

University of Groningen

Use of Data from Predictive Tests following Fetoscopic Endoluminal Tracheal Occlusion for Congenital Diaphragmatic Hernia

Rodrigues, H. C. M. L.; Deprest, J.; Cruz-Martinez, R.; van den Berg, P. P.

Published in:
Fetal Diagnosis and Therapy

DOI:
[10.1159/000324102](https://doi.org/10.1159/000324102)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2011

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Rodrigues, H. C. M. L., Deprest, J., Cruz-Martinez, R., & van den Berg, P. P. (2011). Use of Data from Predictive Tests following Fetoscopic Endoluminal Tracheal Occlusion for Congenital Diaphragmatic Hernia. *Fetal Diagnosis and Therapy*, 29(3), 261-262. <https://doi.org/10.1159/000324102>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Use of Data from Predictive Tests following Fetoscopic Endoluminal Tracheal Occlusion for Congenital Diaphragmatic Hernia

H.C.M.L. Rodrigues^c J. Deprest^a R. Cruz-Martinez^b P.P. van den Berg^c

^aDepartment of Woman and Child, Catholic University of Leuven, Leuven, Belgium; ^bDepartment of Maternal-Fetal Medicine, Hospital Clinic Barcelona, Barcelona, Spain; ^cDepartment of Obstetrics and Gynecology, University Medical Center Groningen, Groningen, The Netherlands

We have read with interest the recent papers by our partners in the European Program on Soft Tissue Engineering for Children (EuroSTEC – www.eurostec.eu) on the prognostic value of pulmonary Doppler in predicting survival and morbidity of fetoscopic endoluminal tracheal occlusion (FETO) in fetuses with severe isolated left congenital diaphragmatic hernia (CDH) and liver herniation. The value of pulmonary circulation assessment for the prediction of outcome of fetal therapy has been investigated either by using Doppler to evaluate blood vessel resistance and/or actual blood flow, or as response to maternal hyperoxygenation [1–3].

On a theoretical basis, the investigation of pulmonary circulation provides independent information that can be combined with that already obtained by measuring the size of the airway compartment and/or the position of the liver. Recent studies also by the FETO consortium confirm that the data obtained with each parameter is not the same. Therefore, adding a combined use of all the different available predictors might improve the prediction of outcome.

These studies are part of ongoing efforts to develop reliable outcome prediction models, both at the time of diagnosis and after prenatal therapy. As suggested [4], we would like to caution the fetal medicine community prior to using this information. First, as shown by the same group, many of these measurements are not easily reproducible [5]. Second, as suggested by the same authors, it would be prudent to wait for external validation of these observations by other, independent researchers [2, 6]. Third, most of the data were collected on a small subset of patients with isolated left-sided CDH and severe pulmonary hypoplasia who underwent prenatal therapy. Clinical experience with FETO has, however, revealed significant individual variability in the response to FETO, both in lung size as well as vascularization [1–3, 7]. Fourth, at fetal surgery centers, the population of patients with less severe hypoplasia, and those who despite severe hypoplasia, are expectantly managed during pregnancy, are under-represented. It would be more comforting to know whether the pulmonary vascular assessment test can perform well also in the latter group of

patients. In our opinion, until there is generalizable agreement upon the value, accuracy and validity of intrapulmonary Doppler, one should refrain from disclosing the prognostic information acquired by this particular investigational method to prospective research participants. The reason against disclosure is that, from an ethical viewpoint, patients have a right to all the information that is necessary to produce voluntary informed consent [8]. Informed consent should be provided only based on reliable, properly validated information. Because the present prediction model has not been validated in a wider research context, it does not provide (yet), when applied to individual patient-research subjects, reliable evidence of correct outcome prediction. In retrospect, patients might otherwise come to the conclusion that they have been wrongly included in a study, because of a wrong prediction of outcome based on an invalidated model. In addition, those with a poor Doppler prognosis after FETO might be misled in their decision either to continue that pregnancy or to terminate it, a legal right that most countries in Europe recognize to

parents in these circumstances. Such situations put researchers at risk of liability and, more importantly, they may harm patients who having been given the correct facts, would either have not consented to participating in the study or would have withdrawn from it.

Centers managing fetuses with CDH, either expectantly or with FETO, would do well to test the proposed model in order to obtain proof of the validity and efficacy of

pulmonary assessment in predicting survival and morbidity irrespective of prenatal intervention. The TOTAL trial (Tracheal Occlusion To Accelerate Lung growth) (www.totaltrial.eu) and the European-based observational study of FETO [9] present a great opportunity to do exactly that. Only when there is consensus and wide professional confidence in the results of the proposed combination of anatomical information (either observed/

expected lung-to-head ratio or volume) should they be used to counsel patients towards their decision for considering FETO, another prenatal intervention, or expectant management during pregnancy. For the time being it seems logical to rely on lung size measurement, and perhaps position of the liver, as the best validated predictors, and informed consent should be provided based on their results [10, 11].

References

- 1 Cruz-Martinez R, Moreno-Alvarez O, Hernandez-Andrade E, Castanon M, Done E, Martinez JM, Puerto B, Deprest J, Gratacos E: Contribution of intrapulmonary artery Doppler to improve prediction of survival in fetuses with congenital diaphragmatic hernia treated with fetal endoscopic tracheal occlusion. *Ultrasound Obstet Gynecol* 2010;35:572–577.
- 2 Cruz-Martinez R, Hernandez-Andrade E, Moreno-Alvarez O, Done E, Deprest J, Gratacos E: Prognostic value of pulmonary Doppler to predict response to tracheal occlusion in fetuses with congenital diaphragmatic hernia. *Fetal Diagn Ther* 2010, E-pub ahead of print.
- 3 Doné E, Allegaert K, Lewi P, Jani J, Gucciardo L, Van Mieghem T, Gratacos E, Devlieger R, Van Schoubroeck D, Deprest J: Maternal hyperoxygenation test in fetuses undergoing FETO for severe isolated congenital diaphragmatic hernia. *Ultrasound Obstet Gynecol* 2010, E-pub ahead of print.
- 4 Moreno-Alvarez O, Hernandez-Andrade E, Oros D, Jani J, Deprest J, Gratacos E: Association between intrapulmonary arterial Doppler parameters and degree of lung growth as measured by lung-to-head ratio in fetuses with congenital diaphragmatic hernia. *Ultrasound Obstet Gynecol* 2008;31:164–170.
- 5 Cruz-Martinez R, Figueras F, Moreno-Alvarez O, Martinez JM, Gomez O, Hernandez-Andrade E, Gratacos E: Learning curve for lung area to head circumference ratio measurement in fetuses with congenital diaphragmatic hernia. *Ultrasound Obstet Gynecol* 2010;36:32–36.
- 6 Claus F, Sandaite I, Dekoninck P, Moreno O, Cruz Martinez R, Van Mieghem T, Gucciardo L, Richter J, Michielsen K, Decraene J, Devlieger R, Gratacos E, Deprest JA: Prenatal anatomical imaging in fetuses with congenital diaphragmatic hernia. *Fetal Diagn Ther* 2010, E-pub ahead of print.
- 7 Cannie MM, Jani JC, De Keyzer F, Allegaert K, Dymarkowski S, Deprest J: Evidence and patterns in lung response after fetal tracheal occlusion: clinical controlled study. *Radiology* 2009;252:526–533.
- 8 Chervenak FA, McCullough LB: Ethics of fetal surgery. *Clin Perinatol* 2009;36:237–246.
- 9 Jani JC, Nicolaides KH, Gratacos E, Valencia CM, Done E, Martinez JM, Gucciardo L, Cruz R, Deprest JA: Severe diaphragmatic hernia treated by fetal endoscopic tracheal occlusion. *Ultrasound Obstet Gynecol* 2009;34:304–310.
- 10 Knox E, Lissauer D, Khan K, Kilby M: Prenatal detection of pulmonary hypoplasia in fetuses with congenital diaphragmatic hernia: a systematic review and meta-analysis of diagnostic studies. *J Matern Fetal Neonatal Med* 2010;23:579–588.
- 11 Mullassery D, Ba'ath ME, Jesudason EC, Losty PD: Value of liver herniation in prediction of outcome in fetal congenital diaphragmatic hernia: a systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2010;35:609–614.