Myelodysplastic Syndromes in Adolescent Young Adults: One Institution's Experience

Joanna Grabska, Bijal Shah, Damon Reed, Najla Al Ali, Eric Padron, Hanadi Ramadan, Jeffrey Lancet, Alan List, Rami Komrokji

Abstract

Little is known regarding myelodysplastic syndromes (MDS) in the younger population. This retrospective review reviewed the characteristics, outcomes, and response to treatment in the adolescent and young adult (AYA) population compared to an older population. MDS was found to be rare and more aggressive in AYA. Karyotype was the most important prognostic factor. Allogeneic stem-cell transplantation offered younger patients the best outcomes.

Introduction: There has been little improvement in cancer survival of adolescent and young adult (AYA) patients, aged 18 to 39 years, possibly reflecting different disease biology. Myelodysplastic syndrome (MDS) is mainly a disease of the elderly. The characteristics, outcomes, and response to treatment are not well described in the AYA population. **Patients and Methods:** This was a retrospective review of patients from the Moffitt Cancer Center MDS database. We compared baseline characteristics and outcomes of the AYA population to older patients. We identified 51 AYA and 1897 older MDS patients. More female subjects and Hispanics were noted in AYA group. **Results:** The AYA patients had higher risk disease, more circulating myeloblasts, and more hypoplastic MDS. Autoimmune disorders were more prevalent in older patients. The median overall survival (OS) was 47 months in the AYA group versus 40 months in the older group ($P = .26$). The median OS was 47 versus 56 months in lower risk AYA group and older group, respectively ($P = .46$). In the higher risk group, median OS was 82 months in the AYA group compared to 17 months in the older group ($P = .001$). Thirty individuals (59%) underwent allogeneic stem-cell transplantation in the AYA group versus 241 (13%) in the older group. The median OS for transplanted patients was 55 months in the AYA group and 46 months in the older group ($P = .4$). In the nontransplanted patients, median survival was 31 months for the AYA group and 39 months for the older group ($P = .9$). The rate of acute myeloid leukemia transformation was 37% versus 28% in the AYA and older groups, respectively ($P = .17$). No differences in use or response to hypomethylating agents were observed. Lenalidomide therapy was seldom used in AYA, as none presented with del5q. In AYA, poor karyotype was the only variable strongly associated with worse outcome. Fifteen patients had poor risk karyotypes (29%). The median OS was 47 months, not reached, and 29 months among patients with good, intermediate, and poor risk cytogenetics, respectively ($P = .035$). **Conclusion:** MDS is rare and tends to be more aggressive in the AYA population. Karyotype was the most important prognostic factor. Allogeneic stem-cell transplantation offered younger patients the best outcomes.

Clinical Lymphoma, Myeloma & Leukemia, Vol. 16, No. S1, S53-6
Keywords: AYA, MDS, Myelodisplasia

Introduction

Approximately 70,000 adolescent and young adult (AYA) cancer patients, aged 15 to 39 years, are diagnosed annually in the United States. Overall, cancer survival of AYA has seen little improvement in the last decades. According to Bleyer et al and Surveillance, Epidemiology, and End Results data, the average annual improvement in 5-year survival rates for invasive cancers was 1.5% for all ages and only 0.5% in the entire AYA population between 1975 and 1997. Moreover, survival decreased by 0.18% in individuals aged 30 to 34 years.[1] In more recent years, research has demonstrated that these patients are at a disadvantage compared to their older counterparts in clinical and supportive care.[2-5] Clearly we need a better understanding of this group's unique characteristics and outcomes. Many reasons have been postulated for why the AYA group may be at a detriment. These include attitudes and beliefs

Moffitt Cancer Center, Tampa, FL

Submitted: Feb 9, 2016; Accepted: Feb 9, 2016

Address for correspondence: Joanna Grabska, MD, Moffitt Cancer Center, 12902 USF Magnolia Drive, Tampa, FL 33612
E-mail contact: Joanna.grabska@moffitt.org

2152-2650/$ - see frontmatter
http://dx.doi.org/10.1016/j.clml.2016.02.022

that shape behavior, as well as daily stressors that may comprise body image concerns, independence from parents, sexual relationships, and personal/career and educational goals.[2] In addition, finances play a unique role in this group: AYA are often too old to be on their parents' insurance and too young to afford their own, affecting access to care.

Myelodysplastic syndromes (MDS) are predominantly diseases of the elderly, and the characteristics, outcomes, and response to treatment are not well described in the AYA population. The purpose of this retrospective review of the Moffitt Cancer Center database was to compare the baseline characteristics and outcomes of the AYA population compared to older patients. We hoped to elucidate some information that will help us provide better care for this population.

Materials and Methods

This retrospective study used data from a single institution, Moffitt Cancer Center, database. The MDS database collects demographic information such as sex, race, and age. It also contains clinical information including diagnostic findings (type of MDS, dates and results of procedures/laboratory tests used for diagnosis and surveillance, staging, extent of disease), therapy history, and follow-up surveillance including additional treatment and patient status.

Descriptive statistics were reported as frequencies and percentages for categorical variables. The chi-square test was used to compare categorical variables and the *t* test for continuous variables. Kaplan-Meier estimates were used for overall survival (OS) and log rank tests for comparison.

Results

The demographic characteristics and outcomes of the study populations (AYA, n = 51; older patients, n = 1897) are reported in Table 1. Of the 51 AYA patients, 25 (49%) were women, whereas in the older group, 34.5% were women. Thirteen (26%) of the AYA patients were Hispanic. The older population was mostly white (n = 1736, 91.5%) ($P < .001$). The rate of therapy-related MDS was similar: for the AYA population it was 19.6%, and for the older population it was 18.9%. No statistical difference was observed by World Health Organization subtype between the 2 groups. However, the AYA group was found to have higher risk disease by the International Prognostic Scoring System (IPSS; 40.4% vs. 31.8%, $P = .011$). No statistical difference was observed when the groups were analyzed by revised IPSS risk. Hypocellular bone marrow was observed in 23.4% of the AYA patients compared to 9.8% in the older group ($P = .009$). None of the patients in the AYA group was found to have an LGL (large granular lymphocytic) clone. The older group harbored the LGL clone in 159 individuals, comprising 8.4% of the population ($P = .033$). Autoimmune diseases were more common in the older population (AYA, n = 8, 15.7%; older patients, n = 500, 26.4%). Approximately 31% of the AYA population was in the poor risk cytogenetic group compared to 23.4% in the older group. No difference was noted in the percentage of patients requiring transfusions between the groups.

The AYA patients had higher risk disease, more circulating myeloblasts, and more hypoplastic MDS. The median OS was 47 months in the AYA group versus 40 months in the older group ($P = .26$). The median OS was 47 months versus 56 months in the lower risk AYA group and older group, respectively ($P = .46$). In the higher risk group, median OS was 82 months in the AYA group compared to 17 months in the older group ($P = .001$). Thirty individuals (59%) underwent allogeneic stem-cell transplantation in the AYA group versus 241 (13%) in the older group. The median OS for transplanted patients was 55 months in the AYA group and 46 months in the older group ($P = .4$). In the nontransplanted patients, median survival was 31 months for the AYA group and 39 months for the older group

Table 1 Characteristics of AYA and Older Patients

Characteristic	AYA (Age 18-39 Years) (n = 51)	Older Patients (Age ≥ 40 Years) (n = 1897)	*P*
Female	25 (49%)	655 (34.5%)	.025
Race			
White	34 (66.7%)	1736 (91.5%)	<.001
Black	2 (3.9%)	47 (2.5%)	
Hispanic	13 (25.5%)	57 (3%)	
Other	2 (3.9%)	41 (2.2%)	
Therapy-related MDS	10 (19.6%)	359 (18.9%)	.902
WHO Subtype			.188
RA	3 (5.9%)	196 (10.4%)	
RARS	1 (2%)	151 (8%)	
RCMD	22 (43.1%)	583 (30.8%)	
Deletion 5q	0 (0%)	51 (2.7%)	
RAEB-1	11 (21.6%)	372 (19.7%)	
RAEB-2	10 (19.6%)	336 (17.7%)	
CMML	0 (0%)	60 (3.2%)	
MDS unclassified	1 (2%)	44 (2.3%)	
MDS/MPN	2 (3.9%)	94 (5%)	
IPSS			.011
Lower risk	28 (59.6%)	1264 (68.2%)	
Higher risk	19 (40.4%)	590 (31.8%)	
IPSS-R			.097
Very low/low	13 (30.1%)	826 (45.3%)	
Intermediate	14 (32.6%)	394 (21.6%)	
High/very high	16 (37.3%)	602 (33%)	
Hypocellular bone marrow	11 (23.4%)	178 (9.8%)	.009
LGL clone	0 (0%)	159 (8.4%)	.033
Autoimmune disease	8 (15.7%)	500 (26.4%)	.055
Karyotype by IPSS			.324
Good risk	24 (50%)	1120 (60.4%)	
Intermediate risk	9 (18.8%)	300 (16.2%)	
Poor risk	15 (31.3%)	434 (23.4%)	
Peripheral blasts	14 (29.8%)	246 (13.2%)	.003
RBC transfusion	36 (70.6%)	1274 (67.3%)	.372

Abbreviations: AYA = adolescent and young adult; IPSS = International Prognostic Scoring System; IPSS-R = revised IPSS; LGL = large granular lymphocytic; MDS = myelodysplastic syndromes; MPN = myeloproliferative neoplasm; RBC = red blood cell; WHO = World Health Organization.