Pregnancy termination rates after fetal diagnosis of single ventricle: A 17-year retrospective review

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Abstract

Background: Contemporary reports of termination rates after Fetal Echocardiographic (FE) diagnosis of congenital heart disease are limited and none have reported temporal trends. Progressive improvements in surgical outcomes were hypothesized to impact termination rates when the diagnosis of hypoplastic left heart syndrome (HLHS)/Single Ventricle (SV) is made early in fetal life.

Methods: We reviewed all fetal echocardiograms performed in a tertiary center pediatric cardiology program between 5/1996 and 1/2013. FE interpretation and all related counseling were performed by a single cardiologist. Annual termination rates were determined and maternal demographics and other identified fetal abnormalities were compared between continued pregnancies and those which were terminated. Review of the medical literature for fetal ultrasound and HLHS/ single ventricle was performed to provide historic comparison of pregnancy termination rates.

Results: 2411 FE were performed with 149 diagnoses of SV (.062%). In 31 cases (21%), the FE diagnosis was made at > 24 weeks’ gestation and these cases are not included in the analysis. Of the remaining 118 cases, 48% were diagnosed with HLHS, 21% hypoplastic right heart, 19% complex single ventricle, and 12% unbalanced atioventricular septal defect. Overall termination rate was 15.4%, with 95% CI (11.67%-20.53%). Termination rates varied from year to year throughout the review period but there was no significant trend over time. There was no statistically significant difference in maternal demographics (age, marital status, ethnicity, gestational age at diagnosis) between continued pregnancies and those which were terminated. Termination rates did not differ when fetal chromosomal abnormalities or high risk cardiac characteristics (severe AV valve insufficiency, intact atrial septum, ventricular dysfunction) were identified.

Conclusions: Over a 17-year period in our center, termination rates in pregnancies with FE diagnosis of SV were consistently low, comparable with previous reports from American centers over the last 20 years. Despite major improvements in cardiac surgical outcomes over this time period, there was no significant trend in termination rates over time. This lack of change suggests that factors other than cardiac prognosis are major determinants in family decision-making after a fetal diagnosis of SV. A significantly higher termination rate reported recently by a single large U.S. referral center suggests that regional differences in counseling may also be important. In over 20% of our cases, the diagnosis of SV was made beyond 24 weeks of gestation, emphasizing the importance of skilled recognition of potential cardiac defects on screening ultrasounds and the need for prompt fetal cardiology referral when any cardiac problem is suspected.

Introduction

Hypoplastic Left Heart Syndrome (HLHS) accounts for 7-8% of all congenital heart disease, and it is one of the most common defects diagnosed prenatally [1,2]. Before the 1980’s, this diagnosis was uniformly fatal, usually in the first week of life [3]. In most centers, parents were informed of this when a fetal diagnosis of HLHS was made and after birth only palliative care was provided. Over the last 3 decades, an effective but high-risk surgical approach, staged palliation beginning with a Norwood procedure shortly after birth, has become the standard management of HLHS and other functional Single Ventricle (SV) diagnoses. Outcomes and survival rates have steadily improved, so prenatal diagnosis now includes specific counseling about this option. However, even with prenatal diagnosis, planning, and a high level of intention to treat, HLHS accounts for up to 25% of all cardiac deaths in the first week of life. Other forms of functional single ventricle defects are less common, but their prognosis with staged palliation is comparable. Additionally, the long-term prognosis for children and young adults remains uncertain and thus, prenatal termination and palliative care after birth are also described to parents as options [4,5].

Despite the evolving prognosis and informed counseling, rates of pregnancy termination for severe congenital heart disease including HLHS in North America have been consistently reported to be between 12-25% over the past 20 years, much lower than rates in Europe, Asia, and Australia [2,5-17] (Table 1). A single U.S. study of SV cases diagnosed between 1995 and 2008 recently reported a higher overall termination rate of 31%, 49% when the diagnosis was made before 24 weeks of gestation [18,19]. With improved outcomes and survival with neonatal palliation and conflicting reports of termination rates, an updated analysis of contemporary pregnancy outcomes in the current era is needed as the most recent series extended only to 2009.

Besides prenatal counseling, several other factors including cultural, religious, and socio-economic factors contribute to parental decisions to terminate [11,20]. To date, there is limited data assessing

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longitudinal trends in pregnancy termination rate, particularly with significant provider and counseling consistency. This information is important as parents need to be optimally informed about the potential outcome of any fetal cardiac diagnosis.

Methods

The URMC fetal echocardiogram database was retrospectively searched from the beginning of routine fetal echocardiography in May 1996 through January 2013. All fetal ultrasounds were interpreted by the same pediatric cardiologist who performed all of the prenatal counseling. Information provided reflected the contemporary status of short- and midterm outcomes after palliative surgery. All fetuses found to have a prenatal diagnosis of HLHS or other functional single ventricle defect requiring staged palliation beginning with a Norwood reconstruction were included. Minor variants of HLHS suitable for biventricular repair were excluded.

A review of the medical record was performed to identify information regarding maternal history (age, gravity, and parity), sonographic findings/diagnosis, gestational age at diagnosis, results of karyotype testing, extra-cardiac anomalies, number of prenatal visits with pediatric cardiologist, as well as pregnancy outcome. Patients were categorized into one of two categories: high-risk or standard-risk. High-risk was defined as the presence of extra-cardiac, genetic, or chromosomal anomalies; or, additional cardiac findings such as intact or highly restrictive atrial septum, severe degree of tricuspid regurgitation, or severe ventricular dysfunction. Standard-risk was defined as the absence of these risk factors. Review of the medical literature for fetal ultrasound and HLHS/single ventricle was performed to provide historic comparison of pregnancy termination rates. Chi-squared analysis or Fisher’s exact test was used to assess differences in maternal demographic, diagnoses, and pregnancy outcomes between high-risk and standard-risk fetuses. Fisher’s exact test was used to compare termination rates in international and American centers. P <0.05 was considered statistically significant.

Results

Over 17 years, 2411 fetal echocardiograms were performed with 149 single ventricle diagnoses (0.062%). In 31 cases (17%), the FE diagnosis was made at >24 weeks gestation and these cases are excluded from the analysis. Initial fetal echocardiography and counseling by the fetal cardiologist were performed at a mean of 21 ± 3.2 weeks' gestation. Mean maternal age at diagnosis was 30 ± 5.6 years. This was the first pregnancy for 26% of the mothers, and 78% were married. Specific diagnoses included 56 (48%) HLHS, 25 (21%) hypoplastic right heart, 23 (19%) complex SV, 14 (12%) unbalanced AV septal defect. Eighty-one fetuses (69%) were standard risk and 37 (31%) were high risk. Of the high-risk fetuses, 27 (73%) had a major extracardiac, genetic, or chromosomal anomaly (Table 2). 7 (19%) had an intact or severely restrictive atrial septum, and 3 (8%) had additional cardiac risk factors (severe AV valve regurgitation or severe ventricular dysfunction).

Overall termination rate was 15.4%, with 95% CI (11.67%-20.53%). Termination rates varied from year to year throughout the review period but there was no significant trend over time (Figure 1). There was no statistically significant difference in maternal demographics (age, marital status, history of previous pregnancy, ethnicity, gender, gestational age at diagnosis) between continued pregnancies and those which were terminated (Table 3). Of terminated pregnancies, 10 (53%) were diagnosed with HLHS, 5 (26%) with HRHS, 3 (16%) with complex single ventricles, and 1 (5%) with an unbalanced AV septal defect (Figure 2). We found no significant difference in proportion of families who chose pregnancy termination between the high-risk and standard-risk groups (Figure 3).

Published pregnancy termination rates from all identified reports of fetal diagnosis of HLHS/SV are displayed in Table 1. Reports include FE diagnoses made between 1995 and 2009. Ten reports were from international centers and 6 were from American centers. All but one [11] were retrospective single center reports. Termination rates ranged from 16 to 79% (mean≈32%) in reports from international centers and from 12.5 to 31% (mean = 18.4%) in American centers (p=0.0003). No previous study reported trends in termination rates over time.

Discussion

Despite improvements in surgical outcomes and counseling consistency provided by a single pediatric cardiologist, we found no significant trend in pregnancy termination rates over the past 17 years after prenatal diagnosis of SV heart defects. Over this time period as awareness has increased, more SV diagnoses are made at an earlier gestational age, and surgical outcomes have improved, changes in pregnancy termination rates would be anticipated; however, we did not
find this to be the case. Previous studies have reported differences in early outcomes between fetuses stratified into high-risk and standard-risk groups [5], and one might also expect to see a higher proportion of families choosing pregnancy termination in the high-risk group. However, as in previous reports, we found no significant difference in the pregnancy termination rate between the high and standard-risk groups. These findings suggest that factors other than cardiac prognosis are the major determinants in family decision-making after a fetal diagnosis of single ventricle. Other factors including cultural, religious, and socio-economic factors are known to be important determinants of parental decision making when considering pregnancy termination.

Additionally, 21% (31/149) of patients were diagnosed after 24 weeks’ gestation, beyond the legal limit for termination in New York State, and the mean fetal age at diagnosis for the remainder was 21 weeks. This emphasizes the importance of recognition of potential cardiac defects on screening ultrasounds and the need for prompt referral to a pediatric cardiologist for diagnosis as soon as any cardiac problem is suspected. Review of the medical literature indicates that the termination rates in this review are similar to those reported for American centers since 1998, consistently and significantly lower than those from international centers with the exception of a single recent report from the Boston Children’s Hospital [18].

Table 2. Extracardiac, genetic, and chromosomal anomalies in the high-risk group

| Anomaly                                      | Number of fetuses affected |
|----------------------------------------------|----------------------------|
| Renal anomaly                                | 4                          |
| Heterotaxy syndrome                         | 4                          |
| Brain anomaly                                | 4                          |
| Skeletal anomaly                             | 2                          |
| Omphalocele                                  | 2                          |
| Congenital cystic adenosomatoid malformation | 1                          |
| Congenital Diaphragmatic Hernia              | 1                          |
| Pentology of Cantrell                       | 1                          |
| Severe non-specific dysmorphism              | 1                          |
| Genetic/Chromosomal                          |                            |
| Trisomy 21                                   | 4                          |
| Trisomy 18                                   | 4                          |
| Trisomy 13                                   | 2                          |

Table 3. Demographic data

| Demographic Data                          | Terminations (n=19) | Continued Pregnancies (n=99) | X2 or Fisher’s Exact Test |
|-------------------------------------------|---------------------|----------------------------|--------------------------|
| Maternal Age in years, mean (+/- SD)      | 31.32 +/- 4.91      | 29.68 +/- 6.29              | p = 0.2856               |
| Gestational age at diagnosis in weeks, mean (+/- SD) | 20.58 +/- 1.71      | 21.16 +/- 2.39              | p = 0.3133               |
| History of previous pregnancy, n (%)      | 14 (74%)            | 68 (69%)                    |                          |
| First pregnancy, n (%)                    | 3 (16%)             | 28 (30%)                    |                          |
| Unknown, n (%)                            | 2 (10%)             | 3 (3%)                      |                          |
| Married status                            |                     | p = 0.3578                  |                          |
| Single, n (%)                             | 17 (95%)            | 75 (76%)                    |                          |
| Unknown, n (%)                            | 2 (5%)              | 23 (23%)                    |                          |
| Ethnicity                                  |                     | p = 0.6757                  |                          |
| White/Non-Hispanic, n (%)                 | 14 (73%)            | 73 (74%)                    |                          |
| White/Hispanic, n (%)                     | 2 (11%)             | 8 (8%)                      |                          |
| Black/African American, n (%)             | 2 (11%)             | 15 (15%)                    |                          |
| Asian American, n (%)                     | 1 (5%)              | 2 (2%)                      |                          |
| Unknown, n (%)                            | __                  | 1 (1%)                      |                          |
| Gender                                     |                     | p = 0.7258                  |                          |
| Male, n (%)                                | 8 (42%)             | 49 (50%)                    |                          |
| Female, n (%)                              | 6 (32%)             | 45 (45%)                    |                          |
| Unknown, n (%)                            | 5 (26%)             | 5 (5%)                      |                          |
family decision making after prenatal diagnosis of single ventricle is not primarily influenced by cardiac prognosis. In order to completely assess pregnancy termination rates, future studies are needed to confirm our findings and to assess all the medical, religious, cultural, and socioeconomic factors that potentially influence parental decision making. While many other factors likely contribute to this difficult parental decision, it remains imperative to provide families with accurate and timely prognostic information in order to optimally support them during this process.

Conclusion

Our review provides an updated analysis of pregnancy termination rates after fetal ultrasound diagnosis of HLHS/SV in an era with improved outcomes and decreased surgical mortality. Over a 17-year period in our center, termination rates in pregnancies with FE diagnosis of SV were low, consistent with reports from American centers dating back to 1998 with no significant trend over time. This lack of change suggests that factors other than cardiac prognosis are major determinants in family decision-making after a fetal diagnosis of SV. We report a significantly lower termination rate than the other contemporary American review, suggesting regional differences in counseling may also affect parental decision making. Additionally, in over 20% of cases, the diagnosis of SV was made beyond 24 weeks of gestation, emphasizing the importance of skilled recognition of potential cardiac defects on screening ultrasounds and the need for prompt fetal cardiology referral when any cardiac problem is suspected.

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