Improvement of relative survival in elderly patients with acute myeloid leukaemia emerging from population-based cancer registries in Switzerland between 2001 and 2013

Annatina Schnegg-Kaufmann a,b,1, Anita Feller c,1, Helen Baldomero d, Alicia Rovo a, Markus G. Manz e, Michael Gregor f, Anna Efthymiou g, Mario Bargetzi h, Urs Hess i, Olivier Spertini j, Yves Chalandon k, Jakob R. Passweg c,d, Georg Stussi i, Volker Arndt c, Nicolas Bonadies a,b,⁎, the NICER Working Group

a Department of Haematology and Central Haematology Laboratory, Inselspital, Bern University Hospital, University of Bern, Switzerland
b Department for BioMedical Research, Inselspital, Bern University Hospital, University of Bern, Switzerland
c Foundation National Institute for Cancer Epidemiology and Registration (NICER) c/o University of Zurich, Switzerland
d Divisions of Hematology, Department of Medicine, University Hospital Basel, Switzerland
e Haematology, University and University Hospital Zurich, Switzerland
f Division of Haematology and Central Haematology Laboratory, Cantonal Hospital Lucerne, Switzerland
g Department of Haematology-Oncology, Cantonal Hospital Fribourg, Switzerland
h Division of Haematology and Transfusion Medicine, Cantonal Hospital Aarau, Switzerland
i Clinic for Haematology and Oncology, Cantonal Hospital St. Gallen, Switzerland
j Service and Central Laboratory of Haematology, Centre Hospitalier Universitaire Vaudois, Lausanne University Hospital, Switzerland
k Department of Oncology, Division of Hematology, Geneva University Hospitals and Faculty of Medicine, University of Geneva, Switzerland
l Clinic of Haematology, Oncology Institute of Southern Switzerland, Switzerland

ARTICLE INFO

Keywords:
Acute myeloid leukaemia
Epidemiology
Classification
Incidence
Mortality
Survival

ABSTRACT

Acute Myeloid Leukaemia (AML) is a rare and heterogeneous haematological malignancy with increasing incidence in the elderly. We performed a population-based, observational analysis of AML cases reported to the Cantonal Cancer Registries in Switzerland. Data was aggregated by the National Institute for Epidemiology and Cancer Registration and stratified for the two time periods 2001–2007 and 2008–2013. Overall, 2351 new AML cases were registered with a stable age-standardised incidence rate (3.0 [95 CI: 2.8-3.2] per 100,000 person-years). This indicates that our observed raise of annual AML cases (+10.9%) is mainly related to demographic ageing and not to an increase of age-specific risks. The fraction of non-classifiable AML cases decreased over time (54.6% to 41.8%) but remained high in elderly patients (65–74 yrs: 44%; 75–84 yrs: 54.2%, 85 + yrs: 59.1%), suggesting less accurate diagnostics and reporting with increasing age. 5 yrs relative survival (RS) correlated with AML risk class (favorable: 61.7%-68.4%; adverse risk: 11.4%-21.9%) and age (< 65 yrs: 42.6–43.3%; 75–84 yrs: 2.0-3.0%), but improved only modestly overall (19.2% to 23.3%). Interestingly, we identified a significant improvement of RS in patients aged 65–74 yrs (5 yrs: 5.2% to 13.5%; p < 0.001). As surrogate for changes in management, we found an increase of allogeneic haematopoietic stem cell transplantations (1.4 to 7%) and clinical trial activities (25 to 29%) for elderly AML patients during the observation period. Our analysis indicates that recent progress made in management of elderly AML patients results in an improvement of survival on a population-based level in Switzerland and that therapeutic nihilism is not justifiable.

1. Introduction

Acute myeloid leukaemia (AML) is a rare and heterogeneous disorder arising from genetic lesions in the haematopoietic stem or progenitor cell compartment. It is a highly malignant condition, characterized by proliferation of immature myeloid precursors and
subsequent displacement of normal haematopoiesis [1]. AML accounts for 1.3% of all incident cancers and 1.8% of all cancer deaths in developed countries [2–4]. Population-based AML registries, such as the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute of the United States [2,3], the Swedish Acute Leukemia Registry [5], and the Dutch PHAROS Registry [6], have provided important epidemiological data from AML patients. Reported incidence rates of AML vary between 1.5 and 5.2 per 100,000 person-years (py), depending on the reference standard population used [7–12]. AML has a male to female ratio of 1.1:1.6 [10] and the incidence increases steadily after the age of 40 years (yrs), reaching peak values of 15–30 per 100,000 py at the age of 75–80 yrs [2,3,5,6]. Survival has substantially improved on a population-based level over the last decades, however these advances are less prominent for elderly patients [5].

Prognosis of AML patients depends on disease- and patient-based factors. Genetic lesions are the main contributors for disease-based prognostic stratification [13]. Roughly 10% of AML patients are therapy related, while another smaller subset of patients develop secondary AML progressing from a previous haematologic malignancy [14–16]. Both entities are associated with adverse outcome. The majority of patients, however, present with “de novo” AML without any identifiable precipitating cause or preceding haematological neoplasm. The most important patient based factors are age and comorbidities, which are both limiting tolerance to intensive treatment approaches [17]. Moreover, AML in the elderly has a more aggressive biology, explained by genetic instability, higher frequency of complex karyotype as well as secondary or therapy related conditions [13,18–20].

The general approach for therapy to young and fit AML patients has almost not changed [15]. It consists of standard induction and consolidation chemotherapy (“3 + 7”) followed by allogeneic haematopoietic stem cell transplantation (allo HSCT) in high-risk AML patients, whereas low-risk AML patients in first remission do usually not require allo HSCT. In contrast, the management of elderly AML patients (> 65 yrs) has substantially changed in recent years. In Switzerland, these patients were treated with hydroxyurea and low-dose cytarabine before 2000. Following activation of clinical trials in elderly AML patients, the general management changed in these patients after 2002. More intensive treatment followed by allo HSCT with non-myeloablative conditioning for eligible, elderly patients stepped in as a potential treatment option. Moreover, based on the results of two phase 3 trials, hypomethylating agents (azacytidine and decitabine) were increasingly integrated into the general management of elderly and unfit patients in Switzerland after 2012 [21,22].

Currently, 18.0% of the Swiss population is 65 yrs and older [23]. This percentage is expected to rise to 22.8% and 26.4% by 2030 and 2045, respectively. All developed, but also an increasing majority of developing countries, face similar demographic trends [24]. Therefore, the prevalence of AML is expected to rise considerably over the next decades with an emerging impact on health system resources.

Here we provide the first population-based data on time trends of classification, incidence, mortality, and survival of AML patients in Switzerland diagnosed between 2001 and 2013 and reported to the Swiss Cantonal Cancer Registries (CCRs). Given the demographic ageing, we were mainly interested to investigate whether elderly patients may have benefited, on a population-based level, from recent changes in AML management.

2. Methods

2.1. Study design

This is a population-based, observational analysis of patients with AML reported to the Swiss Cantonal Cancer Registries (CCRs). Data was aggregated by the National Institute for Epidemiology and Cancer Registration (NICER) [25]. The study population comprised all reported AML cases diagnosed from 2001 (after implementation of ICD-O-3) until the most recent and completely processed dataset. At the time of data-extraction (31.1.2017) complete datasets from the CCRs were available until 2013.

2.2. Data source

The procedure for data collection, processing and analysis was previously reported [26]. In 2001, 13 out of 26 cantons conducted cancer registration, covering 59.3% of the Swiss population. As of 2013, this number increased to 21 cantons, covering 66.3%. Age and sex distribution from the population covered by the CCRs was shown to be identical to the general Swiss population [26]. The following cantons were included in the current analysis: Basel (City and Country, year of incidence 2001–2011), Vaud (2001–2012), Geneva, Glarus, Graubünden, Neuenburg, St. Gallen, Appenzell, Ticino, Wallis, Zürich (all 2001–2013), Jura (2005–2013), Fribourg (2006–2013), Lucerne (2010–2013), Nidwalden, Obwalden, Uri, Zug (all 2011–2013), Thurgau (2012–2013), Aargau (2013). Vital status follow-up was provided by all CCRs with exception of Vaud. Vital status information was collected by passive (linkage with federal mortality data) and active follow-up (verification of vital status with the cantonal registration offices). The Swiss Federal Statistics Office (SFSO) provided canton-specific mid-year estimates of the general population and mortality statistics referring to all persons with permanent residence status in Switzerland by age, sex, and calendar year.

2.3. Classification of AML subtypes

AML classification systems are based on morphologic as well as cytochemical characteristics and genetic lesions have been introduced into the WHO classification system more recently [27]. AMLs are coded in the CCRs according to the International Classification of Diseases for Oncology using the most recent version (currently ICD-O-3.1). The correlation of ICD-O with the WHO classification is shown in supplementary Table 1. Cases with codes ICD-O-3.1 M-9800 (leukaemia, NOS) and ICD-O-3.1 M-9801 (acute leukaemia, NOS) were excluded, as they also include lymphoid neoplasms.

2.4. Classification in prognostic categories

Risk stratification in AML generally depends on patient and disease based factors. In the CCRs the only available patient based risk factor is age, whereas other relevant information, such as comorbidities, are not systematically collected. For the purpose of the present analysis, we classified our AML cases into four age classes: < 65 yrs, 65–74 yrs, 75–84 yrs and 85 + yrs. The most relevant disease based risk factors are cytogenetic alterations, which are partially inferable form the ICO-3.1 codes (supplementary Table 1). We defined four disease-based AML risk-classes considering morphological and cytogenetic features: favorable, intermediate, adverse and non-classifiable. Acute promyelocytic leukaemia cases (APL; ICD-O code 9866) are reported separately in supplementary Table 4. The class of intermediate risk AML comprises cases that could only be classified according to morphological criteria, without consideration of cytogenetic anomalies or driver mutations, since latter are not collected in the CCR database (i.e. FLT3-ITD, mutations in NPM1 and CEBPA).

2.5. Statistical analysis

Crude and age-specific incidence- and mortality-rates were calculated using mid-year population estimates provided by the SFSO, stratified by sex and prognostic categories (age and disease risk), as defined. The expected AML cases for all of Switzerland were extrapolated by applying the observed incidence rates to the population of all cantons under the assumption of homogeneity between cantons with and
Statistical analyses were performed with Stata/MP version 13.1. Exclusion of patients was based on missing follow-up information.

Survival analysis used the method described by Brown et al. [30]. The canton of Vaud was excluded from survival analysis due to missing follow-up information. The mean annual AML case frequency for all of Switzerland increased by 10.9% from 275 to 305 cases (see also Table 3). Median age at diagnosis was 68 and 67 years in the two observation periods (range 0–96 years) with a slight predominance of male sex (male/female ratio: 1.1:1.2). 40.9% and 45.7% were < 65 yrs at diagnosis in female and male patients, respectively. Age distribution of AML cases remained stable over time.

### 3. Results

#### 3.1. Study population

In total, 2351 new AML cases were reported, 1151 and 1200 for the years 2001–2007 and 2008–2013, respectively (Table 1). The proportion of patients reported by death certificate was only 1.2% (n = 28) and decreased slightly from 0.6% to 0% and 7% to 3.6% across the two time periods in patients < 65 and 85+ yrs, respectively. The extrapolated mean annual AML case frequency for all of Switzerland increased by 10.9%, from 275 to 305 cases (see also Table 3). Median age at diagnosis was 68 and 67 yrs in the two observation periods (range 0–96 yrs) with a slight predominance of male sex (male/female ratio: 1.1:1.2). 40.9% and 45.7% were < 65 yrs at diagnosis in female and male patients, respectively. Age distribution of AML cases remained stable over time.

#### 3.2. Classification in AML subtypes and risk-classes

For the whole observation time, 97.8% (n = 2300) AML cases were microscopically verified. Among younger patients (age < 65 years) the proportion increased from 97.8% to 99.8% whereas it remained at 91.8% across the two time periods in patients 85+ years. For the whole observation period, 7.8% (n = 184) could be classified as favorable, 29.5% (n = 693) as intermediate, 14.7% (n = 345) as adverse risk, and 48% (n = 1129) of AML cases had insufficient information and could not be further classified for risk attribution (non-classifiable), respectively (Table 1).

Globally, the percentage of non-classifiable AML cases decreased from 54.6% (n = 628) to 41.8% (n = 501) in the two time periods. In < 65 yrs patients, non-classifiable AML decreased from 47.4% (n = 239) to 30.2% (n = 156), and in 85+ yrs patients from 74.2% (n = 72) to 59.1% (n = 65) (Table 1 and 2). No relevant differences between genders could be observed in all age classes for non-classifiable AML for the two time periods (supplementary Table 2).

Sub-classified AML cases increased from 6.8% (n = 78) to 8.8% (n = 106) for favorable risk, from 27.2% (n = 313) to 31.7% (n = 380) for intermediate risk and from 11.5% (n = 132) to 17.8% (n = 213) for adverse risk (Table 2). Around three quarter of AMLs with favorable risk were reported in younger patients < 65 yrs. In 85+ yrs patients, only one case was recorded in 2001–2007, and none in 2008–2013. Similarly, AMLs with intermediate risk were more frequently reported in < 65 yrs patients, with 31.5% (n = 13) and 20.9% (n = 23) for the two time periods, respectively. Adverse risk AMLs were most frequently reported in older patients and increased in all age classes without relevant differences between genders (supplementary Table 2). Due to the high number of non-classifiable AML cases, robust conclusions for risk-classes remained generally limited.

#### 3.3. Incidence and mortality of AML in Switzerland

The age-standardized (adjusted) incidence and mortality rates were 3.0 and 1.9–2.0 per 100,000 py, respectively, without relevant changes in the two time periods (Table 3). The age-standardized (adjusted) incidence rates per 100,000 py ranged from 3.3 to 3.6 in males and 2.3–2.4 in females, respectively, and were 1.2–1.4 fold higher in males compared to females. The age-standardized (adjusted) mortality rate per 100,000 py ranged from 2.4 to 2.9 in males and 1.5–1.7 in females, respectively, without significant differences in the two time periods. Mortality rates were 1.4–1.5 fold higher in males compared to females. Distribution of incidence and mortality stratified for sex and age classes were comparable over the two time periods. Age-specific (crude) incidence and mortality rates remained low < 65 yrs and increased after the age of 75 yrs, 4–6 fold for the incidence and 5–8 fold for the mortality, respectively (Table 3 and Fig. 1A and B). Distributions of age-

---

**Table 1** Characteristics of AML cases reported to Swiss cancer registries for 2001–2007 and 2008–2013.

<table>
<thead>
<tr>
<th>Age and sex</th>
<th>2001–2007</th>
<th>2008–2013</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>overall</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>females</td>
<td>1151</td>
<td>100</td>
<td>1200</td>
</tr>
<tr>
<td>&lt; 65 yrs</td>
<td>218</td>
<td>18.9</td>
<td>238</td>
</tr>
<tr>
<td>65–74 yrs</td>
<td>121</td>
<td>10.5</td>
<td>140</td>
</tr>
<tr>
<td>75–84 yrs</td>
<td>141</td>
<td>12.3</td>
<td>139</td>
</tr>
<tr>
<td>85+</td>
<td>51</td>
<td>4.4</td>
<td>68</td>
</tr>
<tr>
<td>males</td>
<td>620</td>
<td>53.9</td>
<td>615</td>
</tr>
<tr>
<td>&lt; 65 yrs</td>
<td>286</td>
<td>24.9</td>
<td>279</td>
</tr>
<tr>
<td>65–74 yrs</td>
<td>142</td>
<td>12.3</td>
<td>162</td>
</tr>
<tr>
<td>75–84 yrs</td>
<td>146</td>
<td>12.7</td>
<td>132</td>
</tr>
<tr>
<td>85+</td>
<td>46</td>
<td>4</td>
<td>42</td>
</tr>
</tbody>
</table>

### subtypes and risk-classes

#### favorable

- APL with PML-RARA (FAB M3): 49
- AML with RUNX1-RUNX1T1: 18
- AML with CBFB-MYH11: 11

#### intermediate

- Acute myelomonocytic leukaemia (FAB M4): 313
- AML with maturation (FAB M2): 80
- Acute monoblastic/monocytic leukaemia (FAB M5): 77
- AML without maturation (FAB M1): 54
- AML with minimal differentiation (FAB M0): 14

#### adverse

- Acute myeloid leukaemia, not classified (FAB M7): 132
- AML with MDS-related changes: 66
- Therapy-related myeloid neoplasms (t-MN): 20
- Acute erythroid leukemia (FAB M6): 27
- Acute megakaryoblastic leukemia (FAB M7): 9
- Acute panmyelosis with myelofibrosis: 4
- Myelodysplasia: 4
- AML with MLLT3-MLL: 2
- AML with DEK-NUP214: 0
- AML with RUN1-EVI1: 0
- Acute basophilic leukaemia: 0
- Acute myeloid leukaemia, not classified (9861): 628
- Acute myeloid leukaemia, not classified (9860): 586

---

* Risk stratification according to morphologic and cytogenetic criteria.
specific (crude) incidence and mortality rates were comparable between sexes and the two time periods.

3.4. Survival of AML in Switzerland

Overall, the relative survival (RS) improved modestly at 3 yrs from 21.1% [95% CI: 18.3%–24.1%] to 25.5% [22.8%–28.4%] and at 5 yrs from 19.2% [95% CI: 16.2%–22.3%] to 23.3% [20.6%–26.3%] in 2001–2007 and 2008–2013, respectively (supplementary Table 3 and Fig. 2). Younger patients with < 65 yrs had significantly better 5 yrs RS (range: 42.6–43.3%) compared to patients with 75–84 yrs (range: 2–3%) in both time periods. In patients aged 65–74 yrs the relative survival improved significantly (3 yrs RS: 6% [3.1–10.2%] to 16.9% [12.2–22.4%]; 5 yrs RS: 5.2% [2.4–9.6%] to 13.5% [8.9%–19.1%]; p < 0.001) across the two time periods. When excluding APL cases in patients aged 65–74 yrs, RS remained significantly improved (5 yrs RS: 4.1% [2.0–7.4%] to 12.8% [8.4%–18.3%]; p < 0.001). In all other age classes, RS was not significantly different across the two time periods.

Survival was dependent upon risk-classes; with favorable risk AML patients having significantly better 5 yrs RS (range: 61.7%–68.4%) than
adverse risk patients (range: 11.4%–21.9%). 5 yrs RS for patients with non-classifiable AML was as dismal as for patients with adverse risk AML (range: 11.4%–14.7%) and showed no significant changes over time. Of note, the intermediate and adverse risk AML groups showed also a significant improvement of RS across the two time periods (5 yrs RS: intermediate: 20.4% [14.9%–26.6%] to 27.3% [22.5%–32.4%]; p < 0.001/adverse: 11.4% [5.1%–20.6%] to 21.9% [15.0%–29.7%]; p < 0.001).

3.5. Allogeneic HSCT and clinical trial activities in patients ≥ 65 yrs in Switzerland

Data on treatment is currently not collected in the CCRs on population-based level. To estimate the potential reasons for the improved RS of patients aged 65–74 yrs, we analyzed patient data provided from the national registry of the Swiss Blood Stem Cell Transplant Group (SBST) and the Swiss Group of Clinical Cancer Research (SAKK) coordination office.

For allo HSCT activity, we focused on AML patients ≥ 65 yrs of age (range 65–70 yrs) receiving a first allo HSCT within the period 2001–2013 (supplementary Table 5). During this time, 38 AML patients were transplanted and the frequency increased from 2.2% (6/272) to 9% (32/354) from all transplanted AML patients in Switzerland. On a population based level, the estimated frequency of allo HSCT increased from 1.4% (6/444) to 7% (32/456) for the age class 65–74 yrs. The Kaplan-Meier survival estimator showed a 5 yrs cumulative survival of 47% in all patients transplanted in 2008–2013 with a trend for improved survival compared to 2001–2007 (supplementary Fig. 1).

For clinical trial activities, we analyzed the number of patients recruited to the HOVON/SAKK trials for elderly AML patients during the time period 2000–2017 (supplementary Table 6). 101 and 142 patients were recruited for the two representative time-periods between 3/2002-6/2006 and 8/2007–12/2013, respectively. On a population based level, the estimated frequency of inclusion into clinical trials increased from 25% (110/444) to 29% (133/456). In summary, we found an increase of transplantation and clinical trial activities for elderly AML patients in Switzerland as surrogate for a change in management during the observation period.
4. Discussion

Here we report the first population-based, epidemiologic data of AML patients in Switzerland from 2001 to 2013. Our analysis identified i) a rise of annual AML cases caused by demographic ageing and not by an increase of age-specific risks, ii) improvement of AML classification with less accurate diagnostics and reporting with increasing age, iii) increase of allo HSCT and clinical trial activities in elderly AML patients aged 65–74 yrs as surrogate for changes in management, iv) and improvement of relative survival for elderly AML patients with intermediate and adverse risk AML.

4.1. Strengths and limitations

A very recent and extensive evaluation of Swiss population-based cancer registries demonstrated high completeness across all registries and for most cancer types including myeloid leukaemia [31]. The proportion of patients reported with death certificate only was 1.2% and 97.8% of cases were microscopically verified. Cases reported with death certificate only increased ( < 65 yrs: 0-0.6%; 85 + yrs: 3.6-7%) and microscopically verified cases decreased with age (85 + yrs: 91.8%; < 65 yrs: 97.8–99.4%), without relevant changes during our observation time. The mortality-rates were slightly below the incidence rates, reflecting completeness of registration and a high mortality. Not-classifiable cases and lack of information on treatment and comorbidities remain the most relevant limitations of our dataset.

4.2. Demographics and annual AML case frequency, incidence and mortality

Our observed incidence and mortality rates, as well as the age- and sex-specific distributions, are similar to other population-based registries (supplementary Table 7) [7–12]. Comparison across different studies is however impeded by use of different standard populations for the calculation of age-standardized incidence rates. Using the European Standard 1976, Roman et al. reported an age adjusted incidence rate of 3.48 (95% CI 3.41-3.51) per 100,000 py in the United Kingdom, which is slightly higher than our data [7]. On the other hand, Osca-Gelis et al.
reported a lower age-adjusted incidence rate of 2.91 per 100,000 py using the same European Standard 1976 [9]. Differences in reported incidence rates remain small, and most likely reflect variations in disease reporting within various regions. Although true differences in incidences, for example due to differences in exposures to environmental risk factors, cannot be completely excluded [10]. In our study, age-standardized incidence and mortality rates remained stable over the observation time, demonstrating that the increase of annual cases is mainly caused by demographic ageing of the general population and not by an increase of age-specific risk.

4.3. Classification in AML subtypes and risk stratification

Reporting of cancer diagnosis to registries remains incomplete, either because clinicians renounce in completing the diagnostic work up, or because relevant information may be lost before reaching the CCRs. Such cases will be registered but without accurate classification (non-classifiable AML). As described by others, proper workup and reporting of AML cases is generally better in younger patients and improved in all age classes over time [6].

Another major limitation of our analysis is determination of risk-classes on population-based level. This was related to the high number of non-classifiable AML cases and the assignment of AML risk-classes based on ICD-O codes. The risk classification we applied in this study can be considered appropriate for favorable and adverse risk groups (mainly based on cytogenetic information), but has limitations for the intermediate risk group. For instance, the promyelocytic and core-binding factor leukaemias are faithful representatives of favorable diseases. Additionally, all adverse risk diseases can be identified through the ICD-O code, based on representative cytogenetic or morphological features. In contrasts, NPM1, CEBPA and FLT3 mutation status is currently not collected on our CCR database, which influences correct assignment of patients within the intermediate risk group.

4.4. Survival

Survival of patients with non-classifiable AML was as dismal as in adverse risk AML patients. This may reflect the advanced age as well as relevant comorbidities of patients with non-classifiable AML. We can only speculate, whether these AML patients were retained from adequate diagnostic and therapeutic procedures for disease, patient or management based factors (i.e. advanced disease state with complicated initial presentations or comorbidities), since such information is currently not available from our CCR database.

As expected, we observed a better 5 yrs RS in favorable (61.7%–68.4%) compared to adverse risk AML patients (11.4%–21.9%) and also in younger ( < 65 yrs: 42.6–43.3%) compared to older patients (75–84 yrs: 2.0–3.0%) [2,3,5,6]. Interestingly, we found in elderly AML patients aged 65–74 yrs a significant improvement of RS (3 yrs: 6.0% to 16.9%; 5 yrs: 5.2% to 13.5%; p < 0.001) across the two time periods. The small increase of APL cases found in patients aged 65–74 yrs did not explain this survival advantage. Similarly, patients with intermediate and adverse risk AML showed an improved 5 yrs RS (20.4%–27.3% and 11.4%–21.9%, respectively), while survival remained stable for favorable AML patients. The improvement in survival of intermediate and adverse risk AML patients is most likely a consequence of better survival within the elderly AML population.

Even though treatment information is currently not collected in the CCRs, data from the SBST showed an increase of allo HSCT activity in ≥ 65 yrs patients during the observation period (estimated: 1.4 to 7%). However, the number of transplanted patients remained low and could not completely explain the favorable survival trend observed in elderly patients. Similarly, recruitment of elderly AML patients to clinical trials improved (estimated: 25% to 29%), but did not explain the favorable survival trend. Overall, these observations are surrogates for a general change in management of elderly AML patients during the observation period. They reflect that allocation to more intensive treatment and potentially curative treatment options for eligible, elderly patients has generally improved in Switzerland; a trend that was also observed in other population based registries [5,6]. In the Swedish population-based registry, the 5 yrs RS was 15% and 5% for elderly patients aged 61–70 yrs and 71–80 yrs, respectively. However, in contrast to our study, their survival trend in these age groups remained unchanged between 1988 and 2005 [5]. The 5 yrs RS of 5.2% observed in our Swiss elderly AML population (aged 65–74 yrs) is lower compared to the Swedish data. This suggests that elderly AML patients in Switzerland were not treated intensive enough before 2008. Therefore, recent improvement of survival of elderly AML patients in our country may be multifactorial and mainly caused by an increased allocation to induction/consolidation chemotherapy (including allo HSCT) as well as treatment with hypomethylating agents and improvement in supportive care. As data on treatment is not collected in the CCRs, our interpretation is the best we can achieve with information from Supplementary data sources, but remains speculative. Nonetheless, several clinical trials and population-based data provide sufficient evidence to recommend treatment beyond supportive care for elderly AML patients who tolerate more intensive treatment [2,3,5,6,32].

5. Concluding remarks

In our analysis we could generally reproduce epidemiological data of AML patients reported from other population-based registries. Our survival data indicates that recent progress made in management of elderly AML patients resulted in improved survival on a population-based level in Switzerland and therapeutic nihilism is not justifiable any more. Our available population-based data has limitations. More detailed information on patient-, disease- and management-based factors is warranted to improve conclusions for future health service research studies. Advances in AML management and demographic ageing will further increase AML prevalence. This development has to be taken into account for structural as well as financial recommendations for future health care systems.

Author’s contributions

2 ASK: analyzed data and wrote the paper (equal contribution*); AF: provided data, analyzed data and wrote the paper (equal contribution*); HB: provided Supplementary data; AR: critical revision of the paper; MGM: critical revision of the paper; MG: critical revision of the paper; AE: critical revision of the paper; MB: critical revision of the paper; UH: critical revision of the paper; OS: critical revision of the paper; VA: critical revision of the paper; JRP: provided Supplementary data, analyzed data and critically revised the paper; GS: provided Supplementary data, analyzed data and critically revised the paper; VA: conceptualized the analysis and critically revised the paper; NB: initiated and designed the study, analyzed data and wrote the paper.

Funding

None

Conflicts of interest

None for all authors.

Acknowledgements

The Swiss cancer data used in these analyses was supplied by the Foundation National Institute for Cancer Epidemiology and Registration (NICER) and its partner registries in cantons (alphabetical order) Aargau, Appenzell, Basel, Fribourg, Geneva, Glarus, Graubuenden, Luzern, Uri, Nidwalden, Obwalden, Neuchâtel, Jura, St.

61
Data on stem cell transplantation has been provided and analyzed by the Swiss Blood Stem Cell Transplantation Group.

A. Fuhrer from Swiss Group of Clinical Cancer Research (SACK) coordination office provided data on clinical trials activity.

L. Buetti-Koer from Clinical Trail Units University of Bern supported statistical analysis. F. Galli from NICER assisted in data analysis.

Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version, at https://doi.org/10.1016/j.canep.2017.11.008.

References