Title

Clinical and socioeconomic predictors of pregnancy termination for fetuses with congenital heart defects: A population-based evaluation.

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Bulleted statement.

Most of the literature on TOPFA for congenital heart defects includes single-center hospital-based studies. Moreover, few studies have evaluated both socioeconomic and clinical factors that could be associated with the risk of TOPFA for congenital heart defects.

Using population-based data, we found that, in addition to severity of congenital heart defects, early prenatal diagnosis and maternal characteristics are highly associated with the probability of TOPFA for isolated congenital heart defects.

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ABSTRACT

Objectives. 1) Evaluate the probability and timing of termination of pregnancy for fetal anomaly (TOPFA) for all congenital heart defects (CHD) and categories of CHD; 2) assess clinical and socioeconomic predictors of TOPFA for isolated CHD excluding ventricular septal defects (VSD).

Methods. Using population-based data from the Paris Registry of Congenital malformations, we assessed the probability of TOPFA and gestational age at TOPFA. We used logistic regression to estimate the adjusted effects of maternal characteristics, clinical factors (CHD type, fetal growth restriction, nuchal translucency measurement, and gestational age at prenatal diagnosis) on the odds of TOPFA.

Results. The proportion of TOPFA for prenatally diagnosed CHD was 46% for all CHD combined, 82% for CHD associated with chromosomal anomalies and 27% for isolated CHD-VSD excluded. Isolated CHD-VSD excluded diagnosed before 22 weeks of gestational age had a 3.2-fold higher odds of TOPFA (Adjusted-OR 3.2, 95%CI 1.4–7.1). Maternal occupation was not associated with the odds of TOPFA. Women of African origin had a ten-fold lower odds of TOPFA than women of French origin (Adjusted-OR 0.1, 95% CI 0.02–0.4).

Conclusion. In addition to severity of CHD, early prenatal diagnosis and maternal characteristics were highly associated with the probability of TOPFA for CHD.

Keywords. Termination of pregnancy for fetal anomaly, prenatal diagnosis, congenital heart defects, epidemiology, risk factors.

INTRODUCTION

Congenital heart defects (CHD) are the most frequent congenital anomalies.[1] Progress in fetal ultrasonography has conducted to an increase in the overall proportion of congenital malformations, and in particular CHD, that are prenatally diagnosed. The most severe cases of CHD can be accurately diagnosed during fetal life.[2-4] Ultrasonography screening for CHD at 13/14 weeks of gestation has shown to have good performances and has been proposed to be routinely performed in low-risk population.[5] In case of positive screening, a more detailed scan must be performed by a pediatric cardiologist in the beginning of the second trimester.[6] In high risk population, a specialized scan should be offered in first trimester.[7] The overall effect of prenatal diagnosis on the outcome of fetuses with CHD is difficult to evaluate due to higher severity of cases that are prenatally diagnosed.[8] Nevertheless, the beneficial effect of prenatal diagnosis on morbidity and mortality has been shown for certain CHD such as transposition of great arteries or coarctation of the aorta.[2,9,10]

For the most severe CHD, termination of pregnancy for fetal anomaly (TOPFA) following prenatal diagnosis may be an option to discuss with parents.[6,11,12] Previous studies have shown that timing and accuracy of prenatal diagnosis, existence of associated anomalies, available treatment options and prognosis are factors associated with decision-making regarding TOPFA in case of CHD.[6,12,13] However, most studies have examined TOPFA for CHD with single-center hospital-based data[11,13,14] and few population-based studies exist regarding TOPFA for CHD.[2,3,15] Moreover, few studies have evaluated both socioeconomic and clinical factors that could be associated with the risk of TOPFA for CHD.

Using population-based data from the Paris Registry for Congenital Malformations, we 1) examined the proportion of TOPFA and gestational age at TOPFA for all CHD and categories of CHD and 2) assessed the role of socioeconomic and clinical factors associated with TOPFA and

gestational age at TOPFA for cases of “isolated” CHD excluding ventricular septal defects (i.e., "major" CHD with no other associated anomalies).

MATERIAL AND METHODS

Data

We used data from the Paris Registry for Congenital Malformations which registers all cases of birth defects and chromosomal anomalies among live-borns, still-borns (≥22 weeks of gestation), and TOPFA at any gestational age. The Registry covers the population of women who live in Greater Paris area (Paris and its surrounding suburb) and deliver or have a pregnancy termination in a Parisian maternity unit. The annual number of deliveries in our population is about 38 000. The Paris Registry is a member of the European Network of Registries of Congenital Malformations (EUROCAT)[16,17] and of the International Clearinghouse for Birth Defects Surveillance and Research.[18,19]

The Registry follows the EUROCAT methodology and quality of data is routinely monitored by both EUROCAT and the National Committee of Registries in France. The review of procedures regarding confidentiality of data is overseen by both the National Committee of Registries and the National Committee of Informatics and Freedom. Data are based on medical records and are collected from several sources including maternity units, neonatology wards, and cytogenetic and pathology services.

Our study population comprised women who lived and delivered or had a pregnancy termination in Paris during the period 2001-2007.

Methods

We conducted an observational study to i) describe the proportion of TOPFA after prenatal diagnosis and gestational age at TOPFA and ii) assess predictors associated with the risk (odds) of TOPFA and gestational age at TOPFA.

Proportions of TOPFA and gestational age at TOPFA were estimated for the following categories: i) all CHD combined, ii) all isolated CHD, iii) isolated CHD-ventricular septal defects (VSD)

excluded; the latter category was constituted in order to represent major isolated CHD that often requires intervention , iv) CHD associated with chromosomal anomalies and v) CHD associated with malformations of other systems.

Predictors of the odds of TOPFA were assessed for isolated CHD-VSD excluded. Variables considered as predictors were maternal characteristics (age, occupation, geographic origin and gravidity), clinical characteristics (nuchal translucency, intra-uterine growth retardation (IUGR), gestational age at prenatal diagnosis, gestational age at TOPFA, and category of CHD) and year of TOPFA. Maternal age was coded in three categories (≤ 34, 35-37, ≥38) based on the higher risk of chromosomal anomalies in women aged 35 or more and the fact that at the time of our study reimbursed amniocentesis or chorionic villus sampling was available to all women over 38 years of age in our study population. Maternal occupation comprised the following categories: professional, intermediate, administrative/public service, and none. Maternal geographic origin was coded as: French, African and other countries. Gravidity was coded in two categories: primigravida and multigravida. Nuchal translucency measured at first trimester scan was categorized as: normal, abnormal and not done (i.e. women who had not their 1st trimester scan). IUGR was as noted in medical records and coded in two categories (no/yes). Gestational age at prenatal diagnosis was dichotomized in gestational age ≤ 22 and >22 weeks, as 22 weeks is the recommended term for 2nd trimester scan in France. Gestational age at TOPFA was analyzed as a continuous variable. Isolated cases of CHD were classified into 4 subcategories by a pediatric cardiologist (T.B.) based on the diagnosis recorded in the Registry database: i) functionally univentricular CHD, ii) so-called conotruncal CHD, iii) complex CHD (at least two cardiac defects combined excluding VSD) and iv) other CHD.

Statistical analyses

Data were analyzed using standard descriptive statistics (mean, standard deviation (SD), and frequency). Chi-square test, or Fisher's exact test when appropriate, and ANOVA test were used for univariate analyses of the differences between groups. The associations between clinical and socioeconomic factors and the odds of TOPFA were assessed using logistic regression models. Observations with missing values were excluded from the multivariate analyses. The statistical significance level was set at $\alpha = 0.05$. All analyses were done with Stata 10 software (Statacorp, TX, USA).

RESULTS

During the study period, 1465 cases of CHD were registered, among which 66% (n=968) were isolated CHD, 16% (n=230) were CHD associated with chromosomal anomalies and 18% (n=267) with anomalies of other systems (including genetic syndromes). VSD accounted for half of the cases of isolated CHD (51%, n = 495).

Gestational age at prenatal diagnosis was missing for 0.4% of fetuses. There were no missing data for the outcome of the pregnancy (live-birth, still-birth, TOPFA). Maternal occupation and nuchal translucency were missing for 8% of cases. For the other variables, data were missing for less than 1% of fetuses.

Table 1 summarizes the proportions of prenatal diagnosis and TOPFA for all CHD, and subcategories of CHD. Overall, 48% (703/1465) of cases were prenatally diagnosed and TOPFA occurred for 22% of all cases of CHD (325/1465). Prenatal diagnosis was made for 35% of all isolated CHD (339/968), 58% of isolated CHD - VSD excluded (274/473) and 79% of CHD associated with chromosomal anomalies (182/230).

Among prenatally diagnosed CHD (n=703), TOPFA was performed in 46% (325/703) of cases. The highest proportion of TOPFA was observed for CHD associated with chromosomal anomalies

(82%, 148/182). CHD associated with chromosomal anomalies accounted for 45% of cases of TOPFA (148/325). Proportion of TOPFA for isolated CHD - VSD excluded was 27% (74/274). Among those 74 cases of TOPFA for isolated CHD - VSD excluded, hypoplastic left heart syndrome accounted for half (51%, n=38).

Overall, the mean gestational age at prenatal diagnosis was 20.4 weeks (SD 0.26) for the study population (Table 2). Mean gestational age at prenatal diagnosis was lowest for cases associated with chromosomal anomalies (19.1, SD 0.38) and highest for isolated CHD - VSD excluded (21.9, SD 0.39). The mean gestational age at TOPFA was 23.2 weeks (SD 0.29) for the study population (Table 2). The average gestational age at TOPFA was lowest for CHD associated with chromosomal anomalies (21.7, SD 0.45) and highest for isolated CHD - VSD excluded (24.8, SD 0.46). The mean duration between prenatal diagnosis and TOPFA was 2.8 weeks and was similar for all subcategories of CHD. More than half (57%) of TOPFA for CHD associated with chromosomal anomalies were performed before 22 weeks of gestation vs. 17% for isolated CHD - VSD excluded. We did not find a significant time trend in the gestational age at TOPFA over the study period.

Table 3 summarizes the univariate analyses of the association of TOPFA for isolated CHD - VSD excluded with maternal characteristics and clinical factors. TOPFA was significantly less frequent for mothers of African origin (11% vs. 33% for mother of French origin and 28% for women of other origin, $p=0.003$). TOPFA was significantly more frequent for CHD diagnosed before 22 weeks of gestation (42% vs. 17% for CHD diagnosed after 22 weeks, $p<0.001$), for functionally univentricular CHD and complex CHD (60% and 34 % respectively vs. 21% for conotruncal CHD and 11% for other CHD, $p<0.001$). No statistically significant associations were observed for the other factors, although TOPFA tended to be more frequent in case of IUGR (50% vs. 26%, $p=0.09$).

Table 4 summarizes the multivariate analyses of the association of TOPFA for isolated CHD - VSD excluded with maternal characteristics and clinical factors. CHD diagnosed before 22 weeks of gestational age had a 3.2- fold higher odds of TOPFA than those diagnosed later (adjusted OR 3.2, 95%CI 1.4 – 7.1). IUGR (adjusted OR 6.6, 95%CI 0.9 – 51.0), single ventricle (adjusted OR 21.3, 95%CI 7.7 – 59.0) and complex CHD (adjusted OR 5.8, 95%CI 1.7 – 17.4) were also associated with higher odds of TOPFA but confidence intervals were fairly wide. Maternal occupation was not associated with the odds of TOPFA. However women of African origin had a 10-fold lower odds of TOPFA than women of French origin (adjusted OR 0.1, 95% CI 0.02 – 0.4). There was no significant timr trend in the odds of TOPFA during the study period.

Table 5 summarizes the results of the univariate analyses of predictors of mean gestational age at TOPFA. Sample sizes were relatively small and no statistically significant associations were observed. In particular maternal characteristics were not significantly associated with gestational age at TOPFA whereas an increased nuchal translucency measurement tended to be associated with a lower gestational age at TOPFA although the association was not statistically significant (p=0.13).

DISCUSSION

Using population-based data from the Paris Registry for Congenital Malformations, we found that the overall rate of termination of pregnancy for fetal anomaly (TOPFA) for cases with congenital heart defects (CHD) prenatally diagnosed was 46%. The highest probability of TOPFA was observed for CHD associated with chromosomal anomalies (82%). A prenatal diagnosis before 22 weeks of gestation was associated with a 3.2-higher odds of TOPFA for isolated CHD - VSD excluded. Maternal occupation was not independently associated with the probability of TOPFA. However, mothers of African origin had a 10 fold-lower odds of TOPFA than women of French origin.

It is difficult to know the extent to which our results may be generaliseable to other countries. France represents a particular context for prenatal diagnosis and TOPFA as it pursues an active and highly codified policy of prenatal diagnosis. In contrast to many European countries, TOPFA is authorized in France regardless of gestational age for incurable fetal diseases or life-threatening maternal conditions.[20] Proportions of prenatal diagnosis and TOPFA, in particular for CHD, tend to be higher in France as compared to those observed in other countries[1,15,16] even though differences in the post-natal diagnosis and the period of registration of cases in the postnatal period across countries complicate the interpretation of observed differences in the proportion of prenatal diagnosis for CHD in different countries.

We observed a lower proportion of TOPFA for isolated CHD as compared to CHD associated with chromosomal anomalies or anomalies of other systems, which is consistent with the data from the European surveillance of congenital anomalies (Eurocat) network of registries of congenital anomalies.[4,21] We also observed that the risk of TOPFA was significantly higher for functionally univentricular CHD, which is due to the fact that the outcomes for functionally univentricular CHD remain poor.[22,23]

Socioeconomic factors are known to be associated with the likelihood of TOPFA for chromosomal anomalies, in particular Down syndrome.[24-27] This association has been little studied in the specific case of CHD.[27] In a hospital-based study, Zyblewski *et al.*[13] did not find an association between socioeconomic factors and TOPFA. We found that maternal geographic origin, but not occupation, was strongly associated with the risk of TOPFA for isolated CHD. Access to information about prenatal diagnosis and TOPFA and parental decision making for chromosomal anomalies have been shown to be influenced by preferences and cultural factors[26,28], although the barriers to effective access to full information may also include language barrier since interpreters are often not available. The same association between TOPFA and cultural factors may exist for isolated CHD. We did not observe an association between maternal age and the probability of TOPFA for isolated CHD, suggesting that the overall higher rates of TOPFA for CHD in older women were due to the higher proportions of associated chromosomal anomalies. Prenatal diagnosis and TOPFA occurred earlier in case of CHD associated with chromosomal anomalies.[28,29] This may have been in part due to an increased nuchal translucency measured in the first trimester which is more likely to occur for both chromosomal anomalies and certain CHD. It is also possible that even in the absence of an increased nuchal translucency, cytogenetic studies conducted after prenatal diagnosis of a CHD diagnosed earlier in pregnancy were more likely to reveal an associated chromosomal anomaly.

The average interval between prenatal diagnosis and TOPFA was similar (two weeks) for both isolated CHD and CHD associated with chromosomal anomalies and was consistent with other studies.[4,29] This interval corresponds to the time necessary for a multidisciplinary discussion and for parents to make their decision.

The proportion of TOPFA in fetuses with CHD has been shown to be higher when prenatal diagnosis occurs earlier.[4,5,12] We also found that isolated CHD - VSD excluded diagnosed before

22 weeks had a 3.2-fold higher odds of TOPFA in comparison to those diagnosed later. TOPFA may indeed be more easily accepted by families at an earlier gestational age.[4]In addition, CHD diagnosed earlier may have been on average more severe (associated with poorer prognosis) and hence be more likely to be a candidate for TOPFA. Even though we partially took into account severity of CHD in our analyses, a residual effect of severity as one explanation for the association between earlier timing of prenatal diagnosis and probability of TOPFA cannot be excluded.

For isolated CHD - VSD excluded, gestational age at TOPFA tended to be lower in case of abnormal nuchal translucency. Indeed, a more detailed examination of fetal heart is usually performed after an abnormal nuchal translucency measurement on first trimester ultrasonography and may therefore conduct to the earlier diagnosis of a CHD.[30,31]

Our study has certain limitations. Due to small sample sizes, confidence intervals were fairly wide indicating the limited precision of our estimates. We did not adjust for paternal characteristics due to a high frequency of missing data. Nevertheless, paternal characteristics are strongly correlated with maternal characteristics and are therefore, at least partially, taken into account by maternal adjustment. Data were complete for pregnancy outcome and there were few missing data for the factors included in the analyses. Bias in our estimates due to missing data is therefore unlikely. However, residual bias or residual confusion due to missing data or confounding factors not taken into account in this study cannot be excluded. The strengths of our study are a large sample size and population-based data.

We explored specific associations that may exist between the risks of TOPFA and different categories of CHD defined a priori based on anatomic and/or clinical criteria and classified by a pediatric cardiologist. A caveat that needs to be considered is that our criteria for defining these categories can be arguable. Moreover, alternative and more detailed groupings exist[32,33], which may provide additional information for estimating the probability of TOPFA for CHD. However,

our results suggest that specific associations exist between the categories of CHD as defined in our study and the probability of TOPFA without necessarily implying that the categories investigated in our study are the most appropriate ones to use in this setting.

Diagnostic bias may have occurred as not all fetuses with a prenatally diagnosed CHD resulting in TOPFA had a fetal pathology examination. Therefore, in these cases ascertainment of CHD was based only on prenatal findings. Nevertheless, these cases represented a minority of the overall study population.

CONCLUSION.

In conclusion, TOPFA occurred for 27% of isolated CHD - VSD excluded that were prenatally diagnosed, 82% of CHD associated with chromosomal anomalies and 53% of CHD associated with anomalies of other systems. Prenatal diagnosis of isolated CHD - VSD excluded before 22 weeks of gestation was associated with a 3.2-fold higher odds of TOPFA. Women of African origin had a 10-fold lower odds of TOPFA than women of French origin. The categories of CHD reflecting its severity were also significantly associated with the risk of TOPFA for isolated CHD - VSD excluded. Gestational age at TOPFA tended to be earlier in fetuses with an abnormal nuchal translucency. Timing of TOFPA was explained essentially by timing of prenatal diagnosis and the time interval between prenatal diagnosis and TOPFA appeared to be essentially constant for all the clinical and socioeconomic categories included in our study.

Ethics approval.

No ethics approval was necessary for this study.

Contribution to authorship.

B. K. conceived the study. T.T.T.B. conducted the main statistical analyses. K.T., N. L. and A-C. T. assisted with statistical analysis. K.T. wrote the first draft of the manuscript with T.T.T.B. and B.K. F.G. contributed to the conceptualization of ideas and made suggestions about the required analyses. All of the authors contributed to the interpretation of findings and revisions of the article.

References

1 Dolk H, Loane M, Garne E. Congenital heart defects in Europe: prevalence and perinatal mortality, 2000 to 2005. Circulation. 2011;123:841-9.

2 Khoshnood B, De Vigan C, Vodovar V, *et al*. Trends in prenatal diagnosis, pregnancy termination, and perinatal mortality of newborns with congenital heart disease in France, 1983-2000: a population-based evaluation. Pediatrics. 2005;115:95-101.

3 Garne E, Loane M, Dolk H, *et al*. Prenatal diagnosis of severe structural congenital malformations in Europe. Ultrasound Obstet Gynecol. 2005; 25:6-11.

4 Garne E, Stoll C, Clementi M. Evaluation of prenatal diagnosis of congenital heart diseases by ultrasound: experience from 20 European registries. Ultrasound Obstet Gynecol. 2001;17:386-91.

5 Carvalho JS. Fetal heart scanning in the first trimester.Prenat Diagn. 2004; 24:1060-7.

6 Simpson JM. Impact of fetal echocardiography. Ann Pediatr Cardiol. 2009;2:41-50.

7 Carvalho JS, Moscoso G, Tekay A, *et al*. Clinical impact of first and early second trimester fetal echocardiography on high risk pregnancies. Heart. 2004;90:921-6.

8 Botto LD, Correa A. Decreasing the burden of congenital anomalies/ an epidemiologic evaluation of risk factors and survival. Progress in Pediatric Cardiology. 2003;18:111-21.

9 Bonnet D, Coltri A, Butera G, *et al*. Detection of transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. Circulation. 1999;99:916-8.

10 Franklin O, Burch M, Manning N, *et al*. Prenatal diagnosis of coarctation of the aorta improves survival and reduces morbidity. Heart. 2002;87:67-9.

11 Allan LD, Cook A, Sullivan I, Sharland GK. Hypoplastic left heart syndrome: effects of fetal echocardiography on birth prevalence. Lancet. 1991;337:959-61.

12 Allan LD, Huggon IC. Counselling following a diagnosis of congenital heart disease. Prenat

Diagn. 2004;24:1136-42.

13 Zyblewski SC, Hill EG, Shirali G, *et al*. Chromosomal anomalies influence parental treatment decisions in relation to prenatally diagnosed congenital heart disease. Pediatr Cardiol. 2009;30:1105-11.

14 Tennstedt C, Chaoui R, Korner H, Dietel M. Spectrum of congenital heart defects and extracardiac malformations associated with chromosomal abnormalities: results of a seven year necropsy study. Heart. 1999;82:34-9.

15 Garne E, Khoshnood B, Loane M, *et al*. Termination of pregnancy for fetal anomaly after 23 weeks of gestation: a European register-based study. Bjog. 2010;117:660-6.

16 Khoshnood B, Greenlees R, Loane M, Dolk H. Paper 2: EUROCAT public health indicators for congenital anomalies in Europe. Birth Defects Res A Clin Mol Teratol. 2011;91 Suppl 1:S16-22.

17 Greenlees R, Neville A, Addor MC, *et al*. Paper 6: EUROCAT member registries: organization and activities. Birth Defects Res A Clin Mol Teratol. 2011;91 Suppl 1:S51-S100.

18 Cocchi G, Gualdi S, Bower C, *et al*. International trends of Down syndrome 1993-2004: Births in relation to maternal age and terminations of pregnancies. Birth Defects Res A Clin Mol Teratol. 2010;88:474-9.

19 Registre des Malformations de Paris. Surveillance épidémiologique et diagnostic prénatal des malformations : Evolution sur vingt-sept ans (1981-2007). 2010. [WWW document].URL http://www.unites.inserm.fr/download.asp?download=stockfile/U149/documents/registre/brochure27ans.pdf [accessed on 22 August 2012].

20 Boyd PA, Devigan C, Khoshnood B, *et al*. Survey of prenatal screening policies in Europe for structural malformations and chromosome anomalies, and their impact on detection and termination rates for neural tube defects and Down's syndrome. Bjog. 2008;115:689-96.

21 Garne E, The EUROCAT working group. Prenatal diagnosis of six major cardiac malformations in Europe--a population based study. Acta Obstet Gynecol Scand. 2001;80:224-8.

22 Allan LD, Apfel HD, Printz BF. Outcome after prenatal diagnosis of the hypoplastic left heart syndrome. Heart. 1998;79:371-3.

23 Galindo A, Nieto O, Villagra S, *et al*. Hypoplastic left heart syndrome diagnosed in fetal life: associated findings, pregnancy outcome and results of palliative surgery. Ultrasound Obstet Gynecol. 2009;33:560-6.

24 Khoshnood B, De Vigan C, Vodovar V, *et al*. Advances in medical technology and creation of disparities: the case of Down syndrome. Am J Public Health. 2006;96:2139-44.

25 Khoshnood B, Pryde P, Wall S, *et al*. Ethnic differences in the impact of advanced maternal age on birth prevalence of Down syndrome. Am J Public Health. 2000;90:1778-81.

26 Kuppermann M, Gates E, Washington AE. Racial-ethnic differences in prenatal diagnostic test use and outcomes: preferences, socioeconomics, or patient knowledge? Obstet Gynecol. 1996;87:675-82.

27 Smith LK, Budd JL, Field DJ, Draper ES. Socioeconomic inequalities in outcome of pregnancy and neonatal mortality associated with congenital anomalies: population based study. Bmj.343:d4306.

28 Dommergues M, Benachi A, Benifla JL, *et al*. The reasons for termination of pregnancy in the third trimester. Br J Obstet Gynaecol. 1999;106:297-303.

29 Marret H, Perrotin F, Descamps P, *et al*. [Medical abortion in the second and third trimester. Report of 125 indications from 1992 to 1995]. J Gynecol Obstet Biol Reprod (Paris). 1999;28:245-52.

30 Hyett J, Perdu M, Sharland G, *et al*. Using fetal nuchal translucency to screen for major congenital cardiac defects at 10-14 weeks of gestation: population based cohort study. Bmj.

1999;318:81-5.

31 Weiner Z, Weizman B, Beloosesky R, *et al*. Fetal cardiac scanning performed immediately following an abnormal nuchal translucency examination. Prenat Diagn. 2008;28:934-8.

32 Botto LD, Lin AE, Riehle-Colarusso T, *et al*. Seeking causes: Classifying and evaluating congenital heart defects in etiologic studies. Birth Defects Res A Clin Mol Teratol. 2007;79:714-27.

33 Houyel L, Khoshnood B, Anderson RH, *et al*. Population-based evaluation of a suggested anatomic and clinical classification of congenital heart defects based on the International Paediatric and Congenital Cardiac Code. Orphanet J Rare Dis. 2011;6:64.

Table 1. Prenatal diagnosis and termination of pregnancy for fetal anomaly (TOPFA) for fetuses with congenital heart defects (CHD).

	n	Prenatal diagnosis		Proportion of TOPFA among cases with a prenatal diagnosis	
		%	95% CI	%	95% CI
All CHD	1465	48	46 - 51	46	42 - 50
All Isolated CHD	968	35	32 - 38	16	12 - 19
Isolated CHD-VSD excluded	473	58	54 - 63	27	22 - 32
functionally univentricular CHD	68	93	86 - 99	60	48 - 72
conotruncal defect	53	72	59 - 84	21	8 - 34
complex CHD	48	85	75 - 95	34	19 - 49
other CHD	304	44	38 - 50	11	5 - 16
CHD associated with chromosomal anomalies	230	79	74 - 84	82	77 - 88
CHD associated with anomalies of other systems*	267	73	67 - 78	53	46 - 60

* including genetic syndromes

379

Table 2. Gestational age at prenatal diagnosis and at termination of pregnancy in fetuses with congenital heart defects.

	All CHD	Isolated CHD – VSD excluded	CHD associated with chromosomal anomalies	CHD associated with anomalies of other systems	p
Gestational age at prenatal diagnosis (weeks)					
mean (SD*)	20.4 (0.26)	21.9 (0.39)	19.1 (0.38)	21 (0.51)	< 0.001
median (IQR§)	21 (17 - 23)	22 (21 - 23)	18 (16 - 22.5)	22 (18 - 23)	< 0.001
Gestational age at termination of pregnancy (weeks)					
mean (SD*)	23.2 (0.29)	24.8 (0.46)	21.7 (0.45)	24.1 (0.55)	< 0.001
median (IQR§)	23 (19 - 26)	25 (23 - 26)	21.5 (18 - 25)	24 (20 - 28)	< 0.001
≤ 22	40%	17%	57%	34%	
23 - 25	30%	45%	22%	30%	< 0.001
≥ 26	30%	38%	21%	36%	
Time interval between prenatal diagnosis and termination of pregnancy (weeks)					
mean (SD*)	2.8 (0.14)	2.8 (0.26)	2.6 (0.21)	3.1 (0.3)	0.4
median (IQR§)	2 (1 - 3)	2 (1 - 4)	2 (1 - 3)	2 (1 - 4)	0.6

*SD : standard deviation

§ IQR : interquartile range (25^{th} percentile – 75^{th} percentile)

Table 3. Association between the odds of TOPFA and maternal socioeconomic and clinical factors in fetuses with isolated CHD-VSD excluded.

	n	% of TOPFA	95% CI	p
Maternal age				
≤ 34	184	24	18 - 31	
35 - 37	43	32	18 - 47	0.5
≥ 38	47	30	16 - 43	
Gravidity				
primigravida	99	27	20 - 33	0.8
multigravida	175	26	18 - 36	
Maternal geographic origin				
France	152	33	25 - 40	
Africa	66	11	3 - 18	0.003
Other	56	28	16 - 40	
Maternal occupation				
professional	91	31	21 - 40	
intermediate	36	25	11 - 39	0.12
administrative / public service	51	25	13 - 38	
none	74	15	6 - 23	
Intra-uterine growth retardation				
no	265	26	21 - 31	0.09
yes	10	50	17 - 82	
Nuchal translucency measurement				
normal	206	28	22 - 34	
abnormal	17	35	12 - 59	0.27
not measured	31	16	3 - 29	
Gestational age at prenatal diagnosis (weeks)				
> 22	167	17	11 - 23	<0.001
≤ 22	108	42	32 - 51	
Category of CHD				
other	133	11	5 - 16	
functionally univentricular CHD	63	60	48 - 72	<0.001
conotruncal CHD	38	21	8 - 34	
complex CHD	41	34	19 - 49	

Table 4. Logistic regression analyses of the association between the odds of TOPFA and maternal socioeconomic and clinical factors in fetuses with prenatally diagnosed isolated CHD-VSD excluded.

	Unadjusted OR	95% CI	Adjusted OR	95% CI
Maternal age				
≤ 34	1.0	ref.	1.0	ref.
35 - 37	1.5	0.7 - 3.1	1.0	0.3 - 3.2
≥ 38	1.3	0.6 - 2.7	1.5	0.5 - 4.0
Maternal geographic origin				
France	1.0	ref.	1.0	ref.
Africa	0.2	0.1 - 0.6	0.1	0.02 - 0.4
Other	0.8	0.4 - 1.6	0.8	0.3 - 2.3
Maternal occupation				
professional	1.0	ref.	1.0	ref.
intermediate	0.7	0.3 - 1.8	0.7	0.2 - 2.2
administrative / public service	0.8	0.3 - 1.7	1.2	0.4 - 3.6
none	0.4	0.2 - 0.8	0.5	0.1 - 1.6
Intra-uterine growth retardation				
no	1.0	ref.	1.0	ref.
yes	2.8	0.8 - 10.1	6.6	0.9 - 51.0
Nuchal translucency measurement				
normal	1.0	ref.	1.0	ref.
abnormal	1.3	0.5 - 3.9	1.5	0.3 - 6.2
not measured	0.5	0.2 - 1.3	1.2	0.2 - 5.0
Gestational age at prenatal diagnosis				
> 22	1.0	ref.	1.0	ref.
≤ 22	3.4	1.9 - 5.9	3.2	1.4 - 7.1
Category of CHD				
other	1.0	ref.	1.0	ref.
functionally univentricular CHD	12.9	6.1 - 27.3	21.3	7.7 - 59.0
conotruncal CHD	2.3	0.9 - 5.9	2.1	0.7 - 6.6
complex CHD	4.4	1.9 - 10.3	5.7	1.8 - 17.4

Table 5. Association between gestational age at TOPFA and maternal socioeconomic and clinical factors in fetuses with isolated CHD-VSD excluded.

	n	mean gestational age	SD	p
Maternal age				
≤ 34	45	24.7	0.5	
35 - 37	14	24.5	1.2	0.9
≥ 38	14	25.6	1.3	
Gravidity				
Primigravida	27	24.0	0.5	0.2
Multigravida	46	25.3	0.7	
Maternal geographic origin				
France	50	24.8	0.6	
Africa	7	24.0	1.7	0.8
Other	16	25.1	0.9	
Maternal occupation				
professional	28	24.3	0.8	
intermediate	9	27.1	1.6	0.4
administrative / public service	13	25.1	1.1	
none	11	24.8	0.9	
Intra-uterine growth retardation				
no	69	24.8	0.5	0.7
yes	5	24.2	1.6	
Nuchal translucency measurement				
normal	58	25.3	0.5	
abnormal	6	22.0	1.1	0.13
not measured	5	24.8	2.0	
Type of CHD				
other	14	24.2	1.3	
functionally univentriclar CHD	38	25.2	0.6	0.13
conotruncal CHD	8	26.9	1.3	
complex CHD	14	23.1	1.1	

383

384