Consensus definition and essential reporting parameters of selective fetal growth restriction in twin pregnancy: a Delphi procedure

Asma Khalil[1], Irene Beune[2], Kurt Hecher[3], Klaske Wynia[4], Wessel Ganzevoort[5], Keith Reed[6], Liesbeth Lewi[7], Dick Oepkes[8], Eduardo Gratacos[9], Basky Thilaganathan[1], Sanne J Gordijn[2]

[1]Fetal Medicine Unit, St George's Hospital, St George's University of London, Cranmer Terrace, London SW17 0RE, United Kingdom
[2]Department of Obstetrics and Gynecology, University Medical Center Groningen, University of Groningen, Groningen, Netherlands
[3] Department of Obstetrics and Fetal Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
[4]Department of Health Sciences, Community and Occupational Medicine, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands
[5]Department of Obstetrics and Gynecology, Academic Medical Center Amsterdam, University of Amsterdam, Amsterdam, Netherlands.
[6] Twin and Multiple Births Association (TAMBA), UK
[7]Department of Obstetrics and Gynaecology, University Hospitals Leuven; Department of Development and Regeneration, KULeuven, Belgium
[8] Division of Fetal Medicine, Department of Obstetrics, Leiden University Medical Center, Leiden,The Netherlands
[9] Fetal Medicine Units and Departments of Obstetrics, Hospital Clinic-IDIBAPS, University of Barcelona, Barcelona, Spain

Corresponding author:
Professor Asma Khalil
Fetal Maternal Medicine Unit
St George's University of London
London SW17 0RE
E-mail: akhalil@sgul.ac.uk; asmakhalil79@googlemail.com

Short title: Definition sFGR twins

Key words: selective fetal growth restriction, sFGR, sIUGR, twin, multiple pregnancy

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/uog.19013

ABSTRACT

Objectives: Twin pregnancies complicated by selective fetal growth restriction (sFGR) are associated with increased perinatal mortality and morbidity. Inconsistences in the diagnostic criteria for sFGR employed in existing studies hinder the ability to compare or combine their findings. It is therefore challenging to establish robust evidence-based management or monitoring pathways for these pregnancies. The main aim of this study was to determine, by expert consensus using a Delphi procedure, the key diagnostic features of and the essential reporting parameters in sFGR.

Methods: A Delphi process was conducted among an international panel of experts in sFGR in twin pregnancy. Panel members were provided with a list of literature-based parameters for diagnosing sFGR and were asked to rate their importance on a 5-point Likert scale. Parameters were described as solitary parameters (sufficient to diagnose sFGR, even if all other parameters are normal) and contributory parameters (those that require other abnormal parameter(s) to be present for the diagnosis of sFGR). Consensus was sought to determine the cut-off values for accepted parameters, as well as parameters used in the monitoring, management and assessment of the outcome of twin pregnancies complicated by sFGR. The questions were presented in two separate categories according to chorionicity.

Results: A total of 72 experts were approached, of whom 60 agreed to participate and entered the first round; 48 (80%) completed all four rounds. For sFGR irrespective of chorionicity, one solitary parameter (estimated fetal weight (EFW) of one of the twins less than the third centile) was agreed. For monochorionic (MC) twin pregnancy at least two out of four contributory parameters (EFW less than the 10th centile of one of the twins, abdominal circumference (AC) of one twin less than the 10th centile, EFW discordance of 25% or more, and umbilical artery (UA) pulsatility index (PI) of the smaller twin above the 95th centile) were agreed. For sFGR in dichorionic (DC) twin pregnancy, at least two out of three contributory parameters (EFW of one twin less than the 10th centile, EFW discordance of 25% or more, and UA PI of the smaller twin above the 95th centile) were agreed.

Conclusion: Consensus-based diagnostic features of sFGR in both MC and DC twin pregnancies, as well as cut-off values for the parameters involved, were agreed upon by a panel of experts. Future studies are needed to validate these diagnostic features before they can be used in clinical trials of interventions.

INTRODUCTION

Twin pregnancies complicated by selective fetal growth restriction (sFGR) are at increased risk of perinatal mortality and morbidity.[1] Inconsistences amongst clinicians and researchers with regards to the diagnostic criteria used for the definition of sFGR make the prevalence of this condition difficult to determine. Some studies define sFGR as one twin with estimated fetal weight (EFW) or abdominal circumference (AC) less than the 10th centile, while others use EFW/AC discordance between the twins of more than 20% or 25%.[2-8] While the incidence of sFGR is estimated as 10-15% of twin pregnancies,[9] this incidence is likely to vary according to whether the diagnostic criteria rely only on the EFW/AC of one twin or also incorporate inter-twin discordance. If the latter is the case, the incidence is also likely to vary according to the inter-twin EFW discordance threshold used.

The recent International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) guidance defines sFGR in a dichorionic (DC) twin pregnancy as a condition in which the EFW of one twin is less than the 10th centile, while in a monochorionic (MC) twin pregnancy the definition requires this criterion plus an inter-twin EFW discordance greater than 25%.[10] It seemed acceptable to use different diagnostic criteria for the same condition in DC and MC twin pregnancies, as the pathology leading to sFGR differs according to the type of twin pregnancy. DC twin pregnancies complicated by sFGR have conventionally been managed as for FGR in a singleton pregnancy, but the recent evidence questions this approach.[8] In MC twin pregnancies, sFGR is thought to result mainly from an unequal placental share.[11]

These inconsistencies in the literature with regards to the diagnostic criteria for sFGR make it impossible to compare the findings of existing studies, to combine their results, or to establish robust evidence-based management or monitoring pathways. Recently, a consensus definition of FGR in singletons, derived using the Delphi methodology, has been published.[12] However, there currently exists no gold standard definition for sFGR in a twin pregnancy. In order to attempt to improve the outcomes of these pregnancies, it is imperative that researchers and clinicians first agree a standard definition. The main aim of this study was to reach expert consensus on a definition of sFGR and essential reporting parameters in DC and MC twin pregnancies, using a Delphi methodology. We also attempted to reach expert consensus on the parameters involved in the monitoring and management of these pregnancies, and those representing the key pregnancy outcomes.

METHODS

We used the Delphi methodology, which is based on the scoring of a series of structured statements that are revised, fed back to the participants and repeated in multiple rounds, in increasing detail, until consensus has been reached.[13] This procedure aims at refining the opinions of participating experts, while minimizing confounding factors present in other group response methods.[14] The rationale for using the Delphi procedure is that it is a well-established instrument to reach consensus from a panel of experts for research questions that cannot be answered with empirical evidence and complete certainty.[15] We identified panel members based on their publication record as lead or senior authors in studies of sFGR or twin pregnancies, or by suggestion of confirmed panel members. When inviting panel members, we specifically sought wide geographic representation in order to ensure generalizability of the consensus definitions. The votes of all panel members are weighed equally within the Delphi process. Experts who did not complete a particular round were not invited for subsequent rounds. The results were reported according to the guidelines for reporting reliability and agreement studies (GRRAS).[16]

Data collection

Data were collected in four consecutive rounds by online questionnaires that were presented to panelists through a unique token-secured link for each round. Responses were captured in Limesurvey version 2.50. Non-responders received reminder emails after two and four weeks, and were excluded from subsequent survey rounds if no response was obtained. Each round included the option of offering additional items or suggestions, as well as withdrawal of items from the procedure. Newly suggested items were categorized and carefully considered by the panel for their applicability in this procedure. Details were collected regarding the countries where the experts practise, self-reported expertise, the invasive procedures they perform and the yearly average number of DC and MC twins delivering at their hospitals/institutions. The questions were presented in two separate categories according to chorionicity (DC and MC twins).

First round

Based on a literature review, parameters that could potentially be included in the definition, monitoring, management and assessment of pregnancy outcomes were presented to the panel for agreement. They were also given the opportunity to suggest additional parameters that they considered relevant. In MC twins, some of the included parameters were not specific for the diagnosis of sFGR, but reflect the possible need to exclude other pathologies, such as twin to twin transfusion syndrome (TTTS), as a cause of growth differences. The panel was asked to rate the literature-based parameters for sFGR on a 5-point Likert-scale (1 = very unimportant, 2 = unimportant, 3 = neutral, 4 = important, 5= extremely important). The predefined cut-off for inclusion of parameters in the consensus-based definition for sFGR was a median score of 5 on the Likert-scale.

Second and third rounds

In the second round, accepted and newly recommended items from Round one were presented to the panel with the answer options ‘yes’ or ‘no’. Items that in Round 1 had scored the predefined cut-off of a median Likert score of 5 were considered as inclusions and presented to the panel for verification for inclusion, while items with a median score of 4 were presented to verify exclusion. Items with a median score of 3 or lower were considered

rejected and verification of rejection was requested. A predefined cut-off level of 70% agreement was used to define consensus for these questions. In the third round, parameters that fell within a 60-70% agreement range were presented to the panel for re-consideration.

In the third round, parameters with a median score of 5 were presented to define whether the parameter should be a solitary and/or a contributory parameter. A solitary parameter was defined one sufficient to diagnose sFGR, even if all other parameters are normal. A contributory parameter was defined as one that would require other abnormal parameter(s) to be present to diagnose sFGR. Furthermore, the panel was asked to specify cut-off values for each parameter. The proposed cut-off values were literature based. Experts were also asked to determine these cut-offs for solitary or contributory parameters separately, as these thresholds could potentially differ.

Final round

Possible algorithms to define sFGR were presented to the panel to determine how many contributory parameters were essential for the diagnosis of sFGR in either MC or DC twin pregnancies.

RESULTS

We invited 72 publishing experts to join this Delphi procedure. In the first round an expert panel of 60 participants joined, of whom 48 completed the entire Delphi procedure. Response rates in the following rounds were 92% (55/60) in Round 2, 87% (48/55) in Round 3 and 100% (48/48) in the final round. Thus, 80% (48/60) of participants starting the Delphi finished the complete procedure. Details regarding the self-reported expertise, specialisation and demographic characteristics of the participants are shown in Table 1. Global coverage was achieved, but participants were mainly from Europe, which fairly reflects the geographical distribution of published studies investigating sFGR. A list of the experts is included as supplementary material.

In the first round we presented to the panel 62 and 59 parameters for MC and DC twin pregnancies, respectively (Supplementary Table 1). Figures 1 & 2 and Supplementary Figures 1 & 2 demonstrate the Likert scores of each parameter included in the definition, monitoring, management and outcome of twin pregnancies complicated by sFGR. All the parameters suggested by members of the expert panel were presented in the following round for voting.

Tables 2 & 3 list the agreed conditional parameters for the definition of sFGR in mC and DC pregnancies, respectively. In MC twin pregnancies, the conditional parameters included assessment of the gestational age (GA), TTTS, twin anemia polycythemia sequence (TAPS), structural anomalies, aneuploidy and genetic syndromes. The general parameters included EFW, EFW discordance, AC and umbilical artery (UA) pulsatility index (PI). In DC twins the conditional parameters included assessment of the GA, structural anomalies, aneuploidy, genetic syndromes and congenital infections. The general parameters included EFW, EFW discordance and UA PI.

In the third round, the panel agreed the cut-off values for both the solitary and contributory parameters. Consensus was also reached on the rejection of 41 parameters in MC twins and 27 parameters in DC twins (Supplementary Table 2). In the final round, solitary and contributory parameters and their cut-offs were presented together as possible algorithms. For sFGR in MC twin pregnancy, one solitary parameter (EFW of one twin less than the third centile) and at least two out of four contributory parameters (EFW of one twin less than the 10^{th} centile, AC of one twin less than the 10^{th} centile, EFW discordance of 25% or more, UA PI of the smaller twin above the 95^{th} centile) were agreed upon (Figure 3 and Table 4). For sFGR in DC twin pregnancy, one solitary parameter (EFW of one twin less than the third centile) and at least two out of three contributory parameters (EFW of one twin less than the 10^{th} centile, EFW discordance of 25% or more, UA PI of the smaller above the 95^{th} centile) were agreed upon (Figure 3 and Table 4). In MC twins the percentages of voting at the last round were 62.5% for 2 out of 4 contributory parameters, 35.4% for 3 out of 4 contributory parameters and 2.1% for 4 out of 4 contributory parameters. In DC twins the percentages of voting at the last round were 85.4% for 2 out of 3 contributory parameters and 14.6% for 3 out of 3 contributory parameters.

DISCUSSION

Summary of the study findings

In this study a consensus definition of sFGR in MC and DC twin pregnancy was established through a Delphi procedure. EFW of one twin less than the third centile on its own would establish a diagnosis of sFGR in either MC or DC twin pregnancy. Alternatively, the combination of three out of four parameters (EFW of one twin less than the 10th centile, AC of one twin less than the 10th centile, EFW discordance of 25% or more, UA PI of the smaller twin above the 95th centile) would indicate sFGR in a MC twin pregnancy, while at least two out of three parameters (EFW of one twin less than the 10th centile, EFW discordance of 25% or more, UA PI of the smaller above the 95th centile) are needed in order to diagnose sFGR in a DC twin pregnancy. In addition, lists of parameters considered essential in the monitoring, management and assessment of pregnancy outcome have been established.

Interpretation of the study findings

The prevalence of sFGR varies in the literature, up to 26% in DC twins and 15%-46%[17] in MC twins when defined as birthweight discordance of at least 25% in the absence of TTTS.[9] It is likely that much of this variation is accounted for by differing definitions of sFGR. Fetal medicine specialists should now use consistent definitions of sFGR in MC and DC twin pregnancies, to facilitate comparison of study findings, or pooling of results from different studies. Only then will it be possible to establish robust evidence-based management or monitoring pathways.

One interesting finding of this study is that the expert panel did not choose twin-specific or customised growth charts. In the third trimester, growth in twins is consistently less than in singletons, with the differences most pronounced, and apparent earlier, in MC than in DC pregnancies.[18] Despite this, it is common practice to plot twins' growth on singleton charts. The key question for clinicians is whether this difference in growth represents adaptation or restriction. If adaptation, there is a need for twin-specific growth charts; if restriction, there is a strong argument to use singleton charts to avoid missing FGR in twins. Trial evidence comparing the predictive accuracy of twin-specific versus singleton charts is needed to address this question.

The inclusion of a hemodynamic measure (UA PI >95th centile) is similar to the consensus definition of FGR in singletons.[12] This indicates that the expert group supports the need to differentiate between small for gestational age (SGA) fetuses, the majority of which have normal outcome, and growth restricted fetuses which need close monitoring and likely early delivery. Even in singleton pregnancies, most term stillbirths are not SGA,[19] and therefore not prevented by a policy that relies on fetal size alone. It may be that, as in singletons, the addition of Doppler parameters is of benefit in distinguishing the growth restricted fetus from the well small baby.[20] Interestingly, it has been reported that the normal UA PI reference range in twins differs from that in singleton pregnancies.[21]

Clinical and research implications

These findings could potentially change the way sFGR in twin pregnancies is managed and investigated. Firstly, new definitions for sFGR, specific for MC and DC twin pregnancies, have been agreed. Secondly, a lower centile threshold than that commonly used has been introduced (3rd rather than 10th), reflecting the unfavourable outcomes in severe SGA fetuses in the absence of abnormal functional parameters.[22] Thirdly, a hemodynamic parameter was included. Fourthly, some parameters currently used in monitoring and management of these pregnancies have been rejected as not useful/recommended in routine clinical practice.

Whether the use of these proposed diagnostic criteria will lead to better identification of twin pregnancies destined to develop adverse perinatal outcome should be validated in prospective observational studies.

The consensus definition for MC twins might result in more fetuses diagnosed with FGR than that for DC twins, because of the additional inclusion of AC less than the 10th centile. The definitions are meant to be applicable to FGR in both twins and to sFGR. sFGR can create a dilemma: deliver both babies prematurely for the benefit of the smaller, or observe longer to avoid premature birth of the larger twin. However, growth restriction is unlikely to be selective when there is only a small difference in growth between the twins. With the current definition for MC twins, sFGR can be diagnosed when one twin has an AC/EFW on the 9th centile and the other on the 11th centile. In this case the definition diagnoses FGR and does not address the conflict of interest in sFGR. The outcome of both twins is expected to be good in this case.

Strengths and limitations

The parameters for the diagnosis, monitoring and management of sFGR were assessed separately in MC and DC twin pregnancy. The perinatal mortality rate in MC twins is more than double that in DC twins.[2] This is likely secondary to the marked increase in fetal demise in MC twins, 7.6% versus 1.6%. Furthermore, the overall neonatal morbidity is also higher in MC twins.[23] Conditional parameters were identified which the expert panel considered essential to the assessment of these pregnancies, and essential to include during the design and reporting of research studies investigating sFGR in twin pregnancies.

The main weakness was the potential for selection bias associated with the inclusion of a group of experts who share similar opinions, which is an inherent weakness of the Delphi methodology. Nevertheless, these experts who agreed to participate in the Delphi procedure were those most familiar with the concepts and clinical implications of sFGR in twin pregnancies.

Conclusions

Consensus-based diagnostic criteria for sFGR in both MC and DC twin pregnancies, as well as the cut-off values for those parameters, were agreed by consensus of a large panel of experts using the Delphi methodology. In addition, lists of parameters considered essential in the monitoring, management and assessment of pregnancy outcome have been established. Prospective observational studies are needed to validate these diagnostic criteria before they can be used in clinical trials of interventions.

REFERENCES

1. Buca D, Pagani G, Rizzo G, Familiari A, Fiacco ME, Manzoli L, Liberati M, Fanfani F, Scambia G, D'Antonio F. Outcome in monochorionic twin pregnancies with selective intrauterine growth restriction according to the umbilical artery Doppler pattern of the smaller twin: a systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2016. DOI: 10.1002/uog.17362.

2. Parra-Cordero M, Bennasar M, Martinez JM, Eixarch E, Torres X, Gratacos E. Cord occlusion in monochorionic twins with early selective intrauterine growth restriction and abnormal umbilical artery Doppler: a consecutive series of 90 Cases. *Fetal Diagn Ther* 2016; **39** :186-191.

3. Gratacos E, Antolin E, Lewi L, Martinez JM, Hernandez-Andrade E, Acosta-Rojas R, Enríquez G, Cabero L, Deprest J. Monochorionic twins with selective intrauterine growth restriction and intermittent absent or reversed end-diastolic flow (Type III): feasibility and perinatal outcome of fetoscopic placental laser coagulation. *Ultrasound Obstet Gynecol* 2008; **31** :669-675.

4. Valsky DV, Eixarch E, Martinez JM, Crispi F, Gratacos E. Selective intrauterine growth restriction in monochorionic twins: pathophysiology, diagnostic approach and management dilemmas. *Semin Fetal Neonatal Med* 2010; **15** :342-348.

5. Ortibus E, Lopriore E, Deprest J, Vandenbussche FP, Walther FJ, Diemert A, Hecher K, Lagae L, De Cock P, Lewi PJ, Lewi L. The pregnancy and long-term neurodevelopmental outcome of monochorionic diamniotic twin gestations: a multicenter prospective cohort study from the first trimester onward. *Am J Obstet Gynecol* 2009; **200** : 494 e1-8.

6. Van Mieghem T, Deprest J, Klaritsch P, Gucciardo L, Done E, Verhaeghe J, Lewi L. Ultrasound prediction of intertwin birth weight discordance in monochorionic diamniotic twin pregnancies. *Prenat Diagn* 2009; **29** : 240-244.

7. Chalouhi GE, Marangoni MA, Quibel T, Deloison B, Benzina N, Essaoui M, Al Ibrahim A, Stirnemann JJ, Salomon LJ, Ville Y. Active management of selective intrauterine growth restriction with abnormal Doppler in monochorionic diamniotic twin pregnancies diagnosed in the second trimester of pregnancy. *Prenat Diagn* 2013; **33** :109-115.

8. Vanlieferinghen S, Anselem O, Le Ray C, Shen Y, Marcellin L, Goffinet F. Prognostic value of umbilical and cerebral Doppler in fetal growth restriction: comparison of dichorionic twins and singletons. *PLoS One* 2015. DOI: 10.1371/journal.pone.0123067.

9. Lewi L, Jani J, Blickstein I, Huber A, Gucciardo L, Van Mieghem T, Donè E, Boes AS, Hecher K, Gratacos E, Lewi P, Deprest J. The outcome of monochorionic diamniotic twin gestations in the era of invasive fetal therapy: a prospective cohort study. *Am J Obstet Gynecol* 2008; **199** : 514-518.

10. Khalil A, Rodgers M, Baschat A, Bhide A, Gratacos E, Hecher K, Kilby MD, Lewi L, Nicolaides KH, Oepkes D, Raine-Fenning N, Reed K, Salomon LJ, Sotiriadis A, Thilaganathan B, Ville Y. ISUOG Practice Guidelines: role of ultrasound in twin pregnancy. *Ultrasound Obstet Gynecol* 2016; **47** : 247-263.

11. Lewi L, Cannie M, Blickstein I, Jani J, Huber A, Hecher K, Dymarkowski S, Gratacós E, Lewi P, Deprest J. Placental sharing, birthweight discordance, and vascular anastomoses in monochorionic diamniotic twin placentas. *Am J Obstet Gynecol* 2007; **197** : 587.e1-8.

12. Gordijn SJ, Beune IM, Thilaganathan B, Papageorghiou A, Baschat AA, Baker PN, Silver RM, Wynia K, Ganzevoort W. Consensus definition for placental fetal growth restriction: a Delphi procedure. *Ultrasound Obstet Gynecol* 2016; **48** : 333-339.

13. Murphy MK, Black NA, Lamping DL, McKee CM, Sanderson CF, Askham J, Marteau T. Consensus development methods, and their use in clinical guideline development. *Health Technol Assess* 1998; **2** : 1-88.

14. Sinha IP, Smyth RL, Williamson PR. Using the Delphi technique to determine which outcomes to measure in clinical trials: recommendations for the future based on a systematic review of existing studies. *PLoS Medicine* 2011; **8** : e1000393.

15. Hsu CC, Sandford BA. The Delphi Technique: making sense of consensus. *Practical Assessment, Research and Evaluation* 2007; **12** :1-8.

16. Kottner J, Audigé L, Brorson S, Donner A, Gajeweski BJ, Hróbjartsson A, Robersts C, Shoukri M, Streiner DL. Guidelines for reporting reliability and agreement studies (GRRAS) were proposed. *J Clin Epidemiol* 2011; **64** : 96-106.

17. Chauhan SP, Shields D, Parker D, Sanderson M, Scardo JA, Magann EF. Detecting fetal growth restriction or discordant growth in twin gestations stratified by placental chorionicity. *J Reprod Med*. 2004; **49** :279-284.

18. Stirrup OT, Khalil A, D'Antonio F, Thilaganathan B, Southwest Thames Obstetric Research Collaborative (STORK). Fetal growth reference ranges in twin pregnancy: analysis of the Southwest Thames Obstetric Research Collaborative (STORK) multiple pregnancy cohort. *Ultrasound Obstet Gynecol* 2015; **45** :301–307.

19. Poon LCY, Volpe N, Muto B, Syngelaki A, Nicolaides KH. Birthweight with gestation and maternal characteristics in live births and stillbirths. *Fetal Diagnosis and Therapy* 2012; **32** : 156–165.

20. Khalil AA, Khan N, Bowe S, Familiari A, Papageorghiou A, Bhide A, Thilaganathan B. Discordance in fetal biometry and Doppler are independent predictors of the risk of perinatal loss in twin pregnancies. *Am J Obstet Gynecol* 2015; **213** : 222.e1-222.e10.

21. Mulcahy C, McAuliffe FM, Breathnach F, Geary M, Daly S, Higgins J, Hunter A, Morrison J, Burke G, Higgins S, Dicker P, Mahony R, Tully E, Malone F. Umbilical and fetal middle cerebral artery Doppler reference ranges in a twin population followed longitudinally from 24 to 38 weeks' gestation. *Ultrasound Obstet Gynecol* 2014; **44** : 461-467.

22. Figueras F, Eixarch E, Meler E, Iraola A, Figueras J, Puerto B, Gratacos E. Small-for-gestational-age fetuses with normal umbilical artery Doppler have suboptimal perinatal and neurodevelopmental outcome. *Eur J Obstet Gynecol Reprod Biol* 2008; **136** : 34-38.

23. Hack KE, Derks JB, Elias SG, Franx A, Roos EJ, Voerman SK, Bode CL, Koopman-Esseboom C, Visser GH. Increased perinatal mortality and morbidity in monochorionic versus dichorionic twin pregnancies: clinical implications of a large Dutch cohort study. *BJOG* 2008; **115** :58-67.

Figure Legends

Figure 1. Likert scores of the parameters describing the diagnostic features of selective fetal growth restriction (sFGR) in monochorionic (MC) and dichorionic (DC) twin pregnancy.

Figure 2. Likert scores of the parameters to be included in the management of selective fetal growth restriction (sFGR) in monochorionic (MC) and dichorionic (DC) twin pregnancy.

Figure 3. Consensus-based diagnostic criteria for selective fetal growth restriction (sFGR) in monochorionic (MC) and dichorionic (DC) twin pregnancy.

Supplementary Figure 1. Likert scores of the parameters to be included in the monitoring of selective fetal growth restriction (sFGR) in monochorionic (MC) and dichorionic (DC) twin pregnancy.

Supplementary Figure 2. Likert scores of the parameters to be reported in the outcome of the monochorionic (MC) and dichorionic (DC) twin pregnancies complicated by selective fetal growth restriction (sFGR).

Table 1. Details of the expert panel participants (n=60).

Details of expert panel	**Number (%)**
Region of practice	
Europe	30 (50)
North America	11 (18.3)
South America	5 (8.3)
Asia/Australia	13 (21.7)
Africa	1 (1.7)
Average number of monochorionic twins that deliver annually at the expert's hospital	
<20	8 (13.3)
20-30	11 (18.3)
30-40	11 (18.3)
40-50	8 (13.3)
>50	22 (36.7)
Average number of dichorionic twins that deliver annually at the expert's hospital	
<50	10 (16.7)
50-100	15 (25)
100-200	25 (41.7)
>200	10 (16.7)
Practice level	
General / routine obstetric center	0
Fetal medicine center offering prenatal diagnosis but no fetal therapy	13 (21.7)
Fetal medicine center offering prenatal diagnosis and fetal therapy	47 (78.3)
Invasive procedures performed	
Amniocentesis	59 (98.3)
Chorionic villus sampling	58 (96.7)
Embryo and fetal reduction in multi-chorionic pregnancies	47 (78.3)
Fetoscopic laser photocoagulation	42 (70)
Bipolar cord occlusion	35 (58.3)
Interstitial radio-frequency / laser ablation	39 (65)
Other	15 (25)

Table 2. List of parameters selected in monochorionic twin pregnancy following the Second and Third rounds of the Delphi procedure.

List of parameters	**Voting by the expert panel (% in favor)**
Diagnosis of selective fetal growth restriction	
• *Conditional parameters*	
Gestational age (GA)	87
Exclusion of structural anomalies	95
Exclusion of aneuploidy	91
Exclusion of genetic syndromes	80
Exclusion of twin to twin transfusion syndrome (TTTS)	91
Co-existence of TTTS or twin anemia polycythemia sequence (TAPS)	73
• *General parameters*	
Estimated fetal weight (EFW)	91
EFW discordance	80
Abdominal circumference (AC)	71
Umbilical artery pulsatility index (PI)	84
Parameters essential for monitoring	
Fetal growth	98
Doppler measurements	100
Amniotic fluid (AF) measurements/discordance	80
Cardiotocography (CTG) after viability	82
Interval growth	80
Parameters essential for management	
GA at assessment	98
AF measurement/discordance	73
Umbilical artery PI	96
Gratacos classification of Doppler abnormalities	95
Ductus venosus Doppler	91
GA at first diagnosis	89
AC/EFW discordance	73
CTG	80
Referral to expert center	93
Possibility to offer laser therapy	75
Steroids before 34 weeks' gestation	81
Parameters essential in assessment of the pregnancy outcome	
GA at birth	98
Umbilical artery pH	75
Birthweight	95
Birthweight centiles	96

Necrotizing enterocolitis	75
Brain abnormalities	96
Long-term assessment of twins	100
Indications for delivery	82
Apgar score	76
Lactate level in the umbilical artery	85
Neonatal hemoglobin level	71
Respiratory distress syndrome (RDS) requiring intubation	89
Neonatal length of hospital stay	71
Neonatal death before hospital discharge	95
Intrauterine demise (IUD)	100
GA at IUD	93
Steroids before delivery	84

Table 3. List of parameters selected in dichorionic twin pregnancy following the second and third rounds.

List of parameters	**Voting by the Expert panel (% in favor)**
Diagnosis of selective fetal growth restriction	
• *Conditional parameters*	
Gestational age (GA)	81
Exclusion of structural anomalies	94
Exclusion of aneuploidy	96
Exclusion of genetic syndromes	96
Exclusion of congenital infection	92
• *General parameters*	
Estimated fetal weight (EFW)	100
EFW discordance	73
Umbilical artery pulsatility index (PI)	89
Parameters essential for monitoring	
Fetal growth	100
Doppler measurements	100
Amniotic fluid (AF) measurements	80
Cardiotocography (CTG) after viability	89
Parameters essential for management	
GA at assessment	98
AF measurement/discordance	80
Umbilical artery PI	96
Middle cerebral artery PI	78
Ductus venosus Doppler	93
GA at first diagnosis	80
CTG	89
Steroids before 34 weeks' gestation	81
Parameters essential in assessment of the pregnancy outcome	
GA at birth	100
Umbilical artery pH	93
Birthweight	95
Birthweight centiles	95
Birthweight discordance	80
Necrotizing enterocolitis	84
Brain abnormalities	96
Long-term assessment of twins	100
Indications for delivery	91

Apgar score	80
Lactate level in the umbilical artery	85
Respiratory distress syndrome (RDS) requiring intubation	89

Table 4. Possible algorithms of the diagnostic features of selective fetal growth restriction (sFGR) in twin pregnancies

Dichorionic twin pregnancy	**Monochorionic twin pregnancy**
Solitary	**Solitary**
Estimated fetal weight (EFW) of one of the twins <3rd centile	EFW of one of the twins <3rd centile
Contributory	**Contributory**
EFW <10th centile of one of the twins	EFW <10th centile of one of the twins
EFW discordance ≥25%	Abdominal circumference (AC) of one twin <10th centile
Umbilical artery (UA) pulsatility index (PI) of the smaller twin >95th centile	EFW discordance ≥25%
	UA PI of the smaller twin >95th centile
Algorithms for contributory parameters	**Algorithms for contributory parameters**
A 2 out of 3 contributory parameters are required irrespective of which parameter	**A** 2 out of 4 contributory parameters are required irrespective of which parameter
B all contributory parameters are required	**B** 3 out of 4 contributory parameters are required irrespective of which parameter
	C all contributory parameters are required

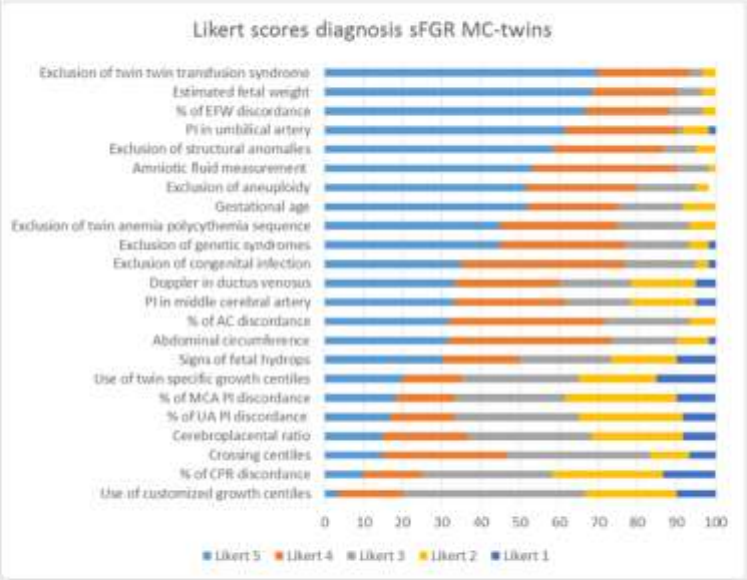

Figure 1a

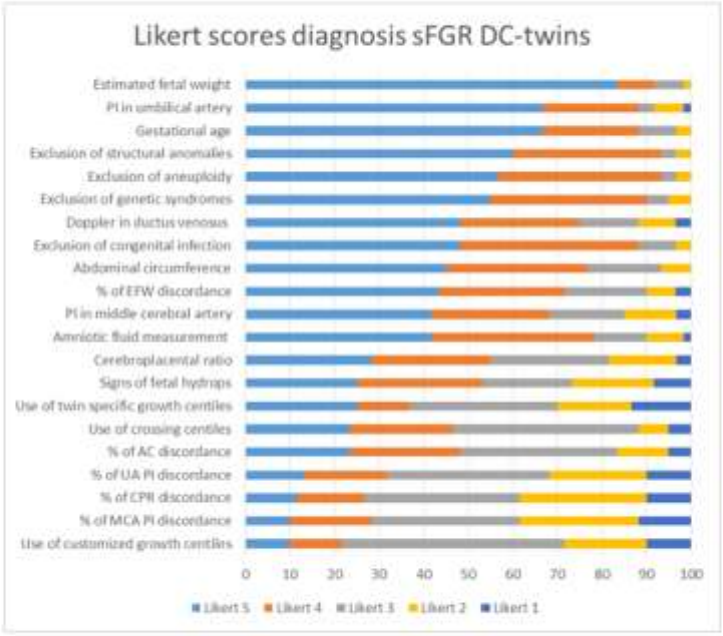

Figure 1b

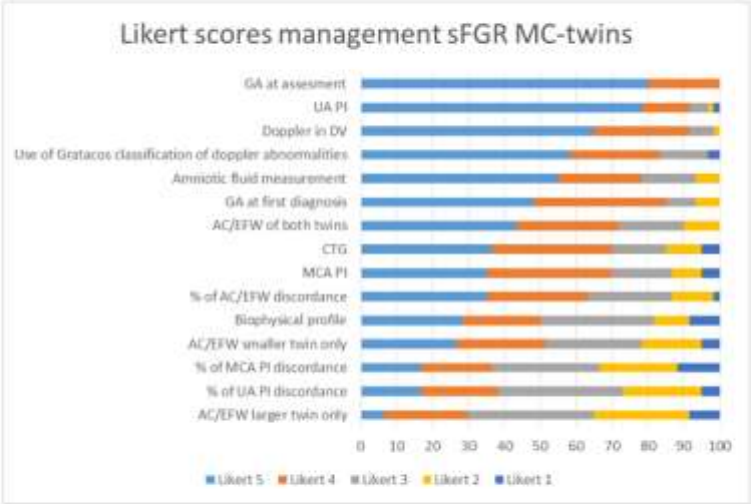

Figure 2a

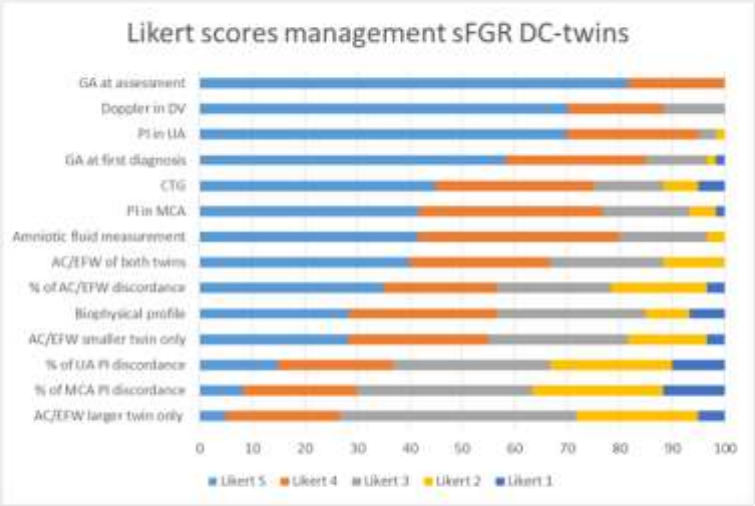

Figure 2b

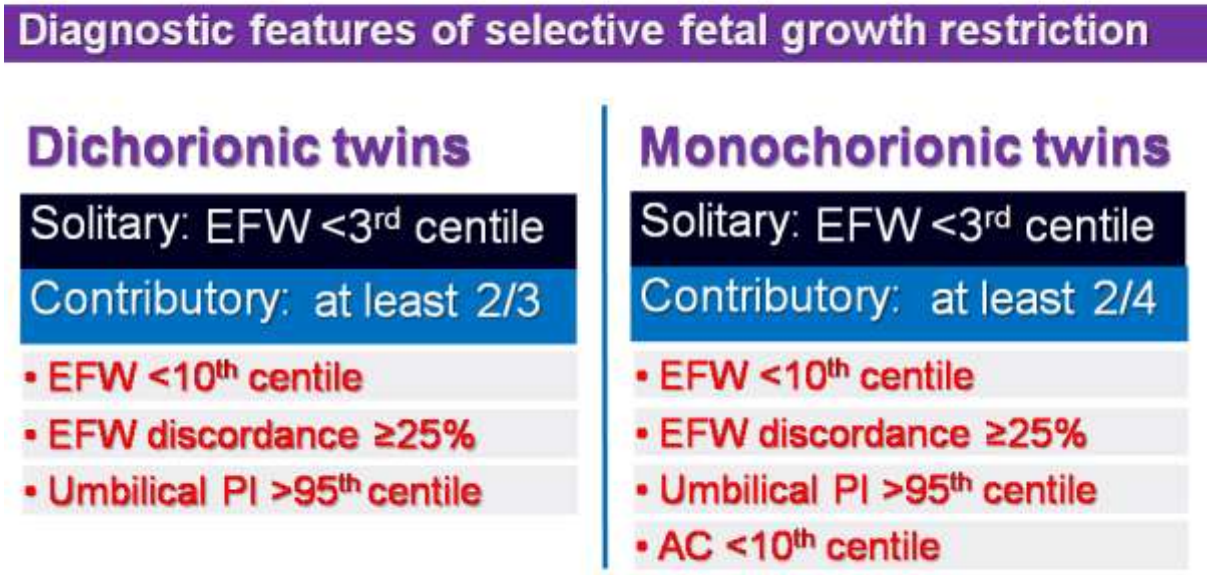

Figure 3