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Reference ranges for serial measurements of umbilical artery Doppler indices in the second half of pregnancy

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Objective: The purpose of this study was to construct new reference ranges for serial measurements of commonly used umbilical artery Doppler indices (pulsatility index, resistance index, and systolic:diastolic ratio).

Study design: This was a prospective longitudinal study of the umbilical artery Doppler indices that were obtained serially at the free-loop of umbilical cord at 4-week intervals at 19 to 42 weeks of gestation in 130 low-risk singleton pregnancies. A total of 513 observations were used to construct the reference ranges with the use of multilevel modeling.

Results: Longitudinally established percentiles of Doppler indices from the present study show a continuous reduction throughout the second half of pregnancy without any plateau or increase near term, as reported previously. There was a significant negative association between Doppler indices and placental weight and neonatal birth weight, but not with gender. The intraobserver coefficients of variation for the umbilical artery pulsatility index, resistance index, and systolic:diastolic ratio were 10.5%, 6.8 %, and 13.0 %, respectively.

Conclusion: New reference ranges for umbilical artery Doppler indices that are based on longitudinal observations appear to be slightly different from cross-sectional studies and are more appropriate for serial evaluation of fetal hemodynamics.

Umbilical artery Doppler velocimetry is one of the most rigorously evaluated and frequently used noninvasive tests of fetal well-being. Although not a good screening tool in the low-risk population,[1] it is a valuable investigation in the surveillance of high-risk pregnancies.[2-5] Several Doppler-derived indices have been used in clinical practice to identify fetuses who are at risk of increased perinatal death and morbidity that may benefit from closer surveillance or elective delivery. Among them umbilical artery pulsatility index (PI), resistance index (RI), and systolic:diastolic (S:D) ratio are used most commonly. The clinical potential of such a tool depends on the availability of suitable reference

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Table I Baseline characteristics of the study population

Parameter	Measure
Maternal	
Age (median, range)	30 Y (18-43 Y)
Nulliparous (n)	60 (46%)
Body mass index at booking (mean ± SD)	25.81 ± 3.98 kg/m^2
Fetal	
Gestational age at delivery (mean ± SD)	39.8 ± 1.36 wk
Birth weight (median, range)	3665 g (1645-4590 g)
Placental weight (mean ± SD)	673 ± 145 g
Umbilical arterial pH (mean ± SD)	7.23 ± 0.148
Umbilical arterial base excess (mean ± SD)	−4.18 ± 3.507 mmol/L
Umbilical venous pH (mean ± SD)	7.33 ± 0.084
Umbilical venous base excess (mean ± SD)	−4.63 ± 3.572 mmol/L

ranges. Several reference ranges of these waveform indices have been published. However, the studies with an adequate number of observations are cross-sectional[6-8] and mostly use routinely collected clinical data.[9,10]

For serial measurements, appropriate reference ranges must be derived from longitudinal studies rather than cross-sectional studies. However, the few longitudinal studies that have been published in the English language are small[11-14] or use continuous wave Doppler imaging without any knowledge of site or angle of insonation[15,16] and the data are mostly analyzed and presented as if they were derived from a cross-sectional study.

The aim of this study was to establish reference ranges for serial measurements of the umbilical artery Doppler indices in the second half of pregnancy based on longitudinal data. In addition, we wanted to examine the effect of neonatal weight, gender, and placental weight on the Doppler indices.

Material and methods

This was a longitudinal study of 130 low-risk pregnancies that were recruited for a detailed study of the umbilical circulation according to a research protocol approved by the Regional Committee for Medical Research Ethics; written informed consent was obtained from all participants.

Inclusion criteria were gestational age confirmed by ultrasound measurement of <20 weeks and no complications in the current pregnancy before recruitment. Maternal smoking, multiple pregnancy, a diagnosed fetal abnormality before recruitment, previous history of preeclampsia, intrauterine growth retardation, abruptio placenta or preterm delivery, and history of any pre-existing medical condition (such as hypertension, diabetes mellitus, renal disease) were reasons for not being included. Each woman was examined 3 to 5 times at approximately 4-week intervals between 19 and 42 gestational weeks.

Doppler ultrasonography was performed with an ultrasound system with a 2.5- to 6-MHz curvilinear transducer (Sequoia 512; Acuson; Mountain View, Calif). A single operator (G.A.) performed all examinations. Color Doppler imaging was used to optimize the insonation by the pulsed Doppler examination. The angle of insonation was kept at <15 degrees in all cases, and angle correction was used if the angle was not zero. The high-pass filter was set at minimum, and a large sample volume (10-12 mm) was used for the pulsed Doppler recording. The Doppler velocity waveforms were obtained from the free-floating loop of the umbilical cord during fetal quiescence. Five to 6 uniform waveforms were obtained ≥3 times in succession, and online measurements were performed. The values that were recorded were an average of 3 consecutive cardiac cycles. The waveform envelope that had the highest measured peak systolic velocity was considered for analysis, assuming that the highest measured velocity represents the lowest angle of insonation. The guidelines of the International Perinatal Doppler Society[17] were followed during Doppler sonographic examinations. The mechanical index was kept at <1.9, and the thermal index was kept at <1.5. Doppler waveform indices were calculated from the maximum velocity waveform with the following computerized planimetry:

PI = (Peak systolic velocity−end-diastolic velocity)/time-averaged maximum velocity[18]

RI = (Peak systolic velocity−end-diastolic velocity)/peak systolic velocity[19]

S:D ratio = Peak systolic velocity/end-diastolic velocity[20]

The outcome of pregnancy was noted and included any complications, gestation at delivery, mode of delivery, neonatal birth weight, sex, Apgar score, umbilical cord blood gases, perinatal complications, and placental weight. All the placentas were collected immediately after delivery and inspected for completeness and any gross abnormalities. The umbilical cord was cut flush with the placental surface, but the membranes were not trimmed. Blood was allowed to drain from the placenta, and the clots were removed. The placenta was weighed on a precision balance by the midwife shortly after delivery. A pediatrician routinely examined the newborn infants on the third postnatal day and noted any abnormalities, if present.

Data analysis was performed with SAS software (version 8.2; SAS Institute Inc, Cary, NC). Normality was checked for each outcome variable, and logarithmic

Table II Reference values for serial measurements of the umbilical artery pulsatility index

	Percentile								
Gestation (wk)	2.5th	5th	10th	25th	50th	75th	90th	95th	97.5th
19	0.97	1.02	1.08	1.18	1.30	1.44	1.57	1.66	1.74
20	0.94	0.99	1.04	1.14	1.27	1.40	1.54	1.62	1.70
21	0.90	0.95	1.00	1.10	1.22	1.36	1.49	1.58	1.65
22	0.87	0.92	0.97	1.07	1.19	1.32	1.46	1.54	1.62
23	0.84	0.89	0.94	1.04	1.15	1.29	1.42	1.50	1.58
24	0.81	0.86	0.91	1.00	1.12	1.25	1.38	1.47	1.55
25	0.78	0.83	0.88	0.97	1.09	1.22	1.35	1.44	1.51
26	0.76	0.80	0.85	0.94	1.06	1.19	1.32	1.41	1.48
27	0.73	0.77	0.82	0.92	1.03	1.16	1.29	1.38	1.45
28	0.71	0.75	0.80	0.89	1.00	1.13	1.26	1.35	1.43
29	0.68	0.72	0.77	0.86	0.98	1.10	1.23	1.32	1.40
30	0.66	0.70	0.75	0.84	0.95	1.08	1.21	1.29	1.37
31	0.64	0.68	0.73	0.82	0.93	1.05	1.18	1.27	1.35
32	0.62	0.66	0.70	0.79	0.90	1.03	1.16	1.25	1.32
33	0.60	0.64	0.68	0.77	0.88	1.01	1.14	1.22	1.30
34	0.58	0.62	0.66	0.75	0.86	0.99	1.12	1.20	1.28
35	0.56	0.60	0.64	0.73	0.84	0.97	1.09	1.18	1.26
36	0.54	0.58	0.63	0.71	0.82	0.95	1.07	1.16	1.24
37	0.53	0.56	0.61	0.69	0.80	0.93	1.05	1.14	1.22
38	0.51	0.55	0.59	0.68	0.78	0.91	1.04	1.12	1.20
39	0.49	0.53	0.57	0.66	0.76	0.89	1.02	1.10	1.18
40	0.48	0.51	0.56	0.64	0.75	0.87	1.00	1.09	1.17
41	0.47	0.50	0.54	0.63	0.73	0.85	0.98	1.07	1.15

or power transformations were performed as appropriate (ln transformation for PI and S:D ratio, square root for RI) to reduce the skewness of residuals. Intraobserver coefficients of variation were calculated from 3 sets of measurements obtained from 513 observations as:

$$\text{Coefficient of variation} = 100\times\sqrt{\sum_i \left(S_i^2/\bar{X}_i^2\right)/n}$$

where S_i^2 = within-subject variance, X_i = mean of all measurements, n = number of observations.[21] Multilevel modeling was used to estimate the reference percentiles.[22] Fractional polynomials were fitted to find the best relationship between Doppler indices and gestational age.

Results

Of a total of 133 recruited participants, 3 participants withdrew because they moved their residence, which left 130 participants with complete data sets for the statistics. All the participants were white. Characteristics of the study population are presented in Table I. Three women (2.3%) had preeclampsia, and 1 woman had gestational diabetes mellitus. Onset of labor was spontaneous in 110 women (84.6%) and was induced in 13 women (10%); 7 women (5.4%) had an elective cesarean delivery before the onset of labor. Seventeen women (13.1%) had an emergency cesarean delivery; 5 women (3.8%) had vacuum delivery, and 1 woman (0.8%) had forceps delivery. Three women (2.3%) were delivered preterm (34-36 weeks of gestation). Four babies (3%) were below the 5th percentile for the gestational age. One fetus was diagnosed with a transposition of the great arteries at 37 weeks of gestation, and 1 fetus was diagnosed with tetralogy of Fallot after birth. There were 66 male (50.8%) and 64 female (49.2%) babies. There was 1 intrauterine fetal death at 42 weeks of gestation. Of 129 liveborn infants, 5 infants (3.9%) had an Apgar score of $<$7 at 5 minutes. Three babies (2.3%) required resuscitation at birth, and 9 babies (6.9%) were admitted to the neonatal care unit.

Gestational age-specific reference values for the 2.5th, 5th, 10th, 25th, 50th, 75th, 90th, 95th, and 97.5th percentiles of the umbilical artery PI, RI, and S:D ratio are presented in Tables II, III, and IV. Curve-fitted percentile charts for each of these variables are shown in Figures 1, 2, and 3. The statistical formulas and the regression equations are presented in the Appendix.

The coefficients of variation for PI, RI, and S:D ratio were 10.5% (95% CI, 9.9%-11.1%), 6.8% (95% CI, 6.4%-7.2%), and 13.0% (95% CI,12.1%-13.9%), respectively.

The Doppler indices decreased continuously with advancing gestational age ($P < .0001$). When the individual values of the Doppler indices that were

Table III Reference values for serial measurements of the umbilical artery resistance index:

Gestation (wk)	Percentile 2.5th	5th	10th	25th	50th	75th	90th	95th	97.5th
19	0.64	0.66	0.68	0.72	0.77	0.81	0.85	0.88	0.90
20	0.63	0.65	0.67	0.71	0.75	0.80	0.84	0.87	0.89
21	0.62	0.64	0.66	0.70	0.74	0.79	0.83	0.85	0.88
22	0.60	0.62	0.65	0.68	0.73	0.78	0.82	0.84	0.87
23	0.59	0.61	0.63	0.67	0.72	0.76	0.81	0.83	0.86
24	0.58	0.60	0.62	0.66	0.71	0.75	0.80	0.82	0.85
25	0.56	0.58	0.61	0.65	0.69	0.74	0.79	0.81	0.84
26	0.55	0.57	0.59	0.64	0.68	0.73	0.78	0.80	0.83
27	0.54	0.56	0.58	0.62	0.67	0.72	0.77	0.79	0.82
28	0.53	0.55	0.57	0.61	0.66	0.71	0.76	0.78	0.81
29	0.51	0.53	0.56	0.60	0.65	0.70	0.75	0.77	0.80
30	0.50	0.52	0.54	0.59	0.64	0.69	0.74	0.76	0.79
31	0.49	0.51	0.53	0.58	0.63	0.68	0.73	0.76	0.78
32	0.47	0.50	0.52	0.56	0.61	0.67	0.72	0.75	0.77
33	0.46	0.48	0.51	0.55	0.60	0.66	0.71	0.74	0.77
34	0.45	0.47	0.50	0.54	0.59	0.65	0.70	0.73	0.76
35	0.44	0.46	0.48	0.53	0.58	0.64	0.69	0.72	0.75
36	0.42	0.45	0.47	0.52	0.57	0.63	0.68	0.71	0.74
37	0.41	0.43	0.46	0.51	0.56	0.62	0.67	0.70	0.73
38	0.40	0.42	0.45	0.50	0.55	0.61	0.66	0.70	0.73
39	0.39	0.41	0.44	0.48	0.54	0.60	0.65	0.69	0.72
40	0.38	0.40	0.43	0.47	0.53	0.59	0.65	0.68	0.71
41	0.36	0.39	0.41	0.46	0.52	0.58	0.64	0.67	0.70

Table IV Reference values for serial measurements of the umbilical artery systolic:diastolic ratio

Gestation (wk)	Percentile 2.5th	5th	10th	25th	50th	75th	90th	95th	97.5th
19	2.73	2.93	3.19	3.67	4.28	5.00	5.75	6.26	6.73
20	2.63	2.83	3.07	3.53	4.11	4.80	5.51	5.99	6.43
21	2.51	2.70	2.93	3.36	3.91	4.55	5.22	5.67	6.09
22	2.43	2.60	2.83	3.24	3.77	4.38	5.03	5.45	5.85
23	2.34	2.51	2.72	3.11	3.62	4.21	4.82	5.22	5.61
24	2.25	2.41	2.62	2.99	3.48	4.04	4.63	5.02	5.38
25	2.17	2.33	2.52	2.88	3.35	3.89	4.45	4.83	5.18
26	2.09	2.24	2.43	2.78	3.23	3.75	4.30	4.66	5.00
27	2.02	2.17	2.35	2.69	3.12	3.63	4.15	4.50	4.83
28	1.95	2.09	2.27	2.60	3.02	3.51	4.02	4.36	4.67
29	1.89	2.03	2.20	2.52	2.92	3.40	3.89	4.22	4.53
30	1.83	1.96	2.13	2.44	2.83	3.30	3.78	4.10	4.40
31	1.77	1.90	2.06	2.36	2.75	3.20	3.67	3.98	4.27
32	1.71	1.84	2.00	2.29	2.67	3.11	3.57	3.87	4.16
33	1.66	1.79	1.94	2.23	2.60	3.03	3.48	3.77	4.06
34	1.61	1.73	1.88	2.16	2.53	2.95	3.39	3.68	3.96
35	1.57	1.68	1.83	2.11	2.46	2.87	3.30	3.59	3.86
36	1.52	1.64	1.78	2.05	2.40	2.80	3.23	3.51	3.78
37	1.48	1.59	1.73	2.00	2.34	2.74	3.15	3.43	3.69
38	1.44	1.55	1.69	1.95	2.28	2.67	3.08	3.36	3.62
39	1.40	1.51	1.64	1.90	2.23	2.61	3.02	3.29	3.54
40	1.36	1.47	1.60	1.85	2.18	2.56	2.96	3.22	3.48
41	1.33	1.43	1.56	1.81	2.13	2.50	2.90	3.16	3.41

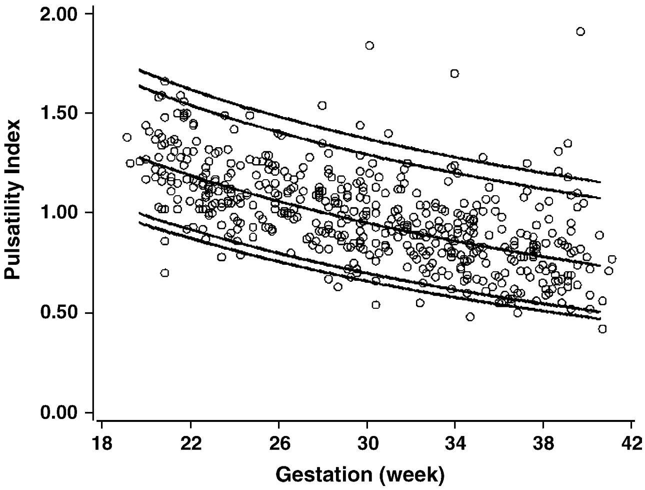

Figure 1 Umbilical artery pulsatility index at the free loop with p2.5, p5, p50, p95, and p97.5. The *dotted lines* represent 95% confidence limits for the mean.

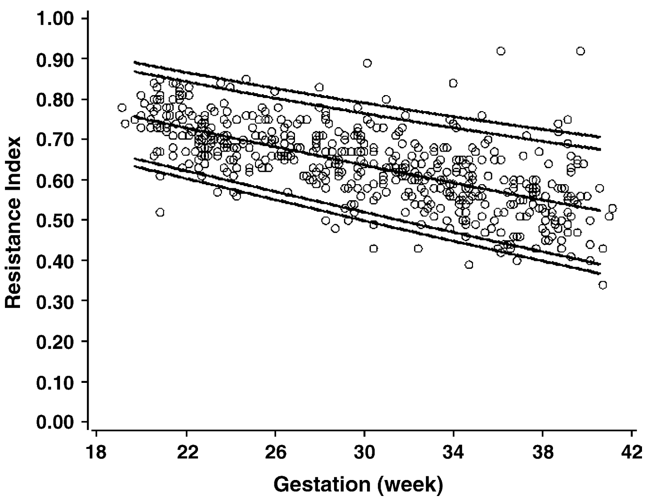

Figure 2 Umbilical artery resistance index at the free loop with p2.5, p5, p50, p95, and p97.5. The *dotted lines* represent 95% confidence limits for the mean.

obtained at the first and last visits were divided into quartiles, 76% of the fetuses remained within ± 1 quartile during the second half of pregnancy. We found no significant association between neonatal gender and the slopes of PI, RI, and S:D ratio (P = .63,.93, and.32, respectively) or their gestational age-specific values (P = .21, .06, and .16, respectively). The slope of the PI was associated negatively with placental weight. The PI was estimated to decrease by 0.01 per gestational week, but this negative slope of PI was associated with placental weight so that, for an increase of 100 g, the slope decreased by -0.002 per week (P = .009). The RI was estimated to decrease by 0.005 per week, but this association was modified by placental weight so that, for an increase of 100 g, the slope of RI decreased by

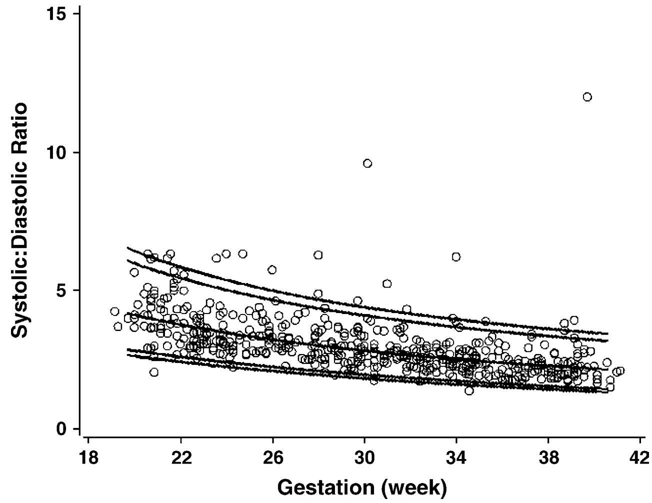

Figure 3 Umbilical artery systolic:diastolic ratio at the free loop with p2.5, p5, p50, p95, and p97.5. The *dotted lines* represent 95% confidence limits for the mean.

-0.001 per week (P = .005). The association between placental weight and the S:D ratio was not statistically significant (P = .14).

We found a significant negative association between birth weight and gestational age-specific values of PI, RI, and S:D ratio (P = .003, .011, .024, respectively) so that the PI, RI, and S:D ratio decreased by 0.035, 0.01, and 0.12, respectively for every 500-g increase in the birth weight. There was no association between the linear slopes of these Doppler indices and birth weight (P = .32-.96).

Comment

We have established reference ranges that were based on longitudinal observations that are suitable for serial measurements of 3 commonly used umbilical artery Doppler indices (ie, PI, RI, and S:D ratio). Currently used references are either based on cross-sectional studies or have common methodologic problems (such as inappropriate design, insufficient information about the study population, inadequate sample size, and handling of the longitudinal data as cross-sectional during statistical analysis without accounting for within-subject changes in Doppler measurements). Our study was designed to overcome many of the methodologic weaknesses that have been noted in fetal measurement studies.[23]

Our longitudinal study showed a continuous reduction of Doppler indices with advancing gestational age, which confirms previous observations. However, our data demonstrate that this reduction continues beyond term, which is in contrast with some of the previously reported large cross-sectional[7] and longitudinal[16] studies that report plateau or a small increase in Doppler indices after 39 to 40 weeks of gestation. On the basis of our observations, it is unlikely that there is an increase in placental vascular impedance in normal pregnancies after 40 weeks of gestation.

The site-dependent variations in the measurement of Doppler indices are well known.[24] Some authors have advised recording the waveforms from the fetal end of the umbilical cord,[25] and other authors have advised to record from the placental end.[26] We chose the free-floating loop of the umbilical cord because it seems to be the preferred technique in many centers. Semiquantitative Doppler indices are not angle dependent, and an insonation angle of <60 degrees does not have any significant effect in their calculation.[27] However, we kept the angle at <15 degrees in all cases.

We had a rare possibility of determining intraobserver variability in 3 sets of examinations in 513 observations at different gestational ages between 19 and 42 weeks. Intraobserver variability was acceptable (coefficients of variance, 6.8%-13% for different indices) and similar to previously reported variability.[28]

Choosing a representative population is important in studies that are intended to construct reference ranges. Our sample was a low-risk population with a uniform ethnic background. Additionally, we did not exclude any of them because of complications that developed during the project to reduce the shift towards a supernormal population. Other characteristics that included an even distribution of the babies' gender and the mean birth weight of 3662 g (median, 3665 g; range, 1645-4590 g), which is at approximately 50th percentile according to Norwegian standards,[29] suggest that this can be considered as a reference population. Because our study population had a relatively uniform socioeconomic and ethic background, it could be argued that our nomograms may not be entirely applicable to other populations. Umbilical artery PI is known to vary with birth weight and placental size, which are parameters that may vary with ethnicity. Taking into account such factors, the impact of other ethnic and socioeconomic characteristics of the population on the Doppler indices is likely to be small.[30] Furthermore, because our data are based on longitudinal observations, conditional reference ranges can be calculated for any individual fetus on the basis of a previous measurement. Therefore, we believe that our nomograms are applicable also outside the Nordic population.

Some investigators would argue that pregnancies that had complications after inclusion should be excluded. However, such a study design has been criticized previously for producing supernormal ranges that were less applicable in the general population. Accordingly, we chose not to exclude such complications in the present study.

A close linear relationship between birth weight and umbilical artery Doppler velocity waveforms has been described previously.[31] The present longitudinal data confirm that relationship.

In clinical practice, the umbilical artery Doppler indices are usually obtained serially when a fetus is deemed to be at increased perinatal risk. The advantage of longitudinal data is that they may be used to calculate conditional reference percentiles (Appendix); ie, it is possible to predict a value including 95% CI for a given gestational age on the basis of a previous measurement, which may be more appropriate in the assessment of individual fetuses.[22]

In short, we have constructed new reference ranges for umbilical artery Doppler indices that are based on longitudinal data. They differ slightly from previously published studies and are more appropriate for serial evaluation of fetal hemodynamics.

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Appendix

Reference interval

If Y_i = velocity at gestational age T_i, then the mean and variance of a transformed velocity Z_i at a transformed time X_i are

$$\mu_i = E(Z_i) = \beta_{0i} + \beta_{1i} X_i$$

$$\sigma_i^2 = Var(Z_i) = \sigma_{\text{int}}^2 + \sigma_{time}^2 X_i^2 + 2\sigma_{\text{int},time} X_i + \sigma_e^2$$

where β_{0i}, β_{1i} are the fixed parameter estimates and σ_{int}^2, σ_{time}^2, $\sigma_{\text{int,time}}$, σ_e^2 are the estimated variance components from the multilevel analysis.

The time specific reference value for Y_i with 95% coverage is

$(\mu_i \pm 1.96\sigma_i)^{1/\lambda}$ if transformation of velocity is $Z_i = Y_i^{\lambda}$

$\exp(\mu_i \pm 1.96\sigma_i)$ if transformation of velocity $Z_i = \ln(Y_i)$

Conditional reference interval

The conditional mean and variance of Z_2 given Z_1 is

$$E(Z_2|Z_1) = \mu_{2|1} = \mu_2 + (Z_1 - \mu_1)\sigma_{12}/\sigma_1^2$$
$$Var(Z_2|Z_1) = \sigma_{2|1}^2 = \sigma_2^2 - \sigma_{12}^2/\sigma_1^2 ,$$

where

$$\sigma_{12} = \text{cov}(Z_1, Z_2) = \sigma_{\text{int}}^2 + (X_1 + X_2)\sigma_{\text{int},time} + X_1 X_2 \sigma_{time}^2$$

The conditional reference interval of Y_2 given Y_1 with 95% coverage is

$\left(\mu_{2|1} \pm 1.96\sigma_{2|1}\right)^{1/\lambda}$ if transformation of velocity is $Z = Y^{\lambda}$

$\exp\left(\mu_{2|1} \pm 1.96\sigma_{2|1}\right)$ if transformation of velocity is $Z = \ln\left(Y\right)$

Pulsatility Index (PI)

PI is log transformed (ie, Z = ln[PI]).

$$\mu_i = E(Z_i) = 1.5075 - 0.2843 T_i^{0.5}$$

$$\sigma_i^2 = Var(Z_i) = 0.0667 + 0.00398 T_i - 0.0276 T_i^{0.5}$$

The conditional mean and variance of Z_2 given Z_1 is

$$\mu_{2|1} = 1.5075 - 0.2843T_2^{0.5} + \left(\ln(PI) - 1.5075 + 0.2843T_1^{0.5}\right) \cdot \left(\frac{0.04616 - 0.0138\left(T_1^{0.5} + T_2^{0.5}\right) + 0.00398T_1^{0.5}T_2^{0.5}}{0.0667 + 0.00398T_1 - 0.0276T_1^{0.5}}\right)$$

$$\sigma_{2|1}^2 = 0.0667 + 0.00398T_2 - 0.0276T_2^{0.5} - \left(\frac{\left(0.04616 - 0.0138\left(T_1^{0.5} + T_2^{0.5}\right) + 0.00398T_1^{0.5}T_2^{0.5}\right)^2}{0.0667 + 0.00398T_1 - 0.0276T_1^{0.5}}\right)$$

Resistance Index (RI)

The transformation of RI is Z = $RI^{0.5}$.

$$\mu_i = E(Z_i) = 1.0079 - 0.007T_i$$

$$\sigma_i^2 = Var(Z_i) = 0.0016 - 0.0000623T_i + 0.00000272T_i^2$$

The conditional mean and variance of Z_2 given Z_1 is

$$\mu_{2|1} = 1.0079 - 0.007T_2 + \left(RI^{0.5} - 1.0079 + 0.007T_1\right) \left(\frac{0.000249 - 0.0000312(T_1 + T_2) + 0.00000272T_1T_2}{0.0016 - 0.0000623T_1 + 0.00000272T_1^2}\right)$$

$$\sigma_{2|1}^2 = 0.0016 - 0.0000623T_2 + 0.00000272T_2^2 - \left(\frac{(0.000249 - 0.0000312(T_1 + T_2) + 0.00000272T_1T_2)^2}{0.0016 - 0.0000623T_1 + 0.00000272T_1^2}\right)$$

Systolic:Diastolic Ratio (SDR)

SDR is log transformed (ie, Z = ln[SDR]).

$$\mu_i = E(Z_i) = 4.16676 - 0.9188\ln(T_i)$$

$$\sigma_i^2 = Var(Z_i) = 0.4851 - 0.2678\ln(T_i) + 0.04115\ln(T_i)^2$$

The conditional mean and variance of Z_2 given Z_1 is

$$\mu_{2|1} = 4.16676 - 0.9188\ln(T_2) + (\ln(SDR_1) - 4.16676 + 0.9188\ln(T_1)) \cdot \left(\frac{0.45537 - 0.1339(\ln(T_1) + \ln(T_2)) + 0.04115\ln(T_1)\ln(T_2)}{0.4851 - 0.2678\ln(T_1) + 0.04115\ln(T_1)^2}\right)$$

$$\sigma_{2|1}^2 = 0.4851 - 0.2678\ln(T_2) + 0.04115\ln(T_2)^2 - \left(\frac{(0.45537 - 0.1339(\ln(T_1) + \ln(T_2)) + 0.04115\ln(T_1)\ln(T_2))^2}{0.4851 - 0.2678\ln(T_1) + 0.04115\ln(T_1)^2}\right)$$