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THE BURDEN OF TREATMENT IN THE LAST SIX MONTHS OF ELDERLY AML-PATIENTS LIVES

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ABSTRACT

Background: Elderly patients with acute myeloid leukemia (AML) have a poor prognosis despite treatment. Intensive chemotherapy is potentially curable; however, hospital admissions and requirements of transfusions are often a byproduct of toxicity of this treatment. As an alternative, non-intensive therapy is known to be less toxic, resulting in fewer complications, though it rarely induces remission of the malignancy, making choice of treatment a therapeutic dilemma. Furthermore, only a few studies have investigated the palliative care of elderly AML-patients. This study examined the burden of hospitalizations, outpatient visits and number of transfusions in the last 180 days of elderly AML patients' lives according to their first line treatment.

Methods: Patients diagnosed with AML in the period 1/1-2010 to 30/6-2020, treated at Aalborg University Hospital, were recruited. All patients have died in the given period. Data with information regarding hospital admissions, transfusions and out-patient visits were obtained by the business intelligence unit (BI-unit). Using a REDcap-survey build for this study, patients were divided into treatment groups; intensive treatment, non-intensive treatment, and palliative treatments. Number of hospital admissions, transfusions and outpatient visits in the last 180 days of the patients' lives were manually categorized. No statistical analyses were made due to poor data registration.

Results: 107 patients were included in this study. Patients receiving intensive treatment had a median of 30 admission days and four outpatients visits. The median number of admission days for patients receiving low dose cytarabine (L-DAC) and azacitidine was 21 and 18, respectively. The L-DAC arm had a median of 8 outpatient visits, while the azacitidine arm had 16 outpatient visits.

Conclusion: Despite a numeric difference in hospital admissions and outpatient visits, this study was not able to draw any conclusions, as a result of poor data quality. Further investigation on the subject is needed.

INTRODUCTION

Acute myeloid leukemia (AML) is a heterogeneous hematologic malignancy due to clonal expansion of myeloid blast cells in the bone marrow and peripheral blood.[1] Though, AML is the most common form of acute leukemia among adults, it primarily affects the elderly with a median age of 73 years in Denmark.[2] Untreated, AML causes death within a few months. Despite treatment, the overall survival (OS) remains poor, with a two-year OS of 31%.[3] For the younger population, survival has improved in the past decades, yet for the elderly patients with AML, survival lingers.[4–6] Especially choice of therapy for this group remains an obstacle, as severe side effects and poor response related to treatment versus expected lifetime must be taken into consideration.

PATHOPHYSIOLOGY

AML may originate from a pre-existing hematological illness, secondary AML(s-AML), or due to prior treatment with chemotherapy or radiation therapy, therapy-related AML(t-AML). However, in the majority of cases, AML arises *de novo*.[5]

AML is caused by excessive proliferation of malignant blast cells, suppressing normal myeloid cells in the bone marrow, resulting in anemia, thrombocytopenia, and leukocytopenia. The 2016 World Health Organization (WHO) defines AML as >20% blast cells in the bone marrow or peripheral blood, with the exception of patients possessing certain genetic abnormalities(t(15;17), t(8;21), t(16;16) and inv(16)) where <20% blast cells are accepted as AML.[1,6]

Diagnostics include immunohistochemistry, cytochemistry and genetic analysis. The immunohistochemistry helps to determine whether the leukemia is of myeloid lineage, lymphoid lineage or ambiguous lineage defined as both myeloid and lymphoid antigen expression of the leukemic cells.[1] The morphology of the cells can further subdivide the type of AML into eight groups according to the French-American-British(FAB)- classification.[7]

The mentioned diagnostic studies help to classify the accurate type of leukemia, whereas the cytogenetic risk profile is the strongest in identifying the prognosis. Complex karyotypes are associated with an adverse prognosis.[1] Furthermore, s-AML and t-AML often have less favorable cytogenetics compared to de novo AML. The proportion of s-AML and t-AML increases by age and thereby elderly AML patients often have a more resistant disease (i.e. complex karyotype is more common in elderly patients) compared to younger patients. A lower rate of elderly AML patients will reach complete remission and relapse is common. Therefore, the prognosis among elderly AML patients is poor despite the fact that they might be eligible for intensive treatment.[8]

Eligibility is often based on performance status (PS) and comorbidities, such as severe heart-, lung-, or kidney disease. Besides being at higher risk for unfavorable cytogenetics, the elderly often have a poor PS and comorbidities, which worsens the prognosis of the disease, as they are of increased risk of treatment-related toxicity and death.[5] The abovementioned must be considered when

choosing the treatment regimen of the elderly AML patients, resulting in a therapeutic dilemma.

TREATMENT OF AML

As aforementioned, the prognosis of AML is poor, however whereas the disease was incurable 50 years ago, there is now a chance of obtaining complete remission (CR) due to better treatment options. Since the implementation of intensive chemotherapy and stem cell transplantation, curing the disease is now possible.[9]

In Denmark, the national guideline divides treatment options into three principles 1) curable intended treatment; intensive chemotherapy 2) non-curable intended treatment; non-intensive chemotherapy, with a slight chance of remission and 3) Basic supportive care (BSC); blood transfusions, antibacterial and antifungal treatment.[10] How to choose between intensive potentially curative treatment and less intensive non-curative treatment is not evident. Hence, some patients will die from treatment-related complications especially among elderly patients if treated with the toxic intensive chemotherapy needed for cure.
Intensive chemotherapy is, at this time, the sole treatment given with the intent to achieve complete remission. Conventional intensive chemotherapy consists of 60 mg/m^2 daunorubicin on for three days and i.v 100 mg/m2 cytarabine for 10 days (3+10) followed by a second induction treatment consisting of 50 mg/m2 daunorubicin for three days and 100 mg/m2 cytarabine for 8 days.[10,11] Hereafter, consolidation treatment with two series of high dose cytarabine 3mg/m^2 every four-six weeks or an allogen stem cell transplantation.[10]

Non-intensive treatment of AML includes low dose cytarabine (L-DAC) and the hypomethylating agent azacitidine. Both treatments have shown superiority compared to BSC and are commonly used for elderly patients with AML. Non-intensive treatment is given seven-ten times every fourth week and the effects take three-six courses to show; less than 20 % will reach CR and relapses are common. The treatment has to continue as long as toxicity and effects are acceptable.[11] Priorly, L-DAC was the standard care of patients, who were not believed fit for intensive therapy. However, since the approval of azacitidine, it has become the more common standard choice of treatment, as azacitidine has shown to be superior to L-DAC when comparing OS and chance of CR.[11,12]

While intensive chemotherapy is the gold standard in younger patients deemed fit, there are no official guidelines for the treatment of elderly patients. Elderly, who receive intensive chemotherapy have a higher OS than those receiving less intensive treatments such as LDAC and azacitidine, however in the performed studies, selection bias must be taken into consideration, as patients receiving non-intensive treatments and palliative care tend to have more comorbidities, and a lower PS, compared to patients treated with intensive therapy.[6,9,13] Though increasing the chance of CR and prolonging the life of AML patients, experts disagree if elderly should undergo intensive treatment, due to

its toxicity and possible harmful side effects.[14] Even though supportive care, such as antibiotics, antifungal and thrombocyte and erythrocyte transfusions, is given immensely, the myeloablative qualities the intensive regimen possesses often results in bleeding, severe infections and several hospitalizations for weeks after administration. A study by El-Jawahri et al. has shown elderly patients receiving intensive chemotherapy spent 30% more time admitted to the hospital compared to patients receiving hypomethylating agents, L-DAC and single-agent therapies on clinical trials.[15] Furthermore, studies have shown, health-related quality of life (HRQoL) worsens in patients who were hospitalized compared to patients with no hospitalizations, and one must therefore consider the burden patients are subjected to, in what may be the last stage of their lives, when choosing intensive treatment.[16] Additionally, if CR is obtained after completing induction and consolidation therapy, an allogen stem cell transplantation is often desirable to decrease the risk of relapse. A procedure that not only requires a matching donor, but also a favorable health, which in most cases eliminates a substantial number of elderly patients.

Due to the poor prognosis, regardless of treatment intensity, it is relevant to investigate the end-of-life care of AML-patients. Only a few studies have been conducted on this subject, making knowledge sparse. Studies have shown patients with solid tumors are more likely to be referred to hospice and palliative units than patients with hematologic malignancies. The referral rate to palliative care of AML-patients varies greatly from 14,2 % to 66 %, which encourages further investigation.[15,17] Hence, this study aims to compare days of hospital admissions, outpatient visits and rate of transfusions in the last 180 days of AML-patients' life >70 years, according to their first line treatment. Furthermore, it is desired to obtain data regarding referral and use of hospice and a palliative care unit.

METHODS

This is a retrospective cohort study of AML patients from the Region of Northern Jutland treated at Aalborg University Hospital in the period 1/1/2010-30/6/2020. Patients included must have received the AML-diagnosis and died during the study period. Data was extracted from Business Intelligence unit (BI-unit) of the region. The BI-unit collects information from the administrative patient system (PAS-system) where patient charts are kept. Patient charts were applied for, with the intent to validate data from the BI-unit and to obtain information regarding palliative care. This was, however, denied.

Code of treatments and diagnosis, date of diagnosis, date of death, number of outpatient visits, days of hospitalization, and whether patients died during admission were extracted from the BI-unit. Data was received in four separate Excel documents.

This study was registered and approved by the Region of Northern Jutland.

The aim of this study was to investigate the impact first line treatment had on the last 180 days of elderly AML patients' lives. Therefore, all patients younger than 70 years were excluded. Furthermore, patients who received chemotherapy for other diseases than AML were excluded.

Data were transferred to a REDcap-survey build for this particular study and sorted by first line treatment. Number of outpatient visits, thrombocyte pools, erythrocyte transfusions, admission days in the last 180 days of their lives were registered. It was also recorded whether patients died while admitted. If death occurred less than 180 days after receiving the diagnosis, the follow up period would be shortened to the date of diagnosis.

Firstline treatment was divided into 1) intensive chemotherapy, 2) non-intensive chemotherapy, or 3) palliative treatment. Intensive chemotherapy was defined as at least one course of daunorubicin and cytarabine (7+3), or a course of high-dose cytarabine, or other courses given with intention of remission. Non-intensive chemotherapy was defined as treatment with L-DAC or azacitidine. Palliative treatment was characterized as patients who received cytostatics with palliative intention (table 1)

Validation of data

Data from the BI-unit are collected for administrative purposes and not priorly validated. By using standard clinical practice, it was decided whether the data was trustworthy. It was expected that patients receiving intensive chemotherapy would receive a minimum of two-three pools of thrombocytes and at least one erythrocyte transfusion every week in three to four weeks after receiving a course of treatment. For those who received non-intensive treatment, a new course of treatment should be administered every fourth week.

There was no way to assess whether the admissions days and outpatient visits were reliable, however these were considered valid, as we may assume, one cannot be hospitalized without any form of registration.

<table>
<tr><th>Intensive AML treatment</th><th>Transfusions</th><th>Treatment for lymfoma</th></tr>
<tr><td>BWHA303: Daunorubicin + Ara-C, 3+7
BWHA304: FLAG-Idarubicin
BWHA237: Doxorubicin(liposomal)
BWHA302: Mitoxantrone + Ara-C
BWHA301: High dose Ara-C
BWHA102: Doxorubicin
BWHA305: mAMSA + etoposid
BWHA178: Cladribine
BWHA30: High dose cytostatics

Additional intensive treatment:
BWHA162: Cytarabin(intraspinal)
BWHA161: Cyt-a + methotrexat + prednisolon(intraspinal)</td><td rowspan="3">Blood Transfusions:
BOQA0: Blood Transfusion
BOQB2: Leukocyte depleted(filtered) erythrocyte suspension
BOQB0: Erythrocyte suspension
BOQB20: Leukocyte depleted(filtered), irradiated erythrocyte suspension
BOQA02: Blood Transfusion up to 5 L

Thrombocyte transfusions:
BOQC0: pooled thrombocyte concentration
BOQC30: Thrombocyte product for intrauterine transfusion
BOQC02: Leucocyte depleted(filtered), irradiated pooled thrombocyte concentration
BOQC01: Leukocyte depleted pooled thrombocyte concentration
BOQC12: Leukocyte depleted pooled thrombocyte concentration from single donor</td><td>BWHA134: Cyclophosphamide + vincristine + prednisolone(CVP)
BWHA119: Cyclophosphamide + doxorubib + vincristine + prednisolone(CHOP)
BWHA219: Methotrexate
BWHA310: BEAM(conditioning)
BWHA109: Carboplatin
BWHA164: Cyclophosphamide + etoposide + vincristine + prednisolone
BWHA105: Cyclophosphamide
BWHB8: Other biologically modified agents
BWHA114: Gemcitabine
BWHA106: Ifosfamide</td></tr>
<tr><td>Low intensive AML treatment</td><td rowspan="3">Treatment for myelomatosis</td></tr>
<tr><td>BWHA158: Low dose Cyt-a
BWHA256: Azacitidine</td></tr>
<tr><td>Palliative AML treatment</td><td>Unspecific cytostatic treatment:</td></tr>
<tr><td>BWHA407: Sorafenib
BWHA181: Hydroxycarbamide
BWHA155: Lomustine
BWHA111: Etoposide
BWHB10A: Interferon-alfa-2a
BWHA438: Venetoclax
BWHA153: Vincristine
BWHA418: Ruxolitinib
BWHB1: Interferons</td><td>BWHA: Cytostatic treatment
BWHA1: Basic cytostatic treatment
BWHA4: Other cytostatic treatment
BWHA2: Complex cytostatic treatment</td><td>BWHA154; Melphalan
BOQE20:unpurified, non stimulated stem cell concentration/ autologous peripheral blood
BWHA31: Conditioning for treatment with stem cell support
BWHA402: Bortezomib
BWHB81: Thalidomide
BWHB82: Lenalidomide
BWHB42: Denosumab</td></tr>
<tr><td>Additional AML treatment:</td><td>Treatment for Chronic myeloid leukemia</td><td>Treatment for breast cancer</td></tr>
<tr><td>BWHB30: Retinoids
BWHA179: Tretinoin
BWHB83: Azathioprin</td><td>BWHA401: Imatinib
BWHA411: Dasatinib
BWHA409: Nilotinib
BWHA429: Ponatinib</td><td>BWHA204: Paclitaxel + epirubicin</td></tr>
</table>

Table 1: Treatment codes. All codes are extracted from data from the BI-unit. Patients receiving treatment for other diseases than AML were excluded.

RESULTS

Between the 1st of January 2010 and the 30th of June 2020, 289 patients were registered in the data received from the BI-unit. A total of 107 patients were included in this study. Patients were excluded due to other hematological illnesses such as lymphoma, chronic myeloblastic leukemia, chronic neutrophilic leukemia or myelomatosis, or due to lack of treatment, hospitalization, and outpatient visits. Some patients could not be divided into a treatment group. Lastly patients were excluded if they were younger than 70 years old

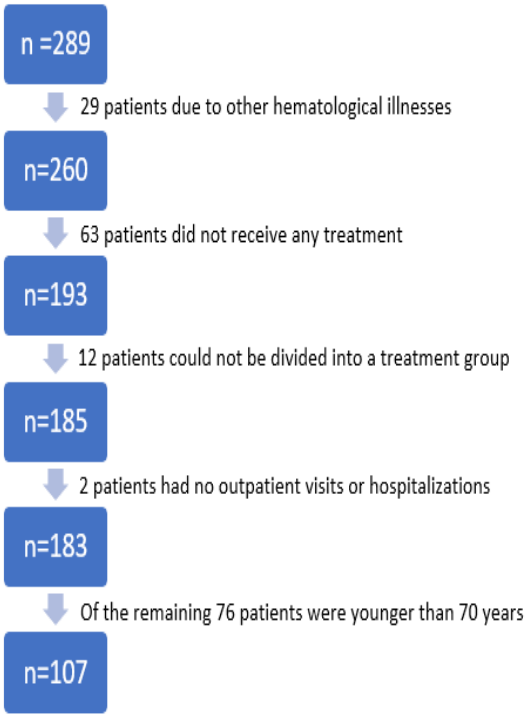

Figure 1: Flowchart of exclusion process

Of the 107 patients, 45 patients received intensive treatment, 44 non-intensive treatment and 19 patients received palliative treatment.

Of the 44 patients receiving non-intensive treatment, 39 patients received L-DAC and four patients received azacitidine. Median

	Intensive treatment n=45	*Non intensive treatment*		*Palliative treatment n=19*	*Total n=107*
		L-DAC n=39	*Azacytidine n=4*		
Age (years)	*74 (70-89)*	*79 (70-89)*	*71 (71-79)*	*84 (73-92)*	*77 (70-92)*
Female, n (%)	*20 (44,44)*	*13 (33,33)*	*2 (50)*	*6 (31,58)*	*41 (38,32)*
Survival (months)*	*2,89 (0,13-49,97)*	*5,32 (0,46-38,43)*	*6,37 (0,03-29,53)*	*1,77 (0-12,39)*	*3,39 (0-49,97)*
Admission days	*30 (0-103)*	*21 (0-64)*	*18 (1-65)*	*7 (0-38)*	*20 (0-103)*
Death during admission, n (%)	*25 (55,55)*	*14 (35,90)*	*3 (75)*	*11 (57,89)*	*53 (49,53)*
Outpatient visits	*4 (0-26)*	*8 (0-32)*	*16 (0-24)*	*2 (0-15)*	*5 (0-32)*
Blood transfusions	*2 (0-25)*	*5 (0-15)*	*6 (1-15)*	*3 (0-18)*	*4 (0-25)*
Thrombocyte pools	*1 (0-18)*	*1 (0-14)*	*2 (0-23)*	*1 (0-5)*	*1 (0-23)*

*Table 2: Overview of results *time from diagnosis to death*

age was 77 years, and 41 patients were women.

Patients receiving intensive treatment had a median survival of 2,89 months and 30 admission days in the last 180 days of their lives. 25 patients died during admission. This group received a median of four outpatient visits, two blood transfusions and one thrombocyte transfusion.

Patients in the non-intensive group received either L-DAC og azacitidine. Survival was 5,32 months and 6,37 months for L-DAC and azacitidine, respectively. Patients receiving L-DAC had a median of 21 days admitted to the hospital in the last 180 days of their lives and 14 patients died in hospital. For the azacitidine group, median admission days was 18 in the last 180 days and three patients died during admission. The L-DAC group had a median of eight outpatient visits, five blood transfusions and one thrombocyte transfusion. For azacitidine, median outpatient visits were 16, six blood transfusions and two thrombocyte transfusions.

In the palliative group, survival was 1,77 months. Median admission days in hospital was seven. 11 patients died during admission. Patients receiving palliative treatment had a median of two outpatient visits, three blood transfusions and one thrombocyte transfusion.

VALIDATION OF DATA

It was expected that patients who received intensive chemotherapy would receive a minimum of two to three thrombocyte transfusions and a minimum of one erythrocyte transfusion each week, however for a number of patients in this study, few or no transfusions were registered. This must be due to a lack of registrations, as intensive chemotherapy is highly myeloablative, resulting in severe bleeding if not given replacement transfusions. When receiving either azacitidine or L-DAC a new course of treatment is administered every fourth week. Without treatment the illness would progress, resulting in death. In this study, not all patients receiving L-DAC or azacitidine had a new treatment course administered every fourth week. Figure 3 shows a treatment interval of almost eight weeks. Some patients had even greater intervals amid treatments. This is considered as wrongful registration.

Unlike patients receiving intensive chemotherapy, blood products are not given systemically, as the bone marrow is not as suppressed, when receiving non-intensive chemotherapy. The need for transfusions is therefore determined individually and registration regarding this matter cannot be validated.

As a result of unreliable data, statistical analysis was not performed, as this study does not want to provide inaccurate data regarding the problem at hand.

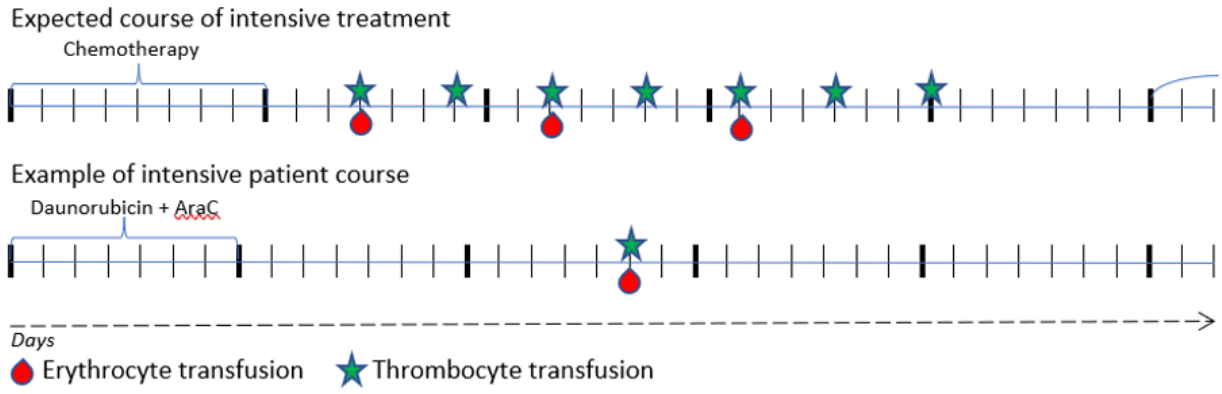

Figure 2: The first timeline shows an expected course of treatment with intensive chemotherapy with the minimum amount of erythrocyte and thrombocyte transfusions. The second timeline represents an example of a patient's treatment course with intensive chemotherapy

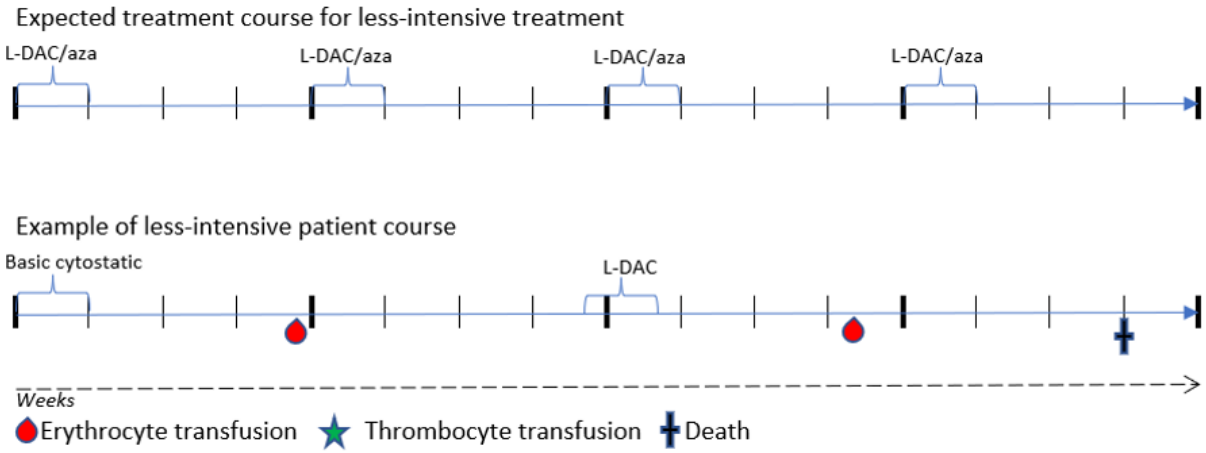

Figure 3: The first timeline shows an expected course of treatment with less-intensive chemotherapy. The second timeline represents an example of a patient's treatment course with L-DAC from the data.

DISCUSSION

In this retrospective study we investigated the burden of hospital admissions, transfusions, and outpatient visits in elderly AML-patients during the last 180 days of life. We found a numeric difference in hospital admissions and outpatient visits according to treatment intensity. Patients in the intensive treatment arm had the highest number of admissions days, with a median of 30 days, whereas patients receiving L-DAC, azacitidine and palliative treatment had a median of 21 days, 18 days and 20 days of their last 180 days of life, respectively. Furthermore, patients in the intensive treatment arm had fewer outpatient visits, a median number of four, compared to the other treatment groups, which might be due to the higher number of admission days seen in this group. Most outpatient visits are discovered in the azacitidine arm with 16 visits during the last 180 days of life.

In the past 10 years, treatment administration has been reorganized to an outpatient setting. Patients receiving azacitidine and L-DAC are now taught to self-administer injections. Furthermore, a change in the production of azacitidine has prolonged the durability from eight hours to 22 hours, meaning patients can collect their medicine for two days per visit instead of collecting medicine each day.[18] The abovementioned, may explain the greater amount of outpatient visits in the azacitidine group.

Not only has administration in azacitidine changed in the past decade, also intensive chemotherapy no longer requires hospitalization in all cases. Eligible candidates receive intensive chemotherapy at home by a medicine pump.[19] This administrative development reduces admission days for patients receiving intensive treatment, while increasing outpatient visits as the pump needs to be refilled daily. In some instances, this will not affect the amount of admission days or outpatient visits as this study merely investigates the last 180 days of patients' lives, and some will have ended treatment beforehand.

Other studies have investigated the admission days for patients from date of diagnosis until death or end of follow-up.[15,20] These studies revealed more admission days for patients in the intensive treatment arm. Lao et. al. compared admission days in patients who received intensive chemotherapy to those who received azacitidine and best supportive care. Patients receiving azacitidine had fewer admission days than the other two groups, but no investigation of outpatient visits was made. They also lacked data on patients receiving L-DAC.[20] Another study by El-Jawahri compared patients who received intensive treatment and non-intensive treatment (azacitidine, L-DAC, and single agent therapy on a clinical trial). Patients in the intensive group spent more time admitted to the hospital and were more likely to be admitted to the intensive care unit. However, they spent less time as outpatients.[15] This correlates with the findings of the current study.[15,20]

The interval between diagnosis and death varies between each patient, this is accounted for in the studies by Lao et al and El-Jawahri et al.. Lao et. al. compares admission days per patient year, and El-Jawahri et al. calculates time from diagnosis to death used in the hospital in percentages. This enables them to compare the treatment groups in each study more precisely. Our study only compares the median admission days and outpatient visit of the groups and does not account for differences in the patients' length of life.

Though it is impossible to comment on the OS of each group, being that long-term survivors were excluded in the study, the poorest survival was found in the intensive treatment arm. The median was 2,43, 3,48 and 0,5 months higher in the L-DAC-, azacitidine- and palliative-arm respectively, which was unexpected. It was discovered that some patients died within a few days of receiving the diagnosis and the first course of treatment. This group of patients had a higher representation in the intensive treatment arm, which might explain the lesser survival in this arm. It could have been considered to exclude patients who died within the first week of diagnosis, since it may be

assumed that the cause of death might be an effect of the disease and not the treatment. However, this has not been practiced in other studies.

DISCUSSION OF METHODS

Data was obtained through the BI-unit in the Region of Northern Jutland, a register with information from patient charts used for administrative purposes. Received data contained codes of treatment and diagnosis, dates of admission and discharge, and dates of outpatient visits. However, during data management, several problems came to attention. The treatment code "Basic cytostatic treatment" was present multiple times. Treatment pattern of this group was analyzed by the authors and a chief physician of the Department of Hematology at Aalborg University Hospital to classify the treatment arm, however for some patients this was not possible. Furthermore, treatment codes differed from clinical practice (Figure 2+3), making the received data unreliable. The data from the BI-unit could have been validated if permission to access the patient charts had been granted, this was, however, denied three times. Meanwhile data extracted from the BI-unit cannot be used exclusively.

Register based research has several advantages, as one may yield a considerable population without selection bias. However, the researchers have no influence in the outcomes available in the register, giving this study certain limitations. To examine the given research question, it would have been beneficial to examine quality of life, whether patients were referred to a palliative care unit, and also examine the disease and patient characteristics such as cytogenetics, comorbidities etc. This information was not present in the used register.

Furthermore, the method does not acknowledge that some patients change course of treatment or achieve CR, meaning the first line of treatment might not have affected the last 180 days of the patient's life.

Some of the above-mentioned limitations could have been solved by going through patient charts, while others would demand another way of conducting the study.

Another option to investigate the effects of treatment intensity on AML patients, would be to conduct a randomized controlled trial (RCT). By doing so, the treatment groups would be comparable, and data on quality of life could be obtained. However, for the project at hand, it would not be possible due to the time limit. The project period was 4 months; therefore, the follow-up period would be too short to make any conclusions. Furthermore, the yearly incidence of AML in Denmark is approximately 250, why only a few patients would be able to participate in this study.[2]

Additionally, a RCT could be considered unethical, due to the fact that intensive chemotherapy is the sole treatment given with the intention of achieving CR, meaning patients eligible to receive intensive chemotherapy could lose their chance of recovery, if placed in the non-intensive group.[10] A study by Wheatley et al. tried to randomize patients between the intensive and non-intensive

group, to examine which patients would benefit from intensive therapy, however only eight patients were randomized between the two treatment arms, as patients chose or were assigned to one of the treatment groups by their clinicians.[21] Minding this, it would be difficult to conduct a RCT, as both patients and psysicians are unwilling to sign up patients for randomization.

A prospective trial, without randomization, would be another approach. Patients would be assigned to each treatment group by their physician, eliminating the ethical dilemma of a RCT, while being able to collect the same amount of data. The short project period would, however, remain a limitation. Furthermore, this method may create a selection bias, as patients in the intensive treatment group often have better prognostic factors.[9]

Otherwise, data could have been obtained through RKKP (The Regions Clinical Quality Program), where the Danish database of Acute Leukemia and Myelodysplastic syndrome are registered. The Danish hematologists are obligated to report each case of AML and which treatment is given. Data on patients receiving intensive treatment is well-reported and therefore reliable, however it has only been common practice to report treatment with L-DAC and azacitidine in the past few years. Hospital admissions, outpatient visits, transfusions, and referral to palliative care facilities are, however, not registered in RKKP, which are the primary outcomes of this study.

The abovementioned methods may have helped to clarify the question at hand, as the current method resulted in unreliable data. Therefore, no conclusions on the subject can be drawn and further investigation is needed, since end-of-life care is poorly enlightened in the literature.
Moreover, a validation study of the information obtained from the BI-unit is recommended before using the data for other future studies.

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