Ref: Ro Med J. 2024;71(3)
DOI: 10.37897/RMJ.2024.3.6

6-month survival of patients with acute myeloid leukemia who received modified chemotherapy at Wahidin Sudirohusodo Hospital

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ABSTRACT

Background and aim. Standard chemotherapy for AML is daunorubicin combined with cytarabine. However, the combination chemotherapy also has side effects that are quite dangerous for AML patients. The purpose of this study is to assess the survival rates of AML patients treated at Wahidin Sudirohusodo Hospital in Makassar using modified chemotherapy regimens.

Methods and material. This study was conducted at Wahidin Sudirohusodo Hospital in Makassar using a prospective cohort design. The study population included AML patients aged 18 years or older who had undergone modified chemotherapy for six months. Data on life expectancy, chemotherapy modifications, age, gender, and AML subtype were collected. Data were analyzed using SPSS version 22.0. Survival analysis was performed using the Kaplan-Meier curve, log-rank, and statistic test.

Results. The cohort consisted of 25 males (51%) and 24 females (49%) with a mean age of 42 years. The 6-month survival rates were 68% for females and 50% for males. Age-based survival rates were 61.3% for patients <45 years, and 55.6 for those >45 years. Survival rates by AML subtype were 40% for M1, 63.3% for M2, 0% for M3, 60% for M4, and 66.7% for M5. The survival curve for the therapy regimen showed a significant relationship (p <0.05), with 86.7% survival for daunorubicin and 47.1% for cytarabine.

Conclusions. Administration of daunorubicin and cytarabine chemotherapy is a variable that significantly determines the 6-month survival of AML patients.

Keywords: acute myeloid leukemia, survival, chemotherapy, prognosis

INTRODUCTION

Acute myeloid leukemia (AML) is a disease characterized by neoplastic transformation and impaired differentiation of progenitor cells of myeloid cells that can infiltrate the bone marrow, blood, and other tissues by abnormally proliferating, cloning, differentiating progenitor cells of the hematopoietic system [1,2]. Abnormal proliferation, differentiation inhibition, and leukemia cell growth that impedes the initial stages of hematopoiesis are the hallmarks of acute leukemia. Hematopoietic precursor cells derived from non-lymphoid cell derivatives can develop acute myeloid leukemia, a malignant hematologic illness [3].

AML patients are usually associated with an unfavorable prognosis, with 2 and 5-year survival rates of 32% and 24%, respectively. The five-year survival for patients without chemotherapy without SCT (Stem Cell Transplantation) is 12%, the survival for the group treated with chemotherapy alone is 37.8% and for those receiving chemotherapy and SCT is 44.1%. Older AML patients were more likely to have relatively poor overall survival (OS), and the majority of

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Article History:
Received: 25 June 2024
Accepted: 26 September 2024

elderly patients (more than 70%) died within 1 year of AML diagnosis [4].

Standard chemotherapy as the first line of treatment for AML is induction therapy with daunorubicin or idarubicin combined with cytosine arabinoside (cytarabine, Ara-C). After induction therapy, patients are often given consolidation therapy, generally by administering high-dose cytarabine or allogeneic hematopoietic stem cell transplantation depending on cytogenetic and molecular classification [5]. However, the combination chemotherapy also has side effects that are quite dangerous for AML patients. Daunorubicin and cytarabine are very strong myelosuppressive agents. It has been reported that AML patients have a high risk of febrile neutropenia and pneumonia after undergoing daunorubicin and cytarabine induction chemotherapy [6,7]. Patients receiving these drugs should be under close medical supervision and, during induction therapy, should have their leukocyte and platelet counts checked daily.

Studies and findings related to the survival of AML patients given only one type of chemotherapy are very limited. This study aims to investigate AML survival including age, gender, AML subtype, and administration of modified chemotherapy to patients at Dr. Wahidin Sudirohusodo Hospital, Makassar.

MATERIAL AND METHODS

This study is an observational study with a prospective cohort approach. The research was conducted at Wahidin Sudirohusodo Hospital Makassar from November 2023 to March 2024. The population of this study was AML patients who were diagnosed and performed modified chemotherapy for 6 months. Inclusion criteria included patients with AML who were diagnosed based on BMP results and had undergone chemotherapy, age >18 years, complete medical record data, and were willing to sign informed consent. Exclusion criteria included patients who could not be contacted by telephone, patients who died not due to the diagnosis of LMA or its complications, and incomplete data. Sampling was conducted in a nonrandom manner.

Data extracted were survival rate, chemotherapy modification, age, gender, and AML subtype. Survival rate is an estimate of the average additional lifespan a person is expected to live from the time of diagnosis until 6 months later. Chemotherapy modification is the administration of one type of chemotherapy based on patient needs, categorized into Cytarabine and Daunorubicin. Age is the length of time lived since birth, categorized into <45 years, and >45 years. Gender is defined as a biological difference based on identification card information matched with physical examination. AML subtypes were classified by FAB (French-American-British) classification based on the presence of dysmyelopoiesis and the quantification of myeloblasts and erythroblasts, categorized into M1, M2, M3, M4, M5, M6 and M7.

Sampling was conducted sequentially throughout the study period until the desired sample size was reached. Furthermore, data were analyzed with SPSS version 22.0 and survival analysis, Kapplan-Meier curve, median survival, log-rank, and test statistics. The results obtained will be displayed in the form of a narrative supplemented by tables and figures.

The Ethics Committee for Biomedical Research on Humans at Hasanuddin University's Faculty of Medicine in Makassar, South Sulawesi, Indonesia, gave its approval for this study. based on the letter of recommendation Number: 914/UN.4.6.4.5.31/PP36/2023, November 29th, 2023, regarding length of the study's authorization from November 29th, 2023 to November 29th, 2024, with protocol number: UH23110844.

RESULT

Study population

Of the 49 samples, 25 (51%) had male patients and 24 (49%) had female patients. The average age of the samples was 42 years. Based on the therapy regimen, daunorubicin was found in 15 (30.6%) patients and cytarabine in 34 patients (69.4%). Survival >6 months was found in 29 (59.2%) patients and <6 months in 20 (40.8%) patients. The subtypes of AML were M2, M4, M1, M5 (30 (61.2%), 10 (20.4%), 5 (10.2%), 3 (6.1%), 1 (2%), respectively.

In the analysis of 6-month survival in AML patients, based on gender, the most experienced events

TABLE 1. Characteristics of the study population (n:49)

Variable			Frequency	
			n	%
Sex		Female	25	51
		Male	24	49
Age	years	<45	31	63.3
	years	>45	18	36.7
Mean age		42 + 14	Max-Min (18-78)	
Chemotherapy		Daunorubicin	15	30.6
		Cytarabine	34	69.4
Survival	months	< 6	20	40.8
	months	>6	29	59.2
AML subtypes		M1	5	10.2
		M2	30	61.2
		M3	1	2
		M4	10	20.4
		M5	3	6.1

n=number of samples

were male gender, namely 50% (12/24) patients compared to female gender 32% (8/25) patients, based on the therapy regimen that experienced the most events found in patients who received cytarabine, namely 52.9% (18/34) patients compared to those who received daunorubicin 13.3% (2/15) patients.

The 6-month patient survival of AML patients based on gender was 60% female (17/25) and 50% male (12/24). Based on the age group of AML patients <45 years old 60% (18/30), 45-60 years old 57.1% (8/14) and >60 years old 60% (3/5). Based on AML subtype, the survival rate of AML patients was M1 40% (2/5), M2 63.3% (19/30), M3 0% (0/1), M4 60% (6/10) and M5 66.7 (2/3). The survival curves of AML patients based on gender, age and AML subtype intersect each other with a p-value (log rank) >0.05, which means that there is no significant association between gender, age and AML subtype with the survival of AML patients.

The 6-month survival of AML patients based on therapy The 6-month survival of patients who received daunorubicin therapy was 86.7% (13/15) compared to those who received cytarabine therapy 47.1% (16/34). The 6-month survival curves of AML patients did not intersect with a p-value (log-rank) <0.05, which means that there is a significant relationship between the therapy regimen and the survival of AML patients.

TABLE 2. 6-month survival of patients with acute myeloid leukemia who received modified chemotherapy based on study variables and survival status

Variable		<6 months		>6 months		Total N		p (log rank)
		n	%	n	%	n	%	
Sex	Female	8	32	17	68	25	51	0.168
	Male	12	50	12	50	24	49	
Chemotherapy	Daunorubicin	2	13.3	13	86.7	15	30.6	**0.01**
	Cytarabine	18	52.9	16	47.1	34	69.4	
Age	<45	12	38.7	19	61.3	31	63.3	0.749
	>45	8	44.4	10	55.6	18	36.7	
AML subtypes	M1	3	60	2	40	5	10.2	0.312
	M2	11	36.7	19	63.3	30	61.2	
	M3	1	100	0	0	1	2.0	
	M4	4	40	6	60	10	20.4	
	M5	1	33.3	2	66.7	3	6.1	

Pearson's Correlation test

DISCUSSION

Table 1 illustrates the characteristics of this study where out of 49 study samples, male gender 25 (51%) patients and female 24 (49%) patients, the average

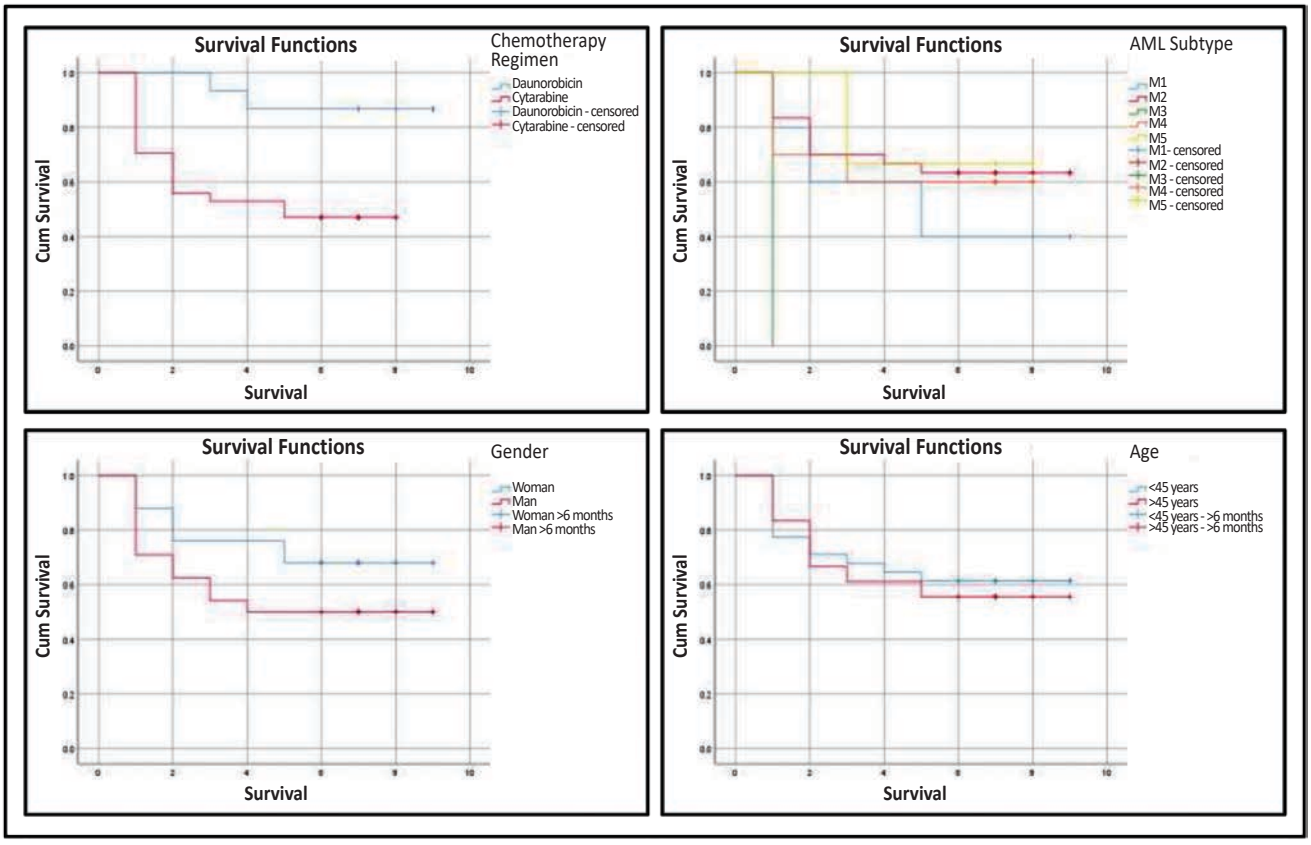

FIGURE 1. 6-month survival of AML patients by sex, age, therapy regimen and AML Subtype with Kaplan Meier Method

age of patients was 42.2 +14 years. Based on the therapy regimen, daunorubicin was found in 15 (30.6%) patients and cytarabine in 34 patients (69.4%). AML subtypes were found to be M2, M4, M1, M5 (30 (61.2%), 10 (20.4%), 5 (10.2%), 3 (6.1%), 1 (2%), respectively. This study is in line with the demographic study conducted by Sultan et al., AML is found more in men than women (60.8%: 32.2%) with an average age of 37.97 ± 20.8 Comparing this conclusion to the findings of the study conducted by Harani et al., which indicated that M2 (30.25%), M3 (10.4%), M1 (8.7%), M0 (7.7%), M5a (3.5%), M5b (2.5%), and M6 (0.8%) were the most prevalent subtypes of AML, AML-M4 being the least common subtype (36.2%) [9].

This study showed that the 6-month survival rate of AML patients was 59.2%. The 6-month survival rate in this study is still lower than the results found by Albuquerque et al. who found the 6-month survival rate of AML patients in Brazil which was 74.9% [10]. While Oran et al. suggested that patients who were treated had a 6-month survival rate compared to patients who were not treated which only reached 2 months [11].

Acute myeloid leukemia (AML) is an aggressive clonal malignancy in which there is a cessation of maturation of granulopoiesis resulting in an increased number of immature myeloblasts in the bone marrow. The disease progresses rapidly and is fatal within weeks or months if left untreated. The survival of AML patients is multifactorial, including age, performance status, and WBC count '[12].

In this study, there was no significant association between AML patient survival and age, gender, and AML subtype. These findings are consistent with a study of 16 AML patients done by Dolatkhah et al. The patient survival rate at six months was 81.3%. The subtype analysis revealed no statistically significant variation in survival rates across the various AML subtypes (P Log-rank = 0.067). Male patients' OS was lower than female patients' (77.8% vs. 85.7%), although the difference was not statistically significant (P Log-rank = 0.640) [13].

This study showed that there was an association between the therapy regimen and 6-month survival of AML patients. Based on the analysis, the p-value (log-rank) <0.05 with curves that do not intersect each other (Figure 1). The survival of patients who received daunorubicin therapy was 86.7% while that of patients who received cytarabine was 47.1%.

The most widely used AML induction chemotherapy regimens are cytarabine and daunorubicin. The effectiveness of AML therapy has been proven in many studies. Research in the last decade tends to look at the efficacy of these therapies at different doses where almost all studies provide consistent results. In patients under 60 years of age, Lee et al. (2016) showed the efficacy of raising the dose of daunorubicin to 90 mg/m^2/day as opposed to 45 mg/m^2/day. The study found that the overall survival rate was 23.7 months as opposed to 15.7 months (p = 0.005), and the overall remission rate was 70.6% as opposed to 57.33% (p <0.001).14 In a different study, patient survival (46.8% vs. 34.6%) was considerably higher in AML, which got 90 mg/m2/day daunorubicin [14].

CONCLUSION

In conclusion, administration of daunorubicin and cytarabine chemotherapy is a variable that significantly determines the 6-month survival of AML patients. Further research is expected to be carried out with a larger sample size and longer research time.

Ethics Committee approval

This research was approved by the Ethics Committee for Biomedical Research on Humans, Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia. Based on recommendation letter Number: 914/UN4.6.4.5.31/PP36/2023, November 29th, 2023, and duration of the study approval from November 29th, 2023 to November 29th, 2024, protocol number: UH23110844.

Authors' contributions:

EDR (idea, planning, availability, materials, gathering and processing of data, interpretation and analysis, literature search, and writing of manuscripts). TH (idea, design, supervision, evaluation and interpretation, and literature search). DB (idea, design, supervision, evaluation and interpretation, and literature search). SB (concept, design, critical review). NM (concept, design, critical review). AAZ (Concept, Design, Analysis and Interpretation, Critical Review).

All authors were involved in drafting the manuscript, revising it, and evaluating its content. They have all read and approved the manuscript, confirming the accuracy and integrity of the research details.

Acknowledgments:

This research was supported by the Department of Internal Medicine, Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia.

Conflict of interest:

Every author certifies that they have no financial relationships (such as stock ownership, equity holdings, consulting, patent/licensing arrangements, etc.) that could create a conflict of interest concerning the submitted work.

Financial support: none

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