Canadian Journal of Cardiology 36 (2020) 1564–1565

Editorial

The Critical Importance of Prenatal Diagnosis of Critical Congenital Heart Disease: Toward 100% Detection in All Regions

Aisling A. Young, MD, FRCPC, and Brian G. Sinclair, MD, FRCPC

University of British Columbia, Vancouver Island Health Authority, Victoria, British Columbia, Canada

See article by Nagata et al., pages 1592–1597 of this issue.

Congenital heart disease (CHD) is the most common congenital lesion, found in 1% of live births.[1] Of this population, critical CHD (CCHD) is found in 25%, requiring early intervention to optimize outcomes. CCHD can be diagnosed postnatally on initial examination, through pulse oximetry screening, when neonates present in cardiogenic shock, or on autopsy. Death from unrecognized CCHD accounted for 4.6 of 10,000 live births in Sweden between 2004 and 2007.[2] Prenatally, ultrasound can diagnose CCHD, with initial publications of *in utero* detection of heart disease, dating from 1980.[3] In Canada, we are fortunate that a mid-gestation screening ultrasound is funded for every pregnancy and that the Society of Obstetricians of Canada and Canadian Association of Radiology guidelines recommend inclusion of a cardiac 4-chamber and outflow views.[4,5] Over the last 40 years, prenatal detection rates have continually improved, but CCHD continues to be undiagnosed *in utero*.

The prenatal detection of CCHD has clear conceptual benefits: Prenatal diagnosis presents opportunities for extensive counselling and preparing and planning for the delivery of a potentially unstable infant. Unfortunately, this benefit has not always been shown in the literature. Of the available literature on prenatal diagnosis of transposition of the great arteries (TGA), a ductal-dependent CCHD, only 2 articles have previously illustrated a benefit to morbidity or mortality from a prenatal diagnosis.[6,7]

The paper by Nagata et al., in the current issue of *the Canadian Journal of Cardiology*,[8] reports the results of a study examining prenatal detection rates of TGA and outcomes in prenatal vs postnatal TGA diagnoses in Ontario, Canada. Prospective databases from the 2 tertiary cardiac centres in the province and the coroner's office were reviewed from 2009 to 2014, and identified 70 prenatal and 76 postnatal cases of TGA. Those with more complex cardiac lesions were excluded. The authors compared prenatal detection rates and outcomes of 5 different regions in Ontario, based on postal code. Outcomes assessed included mortality and a number of markers of morbidity. Data were collected on the need for transfer; mode of transfer; and time to tertiary cardiac centre, cardiac intervention, and cardiac surgery.

In this study by Nagata et al., the median prenatal detection rate of TGA from Ontario was 50% (75 of 151): consistent with previously reported data.[7] This is also consistent with Canadian data from Alberta from the same period for prenatal detection of TGA[9] and critical CHD as a whole.[10] However, Nagata et al. demonstrated a significant regional disparity in prenatal detection rates of TGA, with a rate as high as 72% (21 of 29) in the Greater Toronto Area compared with only 14% (1 of 7) in Northern Ontario.[8] This finding illustrates 2 important issues. First, it is possible to diagnose CCHD prenatally at higher rates: up to 72%. Perhaps the ultimate goal should be to detect all CHD prenatally. A study from Ireland reported a prenatal detection rate of CHD of 91%: something to strive toward or even attempt to surpass.[11] Second, the disparity among regional detection rates highlights the need for further work and delivery of resources in those regions with lower detection rates to improve delivery of care to these mainly rural, remote, and Aboriginal populations in Canada.

Nagata et al. found that, of those with a prenatal diagnosis of TGA, 4 pregnancies were terminated at less than 24 weeks' gestation (5%, 4 of 75) and 1 case born at 24 weeks' gestation had elective withdrawal of care. This finding highlights an important aspect of timely prenatal detection of CHD with regard to counselling families and decision making.

The most important findings of the study by Nagata et al. is the improved 1-year survival in those with prenatal diagnoses of TGA (mortality in 1 of 70 vs 9 of 70, $P = 0.02$). This important finding adds to a growing body of literature that supports the importance of continuing to rigourously diagnose CHD before birth and striving to improve our prenatal detection rates.

Received for publication February 3, 2020. Accepted March 8, 2020.

Corresponding author: Dr Aisling A. Young, Pediatric Cardiology, University of British Columbia, 1 Hospital Way. Victoria, British Columbia V8Z 6R5, Canada. Tel.: 250-893-5717.

E-mail: Aisling.young@viha.ca

See page 1565 for disclosure information.

https://doi.org/10.1016/j.cjca.2020.03.009

One of the weaknesses of the study by Nagata et al. is that there was no difference in preoperative morbidity between those with prenatal vs postnatal diagnoses of TGA. This observation is likely due to the fact that preoperative data were collected from arrival at the treating tertiary centre and not the initial treating facility, as acknowledged by the authors. If the data had been collected at the initial treating facility, they may have provided further evidence in support of prenatal diagnosis of CHD. Also of interest is the higher rate of chylothorax and longer number of days in hospital in the prenatal cohort. These 2 findings are most likely connected, but, unfortunately, the study was not powered to explore this interesting observation further. Nonetheless, the improved overall mortality in those with prenatal diagnoses overshadows these weaknesses.

A strength of the study by Nagata et al. is the inclusion of autopsy cases. The authors identified 4 cases of TGA found at autopsy only. These neonates with TGA were clearly not diagnosed prenatally or postnatally before their death, which further solidifies the importance of prenatal detection. Postnatally, CCHD can be diagnosed clinically or through pulse-oximetry screening before the need for autopsy. A recent joint position statement from the Canadian Pediatric Cardiology Association and the Canadian Cardiovascular Society recommends pulse oximetry screening for infants to enhance postnatal detection of CHD, along with promotion of prenatal screening.[12] However, despite more widespread adoption of pulse-oximetry screening in neonates, it is still not universally performed, and some infants with CCHD may have their conditions go undetected. Importantly, other infants with CCHD may die before the 24-hour timeframe (when pulse oximetry screening is recommended to be performed), particularly those with TGA or hypoplastic left-heart syndrome and restrictive atrial septum. In addition, CCHD may be diagnosed through any of these postnatal methods in locations that are remote from a tertiary cardiac centre, and neonates may not receive the care they need in time. This possibility was highlighted by Nagata et al., who noted a low rate of detection of TGA in Northern Ontario, along with the increased need for transport and the longer time to initiation of prostaglandin therapy, performance of balloon atrial septostomy, and cardiac surgery in those with postnatal diagnoses.

The importance of prenatal detection of CCHD cannot be overstated. At present, there are 5 major opportunities for diagnosis of CCHD: prenatal ultrasound, clinical presentation with cyanosis or shock, postnatal oximetry screening, or on autopsy. The practice of prenatal diagnosis presents great opportunities to enhance care delivery. The study by Nagata et al. is important because it confirms that a prenatal diagnosis of TGA leads to improved survival, and this has not consistently been shown in the previous literature. It also illustrates the disparity in care delivery based on regional differences in detection rates. These findings can be used to advocate for promotion of prenatal detection and resource allocation to support this important endeavour to allow us to approach optimal rates of 100% prenatal detection of CCHD.

Funding Sources

The authors have no funding.

Disclosures

The authors have no conflicts of interest.

References

1. Marelli AJ, Mackie AS, Ionescu-Ittu R, Rahme E, Pilote L. Congenital heart disease in the general population: changing prevalence and age distribution. Circulation 2007;115:163-72.

2. de Wahl Granelli A, Wennergren M, Sandberg K, et al. Impact of pulse oximetry screening on the detection of duct dependent congenital heart disease: a Swedish prospective screening study in 39,821 newborns. BMJ 2009;338:a3037.

3. Allan LD, Tynan MJ, Campbell S, Wilkinson JL, Anderson RH. Echocardiographic and anatomical correlates in the fetus. Br Heart J 1980;44:444-51.

4. Cargill Y, Morin L. Diagnostic Imaging Committee. Content of a complete routine second trimester obstetrical ultrasound examination and report. J Obstet Gynaecol Can 2009;223:272-5.

5. Fong K, Levi C, Mayer LR, et al. Canadian Association of Radiologists. CAR Standard for Performing Diagnostic Obstetric Ultrasound Examinations. 2010. https://car.ca/wp-content/uploads/Ultrasound-Performing-Diagnostic-Obstetric-Ultrasound-Examinations-2010.pdf. Accessed July 31, 2020.

6. 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.

7. van Velzen CL, Haak MC, Reijnders G, et al. Prenatal detection of transposition of the great arteries reduces mortality and morbidity. Ultrasound Obstet Gynecol 2015;45:320-5.

8. Nagata H, Glick L, Lougheed J, et al. Prenatal diagnosis of transposition of the great arteries reduces postnatal mortality: a population-based study. Can J Cardiol 2020;36:1592-7.

9. Ravi P, Mills L, Fruitman D, et al. Population trends in prenatal detection of transposition of great arteries: impact of obstetric screening ultrasound guidelines. Ultrasound Obstet Gynecol 2018;51:659-64.

10. Trines J, Fruitman D, Zuo KJ, Smallhorn JF, Hornberger LK, Mackie AS. Effectiveness of prenatal screening for congenital heart disease: assessment in a jurisdiction with universal access to health care. Can J Cardiol 2013;29:879-85.

11. Corcoran S, Briggs K, O'Connor H, et al. Prenatal detection of major congenital heart disease: optimising resources to improve outcomes. Eur J Obstet Gynecol Reprod Biol 2016;203:260-3.

12. Wong KK, Fournier A, Fruitman DS, et al. Canadian Cardiovascular Society/Canadian Pediatric Cardiology Association position statement on pulse oximetry screening in newborns to enhance detection of critical congenital heart disease. Can J Cardiol 2016;33:199-208.