Why is it important to diagnose chorionicity and how do we do it?

Geoffrey A. Machin* M D, Ph D, FRCPath (UK), FRCP (C)
Emeritus Professor of Pediatric Pathology, University of Alberta, Canada 3931 Cherrilec Cresent, Victoria, British Columbia, Canada, V8N 1R7

Because the monochorionic (MC) placenta is designed for a singleton fetus, and might not provide adequate physiological support for twins, obstetric problems are more frequent in MC than dichorionic (DC) twins. Problems arise because asymmetric cord insertions cause growth discordance as a result of unequal sharing of placental tissue. Approximately 95% of MC twin placentas contain interfetal vascular connections of some kind, sometimes in several combinations. Such connections can cause twin–twin transfusion syndrome and twin reversed arterial perfusion. The survivor can also suffer damage if the co-twin dies spontaneously or from inappropriate methods of selective termination. These complications are progressive and often advanced by 18 weeks gestation. Monoamniotic twins carry greater risks than diamniotic twins, especially entangled cords. MC twins are often discordant for congenital anomalies. Diagnosis of MC twinning is optimal in the first trimester. Optimal management of these MC twin disorders is not yet established; long-term follow-up studies are unsatisfactory. In clinical practice, chorionicity is not always determined in the first trimester.

Key words: twin; twinning; monochorionic; monoamniotic; dichorionic; diamniotic; umbilical cord; velamentous; marginal; demise; termination; ultrasound; twin transfusion; growth discordance; termination of pregnancy.

WHY IS TWIN CHORIONICITY IMPORTANT?

Two-thirds of monozygotic (MZ) twins split more than 2 days post-conception, resulting in twin fetuses who rely on a truly single (monochorionic, MC) placenta. Although such a placenta is optimal for a singleton fetus, the majority of MC twins nevertheless thrive in these unusual conditions. However, certain MC twins suffer from a group of inter-related disorders that are mainly caused by the vascular anatomy that is characteristic of MC twin placentas; these vascular disorders occur only very rarely in dichorionic (DC) twins. Each MC twin placenta is unique in its vascular composition, hence each MC twin pair has a unique clinical status. MC twin vascular disorders are progressive, difficult to manage, vary in severity and timing, and may be fully developed
by 18 weeks of gestation, at the time of dating ultrasound. MC twins and their complications are uncommon in the practice of any individual obstetrician and require specialized care over and above that needed for DC twins. MC twins occur in naturally and in artificially conceived multifetal pregnancies, and are frequent components of naturally conceived higher-order multifetal pregnancies (HOMPs).

When congenital anomalies occur in MZ twins (including MC twins), the twins are usually discordant. Such twins can mistakenly be assumed to be DZ (and DC). Unless special methods are used for selective termination of anomalous MC twin fetuses, both fetuses might be lost.

With some rare exceptions\(^2\), MC twinning is the gold standard in the diagnosis of monozygosity (MZ), which could be important in postnatal life. However, few parents of MC twins are given this information postnatally. Unfortunately, many parents of like-sexed DC twins are told that their twins are DZ, despite the well-known fact that one-third of MZ twins are DC.

For improved outcomes from vascular complications of MC twinning, the diagnosis of monochorionicity should be made as early as possible, so that treatment can be planned before end-stage disease is reached, commonly at 20–24 weeks gestation. The distinction between MC and DC twins is by identification of the so-called ‘twin peak’ (or ‘lambda’) sign by first-trimester ultrasound. Detailed assessment of septal membrane thickness and the number of membrane layers is also possible in the second trimester, although vascular diseases are often advanced by this time.

**CONTRASTING OBSTETRIC OUTCOMES IN DIZYGOTIC AND MONOCHORIONIC TWINS**

Table 1 contrasts outcomes in DC and MC twins pregnancies from recent reports in the literature.\(^3\)–\(^7\)

Another recent study in a health maintenance organization in Colorado, USA, showed that MC twins had higher frequency of adverse perinatal outcomes. MC twins were at significant risk for a very low birth weight (OR = 3.0) similar to that for preterm birth (OR = 3.8).\(^8\)

Additionally, a recent population-based study from Besançon, France, showed that MC twinning (OR = 6.0) and premature ruptured membranes (OR = 4.3) were significant risk factors for neurologic disability in infants born at < 33 weeks.\(^9\)

With one exception, these studies\(^3\)–\(^9\) show marked differences in outcomes of MC and DC twin pregnancies. The excess of adverse outcomes (perinatal death, neurologic morbidity) in MC twins is largely explained by vasculogenic events in MC twin placentas.

**VASCULOGENIC COMPLICATIONS OF MONOCHORIONIC TWINNING**

The principal disorders in MC twinning have overlapping causes and effects:

- severe growth discordance (SGD)
- twin–twin transfusion (TTT)
- twin reversed arterial perfusion (TRAP)
vascular instability in the absence of any of the above, resulting in congenital heart
disease of ‘flow’ type (usually in one twin) and brain lesions (in both twins)
impending fetal demise of a compromised fetus and selective reduction of a
compromised/anomalous fetus, with effects on the co-twin
long-term neonatal and pediatric morbidity from all of the above, affecting brain,
heart and kidneys
monoamniotic (MA) twins have additional risks because of cord complications
special types of ‘blood-borne concordance’ in MC twins who are actually discordant
for congenital abnormalities.

THE VASCULAR STRUCTURES OF MONOCHORIONIC TWIN PLACENTAS

There are two vascular determinants of clinical behavior in MC twins: (i) combinations
of cord insertions; and (ii) types, combinations and flow directions in inter-twin vascular
connections on and in the placenta.

Cord insertions

In singleton placentas, velamentous (1%) and marginal (9%) cord insertions are rare10;
they are far more common in twins. They are thought to arise from a process of
trophotropism, i.e. only that part of the original trophoblastic sphere that is fully
implanted in the endometrium survives as the placenta proper. The remaining chorionic
tissue regresses to form the chorionic membrane. It is not known why a small number of
singleton cord insertion sites do not face the endometrium but velamentous and
margin insertions (VMI) presumably result when the cord insertion is ‘marooned’ from

<table>
<thead>
<tr>
<th>Reference</th>
<th>Location</th>
<th>Study type</th>
<th>Outcome measures</th>
<th>MC</th>
<th>DC</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Nova Scotia, Canada</td>
<td>Population</td>
<td>PND</td>
<td>35/588 (5.9%)</td>
<td>25/1468 (1.7%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean BWD</td>
<td>11.7%</td>
<td>11.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BWD &gt; 25%</td>
<td>8.6%</td>
<td>6.5%</td>
</tr>
<tr>
<td>4</td>
<td>Mumbai, India</td>
<td>Population</td>
<td>PND</td>
<td>18%</td>
<td>9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BWD</td>
<td>35%</td>
<td>14%</td>
</tr>
<tr>
<td>5</td>
<td>Tochigi, Japan</td>
<td>Referral</td>
<td>NND to 1 year</td>
<td>4/88 (4.5%)</td>
<td>6/328 (1.8%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Neurologic disability</td>
<td>5.7%</td>
<td>1.8%</td>
</tr>
<tr>
<td>6</td>
<td>Birmingham, UK</td>
<td>Referral</td>
<td>PND</td>
<td>3/48 (6.2%)</td>
<td>14/190 (6.2%)</td>
</tr>
<tr>
<td>7</td>
<td>Toronto, Canada</td>
<td>Referral</td>
<td>Infants of 24–30-weeks</td>
<td>39%</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>gestation surviving</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>18–24 months; death</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>and neurologic disability</td>
<td></td>
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</tr>
</tbody>
</table>

In ref. 3 there were more double fetal deaths in MC (2.8%) than DC (0.5%) pregnancies. In ref. 6 TTT
was present in 14/44 (32%) MC pregnancies and was responsible for 7/9 adverse outcomes. All MC infants
with adverse outcomes had birth weight discordance ≥ 25% and this was true of 4/12 (33%) DC infants.
The basis for the anomalous result in ref. 7 is not clear. In ref. 8 adverse outcomes were found in 42% of
twins with TTT. BWD, birth weight discordance; DC, dichorionic; MC, monochorionic; NND, neonatal
death; PND, perinatal death; TTT, twin-twin transfusion.
the placenta proper as trophoblast regresses elsewhere for lack of endometrial support. It is easier to see why VMI is more common in DC twins, where there is the likelihood that implanting placentas will collide or interfere with each other's implantation process, with aberrant trophoblastic regression. In MC twinning, however, VMI can be explained by the fact that the intercord distance is already determined before implantation and the single placenta is unable to 'spin' or 'adjust' once it has implanted. If cords are inserted far apart on the early disc, one cord insertion might be exposed by trophotropism. VMI cords are found in 43% of MC twins (Table 2).

The combination of cord insertion sites within MC twin pairs affects clinical outcomes. In SGD, the cord of the larger twin is usually paracentrally inserted (PCI), whereas the smaller twin has a VMI (Figure 1). In TTT, the donor often has VMI and the recipient has PCI, but this not always so and SGD is not a component in the diagnosis of

<table>
<thead>
<tr>
<th>Chorionicity</th>
<th>Marginal or velamentous</th>
<th>Central or eccentric</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC</td>
<td>226</td>
<td>43%</td>
<td>524</td>
</tr>
<tr>
<td>DC</td>
<td>199</td>
<td>23%</td>
<td>858</td>
</tr>
<tr>
<td>Total</td>
<td>425</td>
<td>31%</td>
<td>1382</td>
</tr>
</tbody>
</table>

Figure 1. Postpartum MC/DA placental perfusion, showing unequal sharing secondary to asymmetric cord insertions. Twin A (on the left) has a marginal cord insertion, whereas the cord of twin B is centrally inserted. The vascular equator runs vertically between the cord insertions and is defined by the vascular connections. There is markedly unequal placental sharing in favour of twin B. Placental parenchyma to the left of the equator returns to the twin A.
TTT. TRAP twins usually have closely adjacent cord insertions, allowing the presence of large direct vascular connections between the roots of the cords. Many MA twins also have adjacent cord insertions, and their cords are always entwined. This causes difficulty in rare cases requiring treatment for TTT or in which selective termination is considered. The relative frequency of types of cord insertion in clinical conditions found in MC twins are shown in Table 3.

In a comparison of SGD (>20%) in DC and MC twins, velamentous cord insertion was associated with a 13-fold risk of growth discordance in MC twins. A total of 46% of such cases had growth discordance. In MC twins this can be severe enough to cause oligohydramnios in the restricted twin. However, it should not be confused with TTT, in which both oligohydramnios and polyhydramnios are present.

### Interfetal vascular connections

The primitive villous circulation develops independently of the fetal cardiovascular system. As fetal veins and arteries grow out from the umbilical cord on to the surface of the placenta, they capture cotyledons and connect with the underlying primitive villous sinusoids via scattered foramina in the chorionic plate, one for each cotyledon. Thus, in the course of each artery/vein pair on the chorionic plate, there are only two fixed points: cord insertion and the cotyledonal foramen. Elsewhere, arteries and veins run independently on the chorionic plate, but always converge in artery/vein pairs on the foramina, where they enter and leave the underlying parenchyma via the stem villi. In MC twin placentas, the two sets of fetal arteries and veins emerge from the cord insertions and run across the chorionic plate, seeking to ‘colonize’ or ‘imperialize’ cotyledons. For most zones of MC twin placentas, appropriate artery/vein pairs are connected to each cotyledon. However, the MC twin placenta has a vascular equator, which is a band of tissue running across the placenta at right angles to the intercord insertion line and roughly equidistant between the cord insertions. At the vascular equator, both twins compete to acquire cotyledons—any given foramen can be captured by an artery/vein pair from one twin or by an artery from one twin and a vein from the other twin. This latter arrangement gives rise to the arterio-venous connection.
(AVC), which is the key element in the development of TTT (Figure 2). In an AVC, the artery and vein do not communicate on the surface. Rather, they pass into the cotyledon in the usual way. Net transfusion always occurs in an AVC down the arterio-venous pressure gradient. An AVC can be recognized at fetoscopy or postpartum by the fact that the feeder artery and draining vein traverse a common foramen. The number of AVCs varies in MC twins, and they are often bidirectional (Figure 2).
As arteries grow out across the fetal surface, they might encounter arteries from the other twin and form direct, end-to-end arterio-arterial anastomoses (AAAs). A similar process results in veno-venous anastomoses (VVAs). (Note: veins never form direct, end-to-end connections with arteries on the surface. An AVC consists of an artery and vein from different twins that traverse the same cotyledonary foramen but connect at the capillary level in the villi.) The majority of MC twin placentas contain one AAA, seldom more. In contrast, VVAs are much less common but, when present, there may be several per placenta. The relative rarity of VVAs might result from low flow rates and pressures in chorionic plate veins and VVAs, with spontaneous thrombosis/sclerosis. The structure and function of fetal vascular connections are contrasted in Table 4.

### CLINICAL CORRELATIONS WITH INTERFETAL VASCULAR CONNECTIONS

Interfetal vascular connections are present in 95–98% of MC twin placentas. Clinical outcomes depend on diameters and directions of flow in these various connections. Table 5 shows the mean number and type of vascular connections seen in MC twin placentas of several clinical subtypes.12

#### Table 4. Structure and function of interfetal vascular connections in MC twin placentas.

<table>
<thead>
<tr>
<th>Type</th>
<th>AVC</th>
<th>AAA</th>
<th>VVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Majority of placentas, Up to 2–5 per placenta</td>
<td>Majority of placentas, One per placenta</td>
<td>15–20% of placentas, Up to 2–3 per placenta</td>
</tr>
<tr>
<td>Flow/pressure</td>
<td>Always present, low pressure</td>
<td>High pressure. No net flow if twin cardiac outputs are equal</td>
<td>Low pressure. Not net flow if twin cardiac outputs are equal. Potential for rapid transfusion of large volumes</td>
</tr>
<tr>
<td>Flow direction</td>
<td>Unidirectional in each AVC but different AVCs can flow in opposite directions</td>
<td>Bidirectional, minimal, pulsatile</td>
<td>Bidirectional, minimal, non-pulsatile</td>
</tr>
</tbody>
</table>

AAA, arterio-arterial anastomoses; AVC, arterio-venous connection; VVA, veno-venous anastomoses.

#### Table 5. Mean numbers of vascular connections in MC twin pairs with subtypes of clinical disease.12

<table>
<thead>
<tr>
<th>Clinical status</th>
<th>All connections</th>
<th>AAA</th>
<th>VVA</th>
<th>AVC, both directions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe TTT</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Mild TTT</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>SGD</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Controls</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

AAA, arterio-arterial anastomoses; AVC, arterio-venous connection; SGD, severe growth discordance; TTT, twin–twin transfusion; VVA, veno-venous anastomoses.
Severe growth discordance

Whereas differential cord insertions are the main factor in SGD, these pregnancies have fewer superficial connections than control MC placentas (Table 5).

Antenatal chronic twin–twin transfusion

This occurs when there is steady, unidirectional flow in a dominant (causative) AVC that is compensated inadequately or not at all by any contradirectional flow in coexisting connections elsewhere on the vascular equator. The severity of TTT is variable and is probably determined by the combination and direction of interfetal vascular anastomoses. A single AVC in the absence of any other effective connections dooms the twins to early, severe TTT (Table 5).

There are two routes by which flow in the causative AVC can be compensated: (i) by an AVC in the opposite direction; and (ii) by surface AAAs or VVAs that allow the recipient to download to the donor across a newly established pressure gradient, thereby establishing a dynamic equilibrium. Fortunately, the majority of MC twin placentas contain combinations of these connections. Although transfusion is always taking place across AVVs, the complexity of different connections does not permit imbalance and development of TTT. The presence of an AAA largely protects against the development of TTT14; TTT that occurs in the presence of an AAA or bidirectional AVVs is usually mild. At fetoscopy for laser vascular coagulation, the characteristic anatomy of the AVC is easily seen.

Twin reversed arterial perfusion

Cord insertions are usually as close as 2–3 cm and there is one large AAA and one large VVA between the roots of the cords. The pump twin perfuses the whole of the placenta with normal artery/vein pairs to all cotyledons. The acardiac twin is effectively a side branch from the umbilical vessels of the pump twin. ‘Twice-used’ blood flows back in the VVA from acardiac to pump twin. Simply stated, this blood has perfused both twins without a replenishing cycle through the placenta. Toxic products from the regressing body of the acardiac twin are transferred directly to the brain of the pump twin. Flow in the VVA is also sluggish, with a tendency to thrombosis and the risk of cerebral thromboembolism in the pump twin.

Vascular instability

In the absence of TTT or demise of one twin, MC twin pairs can be discordant for specific types of congenital heart disease thought to result from transient reduced flow through ventricles and great vessels during cardiogenesies, i.e. as early as 4–6 weeks of gestation. These ‘flow’ lesions include left heart hypoplasia and pulmonary atresia.15

Impending fetal demise—selective reduction

When there is impending fetal demise or an indication for selective termination (e.g. TTT, SGD, discordant anomaly), standard technical methods used for singletons and DC twins cannot be applied because the intracardiac toxic agents rapidly reach the intended survivor twin via interfetal vascular anastomoses, resulting in the loss of both
twins. This ‘problem’ becomes an advantage when selective reduction is used in HOMPs containing MC twins, because the high-risk MC twin pair can be selectively reduced by one procedure. However, during spontaneous fetal demise of one MC twin, the other twin might develop cystic encephalomalacia. Fetal rescue should therefore be planned and implemented before fetal demise: the types and directions of interfetal connections should be considered in management options. Selective termination in TRAP is straightforward because placental vascular distribution to and from the placenta by the pump twin is not disturbed when the circulation to the acardiac twin is interrupted. This is because the pump twin is already perfusing the whole placenta. However, in all other MC twin pairs—in which both twins have cardiac activity and have been perfusing their respective placental zones—the death of one twin opens up the body and placental territory of that twin as potential sumps in which blood from the intended survivor could pool. Thus the prognosis for the survivor in TTT is better when the donor dies first than when the recipient dies first (Table 6). Two factors account for this: (i) the causative AVC does not permit retrograde flow back from recipient to donor; and (ii) the placental territory of the donor is frequently small, limiting blood loss from the surviving recipient. The converse applies when the recipient dies first—the surviving donor might bleed across the causative AVC into the recipient and/or its placental zone, with consequent hypotension and bradycardia. It might be necessary to consider ablation of any connecting vessels before cord ablation. When terminating a small fetus with SGD, the small placental zone probably does not pose a threat of significant blood loss by the larger twin.

**Long-term neonatal and pediatric morbidity in surviving monochorionic twins**

*Survival rates and neurologic outcomes*

Despite their high risks, there are few large, population-based studies investigating the long-term health of MC twins. In a comparison between 164 DC and 44 MC twin pairs, the relative rates of death and major neurologic handicap were 3.6% and 10.2%, respectively. The single best predictor of adverse outcome in 59 MC twin pairs was amniotic fluid volume discordance, although hemoglobin discordance also correlates well with adverse outcomes. Vascular instability in the absence of TTT might have caused a concordant Pena-Shokeir phenotype in an MC twin pair of a triplet pregnancy. These studies probably contain MC twins with several vasculogenic disorders, predominantly TTT and SGD.

Follow-up in specific subgroups, such as TTT, is reported in a few small series. In a series of 47 TTT twin pairs, 49 (52%) survived. Of these survivors, 40 were followed; 13 (32%) had specific delayed language development and/or minor neurologic dysfunction whereas nine (22%) had severe psychomotor retardation with cerebral

<table>
<thead>
<tr>
<th>Fate of co-twin</th>
<th>Recipient died first (n = 16)</th>
<th>Donor died first (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-twin fetal demise</td>
<td>9/16</td>
<td>0/10</td>
</tr>
<tr>
<td>Severe anemia of survivor</td>
<td>7/7</td>
<td>1/10</td>
</tr>
<tr>
<td>Brain lesions of survivor</td>
<td>6/7</td>
<td>2/10</td>
</tr>
</tbody>
</table>

Table 6. Vascular anatomy and results of single fetal demise in 16 pairs of MC twins with TTT.
Of eleven TTT pairs with fetal death of one twin, three survivors died in the neonatal period, two had severe neurologic deficits and two had cerebral echodensities by ultrasound. In a study comparing the incidence of echogenic white-matter lesions in twins, 12 (30%) of 40 MC twins and 2 (3.3%) of 62 DC twins were affected. Detailed placental examination showed that superficial vascular connections were present in these cases and that VVA were strongly associated with white-matter necrosis.

The main discussion point in the treatments available for TTT concerns the neurologic status of survivors. A cohort of 89 TTT survivors was tested for neurologic outcome at a median of 21 months. Of these, 69 (78%) were intact, 10 (11%) had minor deficiencies and 10 (11%) had major neurological handicaps. It is certainly clinically valid to consider TTT as displaying a spectrum of severity. ‘Milder’ cases respond to amnioreduction because they have several vascular connections that are re-established by removing amniotic fluid volume and pressure. However, ‘severe’ cases often have a single causative arterio-venous anastomosis and early laser therapy might be the only route to intact survival. However, large series with detailed placental study are required before the role of vascular connections can be fully clarified in terms of outcome.

Cardiac disease

MC twins might have structural congenital heart disease of the ‘flow’ type. Such lesions are not necessarily the result of the abnormal MZ twinning itself, nor do they indicate genetic discordance in MZ twin pairs. Rather, they are thought to rise through abnormal transcardiac flow, either in early cardiogenesis or as the result of chronic antenatal TTT. In a series of 73 TTT pairs, seven (9.6%) of recipients developed right ventricular outflow tract (RVOT) obstruction. Four recipients died with RVOT atresia. In a similar study of 17 TTT pairs, all recipients showed varying degrees of right heart failure in utero and 45% of the surviving recipients had residual right ventricular hypertrophy and/or dilatation that resolved in the ensuing 6 months after birth. A large study of 136 MC twin pairs showed a prevalence of structural congenital heart disease in 6/87 (6.9%) of TTT survivors and 4/177 (2.2%) of MC twins without TTT, whereas the incidence in TTT recipients was 5/42 (12%). One of the non-TTT twins had aortic coarctation but the majority of the other lesions were right-sided obstructions. Assuming that right ventricular obstruction represents a response to decreased forward flow, increased blood viscosity and a combination of these factors, left-sided lesions might have a similar pathogenesis in early disturbed aortic flow during cardiogenesis without overt TTT.

Renal disease

Transient or permanent postnatal oliguria is described in TTT donor survivors, usually on the basis of renal tubular dysgenesis. Abnormal proximal convoluted tubular structure and function is probably caused by renal hypoperfusion. These permanent injuries must already be present in fetal life and might account for paradoxical cases of TTT in which the donor fetus does not appear to respond to adequate treatment.

Whereas neurologic disorders in surviving MC twins can be caused partly by prematurity and partly by placental vascular considerations, cardiac as well as renal structural changes are attributable entirely to the vascular structures of MC placentas, with the added factors of specific clinical conditions such as SGD, TTT and fetal demise.
Monoamniotic twins

In addition to the vasculogenic risks of monochorionicity, monoamniotic (MA) twins (5% of MC twins) incur other potential complications that increase their risks above those of MC, diamniotic (DA) twins. It has been suggested that MA twins do not develop TTT because their close cord insertions ensure that large AAAs and VVAs run between the roots of the cords.32 In general, it is hard to make the diagnosis of TTT in MC/MA twins when oligohydramnios and polyhydramnios cannot be present by definition. However, one potential case of TTT with polyhydramnios and hydrops has been reported in MA twins.33 (In my personal practice, I have seen two such cases, both with atypically remote cord insertions.)

Unlike TTT, TRAP is found quite frequently in MA twins, probably because the close cord insertions are favorable to this condition. Indeed, a recent review of 25 MA twins found 2 cases of TRAP.34 Regardless, virtually all MA twins have entwined cords from early gestation.35 These often quite complex entanglements can cause single or double fetal demise simply through umbilical venous compression. A notched arterial velocity waveform,36 and color flow Doppler detection of extremely high umbilical venous flow37 are clues to cord entanglement. One reason to favor cesarean section for MA twins is the fact that the nuchal cord of the presenting twin might actually belong to the second twin.38 In a series of twelve MA twins pairs diagnosed in the first trimester, the outcomes were poor because four pairs were conjoined, four were discordant for major regional anomalies and four structurally normal pairs had cord entanglement; only two pairs survived.39

Discordance for anuria caused by urinary tract malformation can be particularly confusing because normal urinary production by one twin into the common amniotic cavity masks the effects of anuria on the part of the other twin, including Potter’s oligohydramnios syndrome, especially lethal pulmonary hypoplasia.40

Blood-borne concordance in monochorionic twins

Neonatal hypothyroidism is frequently (85%) caused by defective differentiation and/or migration of the thyroid gland (thyroid dysgenesis). In two large databases of congenital hypothyroidism screening programs, five MZ twin pairs were found to be discordant for thyroid dysgenesis.41 All pairs were MC/DA and had potentially misleading results for thyroid screening, with less elevated thyroid stimulating hormone (TSH) levels than would be expected in the twins with hypothyroidism. At definitive diagnosis, there was a 7-fold increase in TSH levels over those found at screening. This was taken as evidence of a protective effect during fetal life, in which the normal co-twin transfused euthyroid blood to the thyroid-deficient co-twin. Under such circumstances, the diagnosis of neonatal hypothyroidism might be delayed in discordant MC/MZ twins.

Retrospective analysis of newborn blood spots in some leukemic children has identified infrequent monoclonal cells with gene fusion sequences identical in breakpoint with cells from the overt leukemia that subsequently developed.42 Unique and identical breakpoints in fusion genes have now been found in MC/MZ twins who both developed common acute lymphoblastic leukemia at 3 years 6 months and 4 years 10 months of age.43 Transplacental transfusion of mutated cells probably occurred in fetal life.
General comments on vascular structures

In all of these considerations, one must remember that the interfetal vascular connections established in early pregnancy do not remain constant thereafter. Cases of TTT with atypical late onset can be caused by thrombosis in the venous arm of a compensatory AVC, disturbing a previous dynamic equilibrium. It seems likely that there are more AVCs and VVAs in early gestation than later. VVAs are particularly dangerous because they permit large and rapid flows at low resistance. The higher fetal loss rate before 24 weeks gestation in MC/DA versus MC/DC twins (12% versus 2%) could in large part be caused by vascular complications, including TTT. It is crucial to recall that each MC placenta has its own pattern of cord insertions and vascular connections, and that these connections are the cause for the unique and dangerous conditions that largely determine clinical outcomes in MC twins. Further progress is needed to apply available postpartum knowledge to the in vivo MC twin pregnancy. Unfortunately, none of this will be relevant unless MC placentation is diagnosed in early pregnancy.

Diagnosis of monochorionic twin pregnancy, and its complications

The prime objective of obstetric ultrasound in multifetal pregnancy is the unequivocal determination of chorionicity and the ascertainment of MC twins. It is generally recommended that a sequence of factors be considered: fetal external genital sex, placental masses and septal thickness. However, MC twins can be unlike-sexed, either because of anomalous development after in vitro fertilization (IVF) with blastocyst transfer or because of postzygotic chromosome abnormality (heterokaryotypia). Counting placental masses can be unreliable, as evidenced by two reports of bilobed MC twin placentas. (In my own practice, I have seen eight such cases in approximately 600 consecutive MC twin pregnancies. The ultrasound examination in all eight cases concluded that placentation was DC on the basis of two distinct placental masses, despite failure to see a lambda sign. There were no adverse outcomes.) Under these circumstances, diagnosis should principally rest on assessing the membranous septum. Terms such as ‘thick’ and ‘thin’ are best used without absolute quantitative measurements. The two amniotic layers of the MC twin placenta are ‘wispy or faintly seen and visualized in short segments’ (Figure 3a). In contrast, the DC septum is ‘well-defined and imaged over a long segment’ (Figure 3b). The ‘lambda’ or ‘twin peak’ sign for DC, and the ‘T’ sign for MC, are identifiable in the majority of cases. In this series of 150 twin pregnancies diagnosed at 10–14 weeks and with histologic confirmation of chorionicity in like-sexed twin pairs, one DC pair was incorrectly diagnosed as MC on the basis of septal membrane thickness and a ‘T’ sign. No MC pairs were misdiagnosed as DC. Septal thickness was 2.2 mm (range 0.7–4.1) and 0.9 mm (range 0.6–1.2) in DC and MC placentas, respectively.

Whereas it is acceptable to err on the side of caution and to suspect monochorionicity because of thin septal membranes, it is best to avoid the use of imprecise terms such as ‘sacs’, which could imply either chorionic layers or amniotic layers. There might be an undue tendency to concentrate on the number of amnions rather than the number of chorions, such that chorionicity is never actually stated in the report. Considering the rarity of MC/MA twins, it is not justified to look very carefully for amnions at the expense of delineating the number of chorions. MC/DA twins have
Figure 3. First-trimester ultrasound diagnosis of chorionicity. (a) Thin, wispy septal membranes of MC DA twins; (b) 'lambda' or 'twin peak' sign in DC twins.
two yolk sacs whereas MC/MA twins have only one.51 Because cord entwining is almost universal in MC/MA twins, this aids in the diagnosis, making amniography unnecessary.37

SUMMARY

Management of MC twin pregnancy is challenging. Several related disorders occur in 10–15% of cases. These are caused by the special vascular structure of MC placenta, which is unique for each MC placenta. Improved prognosis will best be achieved by first-trimester diagnosis, careful prenatal monitoring, randomized trials for TTT and long-term follow-up studies of MC twin survivors.

REFERENCES


Practice points

† first-trimester ultrasound: (i) lambda sign or T-sign; (ii) assess septal membrane thickness; (iii) number of yolk sacs; (iv) evidence for cord entwining
† second-trimester ultrasound: (i) cord insertions; (ii) differences in amniotic fluid volume; (iii) fetal growth discordance with asymmetric cord insertions; (iv) recognition of TRAP; (v) MZ/MC twins are usually discordant for congenital anomalies; (vi) map AAC by Doppler in known MC twins

Research agenda

† is umbilical arterial Doppler flow measurement appropriate in MC twins?
† the usefulness of seeking AAA by second/third trimester Doppler studies as a diagnostic feature of MC twinning
† the need for separate biometric tables for DC and MC twins
† does early diagnosis of MC twins produce better outcomes through more intensive surveillance?
† what are long-term outcomes following selective terminations in non-TRAP MC twins?
† what are long-term outcomes for MC twin survivors in general?


