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Twin pregnancies and maternal cardiovascular function: literature review and future prospects

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Abstract. Twin pregnancy – with a prevalence nearly doubled in the last decades due to the use of assisted reproductive technology and the increasing age of conception – is associated with physiological cardiovascular adaptations to meet the hemodynamic demands of pregnancy. Compared to singleton pregnancies, increased and earlier in pregnancy risk of developing perinatal complications and maternal cardiac disease is demonstrated due to additional stress on the maternal cardiovascular system due to higher circulation volume. Knowledge on maternal adaptation in twin pregnancies are still lacking and often data derive from research studies on singleton pregnancy and including twins without differentiations. Only a few trials considered the impact of twin pregnancies on the maternal cardiovascular system and included echocardiographic evaluations showing how the changes in left ventricular geometry, systolic and diastolic function were comparable to those observed later in uncomplicated singleton pregnancies or in presence of hypertensive disorders. The present work aimed to review the current state of research on maternal cardiovascular function in twin pregnancies as the basis for a new study focused to find premature echocardiographic parameters able to contribute to the design of effective preventive strategies of complications – such as hypertensive disorders – in pregnancies, particularly on twin pregnancy.

Keywords: twin, pregnancy, cardiovascular system, diastolic function, systolic function.

INTRODUCTION

The Worldwide incidence of multiple pregnancies, especially twins is growing – nearly doubled in the last decades in USA – due to the wide use of assisted reproductive technology and the increased age of conception.

During pregnancy – singleton or multiple – mother's anatomical, metabolic, and physiological changes are necessary for the benefit of the foetus-

es; in fact, physiological cardiac remodelling permits to increase cardiac output and blood volume on one side and decrease the peripheral vascular resistances from the other side (Melchiorre et al., 2016).

Women failing to meet the haemodynamic demands of pregnancy are more likely to develop perinatal or maternal complications and have also an increased risk to develop cardiovascular disease later in life. (Bellamy et al., 2007).

Compared with singleton pregnancy, uncomplicated twin pregnancy has a more pronounced and altered maternal cardiac function, haemodynamic changes, and additional stress on the maternal cardiovascular system due to higher circulation volume; therefore, in twin pregnancies mother's heart has a higher risk of decompensation correlating to increased risk of complication such as pre-eclampsia (Francisco et al., 2017 and Li X et al., 2016).

Trials demonstrated the proportionality of the occurrence of pre-eclampsia and the number of foetuses with a prevalence of 6.5%, 12.7% and 20% in singleton, twin and triples pregnancies respectively (DayMC Barton et al., 2005 and Adank MC et al., 2020) and occurrence at an earlier gestation age, a more quickly progression and an atypical presentation in twin pregnancies; the larger placental size and mass, the stronger inflammatory response, and the possibility to a larger area of placental perfusion damage are the major causes of these findings (Wang et al.2021 and Narang et al., 2021).

We conducted an extensive literature search through PubMed (NCBI) up to 20 June 2023 based on journals evaluating maternal echocardiographic cardiovascular function in twin pregnancies. The keywords used were: twin, pregnancy, echocardiography, systolic and diastolic function (Table 1).

HYPOTHESIS AND THEORY ON MATERNAL CARDIOVASCULAR FUNCTION

Knowledge on maternal cardiovascular function during twin pregnancies are still lacking, women with multiple gestations were often excluded from research studies or included in studies with singletons without differentiation, despite the disproportionate incidence of pregnancy changes and complications in twin pregnancies.

Two of the most dated studies (Robson et al.,1989 and Veille et al.,1985) and then other more recent studies (Kametas et al.,2003 and Kuleva et at,2011) reported variations of the left ventricular (LV) function during gestation such as the increase of cardiac output, stroke volume (SV), heart rate, LV end-diastolic volume and of left atrial area, related to the more hyperdynamic maternal

circulation, increased plasma volume and venous return in twin pregnancies.

Moreover, a recent trial (Orabona et al.,2022) added information on maternal LV dimensions, volumes and LV mass during twin pregnancies demonstrating the progressively increased trend from the first to the third trimester, like in singletons.

Regarding the LV diastolic function, at first, Ghi and Degli Esposti et al (2015) observed the deterioration of diastolic parameters characterized by the reduction of mitral E wave and the increase of mitral A wave and of left atrial pressures.

Recently, Nunez et al confirmed all previous data and taking into consideration the increase of cardiac output, myocardial performance index, LV mass, relative wall thickness (RWT) and the progressive LV diastolic dysfunction demonstrating the increase of isovolumetric relaxation time (IVRT), left atrial area and, the decrease of mitral E/A ratio in twin – dichorionic and monochorionic – pregnancies. No differences were observed in LV myocardial deformation between twin and singleton pregnancies.

Moreover, the impact of chorionicity on the cardiovascular system was examined (Nunez et al and Ghi and Dall'Asta et al.,2019) and dichorionic twin pregnancies seemed to be associated with more accentuated mother cardiac changes.

The impact of pregnancy on maternal right ventricular (RV) systolic and diastolic function was investigated in a recent longitudinal study (Orabona et al.,2022) involving 30 twin pregnancies and no significant differences in RV function (all the parameters such as fractional area change FAC, TAPSE, sPAP, E and A waves, E/A, DT, E/e', IVCT, myocardial performance index and 2D longitudinal strain) were found in twins pregnancies compared to singleton pregnancies.

In general, all trials demonstrated how the maternal cardiovascular changes in twin pregnancies anticipated those encountered in singleton pregnancy later in gestation, suggesting the physiological remodelling in response to the increase in volume loading rather than decompensation of the maternal cardiovascular system.

Recently Giorgione et al (2022) – considering around 830 pregnant women – demonstrated how changes in LV geometry, function and haemodynamics in normotensive twin pregnancy were comparable to those observed in singleton pregnancies complicated by hypertensive disorders of pregnancy (HDP); the cardiac maladaptation in twin pregnancies seemed to be exacerbated in the presence of HDP, compared to normotensive twin pregnancies.

The importance of these findings is related to the precocious evaluation of the functional and structural cardiac changes that could precede complications in pregnancy.

Table 1. Summary of studies on twin pregnancies.

Author	Country	Year	Experimental model	Results
Robson et al.	UK	1989	10 and 13 women with twin and singleton pregnancies respectively.	Heart rate (HR), SV, cardiac output, LV end-diastolic volume, left atrial dimension, RWT, LV mass, systolic and diastolic blood pressure were increased and TVR were reduced compared to non-pregnant values. In twin pregnancies, only heart rate, cardiac output, left atrial dimension were significantly higher compared to singleton pregnancies.
Veille et al.	USA	1985	6 and 16 women with twin and singleton pregnancies respectively.	Heart rate, cardiac index, SV, fractional shortening were increased in the second and third trimester of twin pregnancies. Blood pressure and end-diastolic ventricular size were not affected differently by twin pregnancies.
Kametas et al.	UK	2003	119 women with twin pregnancies and 128 women with singleton pregnancies.	In twin pregnancies, compared to singletons, cardiac output, SV, HR, LV end-diastolic dimensions, ejection fraction, long axis shortening were increased.
Kuleva et al.	Italy	2011	20 women with twin pregnancies and 10 women with singleton pregnancies.	Cardiac output increased during pregnancies, in both twins and singletons. TVR decreased during pregnancy.
Ghi and Degli Esposti et al.	Italy	2015	30 (24 dichorionic and 6 monochorionic) twin pregnancies.	During pregnancy, a reduction of LV ejection fraction, a progressive reduction of pulsed Doppler E-wave velocity and an increase of A-wave were showed from first to third trimester. Higher left atrial pressure was demonstrated.
Ghi and Dall'Asta et al.	Italy	2018	67 twin pregnancies (48 dichorionic and 19 monochorionic).	Compared to dichorionic pregnancies, in the monochorionic sets lower cardiac output and higher TVR were observed. Regarding the diastolic function, higher values were observed for mitral E/A ratio, septal mitral E'/A' ratio, lateral mitral E' in monochorionic pregnancies.
Nunez et al.	UK	2022	155 women with twin pregnancies (86 dichorionic and 69 monochorionic).	In both types of twin pregnancies, compared to singletons, IVRT, left atrial area, RWT, myocardial performance index and LV mass were increased, and mitral E/A ratio decreased.
Orabona et al.	Italy	2022	30 women with uncomplicated singleton and 30 women with uncomplicated twin pregnancies.	During twin pregnancy, maternal LV dimensions and mass increased from first to third trimester, like singletons, while LVEF remained stable. Diastolic function worsened with no differences between twins and singletons, except for higher LV filling pressure in the second trimester in twins. Two-dimensional strains did not vary during gestation in either group, while GLS was altered in one-fourth/one-third in both groups.
Orabona et al.	Italy	2022	30 women with uncomplicated singleton and 30 women with uncomplicated twin pregnancies.	RV function parameters (FAC, TAPSE, sPAP, E, A, E/A, DT, E/E', IVA, IVCT, MPI and 2D longitudinal strain) in twin pregnancies were similar to singletons. Left atrial dimension increased throughout gestation in both twins and singletons.
Giorgione et al.	UK	2022	119 HDP singleton pregnancies, 52 normotensive twin pregnancies and 24 HDP twin pregnancies.	LV mass did not differ between singleton pregnancies complicated by HDP and normotensive twin pregnancies but was higher in HDP twin compared with HDP singleton pregnancies. Left atrial volume and E/e' were higher in HDP twin compared with normotensive twin pregnancies. In normotensive twin compared with HDP singleton pregnancies SV was higher and TVR lower.

Heart rate (HR), cardiac output (CO), total vascular resistances (TVR), hypertensive disorders of pregnancy (HDP).

POTENTIAL FUTURE DEVELOPMENTS IN THE TWIN PREGNANCIES FIELD

Although data on twin pregnancies are still missing, recent knowledge about physiological and pathophysiological changes are emerging.

During singleton and multiple pregnancies physiological adaptations are necessary to ensure adequate uter-

oplacental circulation for foetal growth and development and to respond to higher circulation volume of mothers. In twin pregnancies – compared with singletons – LV mass, end-diastolic volume, SV, cardiac output, and left atrium dimensions increase, but there are also other subtle changes in systolic and diastolic LV function parameters. The typical cardiovascular adaptations in twin pregnancies resemble to those seen in singletons in late gesta-

tion and this concept suggests physiological remodelling in response to the increase in volume.

When mother's physiological changes fail to meet the haemodynamic demands, the risk of complication increases.

Moreover, twin pregnancies have an increased risk of cardiovascular complications -such as pre-eclampsia-, at an earlier gestation age and, a more quickly progression compared to singleton pregnancies.

Understanding the normal cardiovascular changes occurring during pregnancies is essential not only for caring patients with cardiovascular disease but also to try to anticipate the occurrence of complications in the pregnancies of subjects with no pre-pregnancy disorders.

Therefore, we retain that could be useful to establish a new longitudinal study based on transthoracic echocardiography evaluations during the three trimesters of pregnancy to find premature parameters able to contribute to the design of effective preventative strategies for prevention of maternal cardiovascular diseases in high-risk pregnancies such as twins ones.

LEGENDS

HDP hypertensive disorders of pregnancy
 IVCT isovolumetric contraction time
 IVRT isovolumetric relaxation time
 LAVi left atrial volume
 LV left ventricle
 RV right ventricle
 RWT relative wall thickness
 SV stroke volume
 TTE Transthoracic echocardiography
 TVR total vascular resistance

REFERENCES

- Adank MC, Broere-Brown ZA, Goncalves R, Kamran Ikram M, Jaddoe VW, Steegers EAP, Schalekamp-Timmermans S. 2020, Maternal cardiovascular adaptation to twin pregnancy: a population-based prospective cohort study, *BMC Pregnancy and Childbirth*.
- Bellamy L, Casas JP, Hingorani AD, Williams DJ. 2007 Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and metaanalysis. *BMJ*.
- Day MC, Barton JR, O'Brien JM, Istwan NB, Sibai BM. 2005. The effect of fetal number on the development of hypertensive conditions of pregnancy. *Obstet Gynecol*. 106(5 Pt 1):927-31.
- Francisco C, Wright D, Benk ˆo Z, Syngelaki A, Nicolaides KH. 2017. Hidden high rate of pre-eclampsia in twin compared with singleton pregnancy. *Ultrasound Obstet Gynecol*; 50: 88-92.
- Ghi T, degli Esposti D, Montaguti E, Rosticci M, Tancredi S, Youssef A, di Giovanni MV, Pilu G, Borghi C, Rizzo N. 2015. Maternal cardiac evaluation during uncomplicated twin pregnancy with emphasis on the diastolic function. *Am J Obstet Gynecol*; 213: 376.e1-8.
- Ghi T, Dall'Asta A, Franchi L, Fieni S, Gaibazzi N, Siniscalchi C, Pedrazzi G, Montaguti E, Degli Esposti D, Carpano MG, Suprani A, Orabona R, Prefumo F, Vizzardi E, Bonadei I, Sciatti E, Borghi C, Frusca T. 2019. The effect of chorionicity on maternal cardiac adaptation to uncomplicated twin pregnancy: A prospective longitudinal study. *Fetal Diagn Ther*; 45: 394-402.
- Giorgione V, Melichiorre K, O'Driscoll J, Khalil A, Sharma R, Thilaganathan B. 2022. Maternal echocardiographic changes in twin pregnancies with and without pre-eclampsia, *Ultrasound Obstet Gynecol*.
- Kametas N, Mcauliffe F, Krampl E, Chambers J, Nicolaides KH. 2003. Maternal cardiac function in twin pregnancy. *Obstet Gynecol*; 102: 806-815.
- Kuleva M, Youssef A, Maroni E, Contro E, Pilu G, Rizzo N, Pelusi G, Ghi T. 2011. Maternal cardiac function in normal twin pregnancy: a longitudinal study. *Ultrasound Obstet Gynecol*; 38: 575-580.
- Li X, Tan H, Huang X, Zhou S, Hu S, Wang X, Xu X, Liu Q, Wen SW. 2016. Similarities and differences between the risk factors for gestational hypertension and preeclampsia: a population based cohort study in south China. *Pregnancy Hypertens*. 6(1):66-71.
- Melchiorre K, Sharma R, Khalil A, Thilaganathan B. 2016. Maternal cardiovascular function in normal pregnancy: Evidence of maladaptation to chronic volume overload. *Hypertension*; 67: 754-762.
- Narang K, Szymanski LM, 2021, Multiple Gestation and hypertensive disorders of pregnancy: what do we know? *Current Hypertensions reports*.
- Nunez E, Huluta I, Gallardo Arozena M, Wright A, Nicolaides KH, Charakida M. 2022. Maternal cardiac function in twin pregnancy at 19-23 weeks' gestation, *Ultrasound Obstet Gynecol*,
- Orabona R, Sciatti E, Vizzardi E, Bonadei I, Metra M, Sartori E, Fusca T, Pinna A, Bellocco R, Prefumo F. 2022 Maternal left ventricular function in uncomplicated pregnancies: a speckle-tracking imaging longitudinal study. *Journal of Clinical Medicine*.
- Orabona R, Sciatti E, Vizzardi E, Bonadei I, Metra M, Sartori E, Fusca T, Pinna A, Bellocco R, Prefumo F.

2022. Maternal right ventricular and left atrial function in uncomplicated twin pregnancies: a longitudinal study. *Journal of Clinical Medicine*.
- Robson SC, Hunter S, Boys RJ, Dunlop W. 1989. Hemodynamic changes during twin pregnancy. A Doppler and M-mode echocardiographic study. *Am J Obstet Gynecol*. 161:1273–1278.
- Veille JC, Morton MJ, Burry KJ. 1985. Maternal cardiovascular adaptations to twin pregnancy. *Am J Obstet Gynecol*; 153: 261–263
- Wang Y, Wu N, Shen H. 2021. A review of Research process of pregnancy with twins with pre-eclampsia. Risk management and healthcare policy.