

Review Article

Screening for Chorionicity in Twin Pregnancies

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INTRODUCTION

The incidence of twin gestation is about 1% to 2% of all pregnancies¹ but it is increasing due to increased use of assisted reproductive technology² and increasing maternal age over the years.

Zygoty of twin pregnancies is either monozygotic (MZ) which results from fertilization of a single ovum with subsequent splitting into two embryos (i.e. identical) or dizygotic (DZ) which results from fertilization of 2 separate ova (i.e. fraternal).

Chorionicity, on the other hand, refers to the type of placentation in the mother's womb. There are 2 types of chorionicity in twin pregnancies: monochorionic (MC) and dichorionic (DC). Of all the twin pregnancies, about 20% are MC while 80% are DC twins.³ MC twins share the same placenta with vascular anastomoses between the two cord insertions; such vascular anastomoses cause the specific complications peculiar to MC twins. DC twins have separate placentas with no vascular anastomoses between the two cord insertions.

A few basic rules govern the association between chorionicity and zygoty. All monochorionic twins are monozygotic and all dizygotic twins are dichorionic. However not all dichorionic twins are dizygotic (1/3 of monozygotic twins are dichorionic) and not all monozygotic twins are monochorionic (1/4 are

dichorionic).⁴ Monozygotic twins, depending on the number of days from fertilization to splitting of the conceptus, can give rise to monochorionic (2/3 of monozygotic twins), dichorionic or conjoined twins.

Antenatally it is more important to know chorionicity than zygoty as it is the chorionicity that determines the perinatal outcome.¹ Fortunately, chorionicity can be accurately determined by ultrasound scanning in early gestation and confirmed postnatally by placental examination (i.e. for placental vascular anastomoses or histology). Postnatally, it is the zygoty that is more important. The importance of knowing zygoty especially monozygoty can be divided into medical, scientific and individual.⁵ Medically, zygoty is important because it influences the inheritance of specific genetic diseases and possible organ transplant in the future.⁵ Scientifically, determining zygoty facilitates researches and studies. This is particularly true for studies that look at the relative contribution of genetics and environment on the human state by comparing monozygotic twins and dizygotic twins. On an individual basis, most of the parents and the twins themselves would also want to know their zygoty. A good placental examination or histology at delivery that confirms monochorionicity is the best test for monozygoty. However for dichorionic placentas in twins with concordant sex, one would have to resort to ABO status and/or expensive DNA studies to determine the zygoty.

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METHODS FOR CHORIONICITY DETERMINATION

Chorionicity in twins can be accurately determined by transabdominal ultrasound examination during early gestation. However, the success of ultrasonography in chorionicity assessment is inversely proportional to the gestational age⁴ with accuracy reaching 100% in the first trimester⁶ and 80-90% in the mid-trimester.

In the first trimester (7-14 weeks), the most accurate parameter is the ultrasound demonstration of the lambda sign or 'twin peak' sign (see Figure 1). The lambda sign is a triangular projection of echodense placental tissue extending between the layers of



Figure 1. Twin peak sign indicating dichorionic twins



Figure 2. Absence of twin peak sign indicating monozygotic twins

chorion at its origin from the placenta. The lambda sign is indeed just a reflection of the persisting chorion frondosum. The presence of the lambda sign at any point of gestation indicate dichorionicity although as gestation progresses towards the third trimester, it will become harder to identify on ultrasound scan. The presence of the 'twin peak' sign in real-time ultrasound scan had a near 100% positive predictive value for dichorionicity placentation.⁶ Conversely, the absence of the 'twin peak' sign (see Figure 2) indicates monozygoticity. However, the absence of the 'twin peak' sign in later gestation does not necessarily indicate monozygoticity because of the regression of the chorion frondosum to form chorion leave as gestation progresses.

In the second and third trimesters, other parameters are relied upon for the determination of chorionicity. Confident signs of dichorionicity include discordant fetal external genital sexes (indicating dizygosity) and separate placental masses. Occasionally septal thickness or number of layers within the septum on high resolution ultrasound scan may also help in determination of the chorionicity.⁷

While separate discrete placental masses indicate dichorionicity, a single placenta does not necessarily indicate monozygoticity as fusion of separate placental masses in a DC twin pregnancy may appear as a single placenta on ultrasound scan. Indeed, the positive predictive value of a single placenta on ultrasound for monozygoticity is only about 50%.⁸⁻¹⁰ Caution also needs to be exercised when placental masses appear separate on an initial scan as there MC placentas may be bilobed.^{11,12}

Fetal sexes can be established through ultrasound with more than 99% accuracy in the second trimester, provided that a clear visualization of female genitalia is used to diagnose female sex.¹³ The presence of discordant sexes in the twins indicates DC placentas because only DZ twins can be discordant in sexes. On the hand, concordant sex does not necessarily mean monozygoticity because DC twins of the like-sex occur about 45% of the time. Thus with a positive predictive value of only about 40%⁸ when used as the sole diagnostic tool, fetal sex determination has to be combined with other ultrasound parameters to accurately determine chorionicity.

In the second trimester, septal thickness or number of layers can be assessed by high-resolution ultrasound scan to determine chorionicity. In DC pregnancies, the intertwin septa (4 layers) are thicker (2mm or more in a DC placenta)¹⁴⁻¹⁶ than in MC pregnancies (2 layers or less than 2 mm). The 4 layers comprises of 2 outer chorionic membranes (which is absent in MC twins) and 2 inner amniotic membranes resulting in the DC septum being well-defined and imaged over a long segment. Conversely, the MC septum appears wispy and visualized in short segments. In a study involving 150 twin pregnancies, the average septal thickness for DC and MC placentas are 2.2 mm (0.7 - 4.1 mm) and 0.9mm (0.6 -1.2 mm) respectively.¹⁷ In a study done in 1996, Vayssiere et al. reported success in correctly determining chorionicity in 60 out of 63 cases by counting the number of layers in the intertwin septa in the second and third trimesters using high-resolution ultrasound scan.¹⁸ Another study showed a 100% positive predictive value for DC placentation and 95%

Table 1. Summary of PPVs of ultrasonographic parameters in the second and third trimesters for the prediction of chorionicity

| | Monochorionicity | Dichorionicity |
|--|---------------------------|---------------------------|
| Placental masses | Single (~50%) | Separate (~100%) |
| Fetal genitalia sex | Concordant (~40%) | Discordant (~100%) |
| Number of layers in intertwin membrane | 2 (~95%) | 3-4 (~100%) |
| Intertwin membrane thickness | <2mm (~82%) ¹⁶ | >2mm (~95%) ¹⁶ |
| 'Twin peak' sign | Absent (~45%) | Present (~100%) |

for MC placentation.¹⁹ However, determining chorionicity by this method is hampered by great intra- and inter-observer variation and thus limiting its usefulness.

In the third trimester, the use of any single ultrasound parameter cannot accurately predict chorionicity because of poor visibility due to obstruction by fetal body parts. Thus a composite of all the ultrasound parameters is required with a good positive predictive value of 97% in determining monochorionicity.⁸

WHY SCREEN FOR CHORIONICITY?

Compared to DC twins, MC twins contribute disproportionately to the increased perinatal mortality and morbidity in twin pregnancies.¹ The higher complication rates in MC twins include non-specific ones such as miscarriages, preterm labour, intrauterine growth restriction (IUGR) and perinatal mortality, and specific ones such as twin-to-twin transfusion syndrome (TTTS), twin reversed arterial perfusion (TRAP) sequence. Furthermore certain subsets of MC twins such as monoamniotic twins and conjoined twins have a high risk of perinatal mortality. Management of fetal anomalies and impending intrauterine death of one twin is also complicated by monochorionicity.

In today's obstetric practice and medico-legal climate, determination of chorionicity would definitely triage twin pregnancies into low and high risk ones, which allows implementation of different surveillance and management strategies.

Miscarriage and perinatal mortality

Monochorionicity is associated with increased risk of miscarriage.²⁰ The overall miscarriage risk of twin pregnancies with both fetuses viable at early ultrasound scan is about 5%. However, this risk can

be broken down into 2% for DC twins and as high as 12% for MC twins.²¹ This is again probably due to the effects of TTTS and severe growth discordance which is much more common in MC twins. In a study done in 1997,²² it has been shown that in MC pregnancies, the risk of fetal loss before and after 24 weeks is 6 times and 2 times respectively compared to DC pregnancies.

Determination of chorionicity is important for the management in an event of an intrauterine death of 1 twin.²³ For MC twins, the surviving MC twin has a 25% risk of demise and 25% risk of neurological damage (such risk is much lower in DC twins).^{22,24} This is due to secondary haemorrhage into the demised twin through placental vessel connections causing severe hypotension and acute haemodynamic imbalance leading to ischaemia in the surviving twin. As such, survival of the healthy co-twin depends on the extent of superficial anastomoses on the placenta between the MC twins. Management depends on the gestational age. At later gestational ages, early delivery may be considered to reduce distress in parents although damage to the co-twin, if any, is usually present within hours of the event. At earlier gestation, parents have to be prepared psychologically that the surviving twin may suffer from co-twin sequelae such as neurological deficits although the best management is to prolong the pregnancy under close surveillance.

On the other hand, intrauterine demise of a single fetus in DC twins is seldom a risk factor for the survival of the healthy co-twin as there is no placental vasculature anastomoses between them.

Perinatal mortality is also significantly higher (6 times) in MC twin pregnancies compared to DC pregnancies.²¹ This is likely to be due to the higher

incidence of preterm labour that is complicated by TTTS²⁵ and fetal growth discordance. In a population-based cohort study done in Nova Scotia, Canada from 1988 to 1997, it has been found that perinatal mortality of both twins was significantly higher in MC twins compared to DC twins.¹

Twin-to-twin transfusion syndrome (TTTS)

Chronic TTTS is one condition that is unique to MC twins. From the MC twins, the two separate sets of fetal arteries and veins emerge from their respective cord insertions and start attaching to the chorionic plate of the single placenta. At the vascular equator, both twins complete to be attached to the placenta. As a result; several combinations of anastomoses between the fetuses can form-arterio-arterial (AA), veno-venous (VV) and arterio-venous (AV). The formation of AV anastomoses is the key to TTTS.²⁶ Such a connection allows only unidirectional flow down the pressure gradient from the artery to the vein and thus blood flows from the donor twin to the recipient twin.

As a result of such connections, the effects of TTTS usually manifest in the early trimester. Through ultrasound examination, there is a characteristic discordant amniotic fluid volume. This means that the donor twin will experience oligohydramnios with restricted growth and a small bladder. On the other hand, the recipient twin will exhibit polyhydramnios and an enlarged bladder (polyuric).²⁷⁻³⁰ If no intervention takes place and pregnancy is allowed to proceed, the recipient twin will begin to show features of congestive cardiac failure such as cardiac hypertrophy, cardiomegaly, tricuspid regurgitation and hydrops.^{31,32}

Untreated TTTS in MC pregnancies brings about high perinatal mortality of about 60 to 100%.^{28,33,34} Although this condition only affects about 0.0001 to 0.0005% of total pregnancies, it accounts to about 1% of total perinatal mortality.³⁴ Indeed if TTTS is diagnosed early through ultrasound screening and chorionicity determination, such figures can be reduced. The major cause of perinatal mortality in TTTS is due to preterm labour secondary to polyhydramnios in the recipient twin sac. The recipient twin may die from pulmonary hypotension,³⁵ right ventricular outflow obstruction³¹ and renal failure.³⁶ The donor twin is not spared and may suffer from severe intrauterine growth restriction. In addition, TTTS also increases the risk of perinatal morbidity such as sequelae of preterm delivery and acquired intrauterine brain damage leading to neurological handicap.

However, fortunately, TTTS only complicates about 10-15%³⁷ of MC pregnancies when almost all MC twins would have a variable extent of blood vessel

anastomosis between them. This is because TTTS is associated with a paucity of compensatory surface communications that are bi-directional and thus help to keep AV transfusions in check.⁴ The effects of TTTS only develop when there is a chronic haemodynamic imbalance that is build up by deep unidirectional AV anastomoses. Thus if there are enough bi-directional superficial AA or VV anastomoses present, then whatever blood that is pumped into the recipient can be neutralized by a net flux of blood back to the donor through these surface connections.

The diagnosis of TTTS is primarily by ultrasound screening in the early mid-trimester.²¹ Through ultrasound scanning, the diagnosis of TTTS is made when 3 criteria is met. Firstly, there must be a polyhydramnios-oligohydramnios sequence meaning there must be marked discordancy in amniotic fluid volume between the twins. Secondly, a diagnosis of MC twins is preferably made in early gestation, or presumed in concordant sex twins with a single placenta presenting with the first criteria. Thus this underlies the importance of screening for monochorionicity. Lastly, other causes of polyhydramnios such as fetal anomalies and infection have to be excluded.³⁸

There are many treatment options for TTTS, namely amnioreduction, septostomy (puncturing the intertwin membrane) and endoscopic laser ablation.³⁹ The goal of aggressive serial amnioreduction and septostomy is to attempt to normalize the amniotic fluid volume in both sacs. Obviously this form of treatment does not address the underlying pathology. Laser ablation is a recently established treatment for TTTS during which anastomoses between the MC twins are identified on the placenta and ablated through laser energy. This treatment curtails inter-twin transfusion. However, laser ablation has a higher risk of procedure-related fetal loss compared to the other treatment modalities.³⁹ Both laser ablation and amnioreduction has been shown in large cohort studies to have a success rate of 60% to 65%.⁴⁰⁻⁴³ It has recently been suggested that safer, simpler but less effective procedures such as amnioreduction and septostomy are preferred for cases with good prognosis. Laser ablation, which has shown to be slightly more effective but is associated with higher fetal loss, is reserved for cases of TTTS with a poor prognosis.³⁹ The recent Eurofetus randomized controlled trial comparing laser ablation and amnioreduction showed that laser ablation was associated with a higher survival rate than amnioreduction, irrespective of stage.

Acute TTTS usually occur late in the third trimester or during labour (usually in the interval between cord clamping of the first twin and the delivery of the second twin). This condition is usually not lethal but it

represents an acute shift of blood from one twin to the other. The incidence of acute TTTS may be reduced by simultaneous clamping of both umbilical cords at Caesarean section.

Twin reversed arterial perfusion sequence (TRAP)

TRAP, otherwise known as acardiac malformation or twinning is a very rare condition (~1%) in MC pregnancies.^{44,45} It is a congenital vascular abnormality in which cord insertions from the MC twins are so close that a single large arterio-arterial anastomosis between the MC twins forms. This results in an acardiac 'perfused' twin who receives deoxygenated blood from the structurally normal 'pump' twin. As such the 'perfused' twin suffers from underdevelopment of the head, heart and upper limbs due to inadequate nourishment and oxygenation. The 'pump' twin is not spared either because toxic products from the regressing 'perfused' twin is constantly flowing back to the 'pump' twin through veno-venous anastomoses. As a result, the 'pump' twin has a 50% mortality rate due to either cardiac failure, hydrops or prematurity and the 'perfused' twin always die (100%).²¹

There are no randomized control trials to find out what is that optimal clinical management of TRAP. However, case series has recommended fetal ultrasound surveillance and intervention when there is ultrasound evidence that suggest fetal hydrops and polyhydramnios.^{46,47}

The definitive treatment for the TRAP sequence is either cord occlusion or intrafetal cord ablation using a variety of ablative modalities.⁴⁸

Intrauterine growth restriction

Most intrauterine growth restriction (IUGR) is due to chronic placental insufficiency.⁴⁹ Generally, twin pregnancies are 10 times more likely to deliver growth-restricted babies.⁵⁰ It is very common for twins to have a birth weight discordance of around 15%. However, what is pathological growth discordance is still debatable due to different diagnostic criteria. Many believed that discordant fetal weight of more than 30% difference (95th percentile cut off level) is considered pathological.²¹ It is important to monitor IUGR in twin pregnancies because it contributes in causing preterm delivery and high perinatal mortalities and morbidities.

In a recent study, the results showed that MC pregnancies are more likely to suffer from IUGR (34% chance) of at least one twin compared to DC pregnancies (23%). On top of that, the risk of both twins suffering from IUGR is 4 times more in MC pregnancies compared to DC pregnancies.⁵¹

There is also evidence to show that the type of cord insertion also plays a part in growth discordance in MC pregnancies. In severe growth discordance in MC twins, the cord of the larger twin is usually paracentrally inserted and thus occupy a larger portion of the placenta. The smaller twin usually has a velamentous and marginal insertion²⁶ and thus suffers from chronic placental insufficiency.

Thus screening for monochorionicity is important in intrauterine growth because it may be caused by TTTS (which is unique to MC twins), differences in cord insertion and placental insufficiency in MC twins. Management of IUGR is based on serial ultrasound scanning of the twins to monitor fetal growth. In MC twins, scanning starts as early as 16 weeks every fortnightly. Knowledge of chorionicity also dictates management in the case of an impending single intrauterine death as mentioned above.

The phenomenon of intermittent absent/reversed end-diastolic flow (AREDF) in the umbilical artery can be found in MC twins, usually in the presence of an arterio-arterial anastomoses (AAA). In singletons or DC twins, AREDF is the result of progressive increase in fetoplacental flow resistance. This results in fetal malnutrition and thus IUGR. However, in MC twins, AREDF may not have the same implications as singleton or DC twins. This is so because in MC twins there are almost always vascular communications between the fetuses. However, the presence of intermittent AREDF is still a poor prognostic factor in such twins.

Preterm delivery

The average length of singleton pregnancy is 39 weeks but around 35-36 weeks⁵²⁻⁵⁴ for twins. Preterm delivery is the number one most common cause of perinatal mortality in twin pregnancies. Up to 60% of twin pregnancies deliver prematurely and approximately 12% weigh less than 1500g.⁵⁵ MC twins are at a greater risk of premature labour than DC twins.⁵⁶ A study shows that the proportion of MC twins being delivered very preterm (less than 32 weeks) is 9.2% compared to 5.5% in DC twins.⁵⁷ This is likely to be due to a higher incidence of TTTS⁵⁸ causing polyhydramnios⁵⁹ and structural anomalies in MC twins.

Thus in MC pregnancies, mothers and obstetricians alike can expect a higher chance of preterm delivery. As such, management of MC pregnancies can be adjusted to cope with preterm delivery. Measures such as increased surveillance during pregnancy,⁶⁰ cervical cerclage and tocolysis may be implemented. However the usefulness of such measures are questionable although a study demonstrated reduction in preterm labour of up to 20% with early and routine ultrasound screening.⁶¹

Diagnosis and Management of Fetal Anomalies

The incidence of certain congenital malformations such as anencephaly and hydrocephalus are more prevalent in like-sex twins than unlike-sex twins.⁶² Congenital cardiac defects are about twice as common in monozygotic twins than in dizygotic twins. Acardiac and conjoint twinning are specific to MC twins. Although there is no concrete evidence available, the above relationships are likely to be explained by the higher probability of monochorionicity in like-sex twins and monozygotic twins (67%).⁶³ Thus MC pregnancies probably have a higher risk of fetal anomalies.

Monochorionicity also influences the diagnosis of fetal anomalies. Non-invasive screening for Down syndrome in twins mainly involves ultrasound scanning to assess nuchal translucency and biochemical tests. However, it has been reported that using nuchal translucency as a parameter to screen for aneuploidy results in a higher false positive rate in MC pregnancies than in DC pregnancies.⁶⁴ This could be explained by the early development of TTTS in MC twins. Invasive procedures such as amniocentesis and chorionic villus sampling can give definitive diagnosis of Down's syndrome. Determining the chorionicity also influences the choice of technique and interpretation of cytogenetic results concordant for sex.

Determination of chorionicity is also important to the management of fetal anomalies particularly discordant abnormalities. Usually in DC pregnancies, if the parents choose to terminate the abnormal twin, selective fetocide can be performed by intra-cardiac injection of potassium chloride in the abnormal fetus. This is unlikely to affect the normal co-twin because there are no vascular connections. However this is not true for MC twins who share the same placenta and thus inevitably have a variable extent of vascular communications which may allow potassium chloride into the normal twin.⁶⁵ Selective fetocide using potassium chloride is generally discouraged in MC pregnancies. Alternative methods using intravascular injection of fibrin glue, metal coils or ligation of the cord under direct vision can be performed.^{66,67} However these alternatives are limited by the adverse side effects such as intrauterine death, embolic hemorrhage, neurological sequelae of the normal co-twin and total pregnancy loss.

Monoamnionicity and conjoined twins

The prevalence of monoamnionicity in MC pregnancies is about 1-5%.²⁶ Diagnosis of monoamnionicity is possible with ultrasound scanning by showing the absence of an intertwin membrane in MC pregnancies. The accuracy of such screening can be improved by screening for monochorionicity early in pregnancies. Monoamnionicity has its own complications such as entanglement of the umbilical cords, TRAP sequence, congenital anomalies, prematurity, inter-twin locking during labour and rarely TTTS.⁶⁸⁻⁷⁰ These complications cause a high perinatal mortality of as high as 50-70%.^{71,72} Thus by accurately diagnosing monoamnionicity (possible with early monochorionicity screening), serial ultrasound scans can be arranged, which may improve perinatal outcome.

Conjoint twinning is an extremely rare occurrence—about 1.3 per 100000 births. All conjoint twins are MC twins as well. Perinatal survival depends on mainly the age of gestation on delivery and how are the twins joined.

CONCLUSION

Monochorionicity is a type of twin pregnancy, which has its own unique complications, which unfortunately have brought about a higher risk of mortality and morbidity. Comparatively, dichorionic pregnancies can be considered safer. Screening and diagnosing monochorionicity in the early gestation should be carried out routinely because knowledge of monochorionicity influences decisions in diagnosing and management of problems that may arise in the later part of pregnancy. This prepares the obstetrician by increasing surveillance and keeping a lookout for the common complications of monochorionicity. Indeed without chorionicity determination, the diagnosis of many conditions such as TTTS in pregnancies would be less clear.

The advanced and well-established screening methods are safe and can effectively and accurately determine chorionicity early in gestation. Perinatal mortality and morbidity can be reduced if there is early knowledge of can be reduced if there is early knowledge of chorionicity and thus effective management can be tailored for MC pregnancies.

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Editorial Note: It is important to screen and diagnose chorionicity type in the early gestation for twin pregnancy as it has important implications and it may be very difficult to assess chorionicity at the later stage.

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