Maneig del CIR: tenim bons marcadors per finalitzar l'embaràs?

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Maneig del CIR

- PFE
- Doppler
- NST
- Perfil biofísic
- Factors angiogènics

Precoç (<32)

Tardà (>32)

Dificultats per comparar estudis

1996	Brazil	4	1009	BW<3rd centile	Aspirin (60 mg)	Pre-eclampsia
1998	Tanzania	4	1075	BW <2500g	Multivitamin supplementation	Progression of HIV-1 and birth outcomes
2001	France	3	3317	BW <3rd and <10th centile	Aspirin after screening (100mg)	FGR and Pre-eclampsia
2017	Multinational	3	156	BW <5th centile	Low molecular weight heparin	Pre-eclampsia and SGA
2000	UK	3	946	BW <3rd and <10th centile	Aspirin after screening (100mg SR)	GA at delivery, development of pre-eclampsia, APH or SGA
2014	Pakistan	1	193	BW <2500g	Vitamin D	not specified
2016	Cambodia	3	547	BW <10th centile	Dietary supplementation	BW and length
2014	Turkey	1	295	BW <10th centile	Dietary advice	Maternal and perinatal morbidity
2002	Malawi	5	697	BW <2500g	Vitamin A	Birth outcomes
2008	Tanzania	4	913	BW <10th centile	Selenium	Maternal HIV disease progression, pregnancy outcomes and maternal and child survival
2018	Netherlands	3	5296	BW <10th centile	Triaged antenatal care	Preterm birth or SGA
1997	USA	4	4589	BW <10th centile	Calcium	Pre-eclampsia and SGA

Townsend R, et al. Variation in outcome reporting in randomized controlled trials of interventions for prevention and treatment of fetal growth restriction.Ultrasound Obstet Gynecol. 2019 May;53(5):598-608.

Definició de CIR

PFE <p3

PFE p3-10

Doppler

Table 6 Consensus-based definitions for early and late fetal growth restriction (FGR) in absence of congenital anomalies

Early FGR: *GA < 32 weeks, in absence of congenital anomalies*	*Late FGR:* *GA ≥ 32 weeks, in absence of congenital anomalies*
AC/EFW < 3rd centile *or* UA-AEDF	AC/EFW < 3rd centile
Or 1. AC/EFW < 10th centile *combined with* 2. UtA-PI > 95th centile *and/or* 3. UA-PI > 95th centile	*Or at least two out of three of the following* 1. AC/EFW < 10th centile 2. AC/EFW crossing centiles >2 quartiles on growth centiles* 3. CPR < 5th centile *or* UA-PI > 95th centile

Gordijn SJ, et al. Consensus definition of fetal growth restriction: a Delphi procedure. Ultrasound Obstet Gynecol. 2016 Sep;48:333-9

Desenllaç CIR

Items for management	
• Interval between last examination and delivery	69
• Method of monitoring	64
• Administration of steroids to promote fetal lung maturity	64
• Intervals between assessments in longitudinal studies	57
• Administration of low dose aspirin	54
• Frequency of monitoring	44
• Administration of $MgSO_4$	30

Khalil A, et al. Essential variables for reporting research studies on fetal growth restriction: a Delphi consensus. Ultrasound Obstet Gynecol. 2019 May;53(5):609-614.

Desenllaç CIR

Pregnancy outcome	
• Need for emergency cesarean section	66
• Fetal sex	62
• Umbilical artery pH	59
• Signs of fetal distress/hypoxia on fetal heart rate monitoring	56
• Onset of labor	38

Khalil A, et al. Essential variables for reporting research studies on fetal growth restriction: a Delphi consensus. Ultrasound Obstet Gynecol. 2019 May;53(5):609-614.

Maneig del CIR

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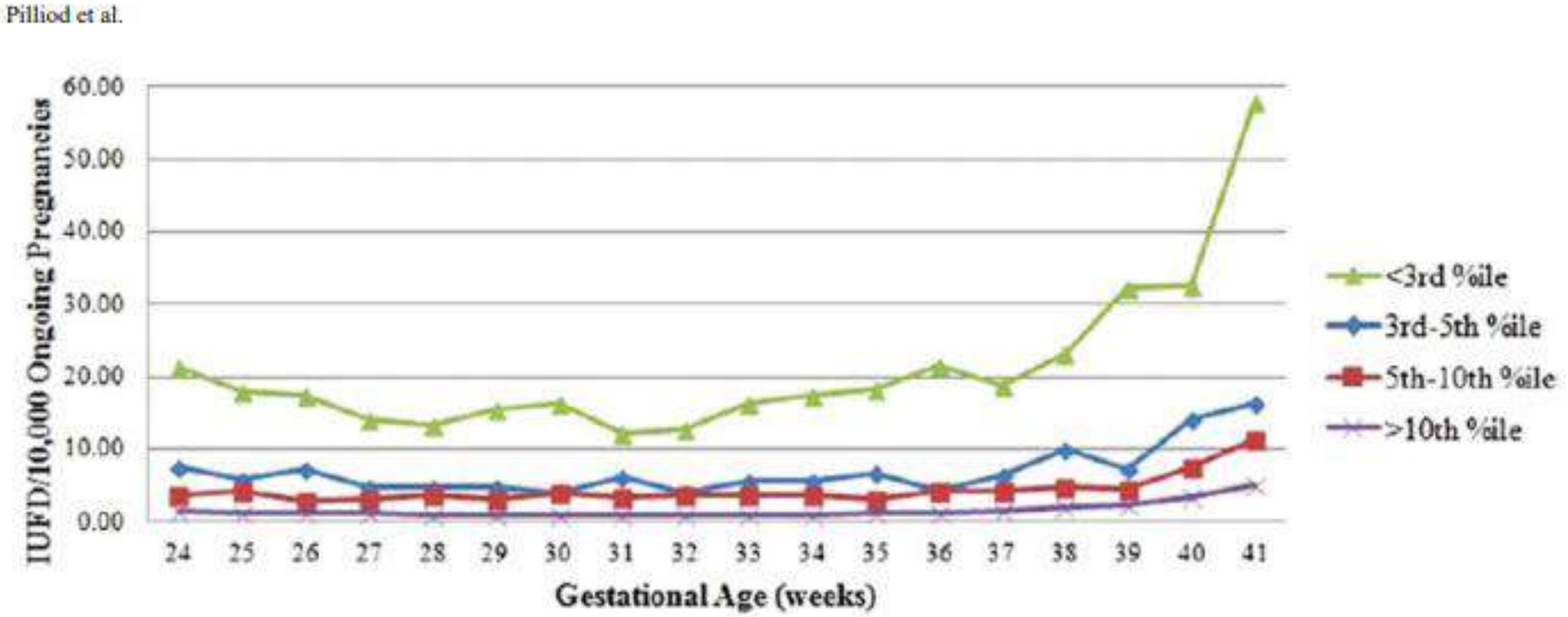
- Factors angiogènics

- Precoç (<32)
- Tardà (>32)

PFE CIR

PFE <p3



FR de MFIU independent del Doppler (precoç/tardà)

Pilliod RA, et al. The risk of intrauterine fetal death in the small-for- gestational-age fetus. *Am J Obstet Gynecol*. 2012

PFE CIR tardà

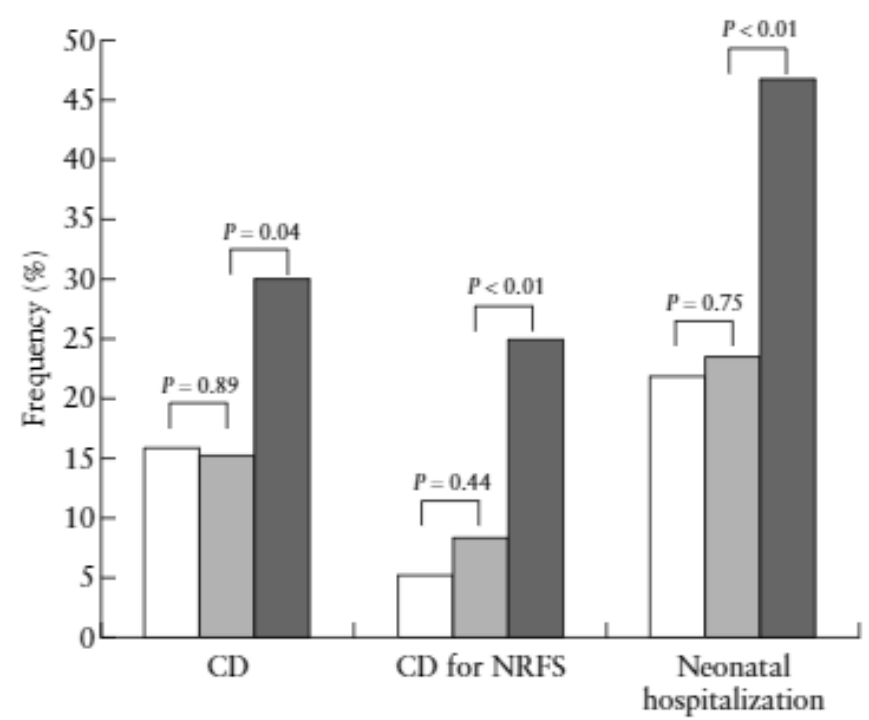


Figure 1 Frequency of intrapartum Cesarean delivery (CD), emergency CD due to non-reassuring fetal status (NRFS) and any period of neonatal hospitalization for controls and for small-for-gestational-age fetuses classified according to estimated fetal weight centile group. □, Controls; ▒, SGA ≥3rd centile; ■, SGA < 3rd centile.

Resultat similar controls i PFE p3-10

Pitjor resultat perinatal si PFE <p3

El PFE no és criteri de finalització per si mateix <37s

PFE CIR tardà: DIGITAT

No té en consideració el Doppler

PFE <p10: 650 (321+329)

Inducció 37 vs conducta expectant (control 2xset)

Resultat neonatal advers compost

Boers KE, et al. Induction versus expectant monitoring for intrauterine growth restriction at term: randomised equivalence trial (DIGITAT). BMJ. 2010

PFE CIR tardà: DIGITAT

Table 3 | Pregnancy outcomes

	Induction of labour group (n=321)	Expectant monitoring group (n=329)	Difference in mean or percentage (95% CI)
Mode of delivery			
Spontaneous vaginal delivery	249 (77.6)	257 (78.1)	−0.5 (−6.9 to 5.8)
Vaginal instrumental	27 (8.4)	27 (8.2)	0.2 (−4.0 to 4.4)
Caesarean section	45 (14.0)	45 (13.7)	0.3 (−5.0 to 5.6)
Indications for caesarean section			
Suspected fetal distress (with or without arrest of labour)	37 (82.2)	40 (88.9)	−6.7 (−21.1 to 7.8)
Arrest of labour	5 (11.1)	2 (4.4)	6.7 (−4.3 to 17.6)
Other	3 (6.7)	3 (6.7)	0.0 (−10.3 to 10.3)
Indications for instrumental vaginal delivery			
Suspected fetal distress (+/− arrest of labour)	21 (77.8)	25 (92.6)	−14.8 (−33.3 to 3.7)
Arrest of labour	6 (22.2)	2 (7.4)	14.8 (−3.7 to 33.3)
Adverse maternal outcome			
Maternal death	1 (0.3)	0	NA
Progression to gestational hypertension	1 (0.3)	6 (1.8)	−1.5 (−3.1 to 0.1)
Progression to pre-eclampsia	12 (3.7)	26 (7.9)	−4.2 (−7.7 to −0.6)*
Eclampsia, lung oedema, thromboembolic events	0	0	NA
Abruption placentae (partial)	1 (0.3)	0	NA
Postpartum haemorrhage	10 (3.2)	15 (4.7)	−1.5 (−4.5 to 1.5)

PFE CIR tardà: DIGITAT

	Induction of labour group (n=321)	Expectant monitoring group (n=329)	Difference in mean or percentage (95% CI)
Neonatal admission			
Intermediate care	155 (48.4)	118 (36.3)	12.1 (4.6 to 19.7) *
Maternal ward	89 (27.8)	116 (35.7)	−7.9 (−15.0 to −0.7)*
No admission	67 (20.9)	78 (24.0)	−3.1 (−9.5 to 3.4)
Length of stay (days)			
Infants in the neonatal intensive care unit	9 (6-14)	13 (6-22)	***
All admissions	4 (2-8)	4 (2-8)	0.2 (−1.4 to 1.8)

Inducció electiva: augmenta ingrés neonatal sense millorar resultat materno-fetal

Conducta expectant: No redueix taxa cesàries, augmenta progressió a PE

Maneig del CIR

PFE

Doppler

NST

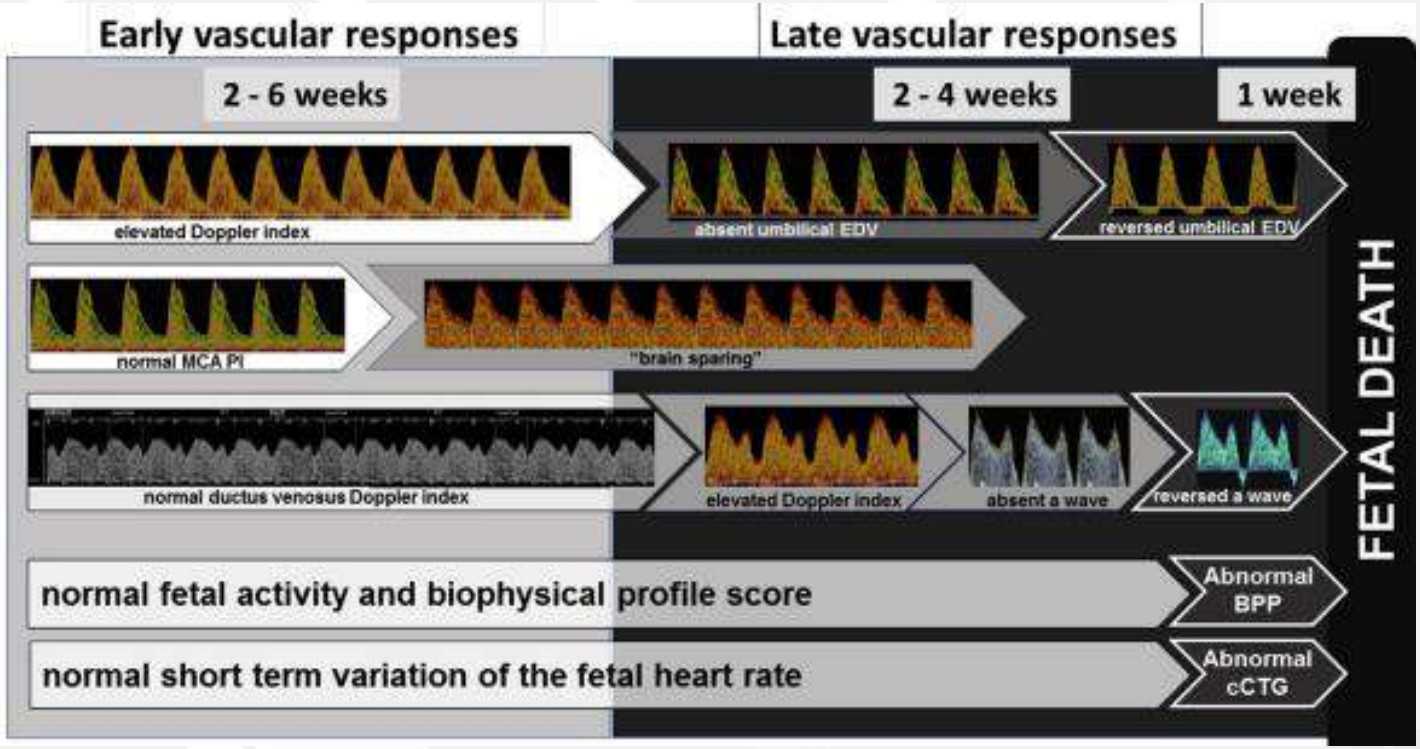
Perfil biofísic

Factors angiogènics

Precoç (<32)

Tardà (>32)

Doppler CIR precoç



Seqüència de degradació coneguda

Velocitat de degradació previsible

Baschat AA. Planning management and delivery of the growth-restricted fetus. Best Pract Res Clin Obstet Gynaecol. 2018

Doppler CIR precoç

United Kingdom	New Zealand	Canada	Ireland	United States	France
Up to 35+6 wk	Up to 34+0 wk	Up to 34+0 wk	Up to 34+0 wk	Up to 34+0 wk	Up to 34+0 wk
Not specified	<30 wk[b]	Not specified	<32 wk	<32 wk	<32–33 wk
AEDV by 32 wk; REDV by 32 wk	AEDV by 34 wk; REDV by 32 wk	AEDV not specified; REDV not specified; "Requires intervention and possibly delivery"	AEDV no later than 34 wk; REDV no later than 30 wk	AEDV ≥34 wk[a]; REDV ≥32 wk	AEDV ≥34 wk; REDV ≥34 wk
Abnormal computerized CTG or DV Doppler	Not applicable —NZMFMN guideline for SGA ≥34 wk	Abnormal BPP, CTG, or DV Doppler	Abnormal computerized CTG	Abnormal fetal surveillance (CTG, amniotic fluid, or BPP)	Abnormal computerized CTG or DV Doppler

AEDV >34s / REDV >30-32s

DV diàstole reversa >26s

McCowan LM, Figueras F, Anderson NH. Evidence-based national guidelines for the management of suspected fetal growth restriction: comparison, consensus, and controversy. Am J Obstet Gynecol. 2018 Feb;218(2S):S855-S868.

Doppler CIR precoç: TRUFFLE

CIR= CA<p10 + Umb >p95, 26-32s

Aleatorització 1:1:1

1. STV reduïda a NSTc

2. DV>p95 +/- NSTc

3. DV ona a absent/reversa +/- NSTc

REDF >32s o AEDF >34s → Finalització

NO diferències en mortalitat perinatal ni neonatal

Grup 3: Major taxa de supervivència sense afectació neurològica als 2a de vida

Lees C, et al. . Perinatal morbidity and mortality in early-onset fetal growth restriction: cohort outcomes of the trial of randomized umbilical and fetal flow in Europe (TRUFFLE). Ultrasound Obstet Gynecol. 2013 Oct;42(4):400-8.

Maneig del CIR

PFE

Doppler

NST

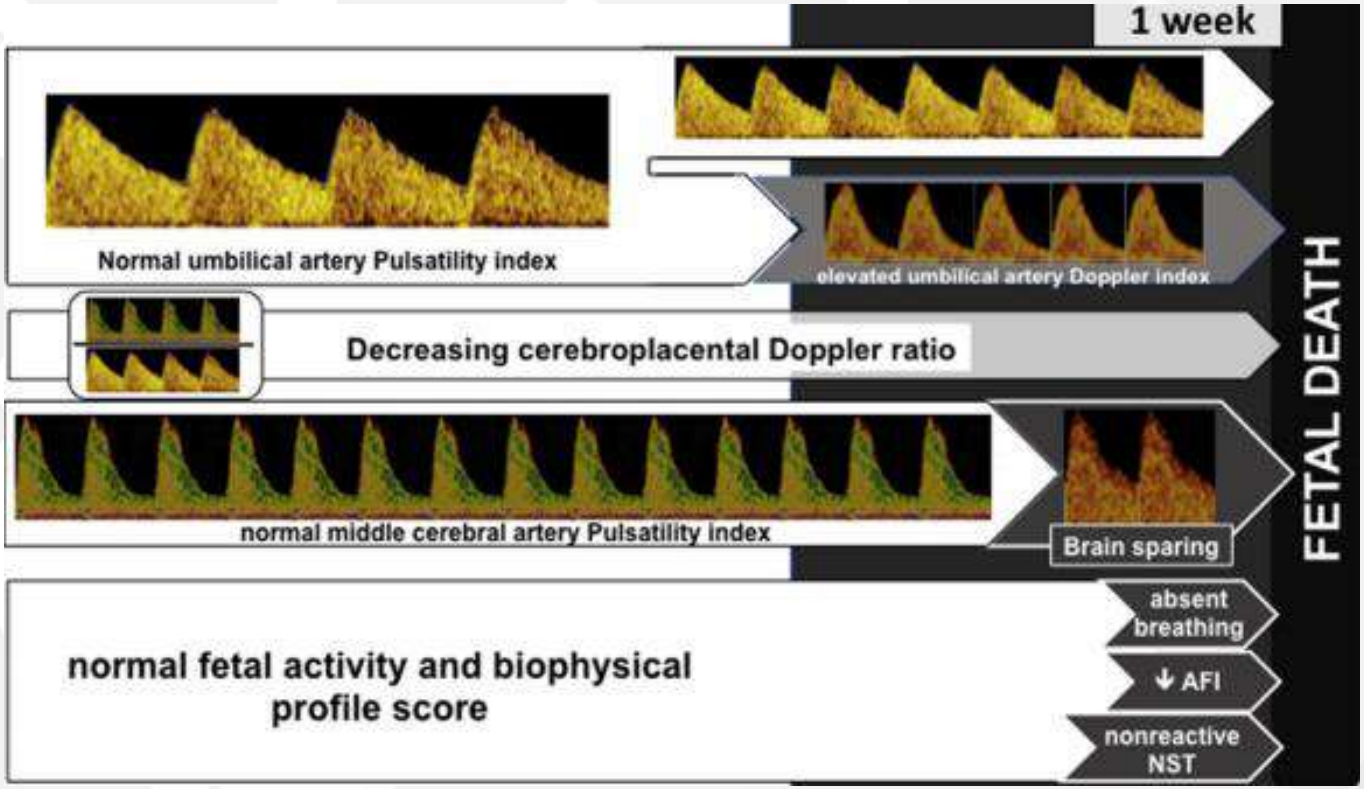
Perfil biofísic

Factors angiogènics

Precoç (<32)

Tardà (>32)

Doppler CIR tardà



Umbilical sol ser normal (ICP/ACM)

Velocitat de degradació variable

Baschat AA. Planning management and delivery of the growth-restricted fetus. Best Pract Res Clin Obstet Gynaecol. 2018

Doppler CIR tardà

Country	United Kingdom	New Zealand	Canada	Ireland	United States	France
Timing of birth Abnormal Doppler[a]	Deliver by 37 wk if MCA PI <5th centile or abnormal UA Doppler	Deliver by 38 wk if UA Doppler >95th, MCA <5th centile, CPR <5th centile, uterine artery >95th	Consider delivery >34 wk if Doppler studies (UA, MCA, DV) abnormal	Abnormal UA PI deliver at 37 wk or earlier if poor interval growth	Consider delivery >37 wk when decreased diastolic flow in UA	Birth from ≥37 wk depending on EFW, amniotic fluid, and Doppler measurements
Timing of birth normal Doppler	If >34 wk deliver if static growth over 3 wk; offer delivery by 37 wk with involvement of senior obstetrician	If EFW <3rd centile deliver by 38 wk; if EFW >3rd and <10th centile deliver at 40 wk unless other concern; if MCA and uterine Doppler studies not available, deliver at 38 wk	Discuss delivery vs ongoing monitoring >37 wk; if amniotic fluid volume or BPP abnormal, consider delivery	Isolated FGR (EFW <10th centile, normal UA Doppler, and AFI), delay delivery until 37 wk, no later than 40 wk	FGR with no additional abnormal parameters, deliver at 38+0 to 39+6 wk	Birth from ≥37 wk depending on EFW, amniotic fluid, and Doppler measurements

PFE<3 o Doppler (UA/ACM/ICP/Ut)>37s

PFE 3-10 o Doppler normal >39s

McCowan LM, Figueras F, Anderson NH. Evidence-based national guidelines for the management of suspected fetal growth restriction: comparison, consensus, and controversy. Am J Obstet Gynecol. 2018 Feb;218(2S):S855-S868.

Doppler CIR tardà

PFE<3 o Doppler (UA/ACM/Ut/ICP)>37s

PFE 3-10 o Doppler normal >39s

- **No assajos clínics aleatoritzats**
- **Basat en estudis observacionals prospectius**
- **Acceptat per la majoria de societats (Risc-benefici)**

Maneig del CIR

PFE

Doppler

NST

Perfil biofísic

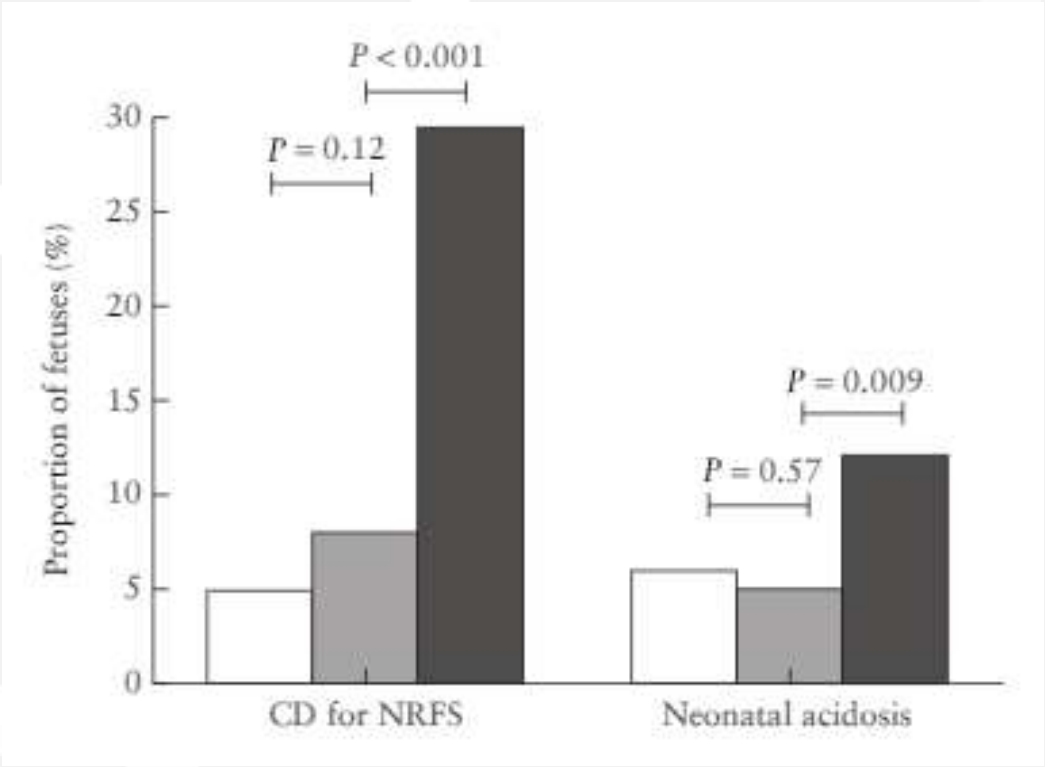
Factors angiogènics

Precoç (<32)

Tardà (>32)

Doppler + PFE CIR tardà

Resultat perinatal segons PFE i Doppler (UA/Ut/ICP)



PFE <p3 o p3-10 + Doppler

PFE p3-10 + Doppler N

PFE >p10

Figueras F, Savchev S, Triunfo S, Crovetto F, Gratacos E. An integrated model with classification criteria to predict small-for-gestational-age fetuses at risk of adverse perinatal outcome. Ultrasound Obstet Gynecol. 2015 Mar;45(3):279-85

Maneig del CIR

PFE

Doppler

NST

Perfil biofísic

Factors angiogènics

Precoç (<32)

Tardà (>32)

NST

Elevada taxa de FP (50%)

No interpretar de forma aïllada (sobretot preterme)→ augmenta MM

cNST en combinació amb Doppler→ Reducció MM

NST convencional: criteri de finalització només si desacceleracions no justificades/silent

Bilardo C, et al. Severe fetal growth restriction at 26-32 weeks: key messages from the TRUFFLE study. Ultrasound Obstet Gynecol. 2017

Evertson LR, Gauthier RJ, Schifrin BS, Paul RH. Antepartum fetal heart rate testing. I. Evolution of the nonstress test. Am J Obstet Gynecol. 1979

Pattison N, McCowan L. Cardiotocography for antepartum fetal assessment. Cochrane Database Syst Rev. 2000

Figueras F, Gratacos E. Stage-based approach to the management of fetal growth restriction. Prenat Diagn. 2014

Maneig del CIR

PFE

Doppler

NST

Perfil biofísic

Factors angiogènics

Precoç (<32)

Tardà (>32)

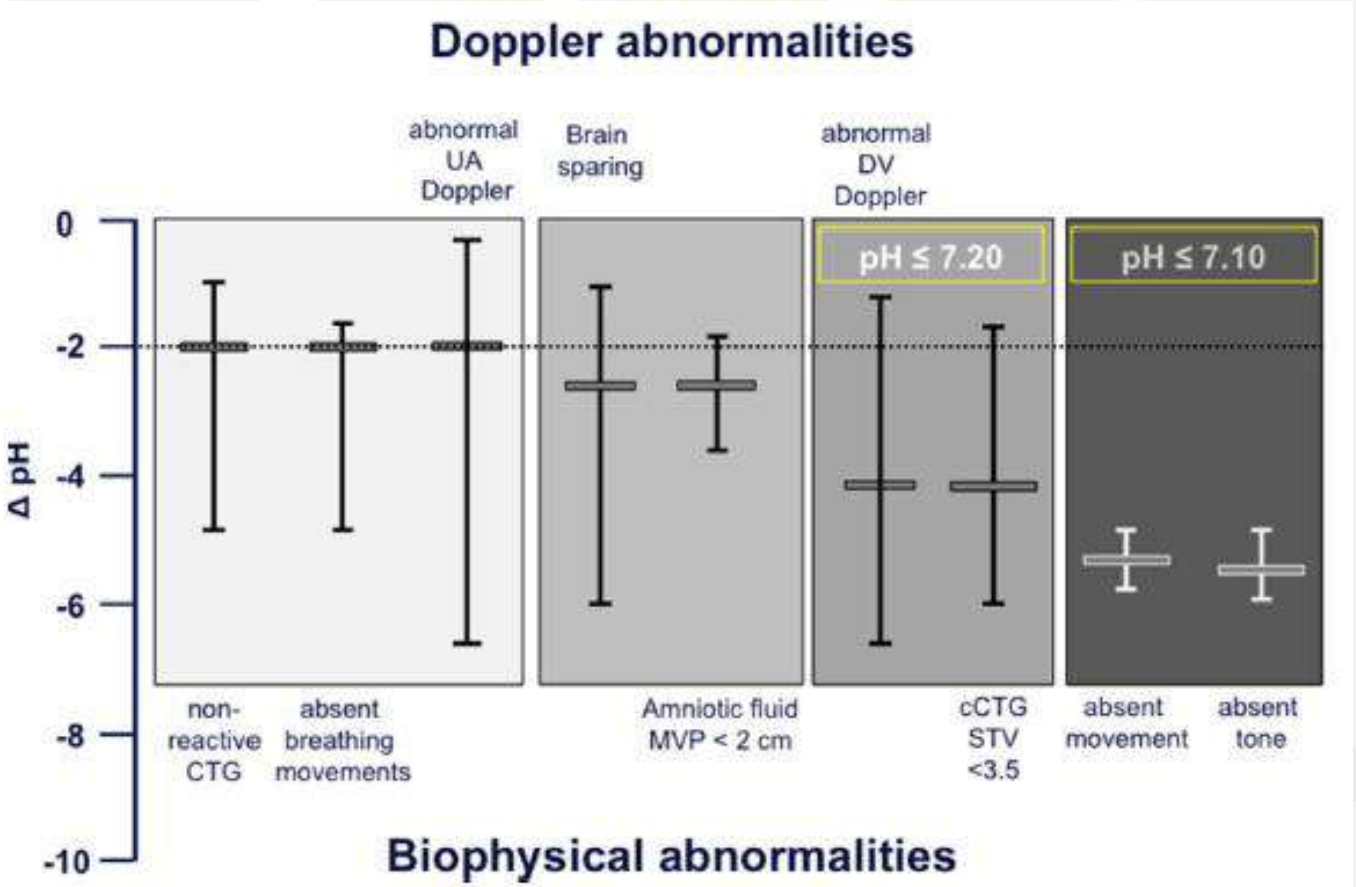
Perfil biofísic

Tabla. Perfil biofisico de Manning		
Parámetro	*Normal (2 puntos)*	*Anormal (0 puntos)*
Movimientos respiratorios fetales	*Al menos un episodio de 30 seg durante 30 min de observación*	*Ausencia o duración <30 seg.*
Movimientos corporales fetales.	*Al menos 3 movimientos (cuerpo/miembros) en 30 seg*	*Menos de 3*
Tono fetal	*Al menos un episodio de extensión/flexión (miembro o tronco)*	*>25 l/m* *Buena adaptación fetal, pero puede llegar al agotamiento*
Reactividad fetal	*Al menos 2 episodios de aceleraciones asociadas a movimientos fetales durante 20 minutos*	*Menos de dos aceleraciones*
Líquido amniótico	*Al menos una bolsa de más de 2 cm*	*Menos de 2 cm*

≤4: patològic; ≥8: normal

Manning FA. Fetal biophysical profile. Obstet Gynecol Clin North Am. 1999

Perfil biofísic



Respiratoris<LA<moviments fetals<To (flexió/extensió)

Baschat AA. Planning management and delivery of the growth-restricted fetus. Best Pract Res Clin Obstet Gynaecol. 2018

Perfil biofísic

Surveillance and timing of birth in late-onset small for gestational age/fetal growth restriction (≥32 wk)

Country	United Kingdom	New Zealand	Canada	Ireland	United States	France
BPP	Do not use	Not as only form of surveillance	Weekly	Not standard	Not as only form of surveillance; if abnormal UA Doppler, twice-weekly CTG and/or BPP[b] every 1–2 wk to assess for deterioration[b]	Not discussed abnormal

Poc utilitzat: principalment a Amèrica del Nord

Perfil biofísic anticipa MFIU en CIR precoç (70%)

Perfil biofísic normal = 75% MFIU en CIR tardà (ACM)

Cochrane: Poca utilitat quan cNST disponible i ús adequat Doppler

McCowan LM, Figueras F, Anderson NH. Evidence-based national guidelines for the management of suspected fetal growth restriction: comparison, consensus, and controversy. Am J Obstet Gynecol. 2018.
Crimmins S, et al. A comparison of Doppler and biophysical findings between liveborn and stillborn growth-restricted fetuses. Am J Obstet Gynecol. 2014
Lalor JG, et al. Biophysical profile for fetal assessment in high risk pregnancies. Cochrane Database Syst Rev. 2008

Maneig del CIR

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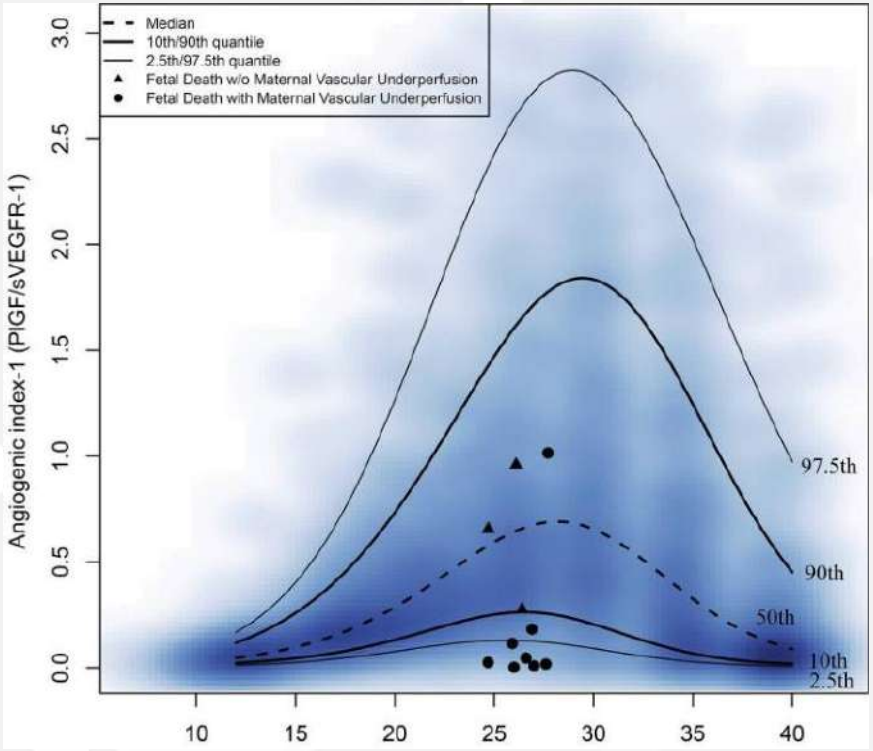
Precoç (<32)

Tardà (>32)

Factors angiogènics

CIR →Nivells baixos de PlGF i elevats de sFlt-1



Elevat sFlt-1/PlGF:

S=96% CIR placentari

PlGF <p5: 6.4% MFIU

PlGF >p5: 0% MFIU

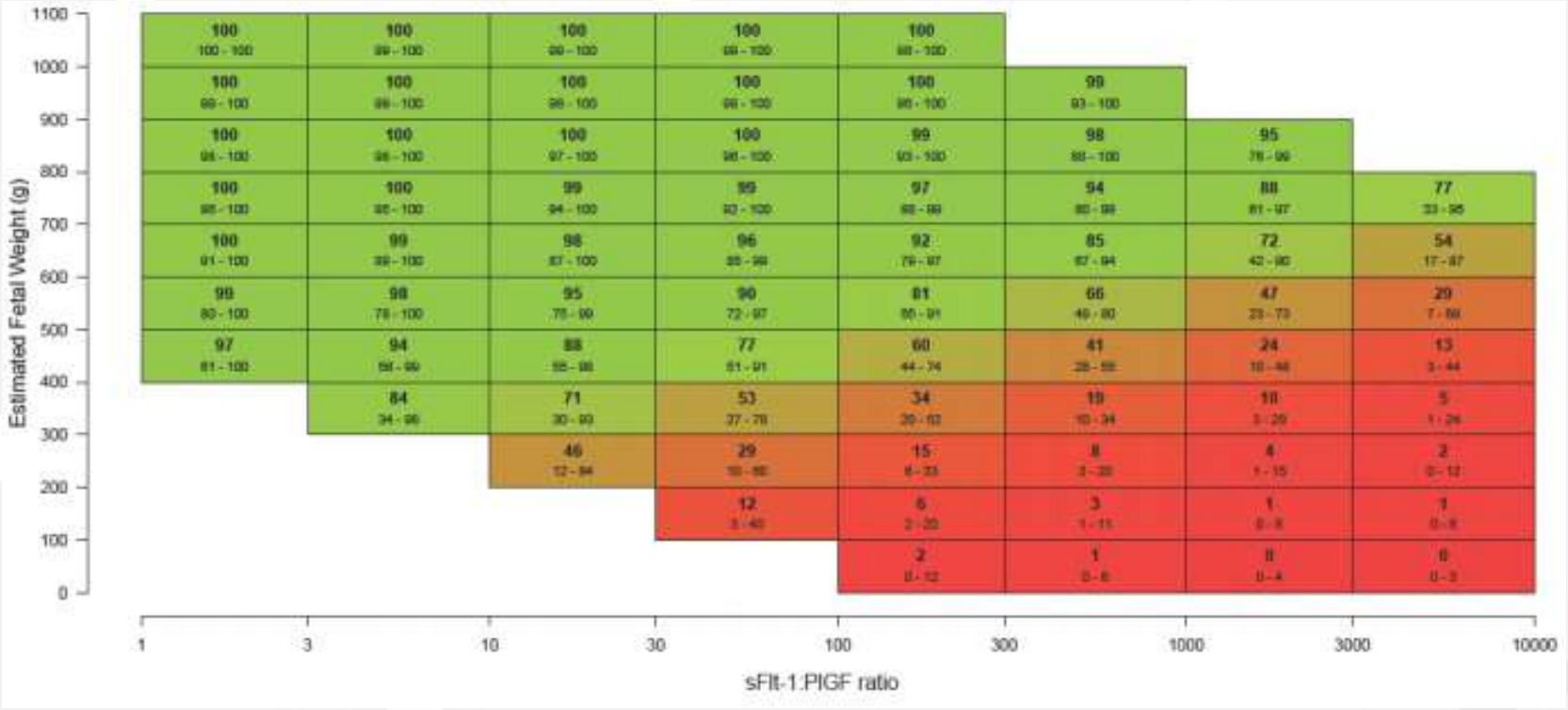
Disbalanç angiogènic:

RR=29 MFIU

Chaiworapongsa T, et al. The prediction of fetal death with a simple maternal blood test at 20-24 weeks: a role for angiogenic index-1 (PlGF/sVEGFR-1 ratio). Am J Obstet Gynecol. 2017

Benton SJ, et al. Placental growth factor as a marker of fetal growth restriction caused by placental dysfunction. Placenta. 2016

Factors angiogènics



PFE i índex sFlt-1/PlGF: predictors independents MM

Sharp A, et al. A prediction model for short-term neonatal outcomes in severe early-onset IUGR Fetal growth conference, Milan, 2018.

Factors angiogènics

Screening for fetal growth restriction using ultrasound and the sFLT1/PlGF ratio in nulliparous women: a prospective cohort study

Francesca Gaccioli, Ulla Sovio*, Emma Cook, Martin Hund, D Stephen Charnock-Jones†, Gordon C S Smith†*

1. PFE<p10 + sFlt-1/PlGF>38

20%

2. PFE <p10 + Doppler

70%

PFE + sFlt-1/PlGF>38: Detecció similar a Doppler, menor TFP

Gaccioli F, et al. Screening for fetal growth restriction using ultrasound and the sFLT1/PlGF ratio in nulliparous women: a prospective cohort study. Lancet Child Adolesc Health. 2018

Maneig del CIR: RESUM

- **Doppler en CIR precoç:** assaig clínic aleatoritzat
- **cNST:** equivalent a Doppler (DV)
- **CIR tardà:** consens basat en risc/benefici
- **NST i perfil biofísic:** No en solitari. Només resultats extrems tenen significat
- **Factors angiogènics:** futurs candidats a reduir iatrogènia

Gràcies

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