

Protesi valvolari cardiache

Daniela Poli

Bologna 26 gennaio 2018

CARDIAC PROSTHETIC VALVES

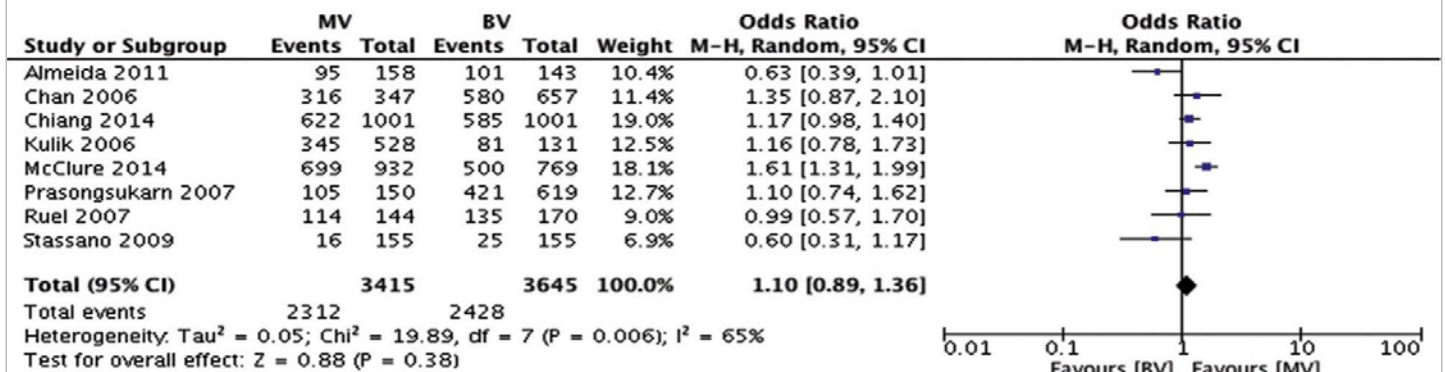
**Mechanical
valves**

**NEED for ANTICOAGULATION
HIGHER THROMBOEMBOLIC RISK**

**Biological
valves**

STRUCTURAL VALVE DETERIORATION
mitral > aortic prosthesis
risk of reoperation slightly higher than first operation

Mechanical Versus Bioprosthetic Aortic Valve Replacement in Patients Aged 40 to 70 Years: A Systematic Review and Meta-Analysis



Forest plot of odds ratio of 15-year survival in mechanical valve (MV) or bioprosthetic valve (BV) patients aged 40 to 70 years. (CI = confidence interval; M-H = Mantel-Haenszel test.)

Wu JJ et al. Ann Thorac Surg, 2016

Mechanical Versus Bioprosthetic Aortic Valve Replacement in Patients Aged 40 to 70 Years: A Systematic Review and Meta-Analysis

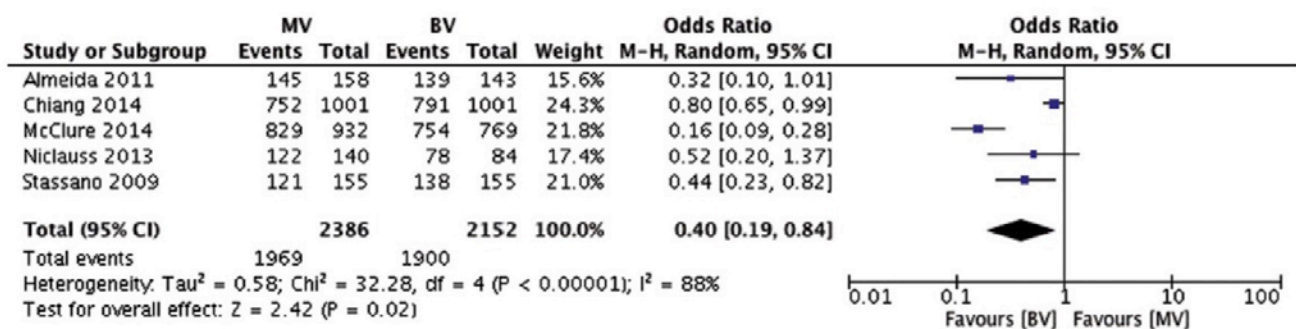


Fig 5. Forest plot of odds ratio of 15-year freedom from major bleeding event in mechanical valve (MV) or bioprosthetic valve (BV) patients aged 40 to 70 years. (CI = confidence interval; M-H = Mantel-Haenszel test.)

Wu JJ et al. Ann Thorac Surg, 2016

Mechanical Versus Bioprosthetic Aortic Valve Replacement in Patients Aged 40 to 70 Years: A Systematic Review and Meta-Analysis

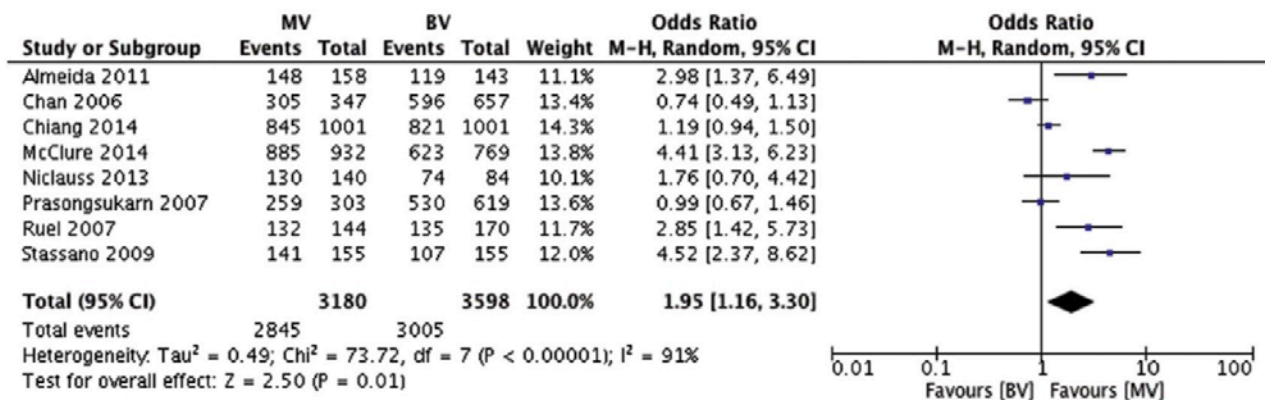


Fig 7. Forest plot of odds ratio of 15-year freedom from reoperation in mechanical valve (MV) or bioprosthetic valve (BV) patients aged 40 to 70 years. (CI = confidence interval; M-H = Mantel-Haenszel test.)

Wu JJ et al. Ann Thorac Surg, 2016



European Heart Journal (2012) 33, 2451–2496
 doi:10.1093/eurheartj/ehs109

ESC/EACTS GUIDELINES 

Guidelines on the management of valvular heart disease (version 2012)

The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: Alec Vahanian (Chairperson) (France)*, Ottavio Alfieri (Chairperson)* (Italy), Felicita Andreotti (Italy), Manuel J. Antunes (Portugal), Gonzalo Barón-Esquivias (Spain), Helmut Baumgartner (Germany), Michael Andrew Borger (Germany), Thierry P. Carrel (Switzerland), Michele De Bonis (Italy), Arturo Evangelista (Spain), Volkmar Falk (Switzerland), Bernard Jung (France), Patrizio Lancellotti (Belgium), Luc Pierard (Belgium), Susanna Price (UK), Hans-Joachim Schäfers (Germany), Gerhard Schuler (Germany), Janina Stepinska (Poland), Karl Swedberg (Sweden), Johanna Takkenberg (The Netherlands), Ulrich Otto Von Oppell (UK), Stephan Windecker (Switzerland), Jose Luis Zamorano (Spain), Marian Zembala (Poland)

Table 17: Choice of the aortic/mitral prosthesis. In favour of a mechanical prosthesis.

| | Class ^a | Level ^b |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|--------------------|
| A mechanical prosthesis is recommended according to the desire of the informed patient and if there are no contraindications for long-term anticoagulation. ^c | I | C |
| A mechanical prosthesis is recommended in patients at risk of accelerated structural valve deterioration. ^d | I | C |
| A mechanical prosthesis is recommended in patients already on anticoagulation as a result of having a mechanical prosthesis in another valve position. | I | C |
| A mechanical prosthesis should be considered in patients aged <60 years for prostheses in the aortic position and <65 years for prostheses in the mitral position. ^e | IIa | C |
| A mechanical prosthesis should be considered in patients with a reasonable life expectancy, ^f for whom future redo valve surgery would be at high risk. | IIa | C |
| A mechanical prosthesis may be considered in patients already on long-term anticoagulation due to high risk of thromboembolism. ^g | IIb | C |

Vahanian A, 2012

Table 18: Choice of the aortic/mitral prosthesis. In favour of a bioprosthesis.

| | Class ^a | Level ^b |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|--------------------|
| A bioprosthesis is recommended according to the desire of the informed patient | I | C |
| A bioprosthesis is recommended when good quality anticoagulation is unlikely (compliance problems; not readily available) or contraindicated because of high bleeding risk (prior major bleed; comorbidities; unwillingness; compliance problems; lifestyle; occupation). | I | C |
| A bioprosthesis is recommended for reoperation for mechanical valve thrombosis despite good long-term anticoagulant control. | I | C |
| A bioprosthesis should be considered in patients for whom future redo valve surgery would be at low risk. | IIa | C |
| A bioprosthesis should be considered in young women contemplating pregnancy. | IIa | C |
| A bioprosthesis should be considered in patients aged >65 years for prosthesis in aortic position or >70 years in mitral position, or those with life expectancy ^h lower than the presumed durability of the bioprosthesis. ^d | IIa | C |

Vahanian A, 2012

Mechanical versus bioprosthetic aortic valve replacement

Stuart J. Head*, Mevlüt Çelik, and A. Pieter Kappetein

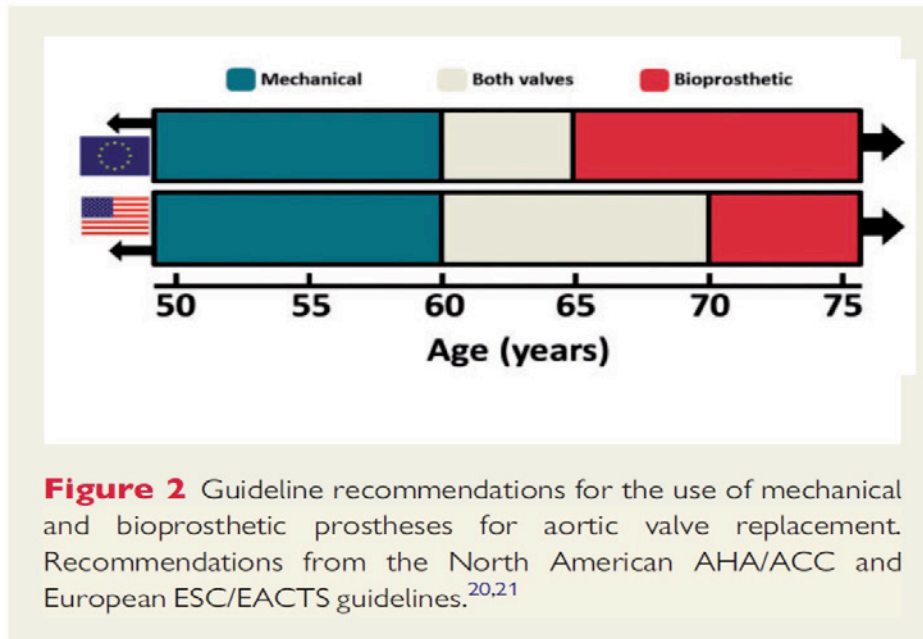


Figure 2 Guideline recommendations for the use of mechanical and bioprosthetic prostheses for aortic valve replacement. Recommendations from the North American AHA/ACC and European ESC/EACTS guidelines.^{20,21}

Europ Heart J, 2017

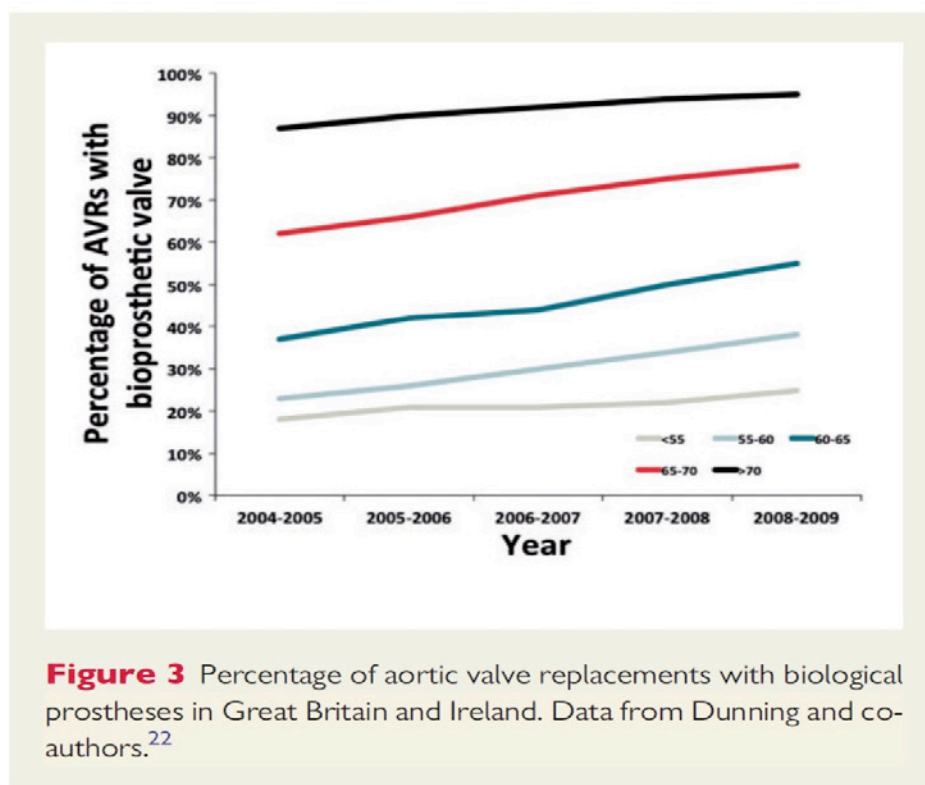


Figure 3 Percentage of aortic valve replacements with biological prostheses in Great Britain and Ireland. Data from Dunning and co-authors.²²

Europ Heart J, 2017

Incidence and risk factors for thromboembolism and major bleeding in patients with mechanical valve prosthesis: A nationwide population-based study



Table III. Rate of stroke/TE and major bleeding events in relation to target INR

| AVR | Stroke/TE | Rate | Major bleeding | Rate |
|---------------------|-----------|-------------------|----------------|--------------------|
| 2.0-3.0 | 139 | 1.29 (1.09-1.52) | 257 | 2.44 (2.15-2.76) |
| 2.5-3.5; 2.0-4.0 | 27 | 1.20 (0.79-1.75)* | 67 | 3.07 (2.38-3.90) † |
| MVR | | | | |
| 2.0-3.0 | 26 | 1.73 (1.14-2.51) | 61 | 4.02 (3.07-5.16) |
| 2.5-3.5; 2.0-4.0 | 8 | 1.77 (1.03-2.83)* | 29 | 2.98 (1.99-4.28) ‡ |

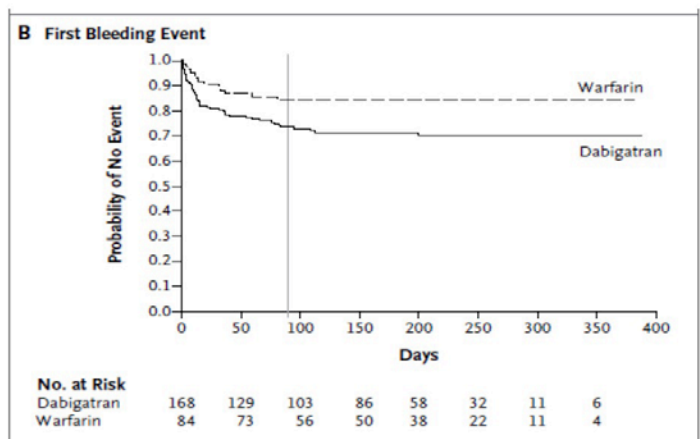
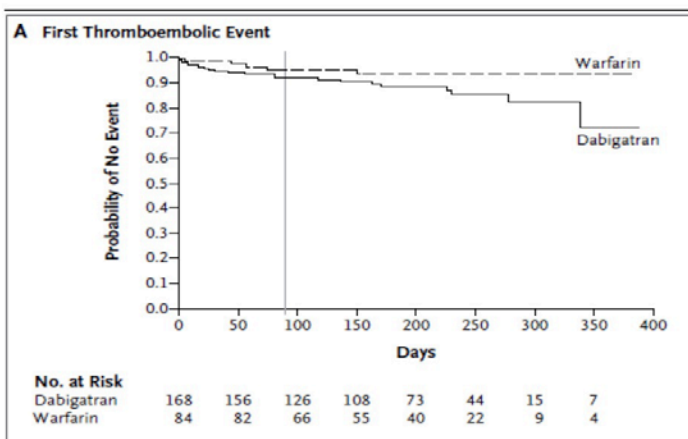
Rate is incidence per 100 patient-years (95% CI). * not significant; † $P = .10$; ‡ $P = .18$.

Labaf A et al, 2016

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dabigatran versus Warfarin in Patients with Mechanical Heart Valves



Eikelboom J et al, RE-ALIGN Study, 2013

3° CONVEGNO DI ANTICOAGULAZIONE.it

ANTICOAGULAZIONE | Attualità cliniche e di laboratorio. Aspetti sociali

BOLOGNA 25-26 GENNAIO 2018 Savoia Hotel Regency - Via del Pilastro 2, 40127 Bologna

Guidelines on the management of valvular heart disease (version 2012)

The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

- Quality of life issues and informed patient preferences must also be taken into account. The inconvenience of oral anticoagulation can be minimized by self-management of the therapy.

Retrospective multicentre FCSA-START –VALVOLE study PLECTRUM Study

Methods

Observational retrospective multicenter study among 33 Centres affiliated to FCSA.

Centres were asked to provide information on each patient in whom a mechanical heart valve or bioprosthesis was implanted.

Quality of anticoagulation, bleeding and thrombotic events occurring during the follow-up were recorded.

Retrospective multicentre FCSEA-START –VALVOLE PLECTRUM Study

33 Centri Partecipanti (n. pazienti)

1. TESTA SOPHIE, PAOLETTI ORIANA Centro Emostasi E Trombosi - A.O. Istituti Ospitalieri di Cremona, Cremona (420)
2. LODIGIANI CORRADO; CELESTE CINZIA; ILARIA QUAGLIA; PAOLA FERRAZZI Centro Trombosi IRCCS-HUMANITAS RESEARCH HOSPITAL Milano (365)
3. DANIELA POLI, ELISA GRIFONI, NICCOLO' MAGGINI Centro Trombosi SOD Malattie Aterotrombotiche Azienda ospedaliero universitaria AOU Careggi; Firenze (300)
4. COFFETTI NADIA ROSA MAROTTA; VARUSCA BRUSEGAN, ORAZIO BERGAMELLI Servizio di Immunoematologia e Medicina Trasfusionale ASST Bergamo Est, Seriate (67+129)
5. FACCHINETTI ROBERTO Laboratorio Analisi Sede Di Borgo Trento Ospedale Civile Maggiore Azienda Ospedaliera Universitaria Integrata Verona (163)
6. SERRICCHIO GIUSEPPINA Centro TAOASST-Lariana PO-CANTU' Como (160)
7. FALCO PIETRO Centro Per La Sorveglianza E Il Controllo Dei Pazienti In Terapia Anticoagulante, Poliambulatorio Specialistico Medical Pontino, Latina (148)
8. CATELLO MANGIONE; BELLOMO GIACOMO Servizio Immunotrasfusionale Presidio Ospedaliero Galatina (Le) (131)
9. MASOTTINI SERENA; COSENZA ALESSANDRA centro per la diagnosi e terapia delle malattie trombotiche Cittadella della Salute Cagliari (120)
10. RUOCCO LUCIA U.O. Analisi Chimico Cliniche, Ambulatorio Antitrombosi CAT-TAO, Azienda Ospedaliero-Universitaria Pisana, Pisa (100)
11. CAFOLLA ARTURO Centro Trombosi - Dip. Di Biotecnologie Cellulari Ed Ematologia, Az. Policlinico Umberto I Università "Sapienza", Roma (95)
12. RUPOLI SERENA; MICUCCI GIORGIA Azienda Ospedaliero-Universitaria Ospedali Riuniti Di Ancona (92)
13. PEDICO PAOLO; ROTUNNO ROSA U.O. Medicina Trasfusionale Ospedale Mons. A.R. Dimiccoli Barletta (Bt) (91)
14. INSANA ANTONIO Servizio Di Patologia Clinica Dipartimento Dei Servizi - Ospedale S. Croce Moncalieri, Ospedale S. Croce, Moncalieri (To) (69)
15. SANTORO ANGELO Direttore U.O.C. Patologia Clinica e Centro Trombosi, Presidio Ospedaliero "A. Perrino", ASL Brindisi (67)

Retrospective multicentre FCSEA-START –VALVOLE PLECTRUM Study

33 Centri Partecipanti (n. pazienti)

16. BARCELLONA DORIS Policlinico Universitario di Monserrato, Università di Cagliari; (65)
17. PENGO VITTORIO, SEENA PADAYATTIL, TISO ENRICO Istituto di Cardiologia, Policlinico Universitario, Università di Padova (58)
18. PAPARO CARMELO Centro Anti Trombosi Ospedale Maggiore, Chieri (TO) (55)
19. BUCHERINI EUGENIO Ambulatorio per il controllo della terapia anticoagulante orale, Presidio Ospedaliero di Faenza AUSLROMAGNA (53)
20. PIGNATELLI PASQUALE, PASTORI DANIELE, VICARIO TOMMASA Centro TAO Clinica Medica Policlinico Umberto I, Roma. (45)
21. MASCIOCCO LUCILLA Centro Controllo Coagulazione - S.C. Medicina Interna, Ospedale Francesco Lastaria, Lucera (FG) (41)
22. TURRINI ANNA Laboratorio Analisi Chimico-Cliniche E Di Microbiologia Ospedale Sacro Cuore Negrar (Vr) (40)
23. TOMA ANDREA UOC di Patologia Clinica Ospedale Civile, Arzignano (VI) (35)
24. PAOLO GRESELE Centro Emostasi e Trombosi Medicina Interna cardiovascolare Università di Perugia (33)
25. LA ROSA LUCIA; RINO MORALES Centro Trasfusionale e ambulatorio emostasi e trombosi; ASST VIMERCATE (30)
26. RONCHI FRANCESCO, ISU GIUSEPPE Centro Tao Servizio Di Patologia Clinica Ns Signora Di Bonaria Asl N. 6 San Gavino Monreale Cagliari (26)
27. FALANGA ANNA, LEREDE TERESA, BARCELLA LUCA Centro per la diagnosi e la terapia delle malattie emorragiche e trombotiche-USC IMMUNOEMATOLOGIA E MED TRASFUSIONALE ASSTT PAPA GIOVANNI XXIII Bergamo (25)
28. RIA LUIGI Centro Trombosi ed Emostasi U.O.C Med. Interna Gallipoli (LE) (18)
29. CRISANTEMO ROSANNA; LUCIANO SURIANO, LUCIANO LORUSSO; MARIO DE SARLO. Servizio di Immunoematologia e Medicina Trasfusionale Ospedale L. Bonomo Andria (15)
30. CARRATO PASQUALE Ist. Polidiagnostico S. Chiara, Agropoli (Sa) (14)
31. ORICCHIO CARMINE Responsabile Centro Immunotrasfusionale, Ospedale Civile L. Curto Polla (SA) (7)
32. GRANDONE ELVIRA, COLAIZZO DONATELLA Centro Trombosi, I.R.C.C.S. Casa Sollievo della Sofferenza, S. Giovanni Rotondo (FG) (6)
33. MOLINATTI MAURIZIO Centro Trombosi e sorveglianza delle terapie Antitrombotiche Clinica Cellini Torino (1)

Retrospective multicentre FCSA-START –VALVOLE study

PLECTRUM Study

Results

| | N (%) |
|-----------------------------------------|-------------------|
| N | 3026 |
| Males | 1664 (55.0) |
| Median age at implantation (IQR) | 61.85 (52.3-69.1) |
| Follow-up (years) | 27.422 |
| Median follow-up (years) (IQR) | 8.45 (3.1-13.1) |
| <i>Type of heart valve</i> | |
| mechanical | 2357 (77.9%) |
| biological | 669 (22.1) |
| <i>Site of implantation (2980/3029)</i> | |
| aortic | 1790 (60.0) |
| mitralic | 851 (28.6) |
| Mitro-aortic | 339 (11.4) |

Mechanical heart valves

| | |
|--------------------------------------------------|-------------|
| Number | 2357 |
| <i>Type of anticoagulant drug</i> | |
| Warfarin | 1929 (81.8) |
| acenocoumarole | 428 (18.2) |
| <i>Intensity of anticoagulation</i> | |
| INR 2.0-3.0 | 604 (26.4) |
| INR 2.5-3.5 | 1484 (64.8) |
| INR 3.0-4.0 | 202 (8.8) |
| Median Time spent within TR (%) (IQR) | 60 (47-74) |
| <i>Events</i> | |
| Death (%) | 174 (7.4) |
| EMG (rate x100 pt-yrs) | 243 (1.0) |
| Stroke/TIA/Peripheral embolism(rate x100 pt-yrs) | 164 (0.67) |
| Re-implatation | 77 (4%) |

MB and thrombotic events in relation to valve position

| Prosthetic valve position | MB (% pt-yrs) | Thrombosis (% pt-yrs) |
|---------------------------|---------------|-----------------------|
| Aortic (%) 1382- 14169 | 144 (1.01) | 72 (0.5) |
| Mitralic (%) 666- 6897 | 62 (0.89) | 74 (1.07) |
| Mitro-Aortic (%)266- 2731 | 33 (1.20) | 17 (0.62) |

Mechanical heart valves

| Prosthesis thrombogenicity | | | |
|----------------------------|-------------|----------------|--------------|
| Prosthetic valve position | Low n(%) | Medium n(%) | High n(%) |
| Aortic (%) | 829 (92.3) | 27 (3.0) | 42 (4.7) |
| Mitralic (%) | 371 (89.8) | 25 (6.1) | 17 (4.1) |
| Mitro-Aortic(%) | 143 (95.3) | 6 (4.0) | 1 (0.7) |

Biological Heart Prosthesis

| | |
|--------------------------------------------------|---------------|
| N. | 612 |
| Males (%) | 324 (52.9) |
| Median age (range) | 71.8 (24-89) |
| Total follow-up patient-years | 3085 |
| Median follow-up (range) | 2.4 (0.5-7.5) |
| <i>Indications for long-term anticoagulation</i> | |
| Atrial Fibrillation | 480 (78.4) |
| History of stroke/TIA | 13 (2.1) |
| Cardiac diseases (*) | 22 (3.6) |
| Other indications for VKA | 6 (1.0) |
| Unknown | 91 (14.8) |

Biological Heart Prosthesis

| | |
|-------------------------------------------------|------------|
| <i>Clinical characteristics</i> | |
| Hypertension | 438 (71.6) |
| Diabetes Mellitus | 121 (19.8) |
| Coronary artery disease-Peripheral Arteriopathy | 246 (40.2) |
| Heart failure | 124 (20.3) |
| Previous stroke/TIA | 77 (12.6) |
| Antiplatelets treatment | 195 (31.9) |
| <i>Adverse events ·(% pt-yrs)</i> | |
| Major bleedings | 34 (1.1) |
| Stroke/TIA | 29 (0.9) |
| Death | 36 (1.2) |

Characteristics of patients undergoing valve prosthesis re-implantation

| | |
|-----------------------------------------------------|--------------|
| N (%) | 46 (7.5) |
| Median age (range) | 59.9 (24-79) |
| Males (%) | 24 (52.2) |
| Median Time interval to re-implant (months) | 84 (1-312) |
| <i>Site of first implantation</i> | |
| Aorta | 30 (65.2) |
| Mitral | 14 (30.4) |
| Both | 2 (4.3) |
| <i>Median Time interval to reoperation (months)</i> | 84 (1-312) |

Characteristics of patients undergoing valve prosthesis re-implantation

| | |
|----------------------------------------------------|--------------|
| <i>Cause of reoperation</i> | |
| Infection | 11 (23.9) |
| Prosthetic valve deterioration | 35 (76.1) |
| Median Time interval to re-implant, months (range) | |
| due to infection | 14 (2-72) |
| due to valve deterioration | 114 (1-312) |
| Median age of patients, years (range) | |
| with infections | 69.8 (31-78) |
| with structural valve deterioration | 55.8 (24-79) |

Characteristics of patients undergoing valve prosthesis re-implantation

| <i>N. of patients with re-implantation in relation to age class (%)</i> | |
|-------------------------------------------------------------------------|---------------|
| ≤60 years | 25/76 (32.9) |
| >60 years | 21/536 (3.9) |
| ≤50 years | 17/31 (54.8) |
| >65 years | 18/476 (3.8) |
| ≤70 years | 37/274 (13.5) |
| >70 years | 9/338 (2.7) |

<60 years vs ≥60 years RR 3.8 (2.1-7.2) p=0.0001

<65 years vs ≥65 years RR 3.1 (1.7-6.0) p=0.0001

<70 years vs ≥70 years RR 3.7 (1.7-8.6) p=0.0001

Clinical characteristics of patients with and without reoperation

| | Patients without reoperation N. 567 (%) | Patients with reoperation N. 45 (%) | p value |
|-------------------------|--------------------------------------------|----------------------------------------|---------|
| Median age (range) | 72.6 (27-89) | 56.7 (24-79) | 0.0001 |
| <i>Valve position</i> | | | |
| Aortic | 335 (59.1) | 29 (64.4) | |
| Mitralic | 157 (27.7) | 14 (31.1) | |
| Both | 75 (13.2) | 2 (4.5) | 0.2 |
| <i>Co-morbidity</i> | | | |
| Hypertension | 402 (70.9) | 36 (80.0) | 0.4 |
| Diabetes mellitus | 110 (19.4) | 11 (24.4) | 0.6 |
| Coronary artery disease | 131 (23.1) | 13 (28.9) | 0.5 |
| Atrial fibrillation | 450 (79.4) | 30 (66.7) | 0.05 |
| Previous Stroke/TIA | 69 (12.2) | 8 (17.8) | 0.3 |
| Heart failure | 113 (19.9) | 11(24.4) | 0.7 |
| eGFR<30 mL/min | 12/273 (4.4) | 1/26 (3.8) | 1.0 |
| Smoking habitus | 118 (20.8) | 12 (26.7) | 0.4 |
| Antiplatelet treatment | 185 (32.6) | 10 (22.2) | 0.2 |

Conclusions

The threshold of 65 years for implanting a BV should be carefully evaluated, considering the high risk for reoperation and the high risk of AF occurrence with persisting need for long-term anticoagulation.

The high risk for reoperation of young patients implanted with BV and the availability of a safe and easy way to conduct VKAs treatment should be considered when the type of valve must be chosen.

OPTIMAL ORAL ANTICOAGULANT THERAPY IN PATIENTS WITH MECHANICAL HEART VALVES

S.C. CANNEGIETER, M.D., F.R. ROSENDAAL, M.D., A.R. WINTZEN, M.D., F.J.M. VAN DER MEER, M.D.,
J.P. VANDENBROUCKE, M.D., AND E. BRIËT, M.D.

Table 1. Characteristics of the Patients at the Beginning of Follow-up.

| CHARACTERISTIC | No. (%) |
|-----------------------------------|-------------|
| No. of patients | 1608 |
| No. of patient-years of follow-up | 6475 |
| Age (yr) | |
| <50 | 343 (21.3) |
| 50–69 | 995 (61.9) |
| ≥70 | 270 (16.8) |
| Sex | |
| Male | 879 (54.7) |
| Female | 729 (45.3) |
| Valve position | |
| Aortic | 961 (59.8) |
| Mitral | 485 (30.2) |
| Both | 158 (9.8) |
| Unknown | 4 (0.2) |
| Valve model* | |
| Caged ball or disk† | 53 (3.0) |
| Tilting disk‡ | 1354 (76.7) |
| Bileaflet§ | 347 (19.6) |
| Unknown | 12 (0.7) |

NEJM 1995

OPTIMAL ORAL ANTICOAGULANT THERAPY IN PATIENTS WITH MECHANICAL HEART VALVES

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J.P. VANDENBROUCKE, M.D., AND E. BRIËT, M.D.

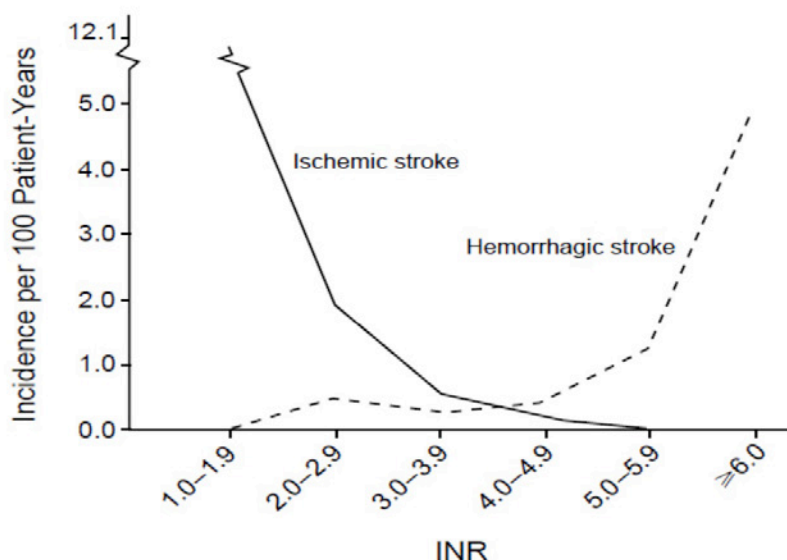


Figure 2. Incidence of Ischemic and Hemorrhagic Stroke According to INR Category.

NEJM 1995

OPTIMAL ORAL ANTICOAGULANT THERAPY IN PATIENTS WITH MECHANICAL HEART VALVES

S.C. CANNEGIETER, M.D., F.R. ROSENDAAL, M.D., A.R. WINTZEN, M.D., F.J.M. VAN DER MEER, M.D., J.P. VANDENBROUCKE, M.D., AND E. BRIËT, M.D.

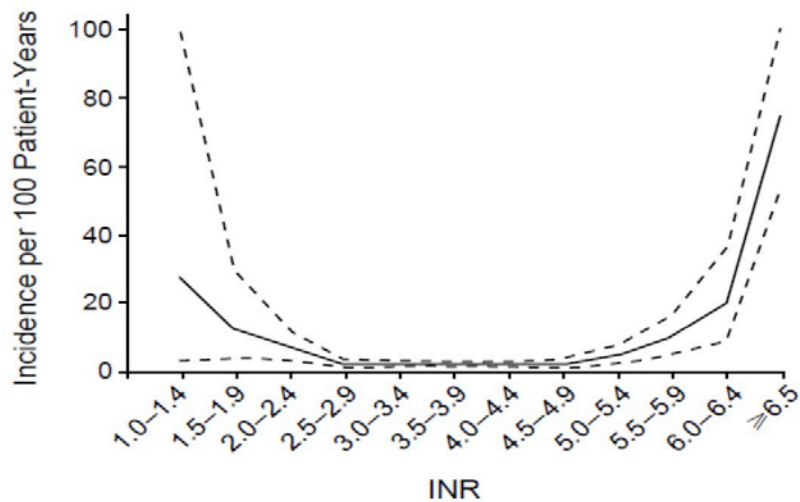


Figure 3. INR-Specific Incidence of All Adverse Events (All Episodes of Thromboembolism, All Major Bleeding Episodes, and Unclassified Stroke).

NEJM 1995

Better anticoagulation control improves survival after valve replacement

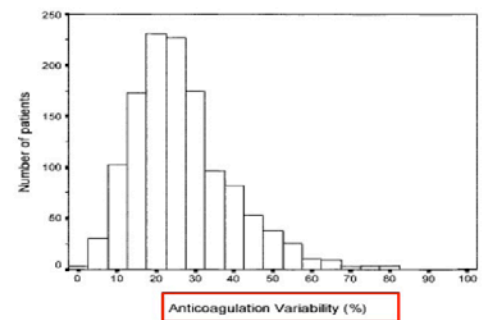


TABLE 2. Valve-related deaths by ACV grouped

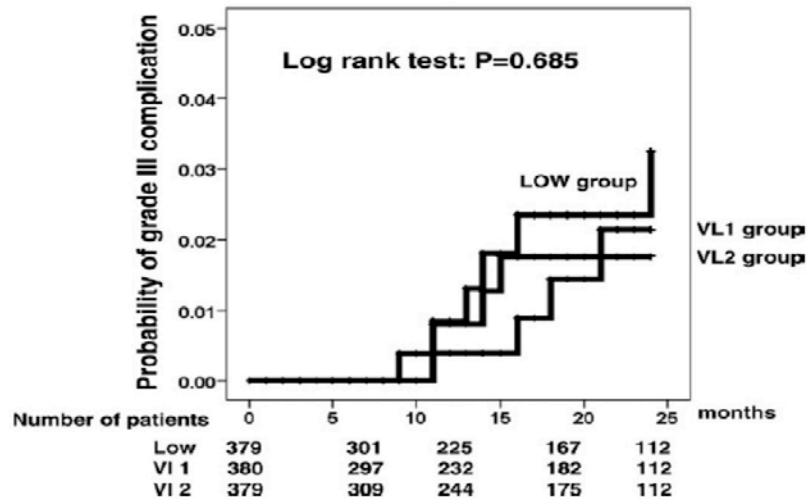
| | Aortic | | Mitral | |
|----------------|-------------------------|-------------------|-------------------------|-------------------|
| | Low/medium ACV n (%/yr) | High ACV n (%/yr) | Low/medium ACV n (%/yr) | High ACV n (%/yr) |
| Patients | 420 | 205 | 436 | 211 |
| Patient-years | 3454 | 1230 | 4106 | 1413 |
| Stroke | 5 (0.1) | 8 (0.7)*** | 8 (0.2) | 5 (0.4) |
| Thrombosis | 0 (0) | 0 (0) | 1 (0.02) | 1 (0.07) |
| Major bleeding | 8 (0.2) | 6 (0.5) | 9 (0.2) | 7 (0.5) |
| PVE | 3 (0.09) | 3 (0.2) | 3 (0.07) | 8 (0.6)*** |
| Total | 16 (0.5) | 17 (1.4)*** | 21 (0.5) | 21 (1.5)*** |

ACV, Anticoagulant variability; PVE, prosthetic valve endocarditis.
*** $P < .001$.

Butchart, 2002

Efficacy and Safety of Very Low-Dose Self-Management of Oral Anticoagulation in Patients With Mechanical Heart Valve Replacement

Heinrich Koertke, MD, PhD, Armin Zittermann, PhD, Otto Wagner, MS, Juergen Ennker, MD, PhD, Werner Saggau, MD, PhD, Falk-Udo Sack, MD, PhD, Jochen Cremer, MD, PhD, Christof Huth, MD, PhD, Maurizio Braccio, MD, PhD, Francesco Musumeci, MD, PhD, and Reiner Koerfer, MD, PhD



low-dose group
AVR INR 1.8-2.8
MVR INR 2.5-3.5

Very low-dose groups
AVR INR 1.6-2.1
MVR INR 2.0-2.5

Fig 1. Freedom from grade III complications beyond postoperative month six.

Ann Thorac Surg, 2010