Biological versus mechanical protheses for aortic valve replacement

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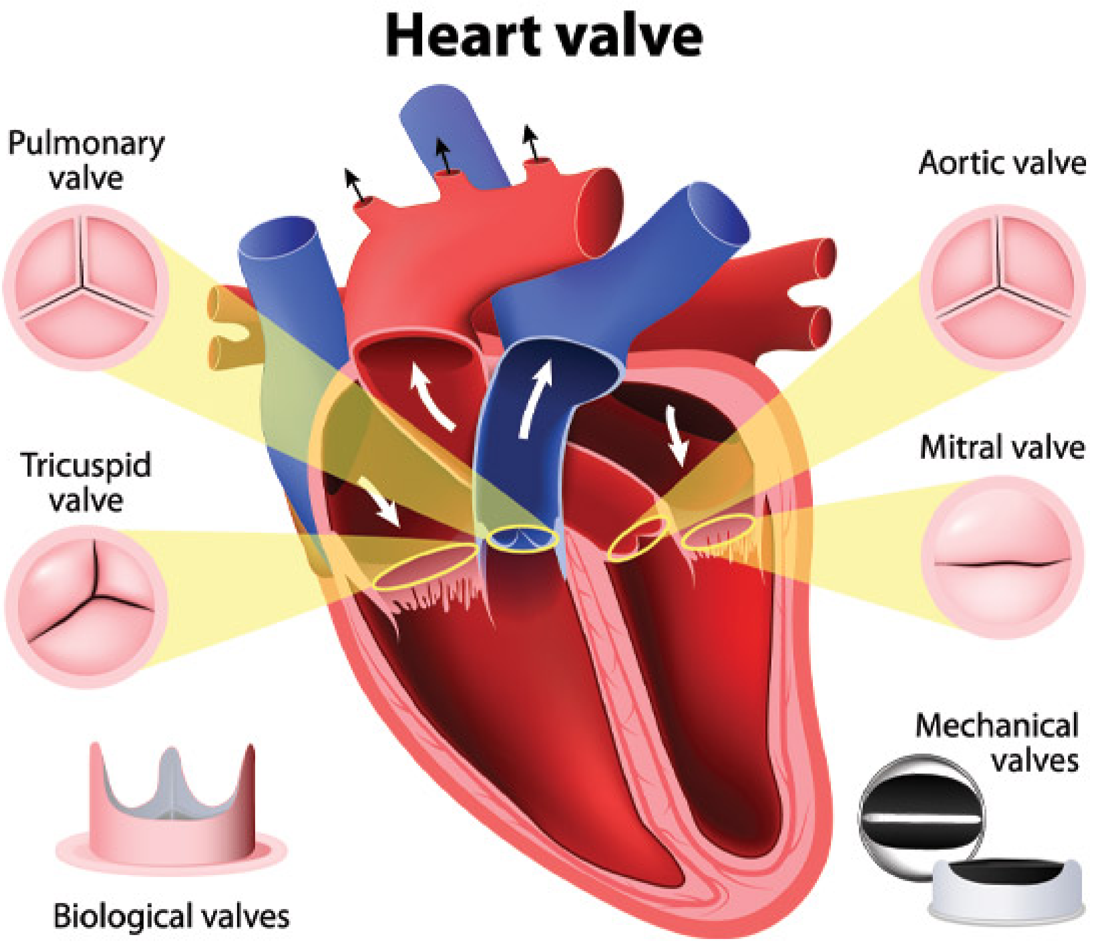
Outline of the presentation

1. Background
    1.1 Anatomy of heart valves
        1.2 Indications for aortic valve replacement
        1.2.1 Aortic stenosis
        1.2.2 Aortic regurgitation
    1.3 Types of bioprosthetic heart valves
    1.4 Types of mechanical heart valves
2. ESC/EACTS Guidelines for heart valve surgery
3. Diploma thesis
4. Ankersmit vs. Rodríguez-Caulo
5. References

1.1 Background- Anatomy of heart valves

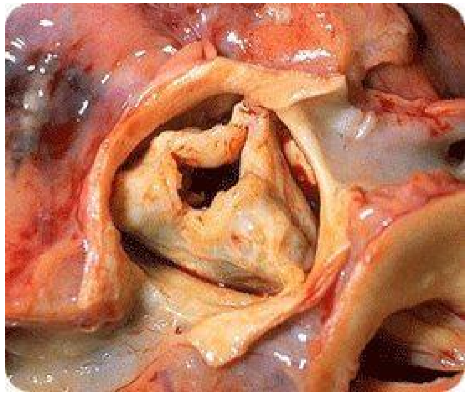


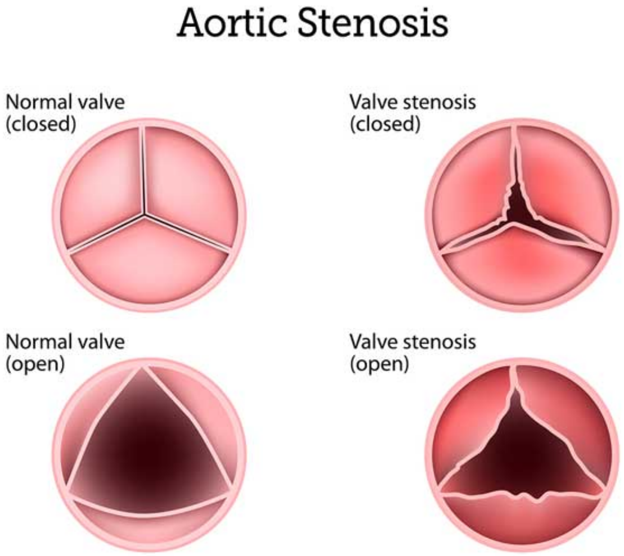
https://www.mountelizabeth.com.sg/specialties/medical-specialties/heart-vascular/heart-valve-repair-replacement-surgery

1.2 Background - Indications for aortic valve replacement

1.2.1 Aortic stenosis (AS)

- **Aetiology**
  - Acquired: arteriosclerosis, rheumatic fever
  - Congenital: mostly valvular aortic valve stenosis with bicuspid aortic valve (80%)
- Typical **symptomtrias:** Syncope, Angina pectoris, Dyspnea
- **Pathophysiology:** Pathological pressure gradient between the prestenotic and poststenotic segments > chronic pressure left ventricle > left heart hypertrophy > dilatation ventricle > heart failure, cardiac arrhythmias
- **Diagnostics:** Pulsus tardus et parvus, small blood pressure amplitude, spindle shaped holosystolic with punctum maximum over 2nd ICR right parasternal
  - Further apparative diagnostics: TEE , X-ray chest, ECG, cardiac catheterization



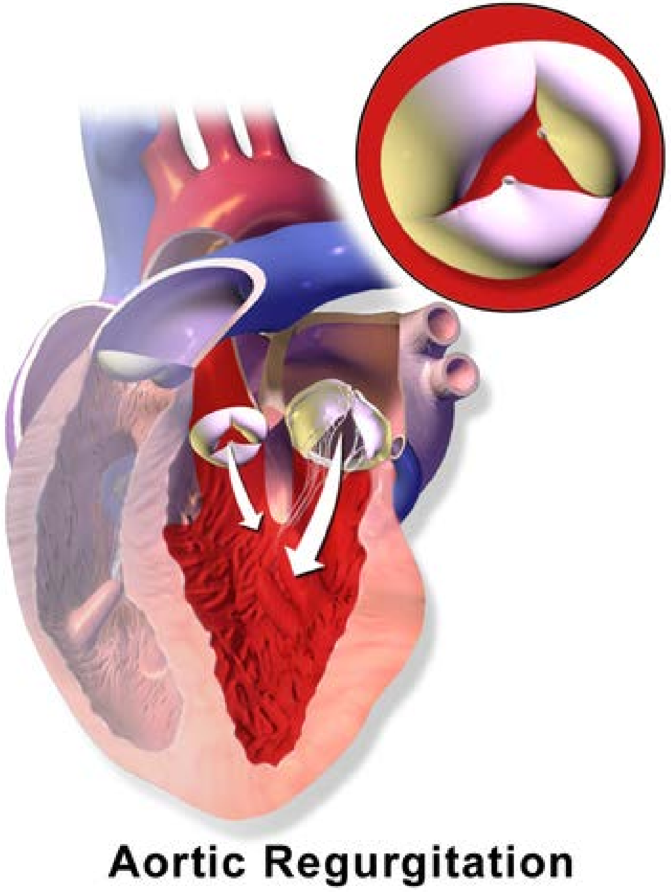


https://www.heart-valve-surgery.com/aortic-stenosis-valve-heart-narrowing.php

1.2 Background - Indications for aortic valve replacement

1.2.2 Aortic regurgitation (AR)

- **Aetiology:** Endocarditis, Rheumatic fever, Lues, dilatation of aortic root/Aorta ascendens, bicuspid apposition of aortic valve
- **Symptoms (in late stages of AR):** decreased performance, palpitations, angina pectoris, dyspnea on exertion
- **Pathophysiology:** Inability of the aortic valve to close > regurgitation into left ventricle > eccentric hypertrophy > progressive heart failure
- **Diagnostics:** diastolic decrescendo heart murmur with punctum maximum above Erb's point, low diastolic blood pressure, pulsus celer et altus
  - Further apparative diagnostics: TEE , X-ray chest, ECG, cardiac catheterization



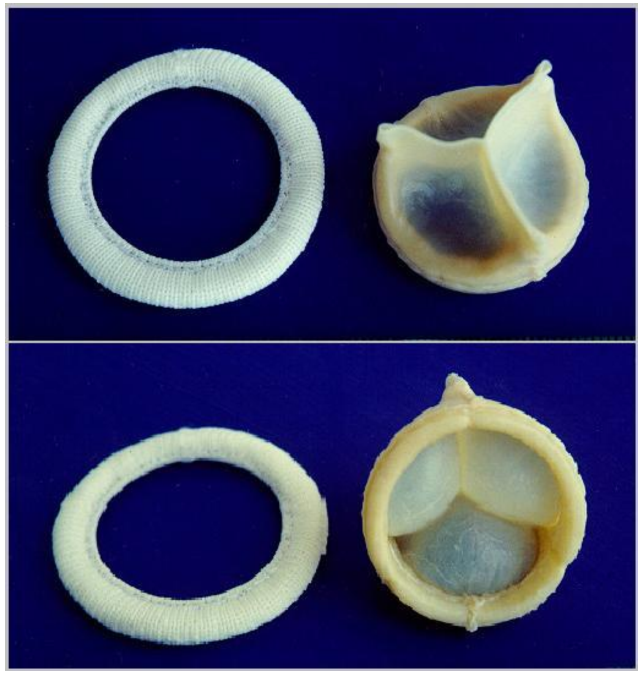
„Aortic Regurgitation" von BruceBlaus.

1.3 Background - Types of bioprosthetic heart valves

Homograft
- Valve harvesting: By heart transplantation or from cadaveric donors
- No anticoagulation necessary after surgery
- Use especially in patients with endocarditis

Xenograft
- Animal material tissue: Pericardium from pork/bovine, aortic valves from pork
- Only temporary anticoagulation necessary

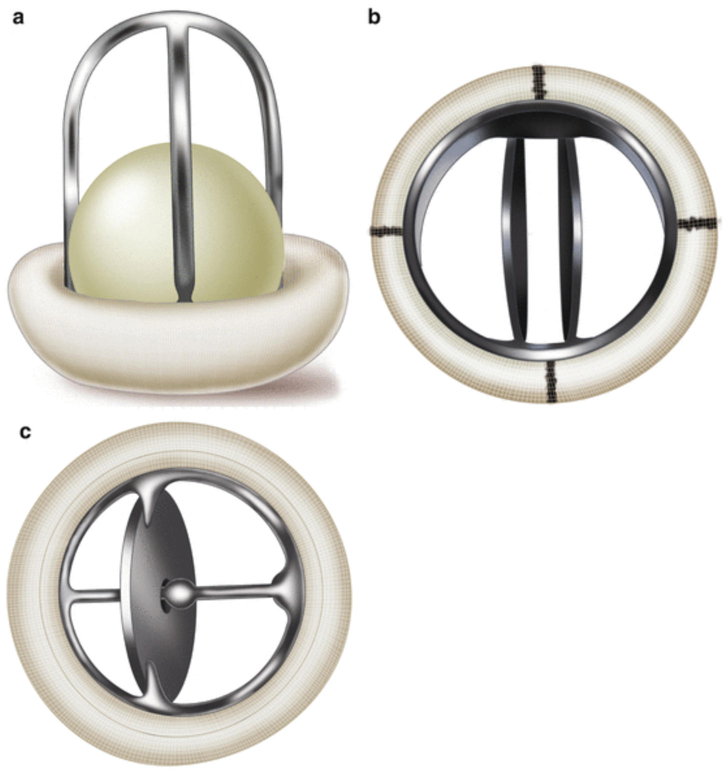
Autograft
- Tissue Engineering
- Donor and recipient of the transplant identical (patient own tissue)
- Ross operation
- Best hemodynamic properties among bioprostheses



Biological Valves ©GNU Free Documentation License

1.4 Background - Types of mechanical heart valves

- First mechanical heart valve was implanted in 1960 by Dr Albert Starr in Portland
- **Structure**
    - Metal body and polyester sleeve
    - Outer ring made of synthetic fabric: Dacron or Teflon
    - Core: pyrolytic carbon (especially of hardened graphite)
- **Benefits:** Lifetime durability
- **Disadvantages:** permanent anticoagulation necessary, risk of embolism and bleeding, valve noise



a Ball in cage design b Bileaflet tilting disc c Tilting disc

Thoracic Key Fastest Thoracic Insight Engine: Prosthetic heart valves, URL: https://thoracickey.com/prosthetic-heart-valves-5/#Fig3. (Status: 14th of 2021)

2. ESC/EACTS Guidelines for heart valve surgery

CLASSES OF RECOMMENDATION

I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.
II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.
IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.
IIb	Usefulness/efficacy is less well established by evidence/opinion.
III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some case may be harmful.

LEVELS OF EVIDENCE

A	Data derived from multiple randomized clinical trials or meta-analyses.
B	Data derived from a single randomized clinical trial or large non randomized studies.
C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

2. ESC/EACTS Guidelines for heart valve surgery

Recommendations for Prosthetic Valve Type: **Bioprosthetic** Versus Mechanical Valve

Class I	By request of the patient (Evidence C)
Class I	Adequate anticoagulation not possible High risk of bleeding (Evidence C)
Class I	Occurrence of thrombosis in mechanical heart valve despite anticoagulation > Reoperation with bioprosthesis (Evidence C)
Class IIa	Expected low-risk reoperation (Evidence C)
Class IIa	Planned pregnancy in young women (Evidence C)
Class IIa	Aortic valve prosthesis: patients > 65 years of age Mitral valve prosthesis: patients > 70 years of age Life expectancy patient < durability bioprosthesis (Evidence C)

2. ESC/EACTS Guidelines for heart valve surgery

Recommendations for Prosthetic Valve Type: Bioprosthetic Versus **Mechanical Valve**

Class I	By request of the patient, no contraindication to lifelong anticoagulation (Evidence C)
Class I	Patients at risk of accelerated structural valve degeneration (Evidence C)
Class I	Patients with a pre-existing anticoagulation indication due to an existing mechanical prosthesis in another valve position (Evidence C)
Class IIa	Patients < 65 years (Evidence C)
Class IIa	Patients with a longer life expectancy > high risk for reoperation (Evidence C)
Class IIb	Existing long-term anticoagulation due to increased risk of thromboembolism, e.g., atrial fibrillation(Evidence C)

3. Diploma thesis

Method of systematic review

Identification

LITERATURE SEARCH

Databases: PubMed, Embase

LIMITS

English language articles only, Publications since 1979 until 2022

KEY WORDS

((biological) OR (mechanical)) AND (replacement) AND ((aortic valve) OR (mitral valve)) NOT (transcatheter)

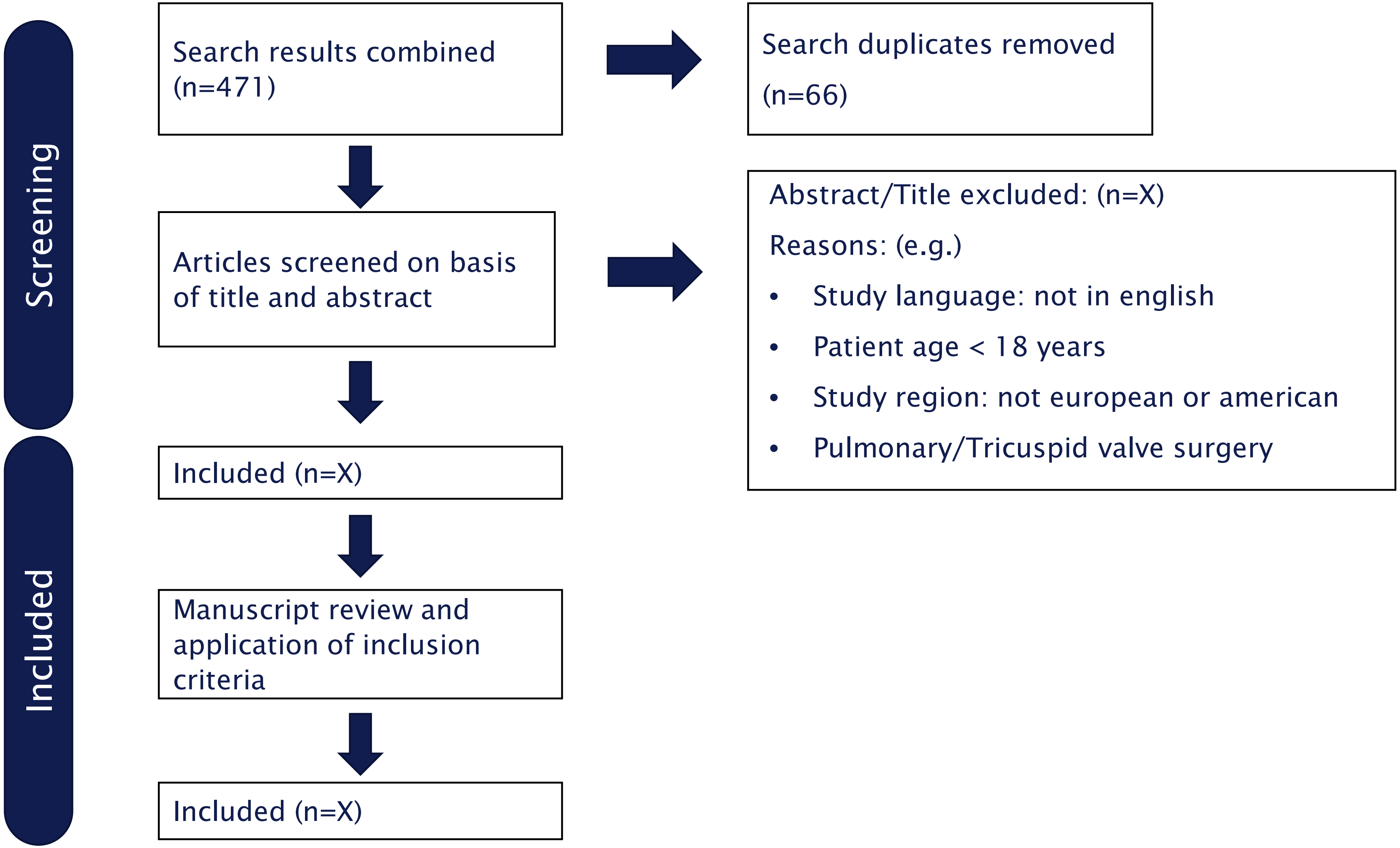
→

Records removed *before screening:*

- Records removed for following reasons:
  - Systematic Review
  - Review
  - Meta-Analysis
  - Books and Documents

↓

3. Diploma thesis



4. Ankersmit vs. Rodríguez-Caulo

Mechanical aortic valve prostheses offer a survival benefit over bioprostheses among 50 to 65-year-olds: the AUTHEARTVISIT study

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Biological versus mechanical prostheses for aortic valve replacement

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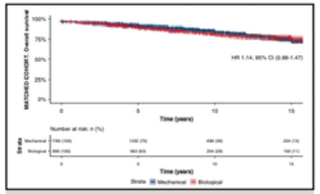
ABSTRACT

Objectives: Long-term real-world outcomes are critical for informing decisions about biological (Bio) or mechanical (Mech) prostheses for aortic valve replacement, particularly in patients aged between 50 and 65 years. The objective was to compare long-term survival and major adverse cardiac and cardiovascular events (ie, stroke, reoperation, and major bleeding) within this population.

Methods: This was a multicenter observational study including all patients aged between 50 and 65 years who underwent an aortic valve replacement because of severe isolated aortic stenosis between the years 2000 and 2018. A total of 5215 patients from 27 Spanish hospitals were registered with a follow-up of 15 years. Multivariable analyses, including a 2:1 propensity score matching (1822 Mech and 911 Bio) and competing risks analyses were applied.

Results: Bio prostheses were implanted in 19% of patients (n = 992). No significant differences were observed between matched groups in long-term survival (hazard ratio [HR], 1.14; 95% confidence interval [CI], 0.88-1.47; $P = .33$). Stroke rates were higher for Mech prostheses, but not significant (HR, 0.72; 95% CI, 0.50-1.03; $P = .07$). Finally, higher rates of major bleeding were found in the Mech group (HR, 0.65; 95% CI, 0.49-0.87; $P = .004$), whereas reoperation was more frequent among the Bio group (HR, 3.04; 95% CI, 1.80-5.14; $P < .001$). Bio prostheses increased from 13% in the period from 2000 to 2008 to 24% in 2009 to 2018.

Conclusions: Long-term survival was comparable among groups in patients between 50 and 65 years of age. Mech prostheses were associated with a higher risk of major bleeding, whereas Bio prostheses entailed higher reoperation rates. Bio prostheses seem a reasonable choice for patients between 50 and 65 years in Spain. (J Thorac Cardiovasc Surg 2021;■:1-9)



Long-term follow-up of overall survival in aortic biological versus mechanical prosthesis.

CENTRAL MESSAGE

Bio prostheses seem a reasonable choice for surgical aortic valve replacement in patients between 50 and 65 years of age in Spain considering long-term survival and risk of major events.

PERSPECTIVE

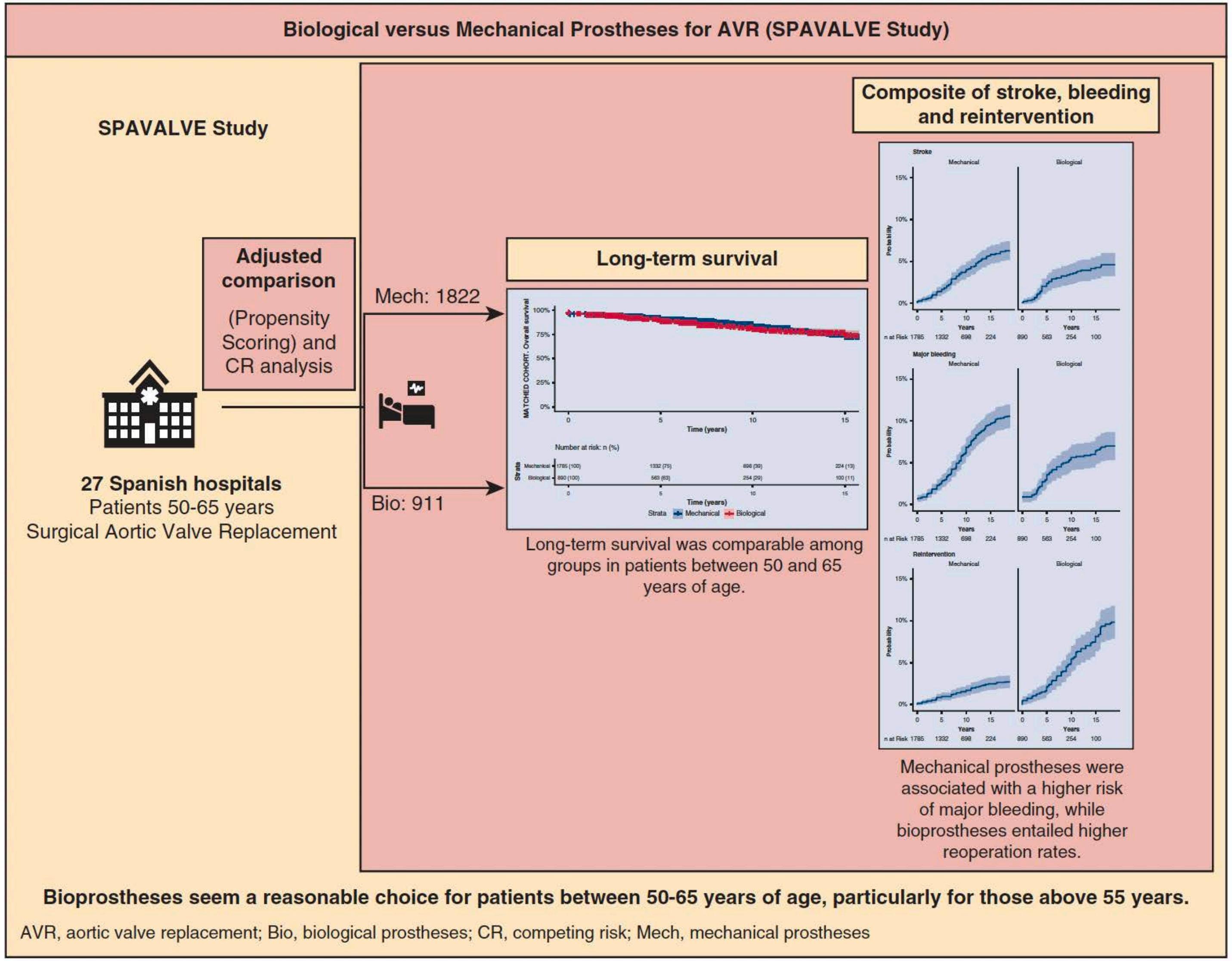
Deciding the type of prosthesis for surgical AVR remains controversial in patients aged 50-65 years. Thus, a comprehensive assessment of long-term survival and the risk of a composite of stroke, bleeding, and reintervention with data from a large multicenter study was conducted. Our find-

ADULT

Methods

	Preprint	Paper
Patient collective	13.993 patients (= 98% of the Austrian population)	5.215 patients from 27 Spanish hospitals
Time period	2010 - 2018	2000 - 2018
Indication	Aortic valve replacement	Aortic valve replacement for severe isolated AS
Exclusion criteria	Patients < 18 years, mitral, tricuspid, or pulmonary valve replacement, concomitant heart surgery	Autonomic change of residence, need for concomitant surgery, previous cardiac surgery, infective endocarditis
Primary Endpoints	Long-term survival	Long-term survival (up to 18 years), stroke, bleeding, reintervention
Secondary Endpoints	Reoperation, stroke, myocardial infarction, risk of heart failure	None

Methods - Paper



Methods - Statistical analysis

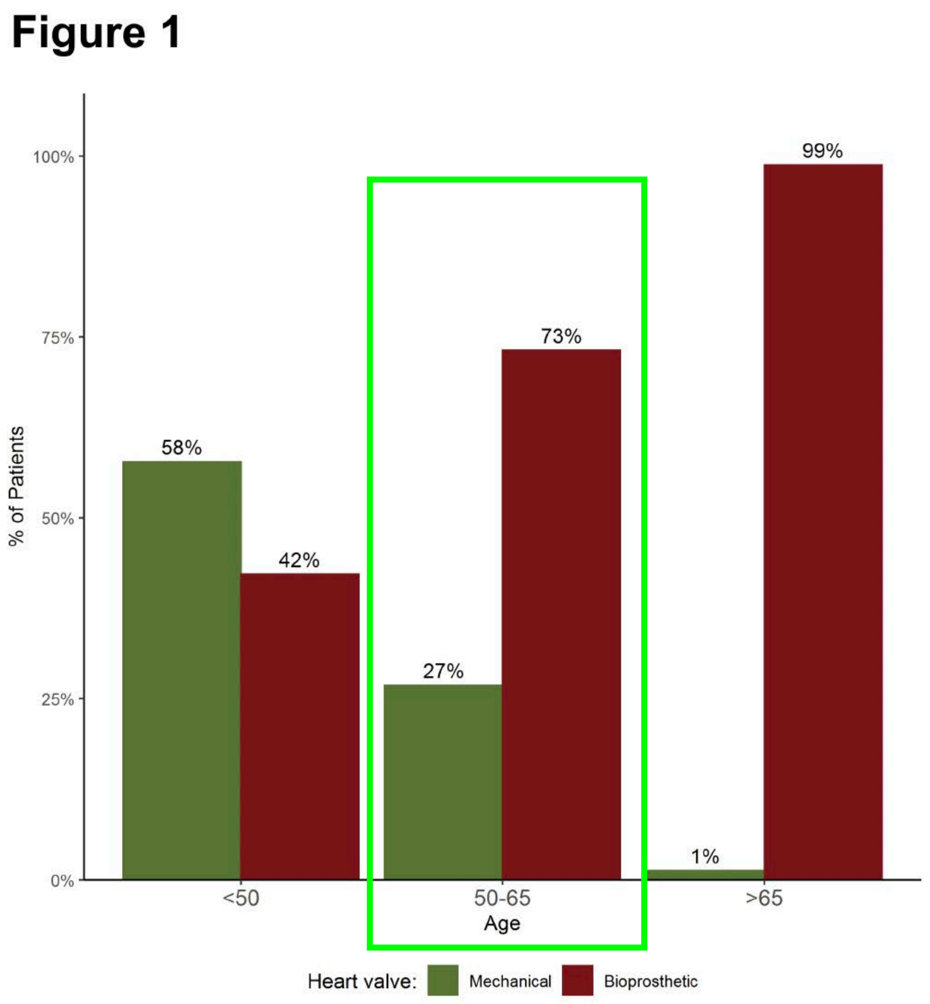
PREPRINT

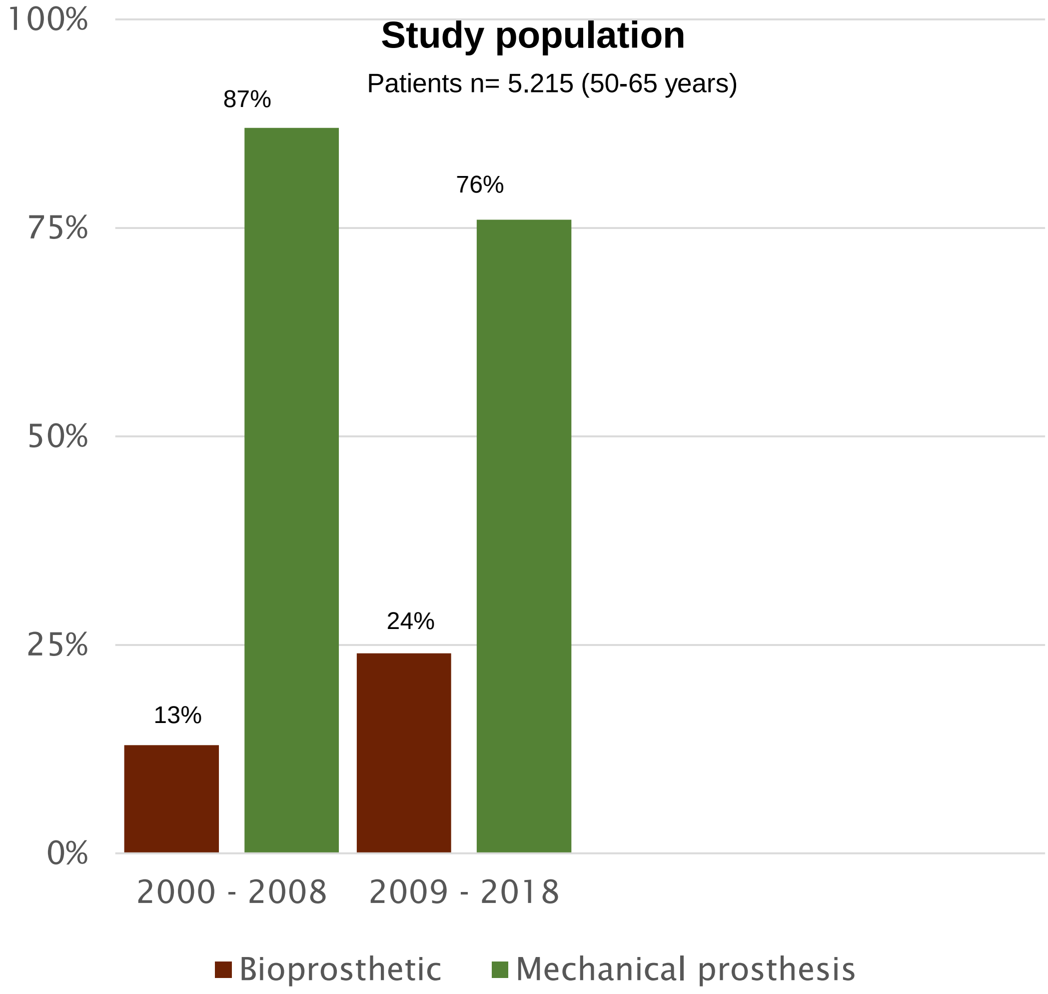
- Descriptive representation of variables as means ± standard deviation (SD), and medians with the interquartile range (IQR)
- Student‘s t-test/Mann-Whitney U-Test: continuous variable
- C2-test: categorical data
- Cox-Regression (Primary Endpoints)
  - Univariable: Overall survival
  - Multivariable: Age, sex, diagnosis of diabetes, heart failure, myocardial infarction, stroke before valve replacement
- Secondary Endpoints: Re-operation, heart failure, myocardial infarction, stroke
  - Multivariable analysis: Age, sex, diagnosis of diabetes, heart failure, myocardial infarction, stroke before valve replacement

PAPER

- Descriptive analysis with continuous variables
- Student’s t-test/c2-test
- Nonparametric tests Mann-Whitney U and Kruskal-Wallis
- 2:1 Propensity Score (PS)
- Logit regression model – Nearest Neighbour Caliper
  - Dependent variable: Prothesis Type (mechanical/bio)
  - Tested covariates: Age, sex, hospital, logistic Euro-SCORE I, hypertension, diabetes mellitus, atrial fibrillation, COPD, hyperlipidemia, previous stroke, previous myocardial infarction, chronic kidney disease, arteriopathy, preoperative mean transaortic gradient, left ventricular ejection fraction, and mean valve size

Methods – Study population





Results PREPRINT - Survival

	Incidence rate		univariable		multivariable	
	Mechanical (n, %)	Biological (n, %)	HR (95% CI)	p-value	HR (95% CI)	p-value
Death (overall)	157 (12·50%)	3948 (31·00%)	2.946 (2·512 – 3·456)	**<0·001**	1·115 (0·939 –1·324)	0·22
Death (<50 years)	31 (7·38%)	38 (12·38%)	1·572 (0·976 – 2·533)	0·06	1·465 (0·903 – 2·378)	0·12
Death (50 – 65 years)	72 (10·26%)	354 (18·53%)	1·866 (1·448 – 2·404)	**<0·001**	1·676 (1·289 – 2·181)	**<0·001**
Death (> 65 years)	54 (40·30%)	3556 (33·8%)	1·194 (0·912 – 1·562)	0·20	0·851 (0·649 – 1·115)	0·24

Results PREPRINT - Survival

univariable		multivariable	
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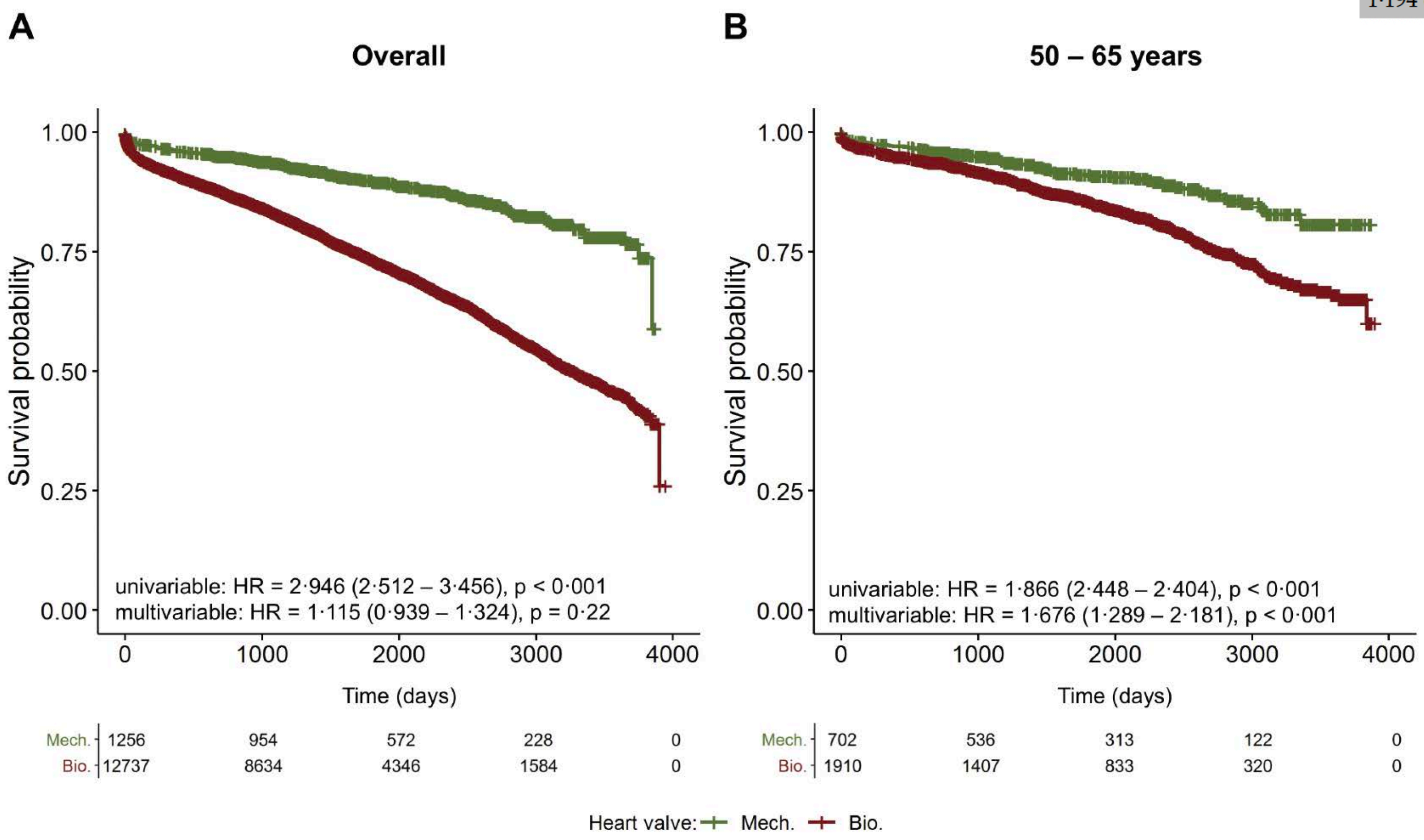
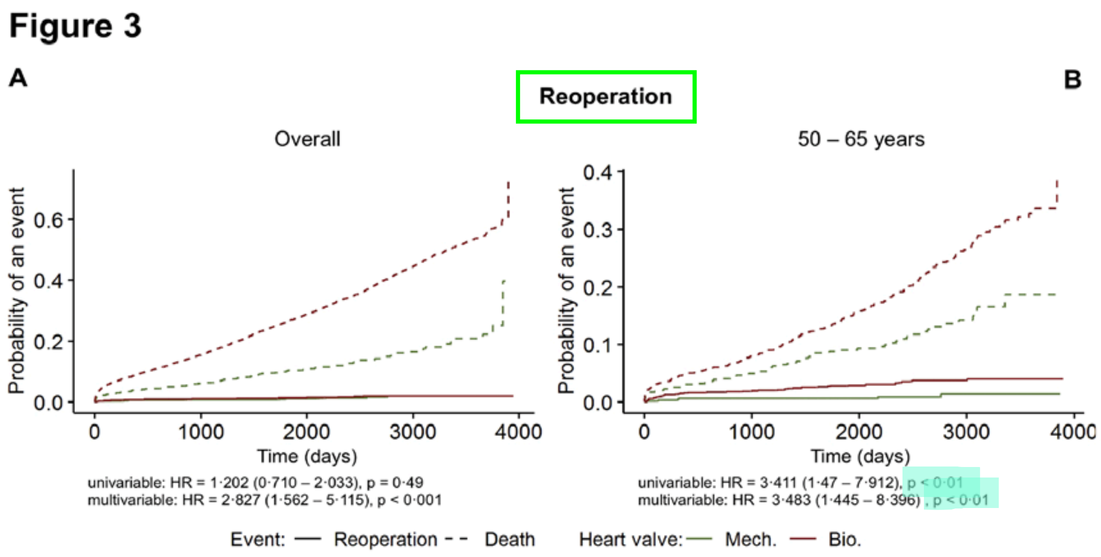
Figure 2

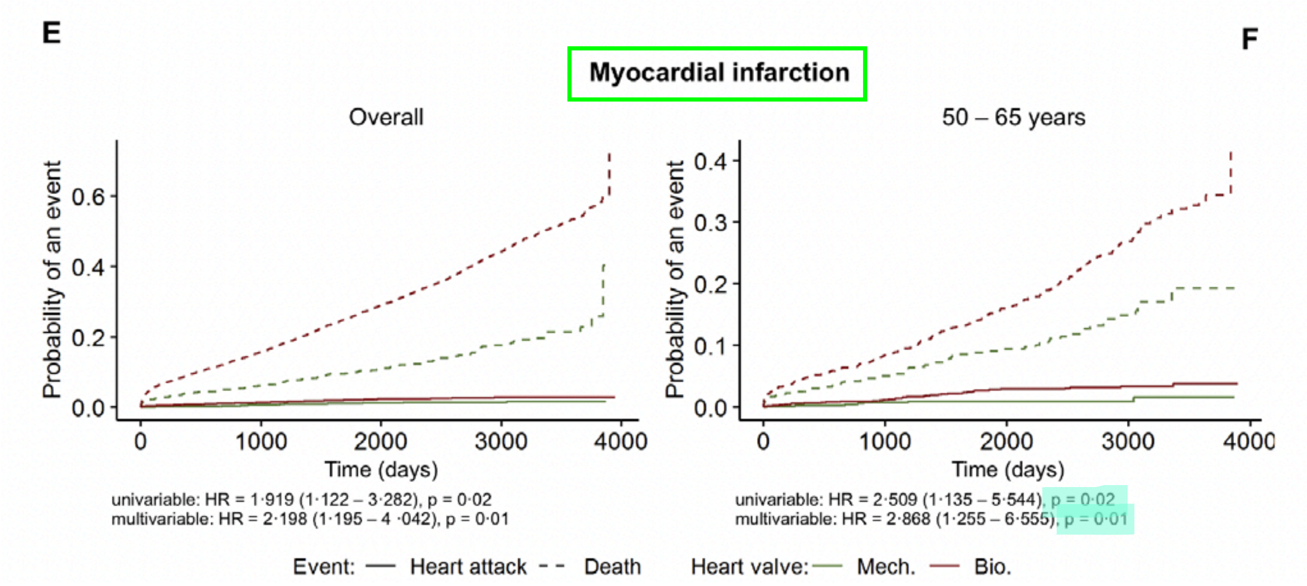


Results PREPRINT - Reoperation, heart failure, myokardial infarction, stroke

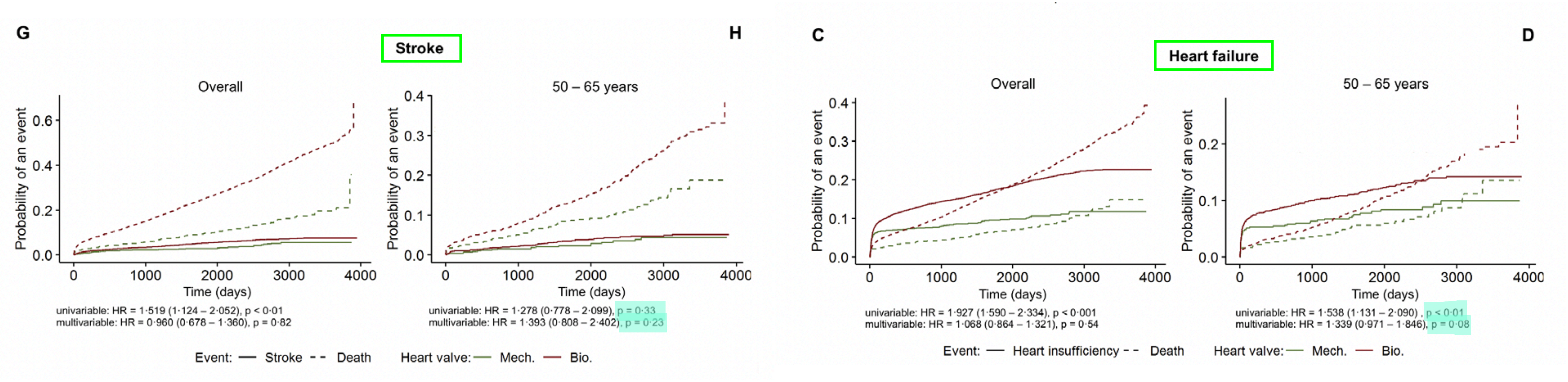
Re-operation (overall)	15 (1·19%)	181 (1·42%)	1·202 (0·710 – 2·033)	0·49	2·827 (1·562 – 5·115)	**<0·001**
Re-operation (<50 years)	5 (1·19%)	13 (4·23%)	3·393 (1·202 – 9·577)	0·02	3·511 (1·240 – 9·938)	0·02
Re-operation (50 – 65 years)	6 (0·85%)	56 (2·93%)	3·411 (1·47 – 7·912)	**<0·01**	3·483 (1·445 – 8·396)	**<0·01**
Re-operation (> 65 years)	4 (2·99%)	112 (1·06%)	0·415 (0·154 – 1·121)	0·08	0·569 (0·204 – 1·584)	0·28
Heart failure (overall)	113 (9·72%)	1965 (17·92%)	1·927 (1·590 – 2·334)	**< 0·001**	1·068 (0·864 – 1·321)	0·54
Heart failure (<50 years)	34 (8·52%)	23 (8·07%)	0·911 (0·539 – 1·540)	0.73	0·897 (0·529 – 1·519)	0·68
Heart failure (50 – 65 years)	51 (7·87%)	205 (11·88%)	1·538 (1·131 – 2·090)	**<0·01**	1·339 (0·971 – 1·846)	0·08
Heart failure (> 65 years)	28 (24·35%)	1737 (19·40%)	0·872 (0·597 – 1·274)	0·48	0·757 (0·518 – 1·106)	0·15
Myocardial infarction (overall)	14 (1·11%)	268 (2·10%)	1·919 (1·122 – 3·282)	0·02	2·198 (1·195 – 4 ·042)	**0·01**
Myocardial infarction (<50 years)	2 (0·48%)	5 (1·63%)	3·150 (0·608 – 16·326)	0·17	3·545 (0·706 – 17·796)	0·12
Myocardial infarction (50 – 65 years)	7 (1·00%)	48 (2·51%)	2·509 (1·135 – 5·544)	0·02	2·868 (1·255 – 6·555)	**0·01**
Myocardial infarction (> 65 years)	5 (3·73%)	215 (2·04%)	0·638 (0·264 – 1·539)	0·32	0·721 (0·298 – 1·749)	0·47
Stroke (overall)	45 (3·58%)	677 (5·32%)	1·519 (1·124 – 2·052)	**<0·01**	0·960 (0·678 – 1·360)	0·82
Stroke (<50 years)	11 (2·62%)	10 (3·26%)	1·235 (0·529 – 2·883)	0·63	1·045 (0·403 – 2·711)	0·93
Stroke (50 – 65 years)	20 (2·85%)	70 (3·66%)	1·278 (0·778 – 2·099)	0·33	1·393 (0·808 – 2·402)	0·23
Stroke (> 65 years)	14 (10·45%)	597 (5·67%)	0·642 (0·380 – 1·083)	0·10	0·569 (0·335 – 0·967)	0·04

Results PREPRINT - Reoperation, Myocardial infarction

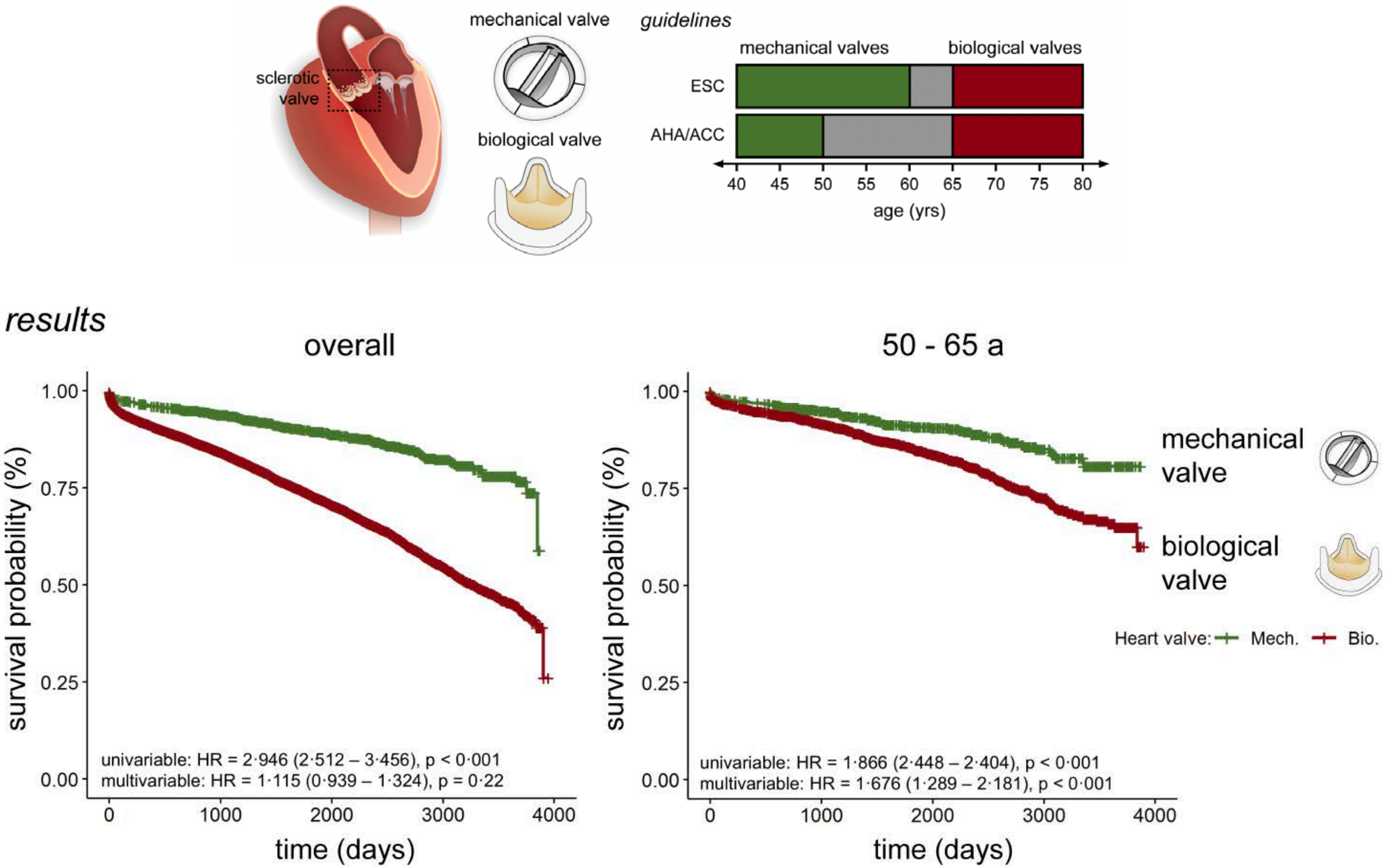




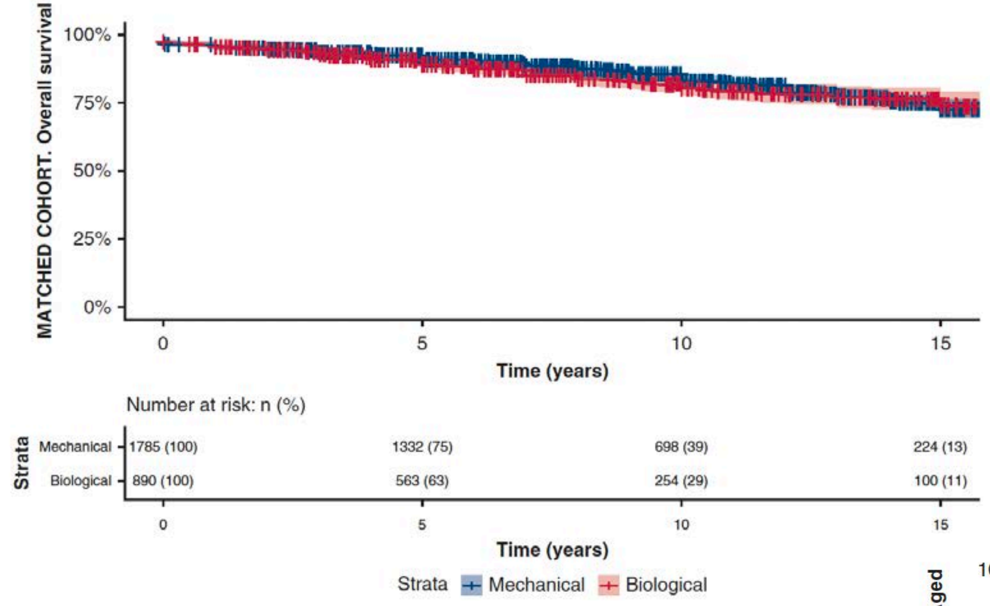
Results PREPRINT - Stroke, Heart failure

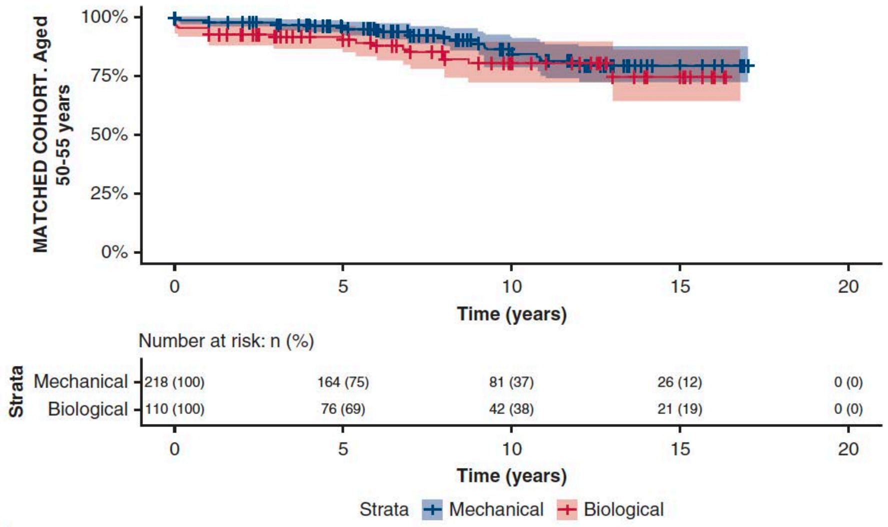


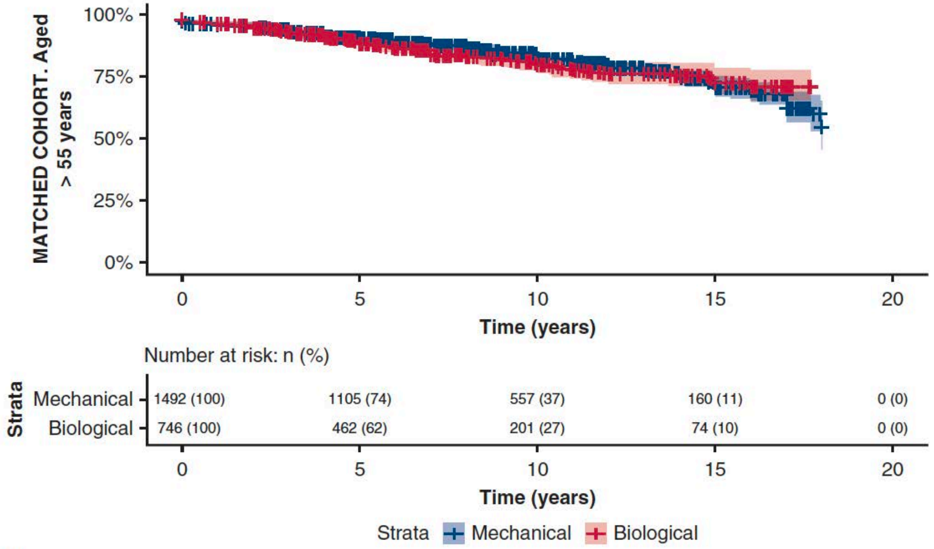
Results PREPRINT



Results PAPER - Long-term survival







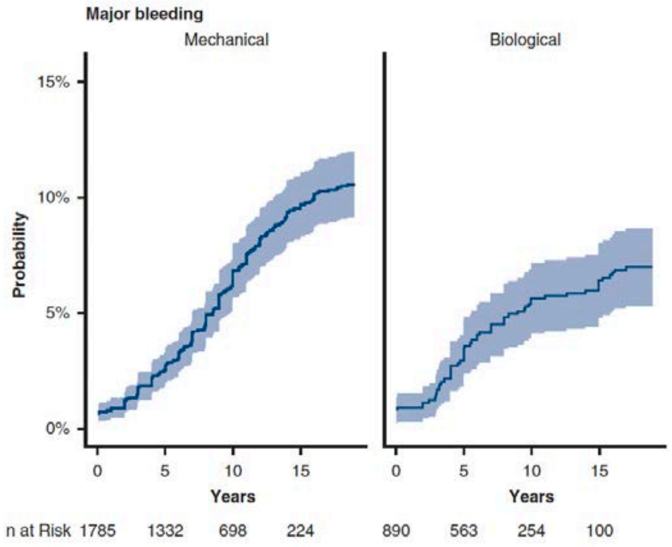
B

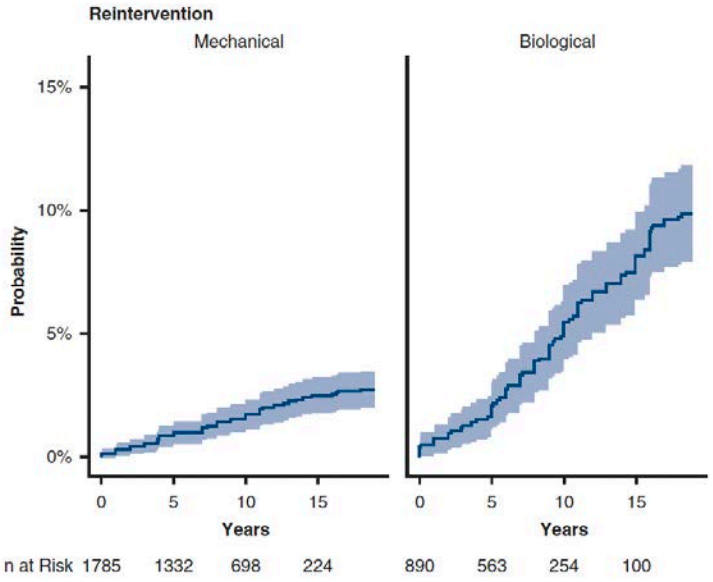
Results PAPER - Bleeding, Reintervention, Stroke

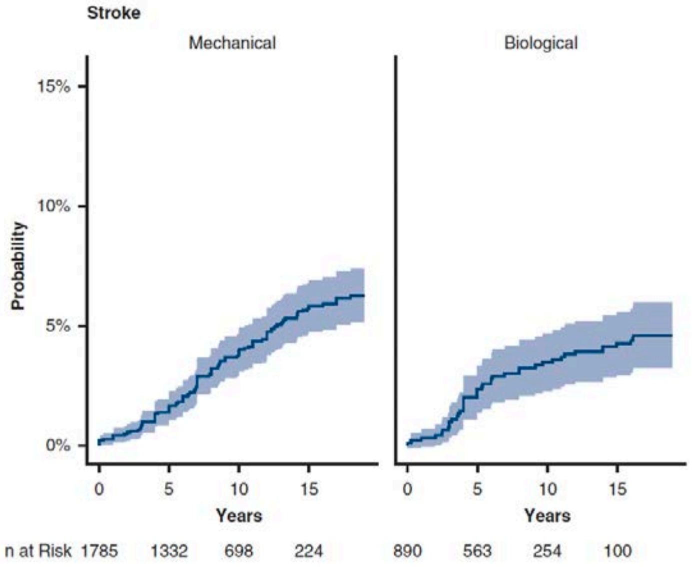
TABLE 2. Follow-up of principal clinical end points (postoperative) in matched sample

End point	Mechanical (n = 1822)	Biological (n = 911)	*P* value
30-Day mortality	55 (3.0)	28 (3.1)	1
Stroke	113 (6.4)	42 (4.7)	.095
Major bleeding	193 (10.9)	63 (7.0)	**.002**
Prostheses reoperation	49 (2.8)	90 (10.1)	**<.001**
Transfusions	390 (22.7)	159 (19.4)	.071
All-cause late mortality	332 (16.9)	164 (16.4)	.808
Cardiac reintervention	262 (14.8)	174 (19.4)	**.003**
Infective endocarditis	47 (2.7)	35 (3.9)	.094
Mean gradient, mm Hg	15.04	16.98	**<.001**
Mean valve size, mm	22.28	22.34	.44
Composite of stroke, bleeding, and reintervention combined for all patients	348 (19.1)	185 (20.3)	.484

Data are presented as n (%), except where otherwise noted. Bold values are statistically significant.







Discussion PREPRINT

- Significantly higher long-term survival in patients with mechanical aortic valve prosthesis than with bioprosthesis
- Implantation of bioprostheses predominates in this age group (contrary to ESC and AHA/ACC guidelines)
- Findings Bioprosthesis:
  - Higher risk of reoperation, myocardial infarction and death after AVR
  - No significantly increased stroke incidence
  - Risk development of heart failure similar for both valve types
- Age limits for implantation of bioprostheses decreased significantly in the last 15 years ➔ Suspected reasons:
  - Relationships between professional societies and the medical device industry
  - Remuneration systems in hospitals

Discussion PREPRINT

- Increased incidence of newly diagnosed heart failure after implantation of a bioprosthesis
- Early immunological host–valve immune reaction
  - Decreased survival rate
  - Increased incidence of reoperation in bioprosthesis recipients
- Alpha-Gal specific immune response ➔ Valve degeneration
- Conservation techniques, development of Gal-free BHVs from pigs with Gal knockout
- Offering humanized valves
- Critical evaluation of overzealous implantation of bioprostheses in patients aged 50-65 years
- Increased mortality with lowering of age limits for bioprosthesis implantation in 50-65 year old patients

Discussion PAPER

- Concordance results: National observational study and ACC/AHA guidelines
- No differences in long-term survival
- Mechanical prostheses: higher risk of stroke, major bleeding
- Bioprostheses: higher risk of reoperation
- Comparison of outcomes before and after 2009: decrease in strokes, major bleeding, and readmissions due to AVR
- Decrease in reoperation risk in patients with bioprostheses due to new anti-calcification properties
- Bio-prosthesis longevity: important factor for prosthesis performance and patient expectation
- Newer oral anticoagulants in bioprostheses : anticoagulation therapy for atrial fibrillation after implantation
- Requirement: Country-specific findings from practice

Conclusion

PAPER

- Bioprosthesis is recommended between 50 and 65 years of age in Spain (mainly patients > 55 years)
- Reason: long-term survival rate and low risk of bleeding compared to mechanical prostheses
- Consideration of risk of reoperation of bioprosthetics > patient education > biological/mechanical prosthesis?

PREPRINT

- No conclusion available so far

5. References

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Thank you for your attention!