Ultrasound schedule and imaging protocol for Monochorionic multiple pregnancies

Purpose:
To provide a standardized imaging protocol and examination schedule for both *complex* and *uncomplicated* monochorionic multiple pregnancies referred to the BC Women's main ultrasound department.

This document also more specifically addresses screening for spontaneous TAPS (sTAPS) in monochorionic twin pregnancies, as there is no current standard approach at our centre.

Site Applicability:
This protocol applies to inpatient and outpatient ultrasound examinations performed through BC Women's main ultrasound department.

Principles:
Monochorionic (MC) multiple pregnancies are susceptible to a subset of specific complications detectable through increased ultrasound surveillance including twin-twin transfusion syndrome (TTTS), selective intrauterine growth restriction (sIUGR) and twin anemia polycythemia sequence (TAPS). This protocol aims to standardize ultrasound screening in MCDA twins with the intent of optimizing outcomes. Triplet or higher order pregnancies involving 2 or 3 monochorionic fetuses should be referred to MFM.

What is unchanged?
- Schedule for serial biometry, amniotic fluid volume, soft markers, anatomical details (including extended heart views) and cervical length screening for uncomplicated MCDAtwin pregnancies.

What is new?
- Routine serial assessment of umbilical artery (UA) Doppler in all MCDA twins starting at 16 weeks
- TAPS screening is now included at the time of biometry, as below:
    - Routine inclusion of MCA PSV and DV Doppler for:
        - "Complex monochorionic twins": Starting at time of diagnosis of complex twins (16 weeks GA or later)
        - "Uncomplicated twins": Starting at 30 weeks GA
    - Routine inclusion of ultrasound markers of advanced TAPS in all MCDA twin pregnancies starting at 16 weeks GA. Assessing for the presence of:
        - Placental dichotomy
        - Cardiomegaly, hydrops
        - Starry sky liver

- <u>Complex MCDA twin pregnancy definition</u>
  MCDA twin pregnancy ≥16+0 weeks and any of the following:
    - IUGR of one or both twins (as defined as either AC or EFW <10th %ile)
    - EFW discordance between twins >20%
    - AEDF or REDF in the UA of either twin
    - TTTS, any stage
    - Amniotic fluid DVP discordance between twins with:
        - GA 16-19+6 weeks: >4cm absolute difference between DVPs
        - GA 20+0 weeks and up: >6cm absolute difference between DVPs

MCDA Twins BCW Imaging protocol & schedule

ALL MCDA TWINS					Complex MCDA + All MCDA ≥30+0	
GA +/- 1 week	**Fetal Anatomy & biometry**	**Screening for TTTS, sIUGR and advanced sTAPS**	**Placenta**	**Cervix length**	**MCA PSV**	**DV**
11-14	• First trimester routine • NT		• Location • Chorionicity	TA	-	-
16, 18	• Biometry • Soft markers assessment	• DVP • Fetal bladder • UA Doppler • Cineclips: -Fetal heart -Fetal liver -Placental sweep	• Location • Chorionicity • Placental cord inserts	EV*	**Complex MCDA twins:** MCA PSV in both twins q2 weeks with biometry	Both twins *at each exam* when: - IUGR or sIUGR with AEDF - Stage 1 TTTS or > - TAPS suspected (stage 0) or confirmed (stage 1-4)
20,22,24	• Biometry • Routine details & extended heart views completed					
26,28	• Biometry			TA		
30,32	• Biometry • Repeat details				**All MCDA twins:** MCA PSV in both twins q2 weeks *with biometry*	
34,36	• Biometry			Not required		

*Cervical length screening: Baseline EV cervical length routinely obtained at 16 weeks **and** 20 weeks. For interim scans <24+0, do EV scan each time unless cervix well seen on TA imaging **and** previous EV length was >3.5cm

APPENDIX 1:

Screening for TAPS: Rationale and explanatory notes

a) What is TAPS?

Twin anemia polycythemia sequence (TAPS) is a recently described complication specific to monochorionic twin pregnancies. TAPS occurs as the result of a chronic unbalanced feto-fetal transfusion from the donor to the recipient twin through minuscule placental anastomoses. This leads to anemia in the donor and polycythemia in the recipient with highly discordant hemoglobin levels at birth (80 g/L or greater)[1]. Unlike TTTS, TAPS occurs in the absence of amniotic fluid discordance.

Both spontaneous and post-laser TAPS are associated with an increased risk of perinatal morbidity and mortality. Data from the international "Twin anemia polycythemia sequence registry"[2] reports a 15% perinatal mortality rate (22% in donors versus 7% in recipients). Severe neonatal morbidity is reported in 33% of cases, with the highest rates in cases with an advanced TAPS stage and a low gestational age at birth.

b) How common is TAPS?

TAPS is most commonly identified following laser surgery for TTTS. The reported incidence of post-laser TAPS (plTAPS) ranges between 2-16%, largely depending on the laser technique utilized[3]. Spontaneous TAPS (sTAPS) has been reported postnatally in approximately 2-5% of monochorionic twin pregnancies[4,5].

Antenatally, the incidence of sTAPS is uncertain because of the following gaps in the literature:

1. There is inconsistent screening practice.
2. Prevalence is estimated based on retrospective case series from referral centres for complex MCDA twins.
3. Prenatal diagnostic criteria for TAPS have evolved over the past 10 years such that antenatally identified cases in earlier literature may not meet contemporary diagnostic criteria[6].

c) How is TAPS diagnosed?

The prenatal diagnosis of TAPS is based on a discrepancy in MCA PSV between donor (presumed anemic) and recipient (presumed polycythemic) twins. Postnatally, the diagnosis is confirmed and based on a difference of hemoglobin between the twins of at least 80 g/L[7]. Antenatally, TAPS can be diagnosed as early at 15 weeks GA and as late as 35 weeks GA with a mean GA at diagnosis of nearly 24 weeks GA[2].

The antenatal diagnosis of TAPS on the basis of MCA PSV alone is limited because:

- MCA PSV is only validated for the detection of severe anemia in singletons (with false positive rates of 12% in the second/early third trimester, and as high as 40% after 34 weeks)[8,9]. PSV is affected by a range of physiologic parameters. MCA PSV has been less studied in TAPS, which comes with its own distinct physiology which could affect the test's performance.
- Low MCA PSV has limited sensitivity in predicting polycythemia[10].

- Evaluation of the diagnostic performance of MCA PSV at early gestational ages is limited by the paucity of data correlating fetal hemoglobin levels with MCA PSV. The gold standard of fetal hemoglobin is not typically available to verify the diagnosis at early GAs when selective feticide is performed, prior to or following fetal laser surgery, or with expectant management. Because of this, sensitivity, specificity, positive and negative predictive values at GA <28 weeks cannot be calculated[11].
- Where data is available, correlation between prenatal and postnatal diagnosis of TAPS is imperfect, with an estimated antenatal diagnosis false positive rate of 17%[6,11,12].

Several thresholds for diagnostic criteria have been proposed for the diagnosis of TAPS. A conservative approach to diagnosis is favored here given the limited evidence guiding best management of pregnancies complicated by TAPS. BCW MFM has opted to adhere to the 2020 Delphi consensus diagnostic criteria[13] as in a comparative study, these criteria were more specific and identified twin pairs more likely to benefit from antenatal intervention (early delivery or other) compared to other proposed criteria, without significant impact on neonatal outcomes[14].

In addition, based on the false positive rate of MCA PSV[13,14] for the detection of anemia in singletons, two consecutive positive MCA measurements are required, within 1-2 weeks of each other, for the diagnosis of TAPS Stage 1.

d) When and who should we screen for TAPS?

Currently, there is no widely accepted screening protocol for TAPS. Much of the existing TAPS literature has been published over the last 5 years and many questions remain to be answered with respect to its diagnosis and management. The latest SOGC[15] and SMFM[16] Guidelines have not made recommendations with respect to screening for TAPS. The 2016 ISUOG Guideline recommends universal routine screening for TAPS in all monochorionic twin pregnancies starting at 20 weeks. This recommendation is not widely endorsed, mainly due to gaps in the literature with respect to diagnosis and the potential for unnecessary intervention and associated morbidity. The 2016 Green Top Guideline[18] proposes screening for TAPS in higher risk, complex monochorionic twin pregnancies, which are typically referred to tertiary care centres for simultaneous monitoring of all MCDA complications.

Given the current limitations of the literature, and limited access to specialized obstetrical ultrasound related to geographical distribution in our province, a pragmatic approach to the surveillance of MCDA twins, with cautious interpretation of results, is advisable. In an attempt to optimize diagnostic accuracy, the following approach is proposed, starting at 16 weeks GA:

(i) MFM referral for all complex MCDA twins: Screening for sTAPS by MCA PSV and signs of advanced TAPS *every 2 weeks (at the time of biometry assessment)*

(ii) ALL MCDA twins: Universal screening for ultrasound signs of advanced stage TAPS (cardiomegaly, hydrops, placental dichotomy, starry sky appearance of fetal liver) *every 2 weeks (at the time of biometry assessment)*. Approximately 86% of cases advanced TAPS will present with at least one of these ultrasound signs[19] (Appendix 2)

(iii) ALL MCDA twins ≥30+0 weeks GA: Universal screening for sTAPS by MCA PSV *every 2 weeks (at the time of biometry assessment)* as:

i. Screening for signs of advanced TAPS can be difficult at advanced gestational ages (for example when the placenta is posterior)
ii. The negative effects of a potential iatrogenic preterm delivery based on a false negative result becomes less significant

TAPS Staging

Two consecutive positive MCA measurements meeting TAPS criteria are recommended <u>within 1-2 weeks of each other</u> for confirming a diagnosis of TAPS due to the significant false positive rate of MCA PSV[5].

TAPS Stage*	Criteria
0 (TAPS suspected)	Single/ first measurement of discordant MCA PSV meeting diagnostic criteria: • Combination of "donor" twin: **MCA-PSV ≥1.5MoM** and "recipient" twin **MCA-PSV ≤0.8MoM *or*** • **PSV discordance of ≥1.0 MoM** AND • No other signs of fetal compromise
1	Two consecutive MCA PSV MoM measurements meeting TAPS diagnostic criteria above, obtained within a 1 – 2 week period: AND No other signs of fetal compromise
2	MCA PSV donor >1.7MoM and MCA-PSV recipient <0.8 MoM AND No other signs of fetal compromise
3	As for stage 1 or 2, with cardiac compromise of donor, defined as a critically abnormal Doppler flow (UA AEDF/REDF; pulsatile umbilical venous flow, absent or reversed "a" wave in DV)
4	Hydrops of donor
5	IUFD of one or both twins preceded by TAPS

*Modified Shlageke staging[7] based on inclusion of Delphi 2020 definition of diagnosis for Stage 1 TAPS

e) What to do when TAPS is suspected or diagnosed?

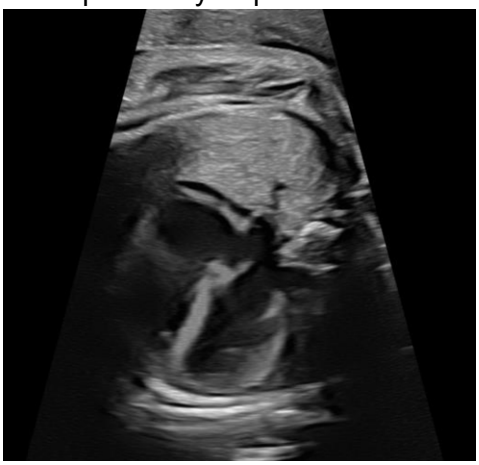
Gestational age, stage of disease and the presence of coexisting MCDA complications are some of the important considerations when considering plans for management of sTAPS. While complications of advanced TAPS include neonatal death, ischemic limb loss, cerebellar disruption and overall perinatal morbidity, more data is required to demonstrate that intrauterine interventions improve outcomes, including the results of an ongoing randomized clinical trial[20,21].

When prenatal diagnosis of TAPS is suspected, a referral to MFM is indicated for consideration of possible management options on a case by case basis, taking into account the presence of other ultrasonographic signs of TAPS[19].

APPENDIX 2: Explanatory notes on additional ultrasound markers for TAPS screening:

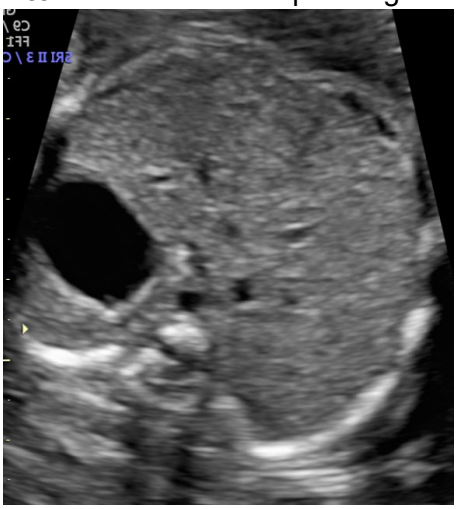
Additional views to assess for the presence of placental dichotomy, fetal cardiomegaly and/or the presence of a starry-sky liver may help improve antenatal detection of sTAPS for all MCDA twins. Views are to be added to the routine biometry scan, starting at 16 weeks GA:

1. **4 chamber cineclip:**
    a. **Rationale**: donor and recipient twins of TAPS or TTTS may demonstrate evidence of cardiac dysfunction that may be evident on a 2D 4 chamber cineclip.
    b. **How to**: Best attempt to include the entire fetal chest to assess for cardiomegaly, contractility and the presence of pericardial effusion at the level of the 4 chamber view. Details of the 4 chamber image are not required to be optimal other than at time of at 20-22 weeks and 28-30 weeks exams or when specifically requested

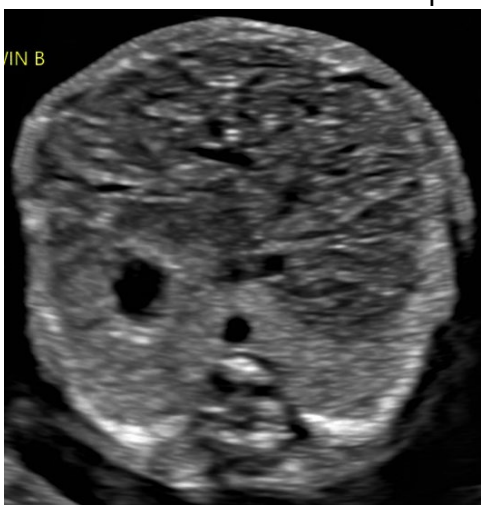


Cardiomegaly and pericardial effusion in TAPS donor twin

2. **Fetal liver cineclip:**
    a. **Rationale**: liver of the polycythemic twin may have a "starry sky appearance". This would be supportive of the diagnosis in cases of TAPS
    b. **How to**: obtain slow sweep through fetal upper abdomen scan in coronal or axial plane



A. Normal appearance of fetal liver

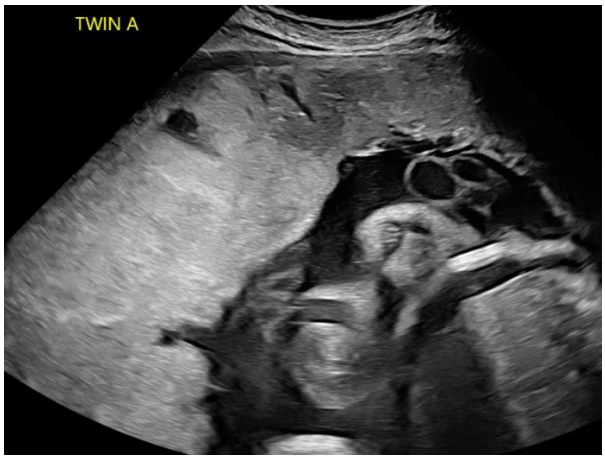


B. Starry sky liver: Clearly identified portal venules (stars) and diminished parenchymal echogenicity (sky)

3. Placental sweep:

a. **Rationale**: Pregnancies affected by sTAPS may demonstrate a "2-tone placenta", referred to as "placental dichotomy", with the anemic twin's part of the placenta being thick and echogenic and the polycythemic twin's being thinner and hypoechoic

b. **How to**: obtain one or more sweeps through the entire placenta focussing on placental thickness and echogenicity.



Placental dichotomy:
Hyperechogenic, thick and hydropic placental share for the donor twin seen to the right of the image and thinner, hypoechoic placental share for the recipient twin identified towards the left

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Definitions

AEDF:	absent end diastolic flow	PI:	pulsatility index
DV:	ductus venosus	plTAPS:	post-laser TAPS
DVP:	deepest vertical pocket	PSV:	peak systolic velocity
EV:	endovaginal	REDF:	reversed end diastolic flow
GA:	gestational age	sIUGR:	selective IUGR
IUFD:	intrauterine fetal death	sTAPS:	spontaneous TAPS
IUGR:	intrauterine growth restriction	TA:	transabdominal
MC:	monochorionic	TAPS:	twin anemia polycythemia sequence
MCA:	middle cerebral artery	TTTS:	twin-twin transfusion syndrome
MCDA:	monochorionic diaminiotic twin gestation	UA:	umbilical artery
		US:	ultrasound

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