Umbilical artery (UA) Doppler indices are surrogate measures of placental function, most commonly used to assess fetal wellbeing in pregnancies with fetal growth restriction. Fetuses with trisomy 21 (t21) are reported to have elevated UA Doppler indices, but reference percentiles are currently lacking for this population. We hypothesized that gestational age-specific values of UA Doppler indices in pregnancies complicated by t21 will be elevated compared to established percentiles based on euploid pregnancies. We aimed to assess UA Doppler indices longitudinally in fetuses with t21 in order to demonstrate Doppler patterns across gestation in this population, compare them with euploid fetuses, and investigate their association with pregnancy outcomes.

Methods: We conducted a retrospective cohort study of singleton pregnancies with confirmed fetal t21 who underwent UA Doppler surveillance antenatally from January 2012 to August 2019. UA Doppler indices, including systolic/diastolic (S/D) ratio, pulsatility index (PI), and resistance index (RI) were extracted from ultrasound reports or directly from ultrasound images. UA S/D, PI, and RI percentiles by gestational week were created from available observations from our cohort via a data-driven approach using a generalized additive model. A secondary analysis was run to statistically compare t21 values to established percentiles based on observations from a historical population of euploid fetuses.

Results: UA Doppler measurements from 86 t21 fetuses and 130 euploid fetuses were included in our analysis. Median (IQR) maternal age in t21 pregnancies and euploid pregnancies were 35 years (29-38) and 30 years (27-33), respectively. As in euploid fetuses, we found a negative association between Doppler indices and gestational age in the t21 fetuses. Maternal tobacco use, obesity, or chronic hypertension had no significant effect on UA Doppler indices. As hypothesized, values for UA S/D ratio, PI, and RI at the 2.5th, 5th, 10th, 25th, 50th, 75th, 90th, 95th, and 97.5th percentiles by gestational week were significantly higher in t21 fetuses compared to euploid fetuses ($p<.001$). Overall, 55.8% (48/86) of the t21 fetuses demonstrated at least one Doppler value above the 95th percentile for gestational age based on euploid reference standard. At birth, eight (9.3%) of the t21 fetuses were small for gestational age. When these pregnancies were removed from analysis, UA Doppler indices remained significantly higher than established percentiles at each week of gestation ($p < .001$). Only three pregnancies ended in fetal demise in the t21 population, two of which had persistently elevated Dopplers above the 95th percentile per established reference percentiles.

Conclusions: At each week of gestation, UA Doppler indices in t21 fetuses were significantly higher than established percentiles from a euploid population. Reference intervals based on euploid fetuses may therefore not be appropriate for antenatal surveillance of fetuses with t21. Prospective studies are needed to investigate the role and impact of serial UA Doppler velocimetry in the surveillance of pregnancies complicated by fetal t21 [1)]

Overexpression of circ-ARFIP2 in human umbilical artery smooth muscle cells (HUASMCs) showed a significant promotion in cell proliferation, migration and invasion. Mechanistically, circ-ARFIP2 targeted miR-338-3p, and circ-ARFIP2 regulated cell behaviors by miR-338-3p. KDR was a direct and functional target of miR-338-3p. Moreover, KDR was a downstream effector of circ-ARFIP2 function. Circ-ARFIP2 regulated KDR expression by targeting miR-338-3p.The findings demonstrated that the increased level of circ-ARFIP2 enhanced HUASMC proliferation, migration and invasion at least in part by the miR-338-3p/KDR axis [2)].

1)
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2)
Qin K, Tian G, Zhou D, Chen G. Circular RNA circ-ARFIP2 regulates proliferation, migration and invasion in human vascular smooth muscle cells via miR-338-3p-dependent modulation of KDR. Metab Brain Dis. 2021 Apr 10. doi: 10.1007/s11011-021-00726-3. Epub ahead of print. PMID: 33837886.