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Doppler studies of the fetal circulation in twin–twin transfusion syndrome

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ABSTRACT

This cross-sectional study investigated the circulatory profile of the donor and recipient fetuses in 20 pregnancies with twin–twin transfusion syndrome presenting with acute polyhydramnios at 17–27 (mean, 22) weeks' gestation. Doppler investigations of the arterial vessels and ductus venosus, inferior vena cava, right hepatic vein, tricuspid and mitral ventricular inflow were performed in both fetuses. Mean values of most blood flow velocities on the venous side showed a significant decrease in both groups of fetuses, and a significant increase in mean values for indices describing waveform pulsatility was found in all three venous vessels in the group of recipients, whereas in the donor group this was only the case in the ductus venosus. Mean values of atrioventricular flow velocities showed a significant decrease in the donor group. The most significant findings on the arterial side were an increased mean umbilical artery pulsatility index and a decreased mean value for aortic blood flow velocity in both groups of fetuses. Five recipients and four donors had absence or reversal of blood flow during atrial contraction in the ductus venosus. All these fetuses showed pulsations in the umbilical vein. Tricuspid regurgitation was present in eight recipients. Absence or reversal of end-diastolic velocities in the umbilical artery was found in four donors. The recipient's circulation showed the characteristics of congestive heart failure due to hypervolemia. The significant decrease of diastolic venous blood flow velocities is compatible with increased end-diastolic ventricular pressure. Alterations in the donor's circulation are consistent with decreased venous return due to hypovolemia and increased cardiac afterload due to increased placental resistance.

INTRODUCTION

Twin–twin transfusion syndrome is a severe complication in monochorionic twin pregnancies. The pathogenesis is based on communicating placental blood vessels connecting the two umbilical circulations. Discordance in fetal size, oliguria with consequent anhydramnios in the donor and polyuria with consequent polyhydramnios in the recipient are the characteristic ultrasound findings[1].

Doppler studies in severe twin–twin transfusion syndrome presenting with acute polyhydramnios during the second trimester of pregnancy have demonstrated increased umbilical artery pulsatility index (PI) and decreased aortic mean velocity in both donor and recipient fetuses, decreased middle cerebral artery mean velocity in donors and decreased PI in recipients[2]. It was suggested that the increased umbilical artery PI in the donor could be the consequence of abnormal placental development and in the recipient it could be the result of polyhydramnios-related compression or placental congestion and edema. Doppler findings in the fetal vessels were compatible with hypovolemia in the donor and congestive heart failure due to hypervolemia in the recipient[2].

The aim of this study was further to investigate the fetal circulation in the donor and recipient fetuses in pregnancies with twin–twin transfusion syndrome by examining intracardiac and venous blood flow. Analysis of these flow velocity waveforms may offer valuable insights into the pathophysiology of this syndrome, particularly as it is still not possible with current techniques to obtain reliable measurements of volume blood flow in the fetal circulation.

MATERIALS AND METHODS

Doppler studies of arterial, intracardiac and venous blood flow were attempted in both fetuses of 20 pregnancies with twin–twin transfusion syndrome. The patients were referred consecutively to our center for endoscopic laser separation of the chorioangiopagus at 17–27 (mean, 22) weeks' gestation, when they presented with acute polyhydramnios. In all cases the following

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ultrasound criteria were fulfilled: twins had a single placenta and no fetal defects but were discordant in size (difference in abdominal circumference as a percentage of that of the smaller twin: range, 14–72%; median, 27%) and the larger twin (presumed recipient) had a distended bladder and was surrounded by polyhydramnios, whereas the smaller twin (presumed donor) appeared to be fixed to the placenta or the uterine wall, because of anhydramnios, and the bladder was not visible. Doppler studies were performed before laser coagulation of the communicating vessels[3]. The subsequent management and outcome of these pregnancies are reported elsewhere as part of a larger study[4].

Color flow imaging and pulsed Doppler velocimetry (Acuson 128, Mountain View, California, USA) were performed. A 3.5-MHz or 5-MHz curved array transducer with spatial peak temporal average intensities below 100 mW/cm^2 was used. The high-pass filter was set at 125 Hz. All recordings used for measurements were obtained in the absence of fetal breathing movements. For velocity measurements, it was aimed to achieve a low angle of insonation, but this was not always possible, because of technical problems imposed by the polyhydramnios and anhydramnios; the limit for acceptance was generally 50° and 30° particularly for atrioventricular inflow Doppler signals. The fetal heart rate was within the normal range of 120–160 beats/min.

Blood velocity waveforms were recorded from the umbilical cord, descending thoracic aorta, middle cerebral artery, ductus venosus, inferior vena cava, right hepatic vein and the atrioventricular valves. In the ductus venosus the sample volume was positioned at its origin from the umbilical vein, in the inferior vena cava in the portion between the inflow of the renal and hepatic veins and in the main stem of the right hepatic vein. For atrioventricular inflow recordings the sample volume was placed at the level of the annulus of the valves. On the venous side of the circulation, priority was given to examination of the ductus venosus.

For the veins, the following parameters were measured as mean values of at least three consecutive uniform waveforms: peak forward velocity during ventricular systole (*S*), peak forward velocity during diastole (*D*), lowest forward velocity or peak reversed velocity during atrial contraction (*a*), time-averaged maximum velocity (Tamx) by following the maximum frequency envelope of the flow velocity waveform of one heart cycle, and intensity weighted time-averaged mean velocity (V_m). In addition, the peak velocity index for veins [PVIV = $(S - a)/D$], and the pulsatility index for veins [PIV = $(S - a)$/Tamx] were calculated[5]. For the atrioventricular valves, peak flow velocities in early diastole (*E*) and late diastole with atrial contraction (*A*) were measured and the *E*/*A* ratio was calculated as a mean value of three heart cycles. For the middle cerebral artery and aorta, intensity weighted time-averaged mean velocity (V_m) and pulsatility index (PI) were measured. For umbilical arterial blood flow, the PI was calculated, and for venous blood flow the presence or absence of pulsations was noted.

Measured values in the donor and recipient twins were expressed as number of standard deviations by which they differed from the appropriate normal mean for gestational age of our normal ranges for singleton pregnancies[5]. The normality of the distribution of measurements was tested. The significance of differences in mean values from normal singletons was tested by Student's *t*-test.

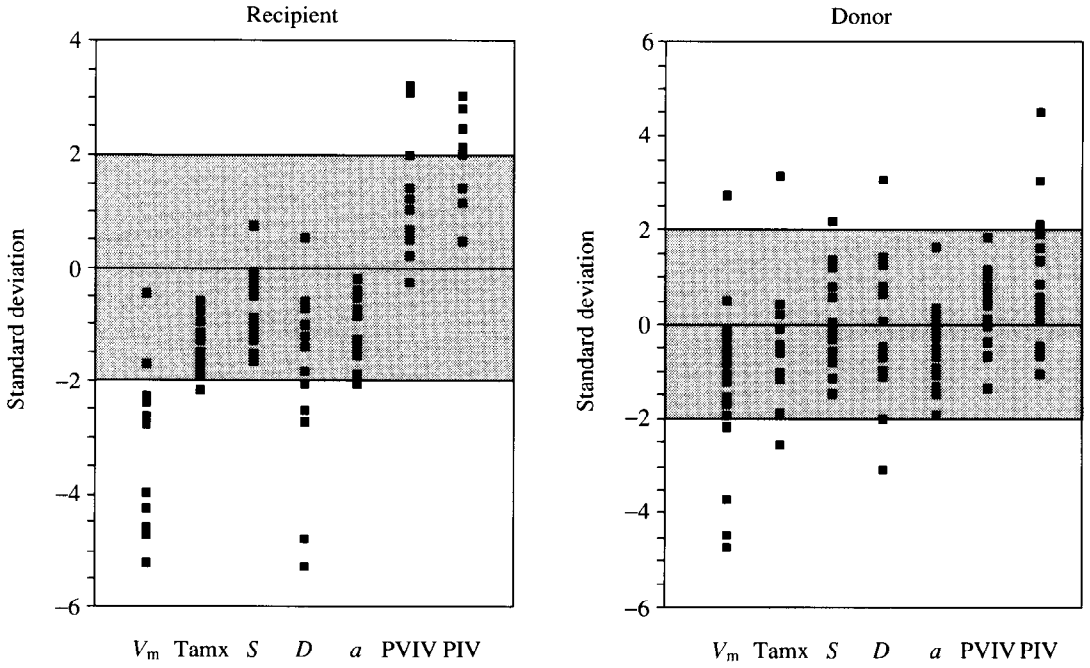

Figure 1 Individual Doppler measurements, expressed in standard deviations from the normal mean for gestational age[5], in the inferior vena cava of recipient and donor twins. Gray area: mean ± 2 standard deviations. V_m, intensity weighted mean velocity; Tamx, time-averaged maximum velocity; *S*, systolic peak velocity; *D*, early diastolic peak velocity; *a*, velocity during atrial contraction; PVIV, peak velocity index for veins [$(S - a)/D$]; PIV, pulsatility index for veins [$(S - a)$/Tamx]

RESULTS

The success rate for obtaining Doppler signals of sufficient quality for calculation of ratios and indices was 60% ($n = 24$) for tricuspid inflow, 73% ($n = 29$) for mitral inflow, 78% ($n = 31$) for the inferior vena cava, 80% ($n = 32$) for the right hepatic vein, 90% ($n = 36$) for the middle cerebral artery, 95% ($n = 38$) for the aorta, 98% ($n = 39$) for the ductus venosus and 100% ($n = 40$) for the umbilical artery.

Figures 1–5 show the differences in standard deviation from the normal mean for gestational age for individual Doppler measurements. Tables 1 and 2 give the results and significance for the mean difference from the normal mean for recipients and donors. On the venous side (Table 1), most velocities were significantly reduced in both fetuses, and both indices describing waveform pulsatility (Figure 6) were significantly increased in all three vessels in the recipient, whereas in the donor this was only the case in the ductus venosus. Velocities through the atrioventricular valves were significantly reduced in the donor. On the arterial side (Table 2), significant differences from normals were increased umbilical artery PI and decreased aortic mean velocity,

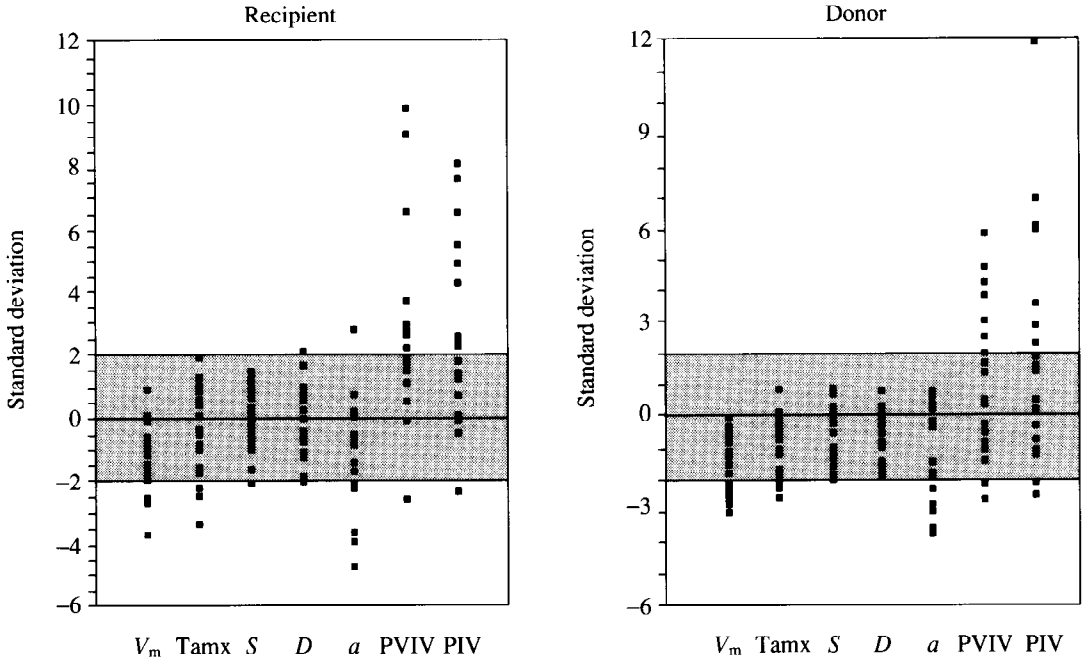

Figure 2 Individual Doppler measurements, expressed in standard deviations from the normal mean for gestational age[5], in the ductus venosus of recipient and donor twins. Gray area: mean ± 2 standard deviations. Abbreviations as in Figure 1

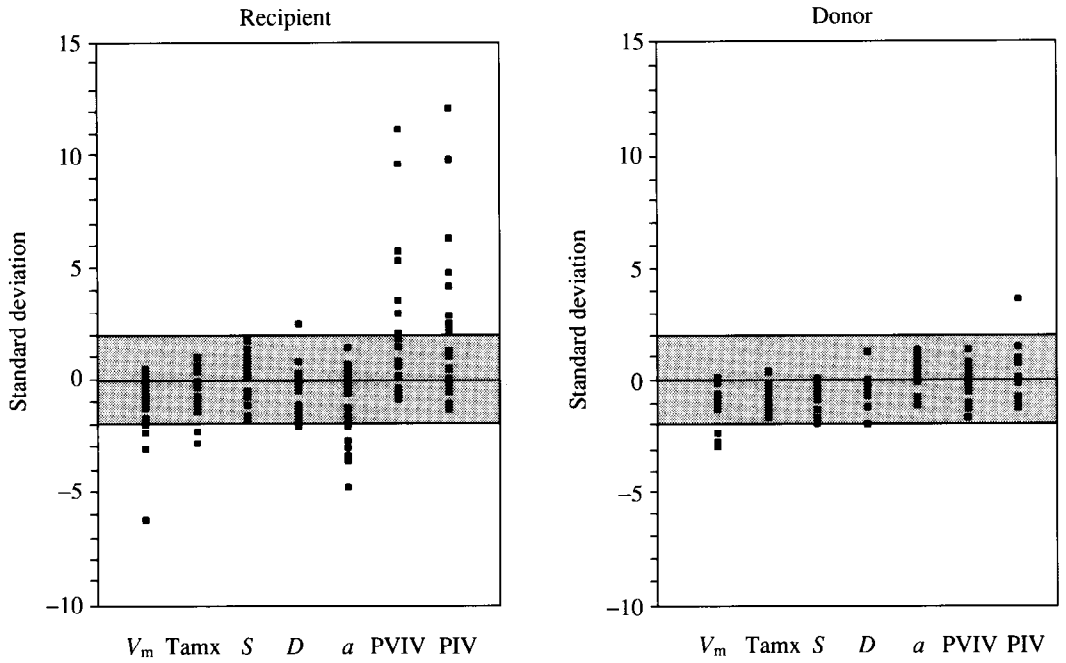

Figure 3 Individual Doppler measurements, expressed in standard deviations from the normal mean for gestational age[5], in the right hepatic vein of recipient and donor twins. Gray area: mean ± 2 standard deviations. Abbreviations as in Figure 1

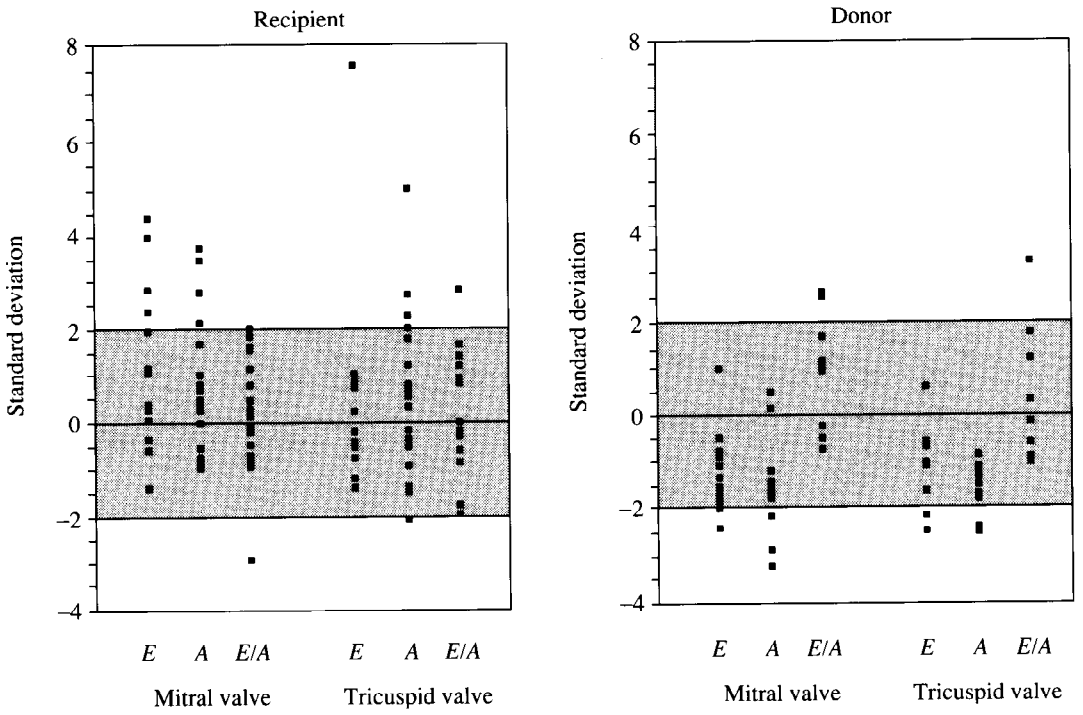

Figure 4 Individual Doppler measurements, expressed in standard deviations from the normal mean for gestational age[5], for mitral and tricuspid ventricular inflow of recipient and donor twins. Gray area: mean ± 2 standard deviations. *E*, early diastolic peak; *A*, late diastolic peak during atrial contraction

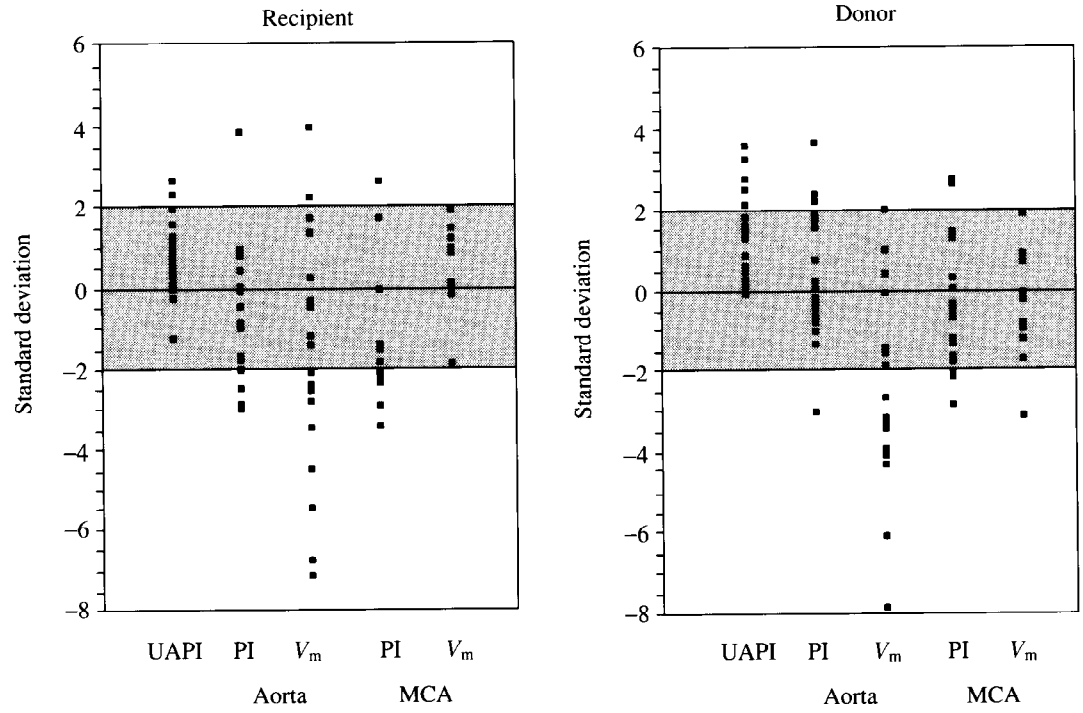

Figure 5 Individual Doppler measurements, expressed in standard deviations from the normal mean for gestational age, for arterial blood vessels of recipient and donor twins. Gray area: mean ± 2 standard deviations. UA, umbilical artery; PI, pulsatility index; V_m, intensity weighted mean velocity; MCA, middle cerebral artery

in both donor and recipient fetuses, and decreased middle cerebral artery PI in recipients.

Five recipients and four donors had absence or reversal of blood flow during atrial contraction in the ductus venosus (Figure 6). All nine fetuses had pulsations in the umbilical vein, four of the recipients showed tricuspid regurgitation and two of the donors had absence of end-diastolic velocities in the umbilical arteries. Overall, tricuspid regurgitation was present in eight recipients, absence or reversal of end-diastolic velocities in the umbilical artery in four donors and umbilical vein pulsations in 12 fetuses (seven recipients and five donors).

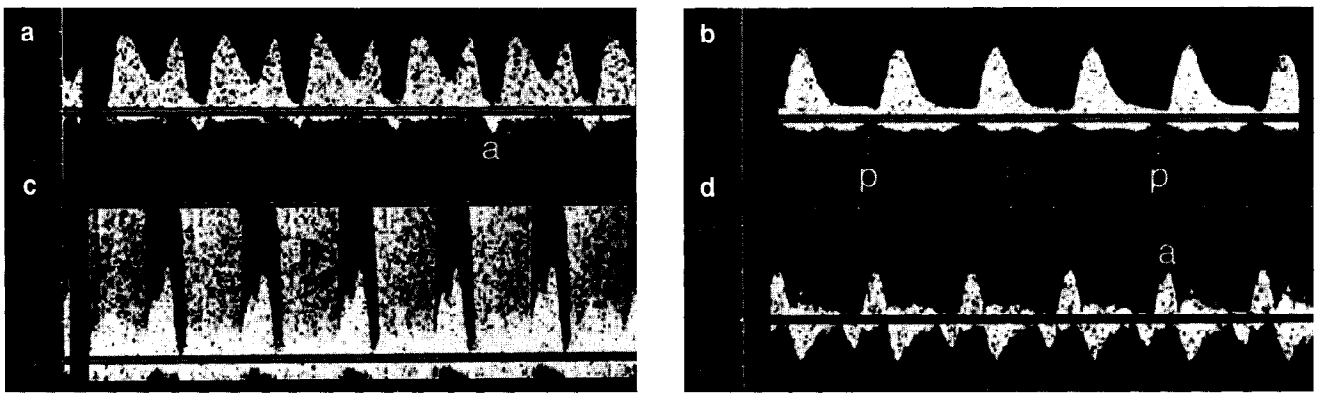

Figure 6 (a) Ductus venosus blood flow velocity waveform with reversed velocities during atrial contraction in a recipient fetus (a); (b) causing pulsations (p) in the umbilical vein; (c) tricuspid regurgitation (R); and (d) velocity waveform of the right hepatic vein with increased reversal of blood flow during atrial contraction (a)

Table 1 Doppler measurements of the venous circulation in recipient and donor twins compared to the appropriate normal mean for gestation. For all parameters, the mean difference from the normal mean is given in standard deviations (SD). SE, standard error

	n	*Recipient mean difference (SD)*	*SE*	*n*	*Donor mean difference (SD)*	*SE*
Inferior vena cava						
V_m	14	−3.0***	0.36	17	−1.3*	0.44
Tamx	14	−1.4***	0.12	17	−0.4	0.30
Systolic peak (*S*)	14	−0.8**	0.18	17	0.0	0.23
Diastolic peak (*D*)	14	−1.9***	0.42	17	−0.1	0.36
a-wave	14	−1.0***	0.17	17	−0.4*	0.20
(*S*–*a*)/*D*	14	1.4***	0.30	17	0.4	0.19
(*S*–*a*)/Tamx	14	1.8***	0.21	17	0.9*	0.34
Ductus venosus						
V_m	20	−1.1***	0.27	18	−1.5***	0.22
Tamx	20	−0.5	0.30	19	−1.0***	0.22
Systolic peak (*S*)	20	0.1	0.22	19	−0.6**	0.20
Diastolic peak (*D*)	20	−0.1	0.26	19	−0.5*	0.21
a–wave	20	−1.4**	0.41	19	−1.2**	0.36
(*S*–*a*)/*D*	20	2.3**	0.69	19	1.7*	0.57
(*S*–*a*)/Tamx	20	2.5**	0.64	19	2.2*	0.99
Right hepatic vein						
V_m	18	−1.4**	0.40	12	−1.1**	0.30
*T*amx	18	−0.6*	0.24	14	−0.7**	0.17
Systolic peak (*S*)	18	0.1	0.26	14	−0.8***	0.17
Diastolic peak (*D*)	18	−0.7*	0.29	14	−0.5*	0.20
a–wave	18	−1.3**	0.41	14	0.4*	0.18
(*S*–*a*)/*D*	18	2.7**	0.80	14	−0.2	0.23
(*S*–*a*)/Tamx	18	2.8**	0.85	14	0.3	0.35
Mitral valve						
E wave	17	0.8	0.42	12	−1.2***	0.42
A wave	19	0.9*	0.35	12	−1.6***	0.35
E/*A*	17	0.2	0.31	12	0.7	0.31
Tricuspid valve						
E wave	13	0.5	0.22	11	−1.2***	0.22
A wave	19	0.7	0.32	11	−1.8***	0.32
E/*A*	13	0.2	0.36	11	0.7	0.36

V_m, mean velocity; Tamx, time-averaged maximum velocity; *E*, early diastole; *A*, late diastole with atrial contraction; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

DISCUSSION

We examined a homogeneous group of pregnancies with typical features of twin–twin transfusion syndrome presenting over a narrow gestational range in mid-pregnancy. The arterial Doppler findings of the majority of these fetuses have been previously reported and discussed in detail as part of a larger study[2]. This report focuses on fetuses in which Doppler studies of venous vessels and atrioventricular flow were performed.

Generally, it has to be acknowledged that with so many parameters measured the problem of multiple

Table 2 Doppler measurements of the arterial circulation in recipient and donor twins compared to the appropriate normal mean for gestation. For all parameters, the mean difference from the normal mean is given in standard deviations (SD). SE, standard error

	n	*Recipient mean difference (SD)*	*SE*	*n*	*Donor mean difference (SD)*	*SE*
Umbilical artery PI	20	0.8**	0.22	20	1.4***	0.23
Thoracic aorta PI	20	−0.8	0.39	18	0.4	0.38
Thoracic aorta V_m	20	−2.2*	0.90	18	−2.6***	0.59
Middle cerebral artery PI	18	−1.1*	0.39	18	−0.3	0.42
Middle cerebral artery V_m	14	0.4	0.29	17	−0.5	0.40

PI, pulsatility index; V_m, mean velocity; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

testing has to be taken into account. With the number of tests of significance presented in the tables there is a possibility of some spurious significant results. Although many parameters show significance in the mean difference from the normal mean, a high percentage of individual measurements is within 2 standard deviations. This may be due, firstly, to the fact that several factors could trigger the development of twin–twin transfusion and, secondly, to the intervention by laser coagulation of the communicating vessels. Therefore, we could not investigate the natural history of the hemodynamic alterations in the fetal circulation in donors and recipients. However, there are certain obvious trends in hemodynamic findings that help in the understanding of the pathophysiology in both groups of fetuses.

We clearly could prove the existence of congestive heart failure in the recipient. The significant decrease of diastolic venous blood flow velocities is compatible with increased end-diastolic ventricular pressure. Blood flow during atrial contraction in the ductus venosus seems to be particularly vulnerable in cardiac disease involving ventricular pump function[6]. Systolic peak velocities did not differ from the normal mean for gestational age, except for the inferior vena cava. These changes resulted in highly pulsatile venous waveforms with increased waveform indices (PVIV and PIV).

Gudmundsson and co-authors[7] described pulsations in umbilical venous blood flow correlated to atrial contraction in six recipients. The right ventricular shortening fraction in fetuses with non-immune hydrops was significantly decreased in fetuses with umbilical vein pulsations compared to those without. These authors also found an increase of the percentage of late diastolic reversed flow in the inferior vena cava compared with the forward flow during systole and early diastole. Recently, the same group of authors showed that umbilical venous pulsations in fetuses with non-immune hydrops, which frequently develops in the recipient during the natural history of the syndrome, are a generic sign of fetal congestive heart failure[8]. Furthermore, these fetuses had decreased ventricular output and peak velocities at the aortic and pulmonary valves, also reported by Rizzo and colleagues[9] for the recipient twin.

Our study provides data for the missing link between the heart and the umbilical vein, which is the ductus venosus. All fetuses with absent or reversed velocities during atrial contraction in the ductus venosus also showed umbilical vein pulsations. Congestive heart failure due to hypervolemia and increased preload in the recipient is furthermore confirmed by abnormal waveforms in the inferior vena cava and right hepatic vein and the high incidence (40%) of tricuspid valve regurgitation.

Tricuspid insufficiency in the recipient occurs during systole and is therefore not directly responsible for the increase of reversed venous flow that occurs during diastole and coincides with atrial contraction. Therefore, both signs seem independently to reflect congestive heart failure. Additionally, the increase of blood flow velocities of atrioventricular inflow (*E*- and *A*-waves) indicates cardiac overload. It is noteworthy that in six out of 19 cases no *E*-wave could be separated from the *A*-wave of tricuspid ventricular inflow in the recipient, which was never the case in the donor (Table 1). The fusion of the two parts of the waveform may be due to an increase of blood flow into the right ventricle. All these findings are in agreement with an increase in heart size and weight in the larger of discordant twins[10,11]. Hypervolemia may cause cardiac hypertrophy as a compensatory mechanism. Eventually, the pumping capabilities of the enlarged heart are exceeded and cardiac failure occurs[10].

In donor twins there is a significant reduction of blood flow velocities in all the vessels examined and in atrioventricular inflow. This is consistent with hypovolemia, but also with increased placental resistance, consecutive increase in cardiac afterload and decrease in venous return. All four donors with absence or reversal of end-diastolic velocities in the umbilical artery had abnormal ductus venosus flow indices and two of them showed absence or even reversal of flow during atrial contraction. This is a typical finding for compromised growth-retarded fetuses suffering from high placental resistance[12].

However, increased placental resistance with consecutive increase in cardiac afterload cannot be the only explanation for abnormal ductus venosus waveforms in the donor, because two fetuses with absence of flow during atrial contraction had normal values for the umbilical artery PI. A possible explanation for this could be a low umbilical venous pressure as a consequence of a decrease in umbilical venous return, due to the chronic twin–twin transfusion. From a recent study, we have drawn the conclusion that umbilical venous pressure is

not necessarily correlated with central venous pressure[13]. The pressure difference between venous blood vessels and the heart seems to be one of the determining factors for venous blood velocity waveforms. Therefore, low umbilical venous pressure may be correlated with abnormal ductus venosus waveforms, due to the fact that the pressure wave during atrial contraction is propagated with more effect into the ductus venosus and even into the umbilical vein, causing pulsations, compared to the inferior vena cava and the hepatic veins.

Doppler studies of the fetal circulation in twin–twin transfusion syndrome show how different mechanisms, such as hypervolemia and hypovolemia, or increased cardiac preload and afterload can cause similar alterations in blood flow velocity waveforms of venous return. Examination of the venous side of the circulation is helpful and supportive for the interpretation of findings on the arterial side, and both are influenced by each other via the heart and the placenta.

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