Ultrasound Obstet Gynecol 2022; **59**: 627–632
Published online 11 April 2022 in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.24857

Maternal cardiac function in twin pregnancy at 19–23 weeks' gestation

E. NUNEZ[1], I. HULUTA[1], M. GALLARDO AROZENA[1], A. WRIGHT[2], K. H. NICOLAIDES[1] and M. CHARAKIDA[1,3]

[1]*Harris Birthright Research Centre for Fetal Medicine, King's College Hospital, London, UK;* [2]*Institute of Health Research, University of Exeter, Exeter, UK;* [3]*School of Biomedical Engineering and Imaging Sciences, King's College London, London, UK*

KEYWORDS: chorionicity; maternal cardiac function; twin pregnancy

CONTRIBUTION

What are the novel findings of this work?
At 19–23 weeks' gestation, twin compared with singleton pregnancy is associated with an increase in cardiac output and reduction in left ventricular systolic and diastolic Doppler function. Cardiac changes are more accentuated in dichorionic compared with monochorionic twin pregnancies.

What are the clinical implications of this work?
Maternal cardiovascular adaptations seen in mid-gestation in twin pregnancy resemble those encountered in singleton pregnancy later in gestation and are mostly related to changes in loading conditions. These findings support the plasticity of the maternal cardiovascular system and its increased ability for remodeling in response to volume loading, without evidence of decompensation.

ABSTRACT

Objectives *To compare maternal cardiovascular indices at 19–23 weeks' gestation between twin and singleton pregnancies and assess the impact of chorionicity on these parameters.*

Methods *This was a prospective observational study in women with twin pregnancy attending for a hospital visit at 19 + 1 to 24 + 3 weeks' gestation. This visit included recording of maternal demographic characteristics and medical history and maternal cardiovascular assessment. In a previous study of 4795 women with singleton pregnancies at 19–23 weeks' gestation, multivariable linear regression models were fitted between the various cardiovascular indices and elements of maternal characteristics and medical history. In this study, we calculated multiples of the median (MoM) and delta values according to the singleton models and assessed the distributional properties of these MoM and delta values in twin as compared with singleton pregnancies.*

Results *The study population of 155 women with twin pregnancy included 86 dichorionic and 69 monochorionic cases. In general, there was a similar distribution of maternal cardiovascular indices in monochorionic and dichorionic twin pregnancies. In both types of twin pregnancy, compared with singleton pregnancy, there was an increase in isovolumetric relaxation time, left atrial area and myocardial performance index, and a decrease in mitral valve E/A. Left ventricular mass indexed for body surface area and relative wall thickness were also increased in twin compared with singleton pregnancy. The magnitude of the increase in left atrial area was greater in dichorionic compared with monochorionic pregnancies. Additionally, mitral valve E was decreased and left atrial volume was increased in dichorionic but not in monochorionic pregnancies, while isovolumetric contraction time was increased in monochorionic but not in dichorionic pregnancies. Left ventricular myocardial deformation was similar between twin and singleton pregnancies.*

Conclusions *In twin pregnancies at mid-gestation, maternal systolic and diastolic function is reduced when compared with singletons. The patterns of cardiovascular adaptation are similar between monochorionic and dichorionic pregnancies and resemble those reported in uncomplicated singleton pregnancy later in gestation.*

INTRODUCTION

During pregnancy, various anatomical, physiological and metabolic changes occur in the mother for the benefit of

Correspondence to: Prof. K. H. Nicolaides, Harris Birthright Research Centre for Fetal Medicine, Fetal Medicine Research Institute, King's College Hospital, 16–20 Windsor Walk, Denmark Hill, London SE5 8BB, UK (e-mail: kypros@fetalmedicine.com)

Accepted: 29 December 2021

the fetus. Cardiac output and blood volume increase by 40%, while peripheral vascular resistance decreases[1–3]. Such changes result in compensatory cardiac remodeling with mild dilatation of all cardiac chambers and increase in left ventricular (LV) mass[1].

Compared with singleton pregnancy, twin pregnancy is thought to pose additional stress on the maternal cardiovascular system due to the higher circulating volume[4]. Consistent with this hypothesis, it has been shown that maternal cardiac output is increased and peripheral vascular resistance is reduced in twin pregnancy compared with singleton pregnancy[3]. In addition, in a relatively small number of uncomplicated twin pregnancies, worsening of LV systolic and diastolic function has been reported with advancing gestation, but the effect of chorionicity remains largely unexplored[5–8]. These findings raise concerns about whether the maternal heart in twin pregnancy is at higher risk of decompensation, which might explain the increased risk of pregnancy complications, such as pre-eclampsia[9], in these women.

The objectives of this study were to examine the effect of chorionicity on maternal cardiovascular indices and compare the values between twin and singleton pregnancies at 19–23 weeks' gestation.

METHODS

Study population and design

This was a prospective observational study in women with twin pregnancy attending for a hospital visit at 19 + 1 to 24 + 3 weeks' gestation at King's College Hospital, London, UK, between January 2019 and December 2020. The women with dichorionic twin pregnancy were booked for pregnancy care in our hospital, whereas many of those with monochorionic twins were booked in other hospitals but were referred to our fetal medicine unit for further assessment and management following their 11–13-week scan in which the diagnosis of monochorionicity was made. The visit at 19 + 1 to 24 + 3 weeks included recording of maternal demographic characteristics and medical history, ultrasound examination for fetal anatomy and growth and maternal cardiovascular assessment. In all cases, an ultrasound scan had also been carried out at 11–13 weeks to determine gestational age based on crown–rump length of the larger twin and chorionicity based on the number of placentae and the presence or absence of the lambda sign at the intertwin membrane–placental junction[10,11]. The women provided written informed consent to participate in the Advanced Cardiovascular Imaging Study (REC No 18/NI/0013, IRAS ID: 237936), which was approved by the NHS Research Ethics Committee.

Data on pregnancy outcome were obtained from the computerized records of patients delivering in our hospital or from other hospitals if delivery was not in our hospital. The inclusion criterion for this study was twin pregnancy resulting in a non-malformed live birth. Pregnancies with aneuploidy, major fetal abnormality, those with one or two fetal deaths and those complicated with pre-eclampsia were excluded.

Maternal cardiovascular assessment

The participants were assessed using two-dimensional and Doppler transthoracic echocardiography at rest in the left lateral decubitus position, and data were acquired during unforced expiration. The protocol included standard parasternal and apical views acquired using a Canon Aplio i900 scanner (Canon Medical Systems Europe BV, Zoetermeer, The Netherlands) as per American Society of Echocardiography and European Association of Cardiovascular Imaging guidelines[12,13]. Echocardiography was performed by fetal medicine fellows who were trained in acquisition and analysis of echocardiograms. In a previous study, we reported excellent interobserver reproducibility of measurement of various cardiac indices[14].

Cardiac output was calculated from stroke volume (derived from the LV outflow tract velocity time integral) multiplied by heart rate. Left atrial area was calculated in end-systole from the four-chamber view and left atrial volume was measured using biplane area-length method[13]. LV mass was calculated with the Devereux formula using measurements of the anatomical M-mode applied in the parasternal long axis. The relative wall thickness was calculated as (2 × posterior wall thickness)/LV diastolic diameter. The mitral peak early (E) and late (A) diastolic flow velocities were measured, and the E/A ratio was calculated. Pulsed tissue Doppler recordings were obtained at the septal and lateral aspects of the basal LV at the junction with the mitral valve annulus in the apical four-chamber view. The E/e′ ratio was calculated using the mean value between septal and lateral peak e′ waves. Speckle tracking was employed to assess global longitudinal systolic strain of the LV using four-, two- and three-chamber projections. Analysis was performed using the Canon semiautomated speckle-tracking analysis software (Canon, Medical Systems, Crawley, UK).

Statistical analysis

Data were expressed as median (interquartile range (IQR)) for continuous variables and *n* (%) for categorical variables. Student's *t*-test and chi-square test or Fisher's exact test were used to compare continuous and categorical data, respectively, between outcome groups.

The following cardiovascular indices were examined: E, A, E/A, E/e′, isovolumetric relaxation time, left atrial area, left atrial volume, myocardial performance index, global longitudinal systolic strain, LV ejection fraction, isovolumetric contraction time, peripheral vascular resistance, LV cardiac output, LV stroke volume, LV mass and relative wall thickness. In a previous study of 4795 women with singleton pregnancies at 19–23 weeks' gestation, multivariable linear regression models were fitted between the various cardiovascular indices and

elements of maternal characteristics and medical history, including heart rate, age, racial origin, method of conception, cigarette smoking during pregnancy, history of chronic hypertension, diabetes mellitus and previous pregnancy with pre-eclampsia[15]. Some of the cardiovascular indices were $\log_{10}$ transformed to achieve homogeneity of variance and approximate Gaussian distributional form. In this study, we used the estimates from the regression models from our study on singletons to calculate multiples of the median (MoM) values for indices that had been $\log_{10}$ transformed and delta values for indices that were not $\log_{10}$ transformed. The statistical software package R was used for data analysis[16].

RESULTS

Maternal and pregnancy characteristics of the study population of 155 twin pregnancies, including 69 monochorionic and 86 dichorionic cases, are summarized in Table 1. In the dichorionic compared with monochorionic group, there was a higher median maternal age and higher proportions of women of black racial origin and cases conceived by *in-vitro* fertilization.

The distribution of MoM or delta values of cardiovascular indices in dichorionic and monochorionic twin pregnancies are shown in Figure 1 and Table 2. The raw data of singleton and twin pregnancies are presented in Table S1. In general, the distribution of indices in monochorionic and dichorionic twin pregnancies was similar. In both types of twin pregnancy, compared with singleton pregnancy, there was an increase in isovolumetric relaxation time, left atrial area, myocardial performance index and LV mass, and a decrease in mitral valve E/A. Relative wall thickness was also increased in twin pregnancies compared with singletons. The magnitude of increase in left atrial area was greater in dichorionic than in monochorionic pregnancies.

DISCUSSION

Principal findings of this study

In this prospective study of uncomplicated dichorionic and monochorionic twin pregnancies, we performed detailed echocardiographic evaluation of maternal LV systolic and diastolic function at 19–23 weeks' gestation. The data demonstrated that, first, there was a similar distribution of values for most cardiovascular indices in the two types of twin pregnancies and, second, women with twin pregnancy compared to those with singleton pregnancy had increased volume loading at mid-gestation and evidence of cardiac remodeling, with an increase in left atrial area and reduction in load-dependent systolic and diastolic cardiac function, similar to that which has been observed in singletons later in gestation[1,2]. These findings suggest that the maternal cardiovascular system in uncomplicated twin pregnancy is able to remodel in response to increased loading conditions without showing signs of cardiac decompensation.

Interpretation of findings

Our findings suggest that, in twin pregnancy, there is evidence of cardiac remodeling in response to increase in loading conditions. In particular, in twins overall

Table 1 Maternal and pregnancy characteristics of the study population of 155 twin pregnancies, overall and according to chorionicity

Characteristic	*All* (n = *155*)	*Monochorionic* (n = *69*)	*Dichorionic* (n = *86*)	P
Age (years)	34.0 (29.0–38.0)	32.0 (28.0–36.0)	36.0 (30.0–39.0)	0.003
Weight (kg)	75.0 (66.9–86.5)	78.2 (65.0–87.3)	74.3 (67.4–85.0)	0.949
Height (cm)	166 (160–170)	164 (160–170)	167 (162–170)	0.102
Body mass index (kg/m^2)	27.5 (24.0–31.2)	28.1 (24.0–31.6)	27.2 (24.0–30.3)	0.689
Gestational age (weeks)	21.1 (20.4–22.6)	21.7 (20.3–23.5)	21.1 (20.4–21.6)	0.576
Racial origin				0.001
White	116 (74.8)	55 (79.7)	61 (70.9)	
Black	20 (12.9)	3 (4.3)	17 (19.8)	
South Asian	6 (3.9)	4 (5.8)	2 (2.3)	
East Asian	2 (1.3)	2 (2.9)	0 (0)	
Mixed	11 (7.1)	5 (7.2)	6 (7.0)	
Medical history				
Chronic hypertension	4 (2.6)	2 (2.9)	2 (2.3)	0.823
Diabetes mellitus	2 (1.3)	1 (1.4)	1 (1.2)	0.359
Smoker	0 (0)	0 (0)	0 (0)	1
Method of conception				0.003
Spontaneous	119 (76.8)	61 (88.4)	58 (67.4)	
In-vitro fertilization	36 (23.2)	8 (11.6)	28 (32.6)	
Parity				0.925
Nulliparous	83 (53.5)	38 (55.1)	45 (52.3)	
Parous, no previous pre-eclampsia	70 (45.2)	30 (43.5)	40 (46.5)	
Parous, previous pre-eclampsia	2 (1.3)	1 (1.4)	1 (1.2)	

Data are given as median (interquartile range) or *n* (%). Dichorionic and monochorionic twin pregnancies were compared using chi-square or Fisher's exact test for categorical variables and Mann–Whitney *U*-test for continuous variables.

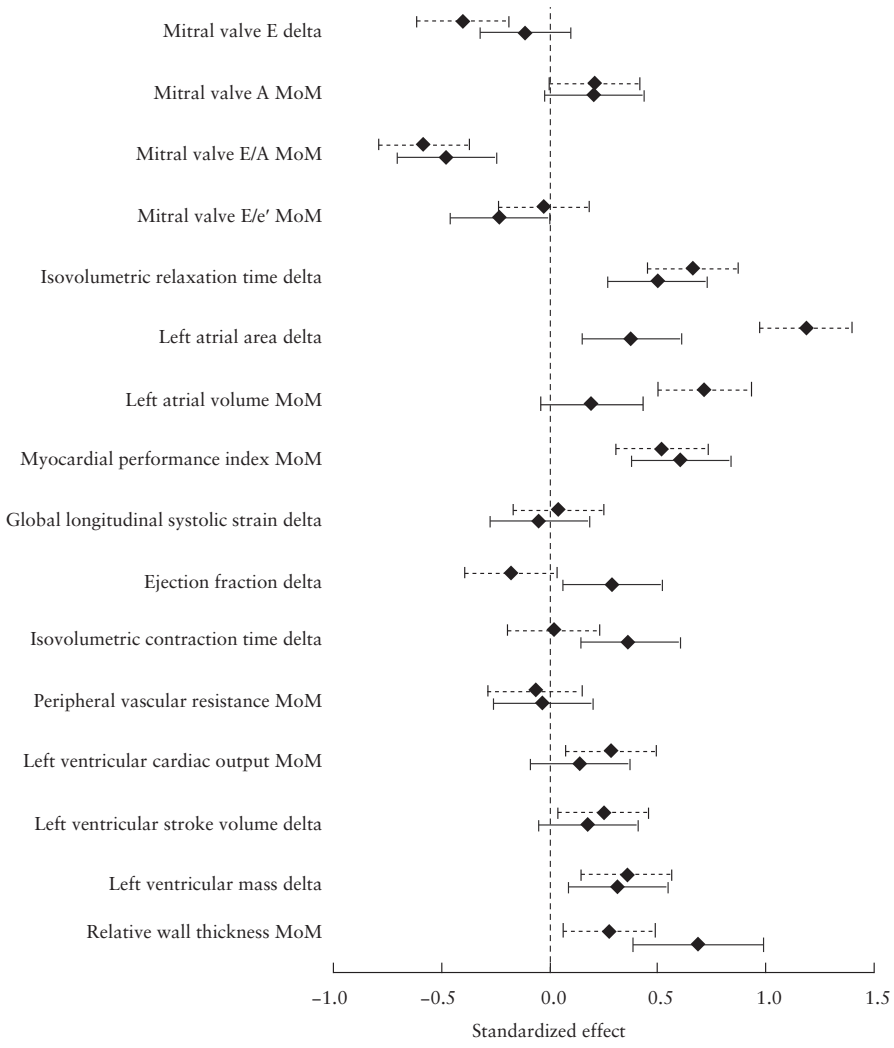

Figure 1 Forest plot of cardiovascular indices (mean and 95% CI) in dichorionic (⟡) and monochorionic (⟡) twin pregnancies adjusted for maternal characteristics and medical history. The vertical line corresponds to a mean of 0.0 in singleton pregnancies. MoM, multiples of the median.

Table 2 Cardiovascular indices of the study population of 155 twin pregnancies, overall and according to chorionicity

Cardiovascular index	*All* (n = *155*)	*Monochorionic* (n = *69*)	*Dichorionic* (n = *86*)
Left ventricular diastolic function			
Mitral valve E delta	−4.113 (−6.862 to −1.364)	−2.518 (−7.603 to 2.566)	−5.393 (−8.217 to −2.569)
Mitral valve A MoM	1.056 (1.012–1.101)	1.054 (0.995–1.116)	1.057 (0.997–1.121)
Mitral valve E/A MoM	0.879 (0.838–0.923)	0.885 (0.801–0.979)	0.875 (0.824–0.928)
Mitral valve E/e′ MoM	0.971 (0.938–1.006)	0.944 (0.889–1.002)	0.994 (0.948–1.043)
Isovolumetric relaxation time delta	7.759 (5.735–9.782)	6.053 (3.254–8.853)	9.127 (6.257–11.996)
Left atrial area delta*	0.867 (0.682–1.053)	0.551 (0.202–0.899)	1.121 (0.919–1.323)
Left atrial volume MoM*	1.127 (1.084–1.172)	1.052 (0.990–1.118)	1.192 (1.131–1.256)
Left ventricular systolic function			
Myocardial performance index MoM	1.118 (1.087–1.151)	1.131 (1.078–1.187)	1.108 (1.063–1.156)
Global longitudinal systolic strain delta	−0.0009 (−0.332 to 0.331)	−0.107 (−0.580 to 0.366)	0.084 (−0.361 to 0.529)
Ejection fraction delta	0.011 (−0.845 to 0.867)	1.269 (0.197–2.341)	−0.998 (−2.181 to 0.185)
Isovolumetric contraction time delta	1.681 (0.090–3.271)	3.564 (1.267–5.861)	0.169 (−1.769 to 2.107)
Hemodynamic parameter			
Peripheral vascular resistance MoM*	0.985 (0.952–1.018)	0.991 (0.941–1.043)	0.980 (0.937–1.025)
Left ventricular cardiac output MoM*	1.034 (1.009–1.060)	1.022 (0.984–1.060)	1.044 (1.010–1.079)
Left ventricular stroke volume delta*	1.510 (0.458–2.562)	1.1003 (−0.430 to 2.636)	1.839 (0.313–3.365)
Structural marker			
Left ventricular mass delta*	3.786 (2.003–5.568)	3.294 (0.816–5.773)	4.179 (1.744–6.615)
Relative wall thickness MoM	1.064 (1.032–1.097)	1.114 (1.062–1.168)	1.040 (1.008–1.073)

Data are given as mean (95% CI). *Indexed for body surface area. MoM, multiples of the median.

(considering mono- and dichorionic twins together), the increase in preload was associated with an increase in left atrial area, stroke volume and cardiac output. LV hypertrophic response was also noted, similar to changes seen in late gestation in normal pregnancy[1,2]. Transmitral A wave Doppler was increased, and E/A ratio was reduced, whereas LV filling pressure assessed by E/e′ ratio was unaltered. With regard to myocardial contractility, variability in responses was noted, with impairment of myocardial performance index, the load-dependent index of LV performance, whereas other load-independent markers, such as global longitudinal systolic strain, were unaffected. Cardiac responses were accentuated in women with dichorionic pregnancy compared to those with monochorionic pregnancy, but a similar pattern was noted between the two groups. Thus, the reported cardiac changes likely reflect beneficial adaptive myocardial responses to increased volume loading. However, they may pose concerns regarding whether the persistent stressor exposure might drive maladaptive remodeling and ultimately lead to decompensation later in gestation, and this remains to be determined.

Comparison with previous studies

Several previous echocardiographic studies, involving small numbers of patients, reported on maternal cardiac indices in twin compared with singleton pregnancies. Veille *et al.* examined 16 uncomplicated twin pregnancies and 17 singletons during the second and third trimesters of pregnancy; they reported that, in twin pregnancies, LV cardiac output and stroke volume were increased[17]. Robson *et al.* performed a longitudinal study from 20 to 26 weeks' gestation in 10 uncomplicated twin pregnancies and 10 singletons; they reported that, in twin pregnancies, LV cardiac output and left atrial area were increased and suggested that their findings were the consequence of increased plasma volume and higher venous return in twin pregnancies[4]. Kametas *et al.* performed a cross-sectional study in 106 uncomplicated twin pregnancies and 125 singletons at 10–40 weeks' gestation and reported that, in twin pregnancies, there was an increase in LV cardiac output, stroke volume, LV mass, ejection fraction and left atrial area[5]. The authors suggested that their findings demonstrate that, in twin pregnancies, the maternal circulation is more hyperdynamic than in singleton pregnancies[5]. Kuleva *et al.* performed a longitudinal study on maternal cardiac function in 20 uncomplicated twin pregnancies and 10 singletons between 20 and 33 weeks' gestation and reported that LV cardiac output was significantly higher in twin pregnancies throughout the examined gestational-age range[6]. In a subsequent study by the same group, 30 uncomplicated twin pregnancies were examined at 11–13, 20–23 and 28–32 weeks' gestation; with advancing gestation, there was a deterioration in LV systolic function, characterized by decreased ejection fraction and longitudinal contractility, and a deterioration in diastolic function, characterized by a reduction in mitral E and an increase in mitral A[7]. There is only one previous study that compared maternal cardiac function in uncomplicated dichorionic *vs* monochorionic twin pregnancies; the authors examined 48 dichorionic and 19 monochorionic twin pregnancies at 11–13, 20–23 and 28–32 weeks' gestation[8]. In both types of twin pregnancy, maternal heart function changed significantly from early pregnancy to the third trimester, but these changes were of greater magnitude in the dichorionic group, including higher cardiac output and lower total vascular resistance in the dichorionic compared with monochorionic group. It was suggested that, in dichorionic pregnancy, the higher total placental mass may be associated with a greater volume overload and heavier burden on maternal heart function[8].

Strengths and limitations

The main strengths of the study are, first, detailed assessment of the maternal cardiovascular system in normal twin pregnancies using standard and advanced echocardiographic techniques and comparison of the results with values from a large population of singleton pregnancies and, second, assessment of the effect of chorionicity on maternal cardiovascular system. The main limitation is that the data are confined to mid-gestation.

Conclusions

In this large cross-sectional study, we showed that, in twin pregnancies compared with singletons, LV mass is increased, but there are only subtle changes in systolic and diastolic LV functional indices. In addition, we demonstrated that the pattern of cardiac changes was similar in monochorionic and dichorionic twin pregnancies. The cardiovascular changes that were observed in twin pregnancies resemble those seen in singletons in late gestation and suggest physiological remodeling in response to the increase in volume loading rather than decompensation of the maternal cardiovascular system.

ACKNOWLEDGMENTS

The study was supported by a grant from the Fetal Medicine Foundation (Charity No: 1037116). The ultrasound machines for fetal echocardiography and the software for speckle-tracking analysis were provided free-of-charge by Canon Medical Systems Europe BV, Zoetermeer, The Netherlands. These bodies had no involvement in the study design, in the collection, analysis and interpretation of data, in the writing of the report or in the decision to submit the article for publication.

REFERENCES

1. Bamfo JE, Kametas NA, Nicolaides KH, Chambers JB. Maternal left ventricular diastolic and systolic long-axis function during normal pregnancy. *Eur J Echocardiogr* 2007; **8**: 360–368.

2. Kametas NA, McAuliffe F, Hancock J, Chambers J, Nicolaides KH. Maternal left ventricular mass and diastolic function during pregnancy. *Ultrasound Obstet Gynecol* 2001; **18**: 460–466.
3. Melchiorre K, Sharma R, Khalil A, Thilaganathan B. Maternal cardiovascular function in normal pregnancy: Evidence of maladaptation to chronic volume overload. *Hypertension* 2016; **67**: 754–762.
4. Robson SC, Hunter S, Boys RJ, Dunlop W. Hemodynamic changes during twin pregnancy. A Doppler and M-mode echocardiographic study. *Am J Obstet Gynecol* 1989; **161**:1273–1278.
5. Kametas N, Mcauliffe F, Krampl E, Chambers J, Nicolaides KH. Maternal cardiac function in twin pregnancy. *Obstet Gynecol* 2003; **102**: 806–815.
6. Kuleva M, Youssef A, Maroni E, Contro E, Pilu G, Rizzo N, Pelusi G, Ghi T. Maternal cardiac function in normal twin pregnancy: a longitudinal study. *Ultrasound Obstet Gynecol* 2011; **38**: 575–580.
7. Ghi T, degli Esposti D, Montaguti E, Rosticci M, Tancredi S, Youssef A, di Giovanni MV, Pilu G, Borghi C, Rizzo N. Maternal cardiac evaluation during uncomplicated twin pregnancy with emphasis on the diastolic function. *Am J Obstet Gynecol* 2015; **213**: 376.e1–8.
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. The effect of chorionicity on maternal cardiac adaptation to uncomplicated twin pregnancy: A prospective longitudinal study. *Fetal Diagn Ther* 2019; **45**: 394–402.
9. Francisco C, Wright D, Benkő Z, Syngelaki A, Nicolaides KH. Hidden high rate of pre-eclampsia in twin compared with singleton pregnancy. *Ultrasound Obstet Gynecol* 2017; **50**: 88–92.
10. Robinson HP, Fleming JE. A critical evaluation of sonar crown rump length measurements. *Br J Obstet Gynaecol* 1975; **82**: 702–710.
11. Sepulveda W, Sebire NJ, Hughes K, Odibo A, Nicolaides KH. The lambda sign at 10-14 weeks as a predictor of chorionicity in twin pregnancies. *Ultrasound Obstet Gynecol* 1996; **7**: 421–423.
12. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish H, Edvardsen T, Flachskampf FA, Gillebert TC, Klein AL, Lancellotti P. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2016; **17**: 1321–1360.
13. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2015; **16**: 233–271.
14. Garcia-Gonzalez C, Abdel-Azim S, Galeva S, Georgiopoulos G, Nicolaides KH, Charakida M. Placental function and fetal weight are associated with maternal hemodynamic indices in uncomplicated pregnancies at 35-37 weeks gestation. *Am J Obstet Gynecol* 2020; **222**: 604.e1–10.
15. Gibbone E, Huluta I, Wright A, Nicolaides KH, Charakida M. Maternal cardiac function at mid-gestation and development of preeclampsia. *J Am Coll Cardiol* 2022; **79**: 52–62.
16. R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/.
17. Veille JC, Morton MJ, Burry KJ. Maternal cardiovascular adaptations to twin pregnancy. *Am J Obstet Gynecol* 1985; **153**: 261–263.

SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Table S1 Comparison of cardiovascular indices in singleton and twin pregnancies

