SHORT FEMUR LENGTH
FOR EFW WORKING GROUP - NOV 2019
Background

- FL is only routine long bone measurement
  - Many scanning guidelines recommend the systematic documentation of the presence and symmetry of all extremities

- Considerations short FL in mid-second trimester
  - Normal variant greater majority (~ two-thirds)
  - Significant FPR up to 13% noted on re-measurement
  - Fetal growth restriction
  - Aneuploidy, Skeletal Dysplasia
  - Other
Hypothesis: Why Short FL in mid trimester?

- Etiologies are likely multifactorial

- Some Hypothesis include:
  - Early adaptive response to chronic hypoxia and placental dysfunction
  - Disorder of vascular origin such as pregnancy induced hypertension or pre-eclampsia
  - Alteration in secretion of growth factors
  - FGF (fibroblast growth factor) receptor may be altered
Define short FL

- **Short FL**
  - Definition is below the 5th percentile which roughly corresponds to below the -2SD
  - Prospective Danish population study, the 5th percentile corresponded to the mean minus 1.645 SD, led authors to suggest that cutoff value closer to -2 SD instead of the 5th percentile should be considered to minimize overdiagnosis
    - Isolated short FL at the 2nd mid-trimester anatomic scan associated with a higher risk of chromosomal anomalies, in particular trisomy 21, and a higher risk for delivery of a small for gestational age infant and early preterm delivery

- **Markedly shortened FL**
  - In Kurtz et al a markedly short FL (≥5 mm below the -2 SD line [equivalent to >-4.3 SD]) was associated with a high likelihood of a skeletal dysplasia, whereas a mildly shortened FL (within 4 mm of the -2 SD line [between -2 and -4 SD below the mean]) in combination with normal interval growth was unlikely to be associated with skeletal dysplasia

Short FL – Non-Isolated

- Literature is limited to retrospective studies
- Isolated short FL is associated with FGR
  - 40% Papageorghiou, 2008
    - Details: <5th percentile, Severe IUGR defined as AC < 5th percentile with abnormal UA Doppler requiring delivery before 37wk
    - High risk severe IUGR requiring PTB accompanied by PET in 1/3
    - Short FL and association of aneuploidy depend on prevalence, thus this population which had all NT found no isolated cases with T21
    - Non-isolated short FL were 1/3 of this group
  - 39% Todros 2004
    - Details: < 10%ile, retrospective 86 cases with overall 32.5% normal, 46.5% structural abnormality, 21% SGA
  - 43% Vermeer 2013
    - Details: < 5th percentile, 112 cases with 78% isolated short FL
    - Non-isolated 6 aneuploidy, 12 MFA, 1 genetic
    - Isolated 43% IUGR with LR 1.2
Isolated Short Femur


- Singleton pregnancies 18-28 weeks with isolated short FL <5th percentile
- 6 retrospective studies, total 3078 cases, control of 222,303 (normal FL)
  - 14.2% IUGR or SGA prevalence vs 5.2% controls, odds ratio ~ 4x
    - 438/3078
- Higher incidence low BW 22.10% vs control group: 8.57%, odds ratio 3.24
- Higher incidence of low APGAR, fetal demise, NICU admission, neonatal death

Conclude:
- Significant association short FL, IUGR, SGA & adverse perinatal outcome
- Conservative counsel as 61% normal outcome
  - Consider closer monitor maternal BP, increase fetal surveillance
  - If placental dysfunction Doppler may aid distinguish “inherent short FL” vs at risk group
  - Need larger prospective trials
    - Limitations: sample size study group 1.4%; although same definition short FL used different biometric charts
    - Could not exclude entirely other reasons for referral
Next Steps:

- Review maternal/parental history, serum tests & markers FGR
- Re-measure to confirm short FL (13% FPR)
- Measure all long bones
- Define pattern over time (3-4 weeks)
  - Normal interim growth albeit along line below normal percentiles but along same growth curve may be constitutional
  - If FL over this interval falls further from the mean, consider severe FGR or skeletal dysplasia
  - Mildly shortened femur is between -2D and -4SD below mean for GA
  - Markedly shortened femur is > 4 SD below mean for GA higher association with skeletal dysplasia

Consider referral to center with expertise

Conclusions: Isolated short FL at time mid-second trimester study

- Associated with an increased risk SGA, IUGR, adverse perinatal outcome in the range of 3-4x

- Consider increased surveillance for maternal hypertension and fetus well being

- Need larger prospective trials to refine our algorithms and management protocols
An Algorithmic Approach to the Initiation of a Prenatal Evaluation of a Short FL

- Positive Family History
- Normal Femur Length
- Serial Measurements
- Abnormal Femur Length or Appearance
  - Normal physiological variant (FP 13%)
  - IUGR
  - Abnormal Karyotype
  - Focal Skeletal Abnormality
  - Skeletal Dysplasia

If FL is < 5 mm below the -2 SD of the mean (-4SD):
- HIGH LIKELIHOOD OF A SKELETAL DYSPLASIA

If the FL is 2 to 4 mm below the -2 SD of the mean:
- RE-ASSESS IN 3-4 WEEKS

NORMAL INTERVAL GROWTH
- Expect 2.5 – 2.7 mm per week of growth 16 – 22 weeks
- Unlikely to be skeletal dysplasia

FURTHER DEVIATION BY > 1 SD
- Concern for skeletal dysplasia
- Concern for severe IUGR
Please address questions and/or referrals pertaining to potential fetal skeletal dysplasia to phyllis.glanc@sunnybrook.ca