Open Access

OBM Transplantation

LIDSEN Publishing Inc.

Research Article

Allogeneic Hematopoietic Stem Cell Transplantation in Patients with Fanconi Anemia: Results of a Single Center with a Fludarabine-Based Conditioning Regimen

Sabrine Mekni *, Lamia Torjemane *, Malek Khayati, Dorra Belloumi, Rimmel Yosra Kanoun, Insaf Ben Yaiche, Rihab Ouerghi, Ines Turki, Saloua Ladeb, Tarek Ben Othman, Nour Ben Abdeljelil

Department of Hematology and Transplantation, National Center of Bone Marrow Transplantation, Tunis, Tunisia; E-Mails: sabrina.mekni@fmt.utm.tn; lamia_torjemane@yahoo.fr; drkhayatimalak@gmail.com; dorrabelloumi@gmail.com; yousr2008@hotmail.fr; benyaicheinsaf@gmail.com; rihabouerghi89@gmail.com; ines.turki.ba@gmail.com; ladebsaloua63@gmail.com; tarek.benothman@fmt.utm.tn; nour.abdejlil@gmail.com

* **Correspondences:** Sabrine Mekni and Lamia Torjemane; E-Mails: sabrina.mekni@fmt.utm.tn; lamia_torjemane@yahoo.fr

Academic Editor: Mobil Akhmedov

Special Issue: Allogeneic Stem Cell Transplantation in Fanconi Anemia and Pediatric Bone Marrow Failure

OBM Transplantation
2024, volume 8, issue 4
doi:10.21926/obm.transplant.2404226

Received: June 29, 2024
Accepted: October 31, 2024
Published: November 11, 2024

Abstract

Allogeneic hematopoietic stem cell transplantation (Allo-HSCT) remains the only curative treatment for bone marrow failure (BMF) and hematologic complications of Fanconi anemia (FA). The evolution remains affected by the toxicity, the risk of graft failure, and clonal evolution. This study aimed to identify factors affecting outcomes in FA patients after allo-HSCT. We included FA patients who underwent allo-HSCT between January 2006 and December 2021. The conditioning regimen was cyclophosphamide/fludarabine (Cy/Flu) ± rabbit anti-thymocyte globulin (ATG). Bone marrow was the stem cell source from HLA-matched related donors in all transplants. Twenty-three patients, 19 with BMF and 4 with MDS/clonal evolution, were included. The median age was 11 years (5–39 years). Five patients

(22%) received serotherapy with the conditioning regimen. Engraftment occurred in all patients without severe regimen-related toxicity. The 100-day cumulative incidence (CI) of grade II-IV acute GvHD (a GVHD) and 5-year CI of chronic GvHD (cGVHD) were 17% and 32%, respectively. The 5-year CI of late secondary graft failure was 10.5%. Two patients developed clonal evolution (AML; n = 2) and one patient developed nephrotic syndrome (n = 1). The 10-year overall survival (OS) and event-free survival (EFS) were 80% and 75%, respectively. There was a trend toward a better EFS in patients aged <10 years compared to patients aged ≥10 years (100% versus 61%; p = 0.06). At the last follow-up, 18 patients were alive, and 4 expired. Causes of death were infections with refractory GVHD (n = 1), graft failure (n = 2), and renal failure (n = 1). Despite the small patient population, we show excellent outcomes, particularly for those transplanted in the first decade.

Keywords
Fanconi anemia; allogeneic stem cell transplantation; outcome

1. Introduction

Fanconi anemia (FA) is a genetically and phenotypically heterogeneous recessive disorder characterized by diverse congenital malformations, progressive pancytopenia, and a predisposition to both hematologic malignancies (myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), and solid tumors [1]. Although allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the only curative option for bone marrow failure (BMF) and other hematologic complications of FA, the risk of solid tumors is still unchanged [2-4]. Over the last three decades, allo-HCT has significantly improved outcomes by optimizing conditioning regimens. Taking into account the high sensitivity of FA patients to DNA alkylating agents, toxicity-related chemotherapy had decreased by reducing the intensity of conditioning regimens by using fludarabine (FLU) and improving Graft versus host disease (GVHD) prophylaxis and supportive care [5-7]. The majority of published series described single-center experiences with small patient populations. However, a significant cohort study conducted by the European Group for Blood and Marrow Transplantation Working Party found that patients who were transplanted before the age of ten, before clonal development, from a matched family donor, and following a fludarabine based conditioning had superior outcomes [8]. Our prior findings with patients transplanted before 2005, using low-dose cyclophosphamide and busulfan as conditioning, revealed 18% and 23% rates for early graft failure and acute GVHD, respectively [9]. We switched then to a fludarabine-based conditioning program with rabbit anti-thymocyte globulin (ATG). Our study aimed to describe the short- and long-term results of allo-HSCT in FA patients.

2. Material and Methods

2.1 Patients-Donors and Inclusion Criteria

We enrolled all patients with FA who underwent allo-HSCT from an HLA-identical matched sibling donor at the Tunisian National Center of Stem Cell Transplantation from January 2006 to December

2021. Lymphocyte chromosome breaks increasing after exposure to DNA cross-linking agents confirmed the diagnosis of FA. In all cases, a molecular genetic approach involving polymerase chain reaction (PCR) amplification and reversed blot (RDB) hybridization (LiPA tests from Innogenetics) was utilized to type HLA class II on donors. All patients or legal guardians have provided informed consent for the transplant procedure and using their data for scientific research. The hospital's Institutional Committee on Hematopoietic Stem Cell Transplantation approved the study.

2.2 Data Collection and Definitions

Data were gathered from medical records on clinical characteristics at the time of transplantation (growth retardation, skin hypopigmentation, and congenital malformations…), indications for stem cell transplantation, hematological status before transplant, transplant-related data, and short- and long-term results. The severity of abnormalities was determined based on the six anatomical areas implicated. Malformations were classified as extensive if they involved at least three sites and limited if they involved fewer than three.

2.3 Transplant Procedures

A conditioning regimen based on fludarabine was administered to all patients, comprising a total dose of fludarabine 120 mg/m^2 and a total dose of cyclophosphamide 40 mg/kg. Five patients received an additional dose of anti-thymocyte globulin (ATG) because they were at high risk of graft failure (presence of specific donor HLA antibodies). Bone marrow was the stem cell source used in all patients. GVHD prophylaxis consisted of methotrexate (MTX 5 mg/m^2 on days 1, 3, and 6) and cyclosporine A (CsA) at a dosage of 3 mg/kg/day i.v. Starting on day 1. Then, when oral intake was possible, CsA was administered orally at a dosage of 6 mg/kg/day in two divided doses, with a gradual tapering throughout 12 to 18 months or longer if the presence of GVHD. Systemic monitoring of CsA levels was performed to maintain a level between 150 and 300 ng/ml. All patients received supportive care (acyclovir and fluconazole prophylaxis, growth factors, and blood products) according to local procedures [9].

2.4 End Points and Statistical Analysis

Engraftment was the first of 3 consecutive days with an absolute neutrophil count greater than 0.5×10^9/L without growth factors and unsupported platelets greater than 20×10^9/L. Primary graft failure was diagnosed if neutrophil recovery was not reached by day 30. Secondary graft failure was defined as recurrent pancytopenia with an absolute neutrophil count $<0.5 \times 10^9$/L without severe GVHD. The GVHD was graded using the Glucksberg revised criteria and the International Bone Marrow Transplant Registry (IBMTR) Severity Index [10, 11]. The c GVHD was diagnosed using published criteria [12].

Overall survival (OS) was defined as the time between the date of allo-HSCT and the date of last patient contact. Event-free survival (EFS) was defined as the time between the date of allo-HSCT and the event (graft failure, secondary malignancy, or leukemia transformation). The probability of survival was calculated using the Kaplan-Meier method. The cumulative incidence (CI) of secondary graft failure and aGVHD and c GVHD were estimated by competing risk function [13]. Kaplan-Meier curves were used to calculate the effect of independent categorical variables on survival. Chi-square

or Fisher's exact tests were used to compare categorical variables. $P \leq 0.05$ was considered to indicate a significant association. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 25.0.

3. Results

3.1 Study Cohort

Twenty-three patients were included (14 females and 9 males). Characteristics of the patients and transplant procedures are summarized in Table 1.

Table 1 Characteristics of patients and transplant procedures.

Covariates	**No (%)**
Age at diagnosis (years, median, range)	10 (5-35)
Age at transplant (years, median, range)	11 (5-39)
Recipient Gender	
Male	9
Female	14
Malformative syndrome	
Yes	21 (91%)
No	2 (9%)
Indication of allo-HSCT	
Bone marrow failure	19 (83%)
Cytogenetic clonal abnormalities	3 (13%)
Myelodysplastic Syndrome	1 (4%)
Pre-transplant status	
Absolute neutrophil count, median × 10^3/L (range)	0.7 (0.3-2)
Hemoglobine, median g/dl (range)	6.8 (2.6-12.8)
Platelet count, median × 10^3/L (range)	23 (3-110)
Infection before transplant	0
Untransfused/transfused patients	7/17
No. of Transfusions prior to allo-HSCT	
Red blood transfusion units	3 (0-15)
Platelet transfusion units	2 (0-11)
Androgen therapy before transplant, yes/no	3/20 (13%)
Donor/recipient Sex	
Female/male	5 (21%)
Others	19 (79%)
ABO compatibility	
Major	4 (17%)
Minor	5 (22%)
Compatible	14 (61%)
Conditioning regimen	
Fludarabine - Cyclosphophamide	18 (78%)

Fludarabine - Cyclophosphamide - ATG	5 (22%)

The median age at diagnosis was 10 years (range 5–35). The median age at the time of transplant was 11 years (range: 5–39), and the median time from diagnosis to transplant was 8 months (range: 2–147). Twenty-one (91%) patients had malformation syndrome. Kidney and urogenital tract malformations were found in 11 (47%) of patients. Indications of transplant were BMF in 19 (83%) patients and clonal evolution in 3 (13%) patients. Abnormalities were: 46, XX karyotype with t (1;9) (n = 1); 46, XX karyotype with +21 and -7 (n = 1); and 45, XX with -7 (n = 1). Only one patient was transplanted with myelodysplastic syndrome with complex cytogenetic abnormalities. Seventeen patients (74%) were transfused before transplantation with a median of 5 units of blood products (range: 1-22). Before allo-HSCT, the median neutrophil count was 0.71×10^3 (0.290-20), and the median platelet count was 23×10^3 (30-1100). The median number of nucleated cell doses infused per kilogram of recipient body weight was 2.93×10^8 (range; 0.8-6.5).

3.2 Short –Term Outcome

Engraftment occurred in all patients. The median time to neutrophil and platelet engraftment were 12 days (range: 10–18) and 14 days (range: 9-21), respectively. Peripheral blood karyotype analysis showed mixed cytogenetic chimerism in 46% of patients.

3.2.1 Regimen-Related Toxicity (RRT)

Mucositis grade 3 requiring morphine occurred in 14 (61%) patients. Liver dysfunction (transient elevation of liver enzymes) occurred in eight patients (35%), mainly after methotrexate administration, without veno-occlusive disease criteria. Acute renal injury grade 0-2, according to the AKIN classification, with increased creatinine less than twice the basal level, occurred in seven patients (30%). Causes of transient acute renal failure were nephrotoxic drugs such as antibiotics or calcineurin inhibitors (n = 6). Two patients developed CsA-induced thrombotic microangiopathy (TMA) and PRESS syndrome, respectively. CsA withdrawal and its replacement by mycophenolate mofetil (MMF) were indicated for the two patients (8.2%). One patient developed acute pancreatitis (n = 1). No other severe toxicities related to cyclophosphamide, such as hemorrhagic cystitis, were observed. There were no deaths related to chemotherapy. The main complications are summarized in Table 2.

Table 2 Complications following allogenic Stem Cell Transplantation.

Type of complication	**N**
Stomatitis requiring morphine	14
Liver Dysfunction without VOD	8
Acute kidney Injury (grade 0-2)	7
Veno-Occlusive Disease (VOD)	0
Pancreatitis	1
Calcineurin Induced TMA	1
PRESS Syndrome	1
Hemorrhagic Cystitis	0

3.2.2 Infections

Febrile neutropenia occurred in all transplants. Bacteremia was documented in only three (13%) patients, and it was gram-positive infections (n = 3). Cytomegalovirus reactivation occurred in four (17%) patients, of whom one patient had underlying severe GVHD and was on systemic corticosteroids. Two patients (9%) developed probable pulmonary aspergillosis. Two patients developed an EBV infection.

3.2.3 Graft-Versus-Host Disease

Grade 2-3 aGVHD occurred in three (13%) patients. The CI of aGVHD was 17% (Figure 1). It was refractory in one patient, leading to his death. In univariate analysis, the occurrence of aGVHD was independent of age (<10 or ≥10 years) (p = 0.7), major ABO incompatibility (p = 0.33), conditioning including ATG or not (p = 0.12), and infection (p = 0.6). Acute GVHD was significantly associated with sex mismatch of donor-recipient (p = 0.018). The CI of c GVHD was 32% at 10 years (Figure 2). It was mainly mild (n = 5) and moderate in only one patient, respectively. None of the factors studied for the occurrence of a GVHD was associated with the occurrence of cGVHD.

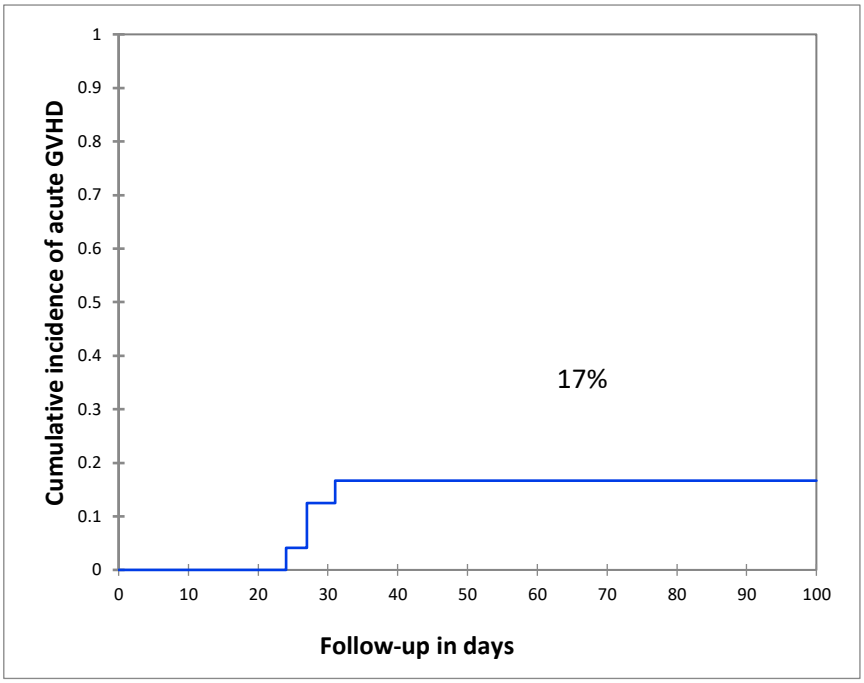

Figure 1 Cumulative incidence of acute GVHD.

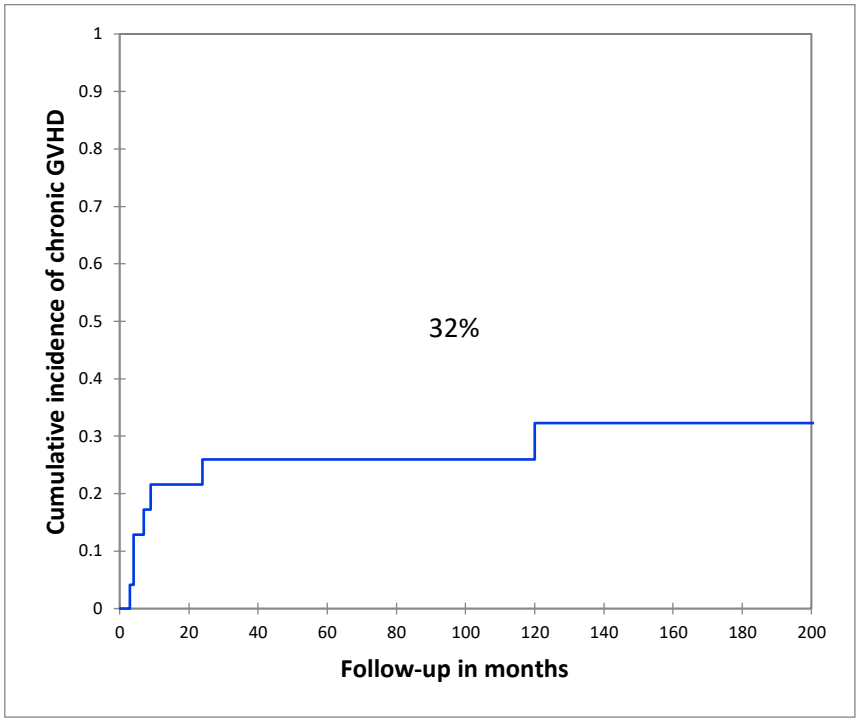

Figure 2 Cumulative incidence of chronic GVHD.

3.3 Long-Term Outcome

3.3.1 Graft Failure

Two patients (one with initially BMF and one with MDS) developed late secondary graft failure, 3 and 5 years after transplant, respectively. The CI of secondary graft failure was 10.5% at 10 years (Figure 3). Graft failure was not associated with age ($p = 0.3$), sex mismatch ($p = 0.45$), ABO major incompatibility ($p = 0.2$), conditioning regimen ($p = 0.45$), clonal abnormalities ($p = 0.37$), aGVHD and c GVHD ($p = 0.5$ and 0.55, respectively).

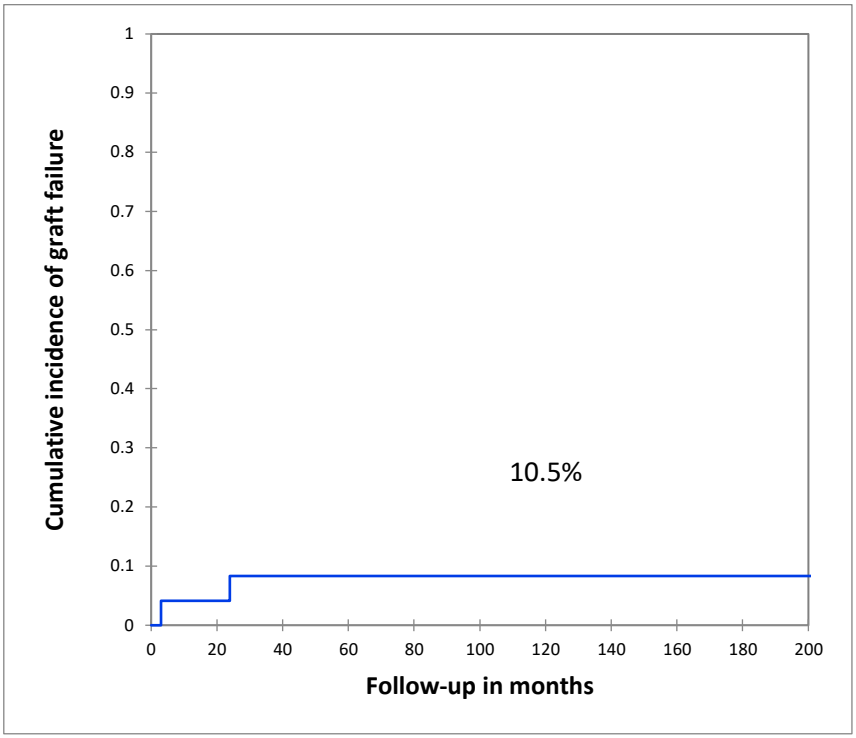

Figure 3 Cumulative incidence of Graft failure.

3.3.2 Clonal Evolution

Clonal evolution to acute myeloid leukemia (AML) occurred in two (8.6%) patients after 32 and 69 months, respectively.

3.3.3 Late Renal Complications

One patient, without initial renal malformations, developed late renal complications, including nephrotic syndrome, and died of renal failure. The main complications were summarized in Table 2.

3.4 Survival Outcomes

After a median follow-up of 120 months (range; 3-242), 19 patients were alive, and 4 patients died. Causes of death were infection associated with refractory GVHD (n = 1), graft failure (n = 2), and renal failure (n = 1). The 10-year overall survival (OS) and event-free survival (EFS) were 80% and 75%, respectively (Figure 4 and Figure 5). In univariate analysis for OS and EFS, clinical abnormalities, time from diagnosis to transplant, conditioning regimen, a GVHD, or c GVHD were not significant predictors. There was a trend towards a better EFS in patients aged <10 years at transplant (100% vs. 61%, respectively; p = 0.06) (Figure 6 and Figure 7).

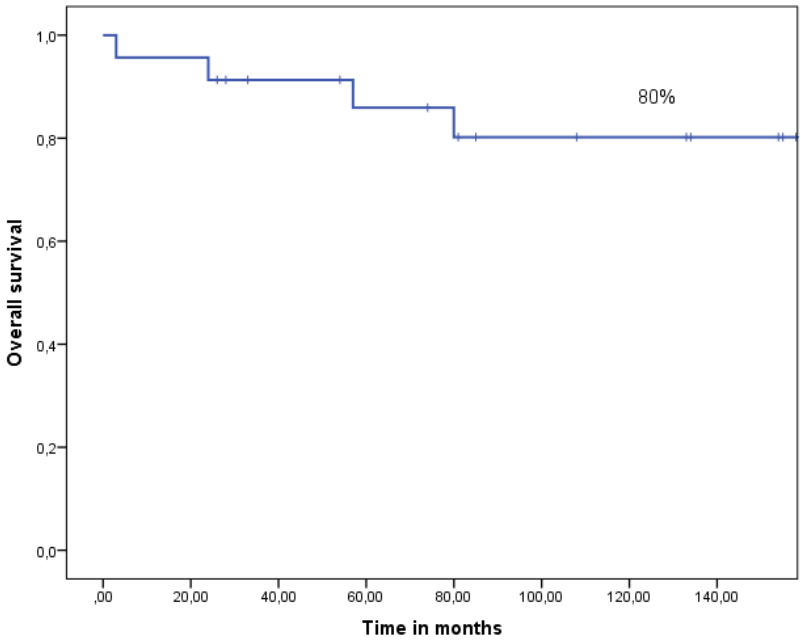

Figure 4 The 10-year Overall survival.

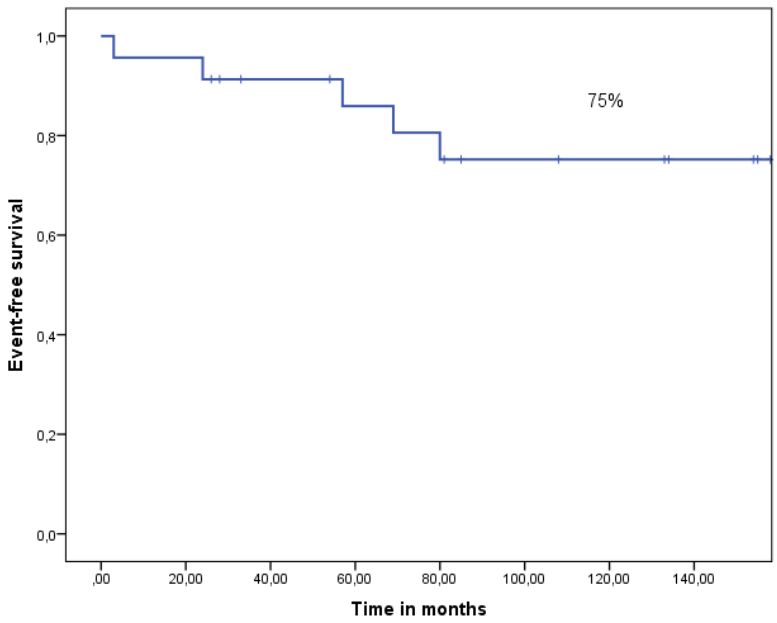

Figure 5 The 10-year Event free survival.

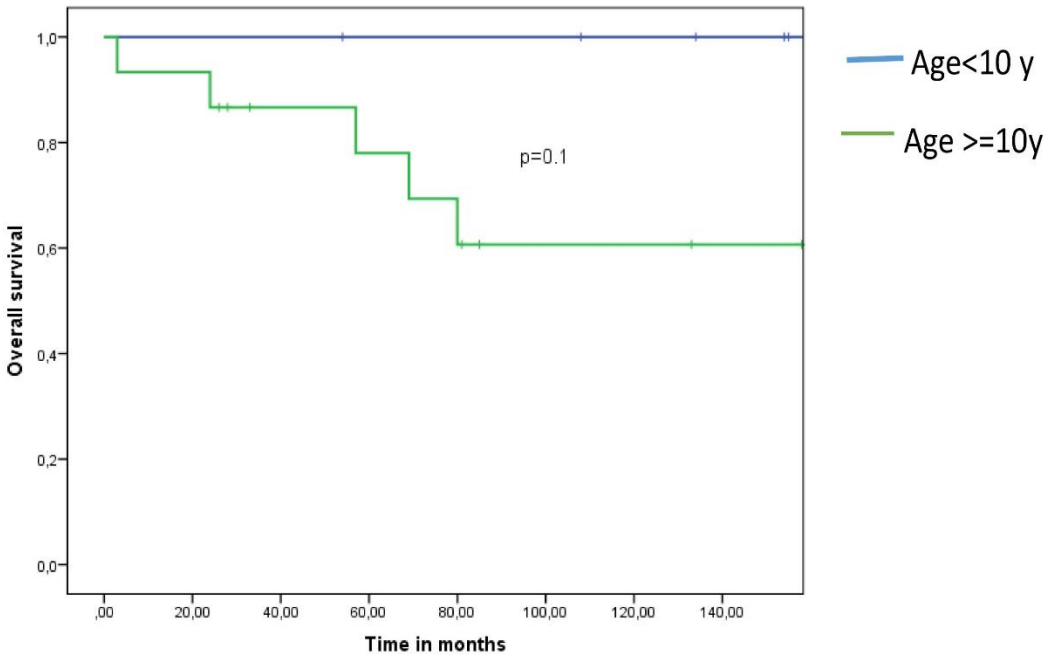

Figure 6 Overall survival according to age.

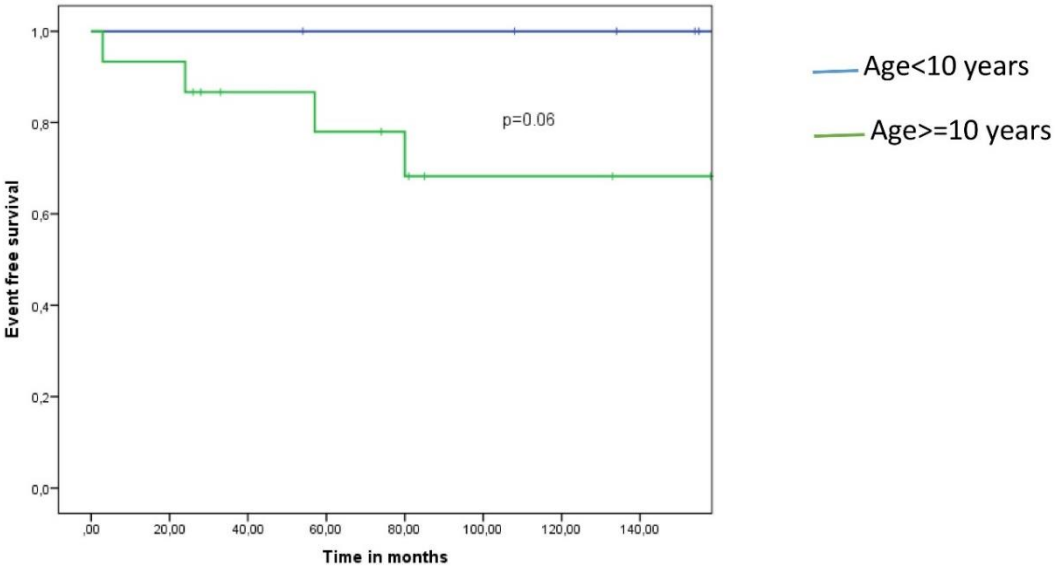

Figure 7 Event-free survival according to age.

4. Discussion

The particular characteristics of our cohort were the presence of malformation syndrome in young children with FA, as well as 47% of renal and/or urinary tract abnormalities.

The main indications for transplantation were bone marrow failure (n = 19), Clonal hematopoiesis with myelodysplastic feature (n = 1), or cytogenetic abnormalities (n = 3). All transplants were done from HLA-matched related donors with bone marrow. A fludarabine-based conditioning regimen resulted in long-term engraftment with mild toxicity in all patients. This regimen improved outcomes in patients with FA, as observed in prior studies [14-18]. The most extensive multicenter study by the European Society for Blood and Marrow Transplantation (EBMT),

including 795 patients transplanted with FA, reported better outcomes for patients transplanted before the age of 10 years, before clonal evolution (i.e., myelodysplastic syndrome or acute myeloid leukemia), from a matched family donor, after a conditioning regimen without irradiation but including fludarabine [8].

Our study added ATG to the conditioning regimen to reduce the risk of primary graft failure in heavily transfused patients with anti-HLA immunization (n = 5). The role of ATG, as in vivo T cell depletion, was to improve engraftment and reduce the incidence of acute and chronic GVHD both in the setting of matched family donors (MRD) as well as in matched unrelated donors (MUD) [7, 15, 19, 20]. Our study omitted busulfan (BU) from the conditioning regimen. The Consensus of German Transplant Centers (CGTC) on HSCT in FA patients also recommended omitting busulfan for low-risk patients defined as cytopenia without evidence of leukemia or cytogenetic aberrations and with an HLA identical donor (i.e., ≥9/10 MSD, MRD, or MUD). However, BU is recommended to facilitate engraftment in patients with mismatched/haplo-identical allografts (<9/10) and as an anti-leukemic agent in patients with bone marrow clonal aberrations and/or MDS/AML. The intravenous formulation is preferred due to its more consistent blood levels after pharmacological monitoring [21].

In our study, the CI of a GVHD and mortality related to severe forms was 17% and 4%, respectively. A lower prevalence of severe GVHD in patients who received the fludarabine-based conditioning was reported [2, 15, 20]. The cumulative incidence of cGVHD was 32% but lower (13%) in our other studies [8, 15, 21, 22]. These different results may be explained by the heterogeneity of the patient population and the use of heterogeneous strategies for GVHD prophylaxis. ATG(s) and alemtuzumab have also been applied as in vivo T cell-depleting agents in FA allo-HSCT to boost engraftment and reduce the incidence and severity of acute and chronic GVHD [23]. To reduce the risk of GVHD, the CGTC recommended in vivo T cell depletion in all FA patients, even those transplanted from an MSD. Alemtuzumab is superior to ATG in FA patients because of its better GVHD prophylactic effect. CSA (day −1 until day +100, then taper) is still employed for GVHD prophylaxis. MMF is added to CSA for unrelated donors only. The continuation or tapering of CSA and MMF depends on the presence or absence of GVHD [21]. In our study, the historical use of methotrexate in GVHD prophylaxis seems to maintain inevitable toxicity (liver, kidneys, and mucosa) without tangible benefits. Thus, GVHD prophylaxis needs to be adapted to avoid an additional risk of interacting with the primary biological defect of FA (i.e., DNA repair processes).

The long-term outcome of our cohort was still affected by other complications, such as clonal evolution with AML (n = 2). FA patients have a markedly higher risk of malignancy, particularly squamous cell carcinomas of the aero esophageal and anogenital tracts, in addition to MDS and AML [3, 4, 24]. GVHD may contribute to epithelioid malignancies. The use of peripheral blood stem cells was strongly associated with secondary cancer. This result is important enough to consider marrow as this population's recommended source of stem cells. Older age was identified by itself as an independent risk factor for secondary cancer [8]. Two patients developed impure nephrotic syndrome (NS) after allo-HSCT with graft failure (n = 1), cGVHD (n = 1), and rapid evolution to renal failure. NS is a rare manifestation of GVHD. Monitoring renal function and kidney biopsy are essential tools for obtaining information about renal pathology and guiding specific treatment [25, 26].

In our study, the 10-year overall survival (OS) and event-free survival (EFS) were 80% and 75%, respectively. Age ≥10 years at the time of transplant seems to be a negative predictor for EFS. Similar

results were reported by single-center and multicenter studies with fludarabine-based conditioning for FA patients [6, 8, 17, 27] but for a shorter follow-up period. Bernard et al. reported an OS of 85.4% with matched-related donors in FA [28]. Also, in a large cohort of 813 patients transplanted for Fanconi anemia, the 5-year OS and EFS were 83% and 78%, respectively, and age ≥ 10 years was an independent factor for worse EFS [29]. Other factors were negative predictors for OS: indication for transplant (BMF vs. MDS/AML), HLA mismatch, conditioning including irradiation, year of transplant, and ex vivo T cell depletion [22].

Our study has limitations: a small sample size of patients, which could be attributed to the disease's rarity. Furthermore, because this is a retrospective research, we had several missing documented data points for some patients. However, the main strength of our study was the long-term follow-up. We conclude with three critical points. First, flu-based protocols are strongly recommended for allogeneic transplantation for FA, which reduces graft failure incidence and severity of GVHD and improves OS with an acceptable toxicity profile. Second, adding ATG, as in vivo T cell depletion, may reduce acute and chronic GVHD incidence and severity. Third and finally, both conditioning regimens and GVHD prophylaxis need to be adapted to the risk factors of each patient taking into account their toxicity and benefits.

Author Contributions

Dr Mekni and Dr Torjemane: writing and editing. Dr Khayati: data collection. All other authors: reviewing and editing.

Competing Interests

The authors have declared that no competing interests exist.

References

1. Auerbach AD. Fanconi anemia and its diagnosis. Mutat Res. 2009; 668: 4-10.
2. Schifferli A, Kühne T. Fanconi anemia: Overview of the disease and the role of hematopoietic transplantation. J Pediatr Hematol Oncol. 2015; 37: 335-343.
3. Rosenberg PS, Socié G, Alter BP, Gluckman E. Risk of head and neck squamous cell cancer and death in patients with Fanconi anemia who did and did not receive transplants. Blood. 2005; 105: 67-73.
4. Rizzo JD, Curtis RE, Socié G, Sobocinski KA, Gilbert E, Landgren O, et al. Solid cancers after allogeneic hematopoietic cell transplantation. Blood. 2009; 113: 1175-1183.
5. Kapelushnik J, Or R, Slavin S, Nagler A. A fludarabine-based protocol for bone marrow transplantation in Fanconi's anemia. Bone Marrow Transplant. 1997; 20: 1109-1110.
6. Aker M, Varadi G, Slavin S, Nagler A. Fludarabine-based protocol for human umbilical cord blood transplantation in children with Fanconi anemia. J Pediatr Hematol Oncol. 1999; 21: 237-239.
7. Socié G, Schmoor C, Bethge WA, Ottinger HD, Stelljes M, Zander AR, et al. Chronic graft-versus-host disease: Long-term results from a randomized trial on graft-versus-host disease prophylaxis with or without anti–T-cell globulin ATG-Fresenius. Blood. 2011; 117: 6375-6382.

8. Peffault de Latour R, Porcher R, Dalle JH, Aljurf M, Korthof ET, Svahn J, et al. Allogeneic hematopoietic stem cell transplantation in Fanconi anemia: The European Group for Blood and Marrow Transplantation experience. Blood. 2013; 122: 4279-4286.
9. Torjemane L, Ladeb S, Ben Othman T, Abdelkefi A, Lakhal A, Ben Abdeladhim A. Bone marrow transplantation from matched related donors for patients with Fanconi anemia using low-dose busulfan and cyclophosphamide as conditioning. Pediatr Blood Cancer. 2006; 46: 496-500.
10. Przepiorka D, Weisdorf D, Martin P, Klingemann HG, Beatty P, Hows J, et al. 1994 consensus conference on acute GVHD grading. Bone Marrow Transplant. 1995; 15: 825-828.
11. Rowlings PA, Przepiorka D, Klein JP, Gale RP, Passweg JR, Henslee-Downey PJ, et al. IBMTR Severity Index for grading acute graft-versus-host disease: Retrospective comparison with Glucksberg grade. Br J Haematol. 1997; 97: 855-864.
12. Lee SJ. Classification systems for chronic graft-versus-host disease. Blood. 2017; 129: 30-37.
13. Gooley TA, Leisenring W, Crowley J, Storer BE. Estimation of failure probabilities in the presence of competing risks: New representations of old estimators. Stat Med. 1999; 18: 695-706.
14. Ayas M, Al-Jefri A, Al-Seraihi A, Elkum N, Al-Mahr M, El-Solh H. Matched-related allogeneic stem cell transplantation in Saudi patients with Fanconi anemia: 10 year's experience. Bone Marrow Transplant. 2008; 42: S45-S48.
15. Stepensky P, Shapira MY, Balashov D, Trakhtman P, Skorobogatova E, Rheingold L, et al. Bone marrow transplantation for Fanconi anemia using fludarabine-based conditioning. Biol Blood Marrow Transplant. 2011; 17: 1282-1288.
16. Smetsers SE, Smiers FJ, Bresters D, Sonnevelt MC, Bierings MB. Four decades of stem cell transplantation for Fanconi anaemia in the Netherlands. Br J Haematol. 2016; 174: 952-961.
17. Chattopadhyay S, Lionel S, Selvarajan S, Devasia AJ, Korula A, Kulkarni U, et al. Fludarabine-based low-intensity conditioning for Fanconi anemia is associated with good outcomes in aplastic anemia but not in MDS-A single-center experience. Mediterr J Hematol Infect Dis. 2023; 15: e2023039.
18. Xu L, Lu Y, Chen J, Sun S, Hu S, Wang S, et al. Fludarabine- and low-dose cyclophosphamide-based conditioning regimens provided favorable survival and engraftment for unmanipulated hematopoietic cell transplantation from unrelated donors and matched siblings in patients with Fanconi anemia: Results from the CBMTR. Bone Marrow Transplant. 2023; 58: 106-108.
19. Tan PL, Wagner JE, Auerbach AD, Defor TE, Slungaard A, Macmillan ML. Successful engraftment without radiation after fludarabine-based regimen in Fanconi anemia patients undergoing genotypically identical donor hematopoietic cell transplantation. Pediatr Blood Cancer. 2006; 46: 630-636.
20. Finke J, Bethge WA, Schmoor C, Ottinger HD, Stelljes M, Zander AR, et al. Standard graft-versus-host disease prophylaxis with or without anti-T-cell globulin in haematopoietic cell transplantation from matched unrelated donors: A randomised, open-label, multicentre phase 3 trial. Lancet Oncol. 2009; 10: 855-864.
21. Chao MM, Ebell W, Bader P, Beier R, Burkhardt B, Feuchtinger T, et al. Consensus of German transplant centers on hematopoietic stem cell transplantation in Fanconi anemia. Klin Padiatr. 2015; 227: 157-165.
22. Cancio M, Troullioud Lucas AG, Bierings M, Klein E, de Witte MA, Smiers FJ, et al. Predictors of outcomes in hematopoietic cell transplantation for Fanconi anemia. Bone Marrow Transplant. 2024; 59: 34-40.

23. Soiffer RJ, Lerademacher J, Ho V, Kan F, Artz A, Champlin RE, et al. Impact of immune modulation with anti-T-cell antibodies on the outcome of reduced-intensity allogeneic hematopoietic stem cell transplantation for hematologic malignancies. Blood. 2011; 117: 6963-6970.
24. Ebens CL, MacMillan ML, Wagner JE. Hematopoietic cell transplantation in Fanconi anemia: Current evidence, challenges and recommendations. Expert Rev Hematol. 2017; 10: 81-97.
25. Beyar-Katz O, Davila EK, Zuckerman T, Fineman R, Haddad N, Okasha D, et al. Adult nephrotic syndrome after hematopoietic stem cell transplantation: Renal pathology is the best predictor of response to therapy. Biol Blood Marrow Transplant. 2016; 22: 975-981.
26. Wong E, Lasica M, He SZ, Bajel A, Roberts AW, Mason KD, et al. Nephrotic syndrome as a complication of chronic graft-versus-host disease after allogeneic haemopoietic stem cell transplantation. Intern Med J. 2016; 46: 737-741.
27. George B, Mathews V, Shaji RV, Srivastava V, Srivastava A, Chandy M. Fludarabine-based conditioning for allogeneic stem cell transplantation for multiply transfused patients with Fanconi's anemia. Bone Marrow Transplant. 2005; 35: 341-343.
28. Bernard F, Uppugunduri CR, Meyer S, Cummins M, Patrick K, James B, et al. Excellent overall and chronic graft-versus-host-disease-free event-free survival in Fanconi anaemia patients undergoing matched related-and unrelated-donor bone marrow transplantation using alemtuzumab–Flu–Cy: The UK experience. Br J Haematol. 2021; 193: 804-813.
29. Lum SH, Samarasinghe S, Eikema DJ, Piepenbroek B, Dalissier A, Ayas M, et al. Outcome of haematopoietic cell transplantation in 813 children with Fanconi anaemia: A study on behalf of the EBMT severe aplastic anaemia working party and paediatric disease working party. Blood. 2022; 140: 657-659.