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RESEARCH ARTICLE

Endocrine Complications in Long-Term Survivors of Allogeneic Hematopoietic Stem Cell Transplantation: Prevalence and Risk Factors

Allojenik Hematopoetik Kök Hücre Nakli Sonrası Uzun Dönem Sağ Kalan Hastalarda Endokrin Komplikasyonlar: Sıklık ve Risk Faktörleri

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ABSTRACT

Objective: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) offers a potentially curative treatment for a range of hematologic disorders. However, long-term survivors of the treatment are increasingly affected by late-onset complications, particularly endocrine dysfunction, which considerably impair quality of life. This study aimed to establish the prevalence and risk factors of late endocrine complications in patients who survived at least 1 year without disease following allo-HSCT.

Materials and Methods: We conducted a retrospective cohort analysis of 79 recipients of allo-HSCT at a single tertiary referral center. Patients with disease relapse or those who died within the first year after allo-HSCT were excluded. Data on demographic and transplant characteristics, graft-versus-host disease, immunosuppressive therapy, and endocrine outcomes were analyzed. Patients with such conditions before transplantation were excluded from the corresponding outcome analyses. Risk factors were evaluated using statistical methods.

Results: The median follow-up duration was 38 months. New-onset endocrine complications were observed in a substantial proportion of patients: dyslipidemia (77.3%), osteopenia or osteoporosis (58.2%), hypogonadism (27.8%), thyroid dysfunction (hypothyroidism or hyperthyroidism: 36.2%), and hypertension (33.5%). Significant risk factors included female sex, corticosteroid exposure, short-term cyclosporine use, and acute graft-versus-host disease. Avascular necrosis was detected in 13.9% of patients and associated with bisphosphonate, mycophenolate mofetil, and steroid use.

Conclusion: Endocrine complications are highly prevalent among patients who have survived beyond 1 year after allo-HSCT. Regular and comprehensive endocrine surveillance is essential, particularly in patients with specific risk factors. Early identification and management of these complications could improve quality of life in this patient population.

Keywords: Allogeneic stem cell transplantation, endocrine complications, graft-versus-host disease

ÖZET

Amaç: Allojenik hematopoietik kök hücre nakli (AKHN), çeşitli hematolojik hastalıklar için potansiyel olarak küratif bir tedavi seçeneğidir. Ancak uzun dönem sağ kalan hastalar, yaşam kalitesini belirgin şekilde bozabilen geç başlangıçlı komplikasyonlardan, özellikle endokrin disfonksiyonlardan, giderek daha fazla etkilenmektedir. Bu çalışmanın amacı, AKHN sonrası en az bir yıl hastalıksız sağ kalan hastalarda geç dönem endokrin komplikasyonların sıklığını ve risk faktörlerini belirlemektir.

Gereç ve Yöntemler: Tek bir üçüncü basamak merkezde AKHN uygulanmış 79 hastayı içeren retrospektif bir kohort analizi yapıldı. Nakil sonrası ilk yıl içinde hastalık nüksü gelişen ve kaybedilen hastalar çalışmaya dahil edilmedi. Demografik ve nakille ilişkili özellikler, graft-versus-host hastalığı, immünsüpresif tedaviler ve endokrin sonuçlara ait veriler analiz edildi. Nakil öncesinde ilgili endokrin hastalığı bulunan hastalar, ilgili endokrin komplikasyon gelişim risk analizlerinden dışlandı. Risk faktörleri tek değişkenli istatistiksel yöntemlerle değerlendirildi.

Bulgular: Medyan takip süresi 38 aydı. Yeni gelişen endokrin komplikasyonlar hastaların önemli bir kısmında saptandı: dislipidemi (%77.3), osteopeni/osteoporoz (%58.2), hipogonadizm (%27.8), tiroid disfonksiyonu (hipotiroidi veya hipertiroidi: %36.2) ve hipertansiyon (%33.5). Anlamlı risk faktörleri arasında kadın cinsiyet, kortikosteroid maruziyeti, kısa süreli siklosporin kullanımı ve akut graft-versus-host hastalığı yer aldı. Avasküler nekroz %13.9 oranında saptandı ve bifosfonat, mikofenolat mofetil ve steroid kullanımı ile ilişkili bulundu.

Sonuç: Endokrin komplikasyonlar, uzun dönem AKHN sağ kalanlarında oldukça yaygındır. Özellikle belirli risk faktörlerine sahip hastalarda düzenli ve kapsamlı endokrin izlem büyük önem taşımaktadır. Bu komplikasyonların erken tanınması ve yönetimi, bu hasta grubunda yaşam kalitesini artırabilir.

Anahtar Kelimeler: Allojenik kök hücre nakli, endokrin komplikasyonlar, graft-versus-host hastalığı

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INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potentially curative treatment for various malignant and non-malignant hematological disorders (1, 2). Enhancements in transplant techniques and supportive care have markedly improved survival rates (1, 2). Nonetheless, patients who survive long-term after allo-HSCT encounter late complications, particularly endocrine dysfunctions that can remain for many years post-transplantation (2, 3). Various endocrine complications, such as thyroid problems, infertility, growth retardation, metabolic syndrome and bone disorders have been observed in patients who have received allo-HSCT (2, 4). Many risk factors, including the use of immunosuppressive medications, ongoing graft-versus-host disease (GVHD), exposure to glucocorticoids, and therapies administered before transplant (eg, total body irradiation: TBI), are associated with these complications (2–5). Recent studies indicate that endocrine sequelae can affect up to 60% of long-term allo-HSCT survivors, resulting in heightened morbidity and diminished quality of life (2, 4).

In pediatric and young adult populations, these issues further affect growth, pubertal development, fertility, and psychosocial wellbeing (4, 5). However, despite increased awareness, standardized guidelines for long-term endocrine surveillance in allo-HSCT recipients remain absent. In this context, our study aimed to evaluate the prevalence and risk factors of late-onset endocrine complications in patients who survived at least 1 year without disease following allo-HSCT. By identifying high-risk categories and prevalent endocrine sequelae, we aimed to facilitate the formulation of effective follow-up techniques and early treatments to improve long-term outcomes.

MATERIALS AND METHODS

Design and Participants:

This retrospective, observational cohort study was performed at a tertiary referral center. The 10-year medical data of patients who underwent allo-HSCT was systematically reviewed. The eligibility criteria were: (a) having received allo-HSCT, (b) disease-free survival for a minimum of 12 months post-transplant, and (c) the availability of comprehensive clinical and laboratory follow-up records. The exclusion criteria were the recurrence or mortality within the first year after transplantation. Between December 2003, and September 2012, a total of 520 HSCTs were performed for 474 patients at our center. Among these procedures, 275 were allo-HSCTs and 245 were autologous HSCTs. For the purposes of our study, only allo-HSCT recipients who survived at least 1 year without disease relapses were considered eligible. After exclusions, 79 allo-HSCT recipients met the inclusion criteria and constituted the study cohort. Endocrine complications were defined using international guidelines. Obesity was classified as a body mass index (BMI) ≥30 kg/m^2. Diabetes was diagnosed according to the American Diabetes Association 2010 criteria (ie, fasting plasma glucose ≥126 mg/dL, random glucose ≥200 mg/dL, or HbA1c ≥6.5%). Hypertension was defined according to the Joint National Committee 7 criteria as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or the use of antihypertensive medication. Metabolic syndrome and dyslipidemia were classified according to the International Diabetes Federation criteria. Thyroid dysfunction was diagnosed according to the Turkish Endocrinology and Metabolism Society guidelines based on abnormal thyroid-stimulating hormone and thyroid hormone levels. Bone metabolism disorders were defined according to World Health Organization criteria based on bone mineral density measurements (T-score or Z-score). Gonadal dysfunction was diagnosed based on clinical symptoms and abnormal sex hormone levels.

Patients with pre-existing endocrine disorders were not excluded from the overall cohort description. However, for each specific endocrine outcome analysis, patients with the condition before transplantation were excluded to allow for the evaluation of de novo post-transplant complications. The date of diagnosis of the endocrine disorder was considered the event time for time-to-event analyses. Pre-transplant bone mineral density and gonadal function assessments were not available; therefore, the onset of obesity, osteoporosis, osteopenia, or hypogonadism was assessed using post-transplantation measurements. Annual bone mineral density results obtained after transplantation were used to determine the presence of low bone density. Demographic data (eg, age and sex), transplant-related variables (eg, underlying diagnosis, conditioning regimen, donor type, and TBI use), and post-transplant clinical parameters (eg, acute and chronic GVHD, immunosuppressive therapies, and endocrine follow-up records) were obtained from the institutional database and patient files. Conditioning regimens were categorized as myeloablative or non-myeloablative, and TBI exposure was recorded for all patients.

Ethical Approval:

This retrospective study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the institutional ethical committee (SBE-07/2013-58). The ethics committee waived the need for individual informed consent because of the retrospective nature of the study that used anonymized patient data. The study strictly protected the privacy of the patients.

Statistical Analysis:

Statistical analyses were performed using SPSS software version 16.0 (IBM Corp, Armonk, NY, USA). Continuous variables were assessed for normality using histograms, Q–Q plots and Kolmogorov–Smirnov or Shapiro–Wilk tests. Variables with a normal distribution were expressed as mean ± standard deviation, whereas non-normally distributed variables were presented as median with minimum and maximum values. Categorical variables were summarized as frequencies and percentages. Comparisons between categorical variables were performed using the Chi-squared (χ^2) test or Fisher's exact test, where appropriate. Comparisons of non-normally distributed continuous variables between two independent groups were performed using the Mann–Whitney U test.

Time-to-event analyses were performed for each endocrine outcome using survival analysis methods. Event was defined as post-transplant development of the endocrine complication. Time was measured from the date of allo-HSCT (day 0) to the first documented diagnosis, or to the date of last follow-up in patients without the event. Time-to-event distributions were estimated using the Kaplan–Meier method, risk factors were evaluated using Cox's proportional hazards regression, and results were expressed as hazard ratios (HRs) with 95% confidence intervals (CIs). A two-sided p-value of <0.05 was deemed statistically significant.

Because the retrospective dataset lacked complete documentation of GVHD severity and organ involvement, GVHD was analyzed as a binary variable, indicating its presence or absence. The duration of cyclosporine A (CsA) treatment in months, served as the continuous variable in Cox's regression models. Tacrolimus was not administered to this particular cohort. Univariable Cox's regression analyses were performed for each endocrine outcome to evaluate potential risk factors, including age, sex, the presence of acute and chronic GVHD, the duration of CsA exposure, the use of corticosteroids after transplantation, and the use of mycophenolate mofetil. Since the study cohort was retrospectively derived from a dataset originally designed in 2013 and as several endocrine outcomes had limited event numbers, multivariable analyses were not performed to avoid model overfitting. Therefore, risk factor assessment was based on univariable Cox's regression analyses.

RESULTS

A total of 79 patients who underwent allo-HSCT and survived at least 1 year without disease relapse were included in the study. The median age at transplantation was 27 years (15–64 years), and 30.4% were female. The median follow-up duration was 38 months (11–98 months). Baseline demographic and transplant-related characteristics, including conditioning regimen intensity and TBI exposure, are summarized in Table 1. Overall Incidence of Endocrine Complications During Follow-up Endocrine complications were common among long-term survivors. The most frequent complications were

Table 1. Baseline characteristics of patients

Characteristic	n=79
Sex, n (%)	
Female	24 (30.4%)
Male	55 (69.6%)
Median age, years (range)	27 (15–64)
Primary diagnosis, n (%)	
Acute myeloid leukemia	31 (39.2%)
Aplastic anemia	15 (19.0%)
Acute lymphoblastic leukemia	14 (17.5%)
Myelodysplastic syndrome	4 (5.1%)
Non-Hodgkin's lymphoma	3 (3.8%)
Others	12 (15.4%)
Pre-transplant radiotherapy, n (%)	7 (8.9%)
Conditioning regimen, n (%)	
Myeloablative	52 (65.8%)
Non-myeloablative	27 (34.2%)
Total body irradiation-based regimen, n (%)	14 (17.7%)
Donor type, n (%)	
Matched related donor	70 (88.6%)
Mismatched related donor	3 (3.8%)
Matched unrelated donor	2 (2.5%)
Mismatched unrelated donor	4 (5.1%)
Graft-versus-host disease prophylaxis regimen, n (%)	
Cyclosporin A + methotrexate	74 (93.7%)
Cyclosporin A + mycophenolate mofetil	5 (6.3%)
Median follow-up duration, months (range)	38 (11–98)
Pre-transplant endocrine diseases, n (%)	
Obesity	12 (15.2%)
Hypertension	5 (6.3%)
Diabetes	3 (3.8%)
Metabolic syndrome	5 (6.3%)
Dyslipidemia	57 (72.2%)
Thyroid disorders	10 (12.7%)
Hypothyroidism (overt or subclinical)	3 (3.8%)
Hyperthyroidism (subclinical)	7 (8.9%)

dyslipidemia (77.3%), bone metabolism disorders (osteopenia or osteoporosis; 58.2%), thyroid dysfunction (hypothyroidism and hyperthyroidism; 36.2%), hypertension (33.5%), and hypogonadism (27.8%). Less frequent complications included diabetes (11.8%), metabolic syndrome (6.8%), and obesity (4.5%). Newly developed endocrine complications after allo-HSCT are summarized in Table 2.

Metabolic Complications:

De novo post-transplant dyslipidemia occurred in a substantial proportion of patients without pre-transplant lipid abnormalities (77.3%). A shorter duration of CsA exposure was significantly associated with an increased risk of post-transplant dyslipidemia (HR 0.919, 95% CI 0.857–0.985, p = 0.018). Post-transplant hypertension developed in approximately one-third of patients (33.5%). Older age (HR 1.038, 95% CI 1.005–1.073, p = 0.024), male sex (HR 3.77, 95% CI 1.14–12.53, p = 0.030), and post-transplant corticosteroid use (HR 3.10, 95% CI 1.19–8.85, p = 0.017) were significantly associated with an increased risk of hypertension. Diabetes, metabolic syndrome and obesity were observed less frequently. Due to the limited number of events, formal risk factor analyses were not performed for these outcomes.

Thyroid Dysfunction:

Post-transplant thyroid dysfunction occurred in 36.2% of patients. Hypothyroidism (17.4%) mostly developed later during follow-up, whereas hyperthyroidism (18.9%) occurred earlier and was often transient. A longer duration of CsA exposure was significantly associated with a reduced risk of post-transplant hyperthyroidism (HR 0.784, 95% CI 0.675–0.911, p = 0.001; Table 3). No other transplant-related variables were significantly associated with thyroid dysfunction.

Bone Metabolism Disorders and Avascular Necrosis:

Post-transplant bone metabolism disorders were observed in 58.2% of long-term allo-HSCT survivors. Osteoporosis was diagnosed in 12 patients (15.2%) and osteopenia in 34 patients (43.0%). For univariable analysis, a shorter duration of CsA

Table 2. Incidence of newly developed endocrine complications after allo-HSCT

Endocrine complication	Patients (n)	Percentage (%)
Dyslipidemia	17	77.3
Bone metabolism disorders (osteopenia or osteoporosis)	46	58.2
Thyroid dysfunction (overall)	25	36.2
Hypothyroidism	12	17.4
Hyperthyroidism	13	18.9
Hypertension	27	33.5
Hypogonadism	22	27.8
Diabetes mellitus	9	11.8
Metabolic syndrome	5	6.8
Obesity	3	4.5
Avascular necrosis	11	13.9

Only patients without the respective condition before transplantation were included in each analysis. Percentages were calculated based on the number of evaluable patients for each complication. Abbreviations: allo-HSCT= allogeneic hematopoietic stem cell transplantation.

Table 3. Univariable cox's regression analysis of risk factors for post-transplantation endocrine complications

Variable	Dyslipidemia		Hypertension		Hypothyroidism		Hyperthyroidism		Bone metabolism disorder		Avascular necrosis		Hypogonadism	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	P	HR (95% CI)	P
Age (years)	1.02(0.98-1.06)	0.51	1.04(1.01–1.07)	**0.024**	1.00(0.94–1.06)	0.999	1.04(1.00–1.09)	**0.053**	1.00(0.97–1.03)	0.80	1.00(0.94–1.06)	0.954	1.00(0.96–1.04)	0.93
Female sex	0.50(0.11-2.28)	0.37	3.77(1.14–12.53)	**0.030**	2.58(0.83–7.99)	0.101	2.25(0.50–10.14)	0.292	0.88(0.47–1.64)	0.687	1.58(0.46–5.40)	0.470	6.40(2.64–15.56)	**<0.00**
Acute GVHD	0.64(0.21-1.97)	0.44	0.97(0.39–2.39)	0.939	2.88(0.84–9.81)	0.092	0.49(0.15–1.60)	0.236	1.64(0.69–3.89)	0.262	2.95(0.86–10.14)	0.085	2.57(1.04–6.34)	**0.041**
Chronic GVHD	1.76(0.64-4.83)	0.270	0.55(0.24–1.21)	0.137	1.85(0.56–6.14)	0.316	1.67(0.55–5.11)	0.369	1.04(0.58–1.85)	0.904	3.27(0.70–15.19)	0.130	1.17(0.50–2.71)	0.718
CsA duration (months)	0.92(0.86-0.99)	**0.018**	0.99(0.97–1.02)	0.551	0.96(0.90–1.02)	0.195	0.78(0.68–0.91)	**0.001**	0.95(0.90–0.99)	**0.032**	1.01(0.98–1.04)	0.484	0.94(0.89–0.99)	**0.019**
Post-transplant steroids	1.06(0.39-2.87)	0.904	3.10(1.19–8.85)	**0.017**	2.39(0.76–7.56)	0.139	0.67(0.21–2.17)	0.503	1.04(0.54–2.01)	0.910	25.93(3.31–203.11)	**0.002**	1.25(0.53–2.99)	0.611
MMF	0.54(0.19-1.47)	0.226	1.84(0.82–4.09)	0.773	1.50(0.40–5.59)	0.546	0.82(0.23–2.99)	0.767	1.49(0.66–3.34)	0.335	7.27(2.11–24.99)	**0.002**	1.07(0.40–2.91)	0.893

Univariable Cox's regression analyses were performed separately for each outcome. A p<0.05 was considered statistically significant (higlighted as bold font). Abbreviations: GVHD=graft-versus-host disease. CsA=cyclosporine A. MMF= mycophenolate mofetil. HR= hazard ratio. CI= confidence interval.

exposure was significantly associated with an increased risk of post-transplant bone metabolism disorders (HR 0.95, 95% CI 0.900-0.990, p = 0.032; Table 3). Avascular necrosis developed in 13.9% of patients. For univariable analyses, post-transplant corticosteroid use (HR 25.93, 95% CI 3.31–203.11, p = 0.002), mycophenolate mofetil use (HR 7.27, 95% CI 2.11–24.99, p = 0.002), and bisphosphonate exposure (HR 6.02, 95% CI 1.82–19.12, p = 0.003) were associated with avascular necrosis (Table 3).

Hypogonadism:

Post-transplant hypogonadism occurred in 27.8% of patients, predominantly within the first year after transplantation. Female sex was associated with an increased risk of hypogonadism (HR 6.40, 95% CI 2.64–15.56, p <0.001). The presence of acute GVHD was also significantly associated with hypogonadism (HR 2.57, 95% CI 1.04–6.34, p = 0.041). A shorter duration of CsA exposure was associated with increased hypogonadism risk in univariable analysis (HR 0.935, 95% CI 0.885–0.989, p = 0.019; Table 3). Univariable Cox's regression analyses for all newly developed endocrine complications are summarized in Table 3, while detailed outcome-specific analyses are provided in the Supplementary Material (Supplementary Tables 1–9).

Hypogonadism usually developed within the first year after transplantation, tended to occur earlier during follow-up, and was often transient. In contrast, hypothyroidism generally developed later, while bone metabolism disorders were more frequently identified during long-term follow-up.

DISCUSSION

Patients who have received allo-HSCT and are surviving longer than 1 year at risk of developing late-onset complications, particularly endocrine disorders. Our study of 79 allo-HSCT recipients showed a markedly higher incidence of endocrine complications. Osteopenia and osteoporosis (58.2%), hypogonadism (27.8%), hypothyroidism (17.4%), and dyslipidemia (77.3%) were the most common complications. These findings correlate with other studies reporting that 60% of long-term transplant survivors have endocrine complications (2, 4). Hypertension developed in 33.5% of patients in our cohort; significant risk variables were post-transplant corticosteroid use, male sex, and age. This finding correlates with other data indicating that steroids induce salt retention and vascular remodeling, hence increasing patients' hypertension risk (6, 7). Long-term survivors show higher sensitivity due to endothelial degradation resulting from extended glucocorticoid administration and conditioning protocols (8). In our cohort, thyroid dysfunction (observed in 36.2% of the patients) was one of the most frequently reported endocrine abnormalities. Hypothyroidism and hyperthyroidism both indicate complex immunological dysregulation and the potential for post-transplant autoimmune thyroiditis (9, 10). Both TBI exposure and chronic GVHD could contribute to thyroid dysfunction (9, 11).

In our group, 15.2% exhibited osteoporosis and 43% had osteopenia, both of which are highly common disorders of bone metabolism. Additionally, 13.9% had avascular necrosis, likely due to treatments with bisphosphonates, mycophenolate mofetil (MMF), and corticosteroids. These findings correlate with the corpus of research identifying the primary causes of bone loss as inadequate calcium and vitamin D metabolism, prolonged corticosteroid exposure, and reduced physical activity (12, 13). Additionally, the capacity of MMF to influence bone remodeling and blood vessel structure might contribute to its correlation with avascular necrosis (14). Some associations, particularly for avascular necrosis, were associated with wide confidence intervals, reflecting the limited number of events and reduced statistical precision. These findings should therefore be interpreted with caution.

Gonadal dysfunction, identified in 27.8% of our patients, remains a major concern, particularly in younger patients. Our hypogonadism findings illustrate the vulnerability of the gonadal axis to several injuries related to transplantation. In the literature, acute GVHD, the use of CsA, and female sex are all associated with hypogonadism (15). The gonadotoxic effects of the alkylating chemical busulfan have been well-documented, particularly in women with diminished ovarian reserves (16). Our study contributes to the literature by providing real-world data from a single-center cohort. These data indicate that long-term surveillance of endocrine systems is crucial. Current guidelines indicate that 1-year post-transplantation, patients who have undergone gonadotoxic treatments or TBI should receive annual evaluations for thyroid function, bone quality, reproductive health, and metabolic parameters (17–19).

Our study revealed that endocrine complications, including post-transplant dyslipidemia and gonadal dysfunction, were more prevalent in patients with shorter duration of CsA exposure. Nonetheless, the standardization of starting doses among all patients using CsA prompts an inquiry into why a short period of treatment increases the incidence of complications. Currently, it is believed that the effects of CsA on the endocrine system might be associated with both cumulative toxicity and rebound effects after the discontinuation of immunological modulation, and inadequate adaptation in hepatic lipid metabolism. A preclinical study shows that CsA affects lipoprotein clearance, resulting in the accumulation of low-density lipoprotein and very low-density lipoprotein, and inhibition of lipoprotein lipase function (20). Accordingly, patients are able to achieve an equilibrium in lipid homeostasis with prolonged use; the early cessation of CsA can interfere with this adaptive mechanism and could cause increased dyslipidemia. In CsA-induced hypogonadotropic hypogonadism (as shown in animal models) early withdrawal of CsA rather than prolonged use could disturb hypothalamic-pituitary feedback pathways, resulting in increased hormonal imbalance (21). Short-term use of CsA could result in a triggering effect on the endocrine system rather than having a protective effect.

When interpreting statistically significant results, it is important to consider the possibility of a type I error, especially when multiple univariable comparisons are used.

Study Limitations:

This study has several limitations. The retrospective design and the fact that it was conducted at a single center could have introduced selection bias, thereby potentially restricting the generalizability of the findings. Additionally, the median follow-up duration of 38 months might not fully capture very late endocrine complications that can occur many years after transplantation. Some biochemical or imaging parameters, particularly related to gonadal function and bone density, could have been inconsistently documented. Furthermore, although the temporal patterns of endocrine complications were described, detailed stratification according to predefined time intervals (eg, 0–1 year, 1–3 years, and >3 years) could not be performed due to the retrospective design and limited number of events for some outcomes.Detailed information regarding specific conditioning agents (eg, busulfan and cyclophosphamide) was not consistently available due to the retrospective nature of the dataset, which might limit the assessment of agent-specific effects on endocrine outcomes. Additionally, detailed information regarding GVHD severity (eg, grading of acute GVHD and classification of chronic GVHD) and organ involvement was not consistently available; therefore, GVHD was analyzed as a binary variable, which could limit the interpretability of its impact on endocrine outcomes. Detailed information regarding CsA dose intensity and therapeutic drug monitoring levels was also not consistently available in this retrospective dataset, potentially limiting a more comprehensive evaluation of immunosuppressive exposure. Lastly, the study cohort was treated between 2003–2012; thus, changes in transplant practices since then could affect comparability with contemporary outcomes.

CONCLUSION

In conclusion, our study reveals that endocrine complications are common in long-term survivors of allo-HSCT. In particular, dyslipidemia, bone loss, and hypogonadism were the common complications and their risk increases with shorter duration or early discontinuation of CsA rather than cumulative exposure and GVHD. These findings suggest that long-term monitoring of endocrine complications is important for these patients.

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