

# TWIN REVERSED ARTERIAL PERFUSION (TRAP) SEQUENCE: BIOLOGY AND MANAGEMENT

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## Pathophysiology

In the usual setting, blood from the placenta enters the fetal circulation through the umbilical veins and exits via the umbilical artery. Very rarely (1% of MC twins or 1:35,000 births), retrograde or reversed arterial perfusion takes place, from the placenta through the umbilical artery of one of the twins, and the twin with the reversed flow receives all of its blood supply from a normal co-twin who gains circulatory predominance—the so-called "pump" twin. This vascular abnormality is termed the twin reversed arterial perfusion (TRAP) sequence.

Whereas the "pump" twin is usually anatomically normal, the heart of the recipient twin is unable to support perfusion of the upper body. Severe reduction anomalies of the upper part of the fetal body are the usual result. Often, these twins lack a heart (acardiac) and head (acephalic), except for a few cases with a rudimentary heart ("hemicardiac"). This is why the TRAP sequence is also called chorioangiopagus parasiticus, and as acardiac twinning.

The TRAP sequence and the twin-twin transfusion syndrome (TTTS) differ in several important aspects. First, in TTTS the shunt is via an arterio-venous anastomosis whereas in TRAP the shunt is via an arterio-arterial connection. Second, the twins in TTTS are usually anatomically normal, whereas in TRAP, the recipient twin is grossly malformed. Finally, the recipient in TTTS suffers from cardiac overload whereas the heart problem in TRAP is present in the donor, who provides for both twins.

Opinions differ whether the underlying pathology is primary cardiac agenesis or cardiac dysmorphogenesis secondary to the reversed flow.<sup>1</sup> Some authors maintain that a lethal heart malformation in early organogenesis – the so-called "cardiac regression sequence" – seems a likely underlying pathology.<sup>2</sup> An alternative view holds that inadequate perfusion of the recipient twin is responsible for the development of the characteristic anomalies. Given the availability of first trimester sonography, the last word has not been said regarding the pathogenesis of TRAP.<sup>3</sup>

In 1981, Bieber and co-workers<sup>4</sup> identified two maternally derived chromosome sets and both maternal histocompatibility antigen haplotypes in the tissues of an acardiac twin. These findings were explained by proposing independent fertilizations, by two different spermatozoa, of a normal haploid ovum and its diploid first-meiotic-division polar body. More recently, however, Fisk et al performed PCR on DNA extraction from 9 sets with the TRAP sequence and calculated that the chance that all acardiac twins resulted from polar body fertilization is <1:100,000.<sup>5</sup>

Despite being anatomically normal, the imposed cardiac overload is a serious threat to the "pump" twin and, if left untreated, it may die in as many as 50 - 75% of cases.<sup>1</sup>

## Diagnosis

Sonographic imaging during the first trimester usually depicts MC twins, with absent or vague heartbeat in one. In a typical missed abortion case, the size of the embryo/fetus decreases with time, but the size of presumed

missed twin is increasing in the TRAP sequence. Color Doppler studies on the umbilical vessels show the characteristic reversed flow in the acardiac twin. Later in pregnancy, the phenotypic characteristics of the acardiac twin are easily recognized.

## Management

The following information should be known before any management decision is made.

- (1) Monoamniotic (MA) variants of MC twinning occurs in only 25% of cases of TRAP sequence.<sup>6</sup> When TRAP occurs in MA pregnancies, treatment of the TRAP alone does not reduce the risks associated with MA twinning and umbilical cord occlusion with transection of the cord is necessary to avoid subsequent entanglement and demise of the "pump" twin.<sup>7</sup>
- (2) Because anomalies are reported in the pump twins as well it is necessary to exclude malformations to avoid unnecessary invasive treatments.
- (3) The well being of the "pump" twin, especially adequate cardiac function should be established.
- (4) The size of the acardiac mass and its umbilical cord in relation to the size of the "pump" twin should be established in order to choose the most appropriate mode of therapy.

### A. Conservative Management

The target of follow-up is the "pump" twin's congestive heart failure, which may lead to polyhydramnios and preterm birth. In one large series of 49 cases, the overall perinatal mortality was 55%, primarily associated with prematurity.<sup>9</sup> Follow up is performed by serial echocardiographic assessments, the purpose of which is to determine when cardiac function deteriorates.

Perinatal outcomes were strongly related to the ratio of the acardiac and pump-twin's weight: the higher the weight of the acardiac twin the more likely is the development of cardiac insufficiency in the pump twin, with a risk of congestive heart failure of 94% when the acardiac twin weighs more than half that of the "pump" twin.<sup>[8]</sup> In the series described by Moore et al, the mean overall ratio of the acardiac to the normal twin weights was  $0.52 \pm 0.42$ ; however, the ratio for patients delivered <34 weeks was 60 vs. 29% ( $p < 0.04$ ). In one quarter of the cases, the twin-weight ratio was  $>0.7$  and the incidence of preterm births in these cases was 90%. As the fetal indices used for sonographic estimations of fetal weight are not applicable to acardiac twins, the authors proposed the following equation:

$$\text{Weight (g)} = 1.2 L^2 - 1.7L$$

where L = longest dimension of the acardiac mass.<sup>9</sup> Rough estimation of the weight of the acardiac twin can be done by comparing the abdominal circumferences of the twins, or by applying any formula that estimates the size of an ellipsoid.

When the acardiac to the normal twin weights ratio is low, delivery at term or near term can be expected. However, when the weights ratio is high, the cardiac dysfunction of the "pump" twin may indicate early delivery.

In a recent publication on 10 cases managed expectantly, Sullivan et al<sup>9</sup> reported on nine women who delivered of healthy "pump" twins (one neonatal death), at a mean gestational age of 34.2 weeks, and mean weights of the "pump" and acardiac twins of 2279 and 1372 g, respectively.

### B. Invasive Procedures

In the past, treatment by selective delivery of the acardiac twin via hysterotomy was advocated.<sup>10</sup> This aggressive modality has been replaced by interruption methods of the blood supply to the acardiac twin. Because of the arrio-arterial shunt in TRAP, the artery must be interrupted, as simple thrombosis is quite difficult to achieve and, if the vein is inadvertently thrombosed, the "pump" twin may suffer from embolization related to the procedure.

Umbilical cord ligation was pioneered by Quintero a decade ago,<sup>11</sup> by tying a knot around the umbilical cord of the acardiac twin by a working instrument. This procedure is associated with 70-80% success rate but also entails risks of technical failure (7.6%), premature rupture of membranes (10%) and bleeding. An alternative

approach is endoscopic coagulation of the umbilical cord vessels of the acardiac twin using a Nd-YAG laser,<sup>12</sup> which was successful in cases treated at 17 and 20 weeks, but failed in pregnancies treated at 26 and 28 weeks. Arias et al<sup>13</sup> reviewed 22 cases treated with invasive procedures. "Pump" twin mortality with endoscopic laser coagulation at  $\leq 24$  weeks and endoscopic or sonographic-guided umbilical cord ligation  $>24$  weeks was 13.6% in comparison with 50% mortality associated with expectant management. A tailored approach was also proposed, whereby conservative treatment was offered to milder cases whereas larger acardiac twin were offered invasive intervention and cord occlusion.<sup>14</sup> Tsao et al<sup>15</sup> proposed radiofrequency ablation of the vessels in the fetal abdomen at the level of the cord insertion site of the acardiac twin. Energy was applied until termination of blood flow to the acardiac fetus was documented by Doppler ultrasound scanning. No major maternal complications were reported in 13 cases, and 12 out of 13 "pump" twins remained alive and well. Recent review of 207 articles published in the English-language literature identified 32 reports involving 74 cases of acardiac twin treated by invasive techniques.<sup>16</sup> The overall median gestational ages at treatment and delivery were 21 and 36 weeks, respectively, with a median treatment-delivery interval of 13 weeks. The overall "pump" twin survival rate was 76%. Intrafetal ablation was associated with increased gestational duration (37 vs. 32 weeks) and longer median treatment-delivery interval (16 vs. 9.5 weeks) compared with cord occlusion techniques. It was also associated with a lower technical failure rate (13 vs. 35%), lower rate of births or rupture of membranes at  $<32$  weeks (23 vs. 58%) and higher rate of clinical success (77 vs. 50%) compared with cord occlusion techniques. This review suggests that intrafetal ablation is the treatment of choice for acardiac twins.

### **C. Delivery Considerations**

The umbilical cord of the acardiac twin is usually very short, and the diameters of this ovoid shaped mass may be larger than the pelvic outlet or even larger than the 10-12 cm uterine incision performed at cesarean section. Accordingly, it seems reasonable to look out for the welfare of normal twin first. This may be accomplished only during a cesarean section.

### **Summary**

Diagnosis and management of the TRAP sequence has changed since the advent of sonography, echography, Doppler flow analysis, and so-called "minimally invasive" instrumentation. It is now possible to tailor the appropriate management by the inter-twin size ratio as well as by direct echographic assessment of the cardiac function of the "pump" twin. Endoscopes, introduced under fetoscopic or sonographic guidance, are currently available for ligation and/or ablation procedures to interrupt the blood flow to the acardiac twin. Expectant management, under close observation, is at present safer than ever before. Consequently, the chance of survival of the "pump" twin has significantly improved with modern perinatal care.

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