XI CONGRESO
SEICAV 2022

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Real Ilustre Colegio de Médicos de Sevilla

SEICAV
Sociedad Española de Infecciones Cardiovasculares

Endocarditis en mujeres ¿En qué son diferentes?

Hospital Universitario Fundación Jiménez Díaz
Grupo quirónsalud

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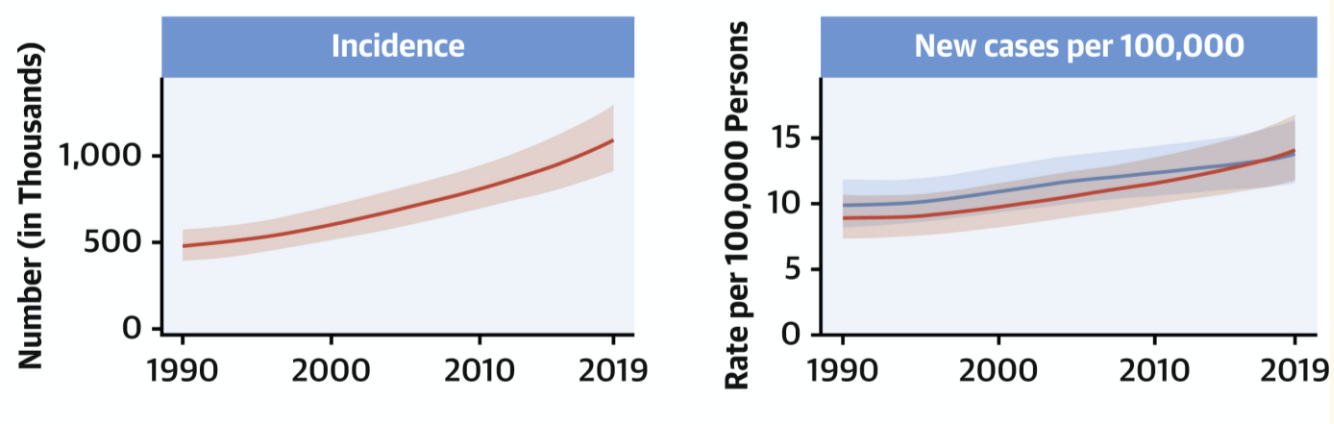
Endocarditis en mujeres ¿En qué son diferentes?

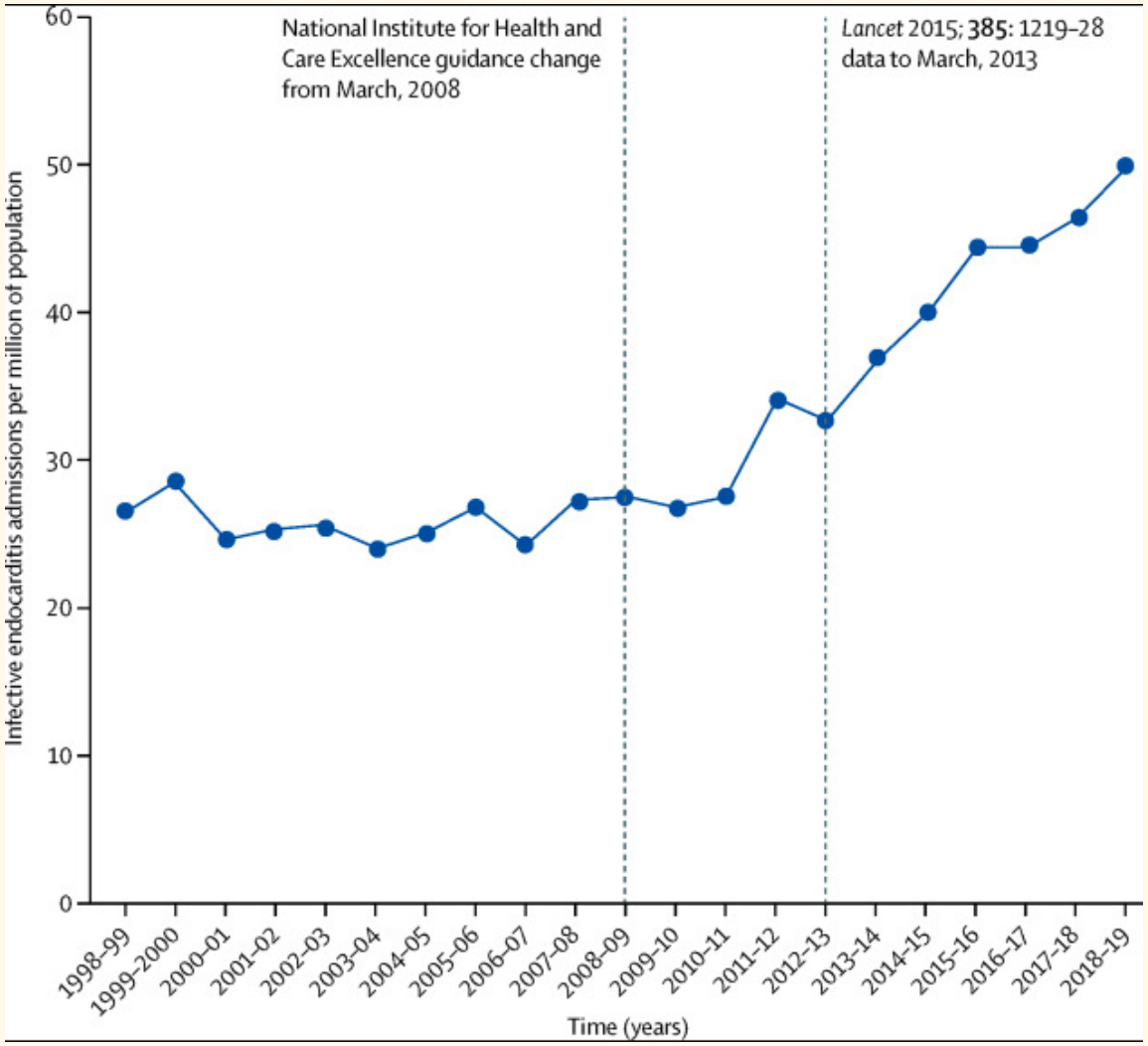
- Epidemiología
- Presentación clínica de la EI
- ¿A que se deben las diferencias en la EI en función del género?
  - Presentación de las enfermedades cardiovasculares
  - Comorbilidades y edad de presentación
  - Etiología
  - Localización
- Sexo femenino como factor pronóstico
- Diferencias en el tratamiento
- Conclusiones

• Epidemiología

- Aumento de la incidencia en los últimos años*
- Mayor severidad de la EI
- Empeoramiento perfil de los pacientes



Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: Update From the GBD 2019 Study



An alarming rise in incidence of infective endocarditis in England since 2009: why?

* Habib G, Erba PA, Iung B Donal E et al. Eur Heart J. 2019;40(39):3222-32.

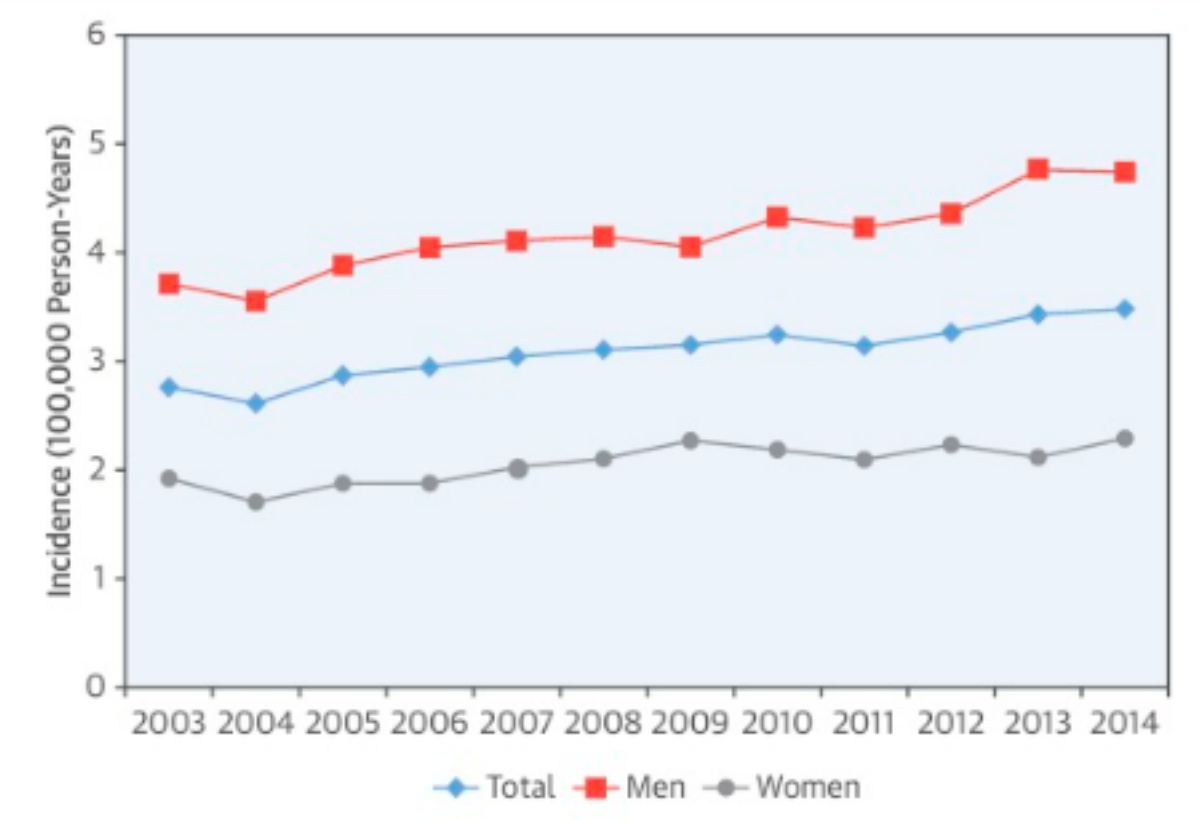
• Epidemiología

- **Diferencias en función del género**

30-40% de las EI en el sexo femenino

	Total (*n* = 3116)
Demography	
Age (years)	
N	3116
Mean ± SD	59.25 ± 18.03
Median (IQR)	63.0 (46.0–73.0)
Age ≥ 65 years	1443/3116 (46.3%)
Age ≥ 80 years	375/3116 (12.0%)
Females (%)	969/3116 (31.1%)

Habib G et al. Results of the ESC-EORP EURO-ENDO registry: a prospective cohort study. Eur Heart J. 2019;40(39):3222-32.



The Evolving Nature of Infective Endocarditis in Spain: A Population-Based Study (2003 to 2014)

- Presentación clínica

Women were older and had a higher proportion of hypertension (HT) and previous valve diseases, whereas men had more chronic obstructive pulmonary disease (COPD), peripheral arteriopathy, liver disease, renal failure, ventricular dysfunction and conduction disturbances.

Regarding IE location, it is important to note that the most affected valves were the aortic valve in men (50.6% vs 32.4% in women) and mitral valve in women (48.7% vs 29.5% in men).

Analysis of sex differences in the clinical presentation, management prognosis of infective endocarditis in Spain. Heart Br Card Soc. 2021

Compared with men, women were older (64.3 years vs 60.4 years, p=0.005), received chronic haemodialysis more often (5.2% vs 1.9%, p=0.04), had a mitral valve IE more often (50.0% vs 35.8%, p=0.02), developed a septic shock less often (4.0% vs 9.0%, p=0.05), underwent EVS less often (37.0% vs 52.4%, p=0.001), and had similar inhospital mortality rate (20.1% vs 20.0%, p=0.96) and 1-year mortality rate

Relationships between sex, early valve surgery and mortality in patients with left-sided infective endocarditis analysed in a population-based cohort study. Heart Br Card Soc. 2014

Diferencias en la presentación afectación y características

Women were older than men, and more women than men were taking immunosuppressants, although more men had human immunodeficiency virus infections than women. Charlson index on admission, rate of nosocomial IE, culprit pathogens, and rate of negative culture were similar in men and women. There were no differences in underlying cardiac disease. Infection more frequently involved the mitral valve in women than in men.

Sex differences in native-valve infective endocarditis in a single tertiary-care hospital. Am J Cardiol. 2010

¿A que se deben estas diferencias en la EI en función del género?

1) Presentación de las enfermedades cardiovasculares en las mujeres

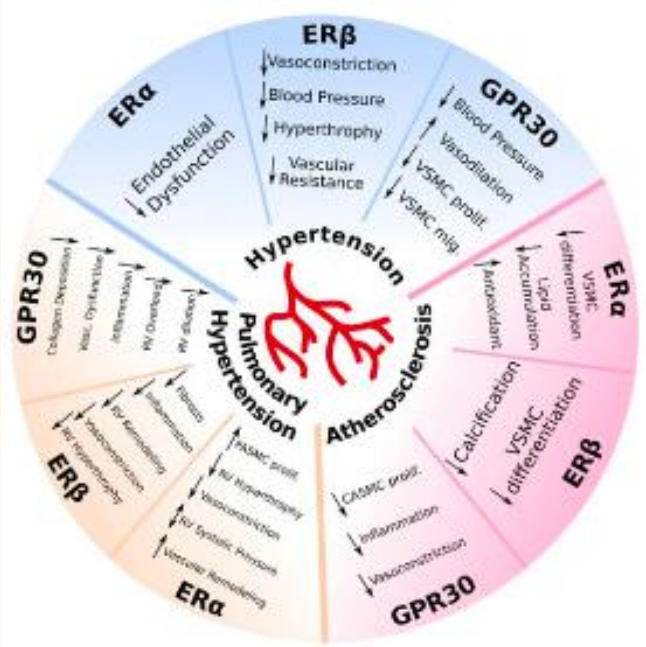
2) Comorbilidades y edad de presentación

3) Etiología

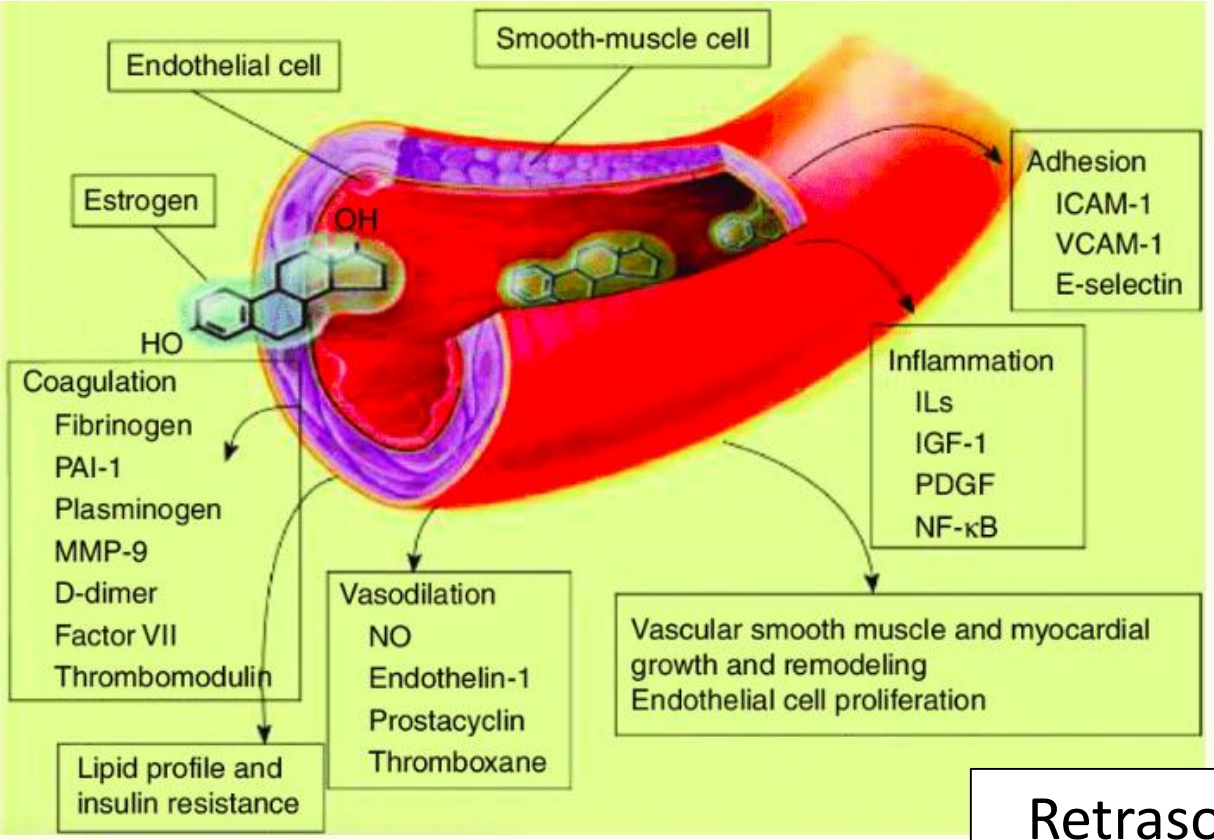
4) Localización

1) Diferente presentación de las enfermedades cardiovasculares

Poder protector de los estrógenos*



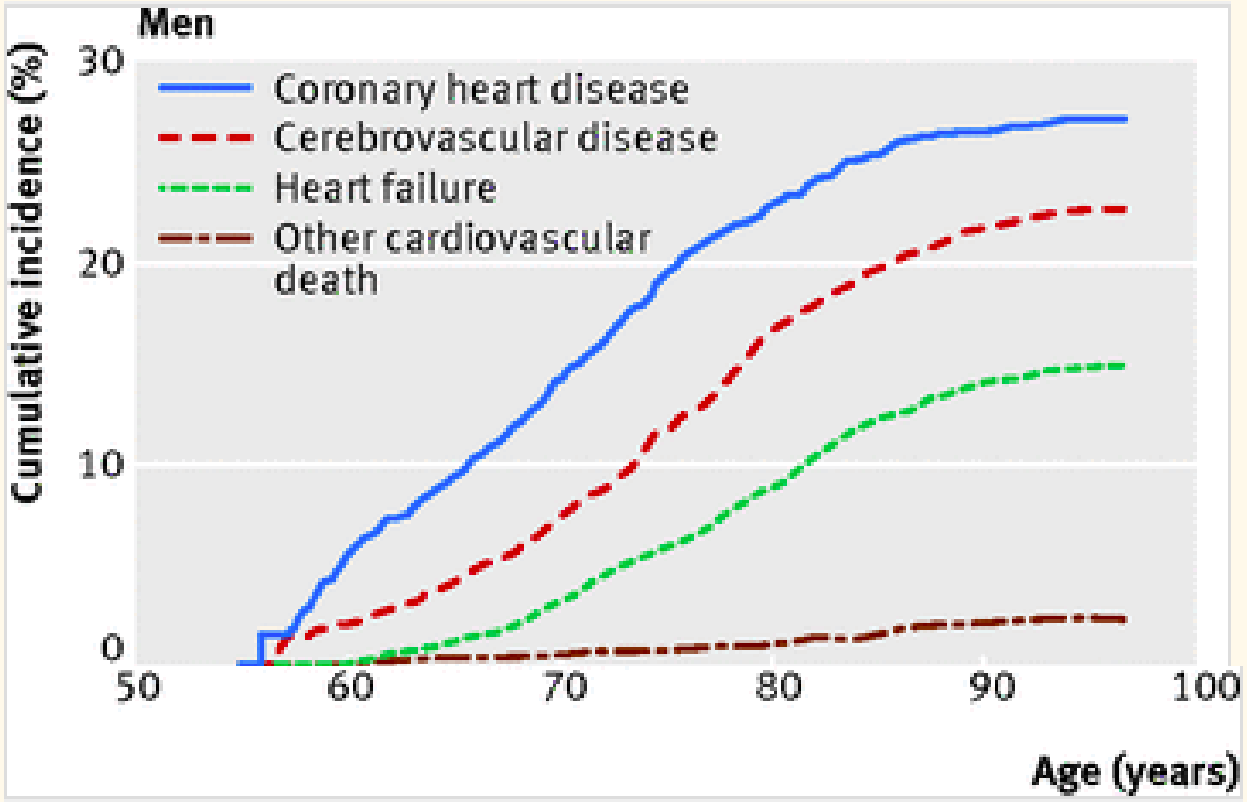
Previene el daño endotelial precoz

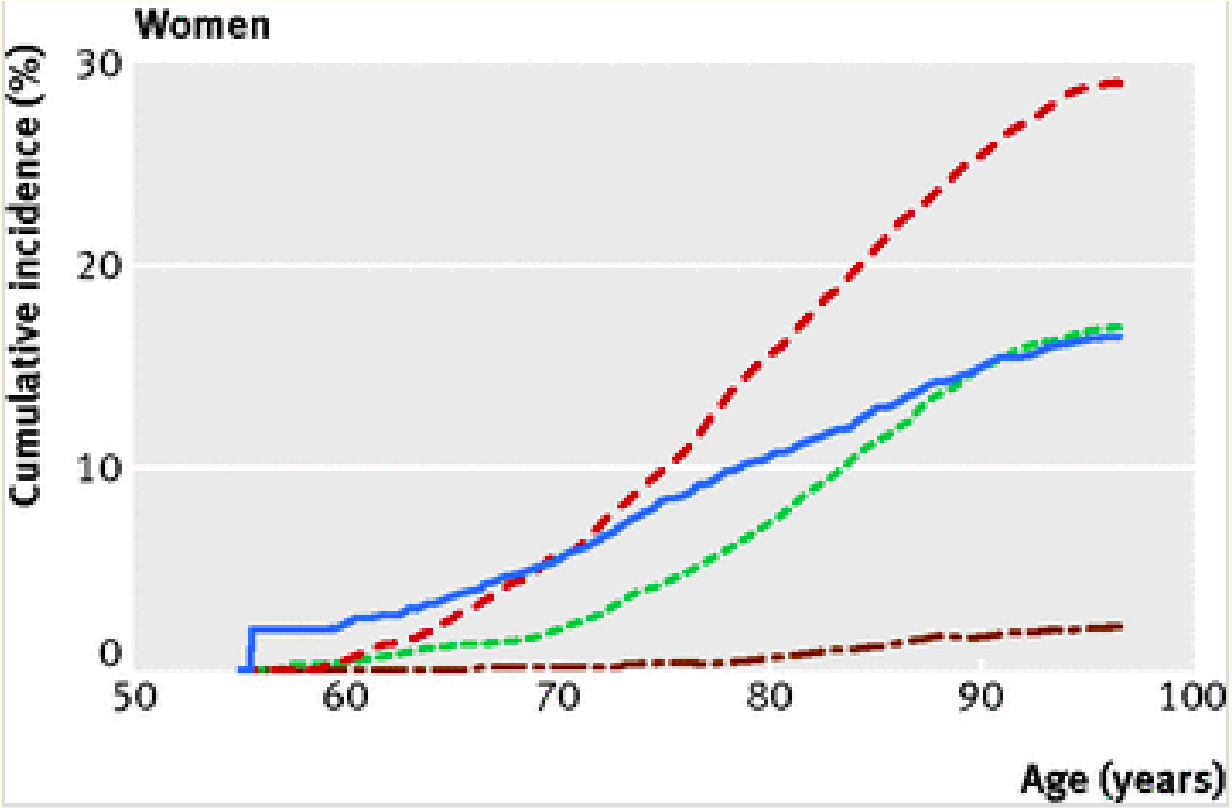


Retraso en la aparición de las enfermedades cardiovasculares

* The Role of Estrogen Receptors in Cardiovascular Disease. Int. J. Mol. Sci. 2020

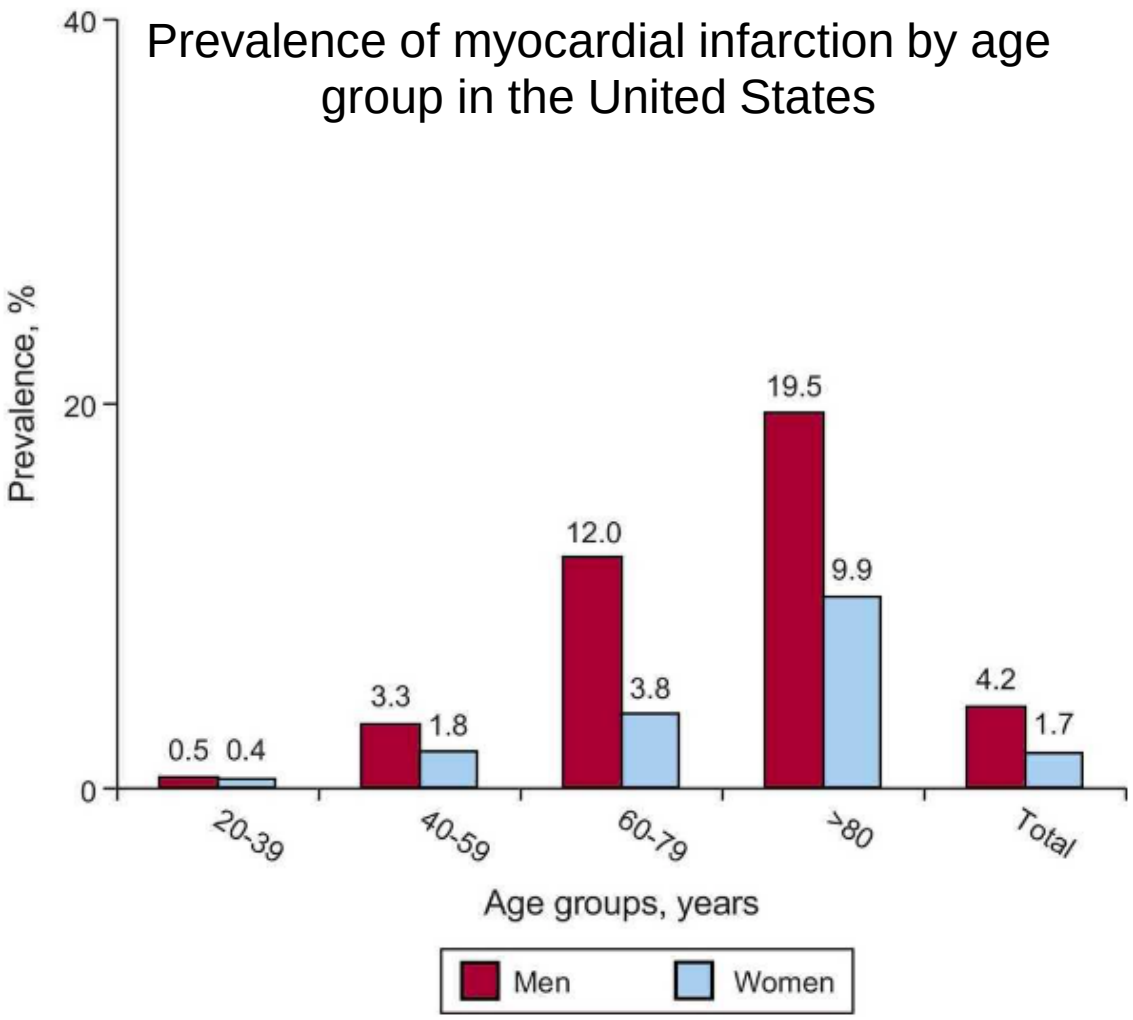
Retraso en la aparición de las enfermedades cardiovasculares



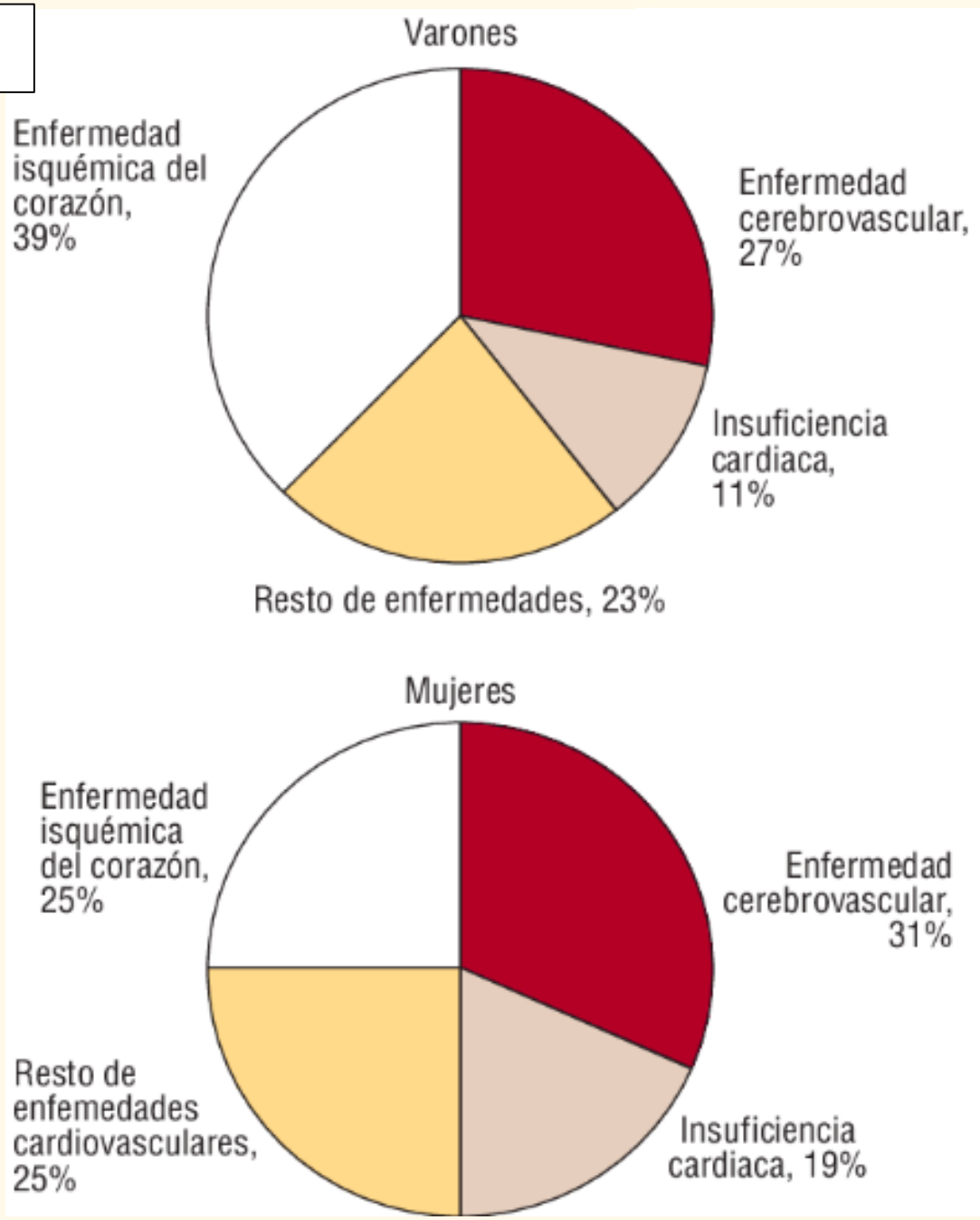


*Sex differences in lifetime risk and first manifestation of cardiovascular disease: prospective population based cohort study BMJ 2014

Diferencia en tipo de enfermedad cardiovascular



The Epidemiology of Coronary Heart Disease. RevEspCardiol 2014



Epidemiología de las enfermedades cardiovasculares en España. RevEspCardiol 2006

CENTRAL ILLUSTRATION: Sex Differences in Valvular Heart Disease

Sex Differences and Similarities in Valvular Heart Disease

Jacqueline T. DesJardin, Joanna Chikwe, Rebecca T. Hahn, Judy W. Hung and Francesca N. Delling

Aortic Valve (women vs men)

Aortic Stenosis

Epidemiology

- Less Valvular Calcium
- More Valvular and intra-myocardial Fibrosis
- Worse Symptoms
- More Advanced NYHA Class

Diagnostics

- Severe AV Calcification > 1,300 Agatston Units (>2,000 for men) on CT imaging
- More concentric remodeling and low-flow low-gradient AS: need for sex-specific stroke volume indexed

Treatment

- Less likely to receive timely intervention
- TAVR: No sex differences in outcomes
- Mortality disproportionately higher for older women and women with pulmonary hypertension
- SAVR: Increased mortality in women

Aortic Regurgitation

Epidemiology

- Rarer
- Less Bicuspid AV, aortopathies, endocarditis
- Older at diagnosis

Diagnostics

Use sex and size-specific LV and aortic dimensions

Treatment

Delayed referral = higher mortality

Bicuspid Aortic Valve

- 2:1 male-female ratio
- More AS
- Less aortopathies and AR
- Aortopathy screening; avoid pregnancy if aorta > 45 mm

Mitral Valve (women vs men)

Mitral Stenosis

Epidemiology

- More common
- More rheumatic heart disease
- More mitral annular calcification (vs men have more leaflet calcification)

Diagnostics

Need for sex and size specific RV and LA dimensions

Treatment

? Sex-differences with balloon valvuloplasty

Mitral Regurgitation

Epidemiology

- More Mitral Valve Prolapse
- Thicker leaflets
- Worse HF symptoms
- Higher risk of MR with LV dilation or myocardial infarction

Diagnostics

- Surgical guidelines are neither indexed to body size nor sex-specific
- Need for indexed and sex-specific parameters (e.g. LV size)

Treatment

- Worse outcomes with MV surgery
- More often receive mitral valve replacement (rather than repair)
- Less reduction in HF symptoms and hospitalizations after transcatheter edge-to-edge repair

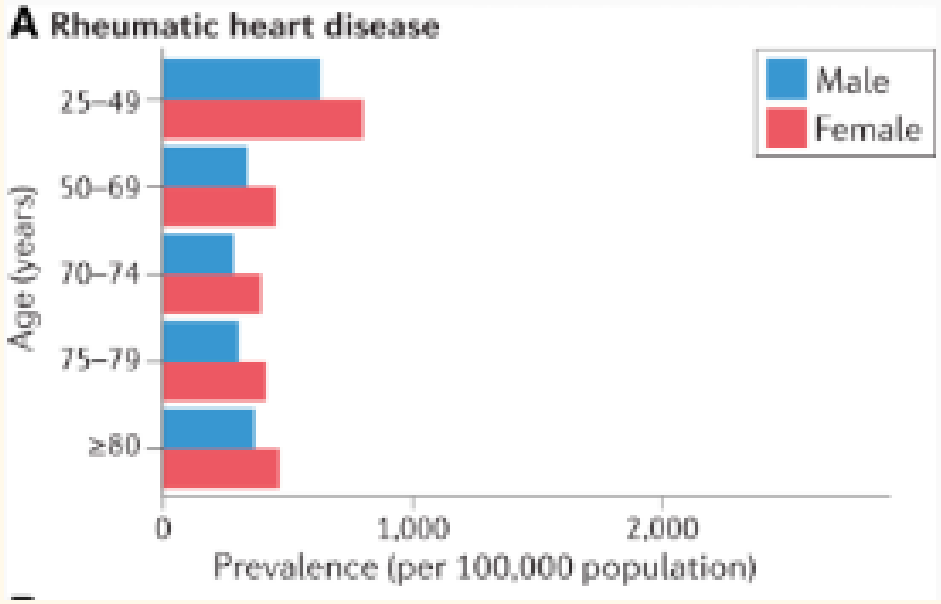
Mitral Valve Prolapse

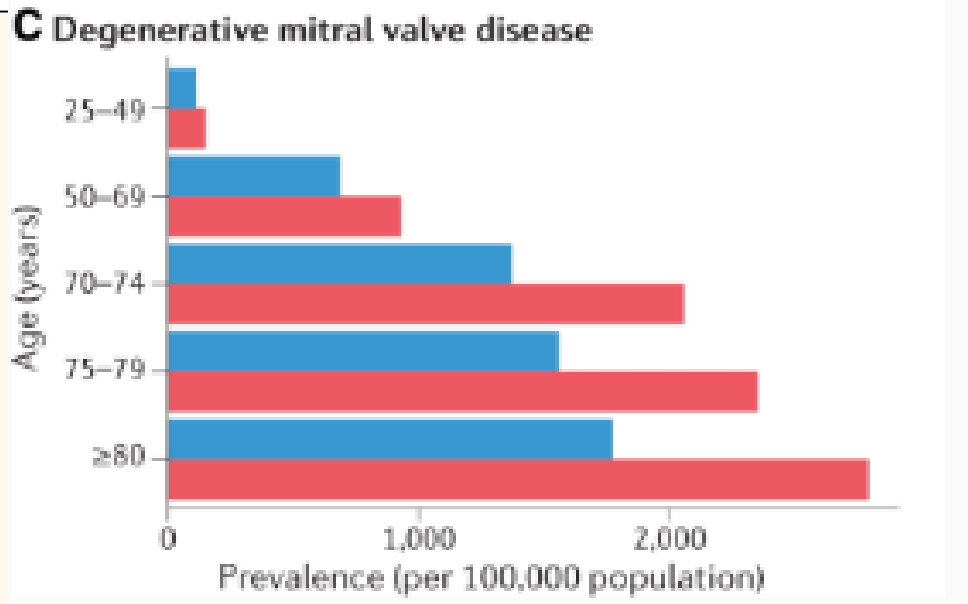
- More common
- Less severe MR
- Less posterior prolapse and flail
- More bileaflet and anterior prolapse

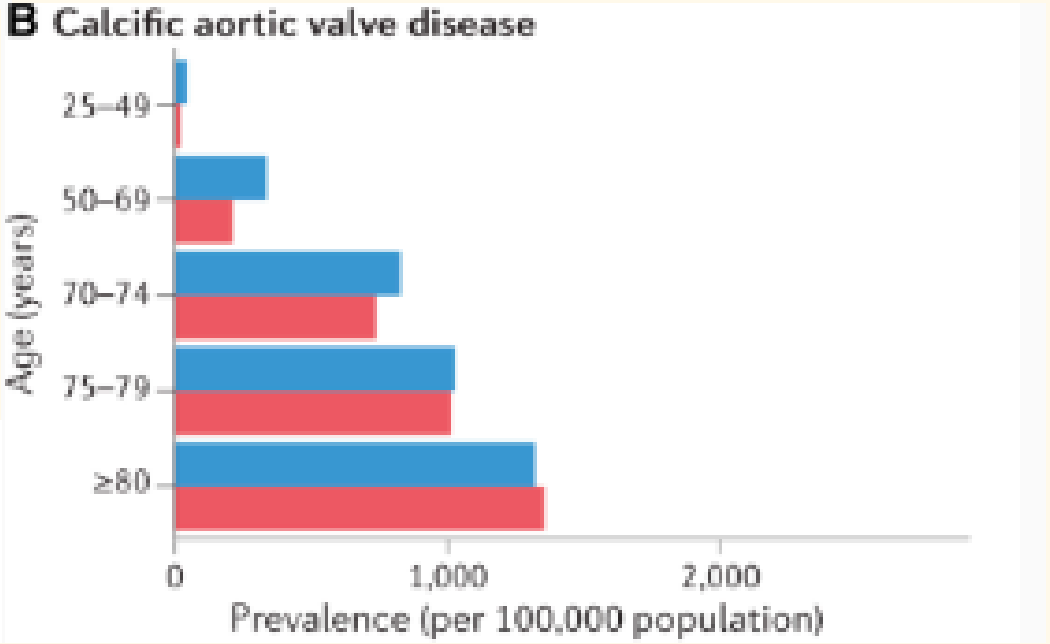
Sex-Based Disparities in Valvular Heart Disease

1. Under-representation in research
2. Lack of sex-specific disease criteria
3. Limited use of BSA-indexed values
4. Under-recognition of severe VHD
5. Delayed referral for intervention
6. Greater symptom burden
7. Worse outcomes in women

Diferencia en tipo de enfermedad cardiovascular







Sex Differences and Similarities in Valvular Heart Disease

Jacqueline T. DesJardin, Joanna Chikwe, Rebecca T. Hahn, Judy W. Hung and Francesca N. Delling

Noticias cardiología

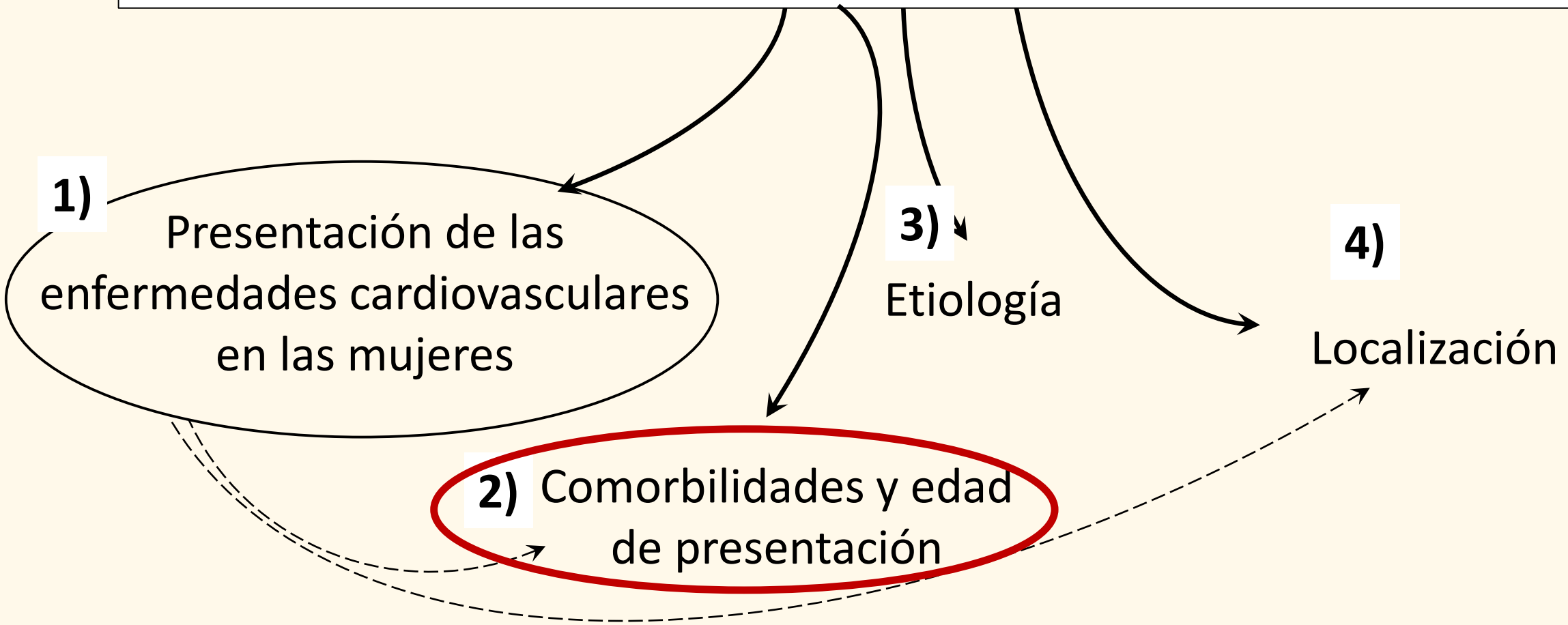
Las mujeres acuden más a urgencias que los hombres, pero ingresan menos en cardiología

Tipo de prueba	Varón (N = 1,3451)	Mujer (N = 1,8481)	p
Ecocardio	284 (21%)	335 (18%)	0,025
Holter	213 (16%)	370 (20%)	0,002
Procedimientos invasivos electrofisiología	27 (2%)	21 (1,1%)	0,045
Procedimientos invasivos hemodinámica	42 (3,1%)	22 (1,2%)	< 0,001
Pruebas detección isquemia	358 (27%)	517 (28%)	0,395
Pruebas de imagen	100 (7,4%)	130 (7%)	0,665
Consulta sucesiva (CAR)	307 (23%)	424 (23%)	0,937

Del total de 6.042 consultas analizadas, el 59% corresponden a mujeres, quienes presentan mayor edad: 64 años de media frente a 59 años en el caso de los hombres. También ellas registran un mayor número de visitas a urgencias durante el seguimiento: el 54,9% frente al 47,7% de los varones. Sin embargo, solo el 6,6% de las mujeres acaban ingresando en el hospital frente al 8,8% de ellos.

"La mayor frecuencia de consultas en urgencias en las mujeres puede explicarse por una mayor conciencia de enfermedad o una mayor preocupación por los síntomas cardiovasculares en ellas. Por el contrario, la menor frecuencia de ingresos hospitalarios en las mujeres puede deberse a una menor preocupación por un padecimiento grave por parte de los médicos que atienden a estas pacientes, en base a los síntomas por los que consultan las mujeres", apunta la especialista en cardiología.

¿A que se deben estas diferencias en la EI en función del género?



2) Edad de presentación y comorbilidades

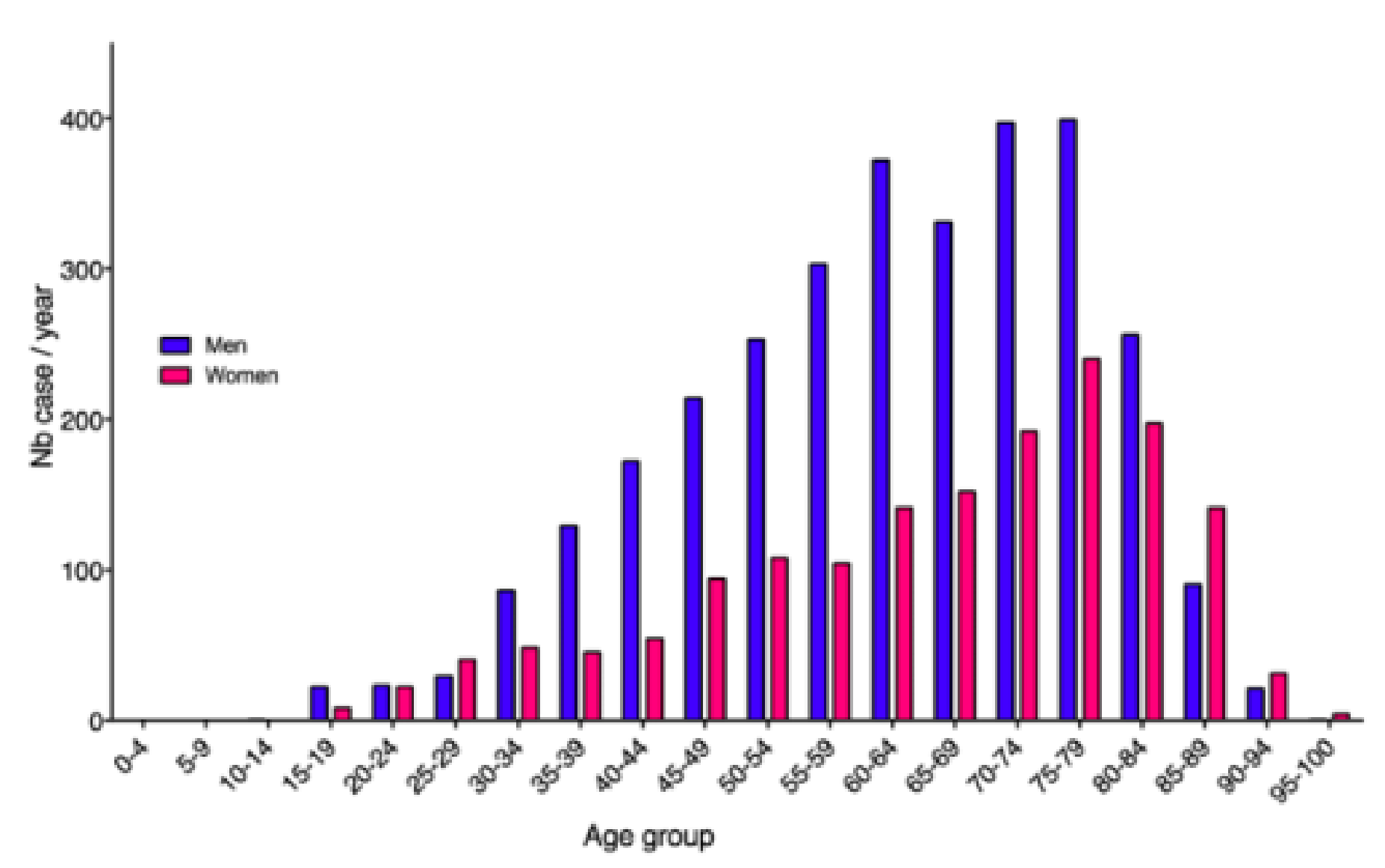
Diferencias en la presentación de las enfermedades cardiovasculares

Comorbilidades

Localización

Edad

Edad de presentación



Epidemiology of infective endocarditis in French intensive care units over the 1997-2014 period - From CUB-Réa Network

Table 1. Baseline Patient Characteristics Stratified by Sex for Infective Endocarditis Hospitalizations From 2004 to 2015

Characteristics	Men (N=45 640)	Women (N=36 302)	*P* value
Age, mean (SD), y	59.85 (17.85)	62.58 (19.62)	<0.001

Sex Differences in the Utilization and Outcomes of Cardiac Valve Replacement Surgery for Infective Endocarditis: Insights From the National Inpatient Sample. J Am Heart Assoc. 2021

Table 1
Differences in clinical and echocardiographic characteristics of infective endocarditis between men and women

Variable	Overall (n = 271)	Women (n = 88)	Men (n = 183)	p Value*
Baseline characteristics				
Age (years)	57 ± 18	63 ± 16	58 ± 18	0.006

Sex differences in native-valve infective endocarditis in a single tertiary-care hospital. Am J Cardiol. 2010

Table 1 Patient characteristics by gender

	Total 3451	Female sex 1105 (32.0%)	Male sex 2346 (67.9%)	P value
Baseline characteristics				
Age (years), mean (SD)	65.7 (14.6)	68.4 (14.9)	64.5 (14.4)	<0.001

Analysis of sex differences in the clinical presentation, management and prognosis of infective endocarditis in Spain. Heart Br Card Soc. 2021

Comorbilidades

Diabetes Mellitus
Fracaso Renal
Inmunosupresión

Table 1 Characteristics of infective endocarditis (IE) according to sex

	Men			Women			
	N=466 (75.2%)			N=154 (24.8%)			
	N	%/mean	SD	N	%/mean	SD	p Value*
(A) Patient's characteristics							
Age (years)	466	60.4	14.5	154	64.3	15.9	0.005
Hypertension	171	36.7		70	45.5		0.05
Diabetes mellitus	83	17.8		38	24.7		0.06
Cancer	62	13.3		24	15.6		0.48
Haemodialysis	9	1.9		8	5.2		0.04
Immunosuppression	29	6.2		10	6.5		0.90
Current smoker	119	26.3		21	14.0		0.002
Intravenous drug users	15	3.2		3	1.9		0.58

Relationships between sex, early valve surgery and mortality in patients with left-sided infective endocarditis analyzed in a population-based cohort study. Heart Br Card Soc. 2014

Table 1
Differences in clinical and echocardiographic characteristics of infective endocarditis between men and women

Variable	Overall (n = 271)	Women (n = 88)	Men (n = 183)	p Value*
Baseline characteristics				
Age (years)	57 ± 18	63 ± 16	58 ± 18	0.006
Co-morbidities				
Type 2 diabetes mellitus	50 (18%)	18 (20%)	32 (18%)	0.67
Hemodialysis	15 (6%)	9 (10%)	6 (3%)	0.05
HIV infection	20 (7%)	1 (1%)	19 (11%)	0.01
Cancer	38 (14%)	12 (14%)	26 (14%)	0.9
Immunosuppression therapy	18 (7%)	12 (14%)	6 (3%)	0.006

Sex differences in native-valve infective endocarditis in a single tertiary-care hospital. Am J Cardiol. 2010

Analysis of sex differences in the clinical presentation, management and prognosis of infective endocarditis in Spain

Laura Varela Barca ,[1] Laura Vidal-Bonnet,[2] MC Fariñas,[3] Patricia Muñoz,[4,5] Maricela Valerio Minero,[4] Arístides de Alarcón,[6] Encarnacion Gutiérrez Carretero,[7] Manuel Gutiérrez Cuadra,[3] Asuncion Moreno Camacho,[8] Xabier Kortajarena Urkola,[9] Josune Goikoetxea Agirre,[10] Guillermo Ojeda Burgos,[11] Luis Eduardo López-Cortés,[12] JC Porres Azpiroz,[13] Jose Lopez-Menendez ,[14] GAMES Investigators

El Aórtica

Mayores
HTA
DM
NYHA>III

	Total 1496	Female sex 354 (23.7%)	Male sex 1142 (76.3%)	p
Age (years), median (SD)	**67.05**	**69.9 (13.19)**	**66.2 (13.76)**	**<0.001**
Vegetations, n (%)	1119 (74.9)	264 (74.6)	855 (74.9)	0.93
HTA, n (%)	**879 (58.9)**	**232 (65.5)**	**647 (56.8)**	**0.005**
Previous surgery, n (%)	674 (45.1)	168 (47.6)	506 (44.4)	0.51
DL, n (%)	595 (39.9)	137 (38.9)	458 (40.2)	0.57
Renal failure, n (%)	571 (38.2)	125 (35.3)	446 (39.1)	0.43
NYHA >III, n (%)	501 (33.5)	127 (35.9)	374 (32.8)	0.28
LEVF disfunction, n (%)	463 (30.9)	82 (23.2)	381 (33.4)	<0.001
Peripheral Embolism, n (%)	454 (30.4)	96 (27.2)	358 (31.4)	0.07
DM, n (%)	**444 (29.7)**	**119 (33.6)**	**325 (28.5)**	**0.14**
Paravalvular abscess, n (%)	408 (27.3)	92 (25.9)	316 (27.7)	0.39
Shock, n (%)	293 (19.6)	70 (19.8)	223 (19.5)	0.92
COPD, n (%)	287 (19.2)	45 (12.7)	242 (21.2)	<0.001
Stroke, n (%)	270 (18.1)	71 (20.1)	199 (17.4)	0.24
S.aureus, n (%)	232 (15.5)	62 (17.5)	170 (14.9)	0.23
Conduction disturbances, n (%)	204 (13.6)	41 (11.6)	163 (14.3)	0.43
Severe regurgitation, n (%)	153 (10.2)	28 (7.9)	125 (10.9)	0.14
Native, n (%)	837 (55.9)	193 (54.5)	644 (56.4)	0.53
Prothesis, n (%)	655 (43.8)	161 (45.5)	494 (43.3)	0.46

Analysis of sex differences in the clinical presentation, management and prognosis of infective endocarditis in Spain

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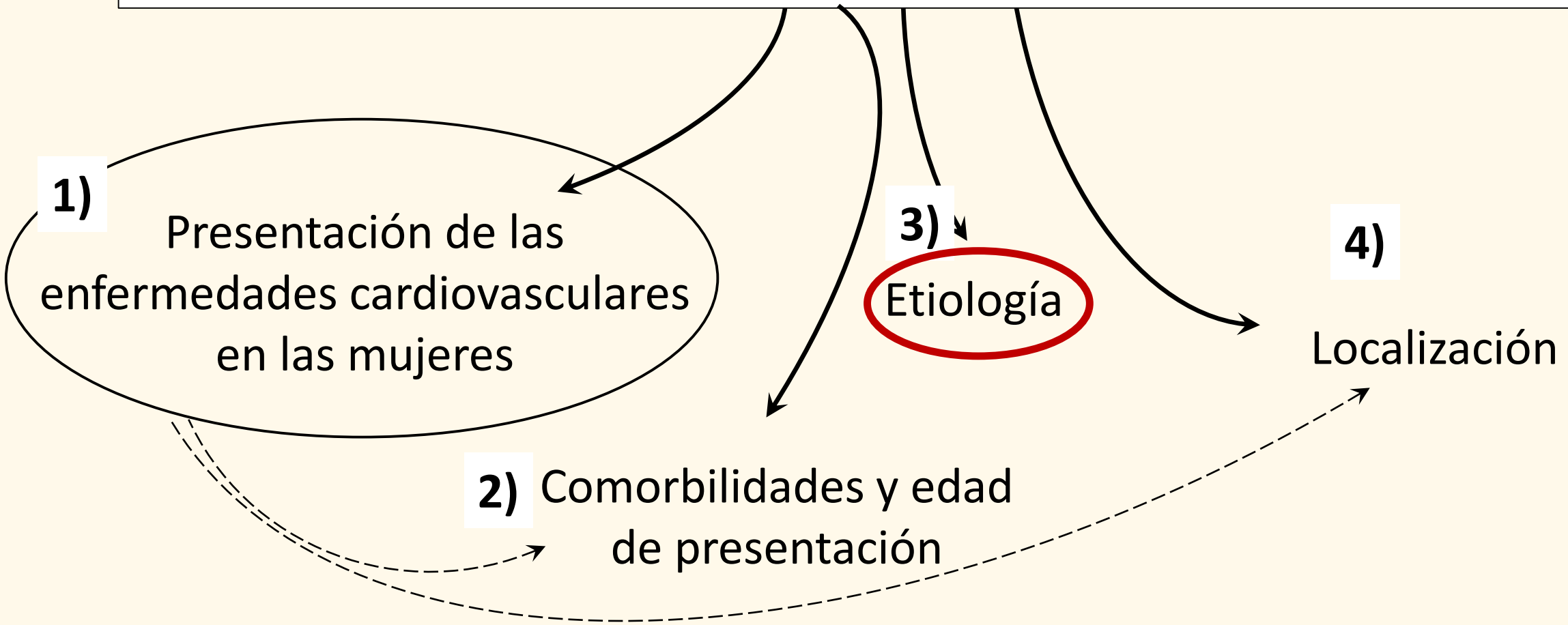
EI Mitral

Mayores
HTA
DM
DL

	Total 1208	Female sex 530 (43.9%)	Male sex 678 (56.1%)	p
Age (years), median (SD)	**66.8 (13,8)**	**70.1 (13.8)**	**64.3 (13.5)**	**<0.001**
Vegetations, n (%)	1022 (84.7)	459 (86.6)	563 (83.2)	0.27
HTA, n (%)	**678 (56.3)**	**331 (62.8)**	**347 (51.3)**	**<0.001**
DL, n (%)	**430 (35.7)**	**207 (39.2)**	**223 (32.9)**	**0.05**
Renal failure, n (%)	414 (34.3)	178 (33.6)	236 (34.8)	0.89
Peripheral embolism, n (%)	412 (34.1)	171 (32.3)	241 (35.6)	0.49
S.aureus, n (%)	372 (30.8)	183 (34.5)	189 (27.9)	0.01
NYHA >III, n (%)	368 (30.5)	180 (33.9)	188 (27.7)	0.02
Previous cardiac surgery, n (%)	364 (30.2)	183 (34.7)	181 (26.7)	0.008
DM, n (%)	**351 (29.1)**	**156 (29.4)**	**195 (28.8)**	**0.14**
LEVF disfunction, n (%)	292 (24.2)	102 (19.3)	190 (28.0)	<0.001
Stroke, n (%)	2281 (23.3)	117 (22.1)	164 (24.2)	0.05
Shock, n (%)	261 (21.6)	127 (23.9)	134 (19.8)	0.08
COPD, n (%)	196 (16.2)	55 (10.4)	141 (20.8)	<0.001
Paravalvular abscess, n (%)	135 (11.2)	66 (12.5)	69 (10.2)	0.34
New conduction disturbances, n (%)	86 (7.1)	39 (7.4)	47 (6.9)	0.69
Severe valve regurgitation, n (%)	79 (6.5)	35 (6.6)	44 (6.5)	0.38
Native, n (%)	922(76.3	381 (71.9)	541 (79.8)	0.001
Prothesis, n (%)	284 (23.5)	149 (28.1)	135 (19.9)	0.001

¿A que se deben estas diferencias en la EI en función del género?



3) Etiología

Mayor porcentaje de Gram negativos y HC negativos en mujeres
Staphylococcus coagula negativo en Hombres

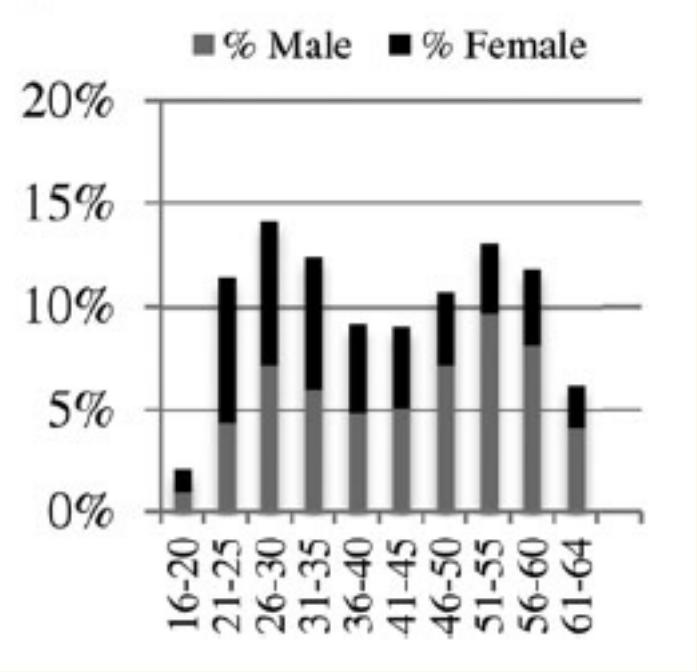
	Males (*n* = 131)	Females (*n* = 83)	*P* Value
Streptococci (*n*, %)	25 (19.7)	20 (25.0)	0.390
Enterococci (*n*, %)	16 (12.6)	10 (12.5)	1.000
Staph. aureus (*n*, %)	33 (26.0)	17 (21.3)	0.506
Coagulase negative staph. (*n*, %)	19 (15.0)	3 (3.8)	0.011
Gram negative bacilli (*n*, %)	6 (4.7)	5 (6.3)	0.753
HACEK (*n*, %)	4 (3.1)	1 (1.3)	0.651
Culture negative (*n*, %)	11 (8.7)	19 (23.8)	0.004
Other (*n*, %)	13 (10.2)	5 (6.3)	0.449
Type of streptococci			
Enterococci	16 (12.6)	10 (12.0)	0.61
Strep pneumoniae	1 (0.8)	1 (1.2)	
Strep viridans	14 (10.7)	4 (4.8)	
Strep oralis	1 (0.8)	3 (3.6)	
Strep group G	1 (0.8)	1 (1.2)	
Strep bovis	6 (4.6)	6 (7.2)	
Strep group B	1 (0.8)	1 (1.2)	
Other strep species	2 (1.5)	3 (3.6)	
Non-strep	90 (68.7)	54 (54.1)	

Sex Differences in Infective Endocarditis. Am J Med Sci. 2021

- Origen genitourinario de la EI en mujeres
- Mayor proporción de EI en ADVP en hombres

↓

Diferencias en agente causal y origen de las EI

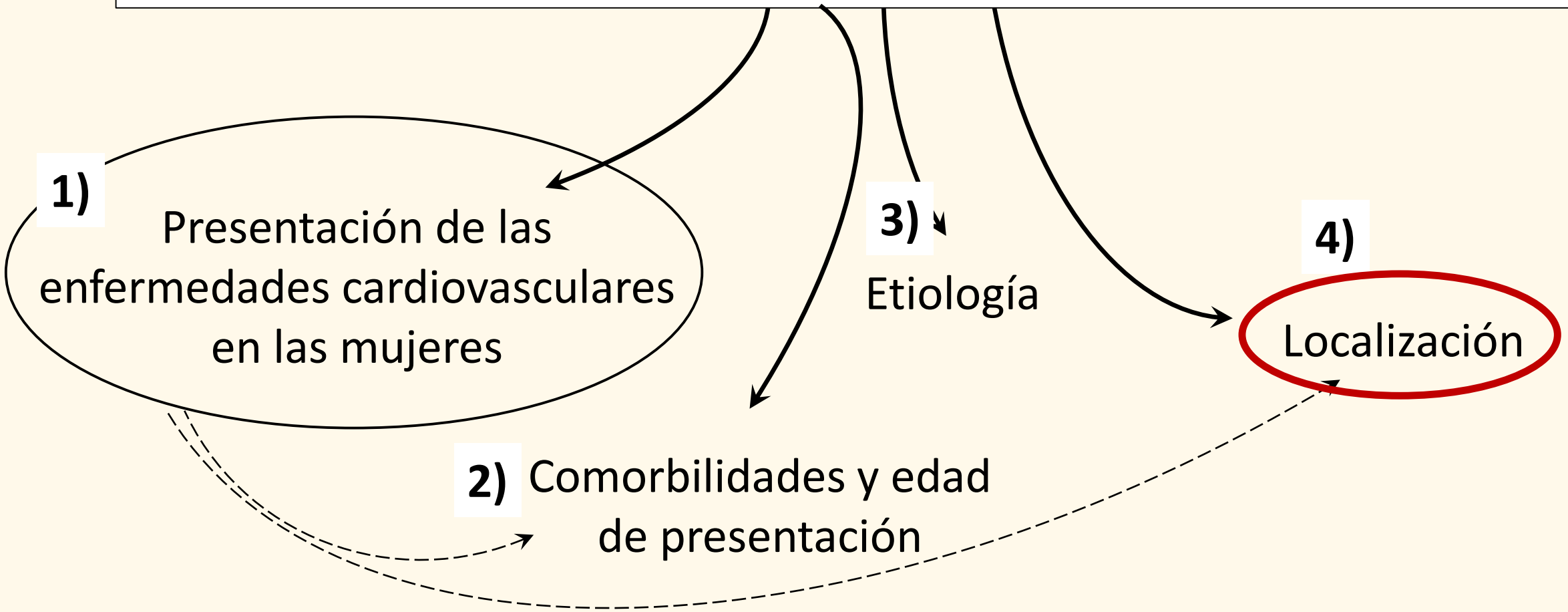


Increasing Infectious Endocarditis Admissions Among Young People Who Inject Drugs. Open Forum Infectious Diseases 2016

Characteristics	Men (N=45 640)	Women (N=36 302)	*P* value
Risk factors and comorbidities			
Drug abuse	19.73%	15.54%	<0.001
Congenital heart disease	5.22%	3.16%	<0.001
Hepatitis C	12.69%	11.39%	<0.001
Chronic rheumatic heart disease	8.83%	9.16%	0.099

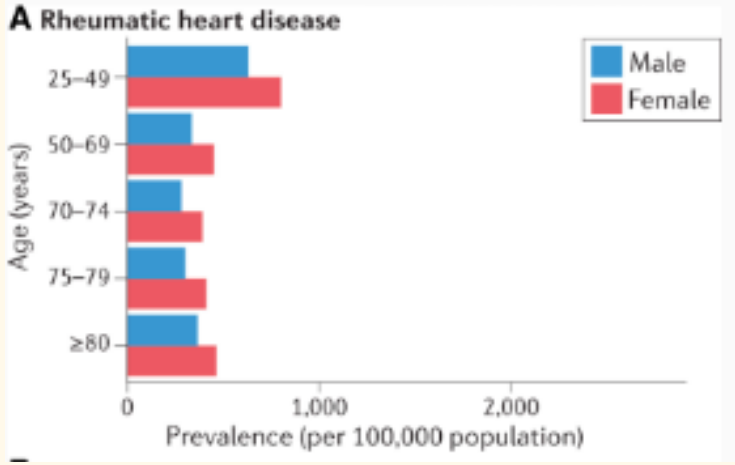
Sex Differences in the Utilization and Outcomes of Cardiac Valve Replacement Surgery for Infective Endocarditis: Insights From the National Inpatient Sample. J Am Heart Assoc. 2021

¿A que se deben estas diferencias en la EI en función del género?



4) Localización de la EI

EI aórtica - sexo masculino
EI mitral -sexo femenino



	Total 3451	Female sex 1105 (32.0%)	Male sex 2346 (67.9%)	P value
Affected valve				
Native, n (%)	2341 (67.9)	731 (66.2)	1611 (68.7)	0.15
Prosthesis, n (%)	1135 (32.9)	383 (34.7)	752 (32.1)	0.13
Aortic, n (%)	**1516 (43.9)**	**358 (32.4)**	**1158 (50.6)**	**<0.001**
Mitral, n (%)	**1231 (35.7)**	**538 (48.7)**	**693 (29.5)**	**<0.001**
Multivalvular, n (%)	**442 (12.8)**	**112 (10.1)**	**330 (14.1)**	**0.001**
Tricuspid, n (%)	152 (4.4)	49 (4.4)	103 (4.4)	0.64
Pulmonary, n (%)	31 (0.9)	0 (0.8)	22 (10.9)	0.64

Analysis of sex differences in the clinical presentation, management and prognosis of infective endocarditis in Spain. Heart Br Card Soc. 2021

TABLA 1. Características generales de la endocarditis infecciosa según el sexo

	Mujeres (n = 104)	Varones (n = 184)
Edad (años)	52 ± 21	50 ± 18
EI previa	7 (6,7%)	12 (6,5%)
Lugar de la infección[a]		
Mitral	56 (54%)	73 (40%)
Aórtica	30 (29%)	92 (50%)
Otras	17 (17%)	19 (11%)

Características clínicas y pronóstico de la endocarditis infecciosa en la mujer. Rev Esp Cardiol. 2008

EI aórtica - sexo masculino
EI mitral -sexo femenino

Absceso
Fistula
Bloqueo AV

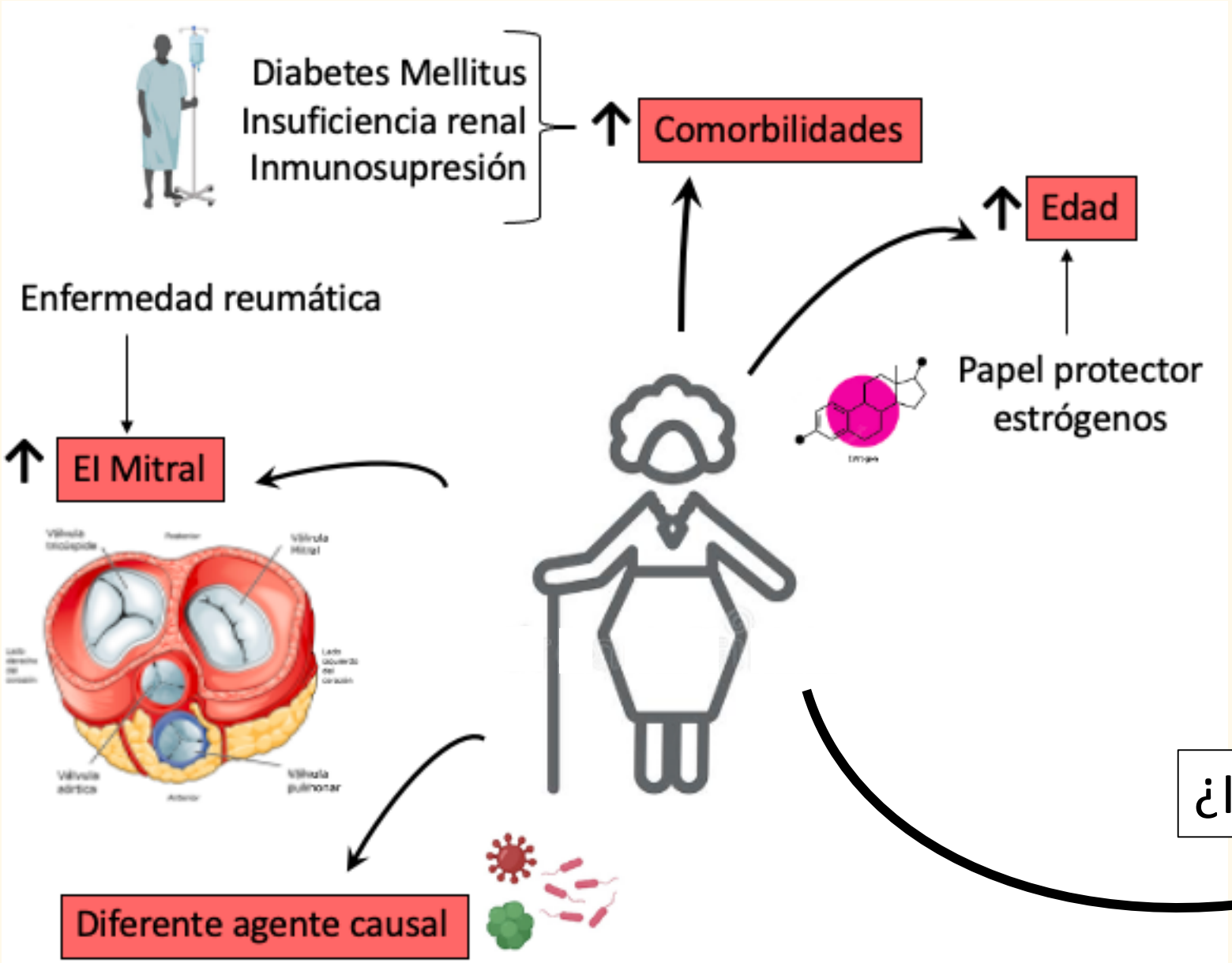
	Total 3451	Female sex 1105 (32.0%)	Male sex 2346 (67.9%)	P value
Local complications				
Paravalvular abscess, n (%)	676 (19.6)	198 (17.9)	478 (20.4)	0.24
Vegetations, n (%)	2727 (79.2)	880 (79.6)	1874 (78.9)	0.44
Severe valve regurgitation, n (%)	280 (24.1)	79 (21.2)	201 (25.5)	0.22
New conduction disturbances, n (%)	**376 (11.0)**	**96 (8.8)**	**280 (12.1)**	**0.01**

Analysis of sex differences in the clinical presentation, management and prognosis of infective endocarditis in Spain. Heart Br Card Soc. 2021

Variable	Overall (n = 271)	Women (n = 88)	Men (n = 183)	p Value*
Paravalvular complications	105 (39%)	23 (26%)	82 (45%)	0.003
Valve perforation	46 (17%)	7 (8%)	39 (21%)	0.006
Abscess	28 (10%)	8 (9%)	20 (11%)	0.41
Valve rupture	33 (12%)	7 (8%)	26 (14%)	0.17
Fistulae	7 (3%)	2 (2%)	5 (2.7%)	1.0

Sex differences in native-valve infective endocarditis in a single tertiary-care hospital. Am J Cardiol. 2010

Las EI en mujeres sí son diferentes



¿Implicaciones en el pronóstico?

- Sexo femenino como factor pronóstico

Características clínicas y pronóstico de la endocarditis infecciosa en la mujer

Juan C. Castillo, Manuel P. Anguita, Mónica Delgado, Martín Ruiz, Dolores Mesa, Elías Romo, Manuel Crespín, Daniel García, José M. Arizón y José Suárez de Lezo

Sex-Specific Risk Factors for Short- and Long-Term Outcomes after Surgery in Patients with Infective Endocarditis

Christine Friedrich [1,*], Mohamed Salem [1], Thomas Puehler [1], B... Herbers [1], Julia Reimers [1], Lars Hummitzsch [2], Jochen Cremer [1] and ...

Sex Differences in Native-Valve Infective Endocarditis in a Single Tertiary-Care Hospital

Antonia Sambola, MD[a,*], Nuria Fernández-Hidalgo, MD[b], Benito Almirante, MD[b], Ivo Roca, MD[a], Teresa González-Alujas, MD[a], Bernard Serra, MD[a], Albert Pahissa, MD[b], David García-Dorado, MD[a], and Pilar Torr...

Analysis of sex differences in the clinical presentation, management and prognosis of infective endocarditis in Spain

Laura Varela Barca, [1] Laura Vidal-Bonnet, [2] MC Fariñas, [3] Patricia Muñoz, [4,5] Maricela Valerio Minero, [4] Arístides de Alarcón, [6] Encarnacion Gutiérrez Carretero, [7] Manuel Gutiérrez Cuadra, [3] Asuncion Moreno Camacho, [8] Xabier Kortajarena Urkola, [9] Josune Goikoetxea Agirre, [10] Guillermo Ojeda Burgos, [11] Luis Eduardo López-Cortés, [12] JC Porras Azpiroz, [13] Jose Lopez Menendez, [14] GAMES Investigators

Sex Differences in the Utilization and Outcomes of Cardiac Valve Replacement Surgery for Infective Endocarditis: Insights From the National Inpatient Sample

Agam Bansal, MD; Paul C. Cremer, MD; Wael A. Jaber, MD; Penelope Rampersad, MD; Venu Menon, MD

El sexo femenino se asocia con un incremento de la mortalidad por EI

Sin embargo…..
Controversia al respecto

ANEXO 1. **Escala de valoración de riesgo. EuroSCORE**

Variables	Puntuación
Variables extracardíacas	
Edad (por cada período de 5 años, total o parcial, por encima de 60)	1
Sexo femenino	1
Enfermedad pulmonar obstructiva crónica	1
Arteriopatía extracardíaca	2
Disfunción neurológica	2
Cirugía cardíaca previa	3
Creatinina sérica > 200 µmol/l	2
Endocarditis activa	3
Estado preoperatorio crítico	3
Variables cardíacas	
Angina inestable con nitratos i.v.	2
Fracción de eyección 30-50%	1
< 30%	3
Infarto reciente (menos de 90 días)	2
Presión arterial sistólica pulmonar > 60 mmHg	2
Variables operatorias	
Emergencia	2
Cualquier operación distinta de cirugía coronaria aislada	2
Cirugía de aorta torácica	3
Rotura septal postinfarto	4

Patient related factors			Cardiac related factors		
Age [1] (years)	0	0	NYHA	select	0
Gender	select	0	CCS class 4 angina [8]	no	0
Renal impairment [2] See calculator below for creatinine clearance	normal (CC >85ml/min)	0	LV function	select	0
Extracardiac arteriopathy [3]	no	0	Recent MI [9]	no	0
Poor mobility [4]	no	0	Pulmonary hypertension [10]	no	0
Previous cardiac surgery	no	0	**Operation related factors**		
Chronic lung disease [5]	no	0	Urgency [11]	elective	0
Active endocarditis [6]	no	0	Weight of the intervention [12]	isolated CABG	0
Critical preoperative state [7]	no	0	Surgery on thoracic aorta	no	0
Diabetes on insulin	no	0			
EuroSCORE II	0				

***Euro*SCORE II**

Variable	Preoperative score	Combined score
Age (for each five years over 55 years)	1	1
BMI 30–40 kg/m²	4	3
BMI 40 kg/m²	9	8
Diabetes	3	3
Renal failure	4	4
Congestive heart failure	3	3
Peripheral vascular disease	2	2
Female gender	2	2
Chronic lung disease	2	3
Cardiogenic shock	6	n/a
Myocardial infarction	2	n/a
Concomitant surgery	4	n/a
Perfusion time 100–200 minutes	n/a	3
Perfusion time 200–300 minutes	n/a	7
Intra-aortic balloon pump	n/a	5

STS, Society for Thoracic Surgeons; BMI, body mass index.

Sin embargo….. Controversia al respecto

	STSS	PALSUSE	De Feo-Cotrufo	Costa	RISK-E	AEPEI	EndoScore°	Spec.ES 1	Spec.ES 2
Edad	-	>70: 1	40-49: 5 50-59: 7 60-69: 9 70-79: 11 > 80: 13	≥ 40: 4	52-63: 0 64-72: 13 ≥ 73: 14	-	60-70: 0.46 70-80: 0.88 >80: 1.53	<60-65: 11 65-70: 22 70-75: 33 75-80: 44 80-85: 56 85-90: 67 90-100: 78	<60-65: 11 65-70: 22 70-75: 33 75-80: 44 80-85: 56 85-90: 67 90-100: 78
Sexo (Femenino)	-	1	-	-	-	-	0.51	-	-
Cirugía urgente	6	1		-	-	-	-	Emerg: 30	42 Emerg: 70
Shock	17 BCIa: 10	∂	EC: 11 NYHA IV: 9	5	15	1,5 NYHA IV: 1,3	1.46	EC: 42 NYHA>I: 26	EC: 37 NYHA>I: 22
Sepsis	-	-	-	6	7	-	-	-	-
Multival.	9	-	-	-	-	-	2: 0.5 3: 1.5	-	-
EI protésica	-	1	No aplicable	-	6	-	-	-	-
CC previa	7	∂	-	-	-	-	-	42	35
DM	ID: 8 NID: 6	-	-	-	-	-	-	-	-
HTA	5	-	-	-	-	-	-	-	-
EPOC	5	-	-	-	-	-	0.68	-	-
IR	12	∂	5		5	2,2	0.5	18	-
HTP	-	-	-	-	-	1	-	48	-
Arritmia	8	-	-	8 BAV: 5	-	-	-	-	-
Cultivos positivos	-	S.A: 1	5	-	S.A: 9 fúngica: 9	-	0.6 S.A: 1.24 fúngica:1.6 P.A: 1.46	S.A: 20	S.A: 19
Absceso	-	1	5	5	5	-	1.09	Fístula: 46	Fístula: 41
Vegetaciones	-	-	-	≥ 10: 4	-	-	-	-	-
EuroScore	-	≥10%: 1	-	-	-	-	-	-	-
Trombopenia	-	-	-	-	7	-	-	-	-
Otros	EI activa: 10	-	-	-	-	IMC>27: 1	-	EI mitral:14	EI mitra:14

El sexo femenino se asocia con un incremento de la mortalidad por EI

¿A que se debe el aumento de la mortalidad?

Mayor edad y presentación de comorbilidades

Mayor afectación mitral

Diferente abordaje terapéutico

Mayor dificultad quirúrgica

Mayor edad y presentación de comorbilidades

Estudios en los que el **sexo femenino** se identifica como **factor independiente de mortalidad** tras ajuste multivariable

El **sexo femenino** se identifica como factor dependiente de mortalidad.

|

Mujeres presentan mayor mortalidad **debido a una mayor edad y comorbilidades**

Sambola et al. Sex differences in native-valve infective endocarditis in a single tertiary-care hospital. Am J Cardiol. 2010

Curlier et al. Relationships between sex, early valve surgery and mortality in patients with left-sided infective endocarditis analyzed in a population cohort study. Heart Card Soc. 2014

Varela et al. Analysis of sex differences in the clinical presentation, management and prognosis of infective endocarditis in Spain. Heart Br Card Soc. 2021

Friedrich et al. Sex-Specific Risk Factors for Short- and Long-Term Outcomes after Surgery in Patients with Infective Endocarditis. J. Clin. Med. 2022

Aksoy et al. Gender differences in infective endocarditis: pre- and co-morbid conditions lead to different management and outcomes in female patients. Scand J Infect Dis. 2007

Weber et al. Severity of Presentation, Not Sex, Increases Risk of Surgery for Infective Endocarditis. Ann Thorac Surg 2019

Analysis of sex differences in the clinical presentation, management and prognosis of infective endocarditis in Spain

Laura Varela Barca ,[1] Laura Vidal-Bonnet,[2] MC Fariñas,[3] Patricia Muñoz,[4,5] Maricela Valerio Minero,[4] Arístides de Alarcón,[6] Encarnacion Gutiérrez Carretero,[7] Manuel Gutiérrez Cuadra,[3] Asuncion Moreno Camacho,[8] Xabier Kortajarena Urkola,[9] Josune Goikoetxea Agirre,[10] Guillermo Ojeda Burgos,[11] Luis Eduardo López-Cortés,[12] JC Porres Azpiroz,[13] Jose Lopez-Menendez ,[14] GAMES Investigators

Mortalidad intra-hospitalaria

Total 27.9% (964)
Mujeres 32.8% (362)
Hombres 25.7% (602)

P<0.001

Análisis multivariable

Tras ajuste: **OR mortalidad 1.25** (IC 95% 1.07-1.47; p<0.01)

Mayor afectación mitral

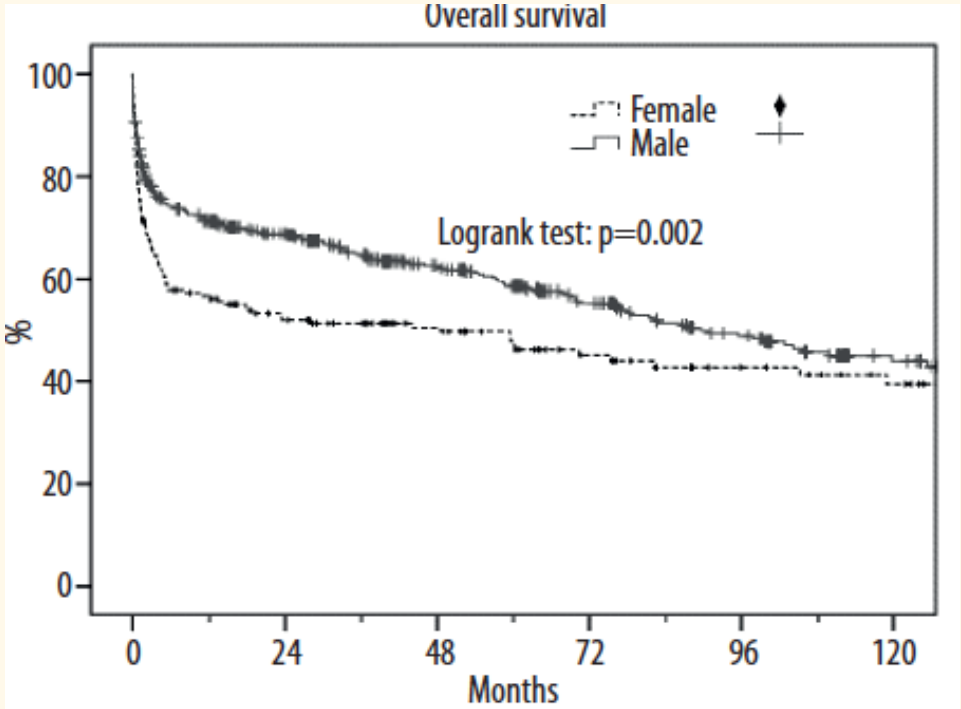
Gender-Based Long-Term Surgical Outcome in Patients with Active Infective Aortic Valve Endocarditis

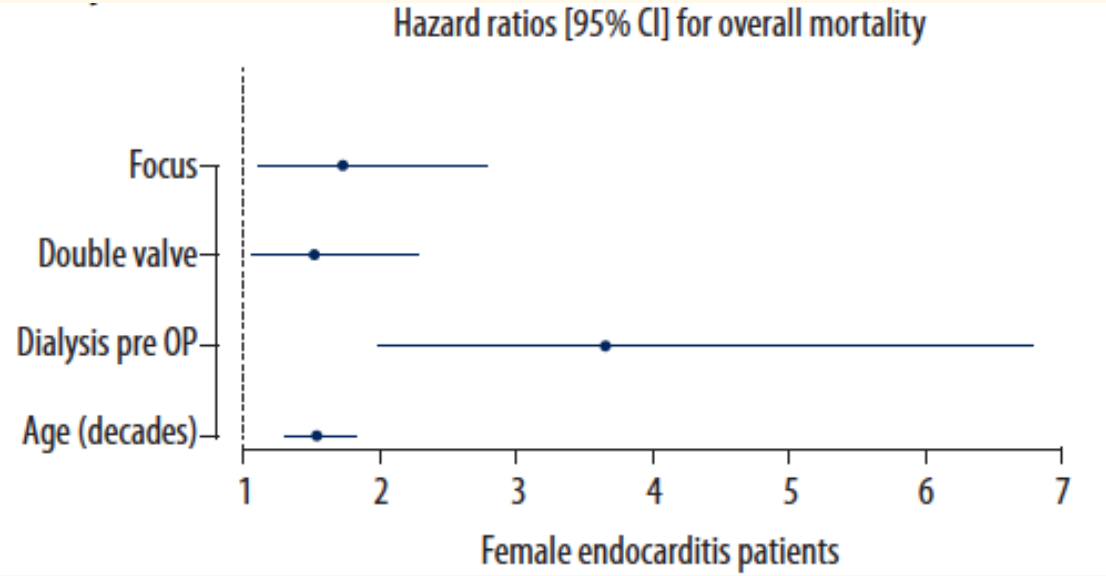
Pascal M. Dohmen*
Christian Binner*
Meinhart Mende
Piroze Daviewala
Christian D. Etz
Michael Andrew Borger
Martin Misfeld
Sandra Eifert
Friedrich Wilhelm Mohr

1 Department of Cardiac Surgery, Leipzig Heart Center, University of Leipzig, Leipzig, Germany
2 Department of Cardiothoracic Surgery, Faculty of Health Sciences, University of The Free State, Bloemfontein, South Africa
3 Coordination Center for Clinical Trial Leipzig (ZKS Leipzig – KKS), University of Leipzig, Leipzig, Germany

Conclusions

This study demonstrated distinct gender-based differences in risk of mortality in patients with AIE who were undergoing surgical treatment. The data also indicate differences in disease patterns, comorbidities, intraoperative surgical treatment strategy, and long-term outcome.





Analysis of sex differences in the clinical presentation, management and prognosis of infective endocarditis in Spain

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Sex differences in mortality were also observed when the affected valves were considered. Mortality was significantly higher in women with aortic valve IE (33.1% vs 25.1%; p<0.001) and mitral valve IE (35.2% vs 25.4%; p<0.001).

	Total 3451	Female sex 1105 (32.0%)	Male sex 2346 (67.9%)	P value
Affected valve				
Native, n (%)	2341 (67.9)	731 (66.2)	1611 (68.7)	0.15
Prosthesis, n (%)	1135 (32.9)	383 (34.7)	752 (32.1)	0.13
Aortic, n (%)	**1516 (43.9)**	**358 (32.4)**	**1158 (50.6)**	**<0.001**
Mitral, n (%)	**1231 (35.7)**	**538 (48.7)**	**693 (29.5)**	**<0.001**
Multivalvular, n (%)	**442 (12.8)**	**112 (10.1)**	**330 (14.1)**	**0.001**
Tricuspid, n (%)	152 (4.4)	49 (4.4)	103 (4.4)	0.64
Pulmonary, n (%)	31 (0.9)	0 (0.8)	22 (10.9)	0.64

Diferente abordaje terapéutico

Se realiza menor tratamiento quirúrgico en las mujeres

Bansal A et al. Sex Differences in the Utilization and Outcomes of Cardiac Valve Replacement Surgery for Infective Endocarditis: Insights From the National Inpatient Sample. J Am Heart Assoc. 2021

Castillo JC et al. Características clínicas y pronóstico de la endocarditis infecciosa en la mujer. Rev Esp Cardiol. 2008

Polishchuk et al. Sex Differences in Infective Endocarditis. Am J Med Sci. 2021

Sousa et al. Gender Based Analysis of a Population Series of Patients Hospitalized with Infective Endocarditis in Portugal – How do Women and Men Compare? Int J Cardiovasc Sci. 2021

Curlier et al. Relationships between sex, early valve surgery and mortality in patients with left-sided infective endocarditis analyzed in a population cohort study. Heart Card Soc. 2014

Varela et al. Analysis of sex differences in the clinical presentation, management and prognosis of infective endocarditis in Spain. Heart Br Card Soc. 2021

Sambola et al. Sex differences in native-valve infective endocarditis in a single tertiary-care hospital. Am J Cardiol. 2010

Friedrichet al. Sex-Specific Risk Factors for Short- and Long-Term Outcomes after Surgery in Patients with Infective Endocarditis. J. Clin. Med. 2022

- La cirugía cardiaca- pilar del tratamiento
- **Indicaciones** bien establecidas

Table 3 Comparison of ACC/AHA and ESC guideline recommendations for timing of surgery in complicated left-sided infective endocarditis

Surgical indication	Recommendation for timing of surgery	
	ACC/AHA	ESC
Valve dysfunction resulting in HF symptoms	Early ('during initial hospitalization and before completion of a full therapeutic course of antibiotics')	Emergency (<24 h)
Highly resistant organism	Early	Urgent/elective
Heart block, annular or aortic abscess, or destructive penetrating lesion	Early	Urgent ('within few days')
Persistent bacteraemia or fever lasting >5 days after onset of appropriate antibiotic therapy	Early	Urgent
Recurrent emboli and persistent vegetations despite appropriate antibiotic therapy	Early	Urgent
Left-sided valve IE who exhibit mobile vegetations >10 mm in length with or without clinical evidence of embolic event	Early	Urgent
Prosthetic valve IE caused by staphylococci or non-HACEK gram-negative bacteria	NA	Urgent/elective
Prosthetic valve IE and relapsing infection without other identifiable source	Early	NA

Infective Endocarditis

15-25% early mortality
30-50% undergo surgery

Similarities in ESC and ACC/AHA Guidelines

Surgical indications

Both ESC and ACC/AHA Guidelines consider heart failure, uncontrolled infection, and embolic risk as surgical indications.

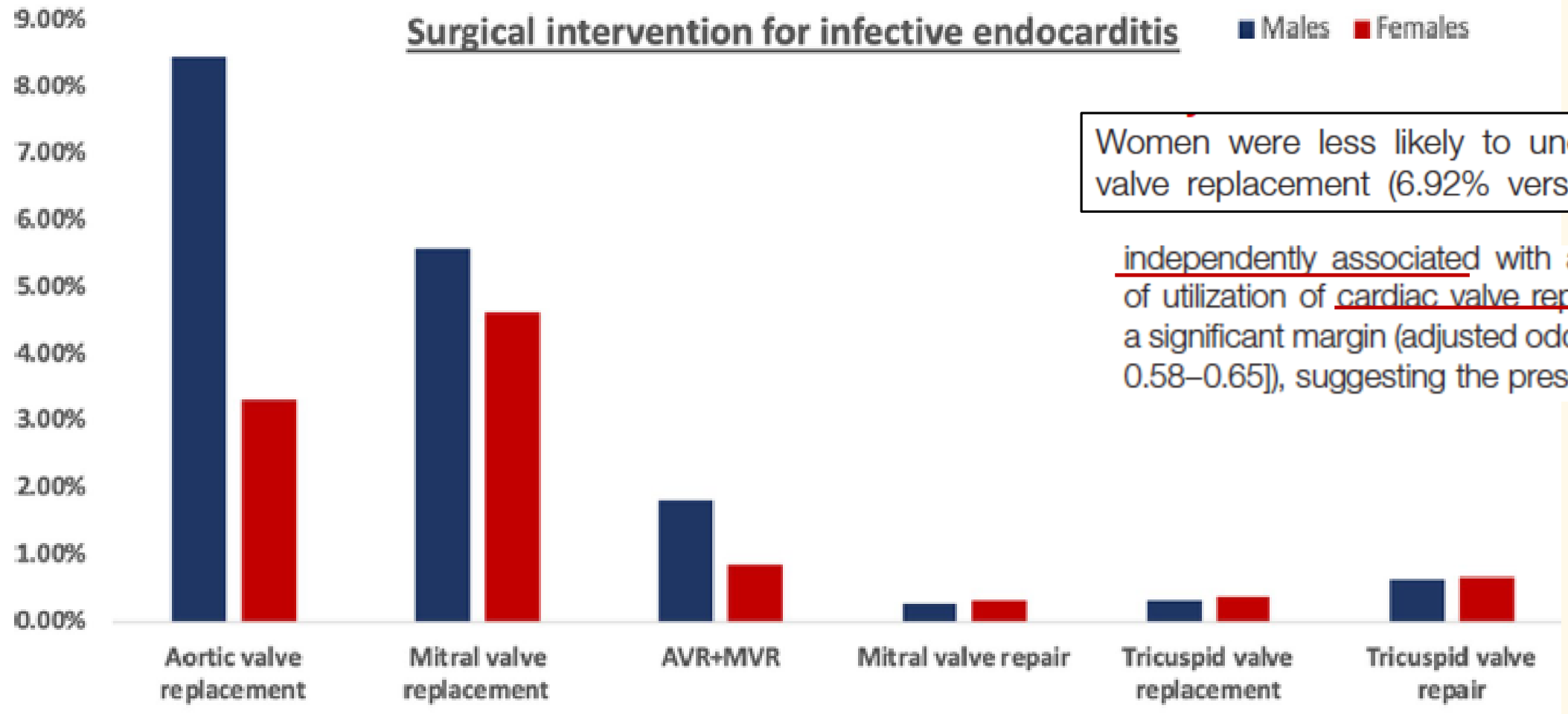
Heart failure	Uncontrolled infection	Embolism risk
Severe valve dysfunction	Antibiotics persistently ineffective	Embolic event
NYHA class	Abscess or fistula	Vegetation size
LV function	Resistant organism	

Dissimilarities in ESC and ACC/AHA Guidelines

	ESC	ACC/AHA
Timing of surgery	Emergent/urgent/elective	Early (before stop antibiotics)
Large vegetation	>30mm	>10mm
Vegetation size and emboli	Emboli+10mm vegetation→surgery	No or ≥1 emboli+10mm vegetation→surger

- **Incremento en la supervivencia**

Current recommendations and uncertainties for surgical treatment of infective endocarditis: a comparison of American and European cardiovascular guidelines. European Heart Journal (2022)



Women were less likely to undergo overall cardiac valve replacement (6.92% versus 12.12%, $P<0.001$), independently associated with a decreased likelihood of utilization of cardiac valve replacement surgery with a significant margin (adjusted odds ratio of 0.61 [95% CI, 0.58–0.65]), suggesting the presence of treatment bias.

Journal of the American Heart Association

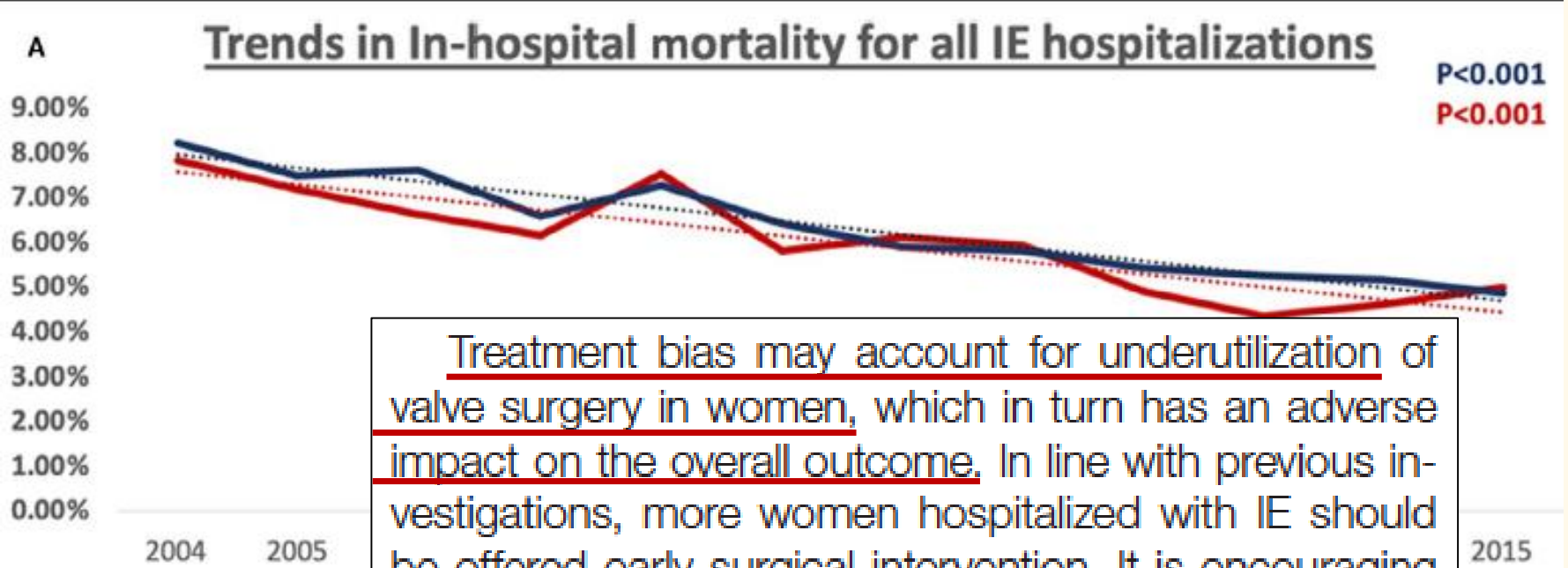
ORIGINAL RESEARCH

Sex Differences in the Utilization and Outcomes of Cardiac Valve Replacement Surgery for Infective Endocarditis: Insights From the National Inpatient Sample

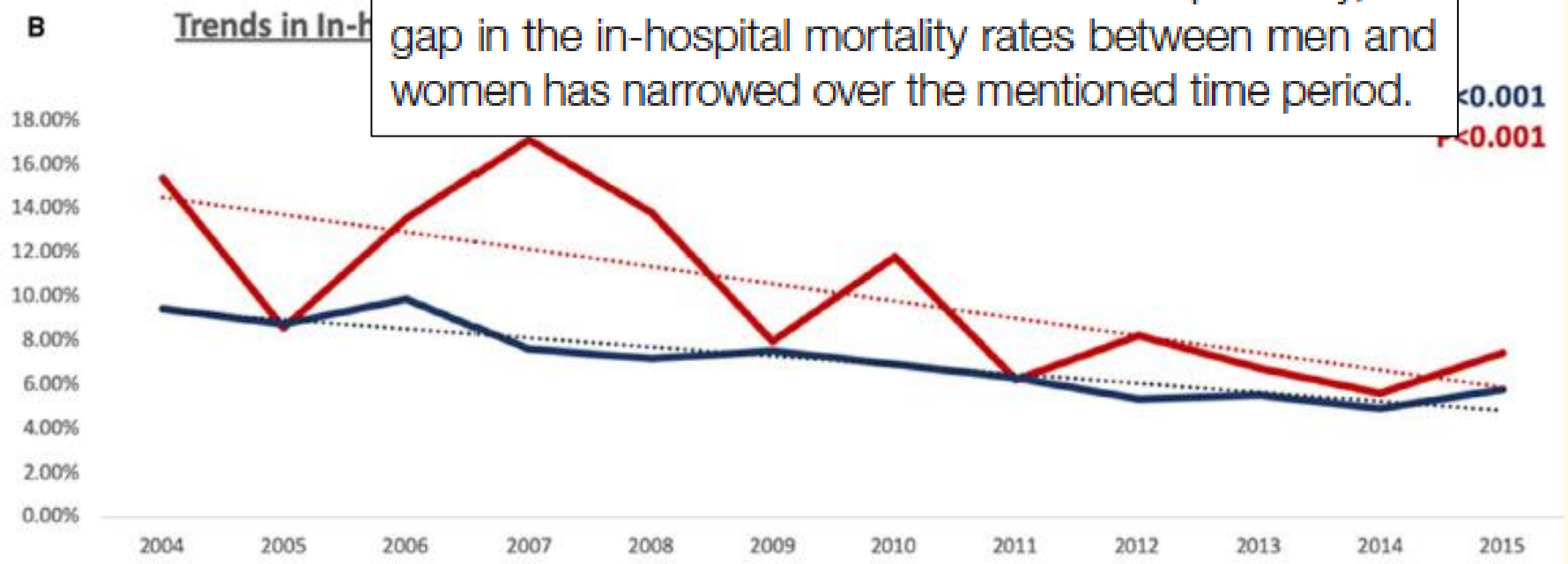
Agam Bansal, MD; Paul C. Cremer, MD; Wael A. Jaber, MD; Penelope Rampersad, MD; Venu Menon, MD

Table 3. Unadjusted and Adjusted Association Between Sex and Likelihood of Undergoing Valve Replacement, In-Hospital Mortality, and Stroke

Variables	Unadjusted association	*P* value	Adjusted association	*P* value
Cardiac valve replacement	0.540 (0.514–0.568)	<0.001	0.614 (0.578–0.652)	<0.001
Aortic valve replacement	0.371 (0.347–0.397)	<0.001	0.422 (0.390–0.456)	<0.001
Mitral valve replacement	0.818 (0.768–0.871)	<0.001	0.963 (0.894–1.036)	0.314
AVR+MVR	0.473 (0.415–0.539)	<0.001	0.559 (0.481–0.648)	<0.001



Treatment bias may account for underutilization of valve surgery in women, which in turn has an adverse impact on the overall outcome. In line with previous investigations, more women hospitalized with IE should be offered early surgical intervention. It is encouraging to find that the rates of valve replacement surgeries have increased from 2004 to 2015 and more importantly, the gap in the in-hospital mortality rates between men and women has narrowed over the mentioned time period.



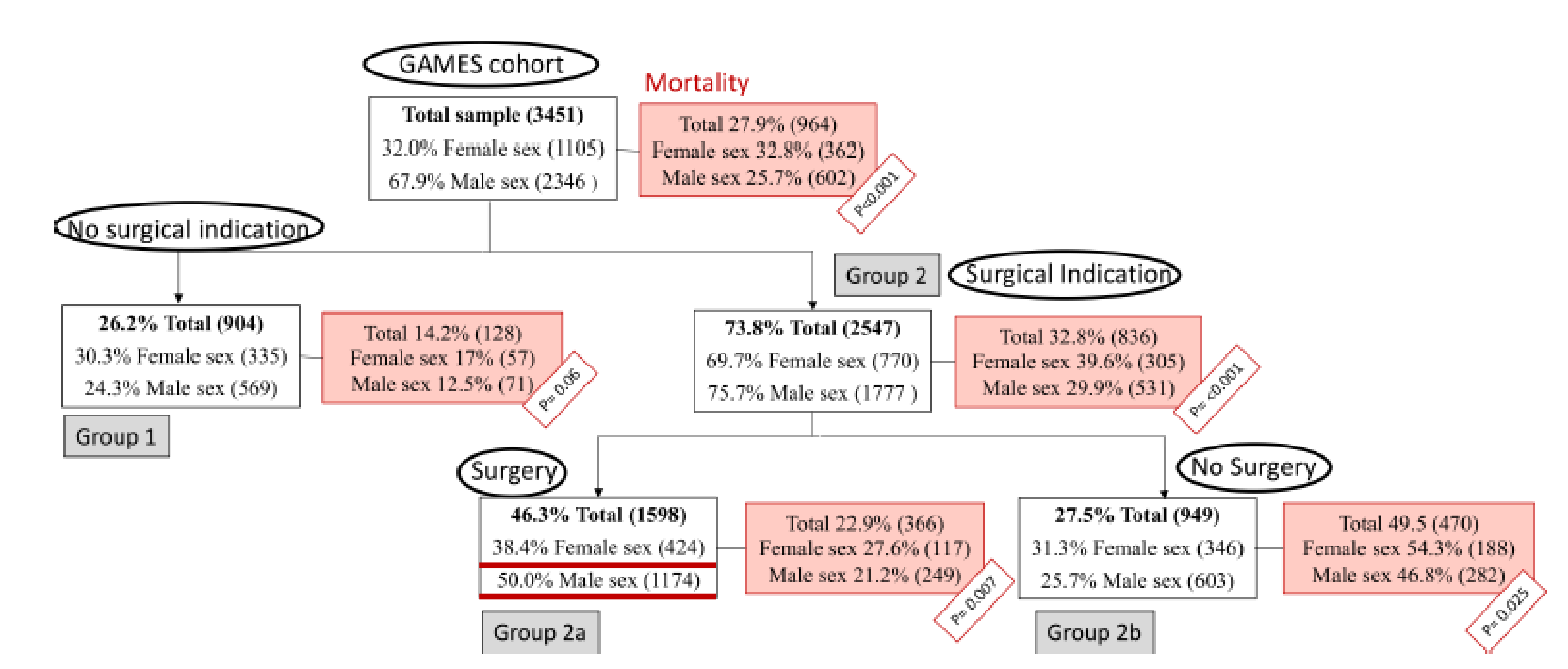
Reducción de la mortalidad (p<0,01):

- Hombres: 8,24 a 4,9 %
- **Mujeres: 7,85 a 4,99 %**

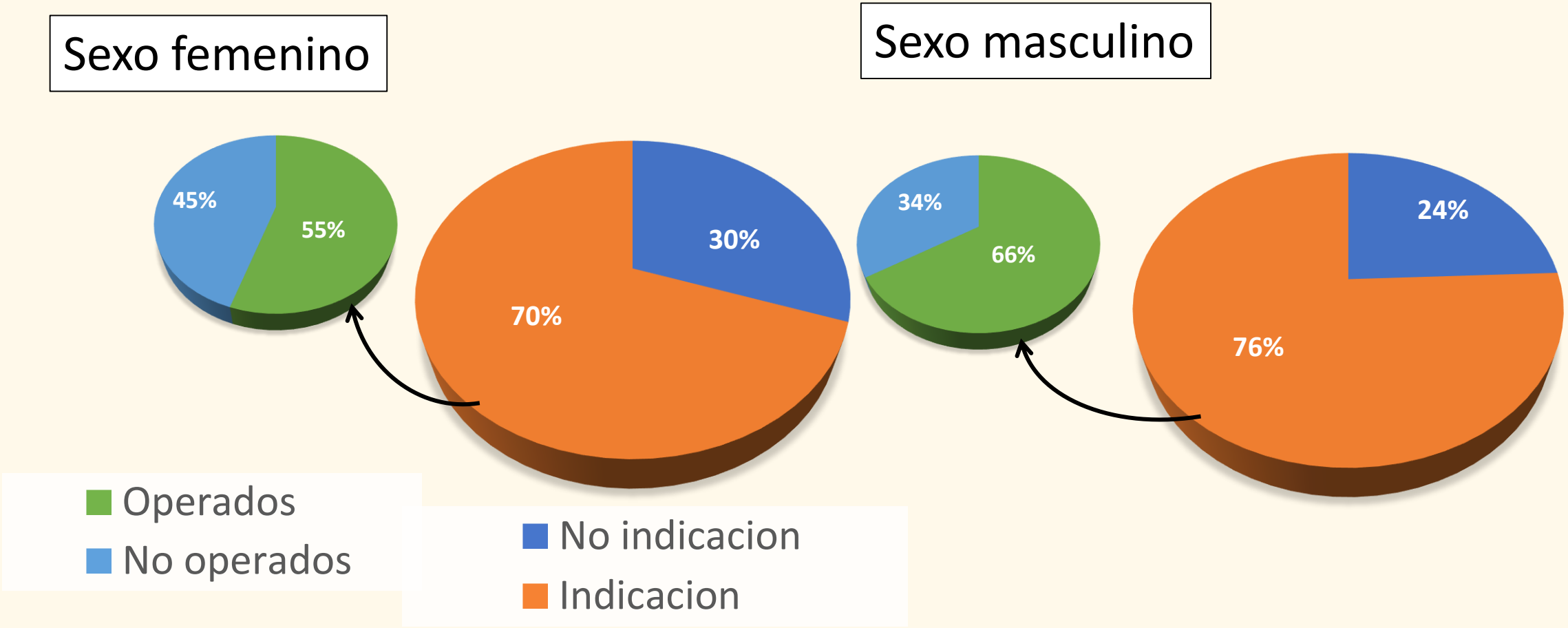
Reducción de la mortalidad (p<0,01):

- Hombres: 9,46 a 5,84 %
- **Mujeres: 15,36 a 7,50 %**

1,5 veces más mortalidad que los hombres (9,94% frente a 6,99%)



- Tratamiento quirúrgico 1598 pacientes (43% de total)
- En las mujeres 38.4% y en los hombres el 50%



Las mujeres con recomendación de cirugía: menos probabilidad de operarse
(OR no cirugía 1.59; IC 95% 1.34 – 1.89; p<0.001)

Tras ajuste de riesgo por **propensity score**: Mujeres menos probabilidad de cirugía
OR cirugía 0.74 (95%IC 0.59-0.91; p=0.05)

¿A que se debe la menor realización de cirugía en las mujeres con EI?

- Alto riesgo estimado de manera preoperatoria
- Estado clínico más avanzado
- Mayor edad
- Más patología mitral
- Comorbilidades
- Fragilidad
- Anatomía
- Rechazo a la intervención

……..

Canadian Journal of Cardiology 38 (2022) 1418–1425

Clinical Research

Sex Differences in Infective Endocarditis After Transcatheter Aortic Valve Replacement

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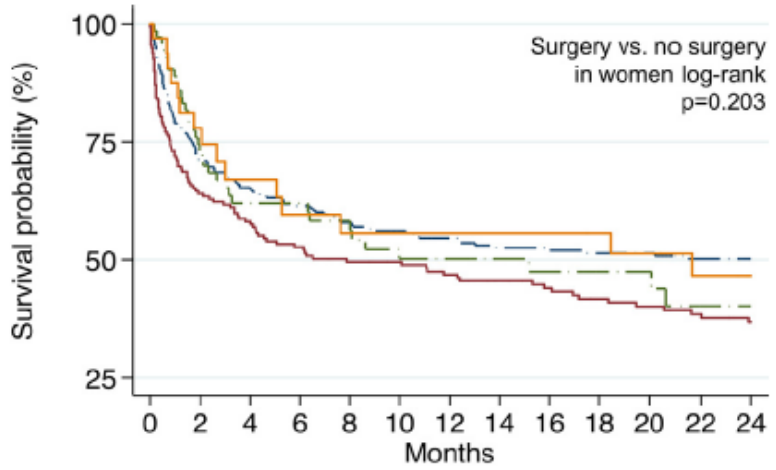
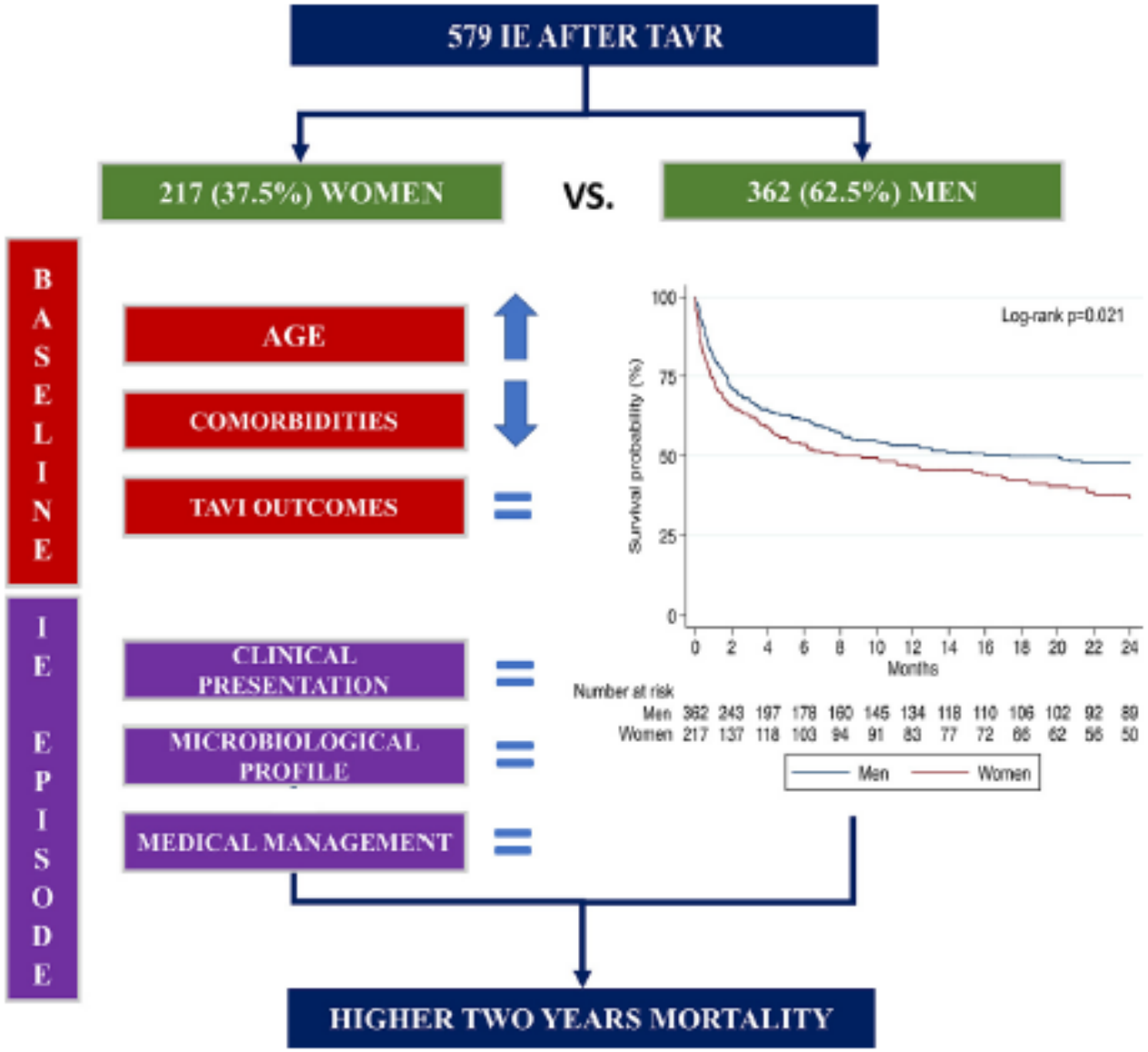


Men no surgery	282	189	156	140	128	118	109	97	92	90	88	81	78
Women no surgery	179	111	97	85	78	76	69	63	58	53	50	46	42
Men surgery	72	49	36	33	29	25	23	20	17	15	13	10	10
Women surgery	32	23	18	15	14	14	14	14	14	13	12	10	8

Men no surgery — Women no surgery
Men surgery — Women surgery



- Sexo femenino: factor independiente de mortalidad
- Cirugía en el 20% de los hombres y el 15% de las mujeres
- La cirugía no resultó un factor protector de mortalidad

Diabetes Mellitus
Insuficiencia renal
Inmunosupresión

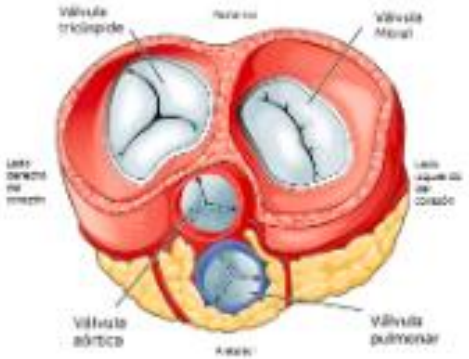
↑ Comorbilidades

↑ Edad

Papel protector estrógenos

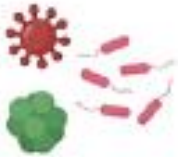
Enfermedad reumática

↑ El Mitral



↓ Tratamiento quirúrgico

Diferente agente causal



Peor pronóstico

- Conclusiones

Endocarditis en mujeres ¿En qué son diferentes?

- Existen diferencias en la **epidemiología** y **presentación clínica** de la EI entre géneros
- Las mujeres presentan **mayor edad y comorbilidades**
- Es más frecuente la **afectación mitral**
- Podría haber diferencias en lo referente a la **etiología**
- Existen diferencias en el manejo, siendo **menos frecuente la cirugía cardiaca**
- **Sexo femenino resultó un predictor de mal pronóstico**

Bias: does it account for low surgical rates in women with infective endocarditis?

Harriette G C Van Spall,[1] Iqbal Jaffer,[1,2] Mamas A Mamas [3]

Disparities in referral and receipt of surgical intervention, along with differences in aetiology, microbiology and comorbidities, may be responsible for the higher risk of mortality in women than in men with IE. Ultimately, awareness of these issues should prompt a self-evaluation of biases on the part of clinicians such that objective, timely surgical referrals are made and interventions are offered regardless of demographic group. While the biology is not modifiable, the biases and care disparities are.

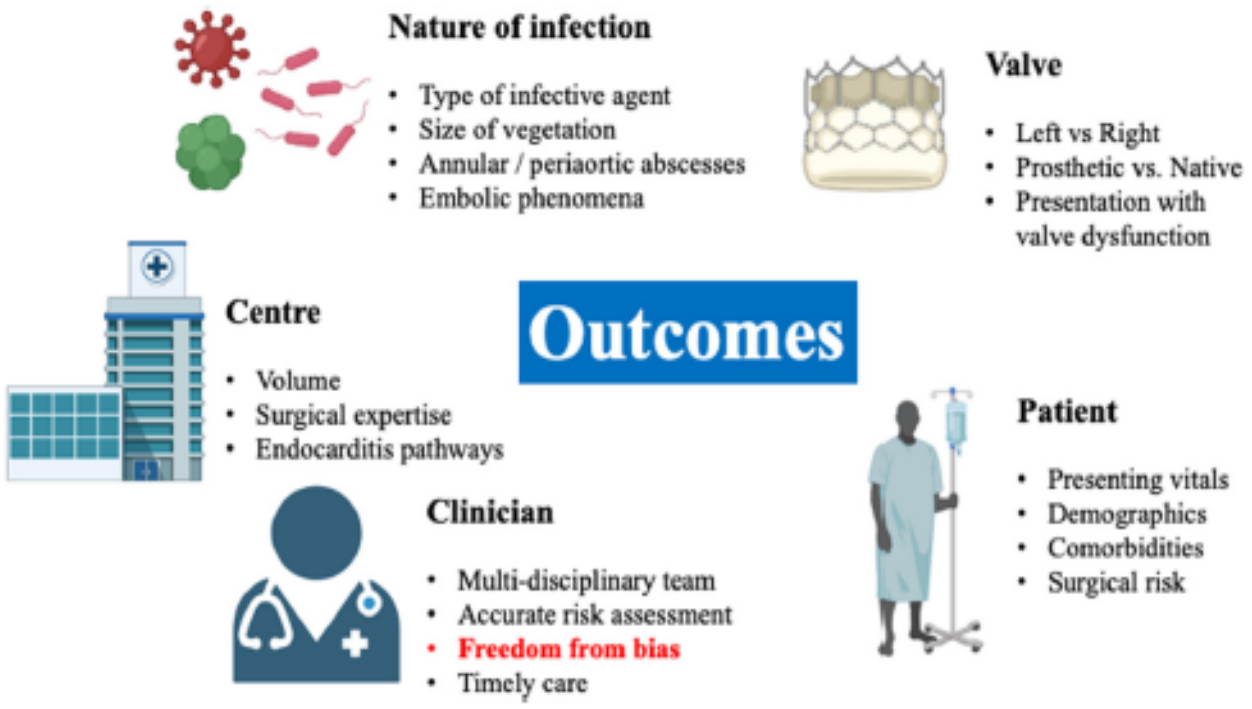


Figure 1 Factors associated with infective endocarditis outcomes

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