HYPOTHESIS

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Why does second trimester demise of a monochorionic twin not result in acardiac twinning?

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Abstract

Background: We previously explained why acardiac twinning occurs in the first trimester. We raised the question why a sudden demised monochorionic twin beyond the first trimester does not lead to acardiac twinning. We argued that exsanguinated blood from the live twin would strongly increase the demised twins' vascular resistance, preventing its perfusion and acardiac onset. However, our current hypothesis is that perfusion of the demised twin *does* occur but that it is insufficient for onset of acardiac twinning.

Methods: We analyzed blood pressures and flows in a vascular resistance model of a monochorionic twin pregnancy where one of the fetuses demised. The resistance model consists of a demised twin with a (former) placenta, a live twin and its placenta, and arterioarterial (AA) and venovenous placental anastomoses. We assumed that only twins with a weight of at least 33% of normal survived the first trimester and that exsanguination of more than 50% of its blood volume is fatal for the live twin.

Results: At 20 weeks, only AA anastomoses with radii $\lesssim 1$ mm keep the exsanguinated blood volume below 50%. Then, perfusion of the deceased body with arterial blood from the live fetus is about 5–40 times smaller than when that body was alive. Beyond 20 weeks, this factor is even smaller. At 14 weeks, this factor is at most 2.

Conclusion: We hypothesize that this small perfusion flow of arterial blood prevents further growth of the deceased body and hence precludes onset of acardiac twinning.

KEYWORDS
AA and VV placental anastomoses, blood perfusion, deceased twin, exsanguination, modeling, monochorionic twin pregnancy, second trimester, vascular resistance model, venous compliance

1 | INTRODUCTION

Monochorionic twin pregnancies consist of monozygotic ("identical") twins that share the same placenta (one chorion). In such twins, embryonic splitting occurred three or more days after fertilization. These pregnancies have in about 95% placental anastomoses that hemodynamically connect the circulations of the two twins (Lewi, Deprest, & Hecher, 2013). The anastomoses can be superficial or deep. Superficially located anastomoses on the placental surface are arterioarterial (AA) and less frequently venovenous (VV), where their flow can be bidirectional. Deep located anastomoses inside the placenta consist of a placental cotyledon shared by the twins, which can be arteriovenous (AV) and venoarterial (VA), and their flow is unidirectional, from one twin's arterial pressure to the other twin's venous pressure. These anastomoses are the source of a number of potentially serious complications (see Lewi et al., 2013, for an excellent overview) and one such complication is acardiac twinning.

An acardiac twin lacks a functional heart but nevertheless grows because its body is perfused by arterial blood from its co-twin, called the pump twin. As the superficial AA anastomoses do not acquire maternal oxygen transfer, the circulation to the acardiac twin is with arterial blood, which is approximately 25% less oxygenated than venous blood that comes from the placenta in live fetuses. The perfusion with arterial blood is the cause of the often bizarre form of acardiacs. Further, an acardiac twin is perfused in a reverse direction in its aorta compared to normal; hence, the name twin reversed arterial perfusion sequence (Van Allen, Smith, & Shepard, 1983). Perfusion of the acardiac twin is only possible when the placenta includes a unique set of AA and VV anastomoses. The incidence of acardiacs is about 1:9,500–11,000 pregnancies (van Gemert, van den Wijngaard, & Vandenbussche, 2015). Without intervention, reported pump twin mortality is about 50% (Healey, 1994; Moore, Gale, & Benirschke, 1990; Van Allen et al., 1983), commonly a result of cardiac failure.

Acardiac onset requires that the future pump twin has a mean arterial pressure that exceeds that of the future acardiac twin. Sufficiently unequal arterial pressures result in the larger twin perfusing part of the smaller twin's placenta (van Gemert, Ross, van den Wijngaard, & Nikkels, 2021; van Gemert, van den Wijngaard, Paarlberg, Gardiner, & Nikkels, 2017), which hampers the smaller twin's development. When this mechanism is sufficiently strong, cardiac arrest occurs in the smaller twin, which forces the larger twin to start a circulation of less oxygenated arterial blood through the AA–VV anastomoses and the demised smaller twin, thus promoting a growing acardiac twin.

The acardiac twin cannot perfuse its placenta anymore, which is henceforth done by the larger pump twin.

In previous work (van Gemert et al., 2021), we provided a pathophysiological mechanism that could explain why acardiac twinning occurs in the first trimester. We gave evidence that first trimester placental resistances are significantly larger than their corresponding embryo resistances, and that acardiac twinning then occurs under appropriate conditions, as explained in the previous paragraph. We also raised the question whether an acardiac twin would develop beyond the first trimester, following the demise for whatever reason of one of the monochorionic twin fetuses. Beyond the first trimester, normal placental weight becomes lower than normal fetal body weight (table 28.1 of Benirschke, Kaufmann, & Baergen, 2006), and because weight is proportional to blood volume, and thus inversely proportional to vascular body resistance, the body resistance becomes *smaller* than the placental resistance under normal conditions. This resistance difference suggests that the body will be more strongly perfused than the placenta. Nevertheless, demise of the smaller twin will markedly increase its venous blood volume because the larger twin will exsanguinate into the venous compartment that has a much larger compliance than the arterial part. We then tacitly assumed (van Gemert et al., 2021) that the demised twin's vascular resistance would concomitantly increase to a significantly larger value than the placental resistance. A much larger resistance of the body than the placenta prevents perfusion of the body, thus preventing its growth, and hence precludes onset of an acardiac twin pregnancy.

Nevertheless, when simulating this scenario, we failed to find convincing arguments that an overloaded demised fetus increases its vascular resistance significantly. Here, we recognized that the fetal vascular resistance is basically the resistance of the arterial and smaller venous vessels but that the larger veins hardly if at all contribute to the body's vascular resistance. And, because the exsanguinated blood enters particularly into the larger veins due to their high compliance rather than the low compliance arterial volume (figure 7 of Struijk et al., 2008), the body resistance of the demised twin will minimally if at all change following exsanguination of the pump twin.

1.1 | Hypothesis

The hypothesis to be discussed in this article is that the mechanism that prevents onset of acardiac twinning beyond the first trimester is the much smaller perfusion flow of the deceased twin compared to when it was alive,

which prevents the necessary growth required for onset of acardiac twin formation.

2 | MATERIALS AND METHODS

2.1 | General

We will evaluate the hypothesis by simulating the pressure-flow distribution of a monochorionic twin pregnancy in a vascular resistance model where twin 1 demises in the second trimester. The demised twin then increases its venous blood volume due to incoming blood exsanguinated from the surviving twin 2 through the AA anastomosis. This blood loss of live twin 2 reduces its cardiac output and thus lowers its arterial and venous pressures, which affects the pressures and flows of all vascular resistances including that of the demised body. Based on the venous compliance of the demised fetus 1, the increase in venous blood volume causes an increase in its venous pressure. The simultaneous occurrence of increasing venous blood volume in the demised body and continuation of its blood perfusion by the live twin is modeled by a simple two-step approach, based on the essential assumption that the vascular resistances of the two placentas, the AA–VV anastomoses and the demised body are independent of the amount of exsanguinated blood.

The analysis requires various assumptions and mathematical relations summarized below in Section 2.2, Section 2.3, Section 2.4, Section 2.5, Section 2.6, and Section 2.7.

2.2 | Vascular resistance model

Figure 1 shows the vascular resistance model of a monochorionic twin pregnancy where twin 1 suddenly demised, and where we assume that all its body properties, except the blood pressures, are still normal. Live twin 2, the larger twin in case of a weight difference, has arterial and venous pressures P_{a2} and P_{v2} (mmHg), and perfuses, respectively, its placenta, resistance R_{p2} (mmHg/[ml/week]), with flow F_{p2} (ml/week), the demised twin's (former) placenta (resistance R_{p1}, flow F_{p1}) through the AA and back through the VV, with flow $F_{AA} = F_{VV}$, and the demised twin's body (R_1, F_1). We did not include umbilical vessels because they are not required to address our hypothesis and simplify the computations.
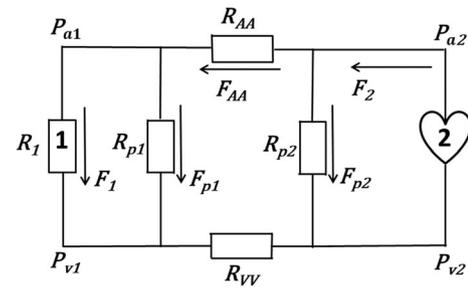

FIGURE 1 Resistance scheme used for a monochorionic twin pregnancy where one of the twins (the left one, 1) demised, with the live twin 2 at the right. For demised twin 1, we included its (former) placenta with resistance R_{p1} and its perfusion flow F_1. For live twin 2, we included its placenta with resistance R_{p2}. Parameters R_{AA} and R_{VV} denote the AA and VV anastomotic resistances. Blood flows are indicated by F, blood pressures by P

2.3 | Blood volumes and pressures

As before, we use that the blood volume of the deceased twin 1, $V_1(t)$ (ml), at gestational age t (weeks), is a factor of $\alpha_1 < 1$ smaller than the blood volume of live twin 2, $V_2(t) = V_N(t)$, assumed to be of normal dimensions (subscript "N"), thus (van Gemert & Sterenborg, 1998)

$$V_1(t) = a_1 \cdot V_N(t) = a_1 \cdot 149 \cdot \left(\frac{t}{31}\right)^3 = 149 \cdot \left(\frac{\sqrt[3]{a_1} \cdot t}{31}\right)^3 \quad (1)$$

In previous work (van Gemert et al., 2021), we argued that a healthy embryo that survives the first trimester has at least a weight of 33% compared to normal, thus

$$a_1 \lesssim 0.33 \quad (2)$$

The arterial and venous blood pressures of the normal live twin 2 are (van Gemert & Sterenborg, 1998)

$$P_{a2} = 60 \cdot \frac{(t-5)}{35} \quad (3)$$

$$P_{v2} = 7.5 \cdot \frac{(t-5)}{35} \quad (4)$$

We use that exsanguination of the live twin into the deceased twin lowers live twin's blood volume to fraction α_2 of its normal volume. So, following exsanguination at gestational age t

$$V_2(t) = a_2 \cdot V_N(t) = a_2 \cdot 149 \cdot \left(\frac{t}{31}\right)^3 = 149 \cdot \left(\frac{\sqrt[3]{a_2} \cdot t}{31}\right)^3 \quad (5)$$

The corresponding blood pressures are then given by

$$P_{a2} = 60 \cdot \frac{\left(\sqrt[3]{a_2} \cdot t - 5\right)}{35} \qquad (6)$$

$$P_{v2} = 7.5 \cdot \frac{\left(\sqrt[3]{a_2} \cdot t - 5\right)}{35} \qquad (7)$$

2.4 | Venous compliance

We estimated the fetal venous compliance, in ml/mmHg, from published intravascular blood transfusions that included venous pressure measurements. We used the results of Weiner, Pelzer, Heilskov, Wenstrom, and Williamson (1989) because they performed two venous transfusions with measurement of the corresponding venous pressures in eight anemic fetuses without hydrops during 20 procedures, summarized in their table 1. Summarizing, mean gestational age: 29.3 ± 1 weeks; estimated fetal blood volume: 116 ml (from table 28.1 of Benirschke et al., 2006); baseline umbilical venous pressure: 6.7 ± 1 mmHg; venous pressure after infusion of 42.5 ± 2 ml blood: 8.1 ± 1.6 mmHg; and after infusion of 93.5 ± 2 ml blood: 10.9 ± 1.4 mmHg. From these data, the curve of $\Delta P_v / P_v$ versus $\Delta V_v / V_v$ can be derived (P_v, V_v are venous pressure and blood volume). We use the three measured values, that is, $\Delta P_v / P_v = (8.1 - 6.7)/6.7 = 0.209$ versus $\Delta V_v / V_v = 42.5/116 = 0.366$, and $\Delta P_v / P_v = (10.9 - 6.7)/6.7 = 0.627$ versus $\Delta V_v / V_v = 93.5/116 = 0.563$. Subsequently, we use from adult physiology that $\Delta V_v / V_v$ can increase about 3.5-fold before the $\Delta P_v / P_v$ starts to increase strongly (https://www.cvphysiology.com/BloodPressure/BP004), and constructed the curve shown in Figure 2. We assumed that this curve holds for all post first trimester gestational ages.

2.5 | Resistances and flows

The resistance of the AA anastomosis is as before (van Gemert & Sterenborg, 1998)

$$
\begin{aligned}
&R_{AA}(t) \\
&= \frac{8 \cdot 0.005}{\pi} \cdot \frac{0.15 \cdot (t-4)/(27 \cdot 1.193)}{[r_{AA}(40) \cdot (t-4)/(27 \cdot 1.193)]^4} \cdot \left(\frac{1}{1.3333 \cdot 10^8 \cdot 60 \cdot 60 \cdot 24 \cdot 7}\right)
\end{aligned}
\qquad (8)
$$

The blood viscosity used as before is 0.005 N·s/m^2 and the AA length at 40 weeks is 0.15 m. The $r_{AA}(40)$ denotes the AA radius at 40 weeks, used as an input parameter in the model. Factor $(t-4)$ indicates that vessel growth of
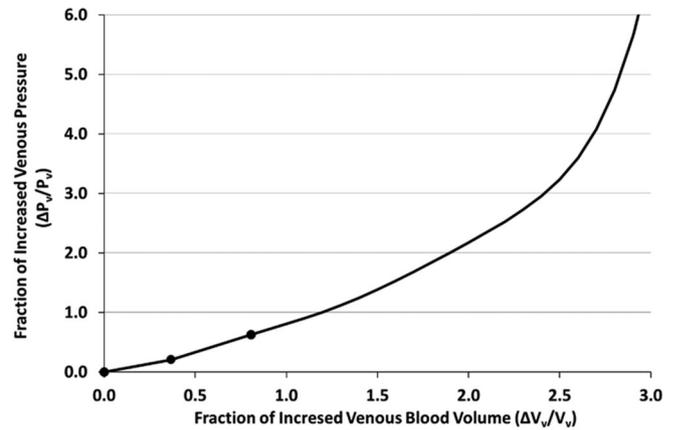

FIGURE 2 Venous compliance relation used, $\Delta P_v / P_v$ versus $\Delta V_v / V_v$, where P_v is venous pressure, and V_v is the venous blood volume. The curve is based on two intravascular blood transfusions of ΔV_v ml in anemic fetuses without hydrops with venous blood pressure measurements (second and third data points) (Weiner et al., 1989). The curve for larger $\Delta V_v / V_v$-values is based on adult physiology of venous compliance (https://www.cvphysiology.com/BloodPressure/BP004)

radius and length is linear with gestation and begins at 4 weeks. The last term between brackets converts the SI value for resistance $[(N/m^2)/(m^3/s)]$ to $[mmHg/(ml/week)]$.

We assumed, arbitrarily, that the VV-anastomotic resistance is a factor of eight smaller than that of the AA, thus

$$R_{VV}(t) = R_{AA}(t)/8 \qquad (9)$$

In previous work (van Gemert et al., 2021), we showed three monochorionic twin placentas that had a set of AA and VV anastomoses, two (van Gemert et al., 2021, figure 2) with about equal diameters, the third (van Gemert et al., 2021, figure 5) with the VV diameter about 60% larger than that of the AA. Our choice implies a factor of $\sqrt[4]{8} = 1.68$ times larger VV than AA diameter. Other AA/VV resistance ratios are discussed in Section 4.

From previous work (appendix A of van Gemert et al., 2017), the resistance relations for the placenta of the smaller twin 1 and for the normal assumed placenta of twin 2 are

$$R_{p1}(t'') = \frac{0.41}{(t''+5) \cdot (t''^2 + 25)} \qquad (10)$$

$$t'' = \sqrt[3]{a_1} \cdot (t-5) + 5 \qquad (11)$$

$$R_{p2}(t) = \frac{0.41}{(t+5) \cdot (t^2 + 25)} \qquad (12)$$

Gestational age $t'' < t$ is defined as follows: the normal twin's blood pressures at t'' are equal to the smaller twin's values at t, see Figure 2b of previous work (van Gemert et al., 2017). Also (equation (2), van Gemert, Ross, Nikkels, & van den Wijngaard, 2016), we use as vascular resistance of the deceased body.

$$R_1(t) = 0.00075/V_1(t) \qquad \text{mmHg/(ml/week)} \quad (13)$$

For V_1, we use the blood volume of fetus 1 before exsanguination. At, for example, 20 weeks and $\alpha_1 = 1$, $V_1(20) = 40$ ml, Equation (1); hence, $R_1(20) \approx 11.3$ mmHg/(ml/s). Using, Benirschke's value (table 28.1 of Benirschke et al., 2006) of 250 g fetal weight, hence, about 25–30 ml blood, would give $R_1(20) \approx 15–18$ mmHg/(ml/s). From Struijk et al. (2008), the downstream aortic arterial peripheral resistance was measured as 8 mmHg/(ml/s). Combination of his resistance value with blood flow data of a healthy fetus, table 3 of Garcia-Canadilla et al. (2014), to, respectively, the lower body and the combined upper body, lungs and brain, of, respectively, 28 and 42%, and assuming 30% enters the placenta, gives that the resistance of upper body, lungs plus brain is $28/42 = 0.67$ times the lower body resistance. Thus, using that the total body resistance in a reversed perfused deceased body is the sum of these lower and upper resistances, with 8 mmHg/(ml/s) of the lower body resistance, gives 1.67 times 8 is 13.3 mmHg/(ml/s) total body resistance, in notable agreement with the value of 11.3 mmHg/(ml/s) we used from Equation (13).

Calculation of the pressures at the placental insertions and the flows through the resistances requires standard resistance network theory. First, the distal resistance, R_{d2}, between the AV pressure source (P_{a2}-P_{v2}) over the placenta of live twin 2 via demised twin 1, is

$$R_{d2} = R_{AA} + R_{VV} + \frac{R_{p1} \cdot R_1}{R_{p1} + R_1} \quad (14)$$

The flow through the AA and VV anastomoses (ml/week) then is

$$F_{AA} = F_{VV} = \frac{(P_{a2} - P_{v2})}{R_{d2}} \quad (15)$$

The arterial and venous pressures of the deceased twin's former placenta as well as the demised twin itself are

$$P_{a1} = P_{a2} - F_{AA} \cdot R_{AA} \quad (16)$$

$$P_{v1} = P_{v2} + F_{VV} \cdot R_{VV} \quad (17)$$

The various flows are

$$F_{p1} = \frac{(P_{a1} - P_{v1})}{R_{p1}} \quad (18)$$

$$F_1 = \frac{(P_{a1} - P_{v1})}{R_1} \quad (19)$$

$$F_{p2} = \frac{(P_{a2} - P_{v2})}{R_{p2}} \quad (20)$$

$$F_2 = F_{AA} + F_{p2} \quad (21)$$

2.6 | Growth of a fetus and of a perfused deceased body

Based on Equation (1), growth of a live fetus (*GrowthL*) of blood volume a_1 times normal, is given by

$$GrowthL(t) = a_1 \cdot \frac{dV_N(t)}{dt} = a_1 \cdot \frac{3 \cdot 149}{31^3} \cdot t^2 = a_1 \cdot 0.015 \cdot t^2 \quad (22)$$

For the growth of a deceased fetal body, we use the previously proposed hypothesis for acardiac twin growth (equation (8) of van Gemert et al., 2016), that acardiac growth is the ratio of acardiac versus normal perfusion multiplied by normal growth, thus

$$\frac{dV_1(t)}{dt} = \frac{F_1(t)}{F_N(t)} \cdot \frac{dV_N(t)}{dt} = \frac{F_1(t)}{F_N(t)} \cdot 0.015 \cdot t^2 \quad (23)$$

where $F_N(t)$ is determined by using that the placenta is approximately perfused by 30% of the blood and the body by 70%, so

$$F_N(t) = (7/3) \cdot F_{p2}(t) \quad (24)$$

Thus, from Equations (22) and (23), the growth of demised fetus 1 versus its growth when it would be alive (*GrowthDvsL*) is

$$GrowthDvsL(t) = \frac{F_1(t)}{F_N(t)} \cdot \frac{1}{a_1} \quad (25)$$

2.7 | Exsanguination of a live fetal twin into its demised co-twin

Exsanguination of blood from a life fetus into a just demised co-twin includes three mechanisms: (a) perfusing the demised body through the AA anastomosis by exsanguinated arterial blood from the live twin,

which (b) lowers the arterial and venous pressures of the live twin because of its reduced blood volume, and (c) compartmentalizing the exsanguinated blood volume primarily into the demised body's venous compartment. These processes continue until the demised body cannot accumulate more external blood or until it dies. Then, when the live twin survives, the deceased body is perfused by blood that enters retrograde through the umbilical arteries and exits retrograde through the umbilical vein.

Demised twin 1 now has one blood pressure, called the filling pressure, which is close to its venous pressure. Exsanguination of blood by the live twin is triggered by the abruptly increased pressure gradient between $P_{\alpha 2}$ and $P_{\alpha 1}$, and begins through the AA anastomosis into the demised twin's umbilical arteries and, via the iliac arteries, respectively retrograde into its aorta and in normal direction into the legs. When AVs from live to demised fetus are present, their blood flow is likely insignificant compared to the AA flow due to their much higher resistance (e.g., appendix of Umur, van Gemert, Nikkels, & Ross, 2002). Through the aorta, the retrograde flow continues until it reaches the heart. Subsequently, it continues in normal caudal direction to perfuse the upper body. Because the aorta valve is closed for retrograde aortic blood flow (see Note section for your reference), the cardiac left ventricle and atrium are not filled with blood coming from this direction. Thus, the aorta in the lower body and thorax is perfused in retrograde direction. Equally so, the ductus arteriosus (ductus Botalli) that connects the pulmonary truncus with the aorta is also perfused in retrograde direction to perfuse the lungs normally. All branching arteries from the aorta into connecting organs are perfused normally.

In the demised fetus, all veins receive their blood in normal direction from the arteries via the capillary bed of the perfused organs. The umbilical vein, as exit channel of the body's perfusion, has a retrograde flow. Inside the body, it is positioned over the proximal abdominal wall until about halfway the liver where it connects with large liver veins and, via the ductus venosus that penetrates through the liver, with the inferior caval vein at the entrance of the right atrium of the heart. Its blood flow continues in normal direction to fill the right atrium and ventricle. Next, normal directed blood flow from the superior vena cava also fills the right atrium and right ventricle. Via the oval foramen in the atrial septum, the left atrium and left ventricle may be filled as well. So, to a good approximation, all veins with the exception of ductus venosus and umbilical vein have their blood flow in normal direction.

When the demised twin's venous compartment collects the exsanguinated excess blood, it will enlarge its volume and increase its pressure, as regulated by the venous compliance, Figure 2. It will also remain perfused by the live twin 2. These two mechanisms will be described in a two-step process. First, the increasing venous volume and pressure is assumed to continue until the venous pressure reaches the arterial pressure, that is, the pressure that exists at the insertion of the umbilical arteries into the body. Second, the demised body's venous pressure difference between post- and pre-exsanguination is added to the body's arterial pressure and to the live twin's arterial and venous pressures. The rational is here that all vascular resistances, that is, the two placentas, the AA–VV anastomoses and the demised body have the same vascular resistances as before the demise, and thus all blood flows have to remain the same too. Finally, the live twin, having lost a known volume of exsanguinated blood, adapts its arterial and venous pressures according to Equations (6) and (7).

Lastly, we assume that exsanguination of the live twin by 50% or more of its blood volume is fatal for a fetus. Support comes from a case report (Ahmed & Abdullatif, 2011) where IUFD occurred following a fetomaternal blood loss of 50 ml/kg, thus about 50 ml per 100 ml (50%) of blood volume, at 35 weeks.

3 | RESULTS

Figure 3 shows α_2, Equation (5), that is, the blood volume of the live fetus post exsanguination compared to normal when the deceased twin reached identical venous and arterial pressures, versus the deceased/live blood volume ratio α_1, at 14 (dashed lines) and 20 weeks (full lines). We recall that $\alpha_1 > 0.33$, Equation (2) (vertical dashed line in Figure 3) and that pregnancies with $r_{AA}(40) \lesssim 1.3$ mm unlikely survive the first trimester (van Gemert et al., 2021). When $r_{AA}(40)$-values are smaller than 1.3 mm, the embryos survive the first trimester; however, at 20 weeks, live twin 2 only survives the demise of twin 1 when $r_{AA}(40) < 1.1$ mm and $\alpha_1 > 0.33$. At 14 weeks, live fetus 2 survives the demised twin 1 at $r_{AA}(40) = 1.3$ mm and $0.33 < \alpha_1 \lesssim 0.44$.

If twin 2 survives demised twin 1, growth relation Equation (25), for $r_{AA}(40) = 0.6–1.1$ mm, shows growth reduction in the demised fetus at $\alpha_1 = 0.33$ compared to being alive by factors varying between 5 and 30 at 20 weeks, but between 2 and 4 at 14 weeks (Figure 4). Thus, once deceased, at least at 20 weeks, the demised fetus will hardly if at all grow. At 14 weeks, the growth reduction of fetus 1 compared to being alive is much smaller, although a factor of at least 2 is still considered significant. Here, we submit that the fact that less oxygenated arterial blood perfuses the body also contributes to its growth reduction. We therefore hypothesize that the demised fetus will not grow but, instead, will macerate, as shown, for example, in figure 6 of previous work (van Gemert et al., 2021).

Interestingly, an estimate of the $r_{AA}(40)$ value from that previous figure 6 gives about 0.13 mm, following from the outer diameter measured in the bending of the parallel AA and VV anastomoses of about 0.42 mm, thus the internal diameter is about 0.58 times smaller (Gansburgskiy & Yaltsev, 2018), or 0.24 mm. Demise, observed at 27 weeks, and birth of a girl of 2,490 g and deceased body of 590 g was at 36 weeks. Hence, $r_{AA}(40) \approx 40/36$ times 0.24/2 or ≈ 0.13 mm and $\alpha_1 \approx 0.56$ (from about 59 ml of the demised twin at 36 weeks, divided by the estimated blood volume of the live girl at 27 weeks, i.e., from Equation (1), about 149 times 27/36 to the third power, or 105 ml). This outcome ($r_{AA}(40) \approx 0.13$ mm, $\alpha_1 \approx 0.56$, at 27 weeks) strongly supports our analysis because growth of the

demised fetus compared to being alive is predicted to be virtually zero (0.021 from Figure 4).

4 | DISCUSSION

Our modeling approach confirms this article's hypothesis that a demised monochorionic twin beyond the first trimester will be minimally perfused by arterial blood from the other live twin at an insufficient level to permit body growth. The basis for this outcome is the following series of complex events.

Monochorionic twins that survive the first trimester are fetuses whose weight is larger than about 33% of normal, so

FIGURE 3 The live twin's remaining blood volume following exsanguination, α_2, expressed as a fraction of its normal value, Equation (5), where demised twin 1 has equal arterial and venous pressures, versus the size of the demised twin 1, expressed as fraction α_1 of the normal value, Equation (1). The values used for $r_{AA}(40)$ are indicated, for 14 weeks with "(14)" behind $r_{AA}(40)$. The dashed vertical line $\alpha_1 = 0.33$ separates surviving- from non-surviving fetuses after the first trimester. Exsanguination to blood volumes less than 50% of normal are assumed to be fatal for the live twin. The calculations are at 14 (dashed lines) and 20 weeks (full lines)
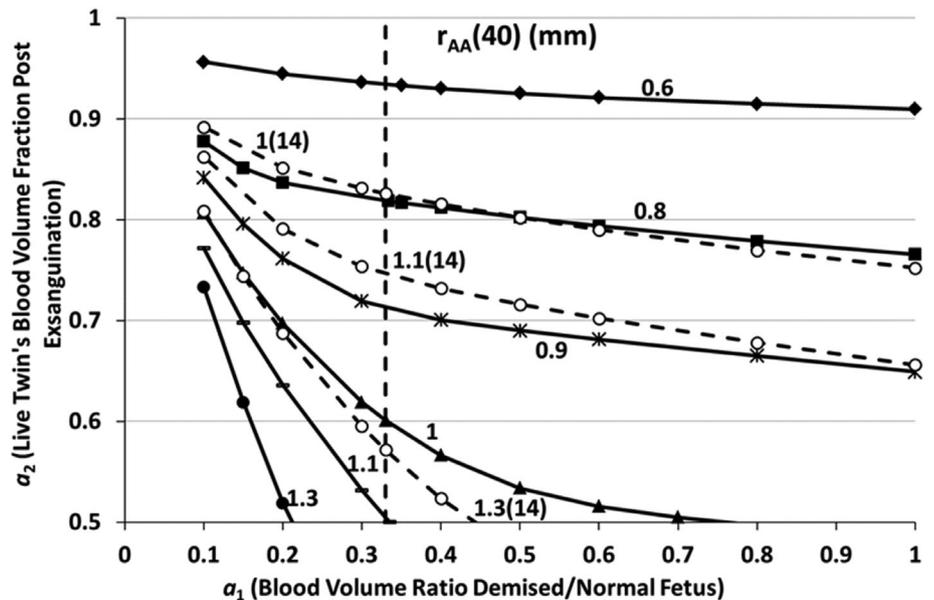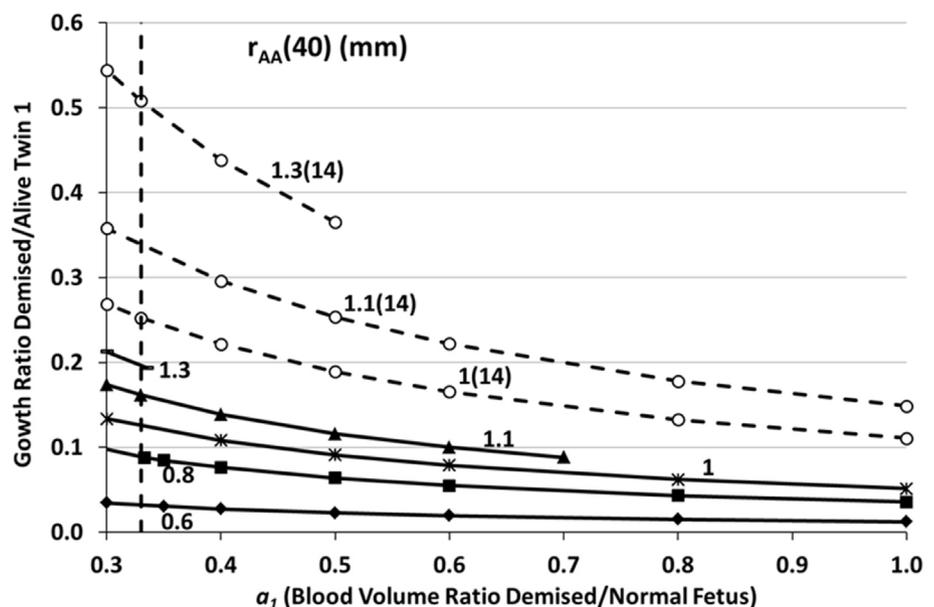

FIGURE 4 Growth of the demised twin 1 versus its growth while alive just before demise, as a function of the relative size α_1 of demised twin 1, for several $r_{AA}(40)$-values. The calculations are at 14 (dashed lines, "(14)" behind $r_{AA}(40)$) and 20 weeks (full lines)

$\alpha_1 \lesssim 0.33$. And, when being connected by AA and VV placental anastomoses, $r_{AA}(40) \lesssim 1.3$ mm (van Gemert et al., 2021). Sudden demise of one of these fetuses causes exsanguination of the other, live, fetus until the venous and arterial pressures of the demised twin have become equal, a consequence of venous compliance. In contrast to our previous statement (van Gemert et al., 2021), the demised twin will then be perfused by the live twin; we calculated this flow by taking all vascular resistances (placentas, AA–VV and demised body) independent of the exsanguinated blood volume. However, our modeling predicts that growth of the demised twin at 14 weeks is 2–4 times smaller-, and at 20 weeks, 5–40 times smaller than its previous growth when it was still alive. Our hypothesis is that this small growth prevents the onset of an acardiac twin.

5 | LIMITATIONS OF THE STUDY

First, we have assumed that the demise of one of the twins was abrupt, so we could conveniently use the normal physiological properties of the other, live, fetus at the gestational age considered. More likely is that a period of fetal deterioration occurs with fetal responses aiming to stay alive as long as possible, some of these mentioned previously (van Gemert et al., 2021) (e.g., hypoxia-mediated neovascularization, brain sparing and peripheral arterial constriction). In that previous work, we included hypoxia-mediated neovascularization, but not in this article. We believe that our outcomes would not change significantly because only the a_1-value would have increased to the a(new)-value defined in van Gemert et al. (2021), figure 6, and we hypothesize that our analysis would give very similar outcomes when $a_1 \approx a$(new), e.g., at 14 weeks, at $r_{AA}(40) = 1.3$ mm and $\alpha_1 = 0.33$, the $\alpha(new) = 0.345$, a 4.5% change without consequences according to Figure 3.

Second, the venous compliance curve of Figure 2 has obvious and unknown uncertainties, because it is based on one set of two intravascular fetal blood transfusions. Also, adult physiology was used to estimate the behavior of the fetal venous compliance at larger $\Delta V_v/V_v$-values ($\lesssim 0.8$) (https://www.cvphysiology.com/BloodPressure/BP004). However, our analyses were limited to exsanguinated blood volumes within $\Delta V_v/V_v$-values of about 1.5, thus close to the expected more accurate part of Figure 2. Third, we presented modeling results at 14 and 20 weeks. However, for later gestational ages, the results for survival of live twin 2 shift to smaller $r_{AA}(40)$-values, for example, at 27 weeks and $\alpha_1 = 0.33$, an $r_{AA}(40) = 0.98$ mm gives $\alpha_2 = 0.5$ (for comparison, $\alpha_2 = 0.62$ at 20 weeks). Finally, the VV-resistance was somewhat arbitrarily taken as 1/8 times, 12.5%, the AA resistance, Equation (8). When, for example, the VV and AA resistances would be equal, the outcomes of Figures 3 and 4 would shift in the direction of larger AA resistances, or to smaller $r_{AA}(40)$-values. Thus, a larger VV resistance retains the outcome of a minimally perfused demised body, precluding acardiac formation. When the VV resistance would be even smaller than 12.5% of the AA resistance, the outcomes of Figures 3 and 4 would shift to slightly larger $r_{AA}(40)$-values. However, the results of previous work, for example, $r_{AA}(40) \lesssim 1.3$ mm, were based on a zero VV resistance (figure 1 of van Gemert et al., 2021), so we submit that increasing the VV resistance from zero to $R_{AA}/8$ will hardly if at all affect our outcomes. Actually, a zero VV resistance at 14 weeks and $\alpha_1 = 0.33$, has an $r_{AA}(40) = 1.117$ mm that gives $\alpha_2 = 0.5$ and growth ratio 0.38 compared to being alive.

6 | CONCLUSION

Sudden fetal demise in a monochorionic twin pregnancy causes exsanguination of the live twin into the venous compartment of the demised twin until its venous pressure has reached its arterial pressure. The vascular resistance of the demised body has been taken independent of the amount of venous blood volume. The demised twin remains perfused by deoxygenated arterial blood from the live twin, however, the predicted perfusion flow is so small that the demised body hardly if at all grows and hence cannot become an acardiac twin. Much more likely is that it will macerate as shown in figure 6 of previous work (van Gemert et al., 2021).

NOTE
We recently found the paper by Gembruch et al. (2003), showing that during exsanguination from a live monochorionic twin fetus into the just demised other fetus, at 25+3 weeks, the heart valves remained open instead of closed as we stated in paragraph 2.7. However, our conclusions remain unaffected as we only included the acardiac resistance from Eq. 13.

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