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Tumor Screening in Beckwith-Wiedemann Syndrome: Parental Perspectives

Kelly A. Duffy[1], **Katheryn L. Grand**[1], **Kristin Zelley**[1], and **Jennifer M. Kalish**[1,2]

[1]The Division of Human Genetics: Children's Hospital of Philadelphia, 3028 Colket Translational Research Building, 3501 Civic Center Blvd, Philadelphia, PA, 19104 USA

[2]The Department of Pediatrics, Perelman School of Medicine, The University of Pennsylvania, Philadelphia, PA, USA, Phone 215-590-1278

Abstract

Children with Beckwith-Wiedemann Syndrome (BWS) and Isolated Hemihypertrophy (IHH) are at an increased risk for developing tumors. Tumor screening in this population is currently being reassessed by several groups and the effect on patients and patient-families has been argued both as a reason to screen and not to screen. Parental perspectives on this topic have never been systematically addressed for the BWS population. Here, we conducted a parent-based survey to evaluate knowledge and attitudes toward tumor screening in patients affected by BWS/IHH. A total of 261 surveys were completed. Overall, parents reported that screening decreased their worry and did not feel that screening increased worry or created a burden. This effect was observed across various demographic variables and other factors examined. Almost all significant differences observed could be attributed to parental knowledge of tumor risk. Parents who correctly identified their child's tumor risk were more likely to agree with stratified screening recommendations according to BWS type and risk, and were less likely to feel worried if recommendations were changed. These results highlight the need to educate families about their child's genetic type and tumor risk in order to facilitate an informed decision about tumor screening.

Keywords

Beckwith-Wiedemann syndrome; Cancer predisposition; Tumor screening

Correspondence to: Jennifer M. Kalish.

Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s10897-017-0182-8) contains supplementary material, which is available to authorized users.

Compliance with Ethical Standards

Conflict of Interest Kelly A. Duffy, Katheryn L. Grand, Kristin Zelley, and Jennifer M. Kalish declare that they have no conflict of interest.

Human Studies and Informed Consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki. Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all patients for being included in the study.

Animal Studies No animal studies were carried out by the authors for this article.

Introduction

Beckwith-Wiedemann Syndrome (BWS, OMIM #130650) and isolated hemihypertrophy/hemihyperplasia (IHH, OMIM #235000) are childhood cancer predisposition disorders with increased risk of embryonal tumors, predominately Wilms tumor and hepatoblastoma. These disorders are caused by a variety of epigenetic and genetic alterations affecting the chromosome 11p15 region: loss of methylation at KCNQ10T1:TSS-DMR (IC2 LOM); gain of methylation at H19/IGF2: IG-DMR (IC1 GOM); paternal uniparental isodisomy of chromosome 11 (pUPD); *CDKNIC* mutations; chromosome abnormalities and translocations; and those with no molecular defect identified. Advancements in the understanding of epi(genotype)-phenotype correlations have led to the stratification of tumor risk according to the molecular cause of BWS. Those with IC1 GOM and pUPD appear to have a high risk (22.8% – 28.6% and 13.8–17.3% respectively) and those with IC2 LOM appear to have a low risk (2.5% – 3.1%) (Brioude et al. 2013; Maas et al. 2016; Mussa et al. 2016b). Tumor risk has been suggested as intermediate for those with no molecular defects identified (6.7%) and *CDKNIC* mutations (6.9% – 8.8%) (Brioude et al. 2013; Maas et al. 2016), although large data sets of these patients are lacking compared to the other subtypes.

Based on the recognized tumor risk in these patients, tumor screening is initiated at the time of diagnosis. Although the recommended frequency of screening has varied among institutions, it has generally been accepted that children with BWS and IHH should receive screening for the development of hepatoblastoma by serial alpha-fetoprotein (AFP) measurements every six weeks to three months until the age of three to four years, and screening for abdominal tumors by ultrasonography until the age of seven to eight years (Beckwith 1998; Brioude et al. 2013; Choyke et al. 1999; Clericuzio and Martin 2009; Cooper et al. 2005; DeBaun and Tucker 1998; Eggermann et al. 2014; Kalish et al. 2017; Lapunzina 2005; Maas et al. 2016; Mussa et al. 2016a, b, c; Rump et al. 2005; Scott et al. 2006; Tan and Amor 2006; Teplick et al. 2011; Weksberg et al. 2010; Zarate et al. 2009). Until recently, these protocols have been implemented regardless of the specific epigenetic and genetic causes of the child's diagnosis. As a result of the stratification of tumor risk according to subtype, some have suggested implementing screening protocols specific to the subtypes at the highest tumor risk and suggested the discontinuation of screening in those with lower risks (Brioude et al. 2013; Maas et al. 2016; Mussa et al. 2016b, c; Scott et al. 2006).

An acceptable risk threshold of >5% has been employed by some in the determination of which subtypes should receive screening (Brioude et al. 2013; Maas et al. 2016; Scott et al. 2006), while others argue for a 1% risk threshold (Kalish and Deardorff 2016; Kalish et al. 2017). Some have recently advocated against the use of AFP screening, citing difficulties with interpretation, the frequency of screening, and invasiveness to the child (Brioude et al. 2013; Maas et al. 2016). While it has been suggested that parental and patient attitudes are factors in successful screening programs, no previous studies have specifically assessed parental attitudes and knowledge of tumor screening in BWS.

For families, tumor screening protocols can promote a sense of control, extra peace of mind that their child is being monitored, and reassurance with negative results (Beckwith 1998;

Everman et al. 2000; Kalish and Deardorff 2016; Maas et al. 2016; McNeil et al. 2001; Shah 1983; Tan and Amor 2006; Teplick et al. 2011; Verge and Mowat 2010). Conversely, families can experience appreciable anxiety around each test and may be burdened with the frequency and long-term commitment required by screening protocols (Brioude et al. 2013; DeBaun et al. 1996; Maas et al. 2016; Mussa et al. 2014; Pappas 2015; Pritchard-Jones 2002; Shah 1983; Tan and Amor 2006; Teplick et al. 2011; Weng et al. 1995; Zarate et al. 2009), leading to lack of adherence to screening protocols (Brioude et al. 2013; Maas et al. 2016; Mussa et al. 2014; Zarate et al. 2009).

The impact of screening on families as a factor in protocol recommendations has been advocated by many groups (DeBaun et al. 1996; Lapunzina 2005; McNeil et al. 2001; Mussa et al. 2016a; Scott et al. 2006) and it has been considered that families may experience anxiety if tumor screening is withdrawn (McNeil et al. 2001; Scott et al. 2006). It appears through anecdotal experience that most families are willing to adhere to screening protocols and support screening (Kalish and Deardorff 2016; Shah 1983; Tan and Amor 2006; Verge and Mowat 2010). As a result, many families choose to continue screening past the recommended age (McNeil et al. 2001; Scott et al. 2006). The frequency of false-positive screening results and the effect on parental anxiety is the most often considered factor in the perception that screening increases parental anxiety (Beckwith 1998; Brioude et al. 2013; Choyke et al. 1999; Clericuzio and Martin 2009; Everman et al. 2000; Maas et al. 2016; Scott et al. 2006; Shah 1983; Tan and Amor 2006; Teplick et al. 2011; Zarate et al. 2009).

To our knowledge, no study has directly asked parents of children with BWS/IHH how they feel about tumor screening recommendations, although this topic has been evaluated in other cancer predisposition disorders. A systematic review by Gopie et al. evaluated the effect of surveillance for individuals with a hereditary cancer risk and found an increased psychological burden in families with rare tumor syndromes, although it was noted that there was a limited number of studies evaluating these populations (Gopie et al. 2012). It was also found that most participants positively viewed screening programs, felt screening offered security and gave a sense of control, and individuals compliant with screening had less fear, regardless if the program was proven to be effective (Gopie et al. 2012).

We sought to evaluate the attitudes of parents of a child who was currently or previously receiving tumor screening due to a clinical or molecular diagnosis of either BWS or IHH. The responses were analyzed to evaluate for factors that influenced parental perspectives, and to potentially identify components related to tumor screening that could be improved in this patient population.

Methods

Instrumentation

A questionnaire was developed by the authors to analyze practices, attitudes, and worry towards tumor screening in patients with BWS/IHH (Online Resource 1). The survey consisted of the following sections: Demographics (7 questions about the child; 10 questions about the parent); Experience with Screening (5 questions); Physician Recommendations and Practice (6 questions); Parental Attitudes and Opinions (5 questions); Parental Worry (7

questions); and Additional Comments (qualitative response). Participants responded to questions in the form of yes/no, multiple choice, and free text comments. All questions were optional, and participants could choose not to answer questions they did not feel comfortable answering. Responses were parent-reported and medical charts were not reviewed. For analysis, some responses were further grouped into categories.

To evaluate how screening affected worry, participants were presented with a series of seven statements regarding their feelings towards tumor screening and responded on a five-point Likert-scale from (1) strongly disagree to (5) strongly agree. For analysis, responses were grouped into three categories: (1) strongly disagree/disagree, (2) neutral, and (3) agree/strongly agree.

Procedures

Recruitment and survey completion primarily occurred online and through email. Patients enrolled in a BWS/IHH patient registry at Children's Hospital of Philadelphia (CHOP) and those who had previously contacted the BWS email account were contacted by email and invited to complete the survey. A link to the survey was also made available on a BWS parent support Facebook group and shared by the Beckwith-Wiedemann Children's Foundation International. A small number of participants were recruited during CHOP genetic clinic appointments and completed a hard-copy of the survey. This survey was available from July – October 2016. Consent was implied when participants completed the survey. This research was approved by CHOP's Institutional Review Board (IRB# 16–013047).

Participants

A total of 261 online or paper surveys were returned. Survey respondents included parents of children diagnosed with BWS and IHH who received tumor screening as part of their care management. Only one parent per family completed the survey. Participants had the option to provide contact information or remain anonymous, and 77.1% provided their contact information. Among participants who provided contact information, 12.4% were CHOP patients and 26.2% were enrolled in the BWS/IHH registry.

Data Analysis

Study data were collected and managed using REDCap (Research Electronic Data Capture) tools hosted at Children's Hospital of Philadelphia. REDCap is a secure, web-based application designed to support data capture for research studies (Harris et al. 2009). The data was exported from REDCap and analyzed using IBM SPSS Statistics (version 24.0).

Descriptive statistics were performed on all variables. Continuous variables were summarized by mean and standard deviation and nominal/categorical variables were summarized by frequencies. Pearson chi-square analyses were performed to evaluate potential factors that could be affecting parental concern. Further analysis was performed to explore the significant relationships identified and included additional Pearson chi-square analyses, Pearson r correlation, and analysis of covariate (ANCOVA) testing. Significance was set at $p \leq 0.05$ when analyzing results.

The following factors and categories were used in this analysis: family location (USA, other); genetic cause (IC2 LOM, other); education groups (associate's degree or less, bachelor's degree, advanced degree); employment groups (unemployed/homemaker, part-time, full-time); marital status (living alone, living with someone); number of children (1 child, two or more); child age groups (less than 4 years, 4–7.99 years, 8 years and over); incurred costs related to screening (no, yes); history of false-positive screen (no, yes); risk threshold to screen (any risk, 1–5%, 6–10%); vary screening by type (no, yes); satisfaction with physician recommendations (no, yes); advocate to receive current screening regimen (no, yes); AFP frequency followed (6 weeks, 3 months); AFP frequency recommended (6 weeks, 3 months); AFP frequency beliefs (6 weeks, 3 months); AFP frequency adherence (no, yes); knowledge of child's tumor risk (correct, incorrect). To assess parental knowledge of their child's tumor risk, the perceived risk reported was compared with the reported genetic type of the child. This was assessed for those types with established risks (IC1 GOM – high risk, pUPD – high risk, IC2 LOM – low risk).

Results

Demographic Characteristics

The demographic characteristics of the children with BWS are summarized in Table 1. Overall, there were more females than males. The majority of children with BWS were under the age of 4 years, with ages ranging from 9 weeks to 21 years. Most children were white and non-Hispanic. The most frequent genetic cause of BWS reported was IC2 LOM.

The demographic characteristics of the parents are summarized in Table 2. The majority of parents were white, non-Hispanic, married females between the ages of 25 and 44 years with two or more children. Most parents reported attaining a bachelor's degree or higher and almost half worked full-time. More than half of parents lived in the United States.

Parental Satisfaction and Experience with Tumor Screening

Tumor screening frequency was assessed in several ways: 1) the frequency recommended by physicians; 2) the frequency being performed (followed); and 3) the frequency parents believed they should be following. These results are summarized in Table 3. For all three evaluations, the majority of responses revealed AFPs were being monitored every 6 weeks or every 3 months and ultrasounds were being performed every 3 months. Participants reported that their physicians recommended an AFP frequency of every 3 months more often than every 6 weeks and slightly more children were following an AFP frequency of every 6 weeks. More than half of parents believed that AFP screening frequency should be every 6 weeks.

The majority of parents (n = 207, 82.5%) were following the same AFP frequency that was recommended by their physician. Among those who were following a different AFP frequency than was recommended (n = 44, 17.5%)), more than half (54.5%) had a child who was receiving AFP screening more frequently than was recommended, 22.7% were receiving AFP screening when it was not recommended, 13.6% were following a less

frequent AFP screening than was recommended, and 9.1% were not receiving AFP screening even though it was recommended.

Less than half of parents (40.5%) reported that they advocated to their physician for their child to receive their current screening regimen, and most parents (88.4%) were satisfied with the screening recommended by their child's physician. Most parents (91.0%) did not have to advocate with their insurance company to receive screening. Less than half of parents (40.9%) incurred costs related to screening and almost all parents (96.9%) reported they were willing to pay for their child to receive screening.

Most children in the survey did not develop a tumor (91.9%). Among those who did develop a tumor ($n = 21$), 76.2% were detected through screening. About one-third of children (32.3%) had a history of a false-positive screen.

Parental Perception and Knowledge of Tumor Risk

Parents were asked to report their child's tumor risk (perceived risk). One- third of parents (33.8%) were unsure of their child's tumor risk, 19.6% reported their child's tumor risk as high, 17.7% reported intermediate, and 28.8% reported low. Parents were also asked to report the genetic cause of their child's diagnosis. More than one-fifth of parents (23.3%) did not know their child's genetic cause, but reported it was confirmed through testing.

Parental knowledge of tumor risk was assessed by comparing the perceived risk with actual risk based on the genetic types of BWS with established risks (IC1 GOM, IC2 LOM, pUPD). Among parents of children with one of these genetic types ($n = 122$), more than half of parents (54.1%) incorrectly identified their child's tumor risk or reported they did not know their child's risk.

Parental Perception of Acceptable Risk

Parents were asked at what risk threshold screening should be performed. Three-quarters (75.4%) of parents believed that a child with any risk of developing a tumor should receive screening, while the other 25% of parents were divided between their beliefs in acceptable risk threshold: 7.2% chose a 1–4% risk threshold; 11.7% chose a 5% risk threshold; 1.2% chose a 6–9% risk threshold; and 4.4% chose a 10% risk threshold.

Parents were also asked if they believed tumor screening should vary by the child's genetic type and subsequent risk. Approximately three-quarters (76.5%) of parents did not think screening should vary by type. Parents who did believe that screening should vary by type ($n = 60$) were asked to choose which type(s) they believed should be screened. The most frequently selected genetic types were pUPD ($n = 32$, 53.3%) and unknown cause ($n = 31$, 51.7%). Similar selection frequencies were observed for *CDKNIC* mutations ($n = 29$, 48.3%), IC1 GOM ($n = 27$, 45.0%), and IC2 LOM ($n = 26$, 43.3%) and "other causes" was selected the least frequently ($n = 21$, 35.0%).

Parental Concern in Tumor Screening

Overall, most parents agreed that they were worried about their child developing a tumor (Table 4). Most parents agreed that screening helped decrease their worry and disagreed that

screening increased their worry. More than half of parents did not report that they felt burdened by the frequency of screening and the majority agreed that the potential of finding their child's tumor early outweighed the stress caused by screening. More than half of parents agreed they would feel more worried if screening recommendations changed and almost all agreed that they would feel more worried if their child did not receive screening.

Analysis of Factors Affecting Attitudes

To analyze factors that could be affecting parental concern, Pearson chi-square analyses were performed. The Likert-scale statements "The potential of finding my child's tumor early outweighs the stress caused by screening" and "I would feel more worried if my child did not receive screening" could not be analyzed further, as more than 90% of parents agreed with these statements and the sample size of parents responding as neutral or disagreeing was too small. Ninety Pearson chi-square tests were performed between the factors and Likert statements. The majority of factors analyzed did not influence parental concern and data is available in Online Resource 2. A total of 10 significant relationships were identified (Table 5). Significant factors that influenced concern included the child's age, number of children, parental education, beliefs about AFP frequency, acceptable risk threshold beliefs, whether screening should vary by genetic type, and parental knowledge of tumor risk.

Knowledge significantly differed in the perception of burden, implying a direct relationship. As four other factors (parental education, beliefs about AFP frequency, acceptable risk threshold beliefs, and whether screening should vary by type) were found to influence burden, analysis of covariate (ANCOVA) testing was performed to control for knowledge and analyze if any of these relationships were still significant after controlling for knowledge. After controlling for knowledge, none of these factors were significant for burden *(data not shown)*.

Additional Exploratory Analysis

Although knowledge was not a significant factor affecting the other Likert statements, we sought to evaluate whether knowledge differed between the remaining controllable factors (acceptable risk threshold beliefs and whether screening should vary by genetic type), suggesting an indirect relationship. A significant difference in knowledge ($p = 0.009$) was found between those who believed tumor screening should vary by type (64.7% correct) and those who did not think screening should vary by type (38.4% correct). Knowledge did not significantly differ in risk threshold beliefs ($p = 0.112$): those who believed in a 6–10% risk threshold correctly identified their child's tumor risk (75.0%) more often than those who believed in a 1–5% risk threshold (54.2% correct) and those who believed in any risk (40.5% correct). As these results suggested a linear relationship, Pearson r correlation was then computed. A small, positive correlation was observed, $r = 0.206$, $n = 116$, $p = 0.026$, indicating that increased knowledge was correlated with increases in risk threshold beliefs.

As knowledge was suggested to influence parental concern, Pearson chi-square analysis was performed to evaluate if any other factors differed in regard to knowledge. Knowledge of child's tumor risk was found to differ significantly among family location ($p = 0.023$), with parents living in a country other than the United States more often correctly identifying their

child's tumor risk (59.1%) compared to parents living in the United States (37.7%). Knowledge did not significantly differ among any other factors analyzed *(data not shown)*.

Discussion

In the context of evolving tumor screening guidelines with new recommendations emerging in the United States (Kalish et al. 2017) and Europe, this study assessed parental attitudes towards tumor screening. Overall, these data demonstrate that parents find screening comforting and few of the factors influence the burden of tumor screening.

The majority of parents were worried that their child would develop a tumor. Most parents agreed that tumor screening helped decrease their worry and disagreed that screening created a burden. Almost all agreed that the potential of finding their child's tumor early outweighed the stress caused by screening, further supporting that screening has an overall positive effect. Parents reported that their worry would increase if screening recommendations were changed and would feel more worried if their child did not receive screening. In addition, almost all parents reported that they would be willing to pay for their child to receive screening, which has been proposed as a method to indirectly evaluate cost-effectiveness of tumor screening and impact the decision to discontinue tumor screening (DeBaun et al. 1996; McNeil et al. 2001).

Most patients were following the reported recommendations of their physician and did not develop tumors. In the survey, about 30% of families responding had a child with the low-risk IC2 form of BWS. Screening was found to be effective in tumor detection as most patients who developed tumors were detected through screening. False-positive results were a common finding in this study and although it has been suggested that the frequency of false-positive results increases parental anxiety (Beckwith 1998; Brioude et al. 2013; Choyke et al. 1999; Clericuzio and Martin 2009; Everman et al. 2000; Maas et al. 2016; Scott et al. 2006; Shah 1983; Tan and Amor 2006; Teplick et al. 2011; Zarate et al. 2009), we did not measure any significant differences in concern between parents of a child who had a falsepositive screen and those who did not.

The majority of factors evaluated were not associated with parental concern suggesting that parents uniformly view tumor screening. Of particular interest, similar responses were observed among parents across the various world region groups. As many countries have differing medical systems and cultural beliefs, the similar responses demonstrate the importance of screening to parents independent of the medical system and system-specific recommendations in which screening is occurring.

To identify components related to tumor screening that could be improved, we grouped the significant factors by those that could not be controlled (i.e. demographic variables) and those that could be controlled (i.e. factors that could potentially be mediated through proper education and genetic counseling). We determined that three significant factors were demographic variables (child's age, number of children, and parental education) and thus could not be controlled. The remaining 4 factors (beliefs about AFP frequency, acceptable

risk threshold beliefs, whether screening should vary by genetic type, and parental knowledge of tumor risk) were determined to be controllable factors.

Knowledge was determined to be the factor that could most readily be controlled and changed among parents. Although parental attitudes cannot entirely be controlled, we suggest that through improved education and knowledge of tumor risk, parental attitudes regarding the other three factors may change.

Recent publications (Brioude et al. 2013; Maas et al. 2016; Mussa et al. 2016b) have delineated different tumor risks based on the molecular types leading to BWS and have suggested different tumor screening protocols based on these risks. Almost a quarter of parents did not know their child's molecular cause and among those who did, more than a half were not able to correctly identify the related tumor risk. Accuracy of parental perception of tumor risk was only calculated for IC1 GOM, IC2 LOM, and pUPD as these are the subgroups that have been stratified for risk. These results suggest that genetic testing results and the associated tumor risk are not being effectively communicated to families.

Patient and family knowledge is crucial to the understanding of their disease and the ability to make informed decisions about their care. Studies have found that patients and parents involved in the care of their children seek information to feel confident about their choices and those with inadequate knowledge lack the skills required to make informed decisions and participate in care (Budych et al. 2012; Jordan et al. 2010; Smith et al. 2009; Woolf et al. 2005). The quality and dynamic of the patient-physician interaction further impacts the effective transmission of information and care decisions (Budych et al. 2012; Jordan et al. 2010; Smith et al. 2009; Woolf et al. 2005). Patients and families of children affected by rare disorders and their physicians face challenges to the traditional patient-physician interaction, where oftentimes the physician has limited knowledge about the disorder and the family becomes the expert through seeking information from other sources. In children with rare diseases, it was found that parents often prefer patient-directed interactions with physicians and wish to have information to participate in the treatment process, often seeking information themselves (Budych et al. 2012). It was also suggested that effective education and information exchange can help the physician and patient reach decisions about their medical care that meets the patient's expectations and in some cases, reduce medical costs by avoiding unnecessary tests (Budych et al. 2012).

Improved and uniform educational practices will likely lead to better parental understanding and shift towards more targeted screening based on tumor risk. Parents who correctly identified their child's tumor risk were more likely to report burden than parents who incorrectly identified risk. This suggests that parents of children with a lower risk may feel that the recommended screening is too frequent or not necessary. Parents with knowledge of their child's tumor risk were also more accepting of stratified tumor screening recommendations according to molecular type and risk, and were less likely to feel worried if recommendations were changed. These results suggest that improved education and effective communication between families and physicians may lead to acceptance of modified screening practices or discontinuation of screening in patients with lower tumor risk and alleviate some of the burden experienced by families.

Within the United States, parents had less knowledge of their child's tumor risk compared to other countries. Knowledge of genetic type did not differ between the United States and other countries. This suggests that while knowledge of the child's molecular cause of BWS is communicated in similar frequencies, the knowledge of tumor risk is not. This difference may be due to differences in medical systems and clinical practice, perhaps specifically due to non-US based physicians beginning to recommend targeted screening based on molecular cause of BWS. Parents also reported they received their tumor screening recommendations from a variety of physician types, suggesting a possible range of knowledge in the diverse medical community who participate in the care of children with BWS/IHH. In an effort to improve education about the genetics and tumor risk associated with their child's diagnosis, it is imperative that all care providers have access to resources about BWS, are knowledgeable in the disorder, and offer consistent education to families regardless of medical system or clinical practices. Genetic counselors may help facilitate proper education and support for families.

Study Limitations

The survey was primarily conducted online in English as a cross-sectional, observational study therefore, participants may differ from those who chose not to participate and parents of children with BWS/IHH who were not aware of the study, which may limit the generalizability of our findings. In addition, the large majority of parents were Caucasian, non-Hispanic females, which limited the ability to assess attitudes by gender and race/ethnicity. Although these limitations exist, we were able to achieve a large sample size of parents ($n = 261$) with a child affected by a relatively rare disorder from a variety of locations, which provides strength in our results and ability to draw conclusions.

All data collected and analyzed was parent-reported and no medical charts were reviewed. In addition, we could not further examine two of the Likert- scale statements ("The potential of finding my child's tumor early outweighs the stress caused by screening" and "I would feel more worried if my child did not receive screening") due to small sample sizes in the groups that felt neutral or disagreed with the statements. Analysis on these statements could have provided additional information about factors that affect parental attitudes toward screening.

Practice Implications

These results demonstrate the importance of physician and parental education regarding genetic causes of BWS and the related tumor risk. At the time of diagnosis or suspected diagnosis effective counseling regarding the genetic types and related tumor risk are instrumental in helping families process risk and develop strategies to manage their worry. Screening is designed to provide early detection however the utility of screening is offset by the possibility of false positive screens, the potential personal cost to families, and the associated worry due to both positive screens and falsepositive screens. In partnership with health care providers, armed with improved education families can make informed decisions about the utility of screening as balanced with their understanding of the risk, worry, and outcomes.

Research Recommendations

Further study is needed to assess the parallel health care providers' attitudes and opinions towards tumor screening in BWS. Additionally, focusing on health care provider knowledge of BWS subtypes and tumor risk is needed along with improved and easily accessible educational materials to augment current knowledge. Tumor screening is one of many aspects of BWS, and family perspectives on other clinical aspects of BWS should be further studied. Finally, BWS is a complex clinical and genetic/epigenetic diagnosis and the study of effective strategies to optimize family and health care provider education would benefit all involved in the care of these children.

Conclusion

To our knowledge, this study is the first to directly evaluate parental attitudes and opinions towards tumor screening in the BWS/IHH population. It is evident that families are comforted by tumor screening and may experience increased worry if their current screening recommendations are changed or if their child does not receive tumor screening. As a result, we suggest that tumor screening be offered to all BWS/IHH patients regardless of the molecular cause of their diagnosis. Families should be properly educated about their child's molecular cause, subsequent tumor risk and the potential benefits (early detection) and risks (false-positive results and potential costs) of the tumor screening. After this education, families can then make an informed decision about whether they would like their child to receive tumor screening. This education may lead some families to choose not to screen and reduce the burden and worry associated with screening. In contrast, other families may choose to receive screening to provide the potential benefit of decreased worry and continued reassurance of negative results. In order to improve patient education from health care providers with diverse medical backgrounds and practice environments, uniform educational tools should be developed for physicians and families.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Demographic characteristics of parent's children

Characteristic	**Mean ± SD or *N* (%)**
Age	3.78 ±3.85 years
Under 4 years	165 (63.0%)
4-7.99 years	60 (22.9%)
8 years and over	37 (14.1%)
Gender	
Male	113 (45.2%)
Female	137 (54.8%)
Race	
White	233 (81.5%)
Black/African American	5 (1.8%)
American Indian or Alaska Native	4 (1.4%)
Asian	8 (2.8%)
Native Hawaiian or Pacific Islander	3 (1.0%)
Two or more races	27 (9.4%)
Other	6 (2.1%)
Ethnicity	
Hispanic/Latino	22 (8.8%)
Not Hispanic/Latino	227 (91.2%)
Genetic Type	
IC2 LOM	77 (30.0%)
IC1 GOM	6 (2.3%)
pUPD 11p15	39 (15.2%)
CDKNIC mutation	5 (1.9%)
Other	7 (2.7%)
Not sure but confirmed through testing	60 (23.3%)
Normal testing	43 (16.7%)
Never received testing	18 (7.0%)
Testing pending	2 (0.8%)

Table 2

Demographic characteristics of parents

Characteristic	*N* (%)
Age	
Below 18 years	1 (0.4%)
18-24 years	12 (4.6%)
25-34 years	113 (43.6%)
35-44 years	110 (42.5%)
45-54 years	20 (7.7%)
55-64 years	3 (1.2%)
Gender	
Male	9 (3.5%)
Female	251 (96.5%)
Race	
White	246 (93.5%)
Black/African American	3 (1.1%)
American Indian or Alaska Native	3 (1.1%)
Asian	4 (1.5%)
Native Hawaiian or Pacific Islander	1 (0.4%)
Two or more races	4 (1.5%)
Other	2 (0.8%)
Ethnicity	
Hispanic/Latino	12 (4.9%)
Not Hispanic/Latino	235 (95.1%)
Education	
Less than High School	1 (0.4%)
High School Diploma/GED	18 (7.0%)
Some College	55 (21.4%)
Associate’s Degree	23 (8.9%)
Bachelor’s Degree	83 (32.3%)
Master’s or Graduate Degree	57 (22.2%)
Law Degree	4 (1.6%)
Doctoral Degree	9 (3.5%)
Other	7 (2.7%)
Employment Status	
Unemployed	7 (2.8%)

Characteristic	***N* (%)**
Homemaker	72 (28.2%)
Part-time	41 (16.1%)
Full-time	125 (49.0%)
Other	10 (3.9%)
Marital Status	
Single (never married)	13 (5.0%)
Living with partner	23 (8.9%)
Married	203 (78.7%)
Separated	4 (1.6%)
Divorced	12 (4.7%)
Widowed	3 (1.2%)
Number of Children	2.28 ±1.11
1 child	49 (19.1%)
2 or more children	207 (80.9%)
Location	
United States	173 (67.3%)
Europe	45 (17.5%)
Australia/New Zealand	26 (10.1%)
Other	13 (5.1%)

Table 3

Screening frequencies recommended, following, and believed by parents

	Recommended[a]	Following	Beliefs
AFP frequency			
6 weeks	98 (37.8%)	107 (41.3%)	141 (55.5%)
2 months	3 (1.2%)	6 (2.3%)	10 (3.9%)
3 months	119 (45.9%)	101 (39.0%)	78 (30.7%)
4 months	1 (0.4%)	2 (0.8%)	1 (0.4%)
6 months	11 (4.2%)	7 (2.7%)	5 (2.0%)
Not recommended	17 (6.6%)	21 (8.1%)	3 (1.2%)
Other	10 (3.9%)	15 (5.8%)	16 (6.3%)
Ultrasound frequency			
6 weeks	7 (2.7%)	7 (2.7%)	6 (2.4%)
2 months	0	0	11 (4.3%)
3 months	229 (88.4%)	225 (86.9%)	219 (86.6%)
4 months	2 (0.8%)	7 (2.7%)	2 (0.8%)
6 months	11 (4.2%)	9 (3.5%)	7 (2.8%)
Not recommended	4 (1.5%)	6(2.3%)	1 (0.4%)
Other	6 (2.3%)	5 (1.9%)	7 (2.8%)

[a]Physician recommendations as reported by participants

Table 4

Parental responses to Likert-scale statements

Statement	Disagree/strongly disagree	Neutral	Agree/strongly agree
“I am worried that my child will develop a tumor.”	31 (12.0%)	40 (15.4%)	188 (72.6%)
“Tumor screening helps decrease my worry.”	18 (7.0%)	27 (10.5%)	213 (82.6%)
“Tumor screening increases my worry.”	164 (63.3%)	45 (17.4%)	50 (19.3%)
“I feel burdened by the frequency of screening.”	174 (67.7%)	42 (16.3%)	41 (16.0%)
“The potential of finding my child’s tumor early outweighs the stress caused by screening.”	11 (4.2%)	11 (4.2%)	237 (91.5%)
“My level of worry would increase if screening recommendations were changed.”	46 (17.8%)	63 (24.3%)	150 (57.9%)
“I would feel more worried if my child did not receive screening.”	5 (1.9%)	4 (1.6%)	249 (96.5%)

Table 5

Significant relationships with parental concern

Factor	Strongly disagree/disagree n (%)	Neutral n (%)	Agree/strongly agree n (%)	*p*-value
Parental concern – worried about tumor development				
Number of children				0.048*
1 child	1/49 (2.0%)	7/49 (14.3%)	41/49 (83.7%)	
2+ children	30/206 (14.6%)	31/206 (15.0%)	145/206 (70.4%)	
Child age groups				0.001***
Under 4 years	11/164 (6.7%)	22/164 (13.4%)	131/164 (79.9%)	
4-7.99 years	12/58 (20.7%)	8/58 (13.8%)	38/58 (65.5%)	
8 years and over	8/37 (21.6%)	10/37 (27.0%)	19/37 (51.4%)	
Parental concern – screening helps decrease worry				
Risk threshold to screen				0.014*
Any risk	11/186 (5.9%)	19/186 (10.2%)	156/186 (83.9%)	
1-5% risk	4/46 (8.7%)	2/46 (4.3%)	40/46 (87.0%)	
6-10% risk	3/14 (21.4%)	4/14 (28.6%)	7/14 (50.0%)	
Parental concern – screening increases worry				
Vary screening by type				0.026*
No	130/195 (66.7%)	27/195 (13.8%)	38/195 (19.5%)	
Yes	31/59 (52.5%)	17/59 (28.8%)	11/59 (18.6%)	
Parental concern – burden				
Education groups				<0.001***
Associate's degree or less	70/96 (72.9%)	18/96 (18.8%)	8/96 (8.3%)	
Bachelor's degree	51/81 (63.0%)	19/81 (23.5%)	11/81 (13.6%)	
Advanced degree	43/69 (62.3%)	4/69 (5.8%)	22/69 (31.9%)	
Vary screening by type				<0.001***

Factor	Strongly disagree/disagree n (%)	Neutral n (%)	Agree/strongly agree n (%)	*p*-value
No	145/194 (74.7%)	29/194 (14.9%)	20/194 (10.3%)	
Yes	27/58 (46.6%)	12/58 (20.7%)	19/58 (32.8%)	
Risk threshold to screen				0.004**
Any risk	132/186 (71.0%)	31/186 (16.7%)	23/186 (12.4%)	
1-5%	32/46 (69.6%)	8/46 (17.4%)	6/46 (13.0%)	
6-10%	5/14 (35.7%)	2/14 (14.3%)	7/14 (50.0%)	
AFP frequency beliefs				0.008**
6 weeks	100/139 (71.9%)	26/139 (18.7%)	13/139 (9.4%)	
3 months	54/77 (70.1%)	6/77 (7.8%)	17/77 (22.1%)	
Knowledge				0.016*
Incorrect	47/64 (73.4%)	11/64 (17.2%)	6/64 (9.4%)	
Correct	29/56 (51.8%)	11/56 (19.6%)	16/64 (28.6%)	
Parental concern – worry will increase if recommendations change				
Vary screening by type				<0.001***
No	27/195 (13.8%)	41/195 (21.0%)	127/195 (65.1%)	
Yes	19/59 (32.2%)	19/59 (32.2%)	21/59 (35.6%)	

*significance at $p \leq 0.050$

**significance at $p \leq 0.010$

***significance at $p \leq 0.001$