Journal Pre-proof

Is Umbilicocerebral Ratio better than Cerebroplacental Ratio for Predicting Adverse Pregnancy and Neonatal Outcomes?

Erkan KALAFAT, MD, Zeynep KALAYLIOGLU, Associate Professor, Basky THILAGANATHAN, Professor, Asma KHALIL, Professor

PII: S0002-9378(20)30434-8

DOI: https://doi.org/10.1016/j.ajog.2020.04.009

Reference: YMOB 13202

To appear in: American Journal of Obstetrics and Gynecology

Received Date: 15 March 2020

Revised Date: 7 April 2020

Accepted Date: 13 April 2020

Please cite this article as: KALAFAT E, KALAYLIOGLU Z, THILAGANATHAN B, KHALIL A, Is Umbilicocerebral Ratio better than Cerebroplacental Ratio for Predicting Adverse Pregnancy and Neonatal Outcomes?, *American Journal of Obstetrics and Gynecology* (2020), doi: https://doi.org/10.1016/j.ajog.2020.04.009.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2020 Published by Elsevier Inc.



1 2	Is Umbilicocerebral Ratio better than Cerebroplacental Ratio for Predicting Adverse Pregnancy and Neonatal Outcomes?
3	
4	Erkan KALAFAT, MD ^{1,2}
5	Zeynep KALAYLIOGLU, Associate Professor ³
6	Basky THILAGANATHAN, Professor ^{1,4}
7	Asma KHALIL, Professor ^{1,4}
8 9	1. Fetal Medicine Unit, St George's Hospital, St George's University of London, UK. Cranmer Terrace, London SW17 0RE
10 11	2. Department of Statistics, Faculty of Arts and Science, Middle East Technical University, Ankara, Turkey
12 13 14 15 16 17	 3. Department of Mathematical Sciences, RMIT University, Department of Statistics, Melbourne, Australia 4. Vascular Biology Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, Cranmer Terrace, London SW17 0RE, UK.
18	Conflict of interests: Authors declare no conflict of interest.
19	CORRESPONDENCE
20	Professor Asma Khalil
21	Fetal Medicine Unit,
22	St George's University of London,
23	London SW17 0RE
24	Telephone: (Work) +442032998256,
25	Mobile: +447917400164.
26	Fax: +442077339534

27 E-mail: <u>akhalil@sgul.ac.uk;</u> <u>asmakhalil79@googlemail.com</u>

- 1 KEYWORDS: Doppler, umbilical artery, middle cerebral artery, biomarker,
- 2 emergency cesarean, and operative delivery.

3

Journal Prevention

Journal Pre-proof

OBJECTIVE: A secondary analysis of the trial of randomized umbilical and fetal flow in Europe suggested that the umbilicocerebral ratio (UCR) provides better differentiation of neurodevelopmental outcome in the abnormal range compared to cerebroplacental ratio (CPR).¹ However, the reported superiority of UCR is controversial.² We aimed to compare the CPR and UCR for predicting operative delivery for presumed fetal compromise and prolonged neonatal unit (NNU) admission in term fetuses suspected to be small for gestational age (SGA).

METHODS: This was a retrospective analysis of singleton pregnancies with 8 estimated fetal weight less than the 10th centile (SGA) at 36 weeks' gestation or 9 beyond at St. George's Hospital in London between 1999 and 2015. CPR was 10 calculated as the ratio of middle cerebral artery and umbilical artery pulsatility index, 11 while UCR was calculated as the inverse of CPR. The outcomes were operative 12 delivery for presumed fetal compromise and prolonged NNU admission (admission to 13 the neonatal unit for longer than 48 hours).³ Multiples of medians (MoMs) were 14 calculated using the reference ranges reported by Acharya et al.⁴ The predictive 15 accuracy was assessed using receiver operating characteristics curves. 16

RESULTS: The analysis included 958 pregnancies. The incidence of operative 17 delivery and prolonged NNU admission were 17.6% (169/958) and 4.7% (45/958), 18 respectively. The CPR (median: 1.63 vs 1.51) and UCR (median: 0.61 vs 0.66) 19 values were significantly different in fetuses who underwent operative delivery for 20 presumed fetal compromise compared to those who did not (P=0.015 for both). 21 There were no statistically significant differences in either UCR or CPR between 22 those with and without prolonged NNU admission (P=0.230 for both). The number of 23 outlier values without MoM correction was significantly more with UCR compared to 24 CPR in those who did not have operative delivery for presumed fetal compromise 25 (5.6%,44/789 vs. 1.6%,13/789 P<0.001) or prolonged NNU admission (5.0%, 46/913 26 vs 1.5%, 14/913 *P*<0.001). 27

The area under the curve (AUC) values of UCR and CPR for predicting operative delivery for presumed fetal compromise (AUC: 0.56, 95% CI: 0.51-0.61) or prolonged NNU admission were the same (AUC: 0.55, 95% CI: 0.46-0.64) (Figure 1).

There was a significant decrease in the AUC values for predicting operative delivery for presumed fetal compromise with UCR MoM (0.56 vs 0.53, *P*<0.001) or CPR MoM

(0.56 vs 0.52, P<0.001) compared to raw values, while there was a significant 1 increase in AUC values for predicting prolonged NNU admission with UCR MoM 2 (0.57 vs 0.55, P=0.036) and CPR MoM (0.58 vs 0.55, P=0.048) compared to raw 3 values. There were no significant differences between UCR and CPR MoMs (P 4 =0.176). 5

CONCLUSION: The AUC values of CPR and UCR for predicting operative delivery 6 for presumed fetal compromise or prolonged NNU admission were essentially the 7 same. MoM standardization for gestational age changed the predictive accuracy for 8 prolonged NNU admission and operative delivery for presumed fetal compromise. 9 However, gestational age adjustment with MoM values may not be appropriate for 10 UCR and CPR when gestational age is an intermediate factor between exposures 11 and outcomes.⁵ The changes in the predictive accuracy are likely to be caused by 12 collider bias and may lead to erroneous conclusions. 13 ournalPr

14

1 **REFERENCES**

2

Stampalija T, Arabin B, Wolf H, Bilardo CM, Lees C, Brezinka et al. Is middle
 cerebral artery doppler related to neonatal and 2-year infant outcome in early
 fetal growth restriction? *American Journal of Obstetrics & Gynecology*.
 2017;216:521.e521-521.e513. doi:10.1016/j.ajog.2017.01.001

- 2. Leavitt K, Odibo A, Odibo L. 334: Comparing cerebro-placental (CPR) and
 umbilico-cerebral (UCR) doppler ratios for the prediction of adverse neonatal
 outcomes. *American Journal of Obstetrics & Gynecology*. 2020;222:S225 S226. doi:10.1016/j.ajog.2019.11.350
- Kalafat E, Morales-Rosello J, Thilaganathan B, Tahera F, Khalil A. Risk of
 operative delivery for intrapartum fetal compromise in small-for-gestational age fetuses at term: An internally validated prediction model. *Am J Obstet Gynecol.* 2018;218:134 e131-134 e138. doi:10.1016/j.ajog.2017.10.022
- Acharya G, Ebbing C, Karlsen HO, Kiserud T, Rasmussen S. Sex-specific
 reference ranges of cerebroplacental and umbilicocerebral ratios: A
 longitudinal study. *Ultrasound Obstet Gynecol.* 2019 doi:10.1002/uog.21870
- 5. Ananth CV, Schisterman EF. Confounding, causality, and confusion: The role
 of intermediate variables in interpreting observational studies in obstetrics. *Am J Obstet Gynecol.* 2017;217:167-175. doi:10.1016/j.ajog.2017.04.016

21

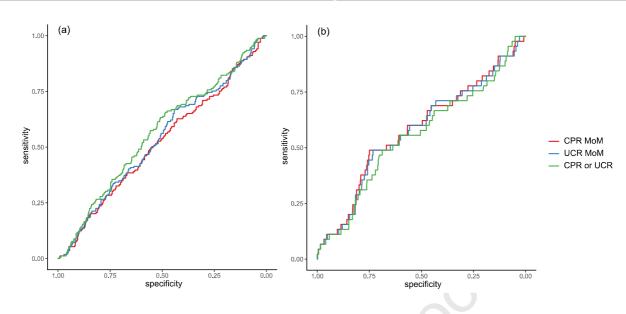


Figure 1. The receiver operating characteristics (ROC) curves for operative delivery 2 for presumed fetal compromise (a) and prolonged neonatal unit admission (>48h) (b). 3 The cerebroplacental ratio (CPR) and umbilicocerebral ratio (UCR) had overlapping 4 ROC curves for operative delivery for presumed fetal compromise or prolonged 5 6 neonatal unit admission. The MoM standardization decreased the area under the curve (AUC) values for operative delivery for presumed fetal compromise (P<0.001 7 for CPR and UCR), while they improved the AUC values for prolonged neonatal unit 8 admission (P<0.05 for CPR and UCR). 9

10 MoM: multiple of median

1

Journal Pre-proof

