Long-term outcomes and conditional survival after allogeneic hematopoietic cell transplantation in patients aged 70 years and older

A single-center analysis of 658 consecutive transplants with a median follow-up of 6.5 years

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STUDY AT A GLANCE

658 consecutive allo-HCT, single center, 2012–2022
44 transplants in patients ≥70 y (vs 106 aged 65–69 y)
79 months median follow-up in survivors
24-month landmark for conditional survival

Beyond two years, the threat is relapse, not toxicity.
Thirteen of the 14 non-relapse deaths occurred within 24 months, while relapse rose from 30% to 39% between 2 and 5 years.

BACKGROUND

- Allo-HCT is increasingly offered beyond 70 years of age, but published series focus on patients aged 60-69 years and rarely report beyond 2-3 years of follow-up.
- Two questions therefore remain unanswered in the clinic: what does the decade after transplantation look like, and has the risk passed for a patient who is alive and in remission at two years?
- Conditional survival answers the second question but has never been reported specifically in septuagenarians.

METHODS

- **Cohort.** 658 consecutive allo-HCTs, single center, January 2012 to December 2022. 44 procedures (6.7%) in patients aged 70 years or older, performed in 42 individuals; the 106 procedures (16.1%) in patients aged 65-69 years served as comparators.
- **Endpoints.** OS, PFS and GRFS by Kaplan-Meier; relapse, NRM and GVHD as competing risks (Aalen-Johansen, Gray test).
- **Models.** Multivariable Cox models on the whole cohort aged 65 years or older (five pre-specified covariables, 96 deaths). Landmark analysis at 24 months in patients alive and progression-free.

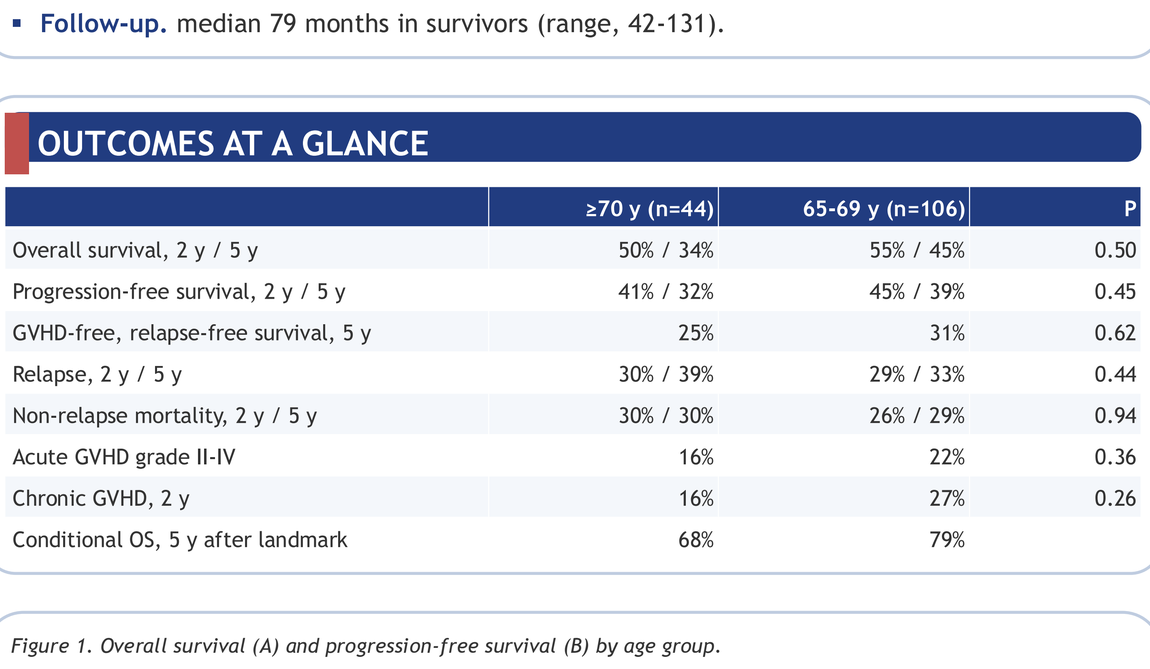
PATIENTS

- **Age.** median 72.1 years (range, 70.4-76.3); 13 patients aged 73 years or older.
- **Disease.** 89% myeloid malignancy; disease risk index high or very high in 41%; 52% not in complete remission; 34% received a sequential regimen for active disease.
- **Comorbidity.** HCT-CI 3 or more in 23%.
- **Transplant.** 61% haploidentical donors, 30% unrelated, 9% matched siblings; 93% peripheral blood; antithymocyte globulin in 89% and post-transplant cyclophosphamide in 59%.
- **Follow-up.** median 79 months in survivors (range, 42-131).

OUTCOMES AT A GLANCE

	≥70 y (n=44)	65-69 y (n=106)	P
Overall survival, 2 y / 5 y	50% / 34%	55% / 45%	0.50
Progression-free survival, 2 y / 5 y	41% / 32%	45% / 39%	0.45
GVHD-free, relapse-free survival, 5 y	25%	31%	0.62
Relapse, 2 y / 5 y	30% / 39%	29% / 33%	0.44
Non-relapse mortality, 2 y / 5 y	30% / 30%	26% / 29%	0.94
Acute GVHD grade II-IV	16%	22%	0.36
Chronic GVHD, 2 y	16%	27%	0.26
Conditional OS, 5 y after landmark	68%	79%	

Figure 1. Overall survival (A) and progression-free survival (B) by age group.



Abbreviations allo-HCT, allogeneic hematopoietic cell transplantation; OS, overall survival; PFS, progression-free survival; GRFS, GVHD-free relapse-free survival; NRM, non-relapse mortality; GVHD, graft-versus-host disease; DRI, disease risk index; HCT-CI, HCT comorbidity index; CI, confidence interval; HR, hazard ratio.

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RESULTS

34% Overall survival at 5 years
32% Progression-free survival at 5 y
78% Conditional OS 3 y after landmark
13/14 NRM deaths within 24 months

- **Survival.** In patients aged 70 years or older, OS was 50% at 2 years and 34% at 5 years, PFS 41% and 32%, and GRFS 34% and 25%. Median OS was 27 months (95% CI, 9-42).
- **Competing risks.** NRM was 30% at 2 years and unchanged at 5 years: 13 of the 14 non-relapse deaths occurred within 24 months. Over the same interval relapse rose from 30% to 39%.
- **GVHD.** Grade II-IV acute GVHD 16%, grade III-IV 7%; chronic GVHD 16% at 2 years, moderate or severe in 14%.
- **Comparison.** No endpoint differed from patients aged 65-69 years, and age was not associated with OS on multivariable analysis (HR 1.21, 95% CI 0.78-1.87). Only a high or very high disease risk index was (HR 1.99, 1.29-3.08).
- **Conditional survival.** Among the 18 patients alive and progression-free at 24 months, conditional OS was 78% three years later and 68% five years later.

Figure 2. Cumulative incidence of relapse (A) and non-relapse mortality (B) by age group.

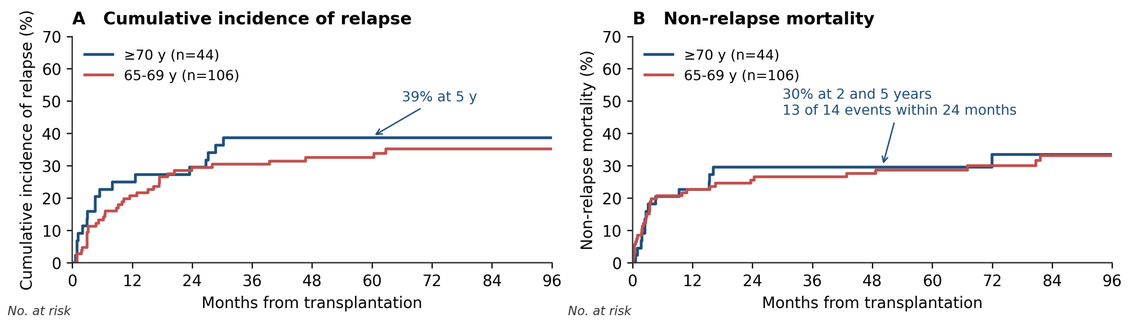
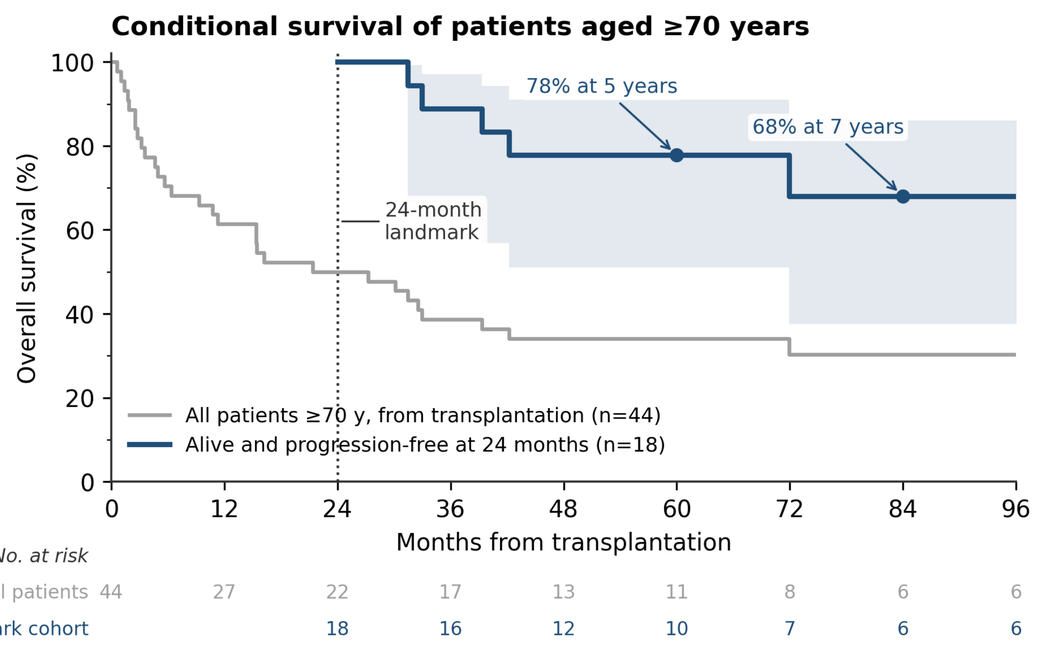


Figure 3. Conditional overall survival from the 24-month landmark.



CONCLUSIONS

- One in three patients transplanted at 70 years or older was alive five years later, despite high-risk or active disease in the majority.
- Risk was concentrated in the first two years. Beyond that point non-relapse mortality became negligible while relapse kept accruing, so the dominant late threat is disease recurrence, not toxicity.
- Two-thirds of the patients who reached the two-year mark in remission were alive five years later, a figure that belongs in follow-up consultations.
- Chronological age alone should not preclude allo-HCT. Post-transplant maintenance strategies deserve prospective evaluation in this age group.
- The study was powered to detect a hazard ratio of 1.87 or greater, so a clinically meaningful difference from patients aged 65-69 years cannot be excluded.