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Longitudinal hemodynamic evaluation of uncomplicated twin pregnancies according to chorionicity: physiological cardiovascular dysfunction in monochorionic twin pregnancy

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CONTRIBUTION

What are the novel findings of this work?

In dichorionic (DC) and monochorionic (MC) twin pregnancy the changes in maternal cardiovascular system are detected as early as the first trimester. In MC twin pregnancy there is a greater cardiovascular effort in the second trimester and a subsequent cross-over with reduction in cardiovascular performance during the third trimester.

What are the clinical implications of this work?

The placenta-cardiac interplay plays a key role in physiological adaptation of pregnancy. Studying the possible influence of chorionicity on maternal hemodynamics could explain the excess risk of complications in twin pregnancies. These findings could be instrumental in evaluation of complicated twin pregnancies with cardiovascular maladaptation.

ABSTRACT

Objective: Maternal cardiac function plays a crucial role in normal placental function and development. The maternal hemodynamic changes in twin pregnancy are more pronounced than in singleton, presumably due to an increased plasma volume expansion. In view of the correlation between cardiac and placental function, it is plausible that chorionicity could influence maternal cardiac function. The aim of this study was to compare the longitudinal maternal hemodynamic changes in dichorionic and monochorionic twin pregnancies.

Methods: 40 monochorionic diamniotic (MC), 35 dichorionic diamniotic (DC) uncomplicated twin pregnancies were included in the study. 531 healthy singleton pregnancies from a cross-sectional study are used as the control group. All participants underwent a hemodynamic evaluation using Ultrasound Cardiac Output Monitor (USCOM®) at three different stages in pregnancy (11-15 weeks, 20-24 weeks and 29-33 weeks) recording mean arterial pressure (MAP), stroke volume (SV), stroke volume index (SVI) heart rate (HR), cardiac output (CO), cardiac index (CI), systemic vascular resistance (SVR), systemic vascular resistance index (SVI), Stroke Volume Variation (SVV), Smith-Madigan Inotropy Index (INO) and potential to kinetic energy ratio (PKR).

Results: Maternal CO (8.33 vs 7.30 l/min, p=0.03) and CI (4.52 vs 4.00 l/min/m^2, p=0.02) were significantly higher in the second trimester in MC compared to DC twin pregnancies. Women with MC twin pregnancies showed significantly higher PKR (24.06 vs 20.13, p=0.03) and SVRI (1837.20 vs 1698.49 d.s.cm^{-5}/m^2, p=0.03) in the third trimester, and significantly lower values of SV (78.80 vs 88.80 cm^3, p=0.01), SVI (47.00 vs 50.31 cm^3/m^2, p<0.01) and INO (1.70 vs 1.87 W/m^2, p=0.03) vs. singleton pregnancies. These differences were not observed in DC twin pregnancies.

Conclusions: Maternal cardiovascular function undergoes significant changes during an uncomplicated twin pregnancy and chorionicity influences maternal hemodynamics. In both twin pregnancies the hemodynamic changes are detected as early as the first trimester. In DC twin pregnancies the maternal hemodynamics remain stable during the rest of pregnancy. On the contrary, in MC twin pregnancies the rise in maternal CO continues in the second trimester to sustain the higher placental growth. There is a subsequent cross-over with a reduction in cardiovascular performance during the third trimester.

INTRODUCTION

Over the last three decades, the incidence of twin pregnancies has steadily increased due to rising maternal age and increased demand for fertility treatments.[1] Twin pregnancy is characterized by marked modifications of all organ systems in the body, and maternal hemodynamic changes are more pronounced compared to singleton, presumably as an effect of an increased plasma volume expansion.[2] The plasma volume expansion reported at earlier stage of pregnancy appears to be the primary trigger of all the cardiovascular adaptation to pregnancy, and higher volume expansion might imply more pronounced hemodynamic changes.[3]

However, twin pregnancy is associated with excess maternal and perinatal mortality and morbidity with a relative risk of preeclampsia 2-3 times higher when compared with singleton pregnancy. This risk might be underestimated because of the lower gestational age at delivery.[4] Moreover, the fetal growth in twins appears reduced compared to singleton pregnancies, and the rate of fetal growth restriction (FGR) is higher.[5] Monochorionic (MC) twin pregnancies are more likely to be complicated by FGR than dichorionic (DC) twin pregnancies.[6]

Maternal hemodynamic changes play an important role in normal placental function and development in singleton pregnancy; hemodynamic alterations are associated with the development of placental insufficiency, hypertensive disorders, and FGR.[7-10] Histopathological studies in twins have demonstrated that FGR and hypertensive disorders are not associated with placental lesions, and therefore, maternal hemodynamics might play a key role.[11]

Based on these considerations, many authors studied maternal hemodynamics in uncomplicated twin pregnancies to describe the physiological adaptative processes and understand the possible pathological mechanisms underlying obstetric complications.[12-15] However, there are only few studies on maternal hemodynamics in twin pregnancies, and the influence of chorionicity is yet to be ascertained.[16] Nevertheless, chorionicity appears to influence the pattern of fetal growth and placental mass development.[17,18] In view of the correlation between cardiac and placental function, it is plausible that chorionicity could influence maternal cardiovascular function.[19,20]

Therefore, the aim of this study was to compare the longitudinal maternal hemodynamic changes between uncomplicated DC and MC twin pregnancies.

METHODS

This was a longitudinal observational study conducted at the Department of Obstetrics and Gynecology, University of Rome Tor Vergata, Policlinico Casilino, Rome, Italy.

We enrolled 104 twin pregnancies referred to our outpatient clinic between January 2018 and December 2021. During the study period, the patients were enrolled in the first trimester and scheduled for subsequent hemodynamic evaluations. Of these, 29 patients were subsequently excluded, and the remaining 75 uncomplicated twin pregnancies completed the 3 steps of hemodynamic assessment

The inclusion criteria were twin pregnancy with viable fetuses and first-trimester pregnancy dating using crown-rump length at 11 to 14 weeks of gestation.

The exclusion criteria were history of maternal heart disease, hypertensive disorders, gestational diabetes, pregnancy complicated by aneuploidy, genetic syndrome, or major structural abnormality in one or both fetuses, intrauterine fetal death, development of twin-to-twin transfusion Syndrome (TTTS), twin anemia polycythemia sequence (TAPS) or selective intrauterine growth restriction (sFGR), amniotic fluid discordance, spontaneous or indicated delivery before 34 weeks, birthweight below the fifth centile of one or both twins.

The sample was divided into 40 monochorionic diamniotic (MC) and 35 dichorionic diamniotic (DC) twin pregnancies. The diagnosis of chorionicity has been determined using an ultrasound scan at 11-14 weeks' gestation.

The study was approved by the local ethics committee (Ethic Committee Lazio 2, ref. 63.17). A written informed consent was obtained from the participants.

All participants underwent a hemodynamic evaluation using Ultrasound Cardiac Output Monitor (USCOM®) (USCOM Ltd, Coffs Harbor, Australia) at three different stages in pregnancy (11-15 weeks, 20-24 weeks and 29-33 weeks). USCOM is a non-invasive Doppler ultrasonic technology for the determination of hemodynamic variables. A non-imaging continuous-wave Doppler transducer is placed at the suprasternal notch to measure transaortic blood flow.[21] The measurements were performed by one trained operator under standardized conditions as described in previous studies.[22,23] The patients were in the left recumbent position to avoid the aortocaval compression in supine position. Maternal blood pressure was obtained from the brachial artery automated machine with the pregnant woman in a resting state.

The following parameters were obtained at each examination: mean arterial pressure (MAP), stroke volume (SV), strove volume index (SVI), heart rate (HR), cardiac output (CO), cardiac index (CI), systemic vascular resistance (SVR), systemic vascular resistance index (SVRI), stroke volume variation (SVV), Smith-Madigan Inotropy Index (INO) and potential to kinetic energy ratio (PKR). The last 2 parameters are calculated from the assessment of maternal cardiovascular potential energy (PE) and kinetic energy (KE). When the heart contracts it transfers 2 types of energy to the circulating blood: PE, which is the portion of output energy that produces arterial pressure, and KE, the energy of blood flow. INO is calculated by the sum of these 2 types of energy adjusted for body surface area and it is a novel approach to assess the inotropy status.[24] PKR represents the ratio between PE and KE and is a measure of the balance between blood pressure and blood flow. In pregnancy complicated by SGA, PKR is increased owing to lower kinetic energy consistent with a low-flow maternal circulatory state.[25]

The obstetric management of the women enrolled was independent of the hemodynamics findings and conducted by physicians not involved in the study. Data on maternal demographics and risk factors were collected from the medical records. Pregnancy outcome data were collected after birth from the hospital electronic records.

From a group of 531 healthy singleton pregnancies enrolled in a previous cross sectional study, we used 95 patients as control in the first trimester (11-15 weeks), 121 as control in the second trimester (20-24 weeks) and 75 as control in the third trimester (29-33 weeks), to compare the hemodynamics between twin and singleton pregnancies.[26]

Statistical analysis

Statistical analyses were performed using MedCalc software (MedCalc Software, West-Vlaanderen, Belgium). Continuous variables were expressed as median and interquartile range, and categorical variables were expressed as numbers and percentages. Comparisons among groups and among trimesters were performed using one-way analysis of variance and using the Kruskal Wallis test where appropriate. Comparison among trimesters in the same group in normally distributed data was performed using ANOVA for repeated measurements with Student-Neuma-Keuls correction for multiple comparisons. The changes in maternal a hemodynamic parameter between the different trimesters were calculated as the difference in percentage of median values. A value of P <0.05 was considered statistically significant.

Radar charts with six hemodynamic parameters (SVR, SVV, HR, CO, INO, PKR) has been constructed for DC and MC according to a method previously described using Z scores mean values[26].

RESULTS

Baseline characteristics

The maternal age (33.00 vs 34.50 years, p=0.26), BMI (23.70 vs 23.04 kg/m^2, p=0.53) at the enrollment, proportion of nulliparous women (71.4% vs 72.5%, p=0.88), those of Caucasian ethnic origin (97.1% vs 92.5%, p=0.71), the proportions of smokers at the enrollment (17.1% vs 17.5%, p=0.78), and the birthweight centile (31.00 vs 26.00, p=0.68) were similar between the two groups as shown in Table 1. The conception modalities were similar in the groups (p=0.49): 27 DC twin patients (77.1%) conceived spontaneously, while 8 (22.9%) using in vitro fertilization (IVF) and one of these from heterologous fertilization; 28 MC twin patients (70.0%) conceived spontaneously, while 12 (30.0%) from homologous IVF. The gestational age at the delivery was significantly higher in DC twin pregnancies than MC (255 vs 253 days, p<0.01), according to local protocol of management of uncomplicated twin pregnancies.

Longitudinal changes in maternal hemodynamics

The results of maternal hemodynamic assessment in DC and MC twin pregnancies are shown in Table 2. In DC twin pregnancies, there was a rise of MAP by 3.45% in the third trimester (p=0.03). The maternal HR gradually increased by 17.7% (p<0.01), while SV was reduced by 7.3% (p=0.05) and SVI by 16.% (p<0.01) in the third trimester. No longitudinal changes were observed in maternal CO (p=0.59), CI (p= 0.36), SVR (p=0.85), SVRI (p=0.47), SVV (p= 0.06), INO (p=0.37) or PKR (p=0.22).

In MC twin pregnancies the maternal MAP didn't significantly change during pregnancy (p=0.06). Maternal CO showed a bimodal pattern with a significant increase by 17.99% from the first to the second trimester and a significant decrease by 10.4% from the second to the third trimester (p<0.01) (Figure 1). This reduction was caused by a decrease by 19.1% in maternal SV during the third trimester ($p<0.01$), while maternal HR increased in the second trimester (by 11.4%, $p<0.01$) and remained stable in the third trimester. SVI showed a significant reduction in the third trimester (by 20.1%, $p<0.01$) and CI reduced by 13.3% ($p<0.01$) from the second to the third trimester. Maternal SVR, SVRI and PKR showed a significant rise, by respectively 23.6%, 19.9% and 26.0%, from the second to the third trimester ($p<0.01$) (Figures 2 and 3). Maternal INO, which remained stable in the second trimester, significantly decreased by 9.6% in the third trimester ($p<0.01$) (Figure 4). No longitudinal changes were observed in SVV ($p=0.56$).

Longitudinal changes in maternal hemodynamics in the three groups are shown in Figures 1-4. The median values of hemodynamic parameters in singleton pregnancies derived from our previous study are summarized in Table 2.

Comparison by chorionicity

Comparison between twin and singleton pregnancies are summarized in Table 2. In the first trimester women with DC twin pregnancies showed significantly lower maternal MAP (87.00 vs 88.00 mmHg, $p=0.04$), SVR (926.88 vs 1082.45 $d.s.cm^{-5}$, $p<0.01$), SVRI (1642.00 vs 1851.19 $d.s.cm^{-5}/m^2$, $p<0.01$), PKR (20.00 vs 25.07, $p<0.01$), and higher SV (96.00 vs 82.35 cm^3, p=<0.01), CO (7.28 vs 6.47 l/min, $p<0.01$) and CI (4.20 vs 4.09 $l/min/m^2$, p =0.02) compared to singleton pregnancies. SVV was reduced ($p=0.03$) in DC comparison to singleton pregnancies. In the third trimester DC twin pregnancies show significantly higher MAP (90.00 vs 86.17 mmHg, $p=0.02$) and HR (93.00 vs 83.32 bpm, $p<0.01$). Women with MC twin pregnancies show significant differences during gestation: in the first trimester they show significantly lower maternal MAP (84.17 vs 88.00 bpm, $p<0.01$), SVR (943.62 vs 1119.00 $d.s.cm^{-5}$, $p<0.01$), SVRI (1650.82 vs 1851.19 $d.s.cm^{-5}/m^2$, $p<0.01$), PKR (19.49 vs 25.07, $p<0.01$), and higher SV (92.94 vs 82.35 cm^3, $p<0.01$) and CO (7.06 vs 6.47 l/min, $p<0.01$) than singleton pregnancies. In the second trimester, they have significantly higher maternal HR (85.00 vs 79.98 bpm, $p<0.01$), CO (8.33 vs 7.12 l/min, $p<0.01$) and CI (4.52 vs 4.11 l/min/m^{2,} $p=0.03$), and significantly lower SVR (803.11 vs 968.64 d.s.cm^{-5}, $p<0.01$), compared to singleton pregnancies. In the third trimester, they show significantly higher PKR (24.06 vs 20.13, $p=0.03$) and SVRI (1837.20 vs 1698.49 d.s.cm^{-5}/m^2, $p=0.03$), and significantly lower values of SV (78.80 vs 88.80 cm^3, $p=0.01$), SVI (47.00 vs 50.31 cm^3/m^2, $p<0.01$) and INO (1.70 vs 1.87 W/m^2, $p=0.03$) in comparison of singleton pregnancies.

Comparison between MC twins, DC twins and singleton pregnancies are displayed with Radar graphs in Figure 5. MC twins showed significantly higher maternal CO (8.33 vs 7.30 l/min, $p=0.03$), CI (4.52 vs 4.00 l/min/m^2, $p=0.02$) in the second trimester compared to DC twins, as shown in Table 2 and Figure 5b.

DISCUSSION

Summary of key findings

The findings of this study suggest that maternal cardiovascular function undergoes significant changes during an uncomplicated twin pregnancy with a hyperdynamic circulation, characterized by high CO and low SVR since the first trimester. Chorionicity appears to influence maternal hemodynamics in the second and third trimesters with a stable hyperdynamic pattern in DC twins, and a "cross-over" pattern in MC twins. In fact, in MC twins the hemodynamic pattern crosses from a hyperdynamic (second trimester) to a more hypodynamic circulation (third trimester) as demonstrated by the reduction of CO and INO, and the rise of SVR and PKR.

Interpretation of study findings and comparison with published literature

According to previous studies, we found early cardiovascular modifications in twin pregnancies with hyperdynamic circulation since the first trimester. Nevertheless, the authors didn't focus on the relationship between chorionicity and maternal hemodynamics.[12,13]

Recently, in a prospective echocardiographic multicenter study, Ghi et al. showed a significant decrease in ejection fraction (EF) in MC twins from the first to the third trimester, while EF remains stable in DC twins.[16] The authors explain the significant EF reduction in MC twins because of measurement variability. In our study, we found a reduction of INO in MC twins during the third trimester, which might be considered (with all due cautions due to the limitations of USCOM with respect to echocardiography in assessing full cardiac function parameters) in line with the reduction of EF found in the above-mentioned study and that reduction might represent a real reduction in systolic function in this group of patients.

Our results should be interpreted considering the correlation between maternal hemodynamics and placental development.[19] It has been widely described the placenta-cardiac interplay in the physiological adaptation of pregnancy, and CO appears to sustain placental development and fetal growth.[27]

Baumann et al. demonstrated the impact of chorionicity on placental weight and growth pattern: MC twins seem to follow a “two-step” growth pattern with an initial rapid increase in the first half of pregnancy, reaching their growth potential at the beginning of the third trimester, and a plateau-like phase until the end of pregnancy.[18] On the contrary, dichorionic placentas continue to develop after 26 weeks and show a gestational age-dependent growth behavior. The authors speculated that monochorionic placentas are intrinsically programmed to supply one fetus, and to support twins’ growth, they must increase their mass reaching earlier the maximal dimensions that the mother can sustain.[18]

These modifications might explain the difference in maternal hemodynamics in MC vs DC twins in our study.

We found that maternal hemodynamics in twin pregnancies has already profoundly changed at the end of the first trimester. In comparison to a singleton pregnancy, maternal CO and SV are significantly higher, while MAP and SVR are reduced. The INO is similar to a singleton pregnancy, but there is a prevalence of kinetic energy with low PKR.

During the second trimester in singleton pregnancy there are profound modifications with a rise in maternal CO and SV, and a reduction in MAP, SVR and PKR. In DC the maternal hemodynamics, already changed in the first trimester and remain stable during the second trimester. On the contrary, MC twin pregnancies showed a further increase in maternal CO and a reduction in SVR.

During the third trimester, the maternal hemodynamic changes remain broadly stable in singleton pregnancies and DC twin pregnancies. After the second trimester, the maternal cardiovascular function in MC twin pregnancies declines: INO and CO reduce, SVR increases, and the circulation becomes more hypodynamic with a rise in PKR.

The hemodynamic modifications in MC twin pregnancies are probably correlated with the increased fetal-placental demand of this pregnancy. The defective MC placenta needs to increase its mass to support the development of the fetuses and its demand continues to increase.[18] Maternal cardiovascular system has to ensure the increased fetal-placental demand, increasing the cardiac work, since the first weeks of pregnancy and in particular in the second trimester where the placenta reaches its maximum mass. This hypothesis is supported by our results that demonstrate higher values of maternal CO in MC twin pregnancies in the second trimester. Nevertheless, during the third trimester the maternal hemodynamic changes in MC twin pregnancies show a cross-over behavior with a reduction in CO and kinetic energy. On the contrary, the maternal hemodynamics in DC pregnancies, which has already changed since the first trimester, remains stable until the third trimester.

Clinical and research implications

In DC twin pregnancy the maternal cardiovascular system works at full capacity since the first trimester and continues to grant fetal demands until term. In MC twin pregnancy the cardiovascular function declines during the third trimester. The reduction in maternal cardiovascular function is probably the cause of the placental growth limitation in the third trimester.[18] This might explain the larger reduction in fetal growth in the third trimester in MC than DC twins when compared with singletons described in previous reports.[28,29]

Strengths and limitations

The strength of this study is the prospective and longitudinal design of the study, with a selected uncomplicated population divided according to chorionicity. This contributed to better understand the "physiological" hemodynamic changes in DC and MC twins.

The main limitation of this study is the lack of placental weight that would be the key element to sustain our hypothesis on the maternal hemodynamics role on placental and fetal growth. The simultaneous evaluation of placental mass and maternal hemodynamics in a larger future study is required to better understand the fetal placental growth patterns.

Another important limitation of this study is the lack of echocardiographic parameters which allow the evaluation of myocardial contractility, diastolic function, cardiac structure and geometry. USCOM parameter for inotropism (INO) is a derived parameter, that quantifies only the 'effective inotropy', being that energy that is delivered to the circulation by the heart.[24]

Conclusions

Twin pregnancies show profound maternal hemodynamic changes since the first trimester compared to singleton pregnancies, with higher maternal CO and lower SVR. In MC twin pregnancies the rise in maternal CO continues in the second trimester, probably to sustain the higher placental growth described by Baumann et al.[18] In the third trimester, there is a subsequent reduction in maternal CO and INO. This cardiovascular limitation to placental growth in MC twins could play a role in the excess risks in these pregnancies, but further studies are required to understand the relationship between cardiovascular function and the development of complications in twin pregnancies.

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FIGURE LEGENDS

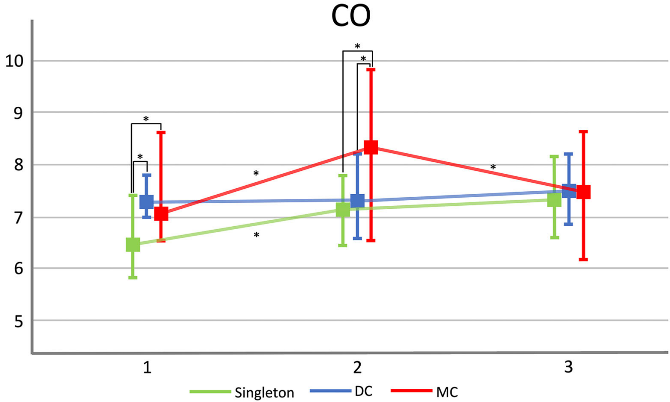
Figure 1. Maternal Cardiac Output (CO) changes in singleton, dichorionic (DC) and monochorionic (DC) twin pregnancies.

Figure 2. Maternal systemic vascular resistance (SVR) changes in singleton, dichorionic (DC) and monochorionic (DC) twin pregnancies.

Figure 3. Maternal Potential to Kinetic Energy Ratio (PKR) changes in single, dichorionic (DC) and monochorionic (DC) twin pregnancies.

Figure 4. Maternal Inotropy Index (INO) changes in singleton, dichorionic (DC) and monochorionic (DC) twin pregnancies.

Figure 5. Radar charts of maternal hemodynamic profile in singleton, dichorionic (DC), and monochorionic (MC) twin pregnancies, in the first trimester (a), second trimester (b), and third trimester (c). Each parameter was expressed in Z score to standardize for GA and mean values were calculated.[26] Systemic Vascular Resistance (SVR), Stroke Volume Variation (SVV), Heart Rate (HR), Cardiac Output (CO), Inotropy Index (INO), and Potential to Kinetic Energy Ratio (PKR).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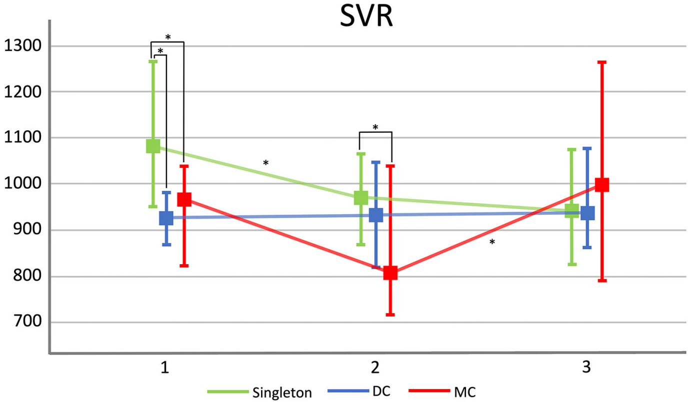
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1300
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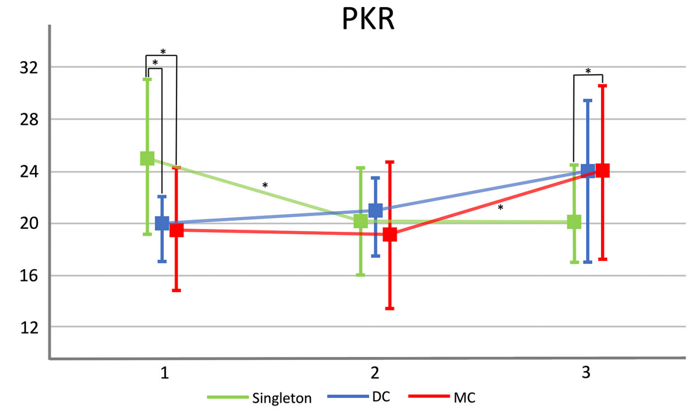
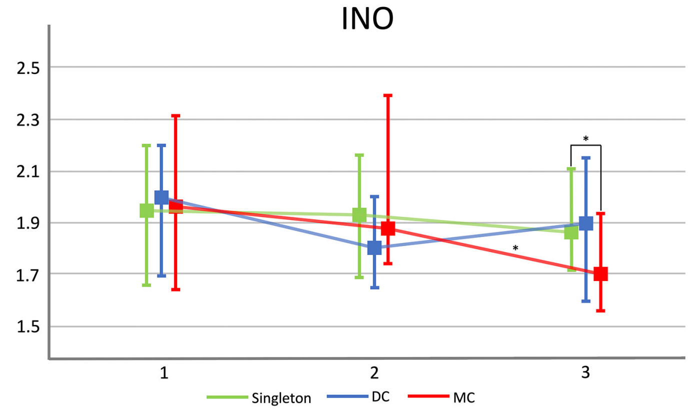
1100
1000
900
800
700
1
2
3
*
Singleton
DC
MC


PKR
32
28
24
20
16
12
1
2
3
Singleton
DC
MC
*
*
*
*
*


INO
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2.3
2.1
1.9
1.7
1.5
1
2
3
*
*
Singleton
DC
MC

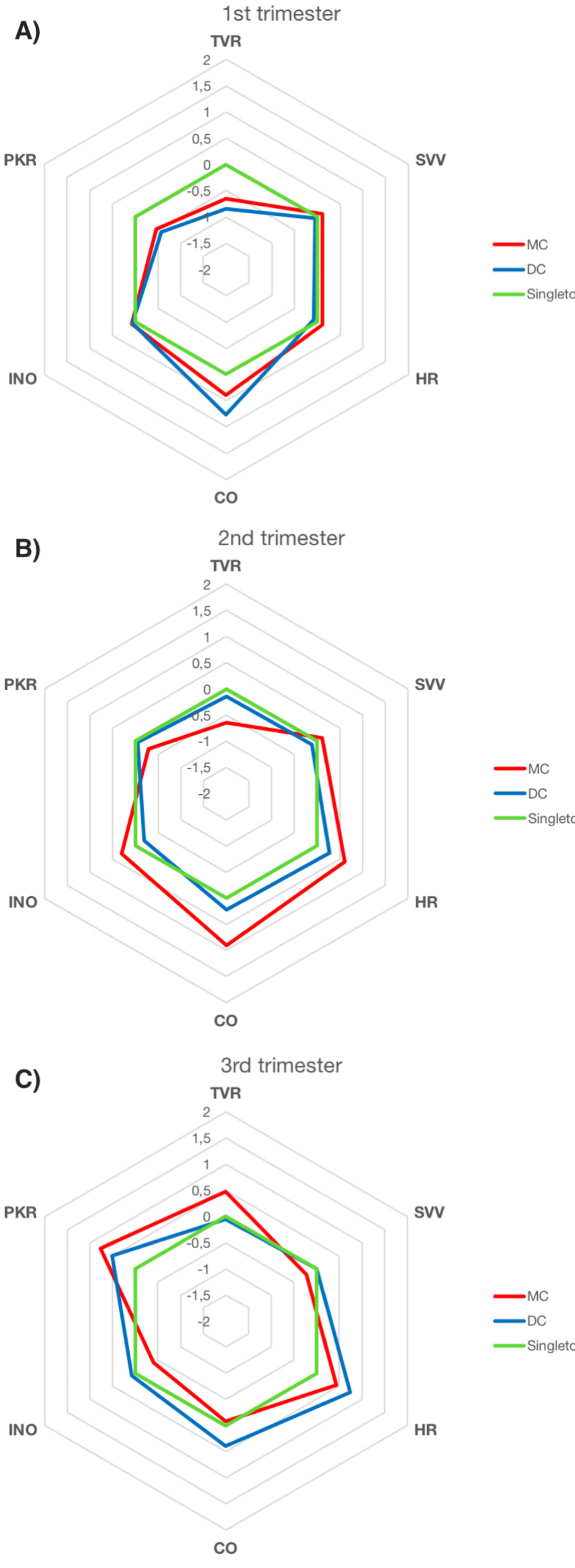
A)
1st trimester
TVR
SVV
HR
CO
INO
PKR
2
1,5
1
0,5
0
-0,5
-1
-1,5
-2
MC
DC
Singleton
B)
2nd trimester
TVR
SVV
HR
CO
INO
PKR
2
1,5
1
0,5
0
-0,5
-1
-1,5
-2
MC
DC
Singleton
C)
3rd trimester
TVR
SVV
HR
CO
INO
PKR
2
1,5
1
0,5
0
-0,5
-1
-1,5
-2
MC
DC
Singleton

Table 1. Baseline characteristics of dichorionic and monochorionic twin pregnancies

	Dichorionic twin pregnancies (N=35)	**Monochorionic twin pregnancies (N=40)**	**P value**
Maternal Age	33.00 (28.75-36.75)	34.50 (31.50-38.50)	0.26
BMI at enrollment	23.70 (20.85-29.30)	23.04 (21.37-26.95)	0.53
Nulliparous	25 (71.4)	29 (72.5)	0.88
Caucasian ethnicity	34 (97.1)	37 (92.5)	0.71
Smoking	6 (17.1)	7 (17.5)	0.78
Conception			0.49
Spontaneous	27 (77.1)	28 (70.0)	
Medically assisted	8 (22.9)	12 (30.0)	
GA at delivery (days)	255.00 (251.50 – 264.25)	253.00 (250.75 – 256.00)	<0.01
Birthweight (grams)	2585.00 (2290.00 – 2765.00)	2460.00 (2267.50 – 2627.50)	0.02
Birthweight (centile)	31.00 (13.00 – 42.00)	26.00 (10.00 – 43.00)	0.68

Data are given as median (interquartile range) or n (%). BMI: Body Mass Index; GA: gestational age

Table 2. Maternal Hemodynamic changes in Monochorionic Twins (n= 40), Dichorionic Twins (n=35) and Singleton Pregnancies (n=291)

	1st trimester	**2nd trimester**	**3rd trimester**	*Comparison among trimesters (P value)*
Dichorionic Twin				
MAP (mmHg)	87.00 (79.00-93.00)*	87.00 (80.00-91.50)	90.00 (86.00-93.00)*	$0.03^{\ddagger\S}$
HR (bpm)	79.00 (71.00-88.01)	85.00 (75.00-90.00)	93.00 (84.00-99.00)*	$<0.01^{\ddagger\S}$
SV (cm^3)	96.00 (87.55-100.77)*	88.00 (82.00-101.50)	89.00 (74.00-97.00)	$0.05^{\ddagger}$
SVI (cm^3/m^2)	56.00 (47.00 – 59.50)	49.00 (43.50 – 53.00)	47.00 (39.00 – 54.00)	$<0.01^{\dagger,\ddagger}$
CO (l/min)	7.28 (7.00-7.80)*	7.30 (6.60-8.20) ¶	7.50 (6.85-8.20)	0.59
CI ($l/min/m^2$)	4.20 (3.85 – 4.49)*	4.00 (3.55 – 4.50) ¶	4.10 (3.70 – 4.50)	0.36
SVR ($d.s.cm^{-5}$)	926.88 (866.01-980.5)*	931.00 (817.00-1047.00)	932.00 (856.00-1073.50)	0.85
SVRI ($d.s.cm^{-5}/m^2$)	1642.00 (1491.58 – 1795.50)*	1755.00 (1436.00 – 1983.00)	1739.00 (1609.00 – 1969.00)	0.47
SVV	17.00 (13.60-21.00)	15.00 (12.00-22.00)* ¶	23.00 (15.50-25.50)	0.06
INO (W/m^2)	2.00 (1.70-2.20)	1.80 (1.65-2.00)	1.90 (1.60-2.15)	0.37
PKR	20.00 (17.09-22.00)*	21.00 (17.50-23.50)	24.00 (17.00-29.50)	0.22
Monochorionic Twin				
MAP (mmHg)	84.17 (80.00-90.00)*	86.67 (82.92-90.00)	91.67 (81.67-95.67)	0.06
HR (bpm)	76.28 (68.78-87.75)	85.00 (80.60-93.71)*	91.63 (81.46-96.22)	$<0.01^{\dagger\ddagger}$
SV (cm^3)	92.94 (80.94-105.11)*	97.46 (81.10-108.46)	78.80 (71.48-94.43)*	$<0.01^{\ddagger\S}$
SVI (cm^3/m^2)	56.00 (47.00 – 59.50)	49.00 (43.50 – 53.00)	47.00 (39.00 – 54.00)*	$<0.01^{\ddagger\S}$
CO (l/min)	7.06 (6.53-8.62)*	8.33 (6.54-9.82)* ¶	7.46 (6.17-8.63)	$<0.01^{\dagger\S}$
CI ($l/min/m^2$)	4.09 (3.65-4.62)	4.52 (3.80 – 5.15) *¶	3.92 (3.33 – 4.60)	$<0.01^{\S}$
SVR ($d.s.cm^{-5}$)	964.48 (823.75-1039.60)*	803.11 (713.75-1038.15)*	994.13 (789.52-1265.15)	$<0.01^{\S}$
SVRI ($d.s.cm^{-5}/m^2$)	1650.82 (1459.21 – 1826.52)*	1532.95 (1302.96 – 1781.11)	1837.20 (1454.27 – 2348.96)*	$<0.01^{\ddagger\S}$
SVV	19.44 (14.12-22.42)	19.33 (15.15-24.79)	17.40 (13.97-23.31)	0.53
INO (W/m^2)	1.96 (1.64-2.31)	1.88 (1.74-2.39)	1.70 (1.56-1.93)*	$<0.01^{\ddagger\S}$
PKR	19.49 (14.84-24.25)*	19.09 (13.47-24.76)	24.06 (17.28-30.59)*	$<0.01^{\ddagger\S}$
Singleton				
MAP (mmHg)	88.00 (82.84-96.67)	86.33 (80.33-90.00)	86.17 (80.67-91.33)	$<0.01^{\dagger,\ddagger}$
HR (bpm)	79.46 (71.57-87.61)	79.98 (74.16-87.65)	83.32 (75.77-93.06)	$0.03^{\ddagger,\S}$
SV (cm^3)	82.35 (72.37-93.66)	90.49 (77.51-101.72)	88.80 (79.67-95.96)	$<0.01^{\dagger,\ddagger}$
SVI (cm^3/m^2)	48.63 (44.28 – 55.93)	52.07 (45.29 – 57.34)	50.31 (43.45 – 55.43)	0.37
CO (l/min)	6.47 (5.83-7.41)	7.12 (6.44-7.79)	7.34 (6.60-8.16)	$<0.01^{\dagger,\ddagger}$
CI ($l/min/m^2$)	3.89 (3.46 – 4.40)	4.11 (3.80 – 4.54)	4.05 (3.78 – 4.76)	0.12
SVR ($d.s.cm^{-5}$)	1082.45 (948.15-1266.58)	968.64 (866.61-1064.30)	940.87(824.48-1075.73)	$<0.01^{\dagger,\ddagger}$
SVRI ($d.s.cm^{-5}/m^2$)	1851.19 (1570.80 – 2103.59)	1663.97 (1483.20 - 1858.36)	1698.48 (1469.65 – 1837.94)	$<0.01^{\dagger,\ddagger}$
INO (W/m^2)	1.95 (1.66-2.20)	1.92 (1.69-2.16)	1.87 (1.71-2.11)	0.71
PKR	25.07 (19.17-31.13)	20.09 (16.09-24.31)	20.13 (17.03-24.57)	$<0.01^{\dagger,\ddagger}$
SVV	18.20 (14.29-23.98)	18.55 (15.86-24.53)	19.90 (14.15-26.36)	0.49

Data are given as median (interquartile range). MAP: Mean Arterial Pressure; HR: Heart Rate; SV: Stroke Volume; SVI: Stroke Volume Index; CO: Cardiac Output; CI: Cardiac Index; SVR: Systemic Vascular Resistance; SVRI: Systemic Vascular Resistance Index; INO: Inotropy Index; PKR: Potential to Kinetic Energy Ratio.

Comparison among trimesters: $p<0.05$ † 1st trimester vs 2nd trimester; ‡ 1st trimester vs 3rd trimester; § 2nd trimester vs 3rd trimester

Comparison among groups: $p<0.05$ ¶DCvsMC; *vs singleton