



La afectación cardiovascular en el lupus y el síndrome Antifosfolípido

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LES a los 26 años

GN lúpica IV (32 a)
(ensayo clínico)

Osteoporosis
Necrosis avascular
Cataratas

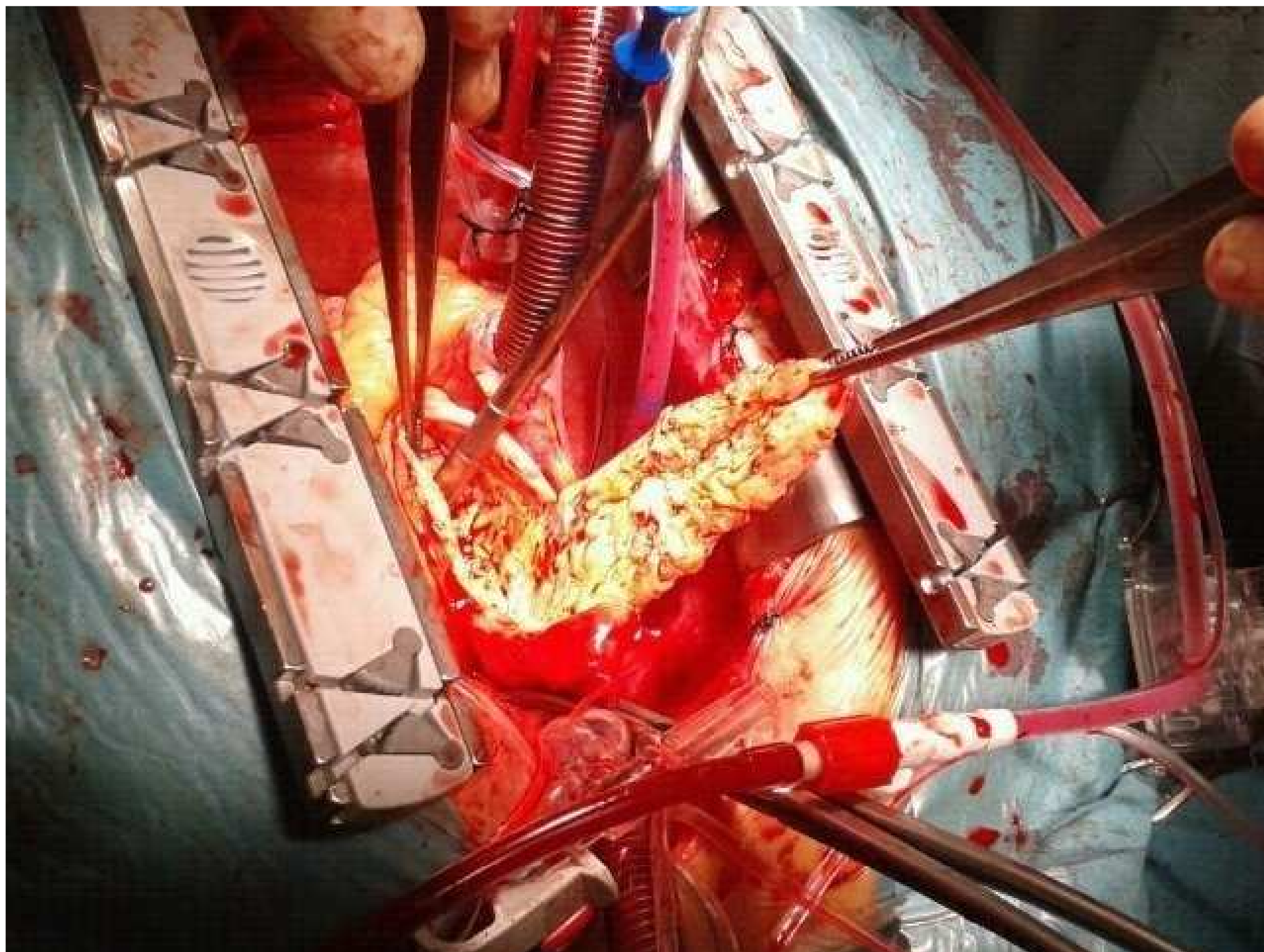
A los 36 años

Disnea progresiva

Estudio ecocardiográfico

Insuficiencia Ao / dilatación raíz Ao







Mortality Associated With Systemic Lupus Erythematosus in France Assessed by Multiple-Cause-of-Death Analysis

Guillemette Thomas,¹ Julien Mancini,² Noémie Jourde-Chiche,² Gabrielle Sarlon,²
Zahir Amoura,³ Jean-Robert Harlé,¹ Eric Jouglu,⁴ and Laurent Chiche¹

Data were collected between 2000 and 2009 in the French Epidemiological Center for the Medical Causes of Death database,

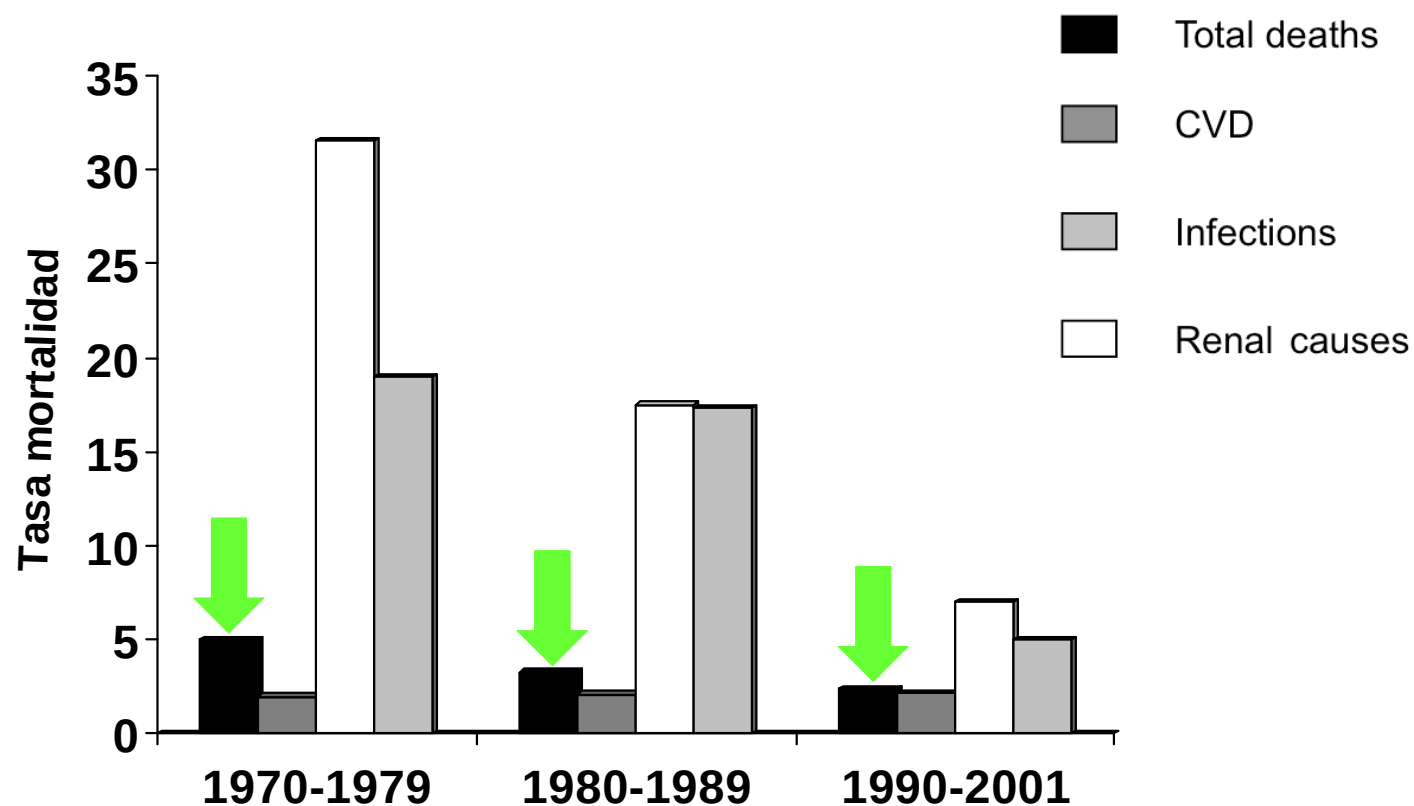
During the study period, 1,593 deaths related to SLE were identified.

Mortality Associated With Systemic Lupus Erythematosus in France Assessed by Multiple-Cause-of-Death Analysis

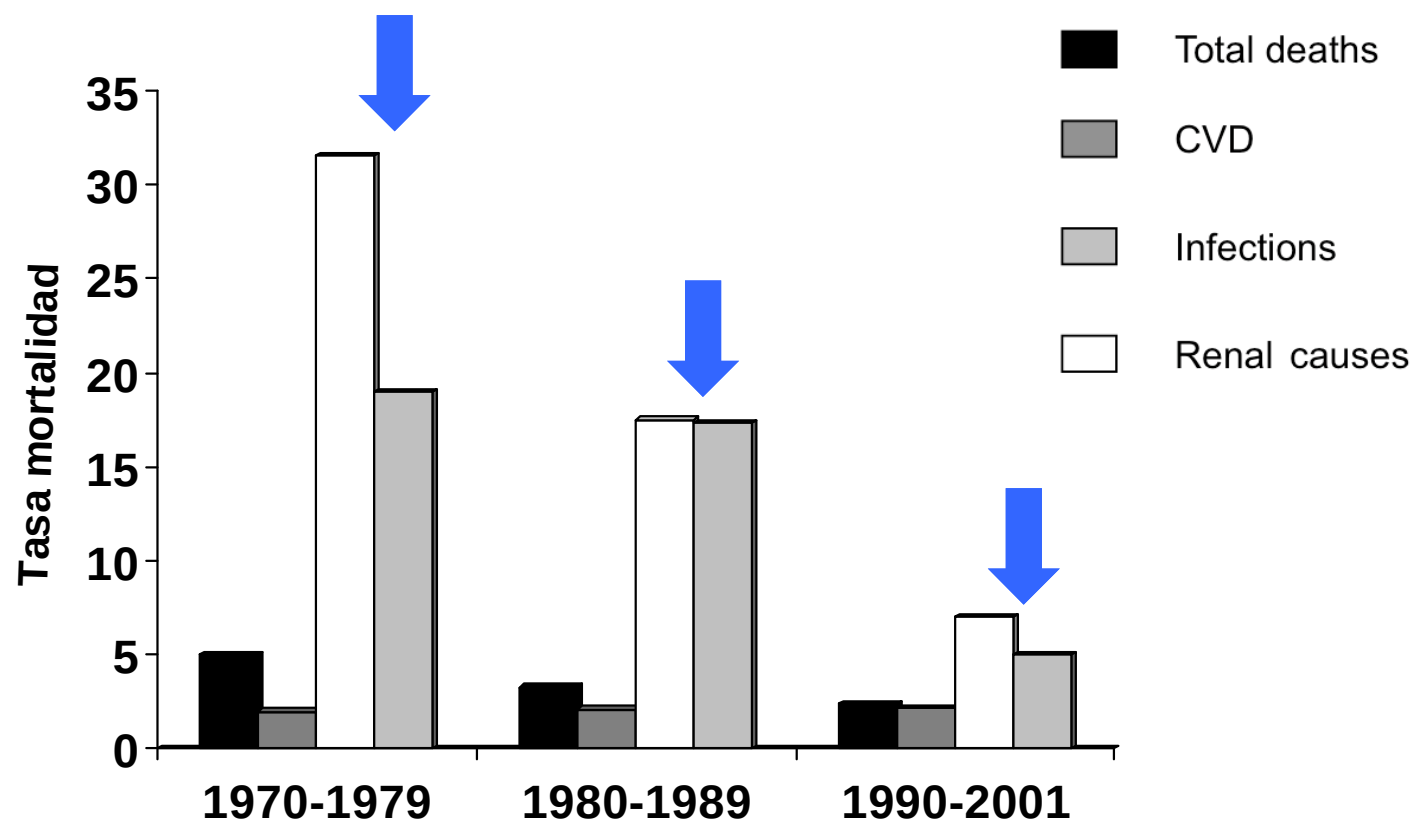
Underlying cause of death	Men (n = 222)	Women (n = 734)	Total (n = 956)	
Infectious disease	21 (9.5)	77 (10.5)	98 (10.3)	10%
Pneumonia	8 (3.6)	24 (3.3)	32 (3.3)	
Other infections	13 (5.9)	53 (7.2)	66 (6.9)	
Cardiovascular disease	73 (32.9)	268 (36.5)	341 (35.7)	36%
Ischemic heart disease	31 (14.0)	61 (8.3)	92 (9.6)	
Cerebrovascular disease	8 (3.6)	64 (8.7)	72 (7.5)	
Other	34 (15.3)	143 (19.5)	177 (18.5)	
Neoplasm	43 (19.4)	90 (12.3)	133 (13.9)	11%
Solid malignant neoplasm	35 (15.8)	69 (9.4)	104 (10.9)	
Hematologic malignancy	8 (3.6)	21 (2.9)	29 (3.0)	
Respiratory disease	10 (4.5)	24 (3.3)	34 (3.6)	
Renal disease	6 (2.7)	23 (3.1)	29 (3.0)	
Other	69 (31.1)	252 (34.3)	321 (33.6)	3%

***Conclusion.* Cardiovascular disease is the leading cause of death associated with SLE in France.**

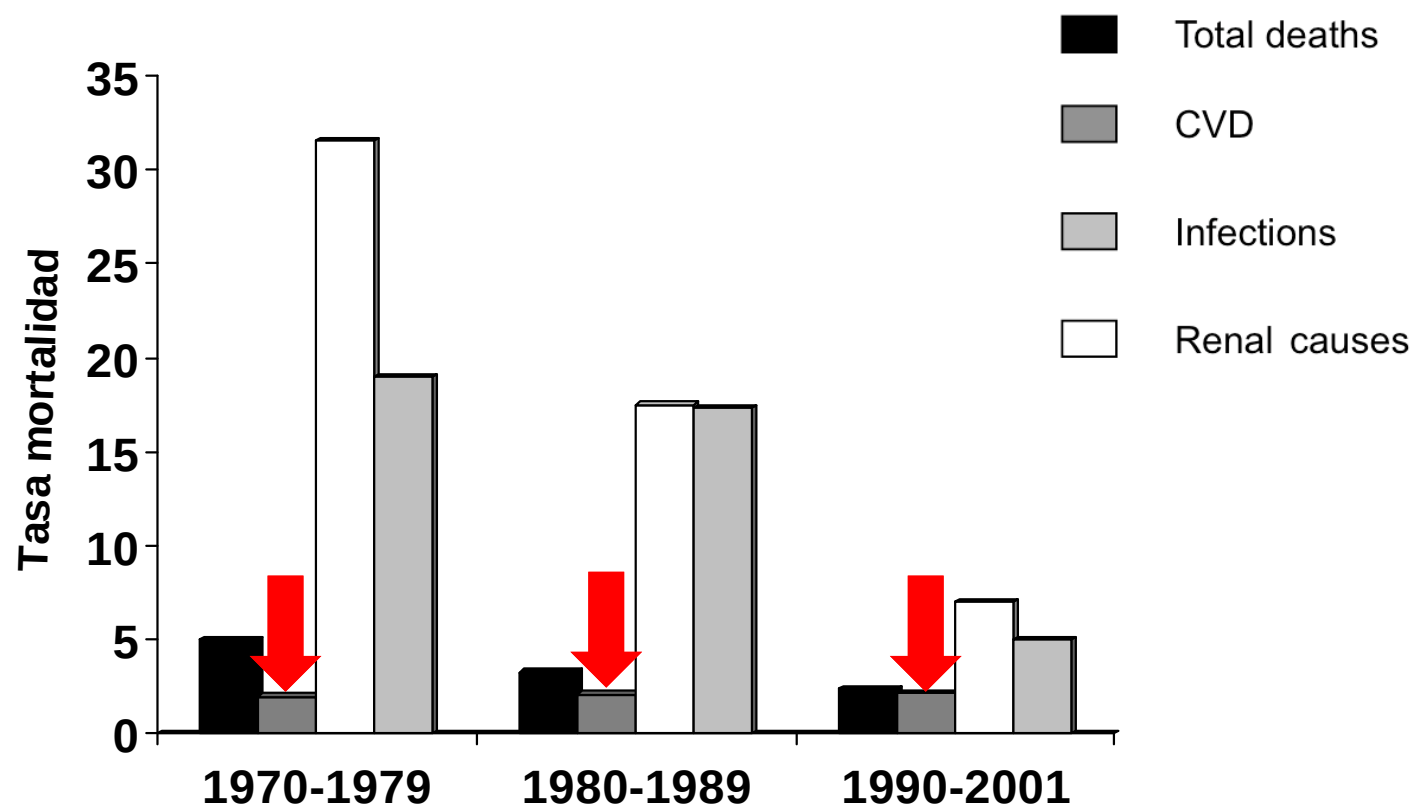
Mortality in Systemic Lupus Erythematosus



Mortality in Systemic Lupus Erythematosus



Mortality in Systemic Lupus Erythematosus



La ECV en el LES es...



FRECUENTE

PRECOZ

ACCELERADA

Los Angeles Times

- La prevalencia de la enfermedad coronaria sintomática en los pacientes con LES es del 6-8%. (*J Rheumatol* 2009;36:2454)
- Las mujeres con LES tienen 5-8 veces más riesgo de sufrir un IAM que las mujeres no lúpicas de edad similar. (*J Rheumatol* 2009;36:2454)
- Este riesgo es 50 veces mayor para las mujeres con edades comprendidas entre los 35 y 44 años. (*Am J Epidemiol* 1997;34:70)
- El riesgo de presentar un ACV en pacientes con LES es 8 veces superior a la de la población general. (*A&R* 2001;44:2331)

Age-specific Incidence Rates of Myocardial Infarction and Angina in Women with Systemic Lupus Erythematosus: Comparison with the Framingham Study



Susan Manzi,¹ Elaine N. Meilahn,² Joan E. Rairie,¹ Claudia G. Conte,¹ Thomas A. Medsger, Jr.,¹ Linda Jansen-McWilliams,² Ralph B. D'Agostino,³ and Lewis H. Kuller²

TABLE 2. Incidence rates of cardiovascular events per 1,000 person-years in the 498 women with systemic lupus erythematosus, University of Pittsburgh, and 2,208 women, Framingham Offspring Heart Study, 1980–1993

Age (years)	SLE*		Framingham		Rate ratio	95% CI
	Rate	95% CI*	Rate	95% CI		
<i>Myocardial infarction</i>						
15–24	6.33	0.2–35.3	0.00	0.0–11.8	∞	
25–34	3.66	0.8–10.7	0.00	0.0–1.2	∞	
35–44	8.39	4.2–15.0	0.16	0.0–0.9	52.43	21.6–98.5
45–54	4.82	1.0–14.1	1.95	0.9–3.6	2.47	0.8–6.0
55–64	8.38	1.7–24.5	1.99	0.6–4.6	4.21	1.7–7.9
65–74	7.94	1.0–28.7	0.00	0.0–17.1	∞	

PRECOZ

Age-specific Incidence Rates of Myocardial Infarction and Angina in Women with Systemic Lupus Erythematosus: Comparison with the Framingham Study



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25–34	3.66	0.8–10.7	0.00	0.0–1.2	∞	
35–44	8.39	4.2–15.0	0.16	0.0–0.9	52.43	21.6–98.5
45–54	4.82	1.0–14.1	1.95	0.9–3.6	2.47	0.8–6.0
55–64	8.38	1.7–24.5	1.99	0.6–4.6	4.21	1.7–7.9
65–74	7.94	1.0–28.7	0.00	0.0–17.1	∞	

PRECOZ

Racial Disparities in Age at Time of Cardiovascular Events and Cardiovascular-Related Death in Patients With Systemic Lupus Erythematosus

Lisabeth V. Scalzi, Christopher S. Hollenbeak, and Li Wang

		Controls versus SLE patients		
		Age difference, years		
	SLE patients*	Control subjects*		<i>P</i>
All women	60.8 (3,627)	71.3 (608,543)	10.5	<0.0001
White	63.5 (2,352) [65]	72.5 (466,056) [76]	9.0	<0.0001
Black	53.9 (786) [21]	65.8 (67,602) [11]	11.9	<0.0001
Hispanic	57.5 (343) [9]	68.6 (48,085) [8]	11.1	<0.0001
Asian	60.6 (55) [2]	71.5 (10,994) [2]	10.8	<0.0001
Other	57.0 (91) [3]	68.6 (15,806) [3]	11.6	<0.0001
All men	60.4 (805)	65.9 (828,608)	5.5	<0.0001
White	63.0 (603) [75]	66.7 (665,999) [80]	3.7	<0.0001
Black	52.3 (114) [14]	61.4 (59,851) [7]	9.1	<0.0001
Hispanic	51.4 (58) [7]	63.5 (59,556) [7]	12.1	<0.0001
Asian	59.2 (8) [1]	65.9 (16,914) [2]	6.7	0.16
Other	55.4 (22) [3]	62.6 (26,288) [3]	7.2	0.009

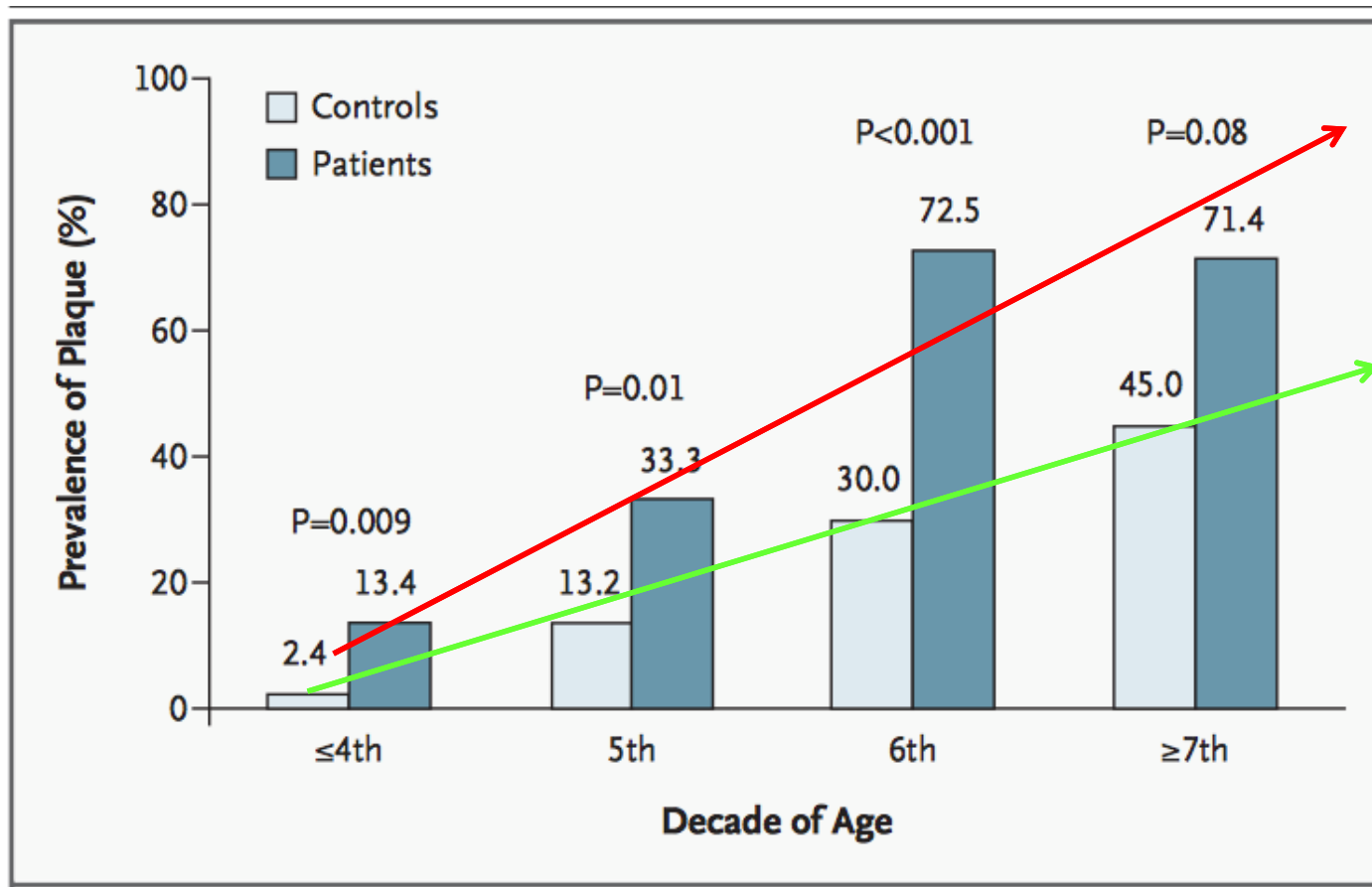
Racial Disparities in Age at Time of Cardiovascular Events and Cardiovascular-Related Death in Patients With Systemic Lupus Erythematosus

Lisabeth V. Scalzi, Christopher S. Hollenbeak, and Li Wang

	SLE patients*	Control subjects*	Controls versus SLE patients	
			Age difference, years	<i>P</i>
All women	63.4 (218)	78.2 (35,003)	14.8	<0.0001
White	67.1 (141) [65]	79.3 (27,142) [78]	12.2	<0.0001
Black	52.8 (47) [21]	72.6 (3,674) [10]	19.8	<0.0001
Hispanic	62.0 (17) [8]	74.9 (2,472) [7]	12.9	<0.0001
Asian	63.8 (9) [4]	77.5 (825) [2]	13.7	0.0004
Other	63.5 (4) [2]	75.4 (890) [3]	11.9	0.07
All men	63.7 (38)	74.7 (35,501)	11.0	<0.0001
White	66.2 (33) [86]	75.7 (28,178) [79]	9.5	<0.0001
Black	52.4 (3) [8]	68.4 (2,785) [8]	16.0	0.05
Hispanic	0	71.0 (2,588) [7]	NA	NA
Asian	45.0 (1) [3]	75.4 (965) [3]	30.4	0.02
Other	36.0 (1) [3]	71.7 (985) [3]	35.7	0.005

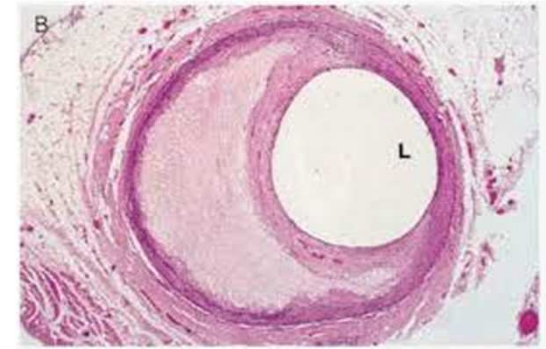
Prevalence and Correlates of Accelerated Atherosclerosis in Systemic Lupus Erythematosus

Mary J. Roman, M.D., Beth-Ann Shanker, A.B., Adrienne Davis, A.B.,
Michael D. Lockshin, M.D., Lisa Sammaritano, M.D., Ronit Simantov, M.D.,
Mary K. Crow, M.D., Joseph E. Schwartz, Ph.D., Stephen A. Paget, M.D.,
Richard B. Devereux, M.D., and Jane E. Salmon, M.D.

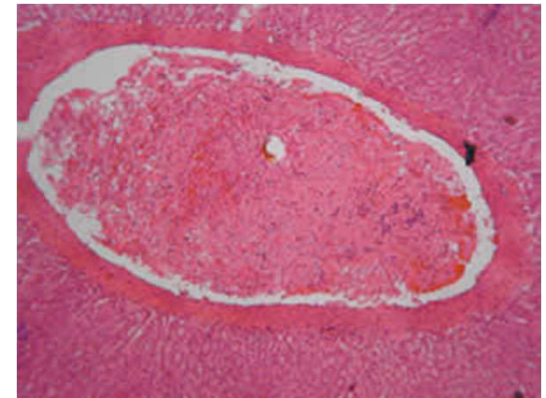




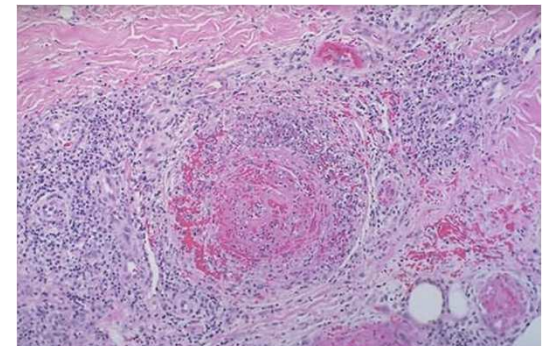
Arteriosclerosis

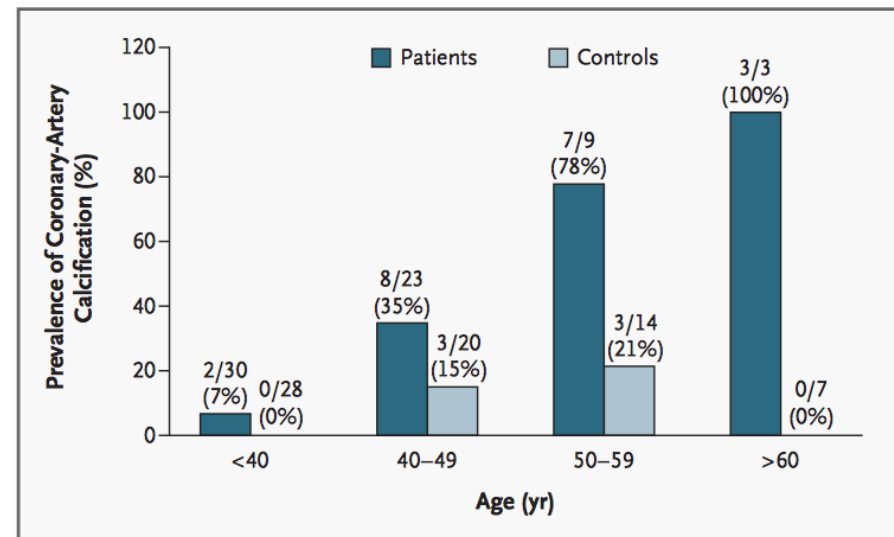
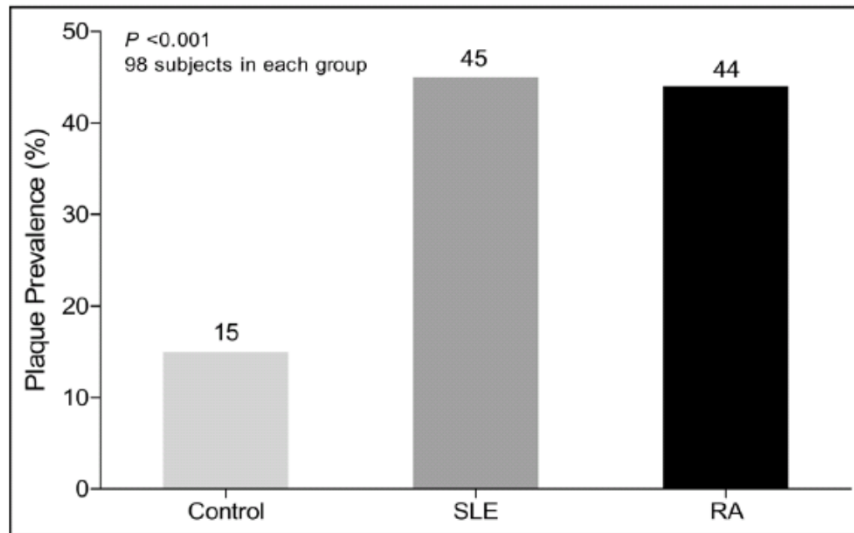


Trombosis

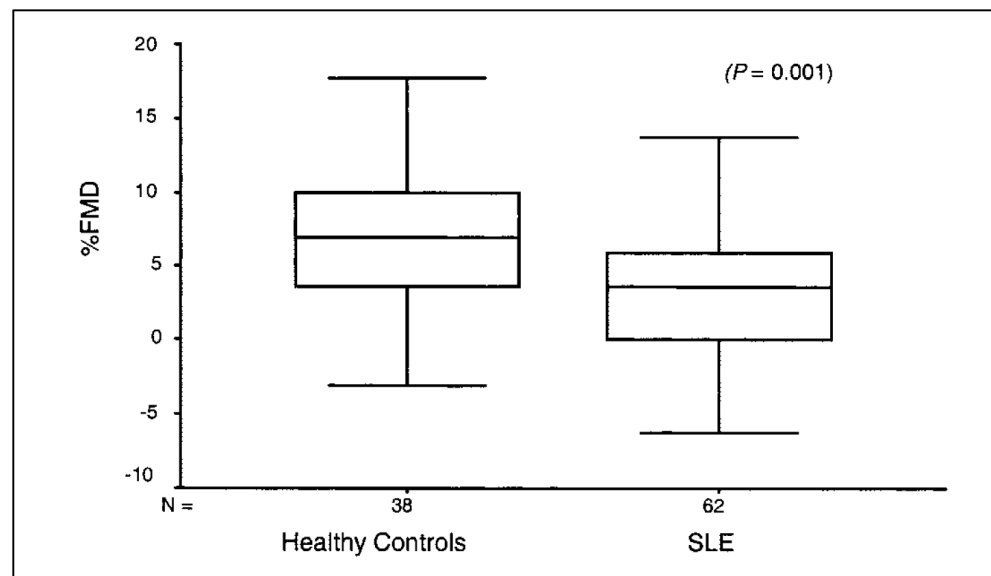


Vasculitis



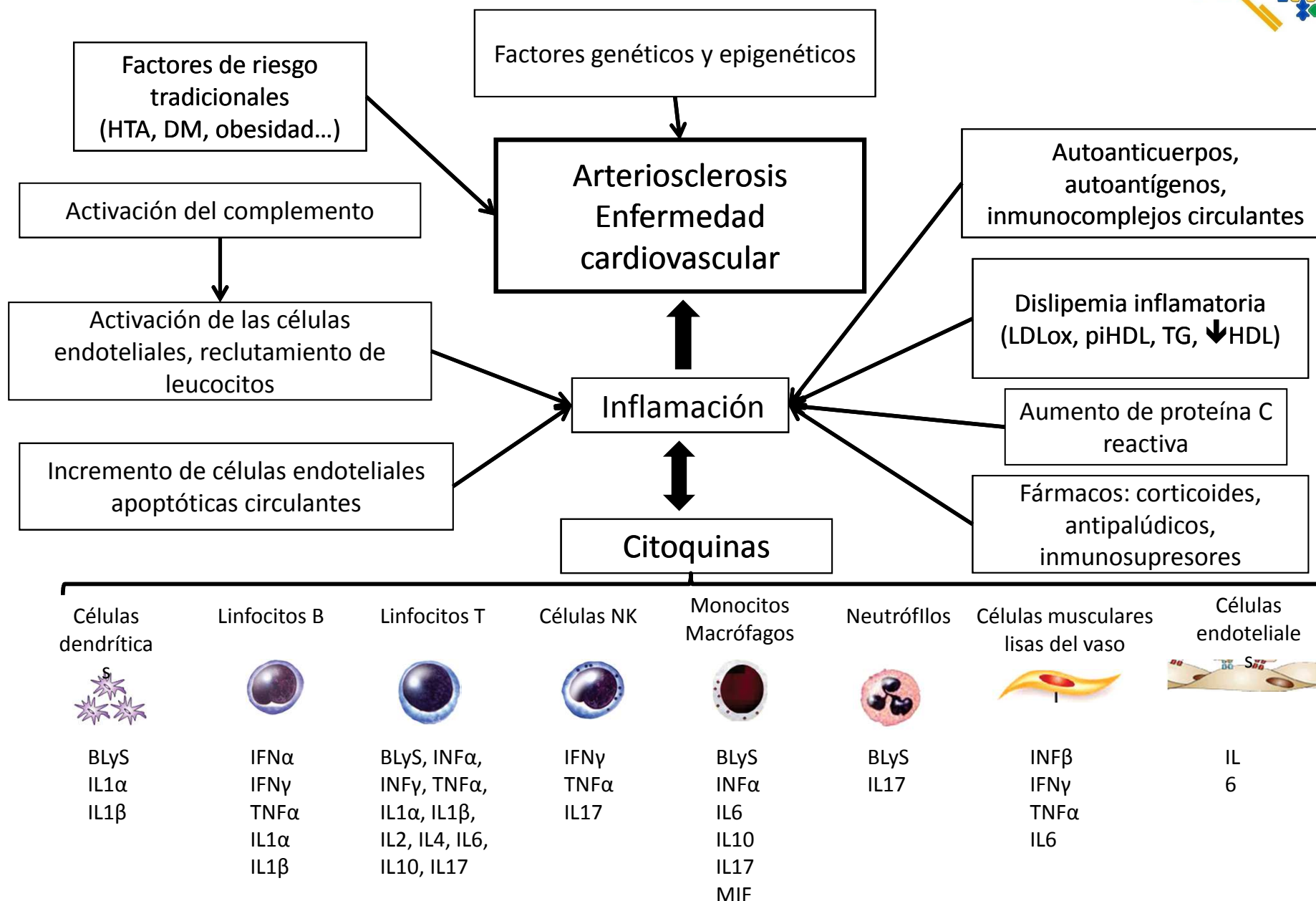


N Engl J Med 2003;349:2407-15.



Circulation. 2004;110:399-404

Figura 1. Etiopatogenia de la arteriosclerosis en el LES



HIPERTENSIÓN ARTERIAL
DISLIPEMIA INFLAMATORIA
MENOPAUSIA
SÍNDROME METABÓLICO
RESISTENCIA INSULINA / DM
HIPERHOMOCISTEINEMIA

FRCV
tradicionales

SEDENTARISMO
OBESIDAD

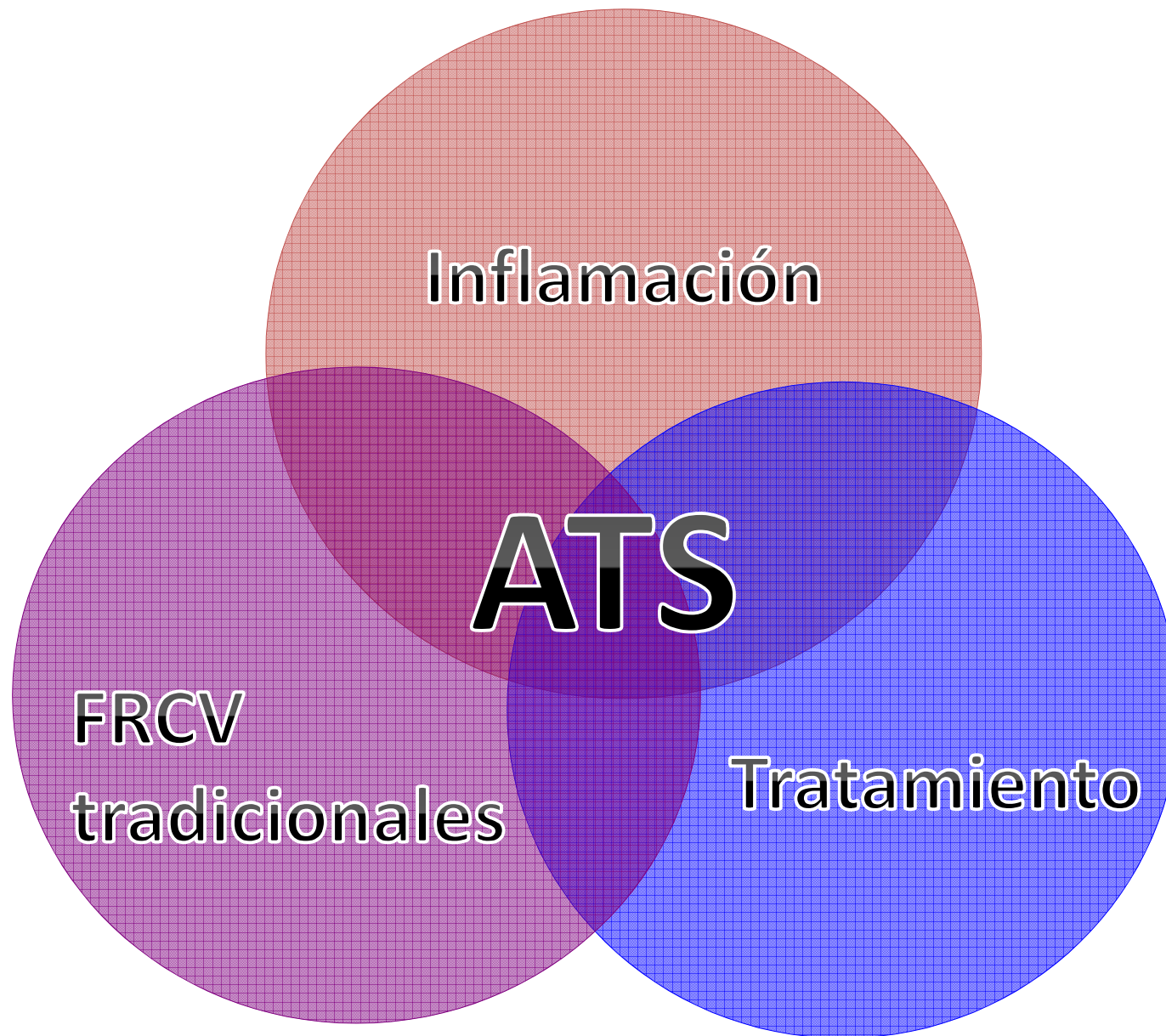
Traditional Framingham Risk Factors Fail to Fully Account for Accelerated Atherosclerosis in Systemic Lupus Erythematosus

John M. Esdaile,¹ Michal Abrahamowicz,² Tamara Grodzicky,³ Yin Li,⁴ Constantina Panaritis,⁴
 Roxane du Berger,⁴ Robert Côté,² Steven A. Grover,² Paul R. Fortin,²
 Ann E. Clarke,² and Jean-Luc Senécal³

Outcome	Observed number of events	Expected number of events	Observed: expected ratio	95% CI
Nonfatal myocardial infarction	17	1.7	10.1	5.8–15.6
Death due to coronary heart disease	12	0.7	17.0	8.1–29.7
Overall coronary heart disease	34	4.5	7.5	5.1–10.4
Stroke	16	2.0	7.9	4.0–13.6

* 95% CI = 95% confidence interval.

FRCV
tradicionales



Mujeres

Hombres

SCORE < 1%

(Riesgo bajo)

94 %

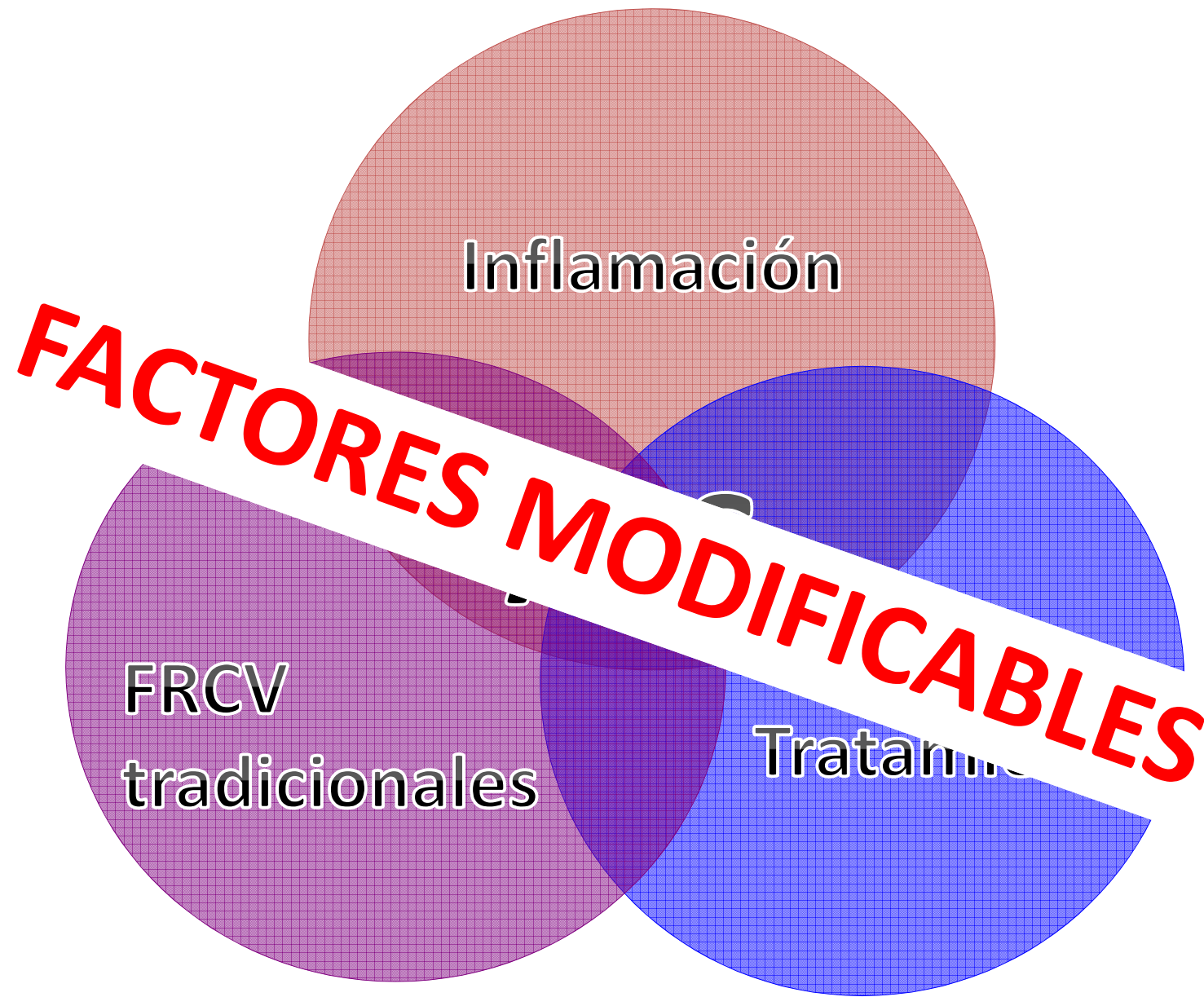
SCORE 1 - 5 %

(Riesgo moderado)

5 %

Colesterol Total

150 200 250 300
mg/dl



Atherosclerotic Vascular Inception Cohort of Sys

- Duración del ttº con PRED
- Hipercolesterolemia
- Hipertensión arterial
- Tabaquismo

- Proteína C reactiva (¿inflamación?)
- Menopausia

	Baltimore (n = 229) (2)	Pitt (n	
Type of cohort	Prevalent	Pre	
Older age at diagnosis	√		
Longer duration of SLE	√		
Male sex			
Longer duration of prednisone use	√		
Hypercholesterolemia	√		
Hypertension	√		
Postmenopausal status			
Smoking			
Neuropsychiatric lupus			
C-reactive protein			
Antiphospholipid antibodies			

- Mayor edad al dx de LES
- Mayor duración del LES
- Género masculino
- Menopausia
- Lupus neuropsiquiátrico
- Anticuerpos antifosfolípido

A medical clipboard with a blue stethoscope is shown. The stethoscope has a blue tube and a silver chest piece. The clipboard has a silver clip at the top and a blue cover. The text is handwritten in black ink on a white sheet of paper.

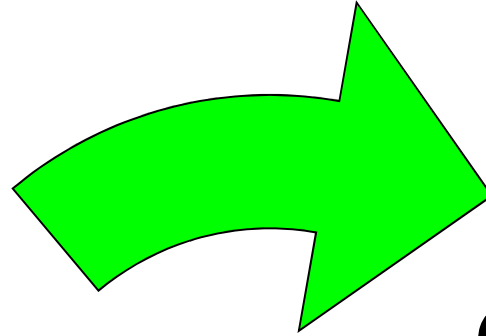
*Comunicación:
asignatura pendiente*

1. Estratificación del riesgo cardiovascular en los pacientes con LES
2. Estudios (ensayos clínicos) que demuestren qué medidas disminuyen la morbi-mortalidad cardiovascular en los pacientes con LES



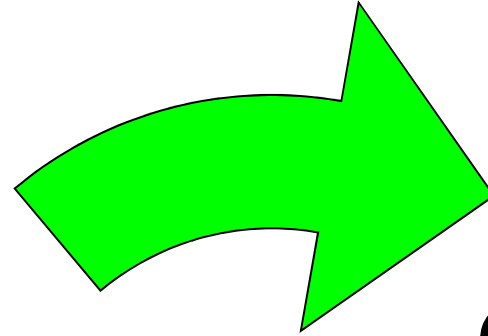
**SENTIDO
COMUN 2.0**

**CONCIENCIACIÓN DE LA
ENFERMEDAD CARDIOVASCULAR
EN LOS PACIENTES CON LUPUS
ERITEMATOSO SISTÉMICO ES UN
PROBLEMA DE PRIMER ORDEN**

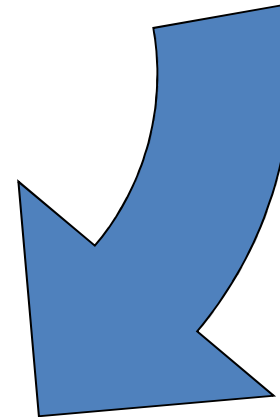


**Control
FRCV**

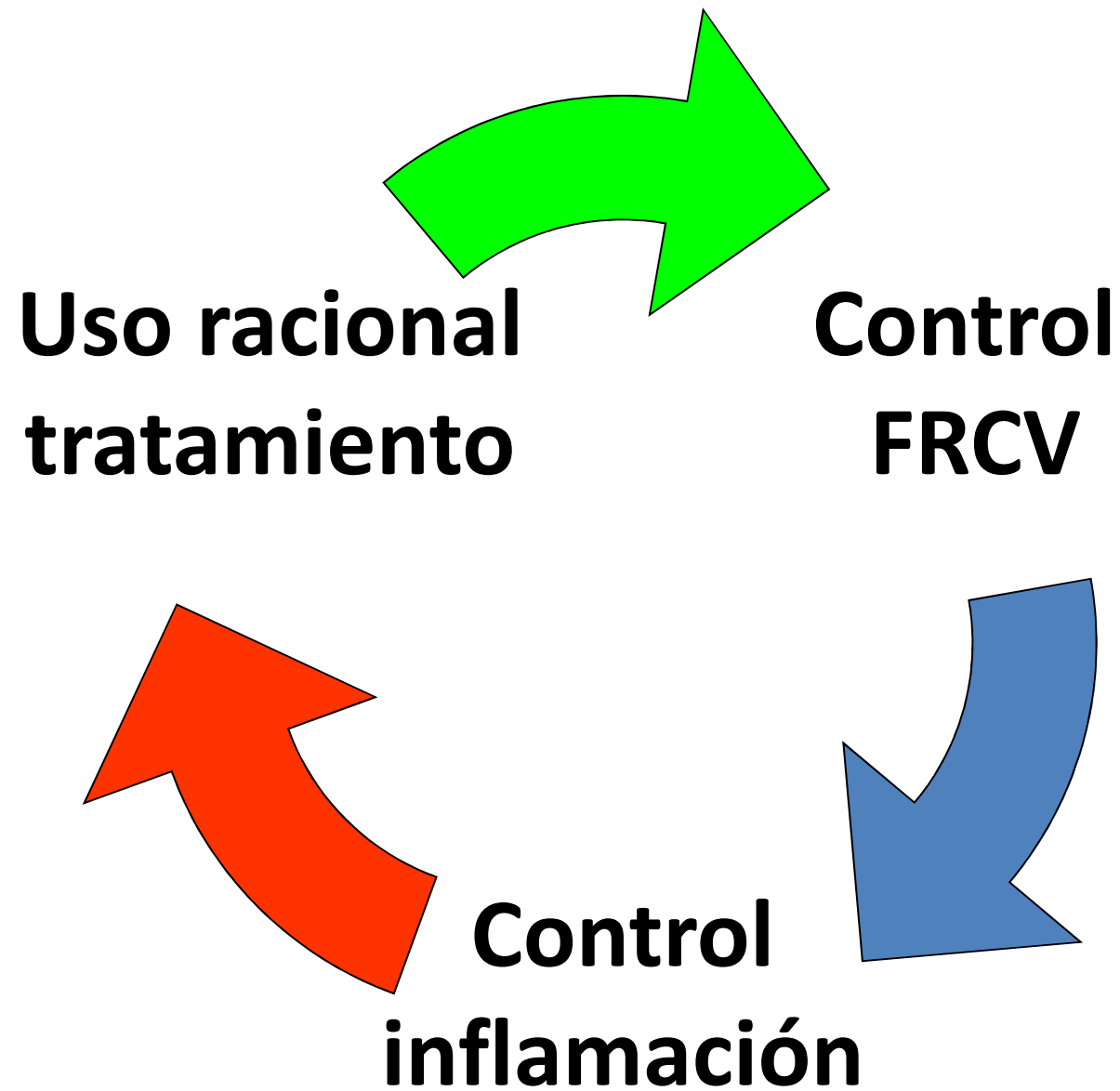
Cholesterol	1. Screening: fasting lipid profile every year; 2. For LDL cholesterol < 100 no treatment; 3. For LDL cholesterol 100–130 mg/dl: therapeutic lifestyle changes. 4. Consider statins when LDL is > 130 mg/dl with or without other risk factors; or when LDL is persistently > 100 mg/dl despite therapeutic lifestyle changes.
Hypertension	1. Blood pressure assessments at every visit to the outpatients clinic; 2. Ideal target is defined as blood pressure at <130mmHg systolic and <80mmHg diastolic. 3. If elevated blood pressure (>140 mmHg systolic or >90mmHg diastolic): lifestyle modification.; 4. If, despite previous measures, the blood pressure is persistently found to be elevated: start antihypertensive medication.
Diabetes mellitus	1. Regular testing for diabetes (1-2 /year); 2. In patients with a fasting glucose ≥ 6.1 mmol/l: glucose tolerance test and lifestyle changes; 3. Referral to a specialist in diabetes.
Weight control	1. Screening for obesity; 2. Lifestyle changes, exercise programmes and behavioral support; 3. If, despite efforts, obesity remains, refer to drug/ bariatric surgery by a multidisciplinary team.



**Control
FRCV**



**Control
inflamación**



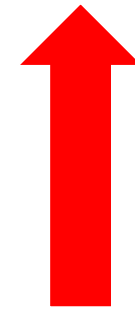


ENFERMEDADES CARDIOVASCULARES ASOCIADAS AL SÍNDROME ANTIFOSFOLÍPIDO

✓ ACCIDENTES CEREBROVASCULARES

✓ CARDIOPATÍA ISQUÉMICA

✓ ENFERMEDAD VASCULAR PERIFÉRICA



AAF

✓ VALVULOPATÍA (Endocarditis de Libman-Sacks)

✓ MIOCARDIOPATÍA DILATADA

✓ HIPERTROFIA Y DISFUNCIÓN VENTRICULAR

✓ HTP SECUNDARIA A TEP CRÓNICO

Morbidity and mortality in the antiphospholipid syndrome during a 10-year period: a multicentre prospective study of 1000 patients

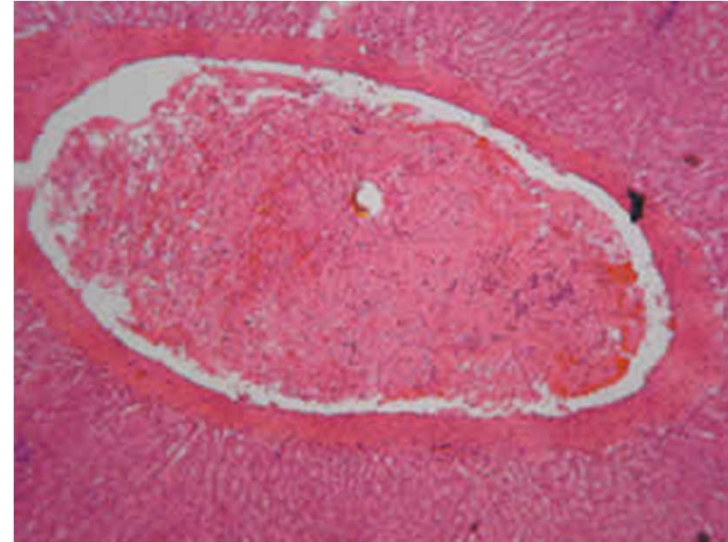
Clinical manifestation*	0 year† (n=1000) No. (%)	0–5 year (n=1000) No. (%)	5–10 year (n=796)‡ No (%)	0–10 year (n=1000) No (%)
Thrombocytopenia (<100 000/ μ L)	296 (29.6)	37 (3.7)	50 (6.3)	87 (8.7)
<i>Livedo reticularis</i>	241 (24.1)	26 (2.6)	55 (6.9)	81 (8.1)
Stroke	198 (19.8)	24 (2.4)	29 (3.6)	53 (5.3)
Transient ischaemic attacks	111 (11.1)	23 (2.3)	24 (3.0)	47 (4.7)
Deep vein thrombosis	389 (38.9)	21 (2.1)	22 (2.7)	43 (4.3)
Pulmonary embolism	141 (14.1)	21 (2.1)	14 (1.7)	35 (3.5)
Epilepsy	70 (7.0)	17 (1.7)	15 (1.9)	32 (3.2)
Skin ulcers	55 (5.5)	17 (1.7)	14 (1.7)	31 (3.1)
Valve thickening/dysfunction	116 (11.6)	17 (1.7)	29 (3.6)	46 (4.6)
Vegetations	27 (2.7)	14 (1.4)	7 (0.9)	21 (2.1)
Myocardial infarction	55 (5.5)	9 (0.9)	10 (1.2)	19 (1.9)
Superficial thrombophlebitis	117 (11.7)	9 (0.9)	8 (1.0)	17 (1.7)
Autoimmune haemolytic anaemia	97 (9.7)	9 (0.9)	31 (3.9)	40 (4.0)

Morbidity and mortality in the antiphospholipid syndrome during a 10-year period: a multicentre prospective study of 1000 patients

Table 5 Main causes of death related to antiphospholipid syndrome (APS) associated with systemic lupus erythematosus (SLE) and primary APS that appeared during the 10-year follow-up (1999–2009) of the 'Euro-Phospholipid' cohort

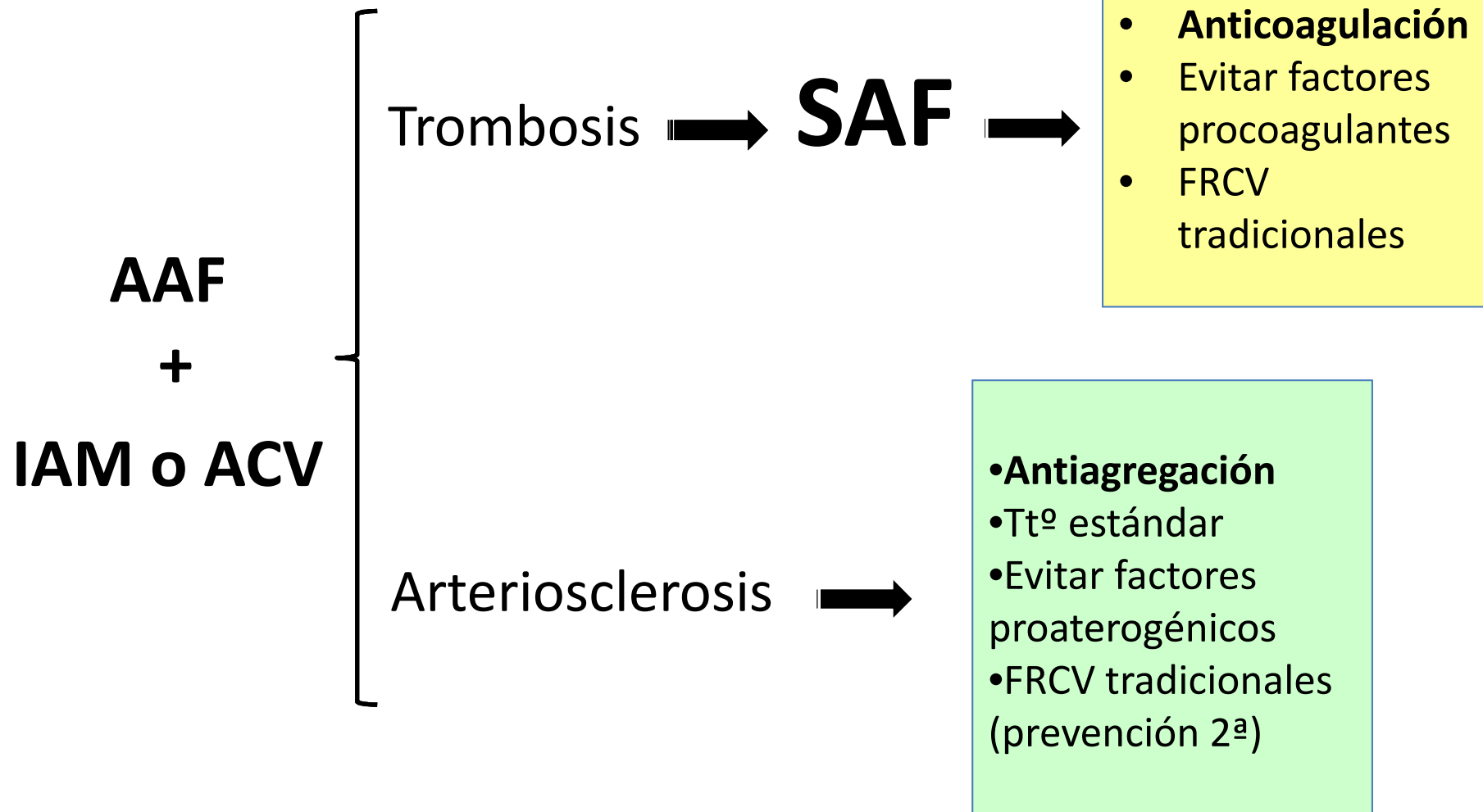
Causes of death*	APS associated to SLE (n=9)† No. (%)	Primary APS (n=30)† No. (%)
Myocardial infarction	0	3 (10)
Stroke	1 (11.1)	3 (10)
SLE renal involvement	1 (11.1)	0
SLE haematological involvement	1 (11.1)	0
Bacterial infection	3 (33.3)	6 (20)
Viral infection	0	3 (10)
Malignancy	1 (11.1)	6 (20)
Haemorrhage	2 (22.2)	7 (23)

Trombosis

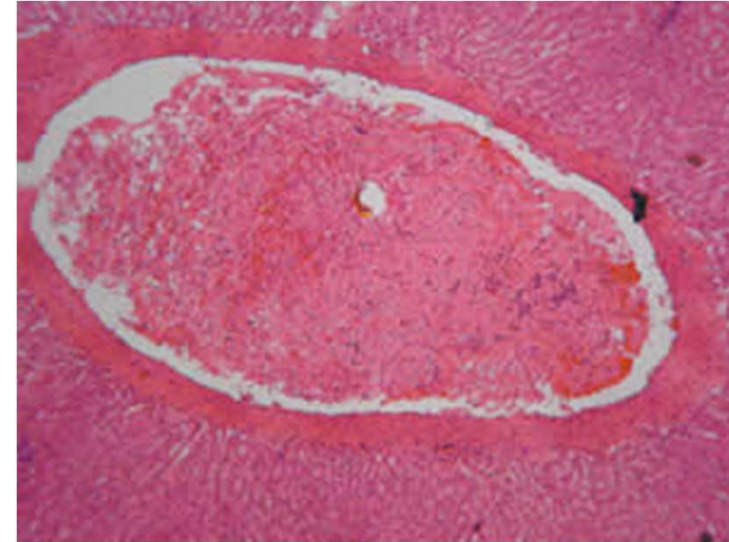


Arteriosclerosis





Trombosis



¿Arteriosclerosis?



Primary antiphospholipid syndrome: a low-grade auto-inflammatory disease?

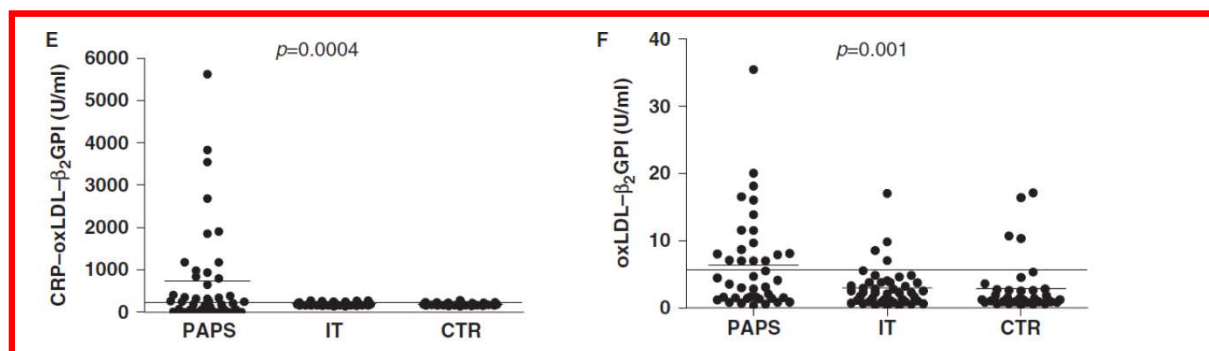


P. R. J. Ames^{1,2}, I. Antinolfi³, A. Ciampa⁴, J. Batuca⁵, G. Scenna³, L. R. Lopez⁶, J. Delgado Alves⁵, L. Iannaccone³ and E. Matsuura⁷



Rheumatology key messages

- Low-grade inflammation and immune activation occur in primary thrombotic antiphospholipid syndrome.
- Immune activation *in vivo* reflects monocyte activation by IgG β_2 GPI *in vitro*.
- Such markers could aid monitoring drug efficacy in interventional trials.



Premature atherosclerosis in primary antiphospholipid syndrome: preliminary data

P R J Ames, A Margarita, K B Sokoll, M Weston, V Brancaccio

Table 2 Intima media thickness in study groups

	CTR (n = 20)	PAPS (n = 20)	p Value
<i>IMT (mm) overall</i>			
CC	0.43 (0.08)	0.53 (0.28)	0.18
B	0.48 (0.09)	0.61 (0.24)	0.04
IC	0.40 (0.08)	0.52 (0.22)	0.01
Disease duration (years)		7 (4)	
<i>IMT (mm) < 31 years</i>			
	CTR (n = 10)	PAPS (n = 10)	
CC	36 (0.05)	0.40 (0.09)	0.31
B	41 (0.04)	0.45 (0.08)	0.30
IC	34 (0.04)	0.41 (0.12)	0.13
Disease duration (years)		5 (3)	
<i>IMT (mm) > 40 years</i>			
CC	0.49 (0.04)	0.67 (0.35)	0.12
B	0.55 (0.06)	0.76 (0.25)	0.0007
IC	0.45 (0.09)	0.63 (0.25)	0.02
Disease duration (years)		9 (4)*	

Ann Rheum Dis 2005;**64**:315–317.

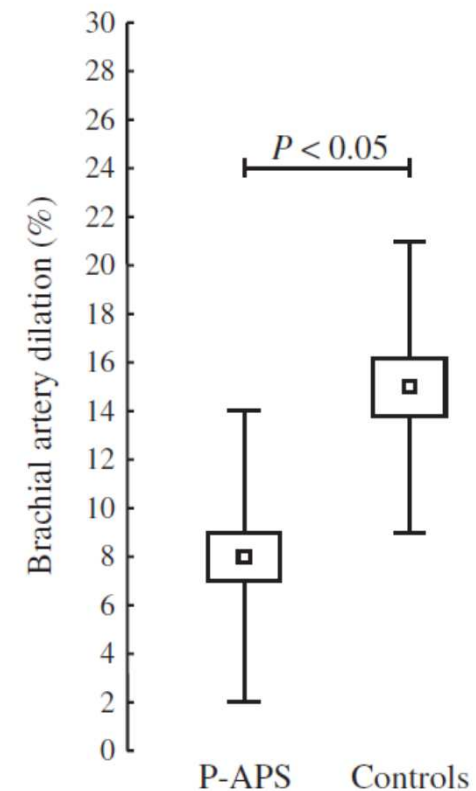
Atherosclerosis in thrombotic primary antiphospholipid syndrome

P. R. J. AMES,* I. ANTINOLFI,† G. SCENNA,† G. GAETA,‡ M. MARGAGLIONES and A. MARGARITA†

	PAPS (n = 49)	CTR (n = 49)	P
Common carotid (mm)	0.487 ± 0.123	0.416 ± 0.085	0.004
Carotid bifurcation (mm)	0.556 ± 0.162	0.481 ± 0.108	0.013
Internal carotid (mm)	0.463 ± 0.118	0.385 ± 0.092	0.001

J Thromb Haemost 2009; **7**: 537–42

Endothelial function is impaired in patients with primary antiphospholipid syndrome



Thrombosis Research (2006) **118**, 455 – 461

Anticardiolipin antibody titre and plasma homocysteine level independently predict intima media thickness of carotid arteries in subjects with idiopathic antiphospholipid antibodies



PRJ Ames^{1*}, A Margarita², J Delgado Alves³, C Tommasino⁴, L Iannaccone⁵ and V Brancaccio⁵

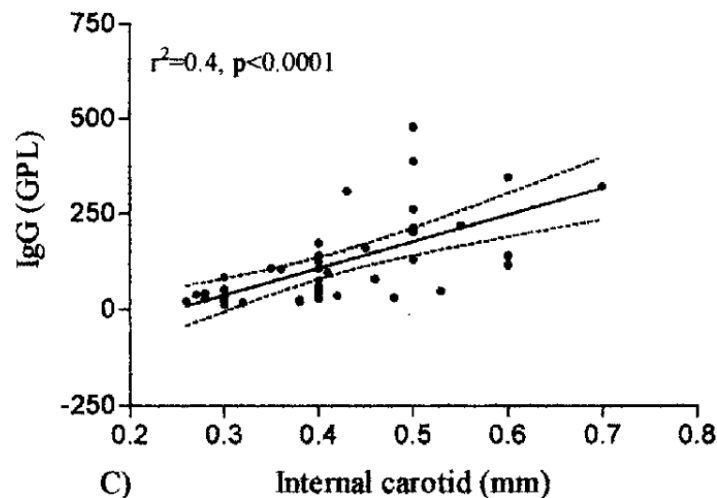
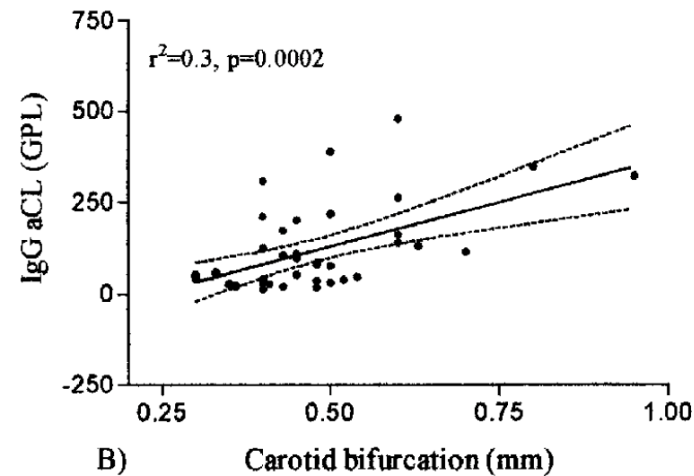
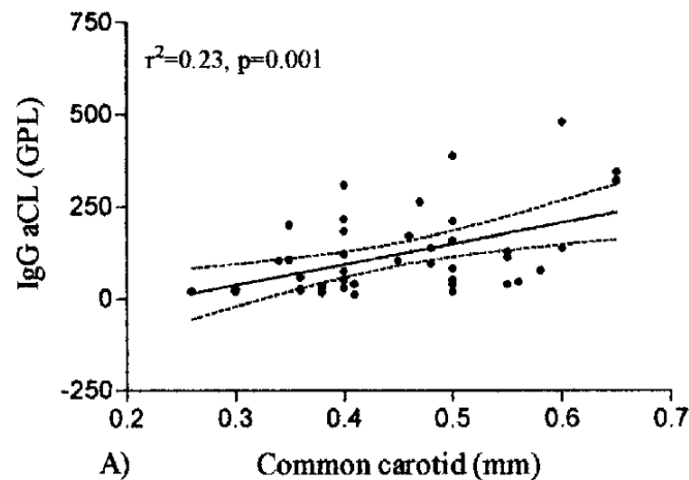


Table 4 Independent predictors of intima-media thickness of carotid arteries generated by a stepwise multiple regression

<i>Dependent variable</i>	<i>Predictor</i>	β	<i>P-value</i>
Common carotid	IgG aCL	0.375	< 0.005
	FNG	0.441	0.001
	HC	0.404	< 0.0001
Carotid bifurcation	IgG aCL	0.337	0.008
	IgG aCL	0.502	< 0.0001
	HC	0.405	< 0.0001
Internal carotid	HC	0.405	< 0.0001
	FNG	0.268	0.03

¿ARTERIOSCLEROSIS EN EL SAF?

A favor	En contra
1. Evidencia experimental de que los AAF podrían producir disfunción endotelial y activación de monocitos en la pared arterial. 2. Evidencia (++)/- de la existencia de arteriosclerosis subclínica.	1. Ausencia de estudios epidemiológicos que demuestren que indiquen que la presencia de arteriosclerosis acelerada en pacientes con SAF primario.

*“Si quieres que
algo cambie, no
hagas siempre
lo mismo”*

