Adolescent and parent perspectives on genomic sequencing to inform cancer care

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Abbreviations:

PEDS-ONCOSEQ	Personalized Medicine based on Molecular Profiling of Pediatric and Young Adult Patients with Cancer
DNA	deoxyribonucleic acid
RNA	ribonucleic acid

Abstract

Next generation sequencing offers opportunities for targeted cancer therapies and may identify pathogenic germline variants. Adolescents' perception of testing is not well understood. We surveyed 16 adolescents and 59 parents regarding motivations, attitudes, and knowledge related to paired tumor/germline sequencing. Participants generally had a good objective understanding of germline genetics and cancer risk, with parents scoring higher than adolescents. Nearly all participants were motivated by a desire to help other patients and to treat their child/themselves. Most adolescents reported involvement in the decision to enroll in the study. Study findings suggest important similarities and differences between parent and adolescent views.

Introduction

Next generation sequencing of pediatric cancers can identify targets for personalized treatment options. While clinically promising, implementation of tumor sequencing presents unique challenges. Such testing is relatively new, and it is common to obtain results where no targeted treatment is available, is only accessible through a clinical trial, or is only approved for a different malignancy.[1,2] Additionally, many genomic sequencing tests can identify germline mutations affecting hereditary cancer risk. A better understanding is needed of patients' knowledge and preferences regarding germline and tumor sequencing. A recent review reported many adults with cancer have limited understanding of sequencing and high expectations for the results and are pleased they participated, even if no actionable results were received.[3]

Adolescents represent a unique population. Most adolescents with cancer enrolling in research feel they have a right to receive results,[4] but their ability to understand the results of sequencing is less studied. A study looking at non-cancer related sequencing found that adolescents have a reasonable understanding of genes and DNA but less robust understanding of genomes and genomic sequencing. They also found that adolescents were motivated to participate, even if sequencing may not yield actionable results.[5] Studies on psychological impacts of genetic testing in adolescents are limited. A small study did not identify any psychological harm from predictive testing for adult-onset hereditary cancer syndromes.[6]

While guidelines exist for genetic testing and results disclosure for adolescent patients,[7,8] few studies have examined tumor sequencing and most surveyed parents.[9] We report responses from adolescents and their parents regarding their motivations, attitudes, and knowledge relating to paired tumor/germline sequencing research.

Methods

Patients aged 14-17 with advanced or refractory cancer enrolled in the PEDS-ONCOSEQ protocol at the University of Michigan and their parents/guardians were recruited consecutively from 10/2015-2/2017 to complete surveys about their participation. Participants were consented in-person by a research coordinator and genetic counselor and were provided these surveys at this same visit. PEDS-ONCOSEQ includes paired tumor-germline exome sequencing (DNA) and transcriptome (tumor RNA).

The surveys (Supplemental Material S1) used both validated measures and items created for this study. The latter were developed by a team of pediatric oncologists, survey methodologists, genetic counselors, and health communication experts. Study measures assessed participant demographics (adapted from NHANES, 2011)[10], understanding of germline genome sequencing and cancer risk (adapted from Kaphingst et al, 2012)[11], motivations, and decision-making regarding study participation (novel items and items adapted from Roberts et al, 2003, McGuire et al, 2009 and deSnoo et al, 2008)[12-14], and preferences for return of results (novel items and items adapted from Fernandez et al, 2014)[15]. Fisher's exact test was used for comparisons of adolescent and parent responses.

Results

Demographics. 20 adolescents and 77 parents (parents of all children enrolled; not exclusive to adolescents' parents) were eligible. Sixteen adolescents (80%) and 59 parents (77%) completed surveys. The study sample predominantly identified as white (93%

adolescents, 90% parents). Most parent respondents identified as female (82%); 29% of adolescent respondents identified as female (Table 1).

Knowledge. Parents and adolescents had good objective understanding of germline genetics and cancer risk based on the questions asked though parents had a better understanding (73% vs. 86% correct, p=0.0051). Adolescents were less likely to recognize that sequencing is not a routine test for cancer care (38% vs. 72% correct, p=0.02). The other differences were not statistically significant (Table 2).

Motivations. Parent and adolescents had similar motivations for participation including helping other children with cancer, helping to treat their child's/their specific cancer, and because of their doctor's recommendation. Thirteen adolescents (81%) reported their participation was motivated by their family's wishes (Table 3).

Decision-making. Data were analyzed for pairs where an adolescent and at least one parent completed the survey. Most adolescents (79%) reported being involved in the decision to participate. Of this group, 55% reported the decision to participate was driven by the parent(s) and adolescent equally, 27% described themselves as more interested in participating, and 18% cited their parents as more interested. (Table 4).

Preferences for information. All adolescents and most parents believed the adolescent should have access to genomic research results for adult-onset conditions (100%, 93%) and most believed adolescents should have access to results without current clinical utility (88%, 87%). Both believed researchers should re-contact adolescents after the age of majority to confirm consent for continued research use of DNA samples (81%, 73%).

Viewpoints diverged on return of results. Most parents (87%) felt it should be up to them to decide whether to share results with their child while 25% of adolescents agreed with

this statement (p=0.001). Responses differed on whether adolescents should receive results if parents objected (88% adolescents vs. 67% parents agreed) and more adolescents agreed they should know the results before their parents (44% vs. 13%). These differences were not statistically significant. (Table 5).

Discussion

Precision oncology research poses challenges for patient education and informed consent. Adolescents are unique given they may be old enough to have preferences regarding study participation, but still require parental consent. Our results are in line with previous, non-cancer related research that suggests that adolescents generally understand relevant genetic information and are motivated to participate and receive their sequencing results.[5]

Adolescents' motivations for participation were similar to those reported by parents; to learn more about their cancer and to help others. Many reported their family's desire for them to participate was important, but most felt the decision was either shared or primarily theirs. These findings are consistent with other studies where adolescents with cancer demonstrated interest in participating in their health care decisions and studies of adult cancer patients who report similar motivations.[3,16,17]

Parents and adolescents expressed preferences for return of individual genomic results that often does not occur in cancer research. For example, they desired disclosure of findings related to risk of adult-onset conditions and/or those that were not clinically actionable. Given that research suggests patients not only prefer but expect such information from precision oncology studies,[18] care should be taken to educate participants about which results will or won't be returned and why. Similarly, whether adolescents will be re-contacted at age 18 for

permission for continued use of their genetic data should be addressed as part of informed consent/assent.

Unsurprisingly, adolescents were more likely than parents to report that they should receive genomic results before their parents and in cases where parents do not want them to access results. This finding likely represents the tension between parents and adolescents as the adolescents grow, mature, and take responsibility for their own health information. Further exploring adolescents' and parents' views and expectations regarding receipt and use of sequencing information may help manage such tensions.

While response rate was high, results represent a small number of patients from a single institution who predominantly identify as non-Hispanic white, limiting generalizability and the ability to compare parent and adolescent responses. Data were collected several years ago and there may have been changes in precision oncology research and practice. Despite these limitations, these findings suggests that adolescents with cancer understand information about precision oncology, want to participate, and have the same desires for information and motivations for participation as adults with cancer. Differences between parental and adolescent expectations for return of results should be explored as part of the consent process.

Conflict of Interest Statement

None of the authors have conflicts of interest related to this work.

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Legends

Supplemental Material S1. Survey distributed to adolescents and parents.

TABLE 1 Demographics

Characteristics	**Adolescents (n=16)**	**Parents (n=59)** [†]
Age in years	Median: 16 Mean: 15 Range: 14-17	Median: 40 Mean: 39 Range: 22-56 Age of respondents' children: Median: 11 years Mean: 9 Range: 6 weeks – 17 years
Race/Ethnicity	White: 93% Non-Hispanic: 93%	White: 90% Non-Hispanic: 90%
Gender	Female: 29%	Female: 82%
Mean psychological distress score (Range: 0-10)	3.2 (SD: 3.4)	5.5 (SD: 3.0)

[†]Two parents answered together. Included separately in demographics but answers recorded once for other items.

TABLE 2 Adolescent and parent survey results: objective knowledge

Objective Knowledge			
	% correct		**p-value, significant at <0.05 (**)**
Survey Item (*correct response*)	**Adolescents (n=16)**	**Parents (n=58)**	
Even if someone has a gene change affecting risk of a type of cancer, s/he may not develop that cancer. (*true*)	81%	97%	0.0643
Once a gene change that affects risk of cancer, that cancer can always be prevented or cured. (*false*)	81%	93%	0.1675
A person's health habits, like diet and exercise, can influence their risk of developing cancer. (*true*)	88%	86%	1.0000
A doctor can tell a person their exact chance of developing cancer based on sequencing results. (*false*)	69%	83%	0.2914
Sequencing may give people info about their chances of developing conditions other than cancer. (*true*)	81%	85%	0.7147
Sequencing all cancer genes is a routine test that doctors can order for most people with cancer. (*false*)	38%	72%	0.0165**
Total Correct	73%	86%	0.0051**

TABLE 3 Adolescent and parent survey results: motivations

Motivations			
I enrolled (my child) in the study…	**n (%) agree or strongly agree**		**p-value, significant at <0.05 (**)**
	Adolescents (n=16)	**Parents (n=58)**	
To help other children with cancer	16 (100%)	55 (94.8%)	1.00
To help researchers better understand how to treat my/my child's type of cancer	15 (94%)	52* (93%)	1.00
Because my/my child's doctor recommended the study	15 (94%)	42 (72%)	0.10
Because my family wanted me to be a part of the study	13 (81%)	N/A	N/A

*Two parents did not answer this question, percentage calculated out of n=56

TABLE 4 Adolescent and parent survey results: shared decision-making process

Shared decision-making process		
Only participants with paired responses available for both adolescents and their parents (aged 14-17) included	**Adolescents (n=14)**	**Parents (n=15)^**
Did you involve your child/Did your parents involve you in the decision to participate in the study?	Yes: 11 (79%) No: 3 (21%)	Yes: 13 (87%) No: 2 (13%)
Adolescents (n=14 unless otherwise indicated)		
Who was more interested in having you participate in the study? *Only adolescents who reported being involved in the decision were asked this question (n=11)*	Both equally: 6 (55%) Me: 3 (%) My parents: 2 (%)	
How much of the decision to participate in the study was made by you? (Scale: 0% = parents/guardians made all the decision, 100% patient made all of the decision)	Mean: 64% (SD 24)	
How involved was your doctor in your decision to be part of the study? (Scale: 0% = not involved, 100% very involved) *One response excluded because it was not on the 0-100 scale (n=13)*	Mean: 76% (SD 25)	
Parents (n=15 unless otherwise indicated)		
Main reason for involving child in decision *Only parents who reported involving their child in the decision were asked this question (n=13)*	I wanted my child to have input into the decision to participate in this study: 5 (38.5%) My child is mature enough to participate in this kind of decision-making with me: 5 (38.5%) My child and I typically make his/her health decisions together: 2 (13%) I value my child's opinion about participating in this study: 1 (7%)	
Main reason for not involving child in decision[#]	It's my job to make these kinds of decisions for my child:	

Only parents who reported not involving their child in the decision were asked this question (n=2)	1 (50%) My child isn't mature enough to make this kind of decision: 1 (50%)

^Separate responses received from both parents for one adolescent

TABLE 5 Adolescent and parent survey results: right to results

Right to results			
***Only responses from parents of adolescents (aged 14-17) included*	**% agree or strongly agree**		**p-value, significant at <0.05 (**)**
	Adolescents (n=16)	**Parents (n=15)**	
I should be allowed to receive my/my child's results for diseases they could get as an adult	16 (100%)	14 (93%)	0.4839
I/my child should receive his/her results even if the doctor says they do not have any impact on me/my child's cancer treatment	14 (88%)	13 (87%)	1.0000
The research team should contact me/my child when I/he/she turns 18 to ask permission to keep using the DNA in studies	13 (81%)	11 (73%)	0.6851
It should be up to the parents and/or doctors to decide whether or not to share the results with me/my child	4 (25%)	13 (87%)	0.0010**
I should be allowed to receive my results even if my parents don't think I should/My child should be allowed to receive his/her results even I don't think he/she should	14 (88%)	10 (67%)	0.1200
I/my child should be the first to know about his/her results, even before the parents	7 (44%)	2 (13%)	0.1134