The Effect of Neurodevelopmental Disorders on the Prognosis of Children Undergoing Heart Transplantation: A Retrospective Analysis of the National Inpatient Sample 2011–2019

Ian Ergui, Fatima Lakhani, Rahul Sheth, Bertrand Ebner, Michael Dang, Karla Inestroza, Louis Vincent, Rosario Colombo, George Marzouka, Luanda Grazette

Abstract

Background: Many international governing bodies recommend against heart transplantation in patients with severe cognitive-behavioral disabilities, however no clear criteria are offered to define severity. Patients with neurodevelopmental disorders may face systematic discrimination when being evaluated for transplant. We set out to investigate whether children with neurodevelopmental disorders that undergo heart transplantation have poorer in-hospital outcomes compared to neurotypical children. Methods: A retrospective analysis of the National Inpatient Sample database was conducted to identify pediatric patients with neurodevelopmental disorders who underwent heart transplantation from 2011–2019. Baseline characteristics and in-hospital outcomes between patients were compared. Binary logistic regression was used to investigate the association between the documented presence of a neurodevelopmental disorder and in-hospital outcomes in children undergoing heart transplantation. Results: We identified a weighted sample of 3770 pediatric cardiac transplant patients, of whom 245 (6.5%) had a documented diagnosis of neurodevelopmental disorder. There was no significant difference in the odds of major adverse cardiovascular events (all-cause mortality, stroke complications or myocardial infarction), surgical complications, infection, venous thromboembolic events, delirium/restraint use, or cardiac dysrhythmia. Patients with neurodevelopmental disorders had lower overall length of stay (44.0 days interquartile range (IQR): 16.0–90.0 vs. 57.08 days IQR: 22.0–112.0, p < 0.050), and cost of stay ($956,031 IQR: 548,559.0–2,129,086.0, p < 0.050). Patients with neurodevelopmental disorders had significantly lower odds of acute transplant complications (adjusted odds ratio (aOR): 0.39, 95% confidence interval (CI): 0.21–0.74, p < 0.050) vascular complications (aOR: 0.36, 95% CI: 0.19–0.66, p < 0.050) and acute kidney injury (AKI) (aOR: 0.52, 95% CI: 0.33–0.83, p < 0.050). Conclusions: These data suggest that patients with neurodevelopmental disorders have overall similar if not potentially improved post-transplant outcomes in the acute setting compared to neurotypical patients, possibly secondary to selection bias in the patient selection process.

Keywords

neurodevelopmental disorder; heart failure; heart transplant; transplant rejection

Introduction

For children with end-stage heart failure refractory to medical management, heart transplantation is the standard of care [1]. The most common indication for transplantation in patients under 1 year of age is congenital heart disease [1]. For older children, conversely, the commonest indication is cardiomyopathy [1]. In-hospital and short-term outcomes after transplant have improved consistently over the past 30 years, and patients that live to 1-year post-transplant have a 60% survival into adulthood [2]. Despite these advances, limited donor availability remains challenging for transplant teams. Patients with 1A status often experience waittimes of up to 80–108 days and wait-list mortality of up to 19.7–21.4% [3]. Most children on the wait-list are aged 12–17 years (28.4%), followed by patients aged 1–5 years (26.4%) and patients younger than 1 year (21.3%) [4]. The majority of children listed for transplant are White (51.3%), followed by Hispanic (21.0%) and African-American children (19.6%) [4]. While the total number of pediatric transplants has risen in recent times (a 36.1% increase from 2010–2021), there are significant concerns regarding mor-
bidity and mortality in various pediatric transplant candidate subgroups [4–6]. Pediatric patients with neurodevelopmental disorders (NDDs) represent a subgroup that is undergoing transplant at increased frequency, yet studies regarding post-transplant prognosis in this group are lacking [7]. The Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) defines NDDs as a group of conditions that begin early in childhood and result in developmental deficits that impair personal, social, academic or occupational functioning [8]. Specific NDDs include autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), intellectual disability (ID), specific learning disorder (SLD), motor disorders (MD) and communication disorders (CD) [8,9].

Epidemiological data from the National Health Interview Survey indicate that 18% of children have some form of NDD as of 2017, a 9.5% increase over the prior 9 years [10]. In terms of specific NDDs, approximately 1 in 36 children aged 8 years have ASD, with male children being 3.8 times more likely to carry the diagnosis [11]. The global prevalence of ADHD is estimated to be anywhere between 4.8% and 9.4% of children and teenagers [12]. Intellectual disabilities are estimated to affect up to 3% of the population [13]. Specific learning disorders, which encompass neurocognitive deficits in verbal and mathematical perception, afflict up to 5–15% of children [8,14]. Similar to IDs, MDs are thought to impact 2–3% of children [15]. Communication disorders are diagnosed more frequently, with an estimated prevalence of 5–10% [16]. NDDs may be associated with an increased risk of developing atherosclerotic heart disease, dyslipidemia, stroke, heart failure and cardiometabolic disease [17–21]. It is unclear what factors contribute to this increased risk of heart disease, but effects of atypical antipsychotics, food selectivity, sedentary lifestyle, disturbed sleep patterns, disparities in the use of guideline directed medical therapy, prematurity, genetic and epigenetic variation, intrauterine growth restriction, autonomic nervous system dysfunction, prenatal infections, maternal obesity and maternal diabetes have all been offered as potential etiologies [17,20–22]. Children with congenital heart disease (CHD) have increased odds of being diagnosed with NDDs [23–28]. Up to 30% of children with CHD have concomitant NDDs [29]. The American Heart Association and American Academy of Pediatrics recommend that clinicians consider enhanced screening for NDDs in children with CHD [23]. While data regarding the prevalence of specific acquired cardiac abnormalities in patients with NDDs is sparse, genetic mouse models of NDDs show altered anterior and posterior wall thickness, differential myocardial fractional shortening and increased left ventricular chamber diameter when compared to wild-type mice [30]. Genetic variants implicated in the pathogenesis of some NDDs, have also been tied to pathologic cardiac morphologic abnormalities [29,31–47]. Although models demonstrating the relationship of these shared neurologic and cardiovascular allelic variants with heart disease in higher mammals have not yet been developed, children with NDDs have been shown to have higher rates of atrial septal defects, ventricular septal defects, and left heart obstructive lesions [24]. Conversely, magnetic resonance imaging (MRI) studies in fetuses with isolated CHD show decreased brain volumes and maturation when compared to controls [48,49].

Many international societies and governing bodies recommend against heart transplantation in patients with severe cognitive/behavioral disabilities, yet criteria to define severity are not offered [50]. Patients with NDDs and end-stage heart failure may face systematic discrimination during evaluation for ventricular assist device (VAD) or transplant. We sought to investigate in-hospital outcomes in pediatric patients with NDDs undergoing heart transplantation. We hypothesized that in-hospital outcomes after transplant would be similar between groups.

**Methods**

**Study Design**

A retrospective cohort analysis was performed using the National Inpatient Sample (NIS) database. The NIS is the largest public all-payer inpatient dataset, encompassing an approximate 20% sample of hospitalizations from US hospitals participating in the Healthcare Cost and Utilization Project. Information on all hospital stays is offered, irrespective of payer. Rehabilitation hospitals and long-term acute care facilities are excluded from the NIS. Patient, hospital, and state identifiers are universally excluded from the NIS, and all information is de-identified. Institutional Review Board oversight and approval was not necessary since patient-level information is de-identified within the database. Data was weighted as recommended by the NIS. Weights are attached to each case by the NIS to approximate a nationwide sampling of patients, and these weights are applied to the sample prior to the application of statistical tests.

The NIS was queried from 1 January 2011 through 31 December 2019, resulting in 324,130,692 weighted cases. Patients undergoing cardiac transplantation were identified based on ICD-9 or ICD-10 procedure codes corresponding to heart transplant (Supplementary Table 1). A total of 25,456 transplant patients were identified, of whom 340 had concomitant documented NDDs (Supplementary Table 2). Patients with individual and mixed NDDs were included in the analysis. To capture all codes used for NDDs, publicly available spreadsheets consisting of all ICD 9/10 codes from the Healthcare Cost and Utilization Project (HCUP) Distributor were cross-referenced against the Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V) [8,51]. Notably, only 95 (27.94%) of the total
NDD coded patients who underwent transplant were adults. Patients older than 18 years of age were excluded from the analysis, as were patients with a medical diagnosis of heart transplant history. After exclusion of transplant recipients aged >18 years, a total of 3770 pediatric cardiac transplant admissions were identified, of whom 245 (6.5%) were coded as having an NDD (Fig. 1).

Baseline characteristics were evaluated, including age, sex, race, elective admission status, hypertension, diabetes mellitus, chronic kidney disease, chronic liver disease, obstructive sleep apnea, asthma, pulmonary hypertension, history of stroke, anemia, obesity, major depressive disorder, history of malignancy, hypertrophic cardiomyopathy, dilated cardiomyopathy, and myocarditis (Supplementary Table 3). Groups were also analyzed at baseline for the presence of congenital heart disease, including atrial septal defect, ventricular septal defect, hypoplastic left heart syndrome, Tetralogy of Fallot, patent ductus arteriosus and a history of prior surgical correction of congenital heart defects.

The primary outcome was a composite of mortality, stroke complications or myocardial infarction (major adverse cardiovascular events, MACE). Secondary outcomes included length of stay, cost of stay, transplant-associated rejection/complications, intraoperative complications/pericardial complications, bleeding, transfusions, infection, postoperative deep vein thrombosis/pulmonary embolism (DVT/PE), delirium/restraint use, ventricular dysrhythmia, atrial fibrillation/flutter, vascular complications, cardiac arrest, cardioversion, acute kidney injury, post procedural cardiogenic shock, post-transplant lymphoproliferative disorders and pneumothorax.

Fig. 1. Flow chart detailing the selection of patients who underwent heart transplantation between 2011 and 2019 with and without neurodevelopmental disorder (NDD).

Baseline characteristics of patients with and without coded NDDs are shown in Table 1.

In patients with NDDs undergoing transplant, 20.4% (N = 50) had mixed or overlapping syndromes. The predominant NDD was ADHD (36.7%, N = 90) followed by ASD (28.6%, N = 70) and then CD (22.4%, N = 55). Intellectual disability was less common in transplant recipients.
Table 1: Baseline characteristics of patients undergoing heart transplant.

<table>
<thead>
<tr>
<th>Variable</th>
<th>No NDD (n = 3525)</th>
<th>NDD (n = 245)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>7.2 ± 6.5</td>
<td>8.9 ± 6.0</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Female</td>
<td>42.0% (1481)</td>
<td>32.7% (80)</td>
<td>0.004*</td>
</tr>
<tr>
<td>Non-white Race</td>
<td>48.6% (1713)</td>
<td>47.3% (116)</td>
<td>0.170</td>
</tr>
<tr>
<td>Elective Admission</td>
<td>16.3% (571)</td>
<td>16.3% (40)</td>
<td>0.990</td>
</tr>
<tr>
<td>Hypertension</td>
<td>28.1% (992)</td>
<td>40.8% (100)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1.4% (45)</td>
<td>9.8% (20)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td>4.4% (155)</td>
<td>10.2% (25)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Chronic Liver Disease</td>
<td>7.5% (265)</td>
<td>14.3% (35)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Obstructive Sleep Apnea</td>
<td>2.8% (100)</td>
<td>8.2% (20)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>On Hemodialysis</td>
<td>N ≤ 10</td>
<td>N ≤ 10</td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>6.1% (214)</td>
<td>20.4% (50)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Pulmonary Hypertension</td>
<td>18.4% (647)</td>
<td>20.4% (50)</td>
<td>0.430</td>
</tr>
<tr>
<td>Prior Stroke</td>
<td>5.4% (190)</td>
<td>N ≤ 10</td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>6.4% (149)</td>
<td>N ≤ 10</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>3.1% (110)</td>
<td>10.2% (25)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Major Depressive Disorder</td>
<td>7.1% (251)</td>
<td>6.1% (15)</td>
<td>0.560</td>
</tr>
<tr>
<td>Congenital Heart Disease</td>
<td>18.9% (666)</td>
<td>6.1% (15)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Personal History of Malignancy</td>
<td>0.7% (25)</td>
<td>N ≤ 10</td>
<td></td>
</tr>
<tr>
<td>Hypertrophic Cardiomyopathy</td>
<td>4.0% (140)</td>
<td>6.1% (15)</td>
<td>0.100</td>
</tr>
<tr>
<td>Dilated Cardiomyopathy</td>
<td>40.8% (1439)</td>
<td>53.1% (130)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>3.0% (105)</td>
<td>N ≤ 10</td>
<td></td>
</tr>
<tr>
<td>History of Myocardial Infarction</td>
<td>0.6% (20)</td>
<td>N ≤ 10</td>
<td></td>
</tr>
<tr>
<td>History of Surgically Corrected Congenital Heart Lesion</td>
<td>6.2% (220)</td>
<td>10.2% (25)</td>
<td>&lt;0.015*</td>
</tr>
</tbody>
</table>

Values are reported as mean ± standard deviation for continuous variables and percentage (number) for categorical variables. p-value < 0.05 is considered significant (asterisk). Cells with values ≤10 are not reported as recommended by the National Inpatient Sample (NIS) and denoted as N ≤ 10.

Patients with NDDs who underwent cardiac transplant had lower rates of MACE, defined as a composite of mortality, stroke complications or myocardial infarction (6.1% vs. 13.7%), acute transplant complications (12.2% vs. 21.4%), intraoperative/pericardial complications (8.2% vs. 13.8%), bleeding complications (10.2% vs. 22.6%), vascular complications (14.3% vs. 26.0%) and acute kidney injury (AKI) (18.4% vs. 33.4%). The average length of stay was shorter in the NDD group as was the average cost of stay. There was no significant difference in blood product transfusions (26.5% vs. 23.7%), postoperative deep venous thrombosis (14.3% vs. 14.9%), ventricular dysrhythmias (28.6% vs. 29.3%), cardioversion (6.1% vs. 4.2%) or pneumothorax (6.1% vs. 8.0%) between groups.

A binary logistic regression model was used to adjust for the prespecified covariates of age, infant status, race, sex, hypertension, diabetes mellitus, chronic kidney disease, chronic liver disease, stroke history, anemia, obesity, obstructive sleep apnea, asthma, congenital heart disease, dilated cardiomyopathy, and history of surgically corrected congenital malformations. The age variable was dichotomized into patients ≤7 years old vs. those >7 for the binary logistic regression model. Infant status was defined as patients <1 year old. The non NDD group contained 972 infants (27.6%) while the NDD group contained 35
Table 2. Outcomes following heart transplant.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No NDD (n = 3525)</th>
<th>NDD (n = 245)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE [A]</td>
<td>13.7% (483)</td>
<td>6.1% (15)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Length of Stay [B]</td>
<td>57 IQR (22–112)</td>
<td>44 IQR (16–90)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Cost of Stay [C]</td>
<td>1,074,793 IQR (599,090–2,129,086)</td>
<td>956,031 IQR (548,559–1,801,412)</td>
<td>&lt;0.030*</td>
</tr>
<tr>
<td>Acute Transplant Complications [D]</td>
<td>21.4% (755)</td>
<td>12.2% (30)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Iatrogenic or Pericardial Complications of Cardiac Surgery</td>
<td>13.8% (488)</td>
<td>8.2% (20)</td>
<td>0.012*</td>
</tr>
<tr>
<td>All Major Bleeding</td>
<td>22.6% (798)</td>
<td>10.2% (25)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Blood Product Transfusion</td>
<td>23.7% (837)</td>
<td>26.5% (65)</td>
<td>0.323</td>
</tr>
<tr>
<td>Infectious Complications [E]</td>
<td>12.0% (423)</td>
<td>N ≤ 10</td>
<td></td>
</tr>
<tr>
<td>Postoperative Deep Venous Thrombosis or Pulmonary Embolism</td>
<td>14.9% (526)</td>
<td>14.3% (35)</td>
<td>0.787</td>
</tr>
<tr>
<td>Delirium or Restraint use</td>
<td>4.4% (156)</td>
<td>N ≤ 10</td>
<td></td>
</tr>
<tr>
<td>Ventricular Dysrhythm</td>
<td>29.3% (1032)</td>
<td>28.6% (70)</td>
<td>0.814</td>
</tr>
<tr>
<td>Atrial Fibrillation/Flutter</td>
<td>6.2% (217)</td>
<td>N ≤ 10</td>
<td></td>
</tr>
<tr>
<td>Vascular Complications</td>
<td>26.0% (916)</td>
<td>14.3% (35)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Cardiac Arrest</td>
<td>9.3% (326)</td>
<td>N ≤ 10</td>
<td></td>
</tr>
<tr>
<td>Cardioversion</td>
<td>4.2% (149)</td>
<td>6.1% (15)</td>
<td>0.160</td>
</tr>
<tr>
<td>Acute Kidney Injury</td>
<td>33.4% (1178)</td>
<td>18.4% (45)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Post Procedural Cardiogenic Shock</td>
<td>1.3% (45)</td>
<td>N ≤ 10</td>
<td></td>
</tr>
<tr>
<td>Post Transplant Lymphoproliferative Disorder</td>
<td>N ≤ 10</td>
<td>N ≤ 10</td>
<td></td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>8.0% (283)</td>
<td>6.1% (15)</td>
<td>0.285</td>
</tr>
</tbody>
</table>

Outcomes reported as median (interquartile range) for continuous variables and percentage (number) for categorical variables. [A] MACE: combined primary endpoint including mortality, all stroke complications, and all acute myocardial infarctions. [B] Length of stay reported in days. [C] Cost of stay reported in USD. [D] Acute transplant complications include rejection, graft dysfunction and allograft vasculopathy. [E] Infectious complications include postoperative infection, sepsis, or septic shock. p-value considered significant <0.05 (asterisk). Cells with values ≤10 are not reported as recommended by the NIS and denoted as N ≤ 10. MACE, major adverse cardiovascular events; IQR, interquartile range.

(14.3%). After adjustment, there was no significant difference in the odds of MACE (aOR: 0.69, 95% confidence interval (CI): 0.34–1.44, p = 0.333), intraoperative/pericardial complications (aOR: 0.79, 95% CI: 0.42–1.49, p = 0.469), or bleeding complications (aOR: 0.64, 95% CI: 0.35–1.16, p = 0.137), between NDD and non-NDD patients. Patient with NDDs had significantly lower odds of acute transplant complications (0.39, 95% CI: 0.21–0.74, p < 0.001) vascular complications (aOR: 0.36, 95% CI: 0.19–0.66, p = 0.003) and AKI (aOR: 0.52, 95% CI: 0.33–0.83, p = 0.004) compared to non-NDD patients during the index admission (Fig. 2). A comorbidity adjusted Brown-Mood median test was conducted to compare the median cost and length of stay between NDD and non NDD groups given the non-parametric distribution of those variables. The median length of stay was shorter in the NDD group (44.0 days interquartile range (IQR): 16.0–90.0 vs. 57.08 days IQR: 22.0–112.0, p = 0.004), and there was no significant comorbidity adjusted difference in the median cost of stay between NDD and non NDD groups ($956,031 IQR: 548,559.0–1,801,412.0 vs. $1,074,793 IQR: 599,089.8–2,129,086.0, p = 0.098).

**Discussion**

We present the only multi-center retrospective cohort study of heart transplantation outcomes in patients with NDDs to date. In this cohort we demonstrate that overall, the presence of NDDs was not associated with increased odds of major adverse cardiovascular events, intraoperative complications, or graft dysfunction. Patients with NDDs, interestingly, had decreased odds of acute transplant complications, vascular complications, and acute kidney injury. This is despite the fact that patients with NDDs had higher rates of comorbidities such as hypertension, diabetes mellitus, chronic kidney disease, chronic liver disease, and asthma. This may be because a higher proportion of the neurotypical patients had concomitant CHD as compared to the NDD patients, whereas the NDD patients had a higher degree of dilated cardiomyopathy. The likely shortened time to transplant for children with dilated cardiomyopathy may explain fewer overall complications being seen in this group [52]. Selection bias in the organ allocation process may also be partly responsible for the improved outcomes in the NDD group in this study. Patients with NDDs may be viewed as sicker than their neurotypical counterparts and
Fig. 2. Adjusted in-hospital outcomes following heart transplant in patients with NDDs. Values <1 favor patients with NDDs. 

may be excluded from the transplant conversation. While the phenomenon of over-diagnosis and under-treatment has been shown in racial minorities [53], there have not been similar studies in patients with NDDs.

Despite the increasing prevalence of NDDs, heart transplantation in neurodivergent populations remains an area of controversy. Several state legislatures in the US have recently passed legislation to protect the rights of patients with NDDs being evaluated for transplant [54]. Up to 43% of pediatric transplant centers consider NDDs when evaluating a patient for transplant, with 14% of centers regarding even mild NDDs a relative contraindication to transplant [55]. Data from the Organ Sharing Network has shown that children with NDDs have longer wait times prior to transplant, but similar survival and graft function after surgery [56]. There is a distinct lack of guidance and standardization regarding the inclusion of neurodevelopmental delay in the transplant evaluation [55]. The low frequency of CHD in the NDD group in this study despite the numerous genetic associations between the conditions raises the question of whether patients with CHD are not being transplanted because of their NDDs. Epidemiological data suggest that up to 18% of US children may have some form of NDD, however patients with NDDs only made up 6.5% of the population of this study [10]. Patient and institution level analyses are needed to assess whether patients with IDs are being excluded from consideration for transplant based on their neurodivergent status [57,58].

Patients with NDDs suffer from persistent difficulties with social interaction, communication, and learning [8,59]. For NDD patients with concomitant heart failure who are in extremis and require transplant for a chance at survival, the pre, peri and post-operative periods can be especially challenging. Overstimulation in the inpatient and intensive care units, higher doses of sedating medications, difficulties communicating symptoms, “picking” at lines or surgical wounds, concerns regarding long term immunosuppressant adherence and problems with dietary and fluid restrictions are all valid concerns for NDD patients facing the possibility of transplant surgery. The results from this retrospective study support the notion that patients with NDDs can benefit from similar in-hospital outcomes to patients without NDDs after cardiac transplant.

Some pediatric transplant centers have had success with limiting the number of patient visitors, minimizing the number of distracting stimuli, decreasing the frequency of vital sign monitoring, and emphasizing the importance of open and empathetic communication with NDD patients [60]. Physicians, case managers, family members, nurses and mental health practitioners are equally important and all play vital roles in serving this vulnerable population. Up to 24% of neurotypical children may suffer from psychological distress after heart transplant, and an individualized approach is needed for all children facing the prospect of such major intervention [61]. One survey of a large pediatric tertiary center showed that nurses with frequent interactions with patients with NDDs have significantly higher
self-reported effectiveness at communicating with and caring for these populations compared to staff with less frequent interactions [62]. Successful strategies reported in that study included partnering with families to understand what techniques were effective to communicate with and calm children with NDDs, as well as better understand what stimuli upset them [62]. Studies in older adults with neurocognitive disorders indicate that one to one specialising and close observation in this population may result in higher quality care, however data regarding specialising and closer observation in pediatric patients with NDDs is not available at this time [63]. Increased supervision, more frequent contact with clinical staff and access to nurses specialized in these behavioral interventions may bely the improved outcomes for the NDD group in this study.

The current study has several limitations. The low sample size of NDD patients reduces the generalizability of this study. A weighted population of 245 NDD patients undergoing transplant ensures that any observations drawn from this study are mainly descriptive and causation cannot be inferred. The accuracy of coding for NDDs is likely heterogeneous between centers. We were unable to evaluate patients with or without NDDs who were considered for transplant and ultimately not listed and therefore cannot estimate the possible role of selection bias on these outcomes. Patients with NDDs being considered for transplant may, for instance, have fewer overall comorbidities and greater performance status at baseline. The former, however, is belied by the higher baseline rates of diabetes mellitus, chronic kidney disease and pulmonary hypertension in the NDD group.

Despite the above-mentioned limitations, in this cohort NDD patients who underwent heart transplant had similar to improved posttransplant outcomes compared to neurotypical patients. Efforts are underway in various governmental bodies to protect the rights of intellectually divergent patients in need of solid organ transplants. The exclusion of patients with NDDs from some transplant programs represents a major disparity in healthcare and transplant teams should consider a multidisciplinary approach to evaluating NDD patients for transplant.

Conclusions

Pediatric patients with neurodevelopmental disorders have similar or potentially improved outcomes post-cardiac transplant when compared to neurotypical patients, however they are transplanted at a lower frequency then would be expected based on epidemiological data.

Availability of Data and Materials

The datasets analyzed in the current study are available from the Healthcare Cost and Utilization Project Central Distributor (https://hcup-us.ahrq.gov/tech_assist/centdist.jsp).

Author Contributions

IE: conceptualization, methodology, software, formal analysis, data curation, writing- original draft, visualization. FL: methodology, formal analysis, data curation, writing- review and editing. RS: formal analysis, writing-review and editing. BE: methodology, software, validation, formal analysis, resources, data curation, writing- review and editing. MD: methodology, software, validation, formal analysis, resources, data curation, writing- review and editing. KI: validation, writing- review and editing. LV: methodology, software, validation, formal analysis, resources, data curation, writing- review and editing. RC: writing- review and editing, project administration, resources, supervision. GM: writing- review and editing, project administration, resources, supervision. LG: conceptualization, methodology, validation, resources, writing- review and editing, supervision, project administration. All authors read and approved the final manuscript. All authors contributed to editorial changes in the manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspect of the work.

Ethics Approval and Consent to Participate

Oversight and approval from the University of Miami institutional review board was not necessary since patient-level information was de-identified within the database.

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Conflict of Interest

The authors declare no conflict of interest.
Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.59958/hsf.7289.

References


