=1038)
Death	29 (6.3%)	59 (10.3%)	88 (8.5%)
Stroke	11 (2.4%)	16 (2.6%)	27 (2.5%)
Renal Failure Requiring Dialysis	23 (5.0%)	69 (11.7%)	92 (8.7%)
Permanent Pacemaker	31 (6.7%)	42 (7.3%)	73 (7.0%)



Circulation

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**One-Year Outcomes of Cohort 1 in the Edwards SAPIEN Aortic Bioprosthesis
European Outcome (SOURCE) Registry : The European Registry of
Transcatheter Aortic Valve Implantation Using the Edwards SAPIEN Valve**

Martyn Thomas, Gerhard Schymik, Thomas Walther, Dominique Himbert, Thierry
Lefèvre, Hendrik Treede, Holger Eggebrecht, Paolo Rubino, Antonio Colombo,
Rüdiger Lange, Rebecca R. Schwarz; and Olaf Wendler

Circulation 2011, 124:425-433: originally published online July 11, 2011

doi: 10.1161/CIRCULATIONAHA.110.001545

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SOURCE Registry -1038 pts

Thomas et al SOURCE Registry of Transcatheter AVI

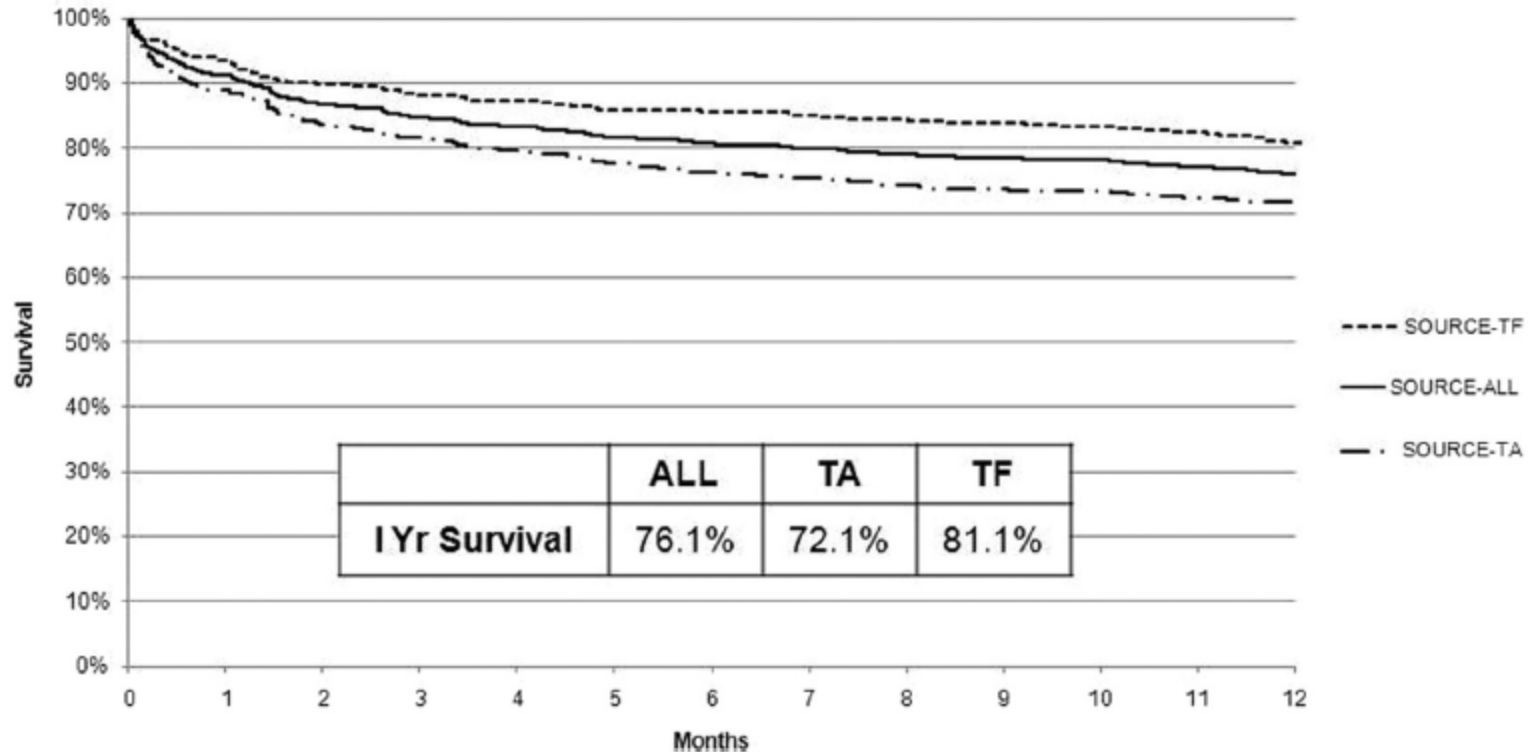
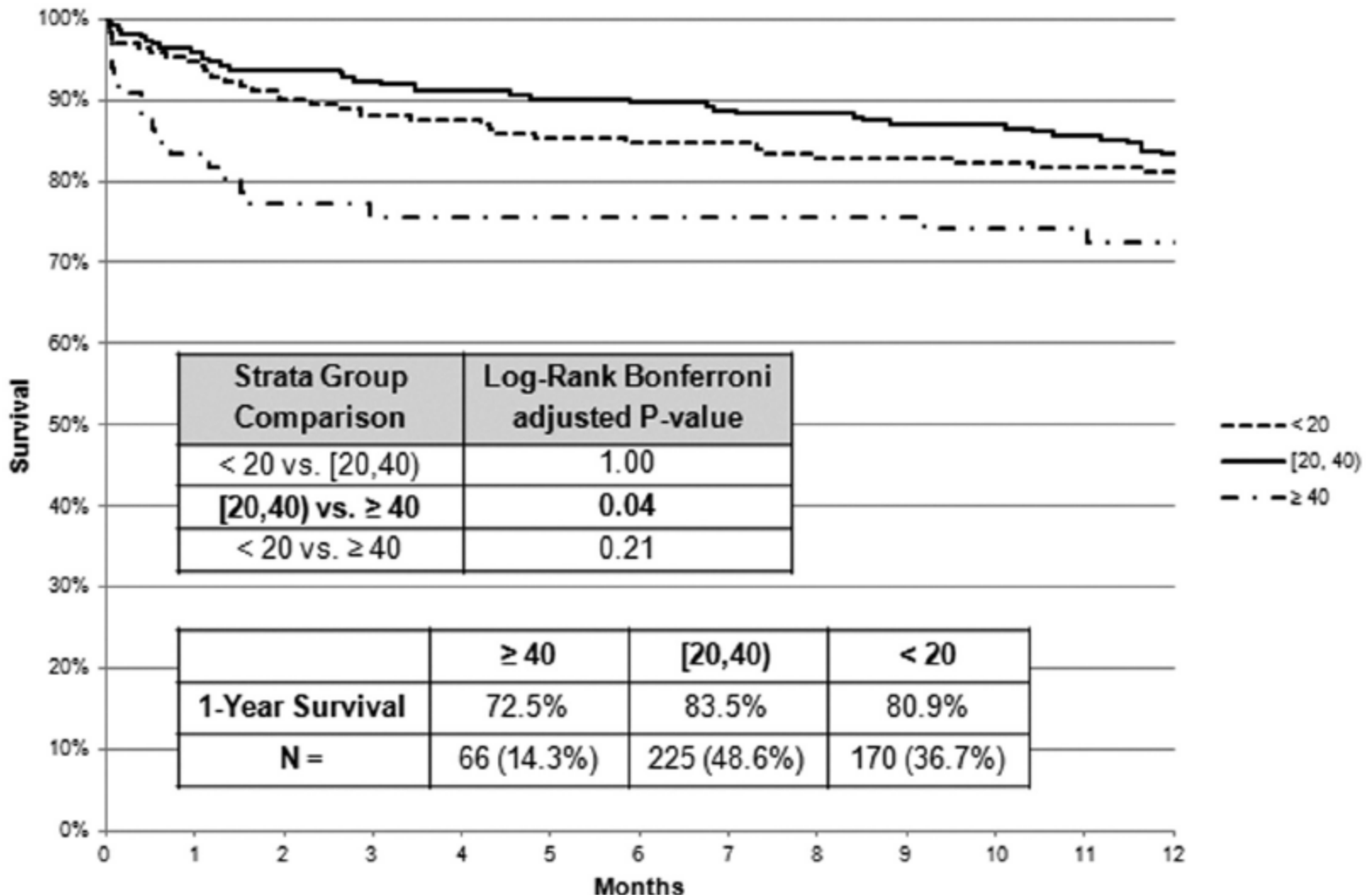


Figure 1. Kaplan-Meier 1-year survival curves. Yr indicates year; TA, transapical; and TF, transfemoral.

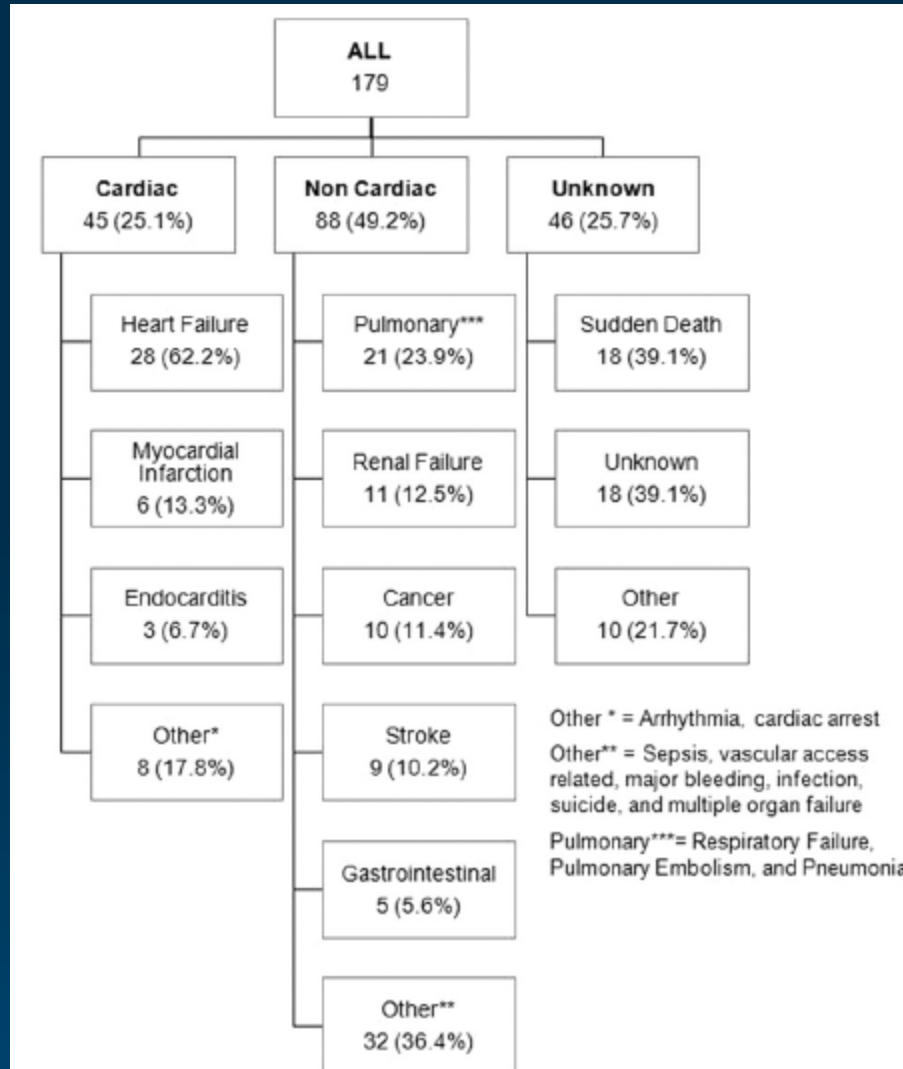
SOURCE Registry

B

All Cause Mortality by EuroSCORE Strata
1 Year Survival - Transfemoral



SOURCE Registry



SOURCE Registry

Table 5. Multivariable Analysis: Variables Associated With Mortality, Transfemoral TAVI

Parameter	<i>P</i>	HR	95% Confidence Limits	
Renal insufficiency/failure	0.001	2.09	1.34	3.26
Hyperlipidemia/hypercholesterolemia	0.03	0.61	0.39	0.95
Systemic hypertension	0.004	0.53	0.35	0.82
Smoking	0.0003	2.42	1.51	3.90
Scaled logistic EuroSCORE (%/10)	0.01	1.19	1.04	1.36
Liver disease	0.04	2.47	1.04	5.85
Carotid artery stenosis (>50%)	0.004	0.07	0.01	0.43
Coagulopathy	0.009	5.09	1.49	17.39

c-index=0.7062.

TAVI indicates transcatheter aortic valve implantation; HR, hazard ratio.

CLINICAL RESEARCH

Intervention in Valve Disease

2-Year Follow-Up of Patients Undergoing Transcatheter Aortic Valve Implantation Using a Self-Expanding Valve Prosthesis

Lutz Buellesfeld, MD,* Ulrich Gerckens, MD,† Gerhard Schuler, MD,‡ Raoul Bonan, MD,§ Jan Kovac, MD,|| Patrick W. Serruys, MD,¶ Marino Labinaz, MD,# Peter den Heijer, MD,** Michael Mullen, MD,†† Wayne Tymchak, MD,‡‡ Stephan Windecker, MD,* Ralf Mueller, MD,† Eberhard Grube, MD§§

Bern, Switzerland; Siegburg, Leipzig, and Bonn, Germany; Montreal, Quebec; Ottawa, Ontario; and Edmonton, Alberta, Canada; Leicester and London, United Kingdom; and Rotterdam and Breda, the Netherlands

Safety & efficacy 18F registry, 9 Eu & Canada centres, 126 pts from 2006-2008

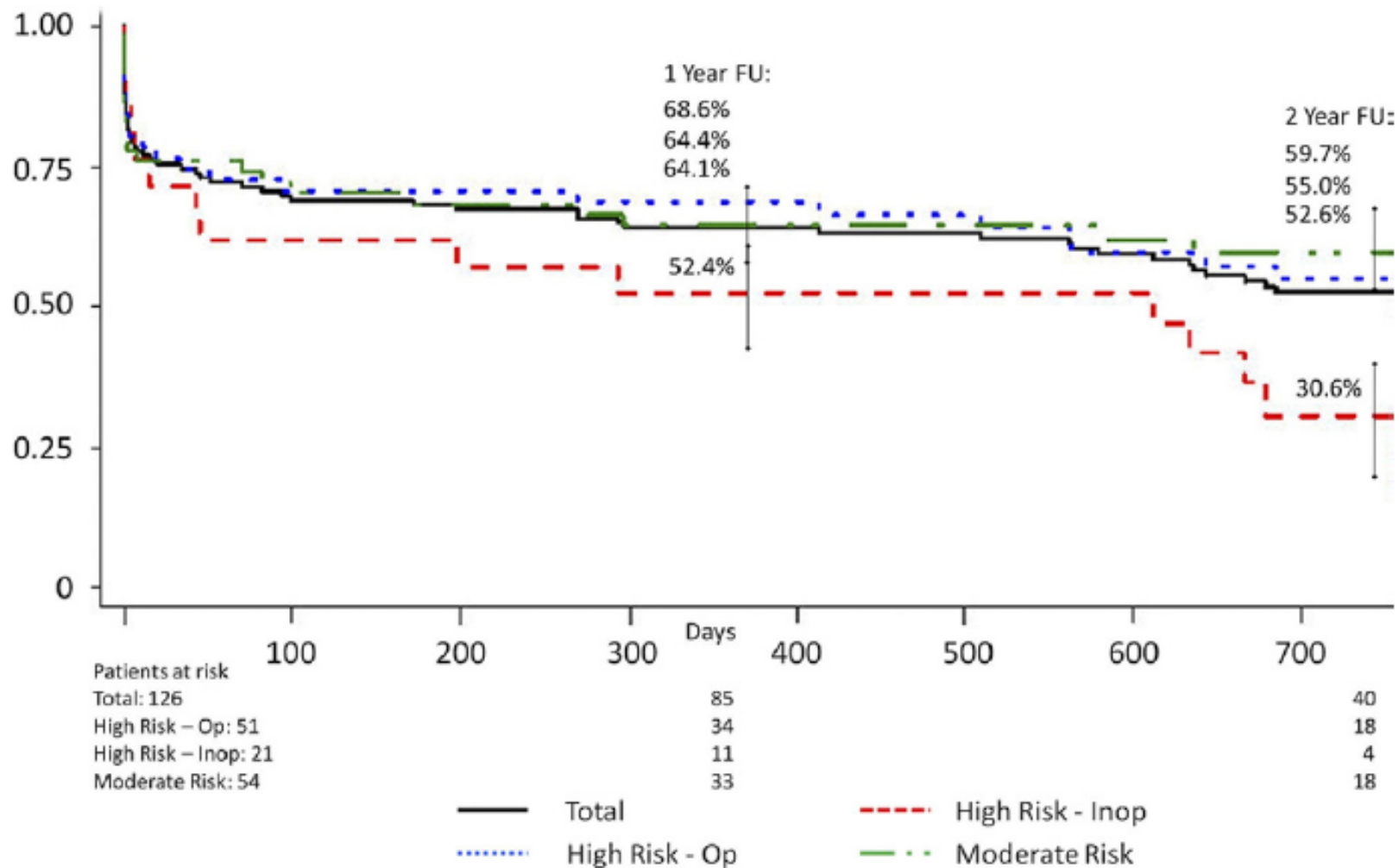


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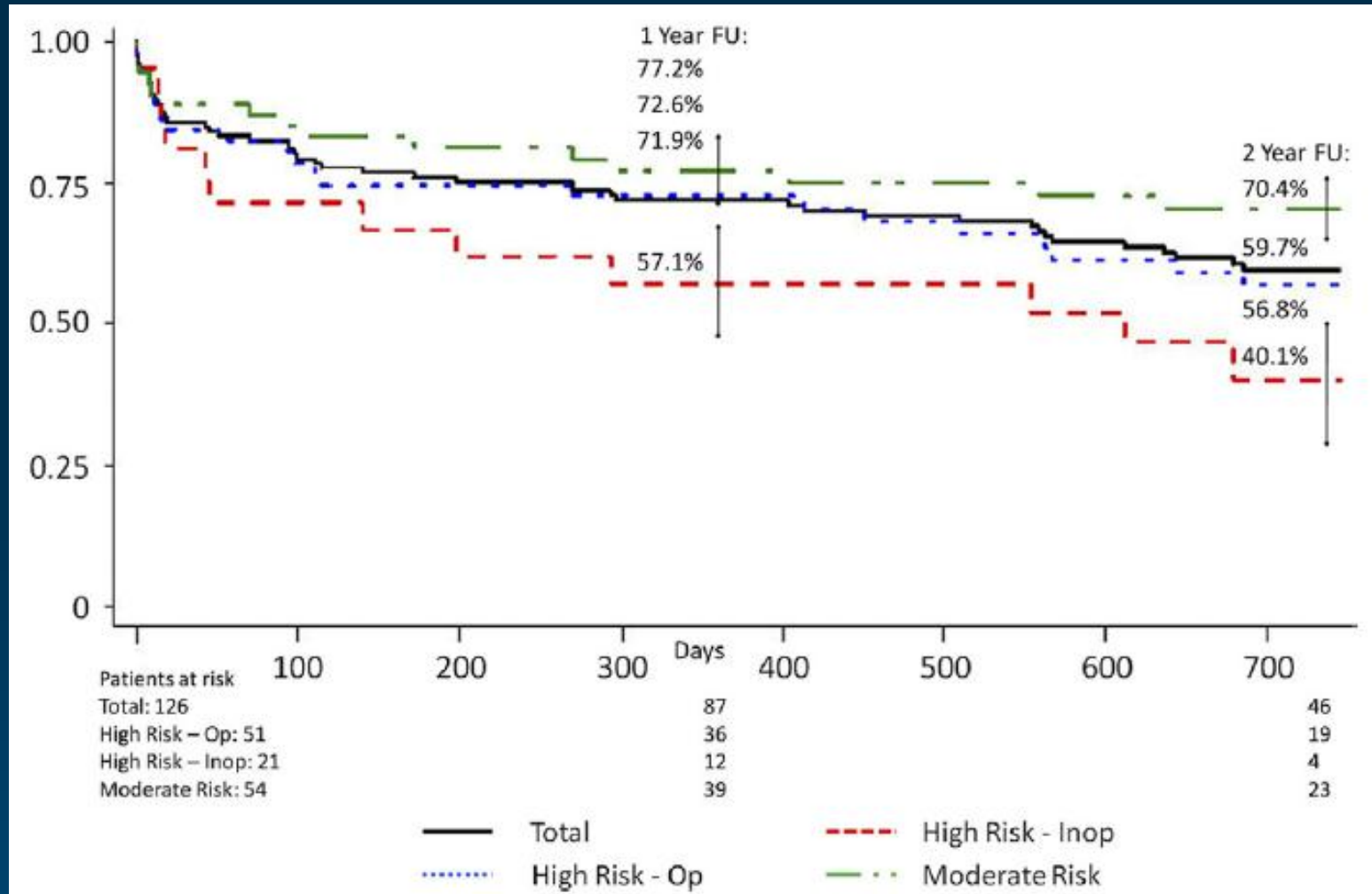
CoreValve 2-year Follow-up

Freedom From MACCE



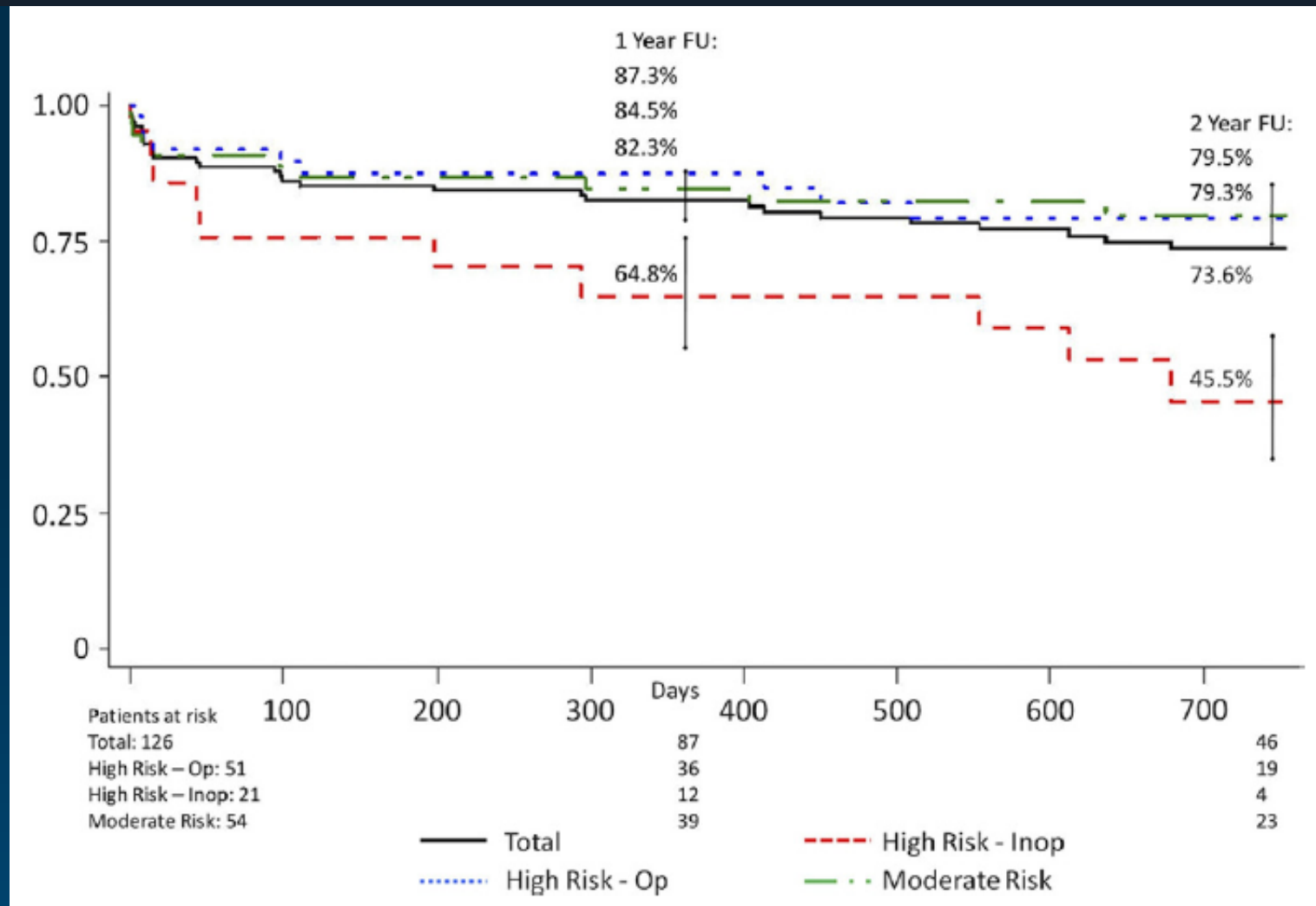
CoreValve 2-year Follow-up

Freedom From All-Cause Mortality



CoreValve 2-year Follow-up

Freedom From Cardiac Mortality

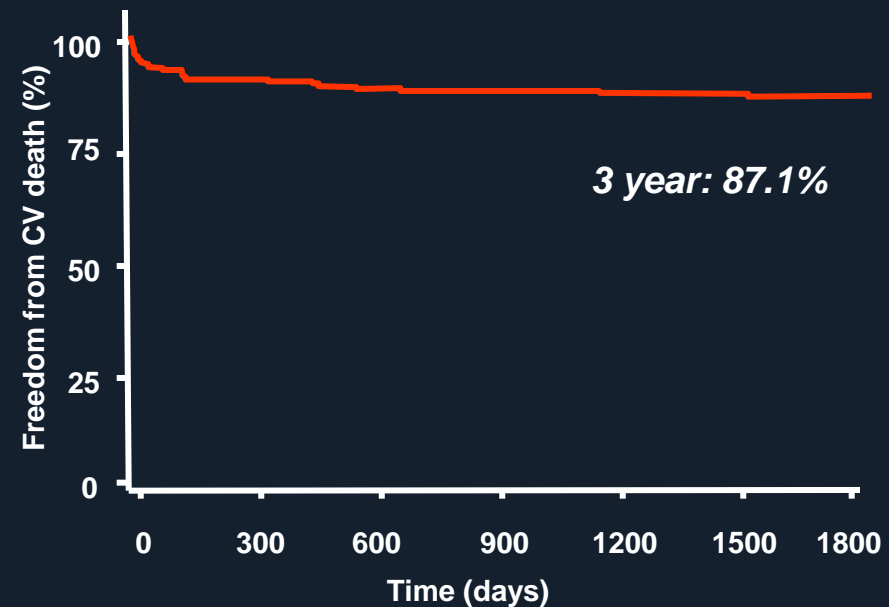
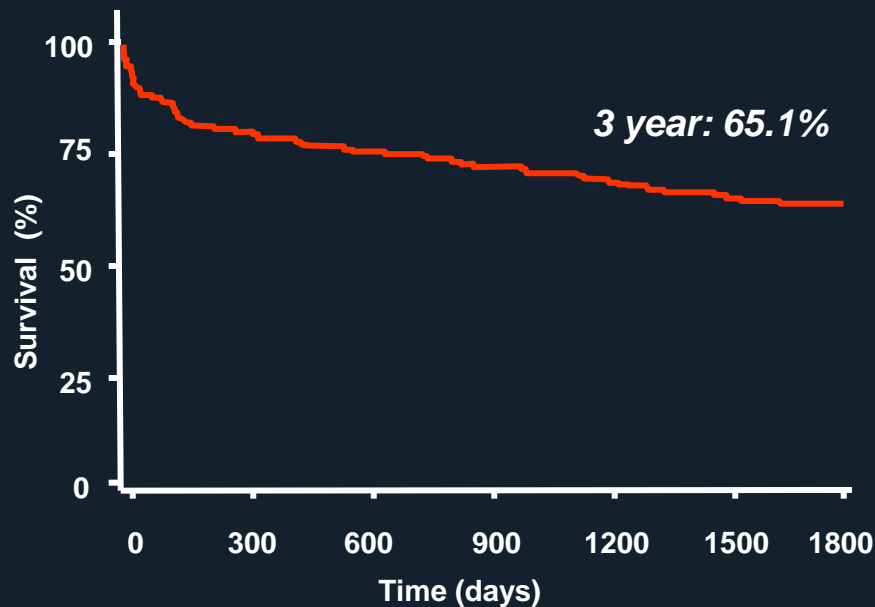


Long-term TAVI

3 year Italian experience



- 181 patients enrolled with at least 3-year follow-up
- VARC definitions
- Less than 2% lost at follow-up

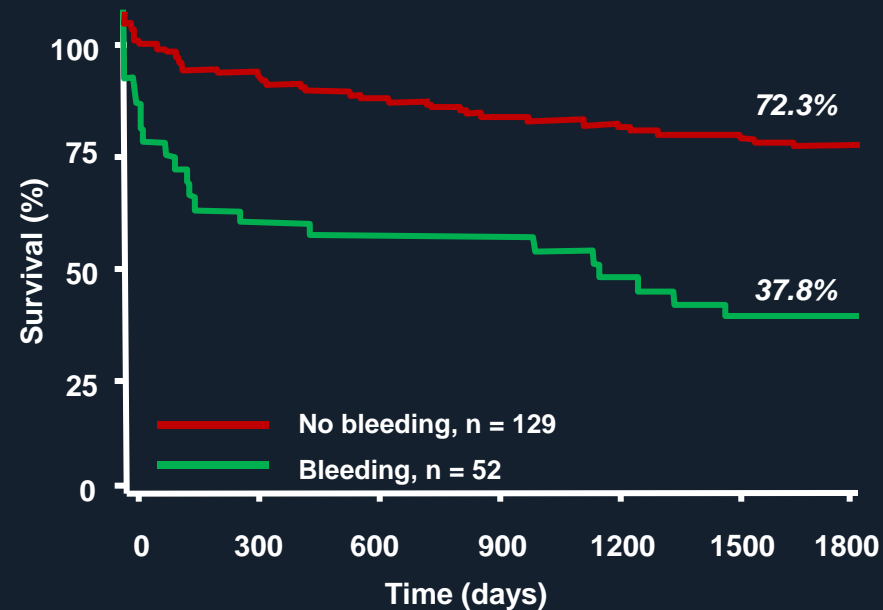
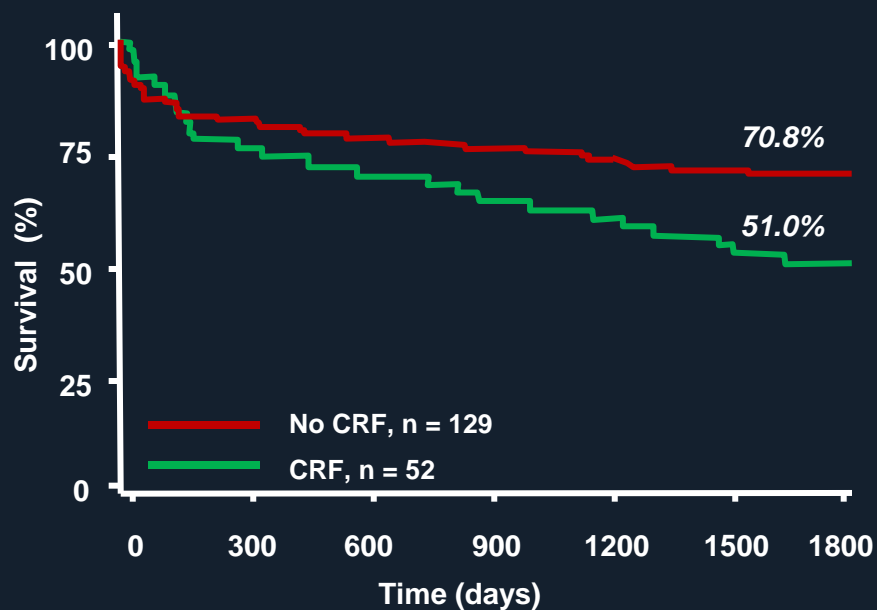


Long-term TAVI

3 year Italian experience

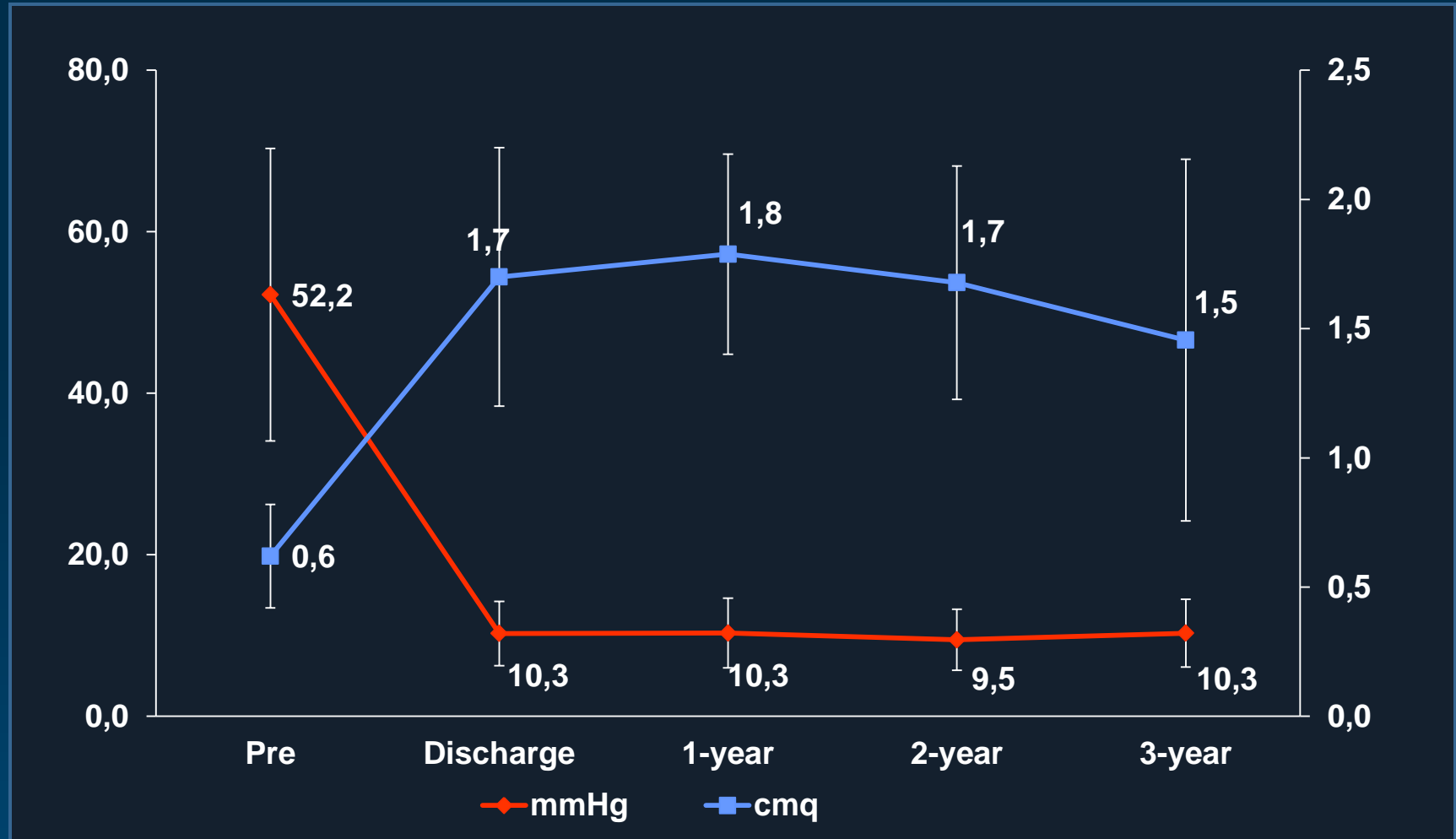


- CRF → adjusted HR 3.89 95% CI 1.38-10.91, $p=0.010$
- Bleeding → adjusted HR 3.61 95% CI 1.07-12.16, $p=0.039$



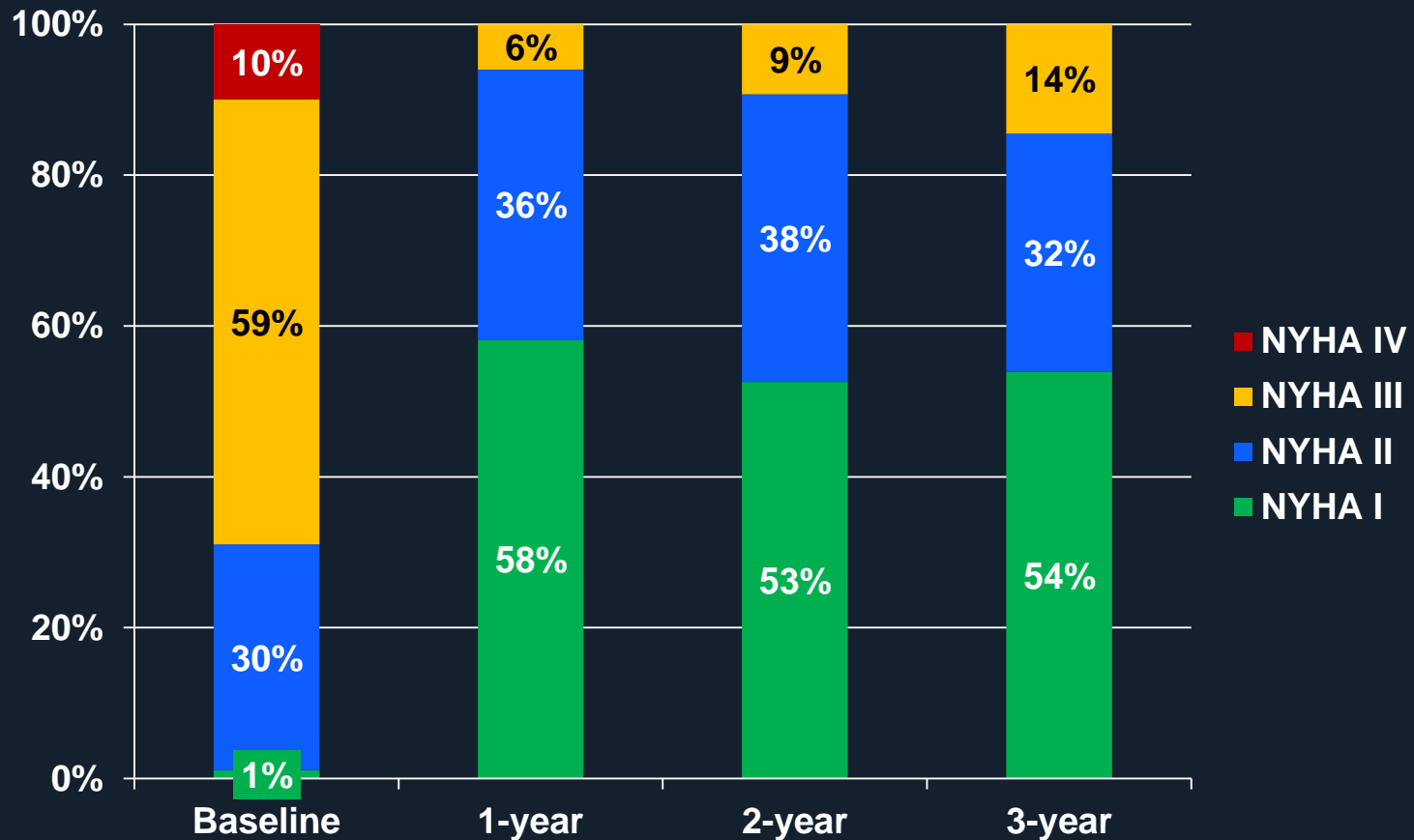
Long-term TAVI

3 year Italian experience



Long-term TAVI

3 year Italian experience



Long-term TAVI

3 year Italian experience

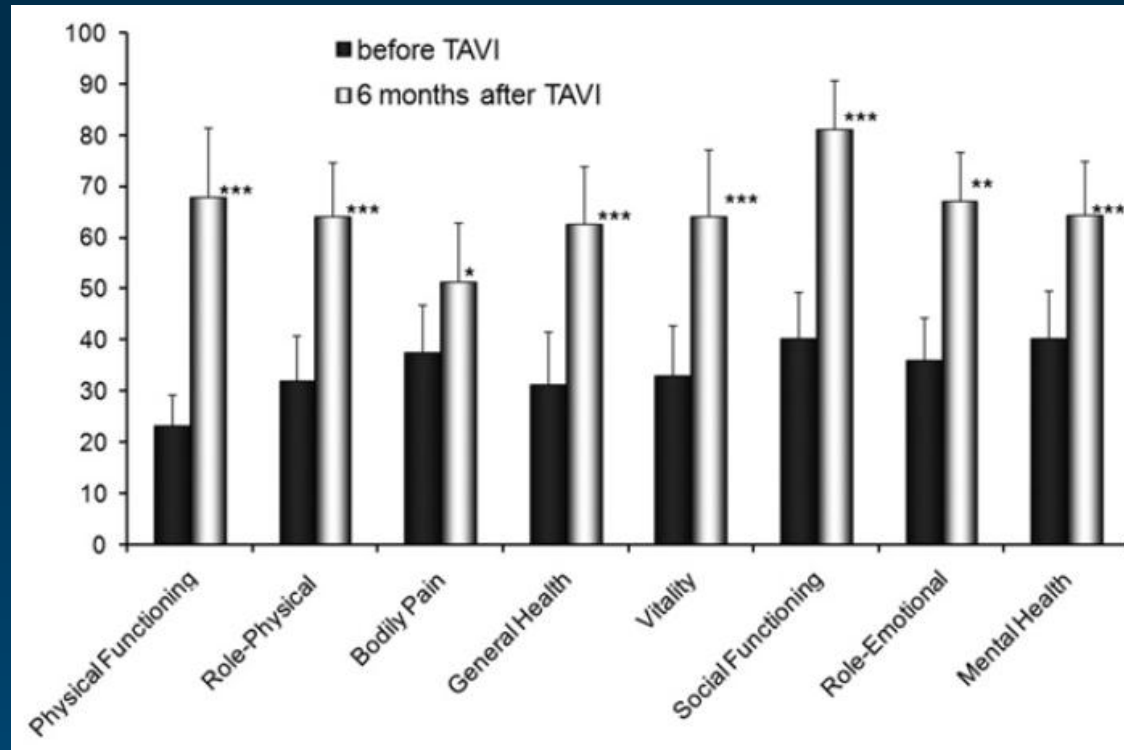


- Intra-procedural bleeding & stroke were procedural independent predictors of 30 day mortality
- Chronic Renal Insufficiency predictor of 3 year mortality
- Paravalvular leak > 2+ increase 1 year mortality
- Increased hospital post procedural admissions
PAPs >60 mmHg/ Mr>3+
- NO structural valve deterioration



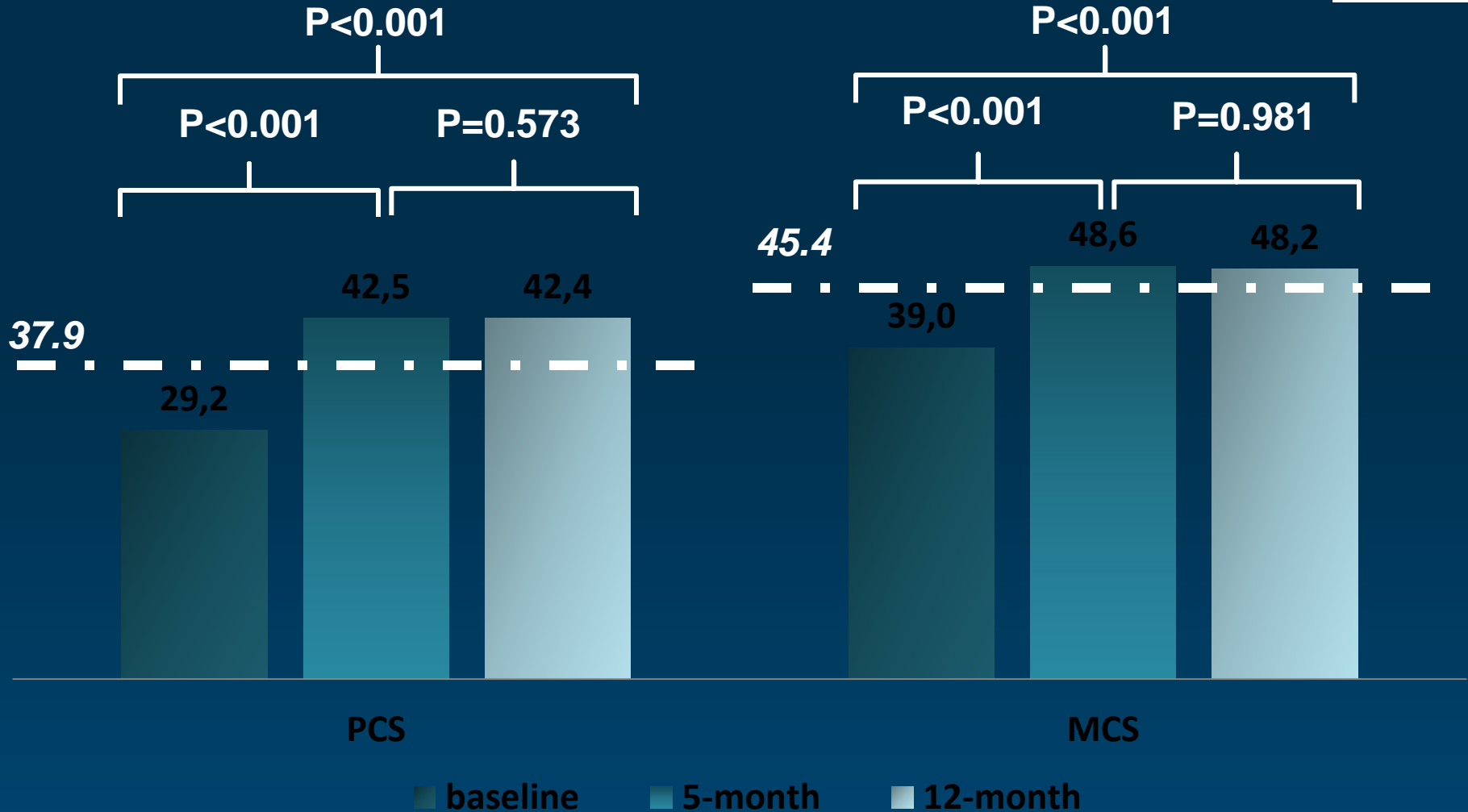
Usefulness of Percutaneous Aortic Valve Implantation to Improve Quality of Life in Patients >80 Years of Age

Raffi Bekerredjian, MD^{a,*}, Ulrike Krumdorf, MD^{a,†}, Emanuel Chorianopoulos, MD^a, Klaus Kallenbach, MD^b, Mathias Karck, MD^b, Hugo Albert Katus, MD^a, and Wolfgang Rottbauer, MD^a



Quality of Life

1-year PCS and MCS



Conclusions

- *TAVI is well beyond “proof of concept” or feasibility already being integrated into high-risk AS standard of care in many parts of the world*
- *Valve performance has exceeded expectations, BUT need long-term durability data*
- *Clinical outcomes have stabilized in experienced hands (5-10% mortality at 30 days), with late mortality reflecting underlying co-morbidities*
- *Undeniable early and sustained clinical benefit*



EURO*bservational* Research Programme

Trans Catheter Valve Treatment Pilot Registry

BE	Prof. Erwin Schroeder	National Coord.
CH	Dr. Peter Wenaweser	National Coord.
CZ	Dr. Petr Kala	National Coord.
DE	Prof. Georg Nickenig	National Coord.
FR	Prof. Helene Eltchaninoff	National Coord.
IL	Dr. Haim Danenberg	National Coord.
IT	Prof. Francesco Romeo	National Coord.
	dr. Gian Paolo Ussia	National Coord.
NL	Dr. Peter den Heijer	National Coord.
PL	Prof. Marian Zembala	National Coord.
SP	Dr. Javier Goicolea Ruigómez	National Coord.
UK	Dr. Bernard Prendergast	National Coord.
SE	Dr. Peter James	National Coord.



Grazie



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Long-term TAVI

3 year Italian experience



Overall outcomes of patients population	N (%)
All cause death, n (%)	67 (37.0)
Cardiovascular death, n (%)	24 (13.3)
Procedural MI, n (%)	7 (3.9)
Spontaneous MI, n (%)	2 (1.1)
Major stroke, n (%)	7 (3.9)
Life-threatening bleeding, n (%)	19 (10.5)
Major bleeding, n (%)	20 (11.0)
In-hospital admission, n (%)*	25 (13.8)
Combined efficacy endpoint, n (%)†	86 (47.5)

