EuroPE Study

Randomized open-label control trial to evaluate if the incorporation of sFlt1/PlGF ratio in the diagnosis and classification of PE improves maternal and perinatal outcomes in women with the suspicion of the disease

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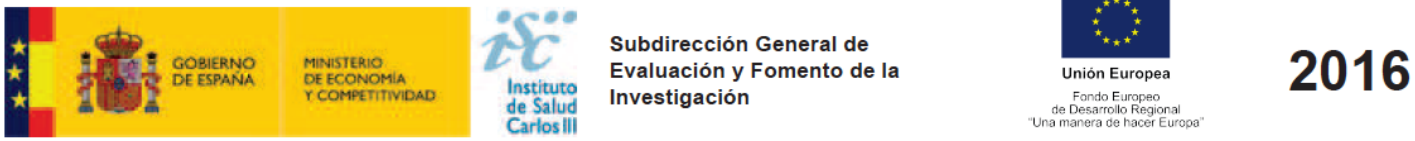
EuroPE Study



CONVOCATORIA DE AYUDAS DE PROYECTOS DE INVESTIGACIÓN EN SALUD
MEMORIA DE SOLICITUD

Expediente Nº PI16/00375

TITULO: **Incorporación del ratio sFlt1/PIGF en el diagnóstico y clasificación de preeclampsia: Ensayo clínico randomizado (EuroPE estudio)**

INVESTIGADOR/A PRINCIPAL: ELISA LLURBA OLIVÉ

- Randomized open-label control trial

- **Experimental intervention**: the incorporation of the ratio in the diagnosis and classification of PE.

- **Control intervention**: Criteria for the definition of PE were those of the International Society for the Study of Hypertension in Pregnancy.

- **Main valuation variable**: Determine levels of sFlt-1 and PIGF and determine ratio sFlt-1/PIGF.

EuroPE Study

Main objective:

The incorporation of sFlt1/PlGF ratio in the diagnosis and classification of PE improves maternal and perinatal outcomes and reduce unnecessary interventions.

EuroPE Study

- **Secondary objectives**:

  - Usefulness in the diagnosis and prognosis of PE.
  - Improve maternal and neonatal outcome.
  - Decreases hospital stay.
  - To elaborate a clinical score for maternal-neonatal prognosis combining prenatal maternal and fetal biomarkers.
  - To establish updated guidelines and protocols for the diagnosis, classification and management of PE with the use of the sFlt1/PlGF ratio.
  - To correlate severity of PE
  - To collect evidence that very high ratios of sFlt-1/PlGF (>655) identify women at risk for life-threatening conditions after admission for severe PE.

EuroPE Study

Key inclusion criteria

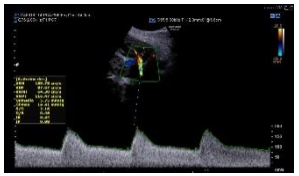
- Suspicious of PE* or PE diagnosed
- > 18 years
- 24-41 weeks

Key exclusion criteria

- Multiple pregnancies
- <24 weeks of gestation
- Fetal chromosomal or congenital abnormalities
- No consent form
- Conditions that require immediate delivery (eclampsia, pulmonary edema, uncontrolled hypertension, severe visual disturbances, severe headache, fetal demise, non-reassuring fetal status….)

EuroPE Study

*Suspicious of PE
New onset of elevated blood pressure
Aggravation of pre-existing hypertension
New onset of protein in urine
Aggravation of pre-existing proteinuria
Preeclampsia-related symptoms: headache, epigastric pain, excessive edema, visual disturbances…
Preeclampsia-related findings: low platelets, elevated liver enzymes.
Abnormal uterine perfusion detected by Doppler sonography in second trimestre
High risk of PE in first trimestre
IUGR



EuroPE Study

Sample size

2536 patients

1268 each group

EuroPE Study: Protocol

Control intervention:

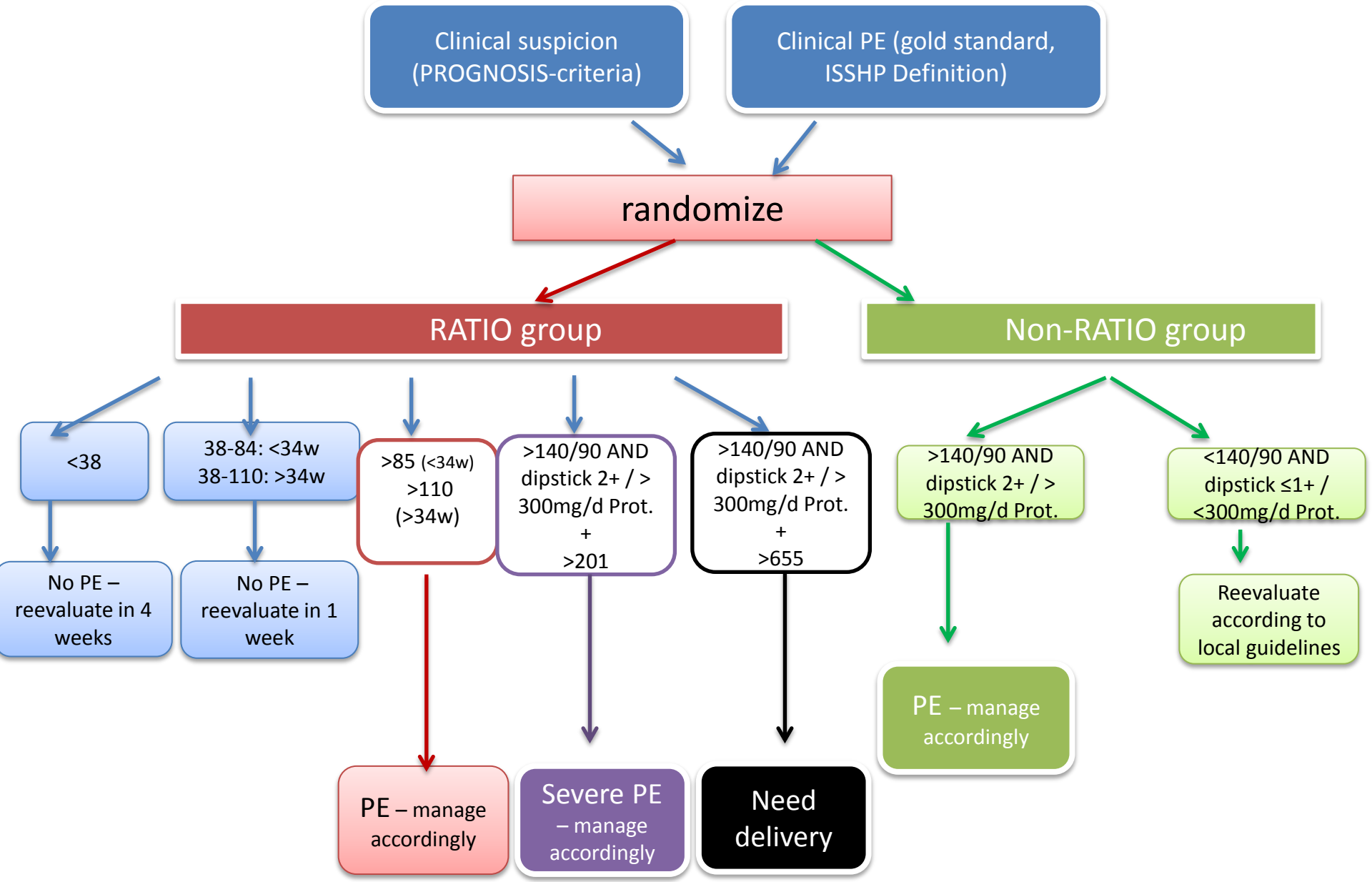
- Suspicious PE: Determine ratio sFlt-1/PIGF at the moment of inclusion, every 4 weeks and at the time of delivery.

- PE diagnosed: Determine weekly ratio sFlt-1/PIGF and at the time of delivery.

EuroPE Study: Protocol

Experimental intervention:

- Ratio sFlt1/PlGF **<38**: No PE. New determination in 4 weeks.
- Ratio sFlt1/PlGF **38-84 (<34w):** No PE. New determination in 1 week.
- Ratio sFlt1/PlGF **38-110 (>34w):** No PE. New determination in 1 week.
- Ratio sFlt1/PlGF **>85 <34w** : PE.
- Ratio sFlt1/PlGF **>110 >34w**: PE.
- Ratio sFlt1/PlGF **>210 + hypertension + proteinuria**: Severe PE.
- Ratio sFlt1/PlGF **> 655 + hypertension + proteinuria**: Need deliver after antenatal corticosteroid therapy.

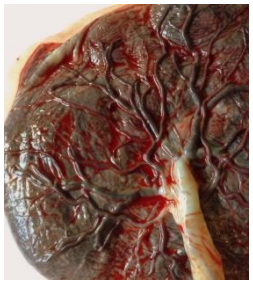

Clinical suspicion (PROGNOSIS-criteria)
Clinical PE (gold standard, ISSHP Definition)
randomize
RATIO group
Non-RATIO group
<38
38-84: <34w
38-110: >34w
>85 (<34w)
>110 (>34w)
>140/90 AND dipstick 2+ / > 300mg/d Prot. + >201
>140/90 AND dipstick 2+ / > 300mg/d Prot. + >655
>140/90 AND dipstick 2+ / > 300mg/d Prot.
<140/90 AND dipstick ≤1+ / <300mg/d Prot.
No PE – reevaluate in 4 weeks
No PE – reevaluate in 1 week
PE – manage accordingly
Severe PE – manage accordingly
Need delivery
PE – manage accordingly
Reevaluate according to local guidelines

Muestras

- **Suero materno** en todas las pacientes incluidas en el estudio para la determinación del ratio sFlt-1/PLGF.

- **Almacenamiento de todas las muestras** de suero obtenidas.

- Subgrupo de pacientes del (HSCiSP): **Muestras de placenta y sangre de cordón** para marcadores apoptosis, estrés oxidativo, hipoxia crónica (HIF-2), factores angiogénicos (PlGF, VEGF), antiangiogénicos (sFlt1, sEnd) y esfingomielina.



Evolución

- Inicio del estudio en febrero 2018
- Total 18 hospitales
- Nuevas incorporaciones: Hospital de Mataró, Hospital de Santiago de Compostela, Hospital Son Espases
- Finalización en 2 años
- **857 pacientes incluidas**

CENTROS	ESTADO	INCLUIDOS	RAMA
Hospital Santa Creu i Sant Pau	Reclutando	164	100 controles/ 64 casos
Hospital Vall d'Hebrón	Reclutando	175	75 controles/ 100 casos
Hospital Las Palmas	Reclutando	130	50 controles/80 casos
Hospital Arnau de Vilanova	Reclutando	102	102 controles
Hospital Son Llàtzer	Reclutando	51	48 controles /3 casos
Hospital Doctor Josep Trueta	Reclutando	36	36 controles
Hospital Sant Joan de Déu de Barcelona	Reclutando	46	46 controles
Consorci Sanitari Parc Taulí	Reclutando	33	33 casos
Hospital Germans Trias i Pujol	Reclutando	21	21 controles
Hospital universitario Lozano Blesa	Reclutando	20	20 controles

Hospital Sant Joan de Reus	Reclutando	28	28 controles
Hospital Santa Lucía de Cartagena	Reclutando	24	24 controles
Hospital Santa Caterina de Salt	Reclutando	22	22 casos
Hospital Joan XXIII	Reclutando	4	4 controles
Hospital General de Catalunya	Reclutando	1	1 caso
Hospital de Cruces	Pendiente iniciar reclutamiento		
Hospital la Paz	Pendiente resolución CEIC		
Hospital Son Espases	Pendiente resolución CEIC		
Hospital de Mataró	Pendiente resolución CEIC		
Hospital de Santiago de Compostela	Pendiente resolución CEIC		
TOTAL PACIENTES		**857**	**554 controles/ 303 casos**

Placental growth factor testing to assess women with suspected pre-eclampsia: a multicentre, pragmatic, stepped-wedge cluster-randomised controlled trial

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- Caso - control
- 1023 pacientes
- PLGF, tiempo desde la sospecha de PE hasta la PE establecida
- Reducción tiempo confirmación preeclampsia
- Menor incidencia resultados adversos maternos
- No mejora resultados perinatales