Original Research

Predicting Fetal Acidemia Using Umbilical Venous Cord Gas Parameters

Jessica Cantu, MD, Jeff M. Szychowski, PhD, Xuelin Li, Joseph Biggio, MD, Rodney K. Edwards, MD, William Andrews, MD, PhD, and Alan T. N. Tita, MD, PhD

OBJECTIVE: To assess the utility of umbilical cord venous blood gas measures for prediction of umbilical artery pH and base deficit acidemia.

METHODS: A retrospective cohort study was conducted of all singletons with valid paired arterial and venous cord gas samples delivered at our institution from January 2006 to March 2012. Fetal acidemia was defined primarily as cord arterial blood gas pH less than 7.0. We also evaluated prediction of acidemia, defined as an arterial base deficit 12 mmol/L or greater. Logistic regression was performed to estimate probabilities of fetal arterial pH and base deficit acidemia given venous blood gas pH or base deficit. Receiver operating characteristic curves were derived to determine predictive ability. Venous blood gas pH and base deficit cutoffs associated with 1% or less, 5%, 10%, and 50% probability of fetal acidemia were identified.

RESULTS: Of 23,506 births, 11,455 (49%) met criteria for inclusion. The frequency of arterial blood gas pH less than 7.0 was 127 (1.1%); arterial blood gas base deficit 12 mmol/L or greater was 245 (2.1%). Venous blood gas pH (area under the curve [AUC] 0.949, 95% confidence interval [CI] 0.920–0.979; $P<.001$) and base deficit (AUC 0.969, 95% CI 0.954–0.983; $P<.001$) were predictors of acidemia based on arterial blood gas pH and base deficit, respectively. Venous blood gas pH cutoffs associated with 1% or less, 5%, or 10% probabilities of arterial blood gas pH less than 7.0 were 7.23, 7.17, and 7.14, respectively. Venous blood gas base deficit values associated with similar probabilities for base deficit 12 mmol/L or greater were 6.3 or less, 8.2 or less, and 9.0 mmol/L or less. For prediction of arterial blood gas pH, adjusting venous blood gas pH for base deficit increased the AUC (0.961, 95% CI 0.938–0.984). Prediction of arterial blood gas base deficit by venous blood gas base deficit was unchanged by adjustment for pH (AUC 0.969, 95% CI 0.955–0.984).

CONCLUSION: We demonstrate that venous blood gas parameters are powerful predictors of arterial blood gas pH and base deficit and can be used to predict the likelihood of fetal acidemia when the cord arterial blood gas is not available.

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Umbilical cord blood gas analysis allows for an objective assessment of fetal acid-base status and determination of fetal well-being at the time of delivery. Current guidelines suggest that physicians should obtain both cord blood samples (arterial and venous) in all high-risk pregnancies and especially in cases of low 5-minute Apgar scores, severe fetal growth restriction, maternal thyroid disease, intrapartum fever, multifetal gestation, or abnormal fetal heart rate tracings.[1,2] Furthermore, universal collection of cord blood gases at every delivery has been adopted at some institutions.[3–5]

According to the American College of Obstetricians and Gynecologists' Task Force on Neonatal Encephalopathy, fetal umbilical artery acidemia, defined as an umbilical artery pH less than 7.0, base deficit 12 mmol/L or greater, or both, increases the probability that neonatal encephalopathy may be associated with an acute intrapartum hypoxic event.[6–8] Importantly, cord arterial blood gas results that are normal or above the predefined thresholds effectively

From the Center for Women's Reproductive Health and the Departments of Obstetrics and Gynecology and Biostatistics, the University of Alabama at Birmingham, Birmingham, Alabama.

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Corresponding author: Jessica Cantu, MD, University of Alabama at Birmingham, Department of Obstetrics & Gynecology, Division of Maternal-Fetal Medicine, 176F 10270C, 619 19th Street S, Birmingham, AL 35209; e-mail: jesscantu27@gmail.com.

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rule out acidemia and the delivery process as a cause of encephalopathy. Therefore, documentation of arterial blood gas in the medical record can be of significant utility, especially from a medicolegal perspective.

Arterial blood gas samples provide a direct measure of fetal pH, whereas the cord venous blood gas reflects placental acid-base status.[2,9–11] Frequently, venous blood gas results but not arterial blood gas results are available, because the comparative size of the vessels makes venous access much easier to obtain compared with arterial access.[10,12,13] Unfortunately, even in settings where it is routine clinical practice to conduct umbilical cord blood gas analyses, up to 20% of results may be inadequate, and these are more likely to occur in at-risk cases and involve absent arterial blood gas specimens or results.[13–15]

Given these difficulties, the ability to predict, or perhaps more importantly exclude, fetal acidemia using venous blood gas results has clinical, medicolegal, and research utility in obstetrics. Therefore, we aimed to identify values for umbilical venous blood gas pH and base deficit that rule out fetal acidemia considering arterial blood gas pH and base deficit as the standards, respectively.

MATERIALS AND METHODS

We conducted a retrospective cohort study of all women who delivered singletons at the University of Alabama at Birmingham Hospital from January 2006 to March 2012 and had a paired cord arterial blood gas and venous blood gas sample obtained. Universal collection of umbilical cord blood gases is performed at our institution. An umbilical cord segment is double-clamped at delivery, and arterial blood gas and venous blood gas samples are obtained using 1-mL heparinized syringes by a trained nurse or technician and sent immediately for analysis in our neonatal intensive care unit laboratory. Radiometer ABL800 Flex analyzers were used to analyze all umbilical cord gas results in this study. All results were then entered into our electronic database by the laboratory technician and double-checked for accuracy. Dedicated trained personnel are responsible for entering demographic and clinical information into our database and ensuring ongoing quality control.

Cord gas values were excluded from the analysis if there was only a single blood gas value or the paired values did not meet stringent criteria for valid collection. Valid collection was defined as a difference in arterial and venous pH of at least 0.02 and a difference in pCO_2 of 4 mm Hg or greater.[16] In addition, the arterial sample had to have a lower pH and higher pCO_2 than the venous sample. If the results indicated the arterial and venous samples were switched (arterial blood gas pH greater than venous blood gas pH and arterial blood gas CO_2 less than venous blood gas CO_2), the values were reversed before analysis. Cord gas values that do not meet these criteria indicate that the same vessel was likely sampled at the time of collection.[17]

The primary outcome variable in our study was fetal acidemia defined by arterial blood gas pH less than 7.0 (pH acidemia). Secondary outcomes included umbilical arterial blood gas pH less than 7.05 and less than 7.10. We also examined fetal acidemia defined as arterial blood gas base deficit 12 mmol/L or greater (base deficit acidemia). Logistic regression analyses were used to model fetal acidemia outcomes, defined by arterial blood gas measures, as functions of venous blood gas measures. The analyses were repeated for all three definitions of pH acidemia (arterial blood gas pH less than 7.0, less than 7.05, and less than 7.10) and for the base deficit-based definition. Statistical significance of the independent variables was based on the Wald test. The area under the curve (AUC) from receiver operating characteristic curves was used to quantify the predictive ability of venous blood gas pH and base deficit for fetal acidemia outcomes based on all these definitions. The estimated regression equations were used to determine venous blood gas values that define less than or equal to a 1%, 5%, 10%, and 50% probability of fetal acidemia. In additional analyses, we examined the predictive models when venous blood gas pH is adjusted for venous blood gas base deficit and vice versa.

Baseline characteristics were compared between acidemic and nonacidemic groups. Statistical comparisons were conducted by using χ^2 tests and Fisher's exact tests for categorical measures. Independent-sample *t* tests and Wilcoxon rank-sum tests were used for continuous measures. SAS 9.2 and 9.3 were used for all statistical analyses. All hypothesis tests were evaluated at a .05 level of significance. Raw *P* values, unadjusted for multiple comparisons, are presented. The study was approved by the institutional review board of the University of Alabama at Birmingham.

RESULTS

Of 23,506 singleton births delivered during the study period, 18,335 (78%) had cord blood gas results reported by the laboratory. Of these, 1,575 (8.6%) had a missing arterial blood gas pH value, 1,081 (5.9%) were missing a venous blood gas pH value, and two were missing both arterial and venous pH. Paired values that did not meet stringent criteria for valid collection were excluded (Fig. 1), leaving 11,455 (62%)

paired arterial and venous blood gas values available for analysis. There were 542 (4.7%) results reported where arterial and venous measures were switched (arterial blood gas pH greater than venous blood gas pH); these were reversed before further analyses. Arterial blood gas pH values range from 6.6 to 7.46 (99.74% or 11,435 of 11,455 were less than 7.41) and venous blood gas pH values ranged from 6.75 to 7.55.

Of the 11,455 neonates, there were 127 (1.1%) cases of fetal pH acidemia (arterial blood gas pH of less than 7.0), 225 (2%) with arterial blood gas pH less than 7.05, and 480 (4.2%) with arterial blood gas pH less than 7.10. The demographic characteristics of the mother–neonate pairs in this study, stratified by whether or not they had fetal pH acidemia, are presented in Table 1. Those with fetal pH acidemia were more likely to be black, obese, preterm, and to be delivered by cesarean (Table 1). As expected, mean venous blood gas pH was significantly lower and base deficit significantly higher in those with fetal pH acidemia. Mean arterial blood gas and venous blood gas base deficit were similar in those without arterial blood gas pH acidemia; mean arterial blood gas base deficit was higher in those with acidemia.

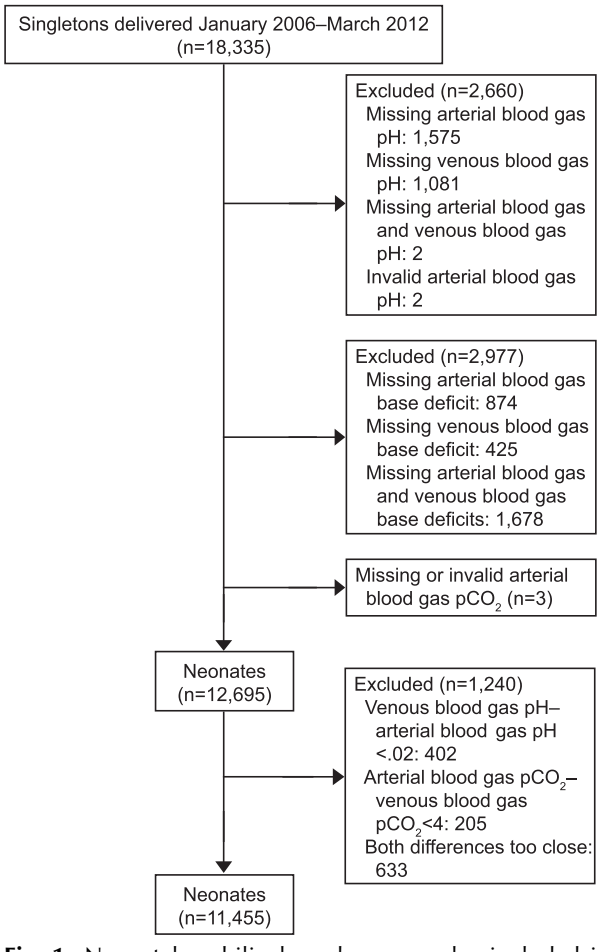

Fig. 1. Neonatal umbilical cord gas samples included in analysis.

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Table 1. Demographic Characteristics Comparing Women With and Without Cord pH Acidemia, Defined as an Arterial Blood Gas pH of Less Than 7.0

Characteristic	Acidemic (n=127)	Nonacidemic (n=11,328)	*P*
Age (y)*	25.3±5.9	25.2±6.0	.91
Race†			
Black	81 (64)	5,945 (52)	**.04**
White	27 (21)	2,997 (26)	
Hispanic/other	19 (15)	2,385 (21)	
Baseline BMI (kg/m²)‡	32.2±9.1	29.0±8.0	**.001**
24.9 or lower	16 (24)	2,516 (37)	**.004**
25–29.9	14 (21)	1,833 (27)	
30 or higher	38 (56)	2,502 (37)	
Parous	65 (51)	6,200 (55)	.42
Gestational age at delivery (wk)§	35.8±5.5	38.2±3.2	**<.001**
Preterm birth at less than 37 wk§	51 (40)	2,116 (19)	**<.001**
Labor‖			
None	33 (28)	1,355 (13)	
Spontaneous	23 (20)	2,034 (19)	**<.001**
Spontaneous with augmentation	38 (32)	4,619 (43)	
Induced	23 (20)	2,727 (25)	
Cesarean delivery	95 (75)	3,383 (30)	**<.001**
Tobacco use¶	20 (25)	2,189 (26)	.78
Venous pH	7.07±0.13	7.32±0.06	**<.001**
Venous base deficit	13.6±5.1	3.4±2.5	**<.001**
Arterial base deficit	17.2±4.0	3.5±2.8	**<.001**

BMI, body mass index.
Data are mean±standard deviation or n (%) unless otherwise specified.
Boldface type indicates $P<.05$.
* Seven missing age information.
† One missing race information.
‡ Four thousand five hundred thirty-six missing BMI information.
§ Nine missing gestational age.
‖ Six hundred three missing labor information.
¶ Two thousand nine hundred sixty-four missing tobacco use information.

Separate logistic regression analyses were used to model the three fetal arterial blood gas pH acidemia outcomes as functions of venous blood gas pH. The estimated logistic regression equations then were used to identify cutoff venous blood gas pH values associated with selected estimated probabilities of fetal acidemia (Table 2). A venous blood gas pH 7.23 or greater is associated with less than a 1% probability (95% confidence interval [CI] of 0.6–1.2%) of fetal

Table 2. Venous Cord pH Cutoffs for Predicted Probability of Acidemia by Logistic Regression Analyses

Definition 1: Arterial Blood Gas pH Less Than 7.0		Definition 2: Arterial Blood Gas pH Less Than 7.05		Definition 3: Arterial Blood Gas pH Less Than 7.10	
Venous pH	Probability (%) of Acidemia (95% CI)	Venous pH	Probability (%) of Acidemia (95% CI)	Venous pH	Probability (%) of Acidemia (95% CI)
7.23 or greater	1 or less (0.6–1.2)	7.26 or greater	1 or less (0.6–1.1)	7.29 or greater	1 or less (0.8–1.2)
7.17 or greater	5 or less (3.5–5.6)	7.20 or greater	5 or less (4.1–6.0)	7.24 or greater	5 or less (4.8–6.4)
7.14 or greater	10 or less (7.9–12)	7.18 or greater	10 or less (7.6–11)	7.22 or greater	10 or less (9.4–12)
7.06 or less	50 or greater (43–60)	7.10 or less	50 or greater (56–69)	7.15 or less	50 or greater (54–63)

CI, confidence interval.

acidemia defined as an arterial blood gas pH of less than 7.0. Venous blood gas pH 7.17 or greater, 7.14 or greater, and 7.06 or greater were associated, respectively, with less than a 5%, 10%, and 50% probability of an arterial blood gas pH less than 7.0. The venous blood gas pH cutoffs associated with predicted probabilities of acidemia based on the alternative definitions of arterial pH less than 7.05 and less than 7.10 are also presented in Table 2.

The receiver operating characteristic curve for the prediction of arterial blood gas pH less than 7.0 from venous blood gas pH is shown in Figure 2A (AUC 0.949, 95% CI 0.920–0.979; $P<.001$). The curves for arterial blood gas pH less than 7.05 and less than 7.10 are also shown in Figures 2B and 2C, respectively. For all three definitions of acidemia, venous blood gas pH was a highly significant predictor of fetal acidemia (all Wald $P<.001$) and demonstrated high predictive power (each AUC 94% or greater).

We further investigated a differential relationship between venous blood gas and arterial blood gas measures between preterm (less than 37 weeks of gestation) and term neonates (37 weeks of gestation or greater). Our logistic regression models were extended to include a main effect for preterm or term status and an interaction term between the venous blood gas measure and preterm or term status. In all models, the interaction term was statistically significant ($P<.005$) and stratified models were subsequently considered. For all three definitions of acidemia,

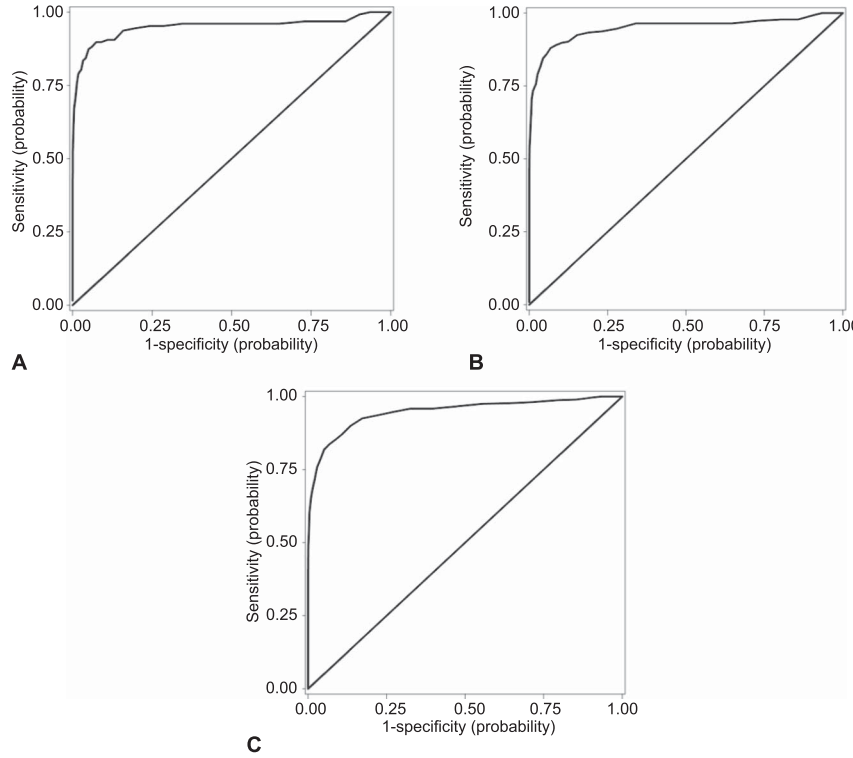

Fig. 2. A. Receiver operating characteristic curve for the prediction of fetal acidemia (umbilical artery pH less than 7) from umbilical vein pH values. Area under curve 0.949 (95% confidence interval [CI] 0.920–0.979). **B**. Receiver operating characteristic curve for the prediction of fetal acidemia (umbilical artery pH less than 7.05) from umbilical vein pH values. Area under curve 0.949 (95% CI 0.928–0.970). **C**. Receiver operating characteristic curve for the prediction of fetal acidemia (umbilical artery pH less than 7.1) from umbilical vein pH values. Area under curve 0.947 (95% CI 0.935–0.960).

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venous blood gas pH was a highly significant predictor of fetal acidemia (all Wald $P<.001$) and demonstrated high predictive power for fetal acidemia in both preterm (each AUC 91% or greater) and term neonates (each AUC 95% or greater).

Next, we examined how venous base deficit performs as a predictor of base deficit acidemia, as defined by an arterial base deficit 12 mmol/L or greater. The demographic characteristics of the study sample comparing those with an arterial base deficit less than 12 and those with a base deficit 12 mmol/L or greater are presented in Table 3. Those with arterial base deficit acidemia were more likely to deliver by cesarean and more likely to be nulliparous. Mean

Table 3. Demographic Characteristics Comparing Those With and Without an Arterial Base Deficit 12 mmol/L or Greater

Characteristic	Base Deficit 12 mmol/L or Greater (n=245)	Base Deficit Less Than 12 mmol/L (n=11,210)	*P*
Age (y)*	25.4±6.1	25.2±6.0	.58
Race†			.37
Black	136 (56)	5,890 (53)	
White	55 (22)	2,969 (26)	
Hispanic or other	54 (22)	2,350 (21)	
Baseline BMI (kg/m²)‡	30.0±8.9	29.0±8.0	.14
24.9 or less	46 (32)	2,486 (37)	
25–29.9	37 (26)	1,810 (27)	.38
30 or greater	60 (42)	2,480 (37)	
Parous	106 (43)	6,159 (55)	**<.001**
Gestational age at delivery (wk)§	37.0±4.7	38.2±3.2	.07
Preterm birth at less than 37 wk§	72 (29)	2,095 (19)	**<.001**
Labor‖			
None	44 (19)	1,344 (13)	**.01**
Spontaneous	40 (17)	2,017 (19)	
Spontaneous with augmentation	83 (36)	4,574 (43)	
Induced	62 (27)	2,688 (25)	
Cesarean delivery	145 (59)	3,333 (30)	**<.001**
Use of tobacco¶	35 (21)	2,174 (26)	.10
Venous pH	7.11±0.11	7.32±0.06	**<.001**
Venous base deficit	12.4±4.2	3.4±2.4	**<.001**
Arterial base deficit	15.4±3.5	3.4±2.7	**<.001**

BMI, body mass index.
Data are mean±standard deviation or n (%) unless otherwise specified.
Boldface type indicates $P<.05$.
* Seven missing age information.
† One missing race information.
‡ Four thousand five hundred thirty-six missing BMI information.
§ Nine missing gestational age.
‖ Six hundred three missing labor information.
¶ Two thousand nine hundred sixty-four missing tobacco use information.

venous blood gas pH was significantly lower and base deficit significantly higher in those with fetal base deficit acidemia. Similar to pH acidemia, mean arterial blood gas base deficit was higher than venous blood gas base deficit in those with arterial blood gas base deficit acidemia. Using logistic regression, venous blood gas base deficit values 6.3 or less, 8.2 or less, and 9.0 mmol/L or less were associated with less than a 1%, 5%, and 10% probability of a cord arterial blood gas base deficit 12 mmol/L or greater, respectively. Venous blood gas base deficit 11.5 mmol/L or less was associated with less than a 50% probability of a fetal arterial blood gas base deficit 12 mmol/L or greater. The receiver operating characteristic curve for the prediction of arterial blood gas base deficit 12 mmol/L or greater by venous blood gas base deficit is shown in Figure 3. Venous blood gas base deficit was a highly significant predictor of arterial blood gas base deficit (AUC 0.969, 95% CI 0.954–0.983; $P<.001$).

A multivariable regression model considering the interaction between venous blood gas base deficit and preterm status indicated no difference in the effect of venous blood gas base deficit between preterm and term neonates ($P=.59$). Thus, no stratified models were constructed.

The estimates from the crude logistic regression model that can be used to formulate an equation to predict arterial blood gas pH acidemia (various

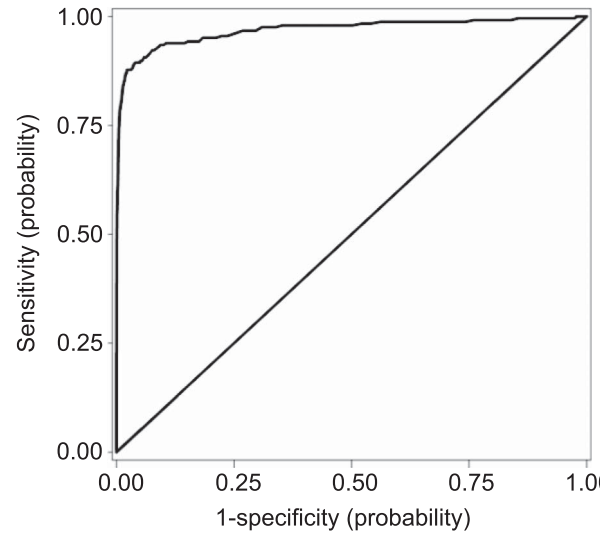

Fig. 3. Receiver operating characteristic curve using venous base deficit (as a continuous variable) for the prediction of arterial base deficit 12 mmol/L or greater. Area under curve 0.969 (95% confidence interval 0.954–0.983).

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definitions) or base deficit acidemia using venous blood gas parameters are shown in the Appendix, available online at http://links.lww.com/AOG/A567.

In additional analyses we applied both cord venous blood gas pH and base deficit to predict fetal acidemia. Venous blood gas pH, adjusting for venous blood gas base deficit, was slightly more predictive of arterial blood gas pH for each of the definitions than venous blood gas pH alone (AUC 0.961, 95% CI 0.938–0.984 for pH less than 7.0; 0.959, 95% CI 0.941–0.976 for pH less than 7.05, and 0.956, 95% CI 0.945–0.967 for pH less than 7.10). However, venous blood gas base deficit adjusting for venous blood gas pH was not more predictive of arterial blood gas base deficit greater than 12 (AUC 0.969, 95% CI 0.955–0.984).

Additional analyses using less stringent criteria to distinguish the arterial from the venous sample (arterial blood gas pH lower than the venous blood gas pH by at least 0.01 and the arterial blood gas pCO_2 higher than the venous blood gas pCO_2 by at least 1 mm Hg) did not materially change the findings (data not shown).

DISCUSSION

Despite a policy of universal cord blood collection in our center, more than one third of patients did not have adequate paired samples or valid results for analysis. Many of these represented single-vessel collections or cases in which arterial and venous samples were not distinguishable. We demonstrate that venous blood gas pH and base deficit are highly powerful predictors of acidemia defined by arterial blood gas pH and base deficit, respectively. Predictive ability may be further improved by adjusting venous blood gas pH for base deficit. Although statistically the arterial blood gas pH prediction is improved in term neonates, venous blood gas pH remains a significant predictor of fetal pH acidemia in both preterm and term neonates (reflected by the AUC 91% or greater). Gestational age is not a modifier of base deficit prediction.

The range of arterial blood gas and venous blood gas values suggests that if the origin is uncertain, pH less than 6.75 would be best classified as arterial, whereas pH greater than 7.46 would be best classified as venous. Any pH values less than 6.6 or greater than 7.55 are outside of our observed ranges. We identify venous pH and base deficit cutoff values associated with low probabilities of fetal acidemia defined by arterial blood gas pH and base deficit, respectively, using simple, easy-to-use models. Although the combination of venous pH and base deficit values was slightly more predictive of pH acidemia, they use a calculated value (base deficit) to predict the measured pH and the added complexity are limiting considerations. The adjustment of the base deficit model for pH yields practically identical results, which is not surprising because the calculation of base deficit already takes pH into consideration.

Our findings suggest that definitions of acidemia using arterial blood gas pH and base deficit identify similar but not identical groups of patients. Findings suggest that patients with worse cord gas parameters are identified using the pH definition. The differences are reflected by the differences observed in the prevalence and patient characteristics associated with pH acidemia compared with base deficit acidemia in Tables 1 and 3.

These findings have important clinical as well as medicolegal and research utility. Our results provide venous blood gas pH and base deficit cutoffs that can be used to determine the probability of acidemia when an arterial sample is not available or only one sample is obtained (presumed to be venous from both a practical and worst-case medicolegal perspective). In addition, our data can be used to predict arterial pH or base deficit for any given venous cord gas values. Our data are consistent with prior reports suggesting that valid cord blood results may not be available in up to 25% of cases.[17] Single-vessel collections comprise an important proportion of inadequate results. In the setting of a single-vessel collection, it is difficult to definitively determine if the result is arterial or venous, although venous origin is more likely considering the relative ease of collection. Westgate et al found that the difference in arterial and venous pH ranged from 0.02 to 0.49 with a median of 0.09. They excluded samples if the pH difference was below the fifth percentile (less than 0.02), which is the same criterion we used to differentiate a venous from an arterial sample.[15]

The strengths of this study include the large number of paired cord gas samples and the criteria we used to confirm valid sampling. Although these stringent criteria helped ensure that a valid arterial and venous sample were obtained, this may be somewhat restrictive when applied to clinical practice, because physiologically the difference in arterial and venous pH and pCO_2 may not differ as much, even if sampled correctly. However, the use of less stringent criteria in additional analyses did not change the results. It is possible that a sudden reduction in umbilical blood flow such as with acute cord compression or bradycardia can cause a large difference between the arterial and venous pH.[10,15,17] Therefore, a normal

venous pH does not exclude the possibility of significant arterial acidosis. A limitation of our study is that we do not have neonatal follow-up data or outcomes with which to correlate blood gas results. However, the objective of the study was to establish the predictive ability of the venous sample and establish cutoffs that would effectively rule out acidemia. In addition, we focused this analysis on the use of pH and base deficit exclusively, because these are the two parameters that are considered when determining pathologic acidemia. Other umbilical blood gas parameters (carbon dioxide partial pressure and oxygen partial pressure) were not included in the logistic regression model. However, models adjusting for base deficit indirectly take into consideration HCO_3 (and CO_2) because HCO_3 is included in the calculation.

Finally, predictive models such as ours should undergo external validation. Thus, we plan to use another database to validate our current findings. Gestational age should be considered as an interaction term when using venous blood gas pH to predict arterial blood gas pH. Adjustments for venous blood gas pH and base deficit as applicable to improve prediction deserve further evaluation.

Our findings, if validated, will help clinicians as well as researchers make more informed decisions about neonatal management and prognosis using predicted arterial parameters when cord gas results are venous-only or of uncertain origin (assumed to be venous). Important medicolegal applications include the ability to estimate the likelihood of parameters that are potentially associated with encephalopathy or cerebral palsy of intrapartum origin. We used primary pH and base deficit cutoffs based on the 2003 American College of Obstetricians and Gynecologists' Task Force document (affirmed in 2014) for our primary analyses.[6,7] The probability of any arterial pH or base deficit cutoffs can be easily estimated using the prediction formula generated by our data.

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