

Impact of New Criteria for Gonadotoxic Risk Stratification on an Oncology Population in a Pediatric Hospital

Alejandra Dumenigo, MD, MS; Olivia Frias, MSN; Karen Burns, MD, MS; Julie Rios, MD



Background

- Gonadal insufficiency secondary to gonadotoxic therapies for childhood cancers is known to cause psychosocial issues and distress among survivors, which can be alleviated through access to fertility counseling and fertility preservation (FP) before treatment
- Patients receive FP counseling based on age, sex, pubertal status, cancer type and cyclophosphamide equivalent dosing (CED)
- In 2020, the Pediatric Initiative Network (PIN) developed the first pediatric, adolescent, and young adult-specific gonadotoxic risk stratification guidelines
- Changes in risk category based on the new guidelines may have impacted prior FP options as some are experimental and only offered to those with high-risk stratification under current IRB protocols

Objectives

- Determine gonadotoxic risk category for each patient using the new stratification system
- Compare gonadotoxic risk categories between the new and previous stratification systems to identify any escalation in risk
- Assess the impact of the new criteria on FP options

The PIN Gonadotoxic Risk Stratification System

Figure 1. Risk Stratification Grid – MALE SEX

		Minimally Increased Risk	Significantly Increased Risk	High Level of Increased Risk
Alkylators CED gm/m ²		CED <4 gm		CED ≥4 gm
Hematopoietic Stem Cell Transplant				Alkylator +/- total body irradiation myeloablative and reduced intensity regimens
Heavy Metal mg/m ²		Cisplatin Carboplatin	Cisplatin >500 mg	
Radiation Exposure	Testicular	0.2-0.6 Gy	0.7-3.9 Gy	≥4.0 Gy
	Hypothalamus	26-29.99 Gy	30-39.9 Gy	≥40 Gy
Surgery			RPLND	

Figure 2. Risk Stratification Grid – FEMALE SEX

			Minimally Increased Risk	Significantly Increased Risk	High Level of Increased Risk
Alkylators CED gm/m ²	Prepubertal		CED <8 gm	CED 8-12 gm	CED >12 gm
	Pubertal		CED <4 gm	CED 4-8 gm	CED >8 gm
Heavy Metal mg/m ²			Cisplatin Carboplatin		
Hematopoietic Stem Cell Transplant					Alkylator +/- total body irradiation myeloablative and reduced intensity regimens
Radiation exposure	Ovary	Prepubertal		<15 Gy	≥15 Gy
		Pubertal		<10 Gy	≥10 Gy
	Hypothalamus		22-29.9 Gy	30-39.9 Gy	≥40 Gy

Results

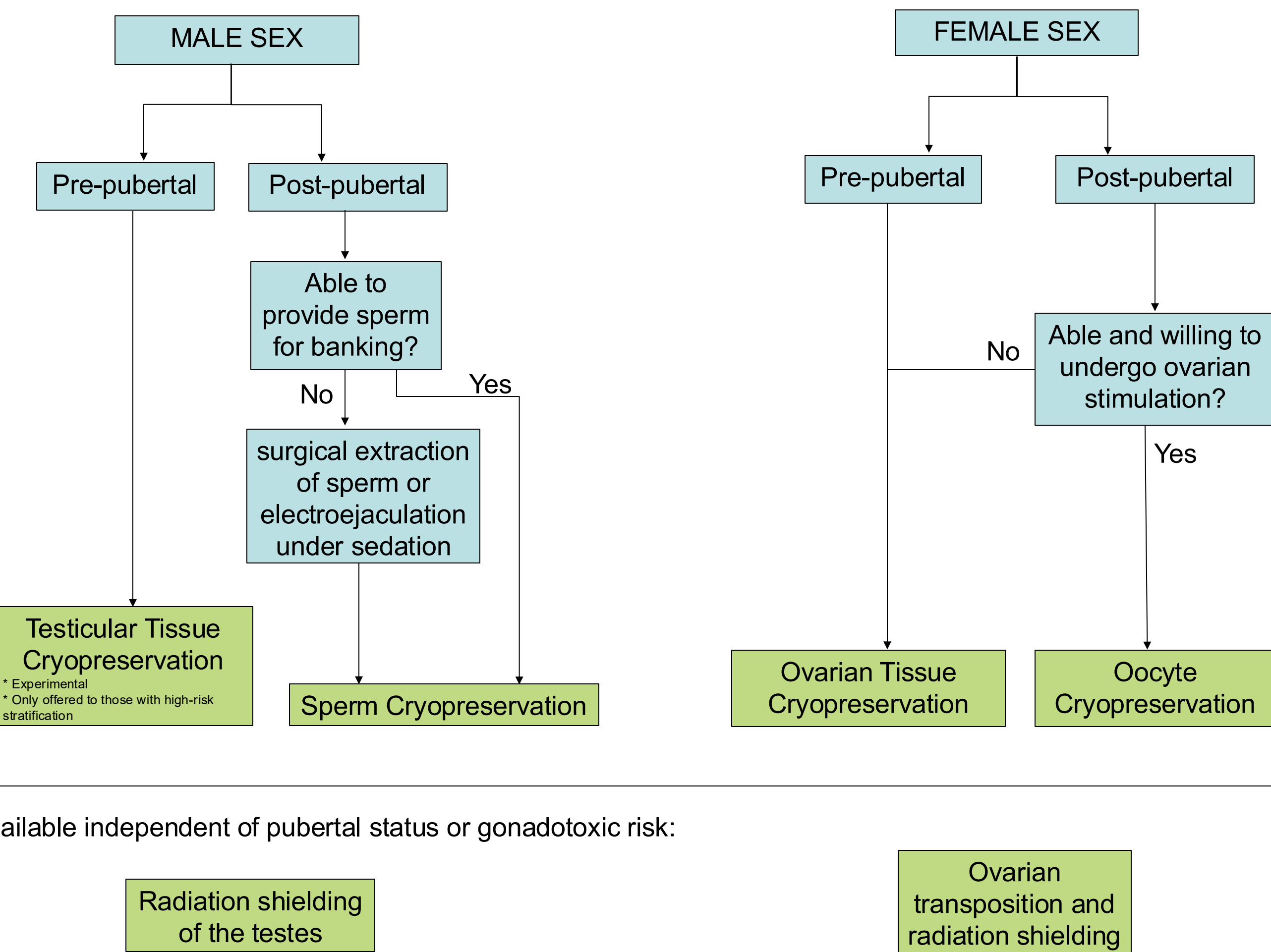
- Of 241 patients, 5.4% (n=13) had a change in risk stratification
- No patients had a reduction in risk assessment from the initial consultation
- As a result of a change to the risk assessment, 6 of these 13 patients qualify for FP protocols for which they previously did not meet the criteria

Table 1. Patients Affected By Change in Risk Stratification

	Female Sex (n=4)	Male Sex (n=9)
Prepubertal	50% (2/4)	55% (5/9)
Low-Significant Risk Change	50% (2/4)	0
Intermediate – High Risk Change	50% (2/4)	55.5% (5/9)
Low – High Risk Change	0	44.4 % (4/9)
Diagnoses	Neuroblastoma (1) T Cell Lymphoma (1) Rhabdosarcoma (1) Osteosarcoma (1)	Lymphoma (5) Neuroblastoma (1) Osteosarcoma (2) Relapsed ALL (1)
Fertility Preservation		
Completed Prior	0/4	2/9
Declined Prior	3/4	2/9
Not Eligible for FP prior*	1/4	5/9

*Patient was not eligible by prior criteria but by new criteria patient would have been eligible for experimental FP protocols

FP Options for Children with Cancer



Methods

- Inclusion criteria: patients within the CCHMC Comprehensive Fertility Care and Preservation Program registry from 2014-2020
- Exclusion criteria: if initial risk assessment was high, as their eligibility for FP would not have been impacted by new criteria or had treatment at an outside facility where total CED could not be determined
- The new risk algorithm was applied and compared to prior risk categorization for 241 patients
- Descriptive statistics were used to compare patients with a change in risk of gonadotoxicity based on the new criteria to patients who did not have a change in risk category
- The Wilcoxon Sum Rank test for continuous variables and Chi-Square or Fisher's Exact for categorical variables were used given small sample size affecting normal distribution. All tests employ a two-tailed, alpha = 0.05, unadjusted for multiple tests

Discussion

- In this study, very few patients experienced a change in risk stratification that impacted FP options
- Male sex patients and those with lymphoma were most affected
- Risk stratification for male sex patients using CED changed from three categories to two, resulting in more patients falling into the high risk category now that the intermediate risk category was eliminated
- The existing data suggests that an increased risk assessment would have heightened the likelihood of these patients pursuing FP options
- The next steps in evaluating the impact of these risk stratification changes involve assessing the psychosocial effects on patients and families, as well as examining how the revised information may have influenced decisions regarding FP