The costs of initial treatment for patients with acute myeloid leukemia in the Netherlands

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A R T I C L E   I N F O

A B S T R A C T

The aim of this study was to calculate the costs of the current initial treatment of acute myeloid leukemia. Resource use was collected for 202 patients who started with intensive chemotherapy in 2008 or 2009. The costs of the first induction course were significantly higher than the costs of the second induction course. Allogeneic transplantation from a matched unrelated donor was significantly more expensive than the other consolidation treatments. In-hospital stay was the major cost driver in the treatment of AML. Research regarding possibilities of achieving the same or better health outcome with lower costs is warranted.

1. Introduction

Acute myeloid leukemia (AML) is an aggressive disease which requires intensive treatment. Treatment of AML generally consists of several induction chemotherapy courses to induce complete remission (CR). Induction treatment is followed by consolidation treatment consisting of high-dose chemotherapy or autologous or allogeneic hematopoietic stem cell transplantation (HSCT) for patients younger than 60–65 years of age. Stem cell sources of allogeneic HSCT are threefold: HLA-identical sibling, matched unrelated donor (MUD) or umbilical cord blood (UCB) [1]. The choice of consolidation treatment depends on the patient's risk of relapse and treatment-related mortality [2].

Insight into the treatment costs is an essential requirement for adequate reimbursement of treatment. In addition, cost calculations are required as input for cost-effectiveness analyses of (new) treatments. The cost-effectiveness factor will become increasingly important due to rising health care expenditures in Western countries [3]. A few studies in the 90s and early 2000s have calculated the total costs of AML treatment [4–6]. However, treatment strategies have changed dramatically [7–10], and an update of the treatment costs is therefore essential. The aims of this study were to gain insight into the current treatment costs and the different cost components of the total treatment costs.

2. Materials and methods

2.1. Patients

All adult patients diagnosed with de novo primary or secondary AML who started with induction chemotherapy in 2008 or 2009 in three university hospitals in the Netherlands were included in this study. Patients with acute promyelocytic leukemia (APL) were excluded because the number of patients was small and these patients were treated differently. Data were collected from diagnosis until relapse, death or last day of registration (June 2011).

2.2. Treatment

The initial treatment of AML was distinguished in three treatment phases: induction treatment, consolidation treatment and follow-up. Induction treatment started at the day of diagnosis. Two different treatment protocols were used based on the patient's age. Younger patients (less than 65 years) received induction and consolidation treatment. Induction treatment consisted of cytarabine and idarubicin in the first course and cytarabine and amsacrine in the second course. Five different consolidation treatments were administered: high-dose chemotherapy, autologous

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Table 1
Patients included in the different treatment phases.

	All patients	"Younger age" protocol	"Older age" protocol
Induction course 1	202	145	57
Induction course 2	167	127	40
Consolidation treatment	126	126	–
High dose chemotherapy	47	47	–
Autologous SCT	18	18	–
Allogeneic SCT from sibling	35	35	–
Allogeneic SCT from MUD	21	21	–
Cord blood transplantation	5	5	–
Follow-up (1 year)	128	101	27
After induction treatment	27	–	27
After high dose chemotherapy	31	31	–
After autologous HSCT	16	16	–
After allogeneic HSCT from sibling	31	31	–
After allogeneic HSCT from MUD	19	19	–
After UCB transplantation	4	4	–

HSCT: hematopoietic stem cell transplantation; MUD: matched unrelated donor.

HSCT, allogeneic HSCT from a sibling donor, allogeneic HSCT from a MUD and UCB transplantation. The choice of treatment depended on the patient's risk of relapse, performance status and the availability of an HLA-identical donor. Older patients received induction treatment consisting of cytarabine and daunorubicin in the first course and cytarabine in the second course. In both age groups, the second induction course was administered to all patients, irrespective of achievement of a CR after the first course. The second induction course started the day after discharge for the first course. In case of a continuous hospitalization, the second course started on the day that cytarabine was given as part of the second course. Consolidation treatment started on the day after discharge for the second induction course. Follow-up started 42 days after induction treatment in older patients and 42 days after consolidation treatment in younger patients. Follow-up was set at 1 year or ended at the date of relapse or death.

2.3. Cost calculation

The microcosting method was used to calculate the direct hospital treatment costs of AML. All medical resource use related to the treatment of AML and its complications was collected and multiplied by the unit cost of each resource use.

Resource use was derived from electronic patient charts and hospital information systems used for financial claims. The hospital information systems contained patient-specific information regarding in-hospital stay, outpatient visits, daycare visits, intensive care, laboratory tests, radiology and administration of blood products. Medication use was derived from electronic patient charts for a random selection of patients (10% of all patients). This selection included both younger and older patients.

Unit prices of laboratory tests, radiology and other hospital activities were derived from national tariffs defined by the Dutch Health Authority [11]. Reference unit prices were used for outpatient visits (€148), daycare treatment (€224), in-hospital stay (€712), intensive care days (€2211) and blood products [12,13]. Unit prices of medications were derived from the Pharmaceutical Compass (Z-index 2010). Unit prices of HLA-typing and donor search were obtained from Blommestein et al. [14]. All unit prices included both capital and labor costs.

Costs were subcategorized into several cost groups: in-hospital stay, hospital visits, diagnostic procedures, medication, blood products, radiation, HLA-typing and donor search. Intensive care costs were included in the costs of in-hospital stay. Hospital visits consisted of daycare treatment, outpatient visits, emergency unit visits and other consults. Diagnostic procedures consisted of laboratory tests, radiology and other activities.

Follow-up data were not always available for 1 year, because only patients diagnosed in 2008 or 2009 were included in this study in order to calculate current treatment costs. If follow-up data were available for at least 100 days in patients alive without relapse, the costs were extrapolated to 1 year based on the average costs per day.

Missing values were imputed according to the average costs per in-hospital day during chemotherapy and transplantation. During follow-up, missing values were imputed according to the average costs per day spent in the hospital, including outpatient visits and daycare treatment. All costs were based on Euro 2010 cost data. Where necessary, costs were updated to 2010 according to the national consumer price index [15].

2.4. Statistical analysis

Mann–Whitney tests were used to test for significant differences in costs, in-hospital stay and treatment duration between treatment protocols, induction courses and consolidation treatments. A probability level <0.05 was considered significant. All analyses were performed using Microsoft Excel 2003 and SPSS 17.0.

3. Results

3.1. Patients

In total, 202 patients were included in this study, of which 145 were treated according to the younger age protocol (Table 1). A second induction course was given to 127 (88%) younger and 40 (70%) older adults. Consolidation treatment was given to 126 patients. A few patients ($N = 8$) received an allogeneic HSCT or UCB transplantation after only one induction course. Most patients received high-dose chemotherapy ($N = 47$) as consolidation treatment. Sufficient follow-up data were available for 101 (70%) younger and 27 (47%) older adults.

3.2. Induction treatment

The average costs of the two induction courses were €46,807 for the first course and €42,395 for the second course (Table 2). Although the first induction course was significantly shorter than the second course, the total costs of the first course were significantly higher. This difference was mainly related to higher costs of diagnostic procedures as costs of diagnosis were included in the first course. In addition, blood products and medication costs were significantly higher during the first course. Although the chemotherapy dose was higher in the second course, the chemotherapy costs were lower due to the lower unit price of the anthracycline used in the second course. Costs of hospital visits were significantly lower in the first course. In-hospital stay did not differ significantly between the two courses. On average patients were hospitalized 33.7 days during the first induction course and 34.1 days during the second course.

Not all patients received both induction courses. The majority of the patients who did not receive the second course were worse off as they died during the first course or were too ill to continue intensive treatment. Although patients receiving only one induction course were worse off, no significant difference in the total costs of the first induction course were found between patients receiving a second course or not (data not shown).

The total costs of the second induction course were significantly higher in older patients compared to younger patients. However, the duration of the second course was significantly longer in older patients; in fact, the total costs per treatment day did not differ significantly between the two age groups. No significant differences in total costs of the first induction course were found between the two age groups. In both induction courses, the chemotherapy costs were significantly higher in younger patients, while the costs of other medications were significantly lower. Duration of