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Review

First-trimester ultrasound determination of chorionicity in twin gestations using the lambda sign: a systematic review and meta-analysis

G.M. Maruotti, G. Saccone, M. Morlando, P. Martinelli *

Department of Neuroscience, Reproductive Sciences and Dentistry, School of Medicine, University of Naples Federico II, Naples, Italy

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ABSTRACT

Objective: To evaluate the accuracy of first-trimester sonographic determination of chorionicity in twin gestations using the lambda sign.

Study design: Electronic databases (MEDLINE, PROSPERO, Scopus, ClinicalTrials.gov, EMBASE, Sciencedirect) were searched from their inception until April 2016. We included only study assessing the accuracy lambda sign in prediction of monochorionicity in the first trimester. Forest plots for pooled sensitivity and specificity with 95% confidence intervals (CI) were generated. In addition, symmetric summary receiver-operating characteristic curves were plotted. The area under the curve (AUC) was also computed to evaluate the overall accuracy of the diagnostic test.

Results: Nine studies, including 2292 twins, were analysed. In all of these studies, identification of the lambda sign was used to diagnose chorionicity on real-time B-mode imaging. Twins were classified as monochorionic if there was a single placental mass in the absence of the lambda sign, and dichorionic if there was a single placental mass but the lambda sign was present or the placentas were not adjacent to each other. In all nine studies, placental histology or discordant fetal sex were used to confirm chorionicity. Pooled results from the meta-analysis showed that sensitivity of the presence of the lambda sign in the prediction of dichorionicity was 99% (95% CI 98–100%), and specificity was 95% (95% CI 92–97%). Pooled sensitivity of the absence of the lambda sign in the prediction of monochorionicity was 96% (95% CI 92–98%) and pooled specificity was 99% (95% CI 98–99%). The AUC for diagnostic accuracy was 0.99, and suggested very high diagnostic accuracy.

Conclusion: The lambda sign predicts chorionicity with a high degree of accuracy before 14 weeks of gestation. Presence of the lambda sign indicates dichorionicity, and absence of the lambda sign indicates monochorionicity. All hospitals should encourage departments providing ultrasound services to determine chorionicity when examining women with twin pregnancies in the first trimester. As determination of chorionicity is most accurate before 14 weeks when the amnion and chorion have not yet fused, the first-trimester scan in twin pregnancy is paramount.

Contents

* Corresponding author. Tel.: +39 0817462966; fax: +39 0817462966.
E-mail address: martinel@unina.it (P. Martinelli).

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Introduction

The incidence of twin gestations in the USA has increased over the past decades [1]. Compared with dichorionic twins, monochorionic twins have inherently different complication rates, including fetal loss, fetal anomalies, intrauterine growth restriction, prematurity, twin anaemia polycythaemia sequence and twin–twin transfusion syndrome [2]. Therefore, accurate determination of chorionicity is vital when managing women with multiple gestations. The sonographic determination of chorionicity is based on the number of placental sites, the visualization of an intertwin membrane (ITM), and the identification of the so-called 'lambda' or 'twin-peak' sign on the one hand or the 'T' sign on the other [3].

The aim of this systematic review and meta-analysis was to evaluate the accuracy of first-trimester ultrasound determination of chorionicity in twin gestations using the lambda sign.

Materials and methods

This review was performed according to a protocol designed a priori and recommended for systematic review [4]. Electronic databases (MEDLINE, PROSPERO, Scopus, ClinicalTrials.gov, EMBASE, Sciencedirect, Cochrane Library, Scielo) were searched from their inception until April 2016 with no language limitations. The following search terms were used: 'twin', 'multiple', 'amnionicity', 'chorionicity', 'gestations', 'ultrasound', 'sonographic', 'pregnancy', 'transvaginal', '2D', 'lambda', 'accuracy', 'cohort', 'case–control', 'prediction', 'first trimester', 'obstetric', 'triplet' and 'sign'. No restrictions were applied for language or geographical location. In addition, the reference lists of all identified articles were examined to identify any studies that were not captured by the electronic search. The electronic search and study eligibility were assessed independently by two authors (GS, PM). Differences were discussed and consensus was reached.

This study considered randomized controlled trials, case–control studies and cohort studies. Studies were included if they reported data allowing construction of a 2×2 table. Only studies that assessed the accuracy of the lambda sign for the prediction of chorionicity in twin gestations during the first trimester were included. Studies that evaluated the accuracy of other signs (e.g. ITM, gestational sac number) for the prediction of chorionicity were excluded. Studies on triplet and high-order multifetal pregnancies were also excluded. The primary outcome of this meta-analysis was planned a priori as the accuracy of the lambda sign for the prediction of chorionicity in twin gestations.

Data abstraction and methodological quality of the included studies were completed by two independent investigators (GMM, PM). Each investigator abstracted data from each study independently. Data from each eligible study were extracted without modification of the original data to custom-made data collection forms. Disagreements were resolved by consensus with a third reviewer (GS). All authors of the original studies were contacted for missing data if possible.

The quality of each included study was assessed using Quality Assessment of Diagnostic Accuracy Studies (QUADAS) criteria [5]. Each item is scored as 'yes', 'no' or 'unclear' (if there is insufficient information to make an accurate judgement) [5]. A quality score was calculated, defined as the total number of items categorized as 'yes' among the seven items of the QUADAS criteria [5]. A study with a score $\geq$5 out of 7 was judged to have low overall low risk of bias [5].

The meta-analysis was reported in accordance with the Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) statement [6]. Before data extraction, the protocol for this review was registered with the PROSPERO International Prospective Register of Systematic Reviews (Registration No. CRD42015027286) following the PRISMA guidelines for protocols (PRISMA-P) [7].

For all included studies, a 2×2 table was constructed to cross-classify the ultrasound measurement of the lambda sign and the prediction of monochorionicity. Forest plots for pooled sensitivity (i.e. detection rate) and specificity of first-trimester lambda sign for the prediction of chorionicity in twins were generated, with 95% confidence intervals (CI). Additionally, symmetric summary receiver-operating characteristic (SROC) curves were plotted. The area under the curve (AUC) and the Q^* index were also computed to evaluate the overall accuracy of the diagnostic test. The AUC of an SROC curve is a measure of the overall performance of a diagnostic test to differentiate accurately between cases with and without the condition of interest. The Q^* index is defined by the point at which sensitivity and specificity are equal, which is closest to the ideal top-left corner of the SROC space. Both values range between 0 and 1, with higher values indicating better test performance [8]. The following guidelines have been suggested for interpretation of AUC values: $0.5 \geq \text{AUC} < 0.7$, low accuracy; $0.7 \geq \text{AUC} < 0.9$, moderate accuracy; and $0.9 \geq \text{AUC} \leq 1$, high accuracy [8]. The authors planned to assess AUC for the sensitivity analysis according to the study design of the included studies.

The degree of between-study heterogeneity was evaluated using the I^2 statistic, which represents the percentage of between-study variation that is due to heterogeneity rather than chance. A value $\geq$30% indicates a substantial level of heterogeneity [4,9]. Potential publication bias was assessed statistically using Begg's and Egger's tests [9].

Data analysis was completed independently by authors (GS, PM) using Meta-DiSc 1.4 (Hospital Universitario Ramon y Cajal, Madrid, Spain). The completed analyses were compared, and any differences were resolved by review of the full data.

Results

The study flow chart is shown in Fig. 1. Thirteen studies were assessed for eligibility [10–22]. Four studies that evaluated the accuracy of ITM for the prediction of amnionicity were excluded [10–12,17]. As such, nine studies, including 2292 pair of twins, were analysed [13–16,18–22].

Begg's and Egger's tests showed no significant publication bias ($p = 0.62$ and $p = 0.71$, respectively). The statistical heterogeneity between the included studies was low ($I^2 = 0\%$). Fig. 2 shows the results of the quality assessment. None of the nine studies had a high risk of bias in patient selection and reference standard. Most studies (5/9) had a low overall risk of bias (i.e. QUADAS score $\geq$5) [13,16,18,19,21].

Table 1 shows the characteristics of the nine included studies. Of the 2292 women with twin gestations, 428 (19%) were monochorionic twins and 1864 (81%) were dichorionic twins. Four studies were from the USA [14,15,18,21]. Four studies were retrospective cohort studies [13–16] and five were prospective cohort studies [18–22]. One study was a secondary analysis of a randomized trial of preterm birth prevention in twins [18]. The method of ultrasound ascertainment was described clearly in all nine studies. Ultrasound scans were performed at <14 weeks of gestation. In seven studies, transvaginal ultrasound scans were performed using a 5-MHz transducer for B-mode imaging by a doctor with appropriate experience in early-pregnancy ultrasound assessment [14,15,18–22]. In the other two studies, ultrasound scans were performed transabdominally [13,16]. In one study, where views were suboptimal with the transabdominal ultrasound, the examination was performed transvaginally with an 8-MHz transducer [16].

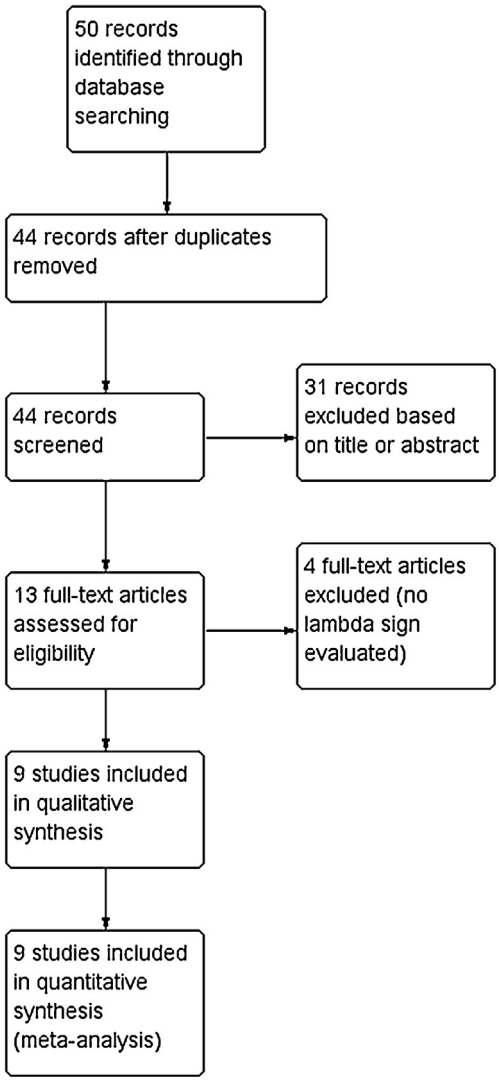

Fig. 1. Study flow diagram.

In all nine studies, identification of the lambda sign was used to diagnose chorionicity on real-time B-mode imaging. If the placentas were fused and a wedge-shaped junction was observed (i.e. lambda sign), this was interpretated as extension of the chorionic tissue into the base of the ITM, and therefore a dichorionic twin pregnancy. Twins were classified as monochorionic if there was a single placental mass in the absence of the lambda sign, and dichorionic if there was a single placental mass but the lambda sign was present or the placentas were not adjacent to each other. In the absence of an ITM, the pregnancy was considered to be monoamniotic. In all nine studies, placental histology or discordant fetal sex were used to confirm chorionicity.

A 2×2 table was constructed for all nine studies for the prediction of chorionicity using the lambda sign in the first-trimester ultrasound scan.

Pooled results from the meta-analysis showed that sensitivity of the presence of the lambda sign for the prediction of dichorionicity ranged from 98% to 100%, and specificity ranged from 82% to 100%. Pooled sensitivity (i.e. detection rate) was 99% (95% CI 98–100%) and pooled specificity was 95% (95% CI 92–97%). Sensitivity of the absence of the lambda sign for the prediction of monochorionicity ranged from 79% to 100%, and specificity ranged from 97% to 100%. Pooled sensitivity was 96% (95% CI 92–98%) and pooled specificity was 99% (95% CI 98–99%).

The AUC for diagnostic accuracy was 0.99, which suggested very high diagnostic accuracy (Fig. 3). Accuracy was also high in the sensitivity analysis of retrospective studies alone (AUC = 0.98) and prospective studies alone (AUC = 0.98).

Comment

This systematic review and meta-analysis showed that the lambda sign has very high diagnostic accuracy for the prediction of chorionicity. The pooled detection rate was 99%.

This study has several strengths. To the authors' knowledge, this is the first meta-analysis to evaluate the accuracy of the lambda sign for the prediction of chorionicity; no similar meta-analyses were found during the systematic review. The number of women included in this study was high, and the overall risk of bias of the included studies was low. All of the included studies had the

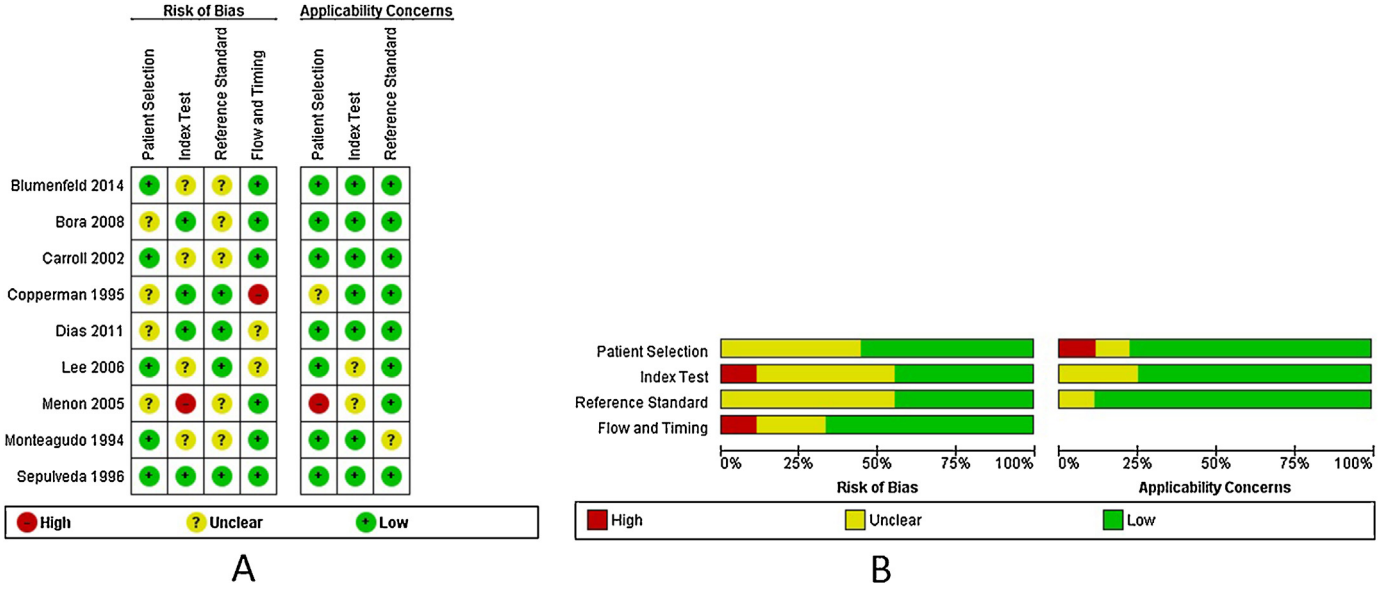

Fig. 2. Review authors' judgement of risk of bias and applicability concerns based on Quality Assessment of Diagnostic Accuracy Studies tool. (A) Summary of risk of bias for each study: +, low risk of bias; –, high risk of bias; ?, unclear risk of bias. (B) Risk of bias graph about each risk of bias item presented as percentages across included studies. Green, low risk of bias; red, high risk of bias; yellow, unclear risk of bias.

Table 1
Characteristics of the included studies.

	Monteagudo 1994 [14]	Copperman 1995 [15]	Sepulveda 1996 [13]	Carroll 2002 [16]	Menon 2005 [22]	Lee 2006 [21]	Bora 2008 [19]	Dias 2011 [20]	Blumenfeld 2014 [18]
Location	USA	USA	UK	Ireland	Malaysia	USA	UK	UK	USA
Study design	PC	PC	PC	PC	RC	RC	RC	RC	RC
Number of twins included	64	47	279	150	463	247	67	613	362
Number of monochorionic twins included	9	3	63	34	50	49	14	146	60
Number of dichorionic twins included	55	44	216	116	413	198	53	467	302
Gestational age at scan (weeks)	5–14	8	10–14	10–14	10–14	<14	7–9	11–14	<14
Placental pathological examination	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

PC, prospective cohort; RC, retrospective cohort.

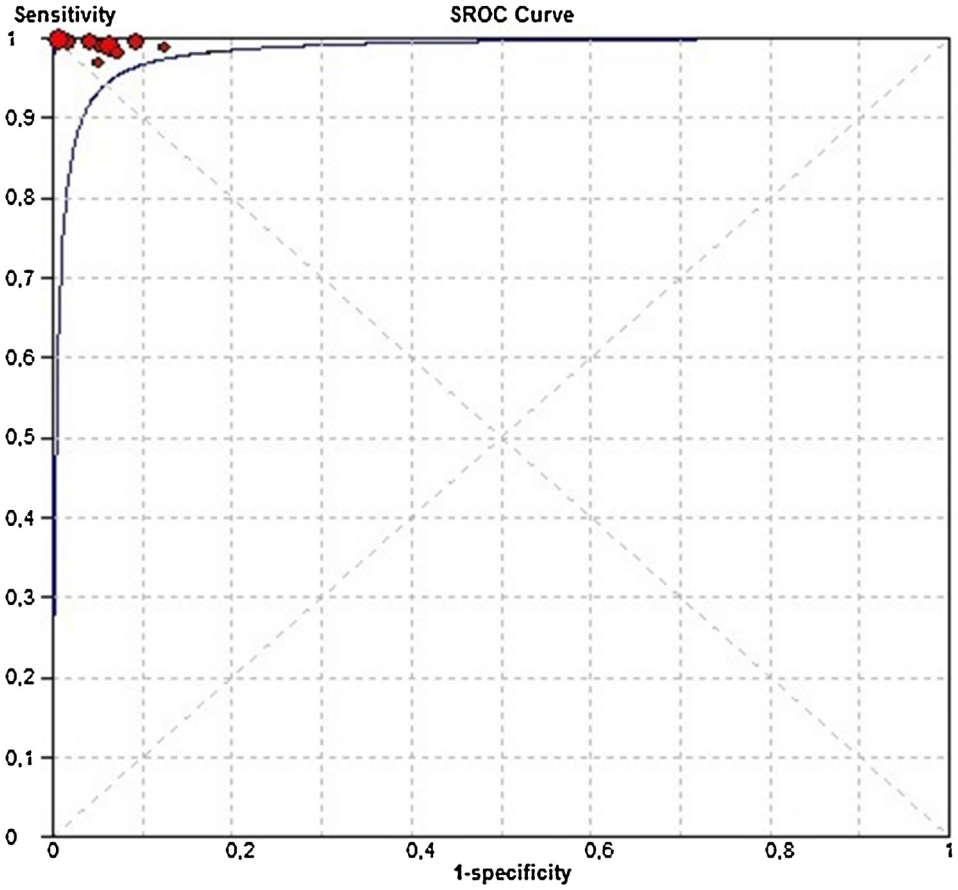

Fig. 3. Symmetric summary receiver operating characteristics curve with 95% confidence interval for the accuracy of first trimester sonographic determination of chorionicity in twin gestations using the lambda sign. Area under the curve (AUC) ± standard error (SE) = 0.999 ± 0.02; Q^* ± SE = 0.994 ± 0.03.

same primary outcome (i.e. prediction of chorionicity). The protocol of this review was registered a priori on PROSPERO. Statistical tests showed no significant potential publication bias. Finally, statistical heterogeneity between the included studies was low, with no inconsistency in the pooled results (I^2 = 0%).

The limitations of this study are mostly inherent to the limitations of the included studies. The quality of the findings is dependent on the quality of the primary studies included. All of the included studies were cohort studies. The generalizability and external validity of these findings may be limited due to the quality of ultrasound equipment at these institutions and the patient population evaluated. No adjustments for potential confounders were made by the original studies. Subgroup analysis according to gestational age was not feasible; only Blumenfeld et al. included second-trimester measurements, but did they not stratify the data by gestational age. However, they showed that for each week increase in gestational age, the odds of misclassification rose by 10% [18]. Hierarchical SROC curves were not assessed.

Twins account for approximately 1% of all pregnancies, with two-thirds of twins being dizygotic (i.e. non-identical) and one-third being monozygotic (i.e. identical) [1]. Over the last 20 years, the rate of twinning has increased, and this increase is most marked for dizygotic twins [1]. Two-thirds of the increase in twins is due to the use of assisted reproduction techniques, and one-third of the increase is due to increasing maternal age [1].

Chorionicity refers to the type of placentation and does not reflect zygosity, which denotes the type of conception. Chorionicity, rather than zygosity, is the main factor that determines pregnancy outcome [23,24]. In dizygotic twins, each fetus has its own placenta and amniotic sac, and therefore dizygotic twins always have a dichorionic placenta [23]. In monozygotic twins, there may be sharing of the same placenta (monochorionic),

amniotic sac (monoamniotic) or even fetal organs (conjoined or Siamese). In monozygotic twins, the type of placentation will depend on when the zygote divides. If the division occurs within the first 3 days of fertilization, dichorionic–diamniotic twins occur; if the split occurs 4–7 days after fertilization, the result is monochorionic–diamniotic twins; and if the division occurs 8–12 days after fertilization, monochorionic–monoamniotic twins occur [23]. Approximately 25% of all monozygotic twin gestations are dichorionic [1].

While all twin pregnancies need increased surveillance compared with singleton pregnancies, monochorionic twins need particular follow-up [2,24]. Twin pregnancies have a monochorionic placenta in 20% of cases, and perinatal mortality is two to three times higher than in dichorionic twins [25,26].

In dichorionic twins, the ITM is composed of a central layer of chorionic tissue sandwiched between two layers of amnion, whereas in monochorionic twins, no chorionic layer is present [3,24]. Determination of chorionicity helps to identify those twins at higher risk, and enables monitoring to be tailored for the early diagnosis of complications [1,25–27]. Being able to predict chorionicity in twin gestations has several potential benefits, as failure to detect chorionicity may be associated with higher rates of neonatal morbidity and mortality [2,24,25,28]. This information may assist birth providers when planning staff coverage [29]. These data may also be helpful for women choosing between planned caesarean delivery and waiting for spontaneous labour to attempt vaginal delivery [29,30]. For pregnant women, this information may help them to arrange their social activities and deal with anxiety.

In summary, the lambda sign predicts chorionicity with a high degree of accuracy before 14 weeks of gestation. The results of this study support the observation that the lambda sign indicates dichorionicity, and the absence of the lambda sign indicates monochorionicity. As there is regression of the chorion laeve and the lambda sign becomes more difficult to identify with advancing gestation [3,13,18,23,30], all hospitals should encourage departments providing ultrasound services to determine chorionicity when examining women with twin pregnancies in the first trimester.

As determination of chorionicity is most accurate before 14 weeks when the amnion and chorion have not yet fused, the first-trimester scan in twin pregnancy is paramount.

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Conflict of interest

None declared.

References

[1] Martin JA, Hamilton BE, Osterman MJ, Curtin SC, Matthews TJ. Births: final data for 2013. Natl Vital Stat Rep 2015;64:1–68.
[2] Danon D, Sekar R, Hack KE, Fisk NM. Increased stillbirth in uncomplicated monochorionic twin pregnancies: a systematic review and meta-analysis. Obstet Gynecol 2013;121:1318–26.
[3] Salomon LJ, Alfirevic Z, Bilardo CM, et al. ISUOG practice guidelines: performance of first-trimester fetal ultrasound scan. Ultrasound Obstet Gynecol 2013;41:102–13.
[4] Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions, Version 5.1.0. Oxford: The Cochrane Collaboration; 2011, March, Available at: www.cochrane-handbook.org [accessed 15.10.15].
[5] Whiting PE, Rutijes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011;155:529–36.
[6] Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62:1006–12.
[7] Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015;349:g7647.
[8] Walter SD. Properties of the summery receiver operating characteristics (SROC) curve for diagnostic test data. Stat Med 2002;21:1237–56.
[9] Zhou Y, Dendukuri N. Statistics for quantifying heterogeneity in univariate and bivariate meta-analyses of binary data: the case of meta-analyses of diagnostic accuracy. Stat Med 2014;33:2701–17.
[10] Watson WJ, Valea FA, Seeds JW. Sonographic evaluation of growth discordance and chorionicity in twin gestation. Am J Perinatol 1991;8:342–4.
[11] Kurtz AB, Wapner RJ, Mata J, Johnson A, Morgan P. Twin pregnancies: accuracy of first-trimester abdominal US in prediction chorionicity and amnionicity. Radiology 1992;185:759–62.
[12] Tannirandorn Y, Phaosavasdi S. Accuracy of ultrasonographic criteria for the prenatal diagnosis of placental amnionicity and chorionicity in twin gestations. J Med Assoc Thail 1993;76:190–5.
[13] Sepulveda W, Sebire NJ, Hughes K, Odibo A, Nicolaides KH. The lambda sign at 10–14 weeks of gestation as a predictor of chorionicity in twin pregnancies. Ultrasound Obstet Gynecol 1996;7:421–3.
[14] Monteagudo A, Timor-Tritsch IE, Sharma S. Early and simple determination of chorionic and amniotic type in multifetal gestations in the first fourteen weeks by high-frequency transvaginal ultrasonography. Am J Obstet Gynecol 1994;170:824–9.
[15] Copperman AB, Kaltenbacher L, Walker B, et al. Early first-trimester ultrasound provides a window through which the chorionicity of twins can be diagnosed in an in vitro fertilization (IVF) population. J Assist Reprod Genet 1995;12:693–7.
[16] Carroll SG, Soothill PW, Abdel-Fattah SA, et al. Prediction of chorionicity in twin pregnancies at 10–14 weeks of gestations. BJOG 2002;109:182–6.
[17] Wan JJ, Schrimmer D, Tache V, et al. Current practice in determining amnionicity and chorionicity in multiple gestations. Prenat Diagn 2011;31:125–30.
[18] Blumenfeld YJ, Momirova V, Rouse DJ, et al. Accuracy of sonographic chorionicity classification in twin gestations. J Ultrasound Med 2014;33:2187–92.
[19] Bora SA, Papageorghiou AT, Bottomley C, Kirk E, Bourne T. Reliability of transvaginal ultrasonography at 7–9 weeks' gestation in the determination of chorionicity and amnionicity in twin pregnancies. Ultrasound Obstet Gynecol 2008;32:618–21.
[20] Dias T, Arcangeli T, Bhide A, et al. First-trimester ultrasound determination of chorionicity in twin pregnancy. Ultrasound Obstet Gynecol 2011;38:530–2.
[21] Lee YM, Cleary-Goldman J, Thaker HM, Simpson LL. Antenatal sonographic prediction of twin chorionicity. Am J Obstet Gynecol 2006;195:863–7.
[22] Menon DK. A retrospective study of the accuracy of sonographic chorionicity determination in twin pregnancies. Twin Res Hum Genet 2005;8:259–61.
[23] Shetty A, Smith AP. The sonographic diagnosis of chorionicity. Prenat Diagn 2005;25:735–9.
[24] American College of Obstetricians and Gynecologists, Society for Maternal-Fetal Medicine. ACOG Practice Bulletin No. 144: Multifetal gestations: twin, triplet, and high-order multifetal pregnancies. Obstet Gynecol 2014;123:1118–32.
[25] Bernirschke K, Kim CK. Multiple pregnancy. N Engl J Med 1973;288:1276–84.
[26] Bernirschke K, Kim CK. Multiple pregnancy. N Engl J Med 1973;288:1329–36.
[27] Carroll SG, Tyfield L, Reeve L, et al. Is zygosity or chorionicity the main determinant of fetal outcome in twin pregnancies? Am J Obstet Gynecol 2005;193:757–61.
[28] Saccone G, Berghella V. Planned delivery at 37 weeks in twins: a systematic review and meta-analysis of randomized controlled trials. J Matern Fetal Neoantal Med 2015;26:15.
[29] Bibbo C, Robinson JN. Management of twins: vaginal or cesarean delivery? Clin Obstet Gynecol 2015;58:294–308.
[30] Hill LM, Chenevey P, Hecker J, Martin JG. Sonographic determination of first trimester twin chorionicity and amnionicity. J Clin Ultrasound 1996;24:305–8.