Peer Review File

Article information: http://dx.doi.org/10.21037/tp-20-264.

Reviewer A

Comments to the authors:

Just a couple comments to the author from this reviewer;

Comment 1: Line 160: "Serial assessment of cardiac function provides an additional tool to monitor TTTs". This is a vague recommendation. The author noted in the sentence before this one that there is not a standard for assessing fetal heart in TTTS cases (pre or postlaser). Would suggest that a more specific appropriate recommendation would be echocardiography, fetal (pre and postlaser) and possibly neonatal pending the fetal finidngs due to the increased risk of developmental cardiac malformations (as the author has pointed out).

Reply 1: This sentence has been modified to be more specific as suggested.

Therefore, fetal echocardiogram is recommended before and after laser surgery to monitor for disease resolution and identify fetuses with persistent cardiac disease that require neonatal echocardiogram and follow up.

Comment 2: TAPS section: The author did not address management of TAPS, which include expectant observation, selective reduction, pregnancy termination, laser, in utero transfusion (with partial exchange transfusion) and early delivery). Results of the interventions have been mixed. There is presently a randomized trial comparing laser to alternative techinques May want to consider adding this, or something similar

Reply 2: The management section was updated to reflect inclusion of TAPS and a statement about the management of TAPS was added to the end of the section.

Management options for TAPS similarly include observation, fetoscopic laser ablation, selective fetal reduction, intrauterine transfusion with or without partial exchange transfusion, termination of pregnancy or early delivery. There is an ongoing international multi-center randomized trial to investigate whether treatment with fetoscopic laser surgery improves outcomes compared to the alternative treatments (ClinicalTrials.gov Identifier: NCT04432168).

Comment 3: Line 223-225: The wording is confusion, aser "intersection point as well as chorionic plate…." The author is describing "solemnization, or clinically dichorionizing the placental surface:

Also, the "85%" is incorrect for double survival rate. That would be the survival rate for "at least one". Double survival rate in the referenced paper is 65%

Reply 3: The sentence has been restructured and statistic updated.

A 400-600µm laser fiber is advanced through the operative channel of the fetoscope and the vessels are coagulated at the site of the anastomosis. The chorionic plate is also coagulated between each vascular anastomosis along the vascular equator (Figure 2). This technique is termed equatorial dichorionization and leads to the highest reported rates of double twin survival of up to 65% (64),

Comment 4: Lines 231-235: Risk of PPROM following laser is 30% (Beck V et al Fetal Diagnosis and Therapy, 2012, 31(1):1-9. This should be added.

Reply 4: The challenge with listing a discrete statistic for the risk for PPROM following laser surgery is that is reported and defined variably among publications and increases with gestational age. The 30% rate in the Beck article includes cases of TTTS, LUTO and TRAP. The three references included all report PPROM by 34 weeks so the highest rate was added to the text for context.

Comment 5: Line 240: add "appears to be" after "26 weeks". The referenced papers are small single center reports. To say "comparable"

Reply 5: This comment seems to be related to line 250 so the language was adjusted as suggested.

However, outcomes for TTTS cases treated before and after 26 weeks appear to be comparable with no differences in duration of surgery, complication rate or delivery timing observed (79,80).

Comment 6: Lines 265: Change "10%" to "15"

Reply 6: This change was made.

Comment 7: Lines 266: Delete “10%”

Reply 7: This change was made.

Comment 8: Remove reference 83. This is a case report that really provides little support for the points the author is making in this section.

Reply 8: This reference is removed.

Reviewer B
Comments to the authors:
Excellent review article.
Some minor points:

Comment 9: Line 75 – comma needed after “cord”

Reply 9: This comma was added.

Comment 10: Line 82 – I don’t think I have ever heard anyone use the phrase “third circulation”

Reply 10: This term is historical but used to help conceptualize that region of the placenta for the readership that may not have a strong foundation of the complexity of the monochorionic placenta.

Comment 11: Line 96 – remove “the” before twin. Twin to twin transfusion syndrome does not require capitalization.

Reply 11: This change was made.

Comment 12: Line 132 – Most centers now use >8 at <20 weeks and >10 at 20 weeks and above.

Reply 12: Recognizing these thresholds are used more contemporarily, particularly among the European centers and to guide intervention, the standard definition for TTTS is used for this review.

Comment 13: Line 204 – regression is actually even more common than that: Ultrasound Obstet Gynecol 2007; 30: 958–964. Stage I twin–twin transfusion syndrome: rates of progression and regression in relation to outcome. K. O'DONOGHUE, E. CARTWRIGHT, P. GALEA and N. M. FISK

Reply 13: This reference is cited (53). The challenge in this reference is the stage 1 cases that spontaneously regressed is not clear. Although 32/46 cases are categorized as either remaining stable or regressed, 18 (39%) had treatment on the first visit of some sort and ultimately 31 (67%) had an amnioreduction. Since these were not really expectantly managed cases this reference likely overestimates the likelihood of stability or regression. The sentence has been restructured to clarify what is known for purely expectant managed cases.

Although stage I disease may remain stable or regress in up to 30 % of expectantly managed cases, progression, fetal demise, or previable birth may occur (52,53).

Comment 14: Line 224 – This dichorionization is most commonly referred to as "Solomonization" Slaghekke F, Lewi L, Middeldorp JM, et al. Residual anastomoses in twin-twin transfusion syndrome after laser: the Solomon randomized trial. Am J Obstet Gynecol 2014;211:285.e1-7.

Reply 14: This sentence is simplified to only refer to the technique as the Solomon technique. This one of the references cited in this sentence.

This is termed the "Solomon technique" and leads to the highest reported rates of double twin survival of up to 65% (64), while also minimizing the risk for residual anastomoses,(65) recurrence or development of post-laser TAPS to <5% (66,67).

Comment 15: Line 265 – another good reference: Ong S, Zamora J, Khan K, Kilby M. Prognosis for the co-twin following single-twin death: a systematic review. BJOG 2006;113: 992–998.

Reply 15: This reference was substituted for reference 83 and also cited in reference 84.