Congenital heart defects and extracardiac malformations

Cardiopatias congênitas e malformações extracardíacas

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ABSTRACT

Objective: To review the association between congenital heart defects and extracardiac malformations.

Data sources: Scientific articles were searched in the Medline, Lilacs, and SciELO databases, using the descriptors "congenital heart disease," "congenital heart defects," "congenital cardiac malformations," "extracardiac defects," and "extracardiac malformations." All case series that specifically explored the association between congenital heart defects and extracardiac malformations were included.

Data synthesis: Congenital heart diseases are responsible for about 40% of birth defects, being one of the most common and severe malformations. Extracardiac malformations are observed in 7 to 50% of the patients with congenital heart disease, bringing a greater risk of comorbidity and mortality and increasing the risks related to heart surgery. Different studies have attempted to assess the presence of extracardiac abnormalities in patients with congenital heart disease. Among the changes described, those of the urinary tract are more often reported. However, no study has evaluated all patients in the same way.

Conclusions: Extracardiac abnormalities are frequent among patients with congenital heart disease, and patients with these alterations may present an increased risk of morbimortality. Therefore, some authors have been discussing the importance and cost-effectiveness of screening these children for other malformations by complementary exams.

Key-words: congenital abnormalities; heart defects, congenital; urinary tract; ultrasonography.

RESUMO

Objetivo: Revisar a associação entre cardiopatias congênitas e malformações extracardíacas.

Fontes de dados: A pesquisa incluiu artigos científicos presentes nos portais Medline, Lilacs e SciELO, utilizando-se os descritores "*congenital heart disease*", "*congenital heart defects*", "*congenital cardiac malformations*", "*extracardiac defects*" e "*extracardiac malformations*". Foram incluídos os artigos de séries de casos que exploravam especificamente a associação entre cardiopatias congênitas e malformações extracardíacas.

Síntese dos dados: A cardiopatia congênita é responsável por cerca de 40% dos defeitos congênitos, sendo uma das malformações mais frequentes e a de maior morbimortalidade. Malformações extracardíacas são observadas em 7 a 50% dos pacientes com cardiopatia congênita, trazendo um risco ainda maior de comorbidade e mortalidade e tornando a cirurgia cardíaca mais arriscada. Diferentes estudos têm tentado avaliar a presença de anormalidades extracardíacas em pacientes portadores de cardiopatia congênita. Dentre as alterações descritas, destacam-se aquelas do trato urinário. Contudo, não houve um estudo que tenha avaliado do mesmo modo todos os pacientes.

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Conclusões: Anormalidades extracardíacas são frequentes em pacientes com cardiopatia congênita, sendo que os portadores de tais alterações podem apresentar um risco maior de morbimortalidade. Consequentemente, alguns autores vêm discutindo a importância e o custo-benefício da triagem destas crianças à procura de outras malformações por meio de exames complementares.

Palavras-chave: anormalidades congênitas; cardiopatias congênitas; sistema urinário; ultrassonografia.

RESUMEN

Objetivo: Revisar la asociación entre cardiopatías congénitas y malformaciones extracardiacas.

Fuentes de datos: Se investigaron artículos científicos presentes en los portales Medline, Lilacs y SciELO, utilizándose los descriptores *«congenital heart disease», «congenital heart defects», «congenital cardiac malformations», «extracardiac defects»* y *«extracardiac malformations»*. Se incluyeron todos los artículos de casos que exploraban específicamente la asociación entre cardiopatías congénitas y malformaciones extracardiacas.

Síntesis de los datos: La cardiopatía congénita es responsable por un 40% de los defectos congénitos, siendo una de las malformaciones más frecuentes y la de mayor morbimortalidad. Malformaciones extracardiacas se observan en 7 a 50% de los pacientes con cardiopatía congénita, trayendo un riesgo todavía más grande de comorbilidad y mortalidad y haciendo la cirugía cardíaca más arriesgada. Distintos estudios vienen intentando evaluar la presencia de anormalidades extracardiacas en pacientes portadores de cardiopatía congénita. Entre las alteraciones descriptas, se destacan aquellas del sistema urinario. Sin embargo, no hubo estudio que haya evaluado del mismo modo a todos los pacientes.

Conclusiones: Anormalidades extracardiacas son frecuentes en pacientes con cardiopatía congénita, siendo que los portadores de estas alteraciones pueden presentar un riesgo mayor de morbimortalidad. Por consiguiente, algunos autores vienen discutiendo la importancia y el costo-beneficio de la selección de estos niños en búsqueda de otras malformaciones por medio de exámenes complementares.

Palabras clave: anormalidades congénitas; cardiopatías congénitas; sistema urinario; ultrasonografía.

Introduction

Congenital heart diseases (CHD) are detected among 3 to 5% newborns[1], and are classified as severe in one out of every 33 livebirths[2]. In developed countries they represent the main cause of mortality in early childhood and are responsible for one fifth of the total deaths[3]. In Brazil, congenital malformations were responsible for nearly 19% of the mortality in children under one year old in 2008, and represented the second most frequent cause of death among this age group[4].

According to the definition proposed by Mitchell *et al* [5], CHD consists of a macroscopic structural abnormality of the heart or the intra-thoracic great vessels, which have significant or potentially significant functional consequences[6]. They comprise about 40% of the congenital defects and represent one of the most frequent malformations[7-9]. The prevalence of CHD range from 4 to 19/1,000 livebirths[6,10-13]. However, according to Bosi *et al*[14], the prevalence of CHD has been increasing due to the greater detection of minor defects by the Doppler echocardiography, which has been widely used. In addition, the advances in intensive, surgical and anesthetic care have allowed a greater survival and, consequently, a greater number of adults with this condition[13,15].

CHD are the congenital malformations with greater impact on children's morbidity and mortality, as well as on the health system's costs[14]. They represent the main cause of death among the congenital malformations[9]. Extra-cardiac malformations (EM), such as intra-abdominal organs defects and/or associated with genetic syndromes, are observed from 7 to 50% of the patients with CHD, and impose a greater risk of morbidity and mortality to these patients, in addition to increasing the risks of surgical correction[16-20]. Also, such patients may need surgical procedures or intensive care regardless of the heart condition[16].

For these reasons, some authors have been discussing the importance and the cost-effectiveness of screening all children with CHD to detect EM using ancillary tests, such as abdominal ultrasound[20,21].

Thus, the objective of this study was to perform a review of the literature regarding the association between CHD and EM. We searched the scientific articles in Medline, Lilacs and Scielo databases using the keywords "congenital heart disease", "congenital heart defects", "congenital cardiac malformations", "extra cardiac defects" and "extra cardiac malformations". The research included all the scientific

papers retrieved in these databases and was not limited to a pre-specified period of time. We included all the case series that specifically analyzed the association between CHD and EM. Case reports were not included.

Studies that evaluated EM in patients with congenital heart defects

Different studies have evaluated the presence of EM in patients with CHD. Studies conducted before the 80's, however, show important limitations, since ultrasound tests were not available yet. The diagnosis of CHD, for instance, was performed according to the physical examination, surgery and catheterism findings, or even autopsy findings[5,22-24].

In the study by Julian and Farrú[25], published in 1986, the diagnostic method used to evaluate the EM was not reported. These authors conducted a retrospective evaluation of 207 children with CHD in a cardiology hospital in Chile and found EM in 31.9% of the patients, 22.7% of which constituted part of some syndrome. The authors did not identify any specific association between the different EM and CHD, except for the classic syndromes. The most frequent EM were observed in the gastrointestinal, musculoskeletal and genitourinary tracts.

In 1987, Ferencz *et al*[26] conducted a case control study of CHD among livebirths in the US. Individuals with CHD (n=1,494) were compared to a sample of neonates without CHD born in the same area (n=1,572). CHD were diagnosed by echocardiography, cardiac catheterization, surgery or autopsy. EM were observed among 26.8% of the individuals with CHD, 8.3% of which were not associated with chromosomal anomalies or any other syndromes. Central nervous system malformations, eye disorders, major defects of the abdominal wall, gastrointestinal and urinary tract defects were more frequent among the patients with CHD.

In 1987, Kramer *et al*[27] prospectively evaluated 1,016 children with CHD up to 16 years old in Germany. The diagnosis was confirmed by echocardiography or cardiac catheterization. In 13.3% of the cases, the heart defect was part of a syndrome, embriopathy, association or sequence. Major EM occurred in 7.7% of the patients without any specific syndrome, embriopathy, association or sequence (the results of the urography were not taken into consideration in these results). The malformations affected mainly the musculoskeletal and central nervous systems, eyes, ears, gastrointestinal, respiratory and urinary tracts. A greater number of EM was identified among individuals with tetralogy of Fallot (p=0.01). A urogram following angiography was performed in 302 individuals for screening of malformations, and revealed abnormalities of the upper urinary tract in 8.9%. Only one of these individuals was symptomatic. The most frequent anomalies of the urinary tract were the total kidney duplication and the duplication of the ureter or renal pelvis. There were no differences in the frequency of the urinary tract malformations in association with any specific heart defect. In the other hand, they found an association (p<0.01) between minor EM and CHD in comparison with healthy children.

In 1898, Stoll *et al*[28] prospectively studied 801 newborns with CHD and a control group in France. The study included fetuses and stillbirths. The diagnosis of heart defect was confirmed by echocardiogram, cardiac catheterization, surgery or autopsy reports. Among the reported cases, 25.7% showed at least one EM, and such abnormalities were ten times more frequent in this group than in the control group. Among individuals with heart defects, 11.5% exhibited some type of syndrome. The most frequent EM affected the kidneys (21.4%) and the digestive system (19.6%). The most frequent abnormalities of the upper renal system were the urethral anomalies, hydronephrosis and unilateral renal agenesis. The presence of olygohydramnios and polyhydramnios and threatened miscarriage (the occurrence of vaginal bleeding before fetal viability) were more frequent among children with CHD and concomitant EM or syndromes.

Following this publication, Murugasu *et al*[21] conducted a prospective study in a Singapore hospital in 1990, including 109 children with CHD who underwent cardiac catheterization and ultrasound of the urinary tract. Important urologic malformations were found in 11.9% of the children, including hydronephrosis, duplication, ectopy, agenesis and renal dysplasia. Five of the 13 patients with renal malformations had some syndrome, four of which were chromosomal. None of the children had any signs or symptoms suggestive of urinary tract disease. The authors concluded that the early identification of the urologic anomalies in these patients would only have been possible using a screening test, such as renal ultrasound or urography.

Later, in 1997, Pradat[29] retrospectively reviewed the data of 2618 children with major CHD obtained in the Cardiology and Congenital Malformations registers in Sweden. All the patients underwent echocardiography, catheterization, heart surgery or autopsy. EM were identified in 720 patients (25.7%); after excluding the children with chromosomal anomalies, 397 (15%) infants remained. Of

these, 27 had a well-recognized syndrome or a well-defined association of malformations. The authors did not identify any association between specific CHD and the main groups of EM, except for a possible relation between spleen abnormalities and endocardic wall defects.

In 1999 Grech and Gatt[16] retrospectively studied 231 patients with CHD in Malta. The diagnosis was confirmed by echocardiography, catheterization, surgery or autopsy. The authors observed that 39 (17%) of the children had EM, 9% of them being chromosomal anomalies, 2% well recognized syndromes and 6% other non-cardiac. The most common EM were the musculoskeletal abnormalities.

In the study of Bosi *et al* in 2003[14], 2,442 livebirths with CHD born from 1980 to 2000 were retrospectively evaluated in Italy. The diagnosis of cardiac malformation was established by physical examination, echocardiography, cardiac catheterization, surgery and/or necropsy findings. Twenty four percent of these patients had EM. Chromosomal anomalies were identified in 9.1% of the newborns. In addition, 4.4% of the patients with CHD were diagnosed with some syndrome and/or sequence. EM were found among 10% of the children with CHD who did not have any syndrome, sequence or chromosomal anomalies. The genitourinary system was the most frequently affected (25.8%).

In 2003, Calzolari *et al*[30] conducted a retrospective study of 1,549 livebirths and stillbirths with CHD, also in Italy. The diagnosis of the cardiac malformation was confirmed by echocardiography, heart surgery, cardiac catheterism and/or necropsy. EM were found in 26% of the cases. Interventricular communication, ostium secundum atrial septal defects and complex heart defects were the cardiac malformations more frequently associated with EM. The most common EM were found in the musculoskeletal (25.3%), genitourinary (22.9%) and gastrointestinal (11.5%) systems. Karyotypical analysis was performed in 19.4% of the cases, and chromosomopathies were detected in 152 patients.

In 2004, Eskedal *et al*[31] studied the prevalence of major EM anomalies in children with CHD and its impact on the survival. The registers of 3527 children with CHD who were born from 1990 to 1999 in Norway were analyzed. All the patients had the diagnosis of the heart defect confirmed by echocardiography, surgery, cardiac catheterization or necropsy. The authors reported the presence of EM in 20% of the children, with the gastrointestinal malformations, mainly intestinal anomalies and esophageal atresia, being the most frequent ones. The authors observed an improvement in the survival of children born from 1995 to 1999 in comparison with those born from 1990 to 1994, except for those with EM, whose survival did not differ between the periods. However, patients with Down's syndrome with CHD and no major EM had a better survival in the second period of the study. Also, children with right atrial isomerism were observed to have a higher risk for asplenia.

Still in 2004, Stephensen *et al*[32] retrospectively evaluated 740 livebirths with CHD from 1990 to 1999 in Iceland. The diagnosis of the heart defect was confirmed by echocardiography, cardiac catheterization or autopsy. EM were observed in 89 individuals (12%), including those with chromosomal anomalies, syndromes and/or other congenital anomalies. Chromosomopathies were observed in 4.9%. Among the patients with chromosomopathies and syndromes, genitourinary and gastrointestinal malformations were the most frequently observed EM. Among those with major heart defects, 18.2% had other congenital anomalies.

Güçer *et al*[33] conducted a retrospective study of 305 autopsies of children who had been born alive and had been diagnosed with a CHD in a Turkey hospital, from a total of 3320 autopsies performed in the study period. The prevalence of CHD was 9.1%. In addition, one or more EM were observed in 45.9% of the cases, with the craniofacial (19.7%) and genitourinary (15.1%) anomalies being the most common ones. The gastrointestinal and spleen malformations comprised 11.1% and 4.6% of the EM, respectively. Intra-atrial and interventricular communication, coarctation of aorta, single ventricle, pulmonary stenosis, hypoplastic right heart syndrome, double outlet right ventricle, atrial and ventricular septal defects, aortic arch anomalies, right and left atrial isomerism were frequently accompanied by EM (>50%). Spleen malformations were significantly more common among the cases of single ventricle ($p<0.002$). Furthermore, gastrointestinal and genitourinary anomalies were significantly associated with conotruncal defects ($p<0.001$).

Still in 2005, Wojtalik *et al*[34] retrospectively studied 1,856 children admitted for heart surgery in the period from 1997 to 2002, in a pediatric tertiary hospital in Poland. The diagnosis of CHD was confirmed by echocardiography. The presence of other malformations was evaluated by physical examination, cranial and abdominal ultrasound, X-Ray or bronchoscopy, and was detected in 84 children (4.5%). Anomalies of the digestive (35.7%) and urinary (22.4%) systems were more frequently observed, with kidney malformations being the most common ones. The authors did

not find any correlation between CHD and concurrent EM. In children with multiple organs malformations, the multivariate logistic regression analysis detected a significant association of age, the primary heart surgery and the type of CHD with mortality. Patients with digestive system malformations had a significant greater number of emergency surgeries (p=0.001). The mortality rate of the total sample was 8.9%, while the mortality of children with EM was 19%, increasing to 50% among newborns in this last group. Therefore, the treatment of children with concomitant CHD and EM is related to high mortality. EM were more frequently observed among children with ventricular septal defects (7.6%, p=0.0012).

In the prospective observational study by Meberg *et al*[19] conducted in Norway in 2007, which evaluated 57,027 births from 1982 to 2005, 662 CHD confirmed by echocardiography or autopsy were observed. Twenty two percent of the individuals with CHD had associated EM. Forty six percent of the EM malformations were not related to any chromosomal anomaly, genetic syndrome, microdeletion or teratogenic syndromes. Atrioventricular septal defects, intra-atrial communication, tetralogy of Fallot and single ventricle were the heart defects most frequently associated with EM. Associated anomalies were observed in 31% of the patients with perimembranous ventricular septal defect. Mortality was significantly higher among patients with CHD associated with other disorders (29%) in comparison with those with isolated heart defects (6%).

In the case control study by Amorim *et al*[2] published in 2008, 277 newborns and 75 stillbirths with CHD diagnosed from 1990 to 2003 in a University Hospital in Minas Gerais, Brazil, were evaluated. The livebirths had a control group, composed by the next newborn of the same gender, with no malformations, born in the same hospital. The CHD was confirmed by postnatal echocardiography or necropsy. Noncardiac anomalies were detected in 31.4% of the livebirths and 48% of the stillbirths in whom no syndromes could be detected. EM constituted part of some syndrome in 23.1% of the livebirthis and 32% of the stillbirths. The most common EM among the newborns were those of the genitourinary system (48.3%). Among the stillbirths with no diagnosed syndromes, EM were more frequently observed in the genitourinary (52.8%) and musculoskeletal systems (52.8%).

In 2009, Gonzalez *et al*[20] conducted a retrospective analysis of the medical charts of 223 neonates with a prenatal diagnosis of structural CHD from 1998 to 2007, in a general and a cardiologic hospital in the US. The CHD was confirmed by postnatal echocardiography. The EM detected by cranial and abdomen ultra-sonogram were classified as significant, moderately significant and nonsignificant (variants of normal). Abdominal ultrasound (performed in 58.7% of the cases) detected some abnormality in 41.2% of the cases, and 36.6% were clinically significant (most of them consisting of renal malformations or heterotaxy disorders). Patients with septal defects were 3.7 times more likely to have abnormal findings in the abdominal ultra-sonogram than those without septal defects. Nearly 50% of the individuals had one or more extra-cardiac or genetic disorders identified by abdominal ultrasound, cranial ultrasound (performed in 134 patients) or karyotype analysis (performed in 158 cases), resulting in a cost-yield ratio of 4,508 USD/patients with extracardiac or genetic abnormalities (the costs of performing the three screening tests was 2,254 USD/patient). The authors concluded, thus, that a universal screening program using the three tests represent a reasonable strategy for the neonates who need a cardiac surgery.

In 2010, Dilber and Malcić[35] retrospectively analyzed 1480 newborns with CHD in the period from 2002 to 2007 in pediatric cardiologic hospitals in Croatia. The diagnosis of CHD was established by physical examination, electrocardiogram, X-Ray, echocardiography, cardiac catheterization or autopsy. Congenital rhythm disturbances and cardiomyopathies were also included. During the five years period, 57 (3.85%) children died due to the CHD or other related problems. Chromosomal defects, syndromes and/or major congenital abnormalities were identified in 14.5% of the patients. Among the individuals who did not have any chromosomal disorder or syndrome, the most common EM were the gastrointestinal defects (8.4%). The CHD most frequently associated with extra cardiac malformations were the major heart defects (33.3%).

In the retrospective study by Miller *et al*[36] in 2011, 7,984 patients with CHD born from 1968 to 2005 were evaluated in the US. The CHD was diagnosed by physical examination, autopsy or echocardiography. Newborns, stillbirths and elective abortions from 20 gestational weeks were included. Data were retrieved from the *Metropolitan Atlanta Congenital Defects Program* (*MACDP*). Among the 7,984 patients, 71.3% had isolated CHD, 13.5% had associated EM, 13.1% had some syndrome and 2% had laterality defects. The frequency of multiple congenital abnormalities was greater in individuals with intra-atrial

communication (18.5%), malrotation of the heart (17.2%) and conotruncal defects (16%). Therefore, 27.8% of the infants with CHD had major EM, including those with syndromes or laterality defects. The most common noncardiac defects were those of the skeleton (35%), gastrointestinal (25.2%) and urinary (23.1%) systems. The clinical information was reviewed by a clinical geneticist, who classified the patients as having isolated CHD, CHD associated with EM or with syndromes. The authors observed a higher frequency of specific combinations, such as hydronephrosis or urethral atresia with cardiac malrotation, right ventricular outlet obstruction, intra-atrial and interventricular communication. When the analysis was limited to the cases with EM who underwent necropsy, the skeleton (46.1%) and urinary system (35.8%) defects were the most frequently observed.

Nevertheless, we must emphasize that none of the studies described herein used the same method to evaluate all the patients. In the present review, we did not find any study that used the dysmorphological physical examination performed by a clinical geneticist, karyotype tests, fluorescent *in situ* hybridization (FISH) test for detection of the 22q11

Table 1 - Studies of extra-cardiac malformations in children with congenital heart diseases published in the literature

Author	Ferencz *et al* [26]	Kramer *et al* [27]	Stoll *et al* [28]	Murugasu *et al* [21]	Pradat [29]	Grech e Gatt [16]	Bosi *et al* [14]	Calzolari *et al* [30]	Eskedal *et al* [31]
Type of study	R	P	P	P	R	R	R	R	R
Períod	1981-84	1981-82	1979-86	NRD	1981-90	1990-94	1980-00	1980-94	1990-99
Country	US	Germany	France	Cingap	Sweden	Malta	Italy	Italy	Norway
n	1,494	1,016	801	109	2,618	231	2,442	1,549	3,527
Age	95% <1 year old	Up to 16 years old	ABOs, BBs and SBs	2 weeks to 20 years old	Up to 1 years old	Up to 1 year old	Up to 2 years old	Up to 5 days – LBs and SBs	Children
Cardiologic diagnosis	ECO, CAT, HS or NEC	PE, ECO, CAT	ECO, CAT, HS or NEC	CAT	ECO, CAT, HS or NEC	ECO, CAT, HS or NEC	PE, ECO, CAT, HS or NEC	ECO, HS or NEC	ECO, CAT, HS or NEC
Controls	+	-	+	-	-	-	-	-	-
Diagnosis of the abdominal malformation	Medical charts and interview	Urogram and medical charts	NR	Urinary US	Medical charts	Medical charts	ND	Medical charts	Medical charts
Pacients who underwent abdominal US	NR	NR	NR	All	NR	NR	NR	NR	NR
% abdominal findings	NR	NR	NR	11.9	NR	NR	NR	NR	NR
Syndromic evaluation	+	+	+	NR	+	+	+	+	NR
Evaluation by a clinical geneticist	NR	NR	NR	NR	NR	NR	NR	NR	NR
% patients with karyotype	ND	ND	19.1	NR	NR	NR	NR	19.4	NR
% chromosomal findings	12.5	5.5	9	ND	12.3	9	9.1	9.8	NR
FISH 22q11	-	-	-	-	-	-	NR	-	NR
% 22q11	-	-	-	-	-	NR	NR	-	NR

Continue...

Table 1 - Continuation

Author	Stephensen *et al*[32]	Güçer *et al*[33]	Wojtalik *et al*[34]	Meberg *et al*[19]	Amorim *et al*[2]	Gonzalez *et al*[20]	Dilber e Malčić[35]	Miller *et al*[36]
Type of study	R	R	R	P	R	R	R	R
Períod	1990-99	1977-02	1997-02	1982-05	NR	1998-07	2002-07	1968-05
Country	Iceland	Turkey	Ploand	Norway	Brazil	US	Croatia	US
n	740	305	1,856	662	352	223	1,480	7,984
Age	Children	1 day to 16 years old - NEC	Children	Neonates	Neonates – LBs and SBs	Neonates	Neonates	ABOs, fetuses, LBs and SBs
Cardiologic diagnosis	ECO, CAT, NEC	NEC	ECO	ECO, NEC	ECO, NEC	ECO	PE, ECG, XRay, ECO, CAT, HS or NEC	PE, ECO, NEC
Controls	-	-	-	-	+	-	-	-
Diagnosis of the abdominal malformation	Medical charts	NEC	Medical charts	NR	NR	Abdominall US	NR	NR
Pacients who underwent abdominal US	NR	NR	NR	NR	NR	Clinical suspicion	NR	NR
% abdominal findings	NR	NR	NR	NR	NR	36.6	NR	NR
Syndromic evaluation	+	+	NR	+	+	NR	+	+
Evaluation by a clinical geneticist	NR	NR	NR	NR	NR	NR	NR	Review of clinical findings
% patients with karyotype	NR	5.2	NR	NR	NR	70.9	NR	NR
% chromosomal findings	4.9	2.6	ND	7.9	NR	NR	7.3	9.2
FISH 22q11	-	NR	-	NR	NR	NR	Some	Some
% 22q11	-	NR	-	NR	NR	NR	0.7	0.7

R: retrospective; P: prospective; NR: not reported; US: United States; Cingap: Cingapure; n: number of patients; ABOs: abortions; LBs: livebirths; SBs: stillbirths; NEC: necropsies; ECO: echocardiography; CAT: catheterization; HS: heart surgery; PE: physical examination; ECG: electrocardiogram; +: present; -: absent; US: ultrasound; abdom: abdominal; KTP: karyotype; FISH: fluorescent in situ hybridization del: deletion .

Chart 1 - Extracardiac malformations most frequently reported among patients with congenital heart diseases[2,14,16,19, 20, 26-36]

Extracardiac malformations
Central nervous system
Hydrocephalus
Corpus callosum agenesis
Defects of the neural tube closure
Craniofacial
Cleft lip/palate
Eyes
Microphtalmia/anophtalmia
Respiratoty
Diaphragmatic hernia
Pulmonary hypoplasia/ agenesis
Tracheoesophageal fistula
Pulmonary segmentation anomalies
Digestive
Esophageal atresia/stenosis
Duodenal atresia/stenosis
Omphalocele
Anal atresia/stenosis
Musculoskeletal
Upper limbs deficiency
Polydactyly/syndactyly
Costovertebral anomalies
Dislocation of the hip
Clubfoot
Genitourinary
Renal duplication
Uretheral/renal pelvis duplication
Hydronephrosis
Renal agenesis/hypoplasia
Cystic kidney disease
Ectopic kidney
Vesicouretheral reflux
Hypospadia
Spleen anomalies
Asplenia/polysplenia

deletion syndrome and abdominal ultrasound in all children with CHD. Table 1 summarizes the main features of these studies. Chart 1 lists the main EM reported among patients with CHD.

Conclusions

In summary, EM, including abdominal abnormalities, are frequent in patients with CHD, and those who have both conditions may present higher risk of morbidity and mortality. Consequently some authors have been discussing the importance and cost-effectiveness of the screening of children with CHD for EM using ancillary tests such as abdominal ultra-sonogram. Only a few studies have evaluated this approach using a universal screening program; however, these studies have indicated that this represents a reasonable strategy, not only for the frequency of EM, but also because many of them, specially the abdominal malformations, may be assymptomatic. Such approach could be helpful to prevent further complications, such as chronic kidney disease. However, almost all the published studies are retrospective and not uniform (*i.e.*, did not use a standardized evaluation method, by using ultrasound in all the studied individuals) and are based mainly in medical charts and population registers. Therefore, further studies are still necessary to evaluate the real importance of performing such a screening.

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