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Outcomes of allogeneic hematopoietic stem cell transplantation in children and adults with prior invasive fungal diseases

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Summary

Invasive fungal diseases (IFD) are a major cause of morbidity and mortality in hematological patients, but prognosis of IFD has improved recently, due to introduction of new antifungals and efficient diagnostic procedures. Number of patients with IFD who are candidates for allogeneic hematopoietic stem cell transplant (allo-HSCT) increased. However, publications on the field are limited and there are no data on results of pediatric allo-HSCT patients with prior IFD. This study focuses on the outcomes of allo-HSCT in children and adults with prior IFD.

Patients and methods

In a prospective study, 504 allo-HSCT recipients were included from Jan 2013 to Jul 2016. The median age was 24 y.o. [2 months to 76 years] including 164 children (<18 yo) and 340 adults. The cohort included 52% male patients. Most patients (74.6%) were diagnosed with high-risk acute leukemia. Allo-HSCT from HLA-matched unrelated donors (MUD) was performed in 58.5%, from matched related donors (MRD), 22.5%; haploidentical HSCT was performed in 19% of patients, predominantly with RIC (67%). EORTC/MSG 2008 criteria for diagnosis and response to therapy were used. In the patients with pre-transplant lung lesions detected by CT scan, bronchoscopy with BAL was used. "Active IFD" means IFD diagnosed just before HSCT.

Results

Incidence of IFD before allo-HSCT was 15% (n=76). According to EORTS/MSG 2008 criteria, 90.8% of patients had probable and 9.2% presented with proven IFD. Etiology of IFD prior to HSCT was as follows: invasive aspergillosis (IA), 75%; invasive candidiasis (IC), 13%; mucormycosis (Mu), 4%; *Pneumocystis pneumoniae* (PCP), 1.3%, and combination of IA with Mu (2 cases), IC (n=1), PCP (n=1). The main sites of infection were lungs (95%), other localizations were predominantly combined with lung involvement: sinuses (9%), spleen (6%), liver (6%), and soft tissues (3%). Antifungal therapy before allo-HSCT was used in 75% patients with median duration of 2 months. Complete response to antifungal therapy was observed in 38.2% of the cases, partial response or stabilization was achieved in 35.5%, and "active IFD" was detected in 26.3% of the patients. After allo-HSCT, all the patients received antifungal therapy or secondary prophylaxis according to the IFD etiology. Cumulative incidence of relapse or progression of IFD after allo-HSCT was observed in 14.5%. Active underlying disease (hematology malignancy) at the moment

of HSCT was the only risk factor for relapse or progression of IFD after allo-HSCT (11.5% *vs* 21.1%, p=0,03). We detected no significant differences in the cumulative incidence of acute, chronic GVHD and relapse in the study group as compared to the patients without history of IFD. 3-year overall survival (OS) after allo-HSCT was 67.5%. The impact of prior IFD on overall survival in allo-HSCT recipients was not statistically significant for the entire group (60.5% *vs* 68.7%, p=0.1), and, separately, for children (50.0% *vs* 57.4%, p=0,3) and adults (63.3% *vs* 74.6%, p=0.09). The worst outcome was observed in the patients with "active IFD" and active underlying disease at the moment of HSCT (3-year OS was 20%, p<0.001 compared to patients without history of IFD). However, in the patients with "active IFD" and remission of underlying disease, OS value was similar to survival rate of patients without history of IFD (80% *vs* 68.7%, p=0.2).

Conclusion

Incidence of IFD before allo-HSCT was 15%. Cumulative incidence of relapse or progression of IFD after allo-HSCT was 14.5%. Prior IFD had no significant impact on transplant-related complications and overall survival in children and adults undergoing allo-HSCT. Active underlying disease at the moment of HSCT was the only risk factor for relapse or progression of IFD and impaired outcome of allo-HSCT.

Keywords

Invasive fungal disease, pre-existing IFD, allogeneic hematopoietic stem cell transplantation, children and adults, clinical outcomes.

Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the most effective treatment method for lymphoid, haematopoietic and related tissue malignancies as well as non-malignant disorders. In 2017, 18.281 number of allo-HSCT were performed in Europe and associated countries reported by 683 centers in 50 countries, with acute leukemia being the main indication [1]. The approachability and outcome of allo-HSCT are steadily improving due to wide application of reduced-intensity conditioning (RIC), new methods of graft-versus-host disease (GvHD) prophylaxis, haploidentical transplantation, and introduction of novel molecules and drugs for bridge therapy before allo-HSCT, along with prevention and treatment of relapses after allo-HSCT both in adults and pediatric patients [2-8] Invasive fungal disease (IFD) is a common infectious complication during remission-induction and/or consolidation chemotherapy for aggressive hematologic malignancies. The patients with acute leukemia and high-risk myelodysplastic syndrome are also at high risk for IFD [9-10]. Some patients with relapsed/refractory lymphoma could be, under some circumstances, also attributed to the high-risk group [11]. Introducing new antifungal drugs and diagnostic procedures has improved prognosis of IFD in hematological disorders. Many of these patients will subsequently be referred for allo-HSCT because of high-risk hematological malignances. The number of patients with IFD who are candidates for allo-HSCT has been also increased, and the problems related to the transplant procedure are pressing now. An observational study of the Transplant Associated Infection Surveillance Network (TRANSNET) suggests that the post-transplant IFD remains problematic, with cumulative incidence rates varying between 5.8 and 7.7% [12]. The role of IFD revealed prior to allo-HSCT is still a subject of controversy. Historically, IFD has been a major barrier for allo-HSCT. Previous studies have shown that invasive aspergillosis (IA) may have a significant role in clinical outcome of allo-HSCT [13-15]. Fukuda et al. have summarized the 10-year experience of Fred Hutchinson Cancer Research Center, having shown that the post-transplant IA occurred in 13 of 45 patients with a pre-transplant IA history (29%) [16]. Nine infectious events were considered to be recurrent by anatomic site and timing. Compared with all other patients who received allo-HSCT over the same period, the patients with IA history had lower 1-year overall survival rate (56% *versus* 77%; P=0.0001), and higher transplant-related mortality (38% *versus* 21%; P=0.0001) by 100 days after HSCT, associated mainly with IA and other pulmonary complications. The CIBMTR data also confirm that 5-year overall survival was 30% (95% Confidence interval (CI): 26-34%) at 5 years in patients with pre-transplant IFD *versus* 45% (95% CI: 44-46%) in control population (p < 0.0001). The lower overall survival seems to be a composite result of higher relapse rates and higher non-relapse mortality in the patients with pre-existing IFD [17].

Historically, pre-transplant IFD was considered a relative contraindication to HSCT. However, recent studies have demonstrated a controversial point, e.g., a single-center study on behalf of CIC 725 suggested that IA prior to allo-HSCT did not impair the outcome of transplantation procedure with effective diagnosis and secondary prophylaxis of IFD, as reported at the 41st Annual EBMT Meeting and 57th Annual ASH Meeting in 2015 [18, 19]. A retrospective EBMT analysis by the Infectious Diseases and Acute Leukemia Working Parties concerning influence of pre-existing invasive aspergillosis upon allo-HSCT outcome in acute leukemia patients (published online in October 2015 in *Bone Marrow Transplantation*) confirm our data that, in general, a history of IA should not be a contraindication when considering allo-HSCT in acute leukemia patients [20]. Penack O. et al. found only a trend toward lower overall survival (P=0.078, hazard ratio (HR) [95% confidence interval (CI): 1.16 (0.98, 1.36)], and higher non-relapse mortality [P=0.150, HR (95% CI): 1.19 (0.94, 1.50)] in allo-HSCT recipients with pre-existing IA [20]. So far, there are no available data on clinical effects of other then IA pre-existing IFD and in pediatric allo-HSCT recipients.

The aim of this study was to estimate impact of prior proven or probable invasive fungal diseases on clinical outcome of allo-HSCT in children and adults.

Patients and methods

We have conducted a prospective single center study, where 504 allo-HSCT recipients were included from Jan 2013 to Jul 2016, with median follow-up time of 20 months and median age of 24 y.o. [2 months to 76 years]. The study cohort included 164 children (<18 yo), 340 adults, 52% were males. Most patients had high-risk acute leukemia (74.6%). Allo-HSCT from MUD was performed in 58.5%; MRD, 22.5%; haplo-HSCT, 19%. Reduced-intensity conditioning regimens (RIC) were predominant (67% of the cases). General characteristics of patients, donors and transplants are outlined in Tables 1, 2. The patients with lymphoid, haematopoietic and related tissue malignancies as well as non-malignant disorders received primary chemotherapy and other treatment in various regions of Russian Federation, from where most of the data including history of prior IFD were collected. All the patients with CT-detectable lesions at the time of transplantation were subjected to diagnostic bronchoscopy with bronchoalveolar lavage (BAL) microscopy, microbiological cultures and galactomannan (GM) test. EORTC/MSG 2008 criteria were used for the diagnosis of proven and probable IFD as well as to evaluate response to therapy. An "active" invasive fungal disease means IFD diagnosed just before allo-HSCT during examination at <1 month before starting the conditioning regimen.

The following primary endpoints were used: incidence of pre-existing IFD, incidence of relapse or progression of IFD after allo-HSCT, and overall survival (OS). The secondary endpoints included influence of pre-existing IFD on other outcomes of allo-HSCT, i.e., acute GvHD, chronic GvHD, relapse of underlying disease.

Overall survival was estimated using the Kaplan–Meier method. Mortality due to any cause was considered as a distinct event. Patients alive at the end of the follow-up were censored at this date. Patients with pre-existing IFD and without pre-existing IFD will be compared by the log-rank test. A Cox regression was applied, in order to compare the outcomes the study groups.

Table 1. Clinical and demographic characteristics of the patients

Patients characteristics	n=504
Age, median (range)	24 [2 mo-76 y]
≤18 19-60 ≥60	177 (35%) 312 (62%) 15 (3%)
Sex Males	262 (52%)
Acute leukemia	376 (74.5%)
AML/ALL CR 1-2 Prim refr/no CR	213/163 262 (70%) 114 (30%)
Myeloproliferative disease	59 (12%)
CR no CR	15 (25%) 44 (75%)
Lymphoproliferative disease	31 (6%)
CR Prim refr/no CR	17 (55%) 14 (45%)
Non-malignant disease	38 (7.5%)
Status of the disease Complete remission No complete remission/primary refractoriness	 299 (60%) 205 (40%)

Table 2. Characteristics of hematopoietic transplants

Transplant characteristics	n=504
Donor type Matched related Mismatched related Matched unrelated Mismatched unrelated	 113 (22.5%) 96 (19%) 194 (38.5%) 101 (20%)
Conditioning regimen Myeloablative Reduced-intensity	 166 (33%) 338 (67%)
Source of the transplant Bone marrow Mobilized peripheral blood stem cells Both	 253 (50%) 241 (48%) 10 (2%)
Dose of CD34+ cells, 10^6/kg, mean±SD	4.9±1.8
GvHD prophylaxis CI + Mtx/MMF +/-ATG CI + MMF + PTCY / mono PTCY	 69 (14%) 435 (86%)
Antifungal prophylaxis Primary: fluconazole Secondary: voriconazole	 262 (61%) 57 (75%)

Abbreviations: AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; CR, complete remission; CI, calcineurin inhibitors; Mtx, methotrexate; MMF, mycophenolate mofetil; ATG, Anti-thymocyte globulin; PTCY, posttransplant cyclophosphamide.

Results

The overall incidence of IFD before allo-HSCT was 15% (n=76). According to EORTS/MSG 2008 criteria 90.8% of patients had probable IFD, and 9.2% exhibited proven fungal invasion. Patients with lymphoma, as well as those with acute myeloid leukemia had a higher rate of pre-existing IFD at the time of allo-HSCT (Fig. 1).

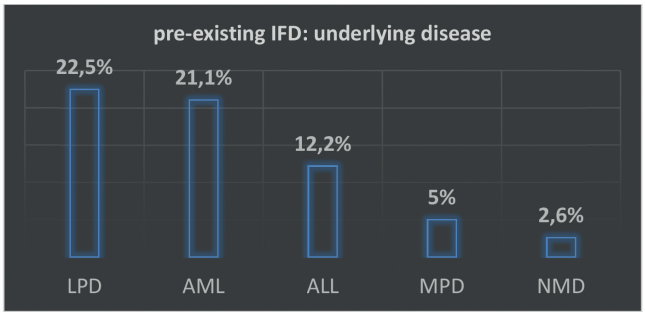

Figure 1. Primary underlying diseases in the patients with pre-existing IFD

Abbreviations: LPD, lymphoproliferative disease; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; MPD, myeloproliferative disease; NMD, non-malignant disease.

The pathogens detected in IFD prior to allo-HSCT were as follows: invasive aspergillosis, 75%; invasive candidiasis (IC), 13%; mucormycosis (Mu), 4%; *Pneumocystis pneumoniae* (PCP), 1,3%; combination of IA with Mu was found in 2 patients, IC in one case, and PCP, in one another case (Fig. 2). The main sites of infection were lungs (95%), other affected sites were predominantly combined with lung lesions, i.e., maxillary or frontal sinuses, 9%; spleen, 6%; liver, 6%, and soft tissues, 3% (Fig. 3).

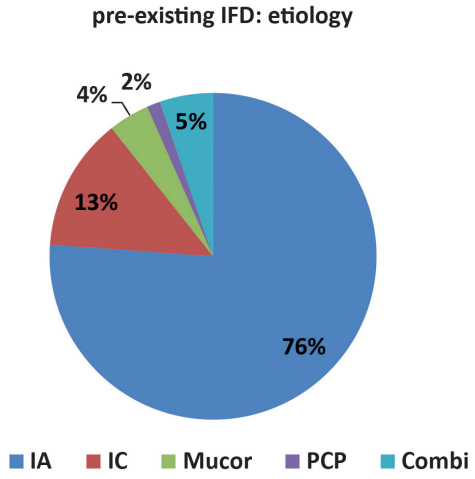

Figure 2. Causative pathogens in pre-existing IFD cases

Abbreviations: IA, invasive aspergillosis; IC, invasive candidiasis; Mu, mucormycosis; PCP, Pneumocystis pneumoniae; Combi, mixed fungal invasion.

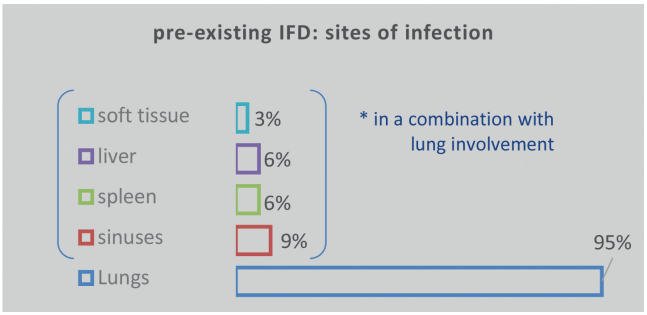

Figure 3. Sites of infections in patients with pre-existing IFD

The median time from IFD to allo-HSCT was 86 days [1 day to 4.5 years]. Antifungal therapy before allo-HSCT was administered in 75% patients. The median duration of antifungal therapy before allo-HSCT was 65 days [1 day-11 months]. Complete response to antifungal treatment was achieved in 38.2% patients, partial response or stabilization were observed in 35.5%, and 26.3% patients had "active IFD". After allo-HSCT, all the patients received antifungal therapy or secondary prophylaxis according to the IFD etiology, with median duration of clinical effect for 78 [21-217] days, and median therapy length for 166 [32 to 394 days].

Cumulative incidence of relapse or progression of IFD after allo-HSCT was 14.5% (Fig. 4). Active underlying disease at the moment of HSCT was the only risk factor for relapse or progression of IFD after allo-HSCT (11.5% *vs* 21.1%, p=0.03) (Fig. 5). We detected no significant differences in cumulative incidence of acute or chronic GVHD, and relapse rates in the study group as compared to the patients without history of IFD. Patients and HSCT characteristics, CMV reactivation, graft hypofunction did not show any significant association with incidence of relapse, or progression of IFD after allo-HSCT. The characteristics related to pre-existing IFD (status of IFD at the HSCT, time from IFD to HSCT, duration of antifungal therapy before HSCT) also had no impact on probability of relapse or progression of IFD after allo-HSCT.

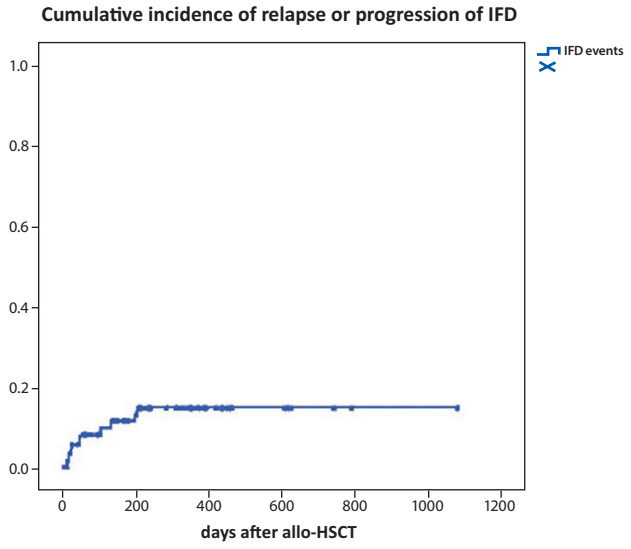

Figure 4. Cumulative incidence of relapse or progression of IFD after allo-HSCT (ordinate). Abscissa, days after HSCT

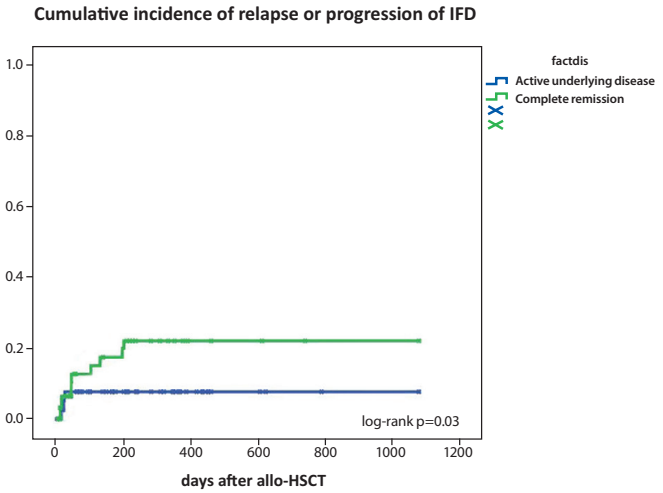

Figure 5. Cumulative incidence of relapse or progression of IFD after allo-HSCT depending on the underlying disease status at the moment of allo-HSCT (ordinate). Abscissa, days after HSCT

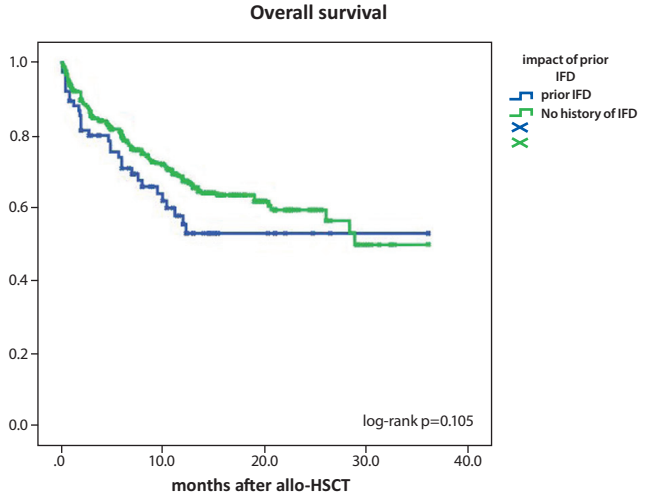

Figure 6. Three-year overall survival after allo-HSCT in the patients with history of prior IFD as compared to patients without history of IFD (ordinate). Abscissa, months after HSCT

Three-year OS after allo-HSCT was 67.5%. The impact of prior IFD upon overall survival in allo-HSCT recipients was not statistically significant in the entire group (60.5% *vs* 68.7%, p=0.1) (Fig. 6). Similar results were obtained for the separate groups of children (50.0% *vs* 57.4%, p=0.3), and adults (63.3% *vs* 74.6%, p=0.09). The main outcomes of allo-HSCT are presented in Table 3.

The worst outcome was observed in patients with "active IFD" and active underlying disease at the moment of allo-HSCT (3-year OS – 20%, p<0.001; HR (95% CI): 5.81 (2.81 – 11.87)). However, OS values in patients with "active IFD" and remission of underlying disease were similar to survival rate of patients without history of IFD (80% *vs* 68.7%, p=0.2, p=0.57, HR [(95% CI): 0.67 (0.16 – 2.71)] (Fig. 7).

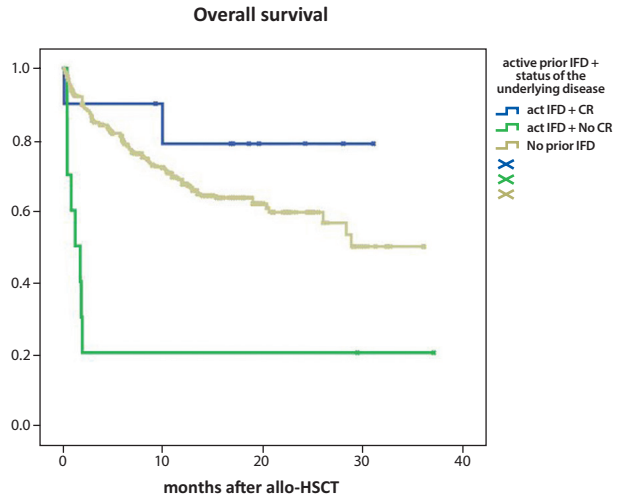

Figure 7. Three-year overall survival after allo-HSCT in the patients with "active IFD" (depending on status of underlying disease at the moment of allo-HSCT) as compared to patients without history of IFD (ordinate). Abscissa, months after HSCT

Comments: blue line is survival curve for the group of patients with "active IFD" and remission of underlying disease; green line is survival curve for the group of patients with "active IFD" and active underlying disease at the moment of allo-HSCT; the yellow line is survival curve for the patients without history of IFD.

Table 3. The main outcomes of allo-HSCT in patients with history of prior IFD as compared to patients without history of IFD

Outcomes of allo-HSCT	Prior IFD		p	HR	(95% CI)
	yes	no			
3y OS (adult + children)	60.5%	68.7%	0.10	1.38	0.93-2.05
3y OS (adult)	63.3%	74.6%	0.09	1.50	0.93-2.42
3y OS (children)	50.0%	57.4%	0.32	1.44	0.69-3.02
Incidence of acute GvHD grade II–IV	18.1%	19.8%	0.28	0.91	0.69-1.20
Incidence of chronic GvHD	27.8%	32.9%	0.25	0.82	0.74-1.07
Relapse of underlying disease	32.6%	30.8%	0.31	1.21	0.89-1.59

Discussion

In the present study, we analyzed large data set of patients with different hematological malignancies and non-malignant disorders undergoing allo-HSCT between 2013 and 2016 in a single BMT center (CIC 725). We would highlight the real-life character of study. The entire cohort of allo-HSCT recipients was included in the observation period without exception of any patients, regardless of underlying disease or status at the moment of allo-HSCT. Also we would emphasize the participation of pediatric cohort that was presented by 164 children.

In our population of allo-HSCT recipients, 15% had proven and probable invasive fungal disease before transplantation. Moreover, most of them (>60%) had signs of the infection at the moment of allo-HSCT. We believe that there are several factors that could contribute to our results. Out BMT team has wide diagnostic opportunities and an active diagnostic strategy related to infections, and is able to perform the on-place assessment of infectious state of the patient before allo-HSCT, because of lacking necessary diagnostic procedures in most regions where the patients were initially treated. Due to successful implementation of such strategy, we are more often prone for active treatment and avoiding delays with allo-HSCT. An unexpected result for us is the fact that a quarter of patients with lymphomas had IFD before allo-HSCT. This result may be due to high pre-treatment burden in these patients, most of them were patients with Hodgkin lymphoma who underwent more than 6 lines of chemotherapy before allo-HSCT.

Our study has also shown that the cumulative incidence of relapse or progression of invasive fungal disease after allo-HSCT was 14.5%. The only risk factor for relapse or progression of IFD was lack of complete remission of the underlying disease at the moment of HSCT. That result corresponded to the earlier reported data [16], but we didn't find any additional risk factors associated with bone marrow transplant procedure or antifungal treatment before allo-HSCT.

In the present study, we demonstrated that invasive fungal disease prior to the allo-HSCT did not impact on outcome of this treatment in children and adults. We suggest that there are several features that may have endow to obtained results.

Firstly, our study included allo-HSCT recipients who have been transplanted over recent years, in comparison with published studies [13-16, 20]. An overall better supportive care management was applied over last years, thus improving, specifically the outcome of allo-HSCT in patients with infectious complications including IFD. We believe that active diagnostic strategy and wide implementation of modern medications for secondary prophylaxis in our center played a role in improving the outcome of allo-HSCT in the patients with pre-existing IFD. It has been shown in several trials that secondary antifungal prophylaxis with voriconazole leads to considerably lower IA relapse rates as compared with those reported in historical controls, since *Aspergillus spp.* is a prevailing pathogen in pre-transplant IFD in our study [21-23].

Secondly, this study demonstrated the central role of the underlying disease status upon outcome of the allo-HSCT, and influence on the course of the infectious complications after HSCT, IFD in our case. Active underlying disease at the moment of HSCT was the only risk factor for relapse or progression of IFD and impaired outcome of allo-HSCT. This hypothesis is supported by publications from a French-Belgium study group, demonstrating that the outcome of severe infectious complications in patients with hematological malignancies has been considerably improved during the last decade and is mostly determined by the status of the underlying disease [24-25].

Thirdly, our study has limitations due to relatively small study cohort from a single center data. That is why the result may be not accurate enough to evaluate the effect of IFD upon allo- HSCT outcome. At the same time, it reflects the situation during certain time which significantly affects the results obtained. Therefore, we cannot exclude the possibility that pre-existing IFD has a higher adverse impact on allo-HSCT outcome than our data may suggest.

In conclusion, we found out no significant impact upon important allo-HSCT transplant outcomes, such as survival, GvHD and relapse. Our data suggest that a history of IFD should not be considered a contraindication for allo-HSCT. We are currently continuous an observational prospective study to be able to more precisely investigate the impact of IFD on allo-HSCT.

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Conflict of interest

No conflict of interests is declared.

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Аллогенная трансплантация гемопоэтических стволовых клеток у детей и взрослых с предшествующими трансплантации инвазивными микозами

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Резюме

Внедрение новых противогрибковых средств и диагностических процедур улучшило прогноз гематологических пациентов с инвазивными микозами (ИМ). Увеличилось число пациентов с ИМ, кандидатов на аллогенную трансплантацию гемопоэтических стволовых клеток (алло-ТГСК). Роль ИМ, развившихся до алло-ТГСК, по-прежнему не определена. Нет опубликованных данных о результатах алло-ТГСК у педиатрических пациентов с предшествующим ИМ. Цель исследования – оценить влияние предшествующего ИМ на результаты алло-ТГСК.

Пациенты и методы

В проспективное исследование были включены 504 реципиента алло-ТГСК в период с января 2013 года по июль 2016 года. Средний возраст составил 24 года (2 месяца – 76 лет), дети (<18 лет) – 164, взрослые – 340, мужчины – 52%. Преимущественно пациенты с диагнозом острый лейкоз группы высокого риска (74,6%). Алло-ТГСК от неродственного совместимого донора были выполнены у 58,5%, совместимого родственного донора – 22,5%, гаплоидентичного – 19%, преимущественно с использованием режима кондиционирования со сниженной интенсивностью (67%). Непосредственно перед алло-ТГСК всем

пациентам с обнаруженными изменениями ткани легких, в результате компьютерной томографии органов грудной клетки, выполнялась бронхоскопия с исследованием жидкости бронхоальвеолярного лаважа: микроскопии, культуры и теста на галактоманнан. Для диагностики доказанного и вероятного ИМ и оценки ответа на терапию были использованы критерии EORTC/MSG 2008. «Активный ИМ» – ИМ, диагностированный непосредственно перед трансплантацией. Медиана наблюдения составила 20 месяцев. Основными конечными точками были общая выживаемость (ОВ), частота рецидива или прогрессирования ИМ после алло-ТГСК; вторичные точки – частота острой и хронической РТПХ, рецидива основного заболевания.

Результаты

Частота ИМ до алло-ТГСК составила 15% (n=76). Согласно критериям EORTS/MSG 2008, 90,8% пациентов имели вероятный и 9,2% доказанный ИМ. Этиология ИМ до трансплантации: инвазивный аспергиллез (ИА) – 75%, инвазивный кандидоз (ИК) – 13%, мукормикоз (М) – 4%, пневмоцистная пневмония (ПП) – 1,3% и комбинация ИА с М диагностирована у 2 пациентов, с ИК – 1, с ПП – 1. Основным органом поражения были легкие – 95%, другие локализации, преимущественно в сочетании с вовлечением легких: синусы – 9%, селезенка – 6%, печень – 6%, и мягкие ткани – 3%. Противогрибковая терапия перед алло-ТГСК применялась у 75% пациентов с медианой продолжительности – 2 месяца. Полный ответ на противогрибковую терапию был достигнут у 38,2% пациентов, частичный ответ или стабилизация – 35,5%, а у 26,3% пациентов был «активный ИМ». После алло-ТГСК все пациенты получали противогрибковую терапию или вторичную профилактику в соответствии с этиологией ИМ. Кумулятивная частота рецидива или прогрессирования ИМ после алло-ТГСК составила 14,5%. Отсутствие ремиссии основного заболевания в момент трансплантации был единственным фактором риска рецидива или прогрессирования ИМ после алло-ТГСК (11,5% против 21,1%, p=0,03). Существенных различий в кумулятивной частоте острой (p=0,28), хронической РТПХ (p=0,25) и рецидива (p=0,31) не было обнаружено в сравнении с группой пациентов без ИМ в анамнезе. 3-летняя ОВ после алло-ТГСК составила 67,5%. Общая выживаемость у реципиентов аллоТГСК без ИМ и имевших ИМ в анамнезе статистически не различалась во всех группах (60,5% против 68,7%, p=0,1), как отдельно у детей (50,0% против 57,4% , P=0,32) так и у взрослых (63,3% против 74,6%, p=0,09). Наихудший результат наблюдался у пациентов с «активным ИМ» и отсутствием ремиссии основного заболевания на момент трансплантации (3-летняя ОВ - 20%, p <0,001). Однако у пациентов с «активным ИМ» и ремиссией основного заболевания ОВ была аналогична выживаемости пациентов без ИМ в анамнезе (80% против 68,7%, p = 0,57).

Выводы

Пятнадцать процентов реципиентов алло-ТГСК имели инвазивный микоз в анамнезе. Кумулятивная частота рецидива или прогрессирования инвазивных микозов после алло-ТГСК составила 14,5%. Предшествующий инвазивный микоз не оказывал существенного влияния на результаты трансплантации и общую выживаемость детей и взрослых после алло-ТГСК. Отсутствие ремиссии основного заболевания на момент трансплантации было единственным фактором риска рецидива или прогрессирования инвазивного микоза, и ухудшения результатов алло-ТГСК.

Ключевые слова

Предшествующие инвазивные микозы, аллогенная трансплантация гемопоэтических стволовых клеток, дети и взрослые, клинические исходы.