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Impact of allogeneic hematopoietic cell transplantation on the outcome of older patients with acute myeloid leukemia

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A B S T R A C T

For younger patients with intermediate- or high-risk acute myeloid leukemia (AML) in first remission, allogeneic hematopoietic cell transplantation (HCT) offers the best chance of cure and therefore is the treatment of choice. The role of allogeneic HCT in the treatment of older patients is less well defined. In this review, four issues concerning the role of HCT in the treatment of older AML patients will be addressed: the frequency of allogeneic HCT in the older AML population in the US; the impact of age on the outcome of HCT; the comparative outcome of allogeneic HCT versus chemotherapy in older AML patients; and some of the barriers to the effective use of HCT in older AML patients.

1. Introduction

According to the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program, 21,380 Americans will be diagnosed with acute myeloid leukemia in 2017 with a median age of 68 [1]. The projected 5-year survival for these patients is 27%, and is very age dependent. A population-based registry from the Swedish Acute Leukemia Registry Group reported 5-year overall survival rates ranging from 60% for those under age 30, to less than 2% for those over age 75 (Fig. 1) [2]. For younger patients with AML, particularly those with intermediate and unfavorable risk disease, allogeneic hematopoietic cell transplantation (HCT) offers the best chance for cure and therefore is the treatment of choice [3,4]. There is less agreement about the proper place of allogeneic HCT in the treatment of older patients. Given the dismal outcome of conventional chemotherapy in older patients, as well as recent improvements in supportive care measures, it seems timely to address the question of the role of allogeneic HCT in this older patient population. Four questions will be addressed in this paper. (1) How frequently is allogeneic HCT currently used to treat AML in the United States (US) according to patient age? (2) With current supportive care measures, how much does age impact the outcome of allogeneic HCT? (3) What is the comparative outcome of allogeneic HCT versus chemotherapy for the treatment of AML in older patients? (4) What are some of the major barriers to the more effective use of allogeneic HCT in older patients with AML?

2. Frequency of allogeneic HCT for the treatment of AML in the US

Table 1 lists the number of new cases of AML in the US in 2015 by age as estimated by SEER. Also shown are the numbers of transplants performed for the treatment of AML by decade as estimated by the Center for International Blood and Marrow

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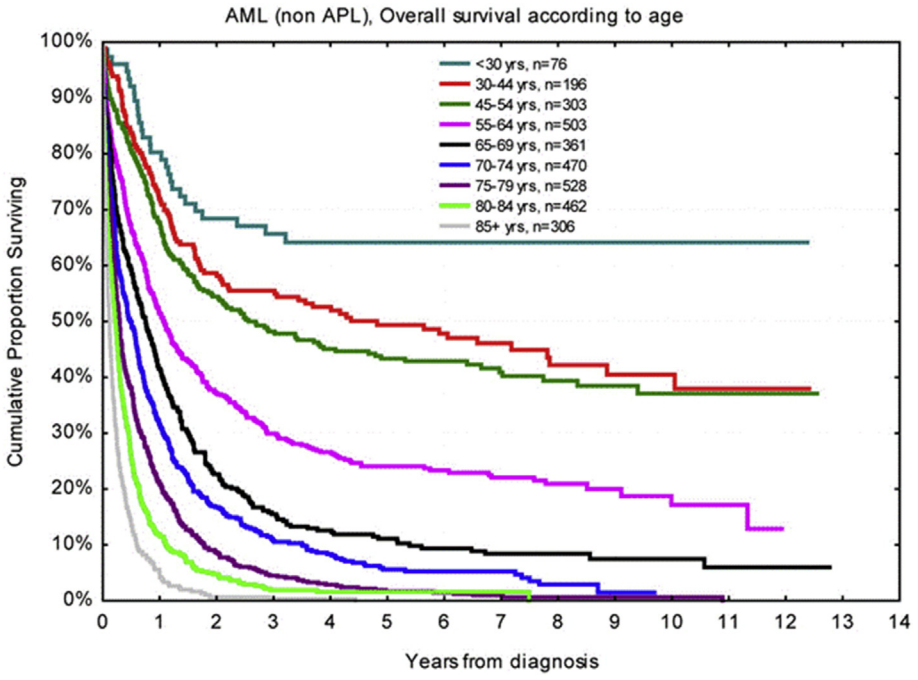

Fig. 1. Overall survival according to age for AML patients diagnosed between 1997 and 2007 [2]. Republished with permission of American Society of Hematology from Juliusson G, Lazarevic V, Horstedt AS, Hagberg O, Hoglund M, Swedish Acute Leukemia Registry G. Acute myeloid leukemia in the real world: why population-based registries are needed. Blood 2012; 119:3890–3899; permission conveyed through Copyright Clearance Center, Inc.

Table 1
Incidence of AML and transplants for AML According to decade of life.

Age	AML Cases	HCT	%
<10	518	143	28
11–20	538	175	32
21–30	798	234	29
31–40	997	279	28
41–50	1596	459	29
51–60	2693	787	29
61–70	3790	978	26
71–80	4389	213	4
>80	4380	1	0

Transplant Research (CIBMTR) in 2015 [5]. With these two numbers, the likelihood of any individual AML patient being transplanted can be easily calculated. As shown in Fig. 2, the percent of AML patients undergoing HCT is remarkably similar in every decade of life up to age 70, and thereafter drops precipitously. Whether patients are in their first, second, third or sixth decade of life, they have about a 30% chance of eventually being treated with HCT. Also, according to CIBMTR data, the source of stem cells is generally constant across age groups with around 30% for transplants being from matched siblings, 15% from other related donors, 45% from unrelated donors, 5%–10% from unrelated cord blood and 1% autografts (Table 2). The only exceptions to the constancy of donor source across age groups are an increased use of cord blood among patients below age 10 where their use makes up almost 35% of grafts, and a decrease in the use of matched related donors in the oldest age group, likely due to decreased availability of healthy, willing siblings as patients age.

3. Impact of patient age on outcome of HCT

As noted above, the median age of patients diagnosed with AML is 68. Prior to the advent of reduced intensity conditioning regimens in the late 1990's, transplantation was arbitrarily restricted to patients less than age 50–55, with little hard data to support this limit. Given the age distribution shown in Table 1, this means that only about 25% of patients with AML were in the age range for which transplantation was used. With the development of better supportive care measures and reduced intensity preparative regimens, transplants are increasingly being performed in patients in their seventh and even eighth decade of life, thus raising the question of how much does age per se influence the outcome of transplantation. A study from

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