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PREDICTORS OF THERAPY-RELATED MYELODYSPLASIA AND ACUTE MYELOID LEUKEMIA (T-MDS/AML) AFTER AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANTATION (AHCT) FOR HEMATOLOGIC MALIGNANCIES

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Background: t-MDS/AML is the major cause of non-relapse mortality after aHCT for hematologic malignancies. Independent contributions by pre-aHCT therapeutic exposures and aHCT-related factors (stem cell mobilization, conditioning) to t-MDS/AML risk are unknown.

Methods: From 1986 to 2006, 2104 consecutive patients (median age: 49 yr) received aHCT for NHL (n = 1029), MM (n = 612), or HL (n = 463), at City of Hope (COH). Information regarding t-MDS/AML diagnosis was procured from medical records and California Cancer Registry to ensure complete capture. A retrospective cohort design described the cumulative incidence of t-MDS/AML. A nested case-control design evaluated the role of pre-aHCT therapeutic exposures and aHCT-related factors. Cases (t-MDS/AML post-aHCT) were matched to controls (no t-MDS/AML post-aHCT) for primary diagnosis, age at aHCT, year of aHCT, and race/ethnicity.

Results: By 2008, 97 patients had developed t-MDS/AML (cumulative incidence: 5.5% at 10 years [HL: 7.0%, NHL: 6.4%, MM: 2.4%]). Cohort study: multivariable analysis revealed the following to be associated with t-MDS/AML risk: diagnosis of HL (RR = 2.0, 95%CI, 1.2-3.5; ref grp: NHL), older age at aHCT (60+ yr: RR = 4.7, 95%CI, 2.1-10.1; ref grp: < 40 yr), use of PBSC (RR = 4.7, 95%CI, 1.9-11.5; ref group: BM/BM+PBSC), and exposure to TBI (RR = 1.7, 95%CI, 1.0-2.9). Case-control study: multivariable analysis revealed pre-aHCT alkylating agent (high dose: OR = 2.3, 95% CI, 1.2-4.3) and topoisomerase II inhibitor (high dose: OR = 2.1, 95% CI, 1.0-4.1), stem cell mobilization with etoposide (OR = 7.7, 95% CI,1.7-34.8) and conditioning with TBI (OR = 4.0, 95% CI, 2.0-8.2) to be associated with t-MDS/AML risk. Sub-analyses by cytogenetic abnormalities revealed pre-aHCT exposure to alkylating agents (OR = 2.7, 95%CI, 1.1-6.4) and TBI (OR = 4.1, 95%CI, 1.7-9.8) to be associated with increased risk of alkylating-agent associated t-MDS/AML (5/7); and mobilization with etoposide (OR = 14.2, 95%CI, 1.0-192) and TBI (OR = 9.9, 95%CI, 1.7-57) to be associated with topoisomerase inhibitor-associated t-MDS/AML (11q23/21q22). Of the 97 t-MDS/AML patients, 76 have died (median survival: 10 months from t-MDS/AML) by the end of 2009; overall survival was 22% at 5 years.

Conclusions: This large study with near-complete ascertainment of cases, demonstrates the role of pre-aHCT therapeutic exposures, use of etoposide for stem cell mobilization, and exposure to TBI to collectively and independently increase the risk of t-MDS/AML.

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TRANSPLANT PHYSICIAN PERCEPTIONS AND PRACTICE PATTERNS REGARDING FERTILITY PRESERVATION IN HEMATOPOIETIC-CELL TRANSPLANT (HCT) RECIPIENTS

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HCT recipients are at risk for impaired fertility. Physician perceptions and practices can be a barrier to informing patients about fertility preservation options. We conducted a survey of HCT physicians in the United States to evaluate knowledge of fertility preservation and to describe practice behaviors and barriers to discussing fertility preservation with HCT recipients of child-bearing age. Using CIBMTR email list, 1035 transplant physicians were invited by email to participate in a 29-item web survey. Of these, 185 participants completed the survey (response rate 18%). 69% and 31% of respondents were male and female, 68%, 22% and 10% took care of adult, pediatric and both adult and pediatric patients, and 55% and 45% had graduated from medical school before and after 1990, respectively. 64% of respondents had access to infertility specialist at their own center, 28% in another institution in the community and 8% had no access to infertility specialist. 83% respondents felt that patients were interested in learning about effects of HCT on fertility. 80% always or often felt comfortable discussing fertility preservation with their patients. 88% always or often discussed the impact of HCT on fertility and 51% always or often discussed fertility issues with patients even when prognosis was poor. However, 48% rarely or never provided their patients with educational materials about fertility preservation. 30% always or often consulted and 54% always or often referred their patients to an infertility specialist. 40% were unaware of ASCO fertility preservation guidelines for cancer patients and 29% rarely or never used these guidelines. Common barriers to discussing fertility preservation with patients were: patient being too ill to delay treatment (55%), insurance not covering fertility preservation (35%), patients inability to afford fertility preservation (33%) and time constraints (27%). On univariate analysis, access to infertility specialist was associated with consultation and referral practices for fertility (Table 1). Our study highlights the variation in transplant physician perceptions and practice behaviors regarding fertility preservation. Although relatively low response rate is a limitation of our study, HCT physicians in general are interested in discussing fertility issues with their patients but lack educational materials. Informational materials and guidelines on fertility preservation specifically targeted to HCT physicians are needed.

Table 1. Characteristics of respondents who consult or refer their patients to an infertility specialist

Physician Characteristics	Always/ Often	Sometimes	Rarely/ Never	P-value[#]
Consult infertility specialist with questions about fertility issues				
Gender				
Male, N (%)	36 (31)	37 (32)	43 (37)	0.45
Female, N (%)	13 (25)	22 (42)	18 (34)	
Practice type				
Adult, N (%)	30 (27)	40 (35)	43 (38)	0.59
Pediatric, N (%)*	18 (34)	18 (34)	17 (32)	
Access to specialist				
In same institution, N (%)	39 (36)	37 (35)	31 (29)	<.0001
In another institution, N (%)	10 (21)	21 (45)	16 (34)	
No access, N (%)	0	0	13 (100)	
Refer patients who have questions about fertility to an infertility specialist				
Gender				
Male, N (%)	64 (55)	31 (27)	21 (18)	0.89
Female, N (%)	28 (53)	16 (30)	9 (17)	
Practice type				
Adult, N (%)	60 (53)	30 (27)	23 (20)	0.53
Pediatric, N (%)*	30 (57)	16 (30)	7 (13)	
Access to specialist				
In same institution, N (%)	63 (59)	32 (30)	12 (11)	<.0001
In another institution, N (%)	29 (62)	12 (26)	6 (13)	
No access, N (%)	0	2 (15)	11 (85)	

*Includes physicians who take care of both adult and pediatric patients
[#]Chi-square or Fisher's test p-value, as appropriate

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SECONDARY MALIGNANCY AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT): 30 YEARS EXPERIENCE FROM A SINGLE CENTER

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