

IMPLICACIONES Y MANEJO DE ANTI RO EN LA GESTACIÓN

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AC ANTI RO

Table 1

Prevalence of anti-Ro/SSA and anti-La/SSB antibodies in different autoimmune rheumatic diseases

	Anti-Ro/SSA	Anti-La/SSB	Ref.
Sjögren's syndrome	60–90%	30–60%	Routsias JG, et al. <i>Clinic Rev Allerg Immunol</i> 2007
Systemic lupus erythematosus	30–50%	10–40%	Franceschini F, Cavazzana I. <i>Autoimmunity</i> 2005
Systemic sclerosis	12%	4%	Codullo V, et al. <i>Future Rheumatol</i> 2006
Rheumatoid Arthritis	11%	–	Franceschini F, Cavazzana I. <i>Autoimmunity</i> 2005
Undifferentiated connective tissue disease	8–30%	–	Belfiore N, et al. <i>J Bone Spine</i> 2000

EMBARAZO Y AC ANTI RO +

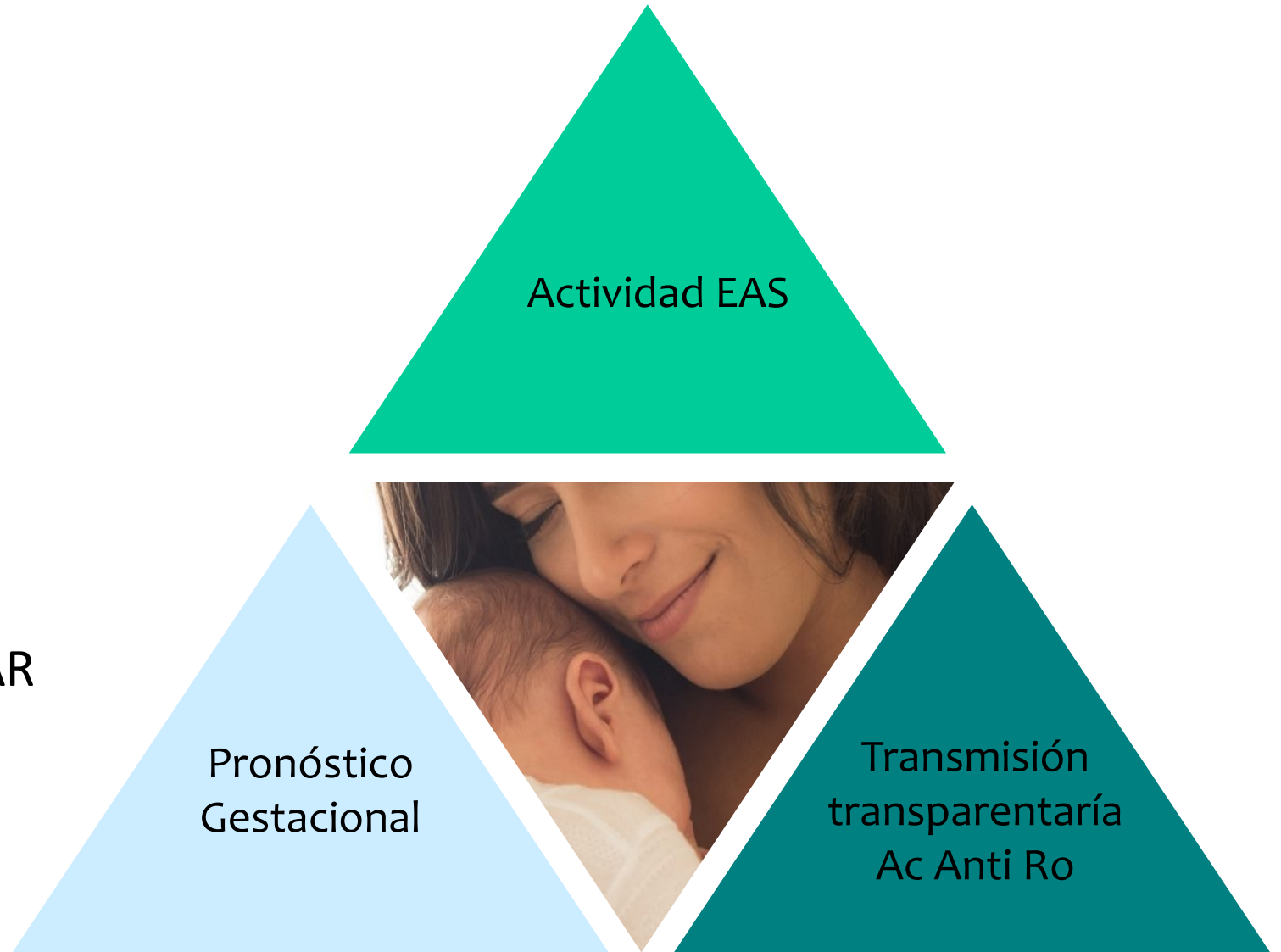
SITUACIÓN DE RIESGO



BINOMIO MADRE/HIJO



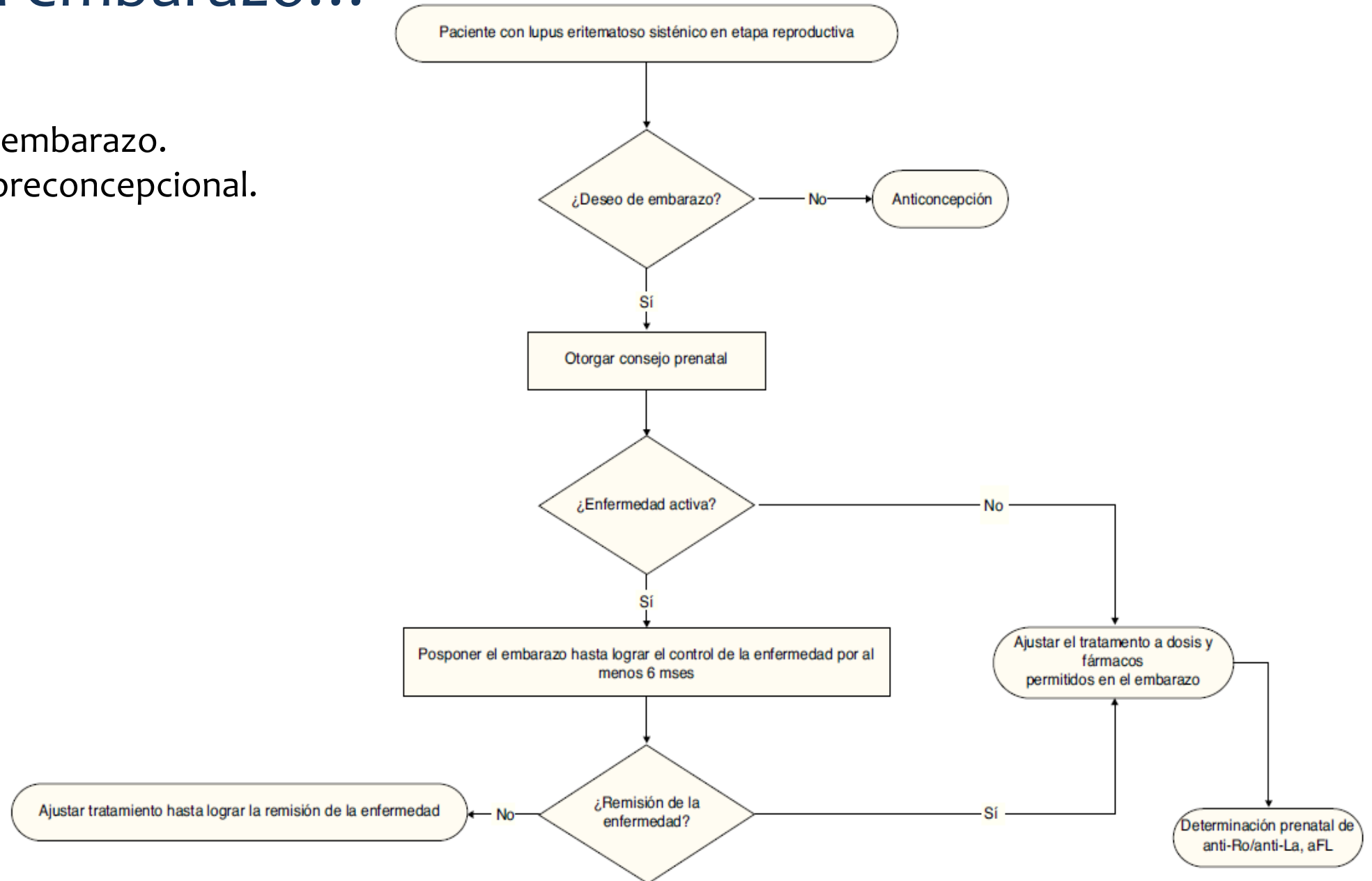
ABORDAJE MULTIDISCIPLINAR



Previo al embarazo...

M.Á. Saavedra Salinas et al. / Reumatol Clin. 2015;11(5):295-304

Planificar el embarazo.
Evaluación preconcepcional.



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Table 2 Pregnancy outcome of all anti-Ro/SSA positive vs all anti-Ro/SSA negative women

	<i>Ro/SSA positive women</i>		<i>Ro/SSA negative women</i>	
	n	% ^a	n	% ^a
Number of women	100		107	
Number of pregnancies	122		140	
Twin pregnancies	4		2	
Living newborns	116	95.1%	125	89.3%
Total spontaneous pregnancy losses	10	8.2%	17	12.1%
Pregnancy losses < 10 weeks	7	5.7%	10	7.1%
Pregnancy losses > 10 weeks	3	2.4%	7	5.0%
Therapeutical abortions	0	0	1	0.7%
Prematurity < 37 weeks	19	15.6%	16	11.4%
Prematurity < 34 weeks	3	2.5%	2	1.4%
Mean gestational age at delivery; weeks (range)	38 (30–42)		38.4 (33–42)	
Maternal mean age at delivery; years (range)	31.2 (25–40)		29.8 (20–41)	
<i>Previous pregnancies (retrospective analysis)</i>				
Total pregnancies	44		44	
Pregnancy losses < 10 weeks	16	36.3%	9	20.4%
Pregnancy losses > 10 weeks	5	11.4%	8	18.1%
Total spontanous pregnancy losses ^b	21	47.7%	17	38.6%
Therapeutical abortions	3	6.8%	5	11.4%

^aPercentages are expressed on the number of pregnancies: prospective, 122 for Ro/SSA positive and 140 for Ro/SSA negative women; 44 retrospective pregnancies for both.

^bTotal spontanous pregnancy losses: in anti-Ro/SSA positive women, prospective (10/122) vs retrospective (21/44), $P < 0.001$; in anti-Ro/SSA negative women, prospective (17/140) vs retrospective (17/44), $P < 0.001$.

Ac Anti Ro/SSA no relacionados con infertilidad

Ac Anti Ro/SSA no influye en el pronóstico de la gestación (excepto LN cardíaco).

AC ANTI RO Y EMBARAZO

Table 3 Pregnancy outcome of non-SLE anti-Ro/SSA positive vs non-SLE anti-Ro/SSA negative women

	<i>Ro/SSA positive women</i>		<i>Ro/SSA negative women</i>	
	n	% ^a	n	% ^a
Number of women	47		49	
Number of pregnancies	61		54	
Twin pregnancies	3		2	
Living newborns	60	98.4%	55	101.8%
Total spontaneous pregnancy losses	4	6.6%	1	1.8%
Pregnancy losses < 10 weeks	3	4.9%	0	0
Pregnancy losses > 10 weeks	1	1.6%	1	1.8%
Therapeutical abortions	0	0	0	0
Prematurity < 37 weeks	6	9.8%	4	7.4%
Prematurity < 34 weeks	1	1.6%	1	1.8%
Mean gestational age at delivery; weeks (range)	38 (34–42)		39.3 (33–41)	
Maternal mean age at delivery; years (range)	30 (24–37)		29.6 (24–41)	
Positivity for aPL	2	3.3%	5	10.2%
<i>Previous pregnancies (retrospective analysis)</i>				
Total pregnancies	23		22	
Pregnancy losses < 10 weeks	9	39.1%	6	27.3%
Pregnancy losses > 10 weeks	2	8.7%	3	13.7%
Total spontanous pregnancy losses ^b	11	47.8%	9	40.9%
Therapeutical abortions	2	8.7%	0	0

^aPercentages are expressed on the number of pregnancies: prospective, 61 for Ro/SSA positive and 54 for Ro/SSA negative women; retrospective, 23 for Ro/SSA positive and 22 for Ro/SSA negative women.

^bTotal spontanous pregnancy losses: in anti-Ro/SSA positive women, prospective (4/61) vs retrospective (11/23), $P < 0.001$; in anti-Ro/SSA negative women, prospective (1/54) vs retrospective (9/22), $P < 0.001$.

Ac Anti Ro/SSA no relacionados con infertilidad

Ac Anti Ro/SSA no influye en el pronóstico de la gestación (excepto LN cardíaco).

AC ANTI RO Y EMBARAZO

Review > Expert Rev Clin Immunol. 2019 Jun;15(6):617-627.

doi: 10.1080/1744666X.2019.1601557. Epub 2019 Apr 19.

Clinical outcomes and predictors of maternal and fetal complications in pregnancies of patients with systemic lupus erythematosus

Maddalena Larosa ¹, Teresa Del Ross ¹, Antonia Calligaro ¹, Maria Favaro ¹, Elisabetta Zanatta ¹, Luca Iaccarino ¹, Andrea Doria ¹

Aumento del riesgo de actividad de EAS/LES

Factores relacionados con aumento del riesgo de actividad:

- Actividad de la enfermedad en los 6 meses previos. Nefritis lúpica
- Elevado número de brotes previo al embarazo
- Índice SLEDAI > 5 puntos
- Interrupción de tratamientos en la gestación (Hidoxicloroquina GRA)

PRONÓSTICO GESTACIONAL/LES

Published in final edited form as:

Am J Obstet Gynecol. 2008 August ; 199(2): 127.e1–127.e6. doi:10.1016/j.ajog.2008.03.012.

A National Study of the Complications of Lupus in Pregnancy

Megan E. B. Clowse, MD, MPH, Margaret Jamison, PhD, Evan Myers, MD, MPH, and Andra H. James, MD, MPH

Medical complications in SLE pregnancies

Medical Complication	Percentage of SLE pregnancies with the complication	Percentage of non-SLE pregnancies with the complication	Odds Ratio	95% CI	p-value
Thrombotic Complications					
Stroke	0.32%	0.03%	6.5	2.8 to 10.3	<0.001
Pulmonary Embolus	0.4%	0.04%	5.5	2.8 to 10.8	<0.001
DVT	1.0%	0.01%	7.9	5.0 to 12.6	<0.001
Infectious Complications					
Sepsis	0.5%	0.1%	3.5	2.0 to 6.0	<0.001
Pneumonia	1.7%	0.2%	4.3	3.1 to 5.9	<0.001
Hematologic Complications					
Transfusion	2.7%	0.5%	3.6	2.8 to 4.2	<0.001
Postpartum hemorrhage	4.5%	3.3%	1.2	1.0 to 1.5	0.01
Antepartum bleeding	2.0%	0.4%	1.8	1.3 to 2.4	<0.001
Anemia at delivery	12.6%	6.8%	1.9	1.7 to 2.2	<0.001
Thrombocytopenia	4.3%	0.4%	8.3	6.8 to 10.1	<0.001

PRONÓSTICO GESTACIONAL/LES

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Am J Obstet Gynecol. 2008 August ; 199(2): 127.e1–127.e6. doi:10.1016/j.ajog.2008.03.012.

A National Study of the Complications of Lupus in Pregnancy

Megan E. B. Clowse, MD, MPH, Margaret Jamison, PhD, Evan Myers, MD, MPH, and Andra H. James, MD, MPH

Pregnancy complications in SLE pregnancies

Pregnancy Complication	Percentage of SLE deliveries with the complication	Percentage of non-SLE deliveries with the complication	Odds Ratio	95% CI	p-value
Cesarean section	36.6%	25.0%	1.7	1.6–1.9	<0.001
Preterm labor ¹	20.8%	8.1%	2.4	2.1–2.6	<0.001
Intrauterine (fetal) growth restriction	5.6%	1.5%	2.6	2.2–3.1	<0.001
Preeclampsia	22.5%	7.6%	3.0	2.7–3.3	<0.001
Eclampsia	0.5%	0.09%	4.4	2.7–7.2	<0.001

¹Preterm labor indicates women admitted for preterm labor, but is not an accurate proxy for preterm birth.

Co-morbid illnesses in women with SLE

Co-morbid illness	Percentage of SLE deliveries with the condition	Percentage of non-SLE deliveries with the condition	Odds Ratio	95% CI	p-value
Pre-gestational diabetes	5.6%	4.2%	1.7	1.2–2.2	<0.001
Hypertension	3.9%	0.7%	5.5	4.5–6.8	<0.001
Pulmonary hypertension	0.2%	0.01%	10.9	3.9–30.0	<0.001
Renal Failure	0.2%	0.002%	36.9	25.0–52.3	<0.001
Thrombophilia	4.0%	0.04%	34.7	27.7–43.4	<0.001

PRONÓSTICO GESTACIONAL/LES

Observational Study > [Lupus. 2019 Oct;28\(12\):1417-1426. doi: 10.1177/0961203319877247.](#)

Epub 2019 Sep 24.

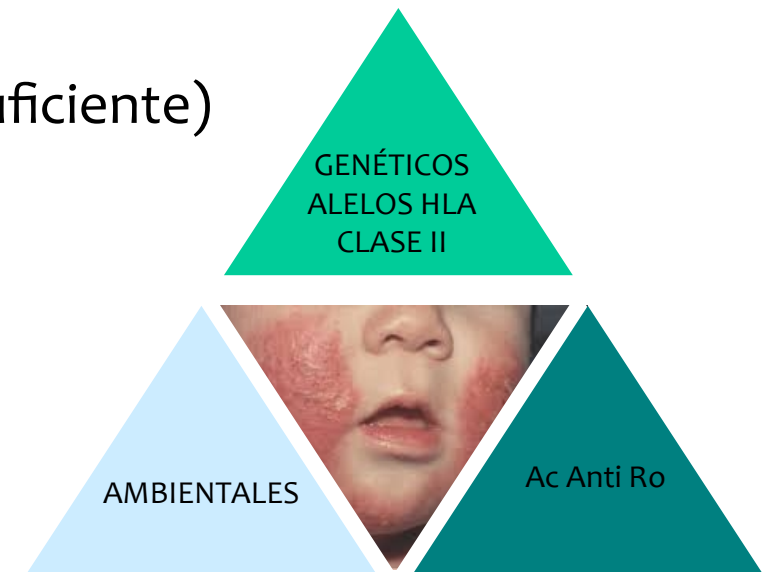
Systemic lupus erythematosus and pregnancy: the challenge of improving antenatal care and outcomes

D E A Pastore ¹, M L Costa ¹, F G Surita ¹

- 102 embarazos
- ↑ abortos y prematuridad
- No influye tratamiento inmunosupresor

LUPUS NEONATAL (LN)

- Enfermedad inmune adquirida del feto.
- Epidemiología:
 - Prevalencia 1/12500 r.n. vivos. Infradiagnosticada.
 - Mortalidad variable. Afectación cardíaca
- Paso transplacentario de Ac maternos de clase IgG (no suficiente)
 - Anti-Ro/SSA 95%
 - Anti-La/SSB 50-70%
 - Anti U1 RNP



- **Buyon et al.: estudio multicéntrico**

- Títulos más altos (ELISA) de Acs anti-Ro/SSA y anti-La/SSB en madres con hijos con LN que en aquellas con hijos sanos

LN. MANIFESTACIONES CLÍNICAS

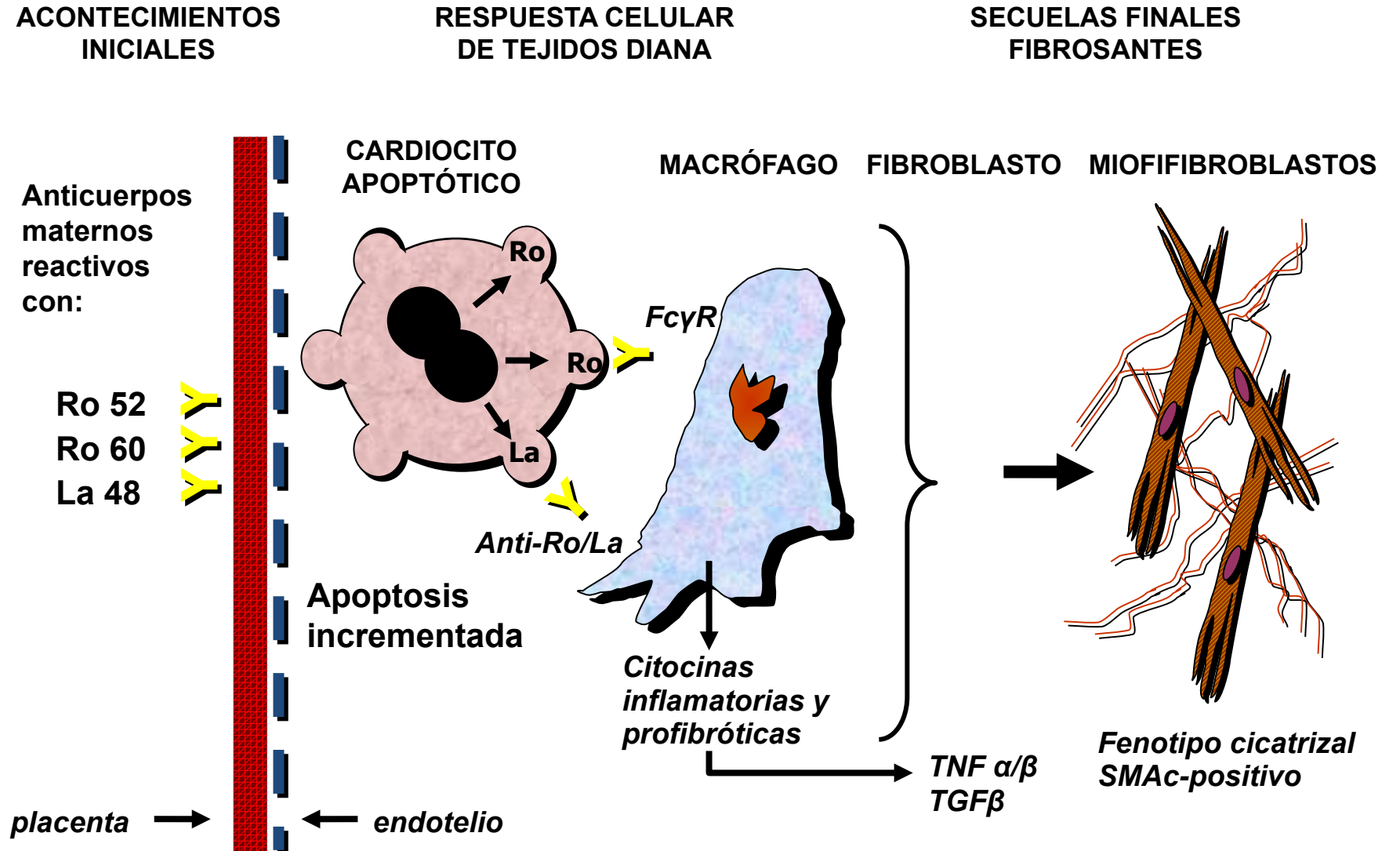
Clinical feature		Reported frequency (%)	Duration
Lupus dermatitis	Face	17/18 (94%) ^a to 57/57 (100%) ^d 15/18 (83%) ^a with 'owl's eye' sign 33/57 (58%) ^d with mask-like distribution	Transient
	Scalp	31/57 (54%) ^d to 15/18 (83%) ^a	Transient
	Trunk/groin	15/57 (26%) ^d to 6/18 (33%) ^a	Transient
	Limbs	13/57 (23%) ^d to 13/18 (72%) ^a	Transient
	Photosensitivity	12/18 (66%) ^a to 45/48 (94%) ^d	Transient
Cutis marmorata telangiectatica		4/18 (22%) ^a	Chronic, but resolves by 12 months of age ^a
Telangiectasia (at sites of lupus dermatitis and arising <i>de novo</i>)		4/18 (22%) ^a	Persistent
Dyspigmentation		3/18 (17%) ^a	Postinflammatory hyperpigmentation clears spontaneously; hypopigmentation may persist for >3 years ^a
Complete heart block		Approximately 2% ^b in primigravidae with anti-Ro or La antibodies; approximately 20% ^b in women having had a previous child with congenital heart block	Develops <i>in utero</i> , perinatally or rarely postnatally; ^c first- and second-degree block may progress to third-degree block which appears to be irreversible
Cardiomyopathy and myocarditis		10–20% ^b of infants with NLE	Persistent and associated with considerable morbidity/mortality
Cholestatic hepatitis		3/18 (17%) ^a	Transient May occur together as part of the HELLP syndrome
Thrombocytopenia		4/18 (22%) ^a	Transient

LN. Manifestaciones cutáneas



LN. Manifestaciones cardíacas

*Semanas 14-16
gestación*



LN. Manifestaciones cardíacas



Bloqueo cardíaco congénito completo

BAV de 1 y 2º grado: reversibles.

Bradicardia sinusal (por afectación del nodo sinusal)

Síndrome de QT largo.

Miocardiopatía, Fibroelastosis

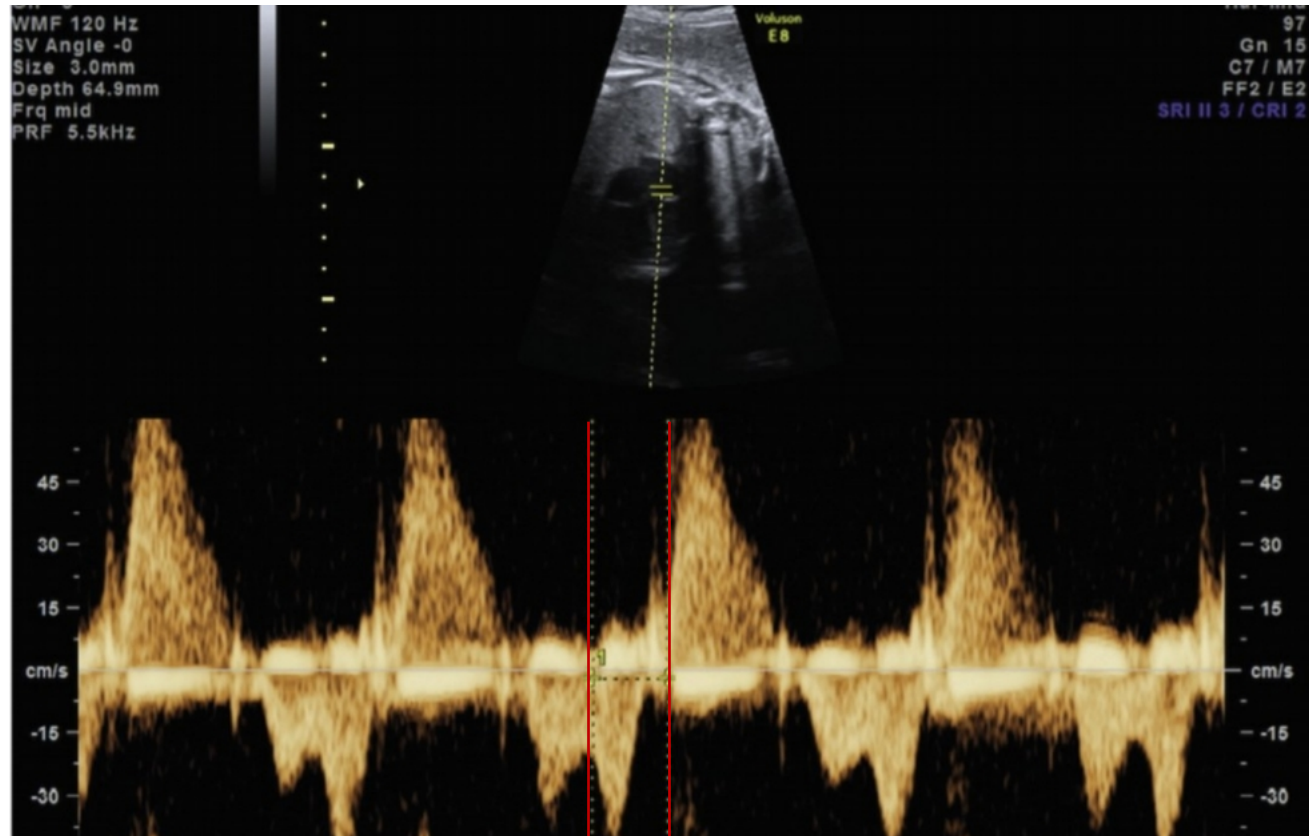
Ac anti Ro/SSA 52Kd 85% casos (p200)

Bloqueo Cardíaco Congénito



DIAGNÓSTICO

- Ecocardiografía fetal
- Medición intervalo PR mecánico (Normal $< 150\text{mseg} \pm 3\text{DE}$)



Diagnóstico precoz

Estudios limitados

BCC completo es IRREVERSIBLE

BCC incompleto: beneficio de tratamiento precoz

Monitorización cardíaca fetal cada 1- 2 semanas a partir de las semanas 14-16 de gestación

Congenital Heart Disease

Utility of Cardiac Monitoring in Fetuses at Risk for Congenital Heart Block The PR Interval and Dexamethasone Evaluation (PRIDE) Prospective Study

Deborah M. Friedman, MD; Mimi Y. Kim, ScD; Joshua A. Copel, MD; Claudine Davis, BS;
Colin K.L. Phoon, MPhil, MD; Julie S. Glickstein, MD; Jill P. Buyon, MD;
for the PRIDE Investigators

Mujeres de alto riesgo :

- Ac anti-Ro/SSA (52 Kd) títulos elevados y/o anti-La/SSB y anti U1 RNP
- Ac anti-Ro/SSA 52Kd (p 200)
- Antecedente de un hijo LN (riesgo de BCC 1-2%→20-25%)

TRATAMIENTO

CORTICOIDES

- Dexametasona 4mg/día, Betametasona 3mg/día
- Efectos adversos maternos y fetales

Review > Curr Opin Rheumatol. 2009 Sep;21(5):478-82. doi: 10.1097/BOR.0b013e32832ed817.

Prevention of complete heart block in children of mothers with anti-SSA/Ro autoantibodies: detection of

degree atrioventricular block

Dror Mevorach¹, Uriel Elchalal, Azaria J J T Reijnders

Ultrasound Obstet Gynecol 2004; 24: 467-472
Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/uo

Treatment of fetal heart block with medical therapy: case report and review of the literature

J. M. P. J. BREUR*, G. H. A. VISSER*, A. A. KRUIZE†, P. STOKER‡
Departments of *Obstetrics and †Rheumatology and Clinical Immunology, University of Lausanne, ‡Division of Pediatric Cardiology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

ARTHRITIS & RHEUMATISM
Vol. 50, No. 7, July 2004, pp 2223-2226
DOI 10.1002/art.20341
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First-Degree Heart Block in the Fetus of an Anti-SSA/Ro-Positive Mother

Reversal After a Short Course of Dexamethasone Treatment

Samo Vesel, Uroš Mazić, Tanja Blejec, and Tomaž Podnar

BCC incompleto o BCC completo con complicaciones

Isolated Atrioventricular Block in the Fetus

A Retrospective, Multinational, Multicenter Study of 175 Patients

Håkan Eliasson, MD; Sven-Erik Sonesson, PhD, MD; Gurleen Sharland, MD;
Fredrik Granath, PhD, MD; John M. Simpson, MD; Julene S. Carvalho, PhD, MD; Hana Jicinska, MD;



No diferencias significativas en SV de fetos con afectación cardíaca, independientemente del grado de BC, el CC o la dosis.

Paediatric Rheumatology

Fluorinated steroids are not superior to any treatment to ameliorate the outcome of autoimmune mediated congenital heart block: a systematic review of the literature and meta-analysis

A. Hoxha¹, E. Mattia², A. Zanetti³, G. Carrara⁴, N. Morel⁵, N. Costedoat-Chalumeau⁶, A.L. Brucato⁷,
A. Ruffatti⁸

Hoxha et al. *Clin Exp Rheumatol*. 2020; 38 (4): 783-791



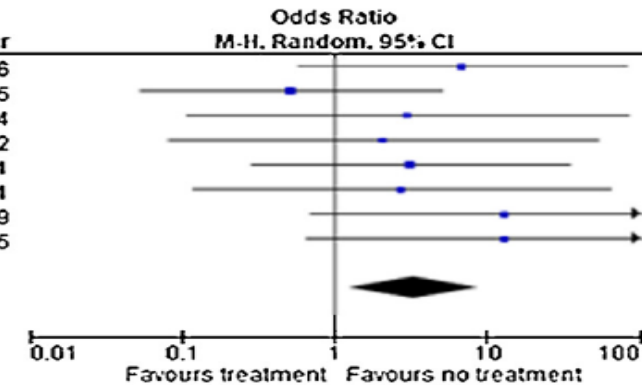
Metaanálisis 747 pacientes BCC diferentes grados: no diferencias en tasa natalidad, supervivencia, progresión del BCC e implante de MP

Use of antenatal fluorinated corticosteroids in management of congenital heart block: Systematic review and meta-analysis

Armia Michael^a, Ahmad A. Radwan^a, Ahmed Kamel Ali^a, Ahmed Yassien Abd-Elkariem^a, Sherif A. Shazly^{b,*}, Middle-East Obstetrics and Gynecology Graduate Education (MOGGE) Foundation Research Group

II. Downgrade of heart block

Study or Subgroup	Treatment		No treatment		Weight	Odds Ratio M-H, Random, 95% CI	Year
	Events	Total	Events	Total			
Van den Berg et al. 2016	2	14	1	42	15.6%	6.83 [0.57, 82.02]	2016
Levesque et al. 2015	1	79	3	123	18.5%	0.51 [0.05, 5.02]	2015
Perin et al. 2014	1	10	0	9	8.7%	3.00 [0.11, 83.36]	2014
Miyoshi et al. 2012	1	46	0	31	9.2%	2.08 [0.08, 52.65]	2012
Izmirly et al. 2011	4	13	1	8	16.6%	3.11 [0.28, 34.42]	2011
Trucco et al. 2011	4	15	0	3	9.6%	2.74 [0.12, 64.39]	2011
Saleeb et al. 1999	6	28	0	22	11.2%	13.00 [0.69, 244.73]	1999
Buyon et al. 1995	3	27	0	45	10.7%	13.00 [0.64, 262.06]	1995
Total (95% CI)		232		283	100.0%	3.27 [1.23, 8.71]	
Total events	22		5				
Heterogeneity: Tau ² = 0.00; Chi ² = 4.64, df = 7 (P = 0.70); I ² = 0%							
Test for overall effect: Z = 2.47 (P = 0.02)							



Regresión del BCC. Tratamiento CC combinado (p < 0.05)

TRATAMIENTO

INMUNOGLOBULINAS

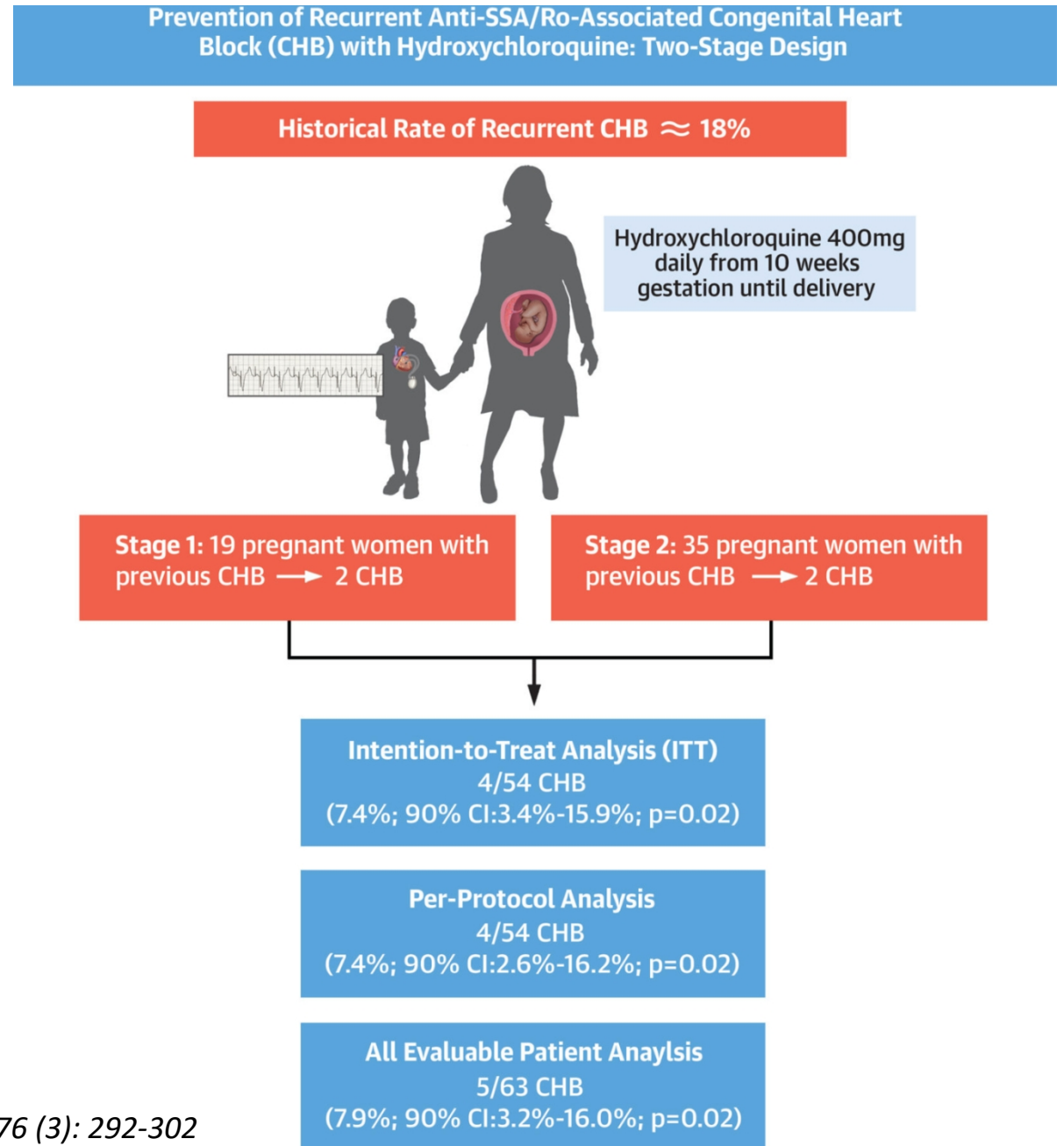
- Series cortas de casos: BCC incompletos
(Yu et al. *Asian Pac J Allergy* 2016; 34:174-8)
- No utilidad como tratamiento preventivo
(Friedman et al. *Arthritis Rheum* 2010; 62: 1138-46.
Pisoni et al. *Arthritis Rheum* 2010; 62: 1147-52)
- Tratamiento combinado \pm DXM \pm plasmaféresis
(Trucco et al. *J Am Coll cardiol.* 2011; 57:715-23)

TRATAMIENTO

HIDROXICLORIUINA

- Mujer Ac anti Ro +
- 400mg/día
- < 10 semana de gestación
- Reducción recurrencia > 50%

J Am Coll Cardiol. 2020; 76 (3): 292-302



CONCLUSIONES

1. Planificación del embarazo.
2. Seguimiento estrecho clínico y analítico de la mujer durante la gestación.
3. Tratamiento con Hidroxicloroquina 400mg/día (< semana 10)
4. Monitorización ecocardiográfica fetal (semana 16)
5. Tratamiento en BCC incompletos : HQ CC GG
6. Tratamiento BCCC sólo si complicaciones

