Predictive Value Of Autograft Absolute Monocyte Count In Patients Underwent Autologous Stem Cell Transplantation

Asmaa Fawzey[1], Elbaiomy MA[2], Shimaa R. Hendawy[3], Reham AL-Ghandour[1], Elkhodary TR[1]

[1]*Medical oncology Unit, Oncology Center Mansoura University, Faculty of Medicine, Mansoura University, Mansoura, Egypt*
[2]*Consultant Medical Oncology, king Salaman Bin Abdelaziz Medical City, Medinah, KSA. Professor of Medical Oncology, Mansoura University, Egypt*
[3]*Clinical pathology department, Faculty of Medicine, Mansoura University, Egypt*
**Corresponding author: Asmaa Fawzey, E-mail: asmaafawzey@mans.edu.eg*

KEYWORDS
Autologous Stem Cell Transplantation, Autograft Absolute Monocyte Count, platelet engraftment, hospital stay, disease-free survival, progression-free survival.

ABSTRACT
Background: Autologous stem cell transplantation (ASCT), following intensive chemotherapy, is a common treatment for patients with hematologic cancers such as lymphoma and multiple myeloma. The Autograft Absolute Lymphocyte Count (A-ALC) has been recognized as an important prognostic marker for survival in patients undergoing ASCT. In this article, we studied the predictive value of Absolute Monocyte count (A-AMC) in engraftment kinetics and survival in patients who underwent ASCT. **Methods:** This is a prospective study applied to adult patients who underwent ASCT at the Oncology Centre, Mansoura University, Egypt within 2 years from June 2021 to June 2023. A-AMC was calculated and prognostic factors that may influence the course of the disease were chosen. **Results:** There were 49 patients, 21 patients (42.9%) were male and 28 patients (57.1%) were female with a median age of 42 (19-64). 20 patients (40.8%), 16 patients (32.7%) and 13 patients (26.5%) were diagnosed with multiple myeloma, Hodgkin lymphoma and Non- Hodgkin lymphoma respectively. Patients underwent ASCT after the first complete response or the second complete response according to the type of disease. The median cut-off value of A-AMC was 60.7. High A-AMC was associated with rapid platelet engraftment with a mean of 12.25 days vs. 15.25 days with low A-AMC which is statistically significant (P-value 0.029). Also, high A-AMC was associated with shorter hospital stay duration with a mean of 14.96 days vs. 18 days with low A-AMC which is also statistically significant (P-value 0.033). On the other hand, 2 years disease-free survival (DFS) was about 82% with low A-AMC vs. 58% with high A-AMC in lymphoma that was borderline statistically significant (P-value 0.05). 2 years progression-free survival (PFS) was 100% with low A-AMC vs. 80% with high A-AMC in MM that was not statistically significant (P -value 0.18) as shown in Figure 1 and Figure 2. **Conclusion:** A-AMC was identified as a useful prognostic factor for platelet engraftment, hospital stay duration, DFS and PFS in patients who underwent ASCT.

Introduction

Autologous stem cell transplantation (ASCT) plays an important role in the treatment of patients with hematological malignancies such as lymphoma and multiple myeloma (MM) both in the upfront and relapsed/refractory settings. ASCT involves the collection and subsequent reinfusion of a patient's own hematopoietic stem cells following high-dose chemotherapy (Nagayama et al., 2020). Despite the overall success of ASCT, treatment outcomes vary significantly, with some patients achieving long-term remission while others face disease relapse or experience complications related to the treatment (Oliver-Caldes et al., 2022). One hypothesis for the high relapse rate observed in ASCT is the presumptive lack of graft-versus-tumor (GVT) effect present in allogeneic stem cell transplantation (Allo-SCT), where it is associated with a significant

therapeutic impact on clinical outcomes (Baron et al., 2005). Currently, various prognostic factors, including disease stage, cytogenetic abnormalities, and performance status, are utilized to inform treatment decisions in ASCT (Thurlapati et al., 2023). However, there is a need for additional reliable and easily measurable markers to refine risk stratification and personalize therapeutic strategies. In addition to patient and disease-related factors, the composition of the infused cell product such as dendritic cell content, lymphocyte to monocyte ratio and immune reconstitution following ASCT have recently been identified as independent predictors of survival in Non-Hodgkin lymphoma (NHL) (Herr et al., 2020). Monocytes, a vital part of the innate immune system, are essential for immune surveillance, inflammation, and tissue repair. Research has indicated that monocytes and their subsets may affect the tumor microenvironment and influence treatment responses in cancer patients (Austermann et al., 2022). The autograft absolute lymphocyte count (A-ALC) has been identified as a prognostic factor for survival in patients undergoing ASCT (Porrata et al., 2021). In this article, we studied the predictive value of Absolute Monocyte count (A-AMC) in engraftment kinetics and survival in patients who underwent ASCT.

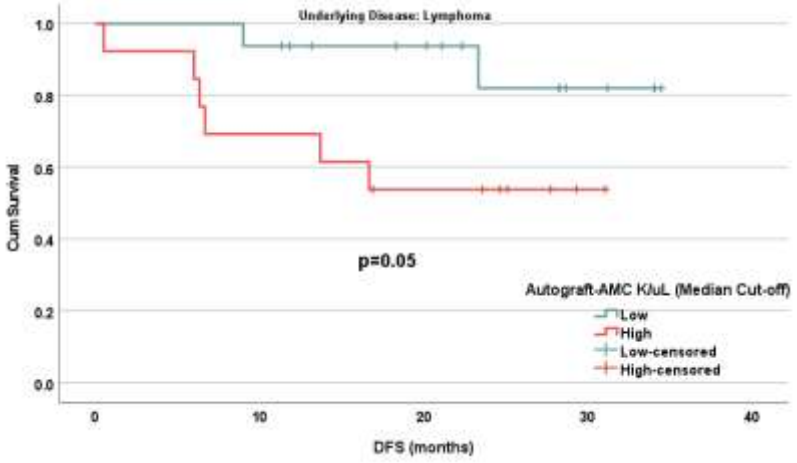

Figure 1. Impact of A-AMC on DFS in lymphoma after ASCT

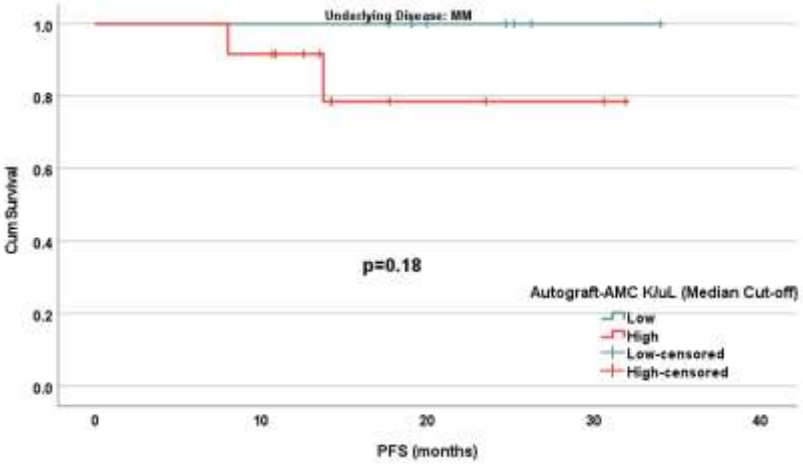

Figure 2: Impact of A-AMC on PFS in MM after ASCT

PATIENTS AND METHODS

This is a prospective study applied to adult patients who underwent ASCT at the Oncology Centre, Mansoura University, Egypt within 2 years from June 2021 to June 2023. Inclusion criteria involved patients aged ≥ 16

years with hematological malignancies with Eastern Cooperative Oncology Group performance status (ECOG) < 2 and the source of stem cells is peripheral blood stem cells (PBSCs). Exclusion criteria involve Patients above 70 years of age with other sources of stem cell rather than PBSCs. Demographic data, including age, sex, and comorbidities and Disease characteristics, including diagnosis and disease stage were collected. The absolute monocyte count in the autograft sample was measured and post-transplant outcomes, including engraftment kinetics, duration of hospital stay, progression-free survival (PFS) and disease-free survival (DFS) were assessed. Statistical analysis employs SPSS using various tests such as Chi-square, t-tests and correlation analysis. The association between A-AMC and clinical outcomes was evaluated using Kaplan-Meier analysis and log-rank tests.

RESULTS

This study included 49 patients, 21 patients (42.9%) were male and 28 patients (57.1%) were female with a median age of 42 (19-64). Patients' characteristics are shown in Table 1.

Table 1. Patients' characteristics:

		N	%
Sex	Male	21	42.9%
	Female	28	57.1%
Hypertension	Absent	45	91.8%
	Present	4	8.2%
DM	Absent	45	91.8%
	Present	4	8.2%
HCV	Absent	39	79.6%
	Present	10	20.4%

20 patients (40.8%), 16 patients (32.7%) and 13 patients (26.5%) were diagnosed with MM, Hodgkin lymphoma (HL) and NHL respectively. Disease characteristics and impact of disease type in engraftment kinetics, duration of hospital stay and duration of Intravenous (IV) antibiotic treatment are shown in Table 2 and Table 3.

Table 2. Disease's characteristics.

		N	%
Underlying Disease	HL	16	32.7%
	NHL	13	26.5%
	MM	20	40.8%
BM Involvement (Lymphoma)	Absent	25	86.2%
	Present	4	13.8%
Staging (Lymphoma) (Ann Arbor staging)	I	3	10.3%
	IB	1	3.4%
	II	6	20.7%
	III	10	34.5%
	IV	9	31.0%
Staging (Myeloma) (ISS)	I	6	30.0%
	II	1	5.0%
	III	13	65.0%

Table 3: Impact of disease type in engraftment kinetics, duration of hospital stay and duration of Intravenous (IV) antibiotic treatment.

	Underlying Disease	Mean	SD
Neutrophil Engraftment (Days)	HL	10.56	0.964
	NHL	11.42	2.644
	MM	10.10	0.308
Hemoglobin Recovery	HL	3.38	3.202
	NHL	3.31	6.019
	MM	0.80	1.473
Platelet Engraftment (Days)	HL	13.63	1.408
	NHL	16.25	8.986
	MM	12.35	1.725
Antibiotic Treatment Duration (Days)	HL	9.88	1.708
	NHL	10.69	2.496
	MM	7.75	3.279
Hospital Stay (days)	HL	16.19	1.642
	NHL	19.08	9.041
	MM	14.95	1.791

Patients underwent ASCT after the first complete response or the second complete response according to the type of disease.

The median cut-off value of A-AMC was 60.7. High A-AMC was associated with rapid platelet engraftment with a mean of 12.25 days vs. 15.25 days with low A-AMC which is statistically significant (P-value 0.029). Also, high A-AMC was associated with shorter hospital stay duration with a mean of 14.96 days vs. 18 days with low A-AMC which is also statistically significant (P-value 0.033) as shown in Table 4.

Table 4: Impact of A-AMC value on engraftment kinetics, duration of hospital stay and duration of Intravenous (IV) antibiotic treatment.

	Autograft-AMC K/uL (Median Cut-off)	Mean	SD	p-value
Neutrophil Engraftment (Days)	**Low**	10.71	1.853	0.569
	High	10.46	1.062	
Hemoglobin Recovery	**Low**	2.88	5.059	0.314
	High	1.76	2.067	
Platelet Engraftment (Days)	**Low**	15.25	6.319	0.029
	High	12.25	1.648	
Antibiotic Treatment Duration (Days)	**Low**	9.55	1.820	0.932
	High	9.48	3.400	
Hospital Stay (days)	**Low**	18.00	6.769	0.033
	High	14.96	1.457	

Table 5 and Table 6 show the impact of A-AMC on post-transplant complications such as engraftment syndrome (ES) or severe toxicities such as GII-GIV cardiac toxicity, GIII-GIV diarrhea and mucositis.

Table 5: Impact of A-AMC in engraftment syndrome.

		ES				P-value
		Absent		Present		0.136
		N	%	N	%	
Autograft-AMC K/uL (Median Cut-off)	Low	17	43.6%	7	70.0%	

	High	22	56.4%	3	30.0%	

Table 6: Impact of A-AMC in severe toxicities.

		Severe Toxicity				P-value
		Absent		Present		0.682
		N	%	N	%	
Autograft-AMC K/uL (Median Cut-off)	Low	7	53.8%	17	47.2%	
	High	6	46.2%	19	52.8%	

Moreover, we studied the effect of A-AMC on survival; 2 years disease-free survival (DFS) was about 82% with low A-AMC vs. 58% with high A-AMC in lymphoma that was borderline statistically significant (P-value 0.05). 2 years progression-free survival (PFS) was 100% with low A-AMC vs. 80% with high A-AMC in MM that was not statistically significant (P -value 0.18) as shown in Figure 1 and Figure 2.

DISCUSSION

ASCT plays a critical role in the treatment of hematological malignancies such as lymphoma and multiple myeloma, as well as in non-malignant disorders like autoimmune diseases (Henes et al., 2021). In recent years, the number of ASCT procedures has increased in Egypt, with lymphoma and multiple myeloma being the most frequently treated malignancies in both Egypt and the broader Middle East (Mahmoud et al., 2020). We studied patients who underwent ASCT from June 2021 to June 2023. There was a decrease in the flow rate of patients due to the prevalence of COVID-19 infection and subsequent complications, especially in the early time of the study.

Our study included 49 patients, 28 patients were female and 21 patients were male with a median age of 42 years (range, 19-64 years). HCV infection was present in 10 % of patients, which is close to the prevalence of HCV infection in Egypt (Elgharably et al., 2017). The median duration of neutrophil and platelet engraftment were 10 and 13 days respectively which is the same results from (Ergene et al., 2007). Our study identified the associations between high A-AMC and rapid platelet engraftment and short hospital stay duration after ASCT. On the other hand, we observed that there was no significant relationship between A-ALC and engraftment of neutrophils and platelets that is compatible with the results from (Yoon et al., 2009). A-ALC has been reported to be a prognostic factor for survival after ASCT in multiple studies (Hiwase et al., 2008; Porrata et al., 2021). These results suggest that host immunity affects the clinical outcomes of patients treated with ASCT.

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