

The key factors influencing patients in selecting autologous hematopoietic stem-cell transplantation as the main therapy for multiple myeloma: A population-based epidemiological study

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Abstract

Autologous hematopoietic stem-cell transplantation (ASCT) is one of the most effective therapies for the treatment of multiple myeloma (MM). In this study, we explored factors influencing patients in selecting ASCT by analyzing population-based epidemiological data on patients' sociodemographic and clinical variables. This multicenter study was conducted across 14 medical centers in Zhejiang Province in China. Patient survey was conducted via face-to-face interviews, telephone interviews, or online completion of questionnaire with patients' informed consent. Patients were divided into transplantation (TR) and non-transplantation (non-TR) groups. The difference in education levels, occupational status, and annual income between the TR group and non-TR group was significant (P < 0.01). The main reasons that patients had chosen transplantation were "to delay recurrence, improve quality of life, prolong survival" and "trust the treatment provided by doctors", the main reason that patients had rejected transplantation was "worried about the physical condition", followed by "risk of relapse", "side effects" and "family burden". In addition to discussing therapy with their primary physician, patients in TR group tended to obtain relevant information from other sources. Education levels, occupational status, and annual income were the main factors affecting transplantation therapy choice among patients with MM.

Introduction

Multiple myeloma (MM) is a malignancy affecting plasma cells. Clonal proliferation of plasma cells is associated with production of a monoclonal antibody, causing end-organ damage [1]. The treatment of MM is rapidly evolving with the approval of multiple new drugs [2]. The front-line management includes induction regimen, maintenance therapy, and hematopoietic stem cell transplantation. In young patients with MM, the extended use of high-dose chemotherapy followed by autologous hematopoietic stem-cell transplantation (ASCT) is associated with high response rates and prolonged progression-free survival (PFS) and overall survival (OS). The treatment is also effective for patients up to 70 years old with newly diagnosed MM [3, 4]. ASCT, due to an antitumor effect achieved through associated high-dose chemotherapy, may help improve the bone marrow microenvironment and immune reconstitution [5]. In the real-world practice, however, the proportion of patients who are accepting ASCT is very low. As MM is a heterogeneous disease, treatment preferences and goals may differ between patients, depending on multiple patient-related, disease-related, and treatment-related factors [6, 7]. These factors include clinical symptoms, treatment burden, and toxicities, ability to participate in daily activities, financial burden, accessibility to treatment, and convenience of treatment [8] and could affect treatment goals and patients' treatment choices, and eventually affect the quality of life.

To explore the factors that most influence the selection of ASCT by patients, we conducted a population-based epidemiological study on patients' sociodemographic and clinical variables. Our findings could help decision-making in the selection of therapeutic strategies and improve the overall outcome in the treatment of MM.

Methods

Patients

This retrospective study was conducted across 14 medical centers in Zhejiang Province in China. A total of 747 patients with MM who were > 18 years old were enrolled in this study. Eligible patients were assessed for diagnosis and disease progression according to standard International Myeloma Working Group criteria. The survey was conducted via face-to-face interviews, telephone interviews, or online completion of the questionnaire. Patients under 18 years of age or those who could not efficiently communicate were excluded from the study. Of the 747 questionnaires completed, 5 were excluded in the statistical analysis due to obvious logical errors.

Sociodemographic and clinical variables

We analyzed patients' gender, age, education levels, occupational status, household status, parenting situation, children's situation, education levels of the children, occupational status of the children, average annual income, insurance status and treatment cost. Clinical data included presenting symptoms, consultation department and whether to transplant or not.;

Statistical analysis

SPSS Statistics version 23 was utilized for statistical analysis. Patient baseline characteristics were analyzed using Chi-square test. P<0.05 was considered to be statistically significant.

Results

Baseline demographic and clinical characteristics of the MM patients

The main demographic, socio-economic, and clinical features of the patients are listed in Table 1. Our cohort included 742 patients, of which 90% were from Zhejiang Province; 44% were female, 56% were male, and the proportions of male and female in the TR group and non-TR groups were similar (P>0.05); and 70% were older than 55 years (Table 1 and Figure 1A). More than 70% had been working in agriculture or were unemployed, retired, or working as freelancers. Compared to the non-TR group, the TR group had more employees in enterprises and institutions (34% vs 18%, P<0.01) and slightly more retirees (24% vs 22%, P>0.05), but fewer agricultural workers (18% vs 34%, P<0.01) (Figure 1B). The proportion of patients in the TR group who had bachelor degree or above was larger than that in the non-TR group (14% vs 6%, P<0.01), although the junior high school was the highest level of education among 75% of all the patients in this study (Figure 1C). Most patients (87%) lived with their spouses, of which 39% lived also with children (Figure 1D). Almost all patients (99%) had children and 94% of their children were adults

and 87% of their children had jobs. Moreover, 57% of patients' children had a bachelor's degree or above (68% in TR group vs 52% in the non-TR group, P<0.01). (Figure 1E).

The socioeconomic status of the patients is shown in Supplementary table 1. The annual income of 58% patients was less than 100,000 RMB; that of 32% patients was 100,000-300,000 RMB. Seventy one percent of patients in the non-TR group had an annual income <100,000 RMB whereas only 45% in the TR group had such low income (P<0.01). Almost all patients were medical insurance covered but the out-of-pocket payments were still significant. Most patients (73%) spent more than 100,000 RMB out-of-pocket money for treatment. Twenty-seven percent of patients had 50,000-100,000 RMB and 21% of patients had 110-150,000 RMB direct out-of-pocket cost in the first year. Patients in the TR groups paid more than those in the non-TR group. For the total cost, e.g., the largest subgroup of patients in the TR group was in between 310,000 and 500,000 RMB (22%), whereas that in the non-TR group was in between 50,000 and 100,000 RMB (23%). The direct out-of-pocket cost after the first recurrence exceeded 150,000 RMB in 32% of the patients in the TR group whereas this occurred only in 20% in the non-TR group.

The main symptoms and the consultation departments that initially enrolled patients with MM are listed in Supplementary table 2. The patients' initial symptoms were mainly bone pain (46%) and elevated serum or urine protein (13%). Orthopedics (36%) and hematology (27%) were the most common departments for the patients' first visits (Figure 2).

Communication between doctors and patients

Before treatment, more than 70% of patients were told by their doctors that 1) patients with MM need long-term treatment, 2) MM is a malignant tumor with abnormal proliferation of plasma cells in the bone marrow, 3) MM is currently an incurable disease and will relapse in almost all patients after treatment. Fifty-seven percent of patients were receiving chemotherapy at the time of survey, while the patients under maintenance treatment and waiting for treatment accounted for 18%. Bortezomib (71%) and dexamethasone (63%) were the most commonly used therapeutic drugs (Figure 3A).

ASCT, due to associated intensive chemotherapy that can maximally reduce tumor cells, can also prolong survival and improve prognosis. 73% of patients were recommended for ASCT by their doctors. One of the main points that doctors communicated to their patients was that ASCT is a preferred treatment option for patients with good physical status, i.e., patients are younger than 65 years old or older than 65 years but in good physical condition, and may prolong survival and improve prognosis (Figure 3B).

Reasons for choosing or not choosing ASCT and the main concerns of patients

Thirty-eight percent of patients who were diagnosed within one year accepted ASCT. "Believe that autologous transplantation has a better curative effect, delays disease recurrence, improves quality of

life, and prolongs survival (90%)" and "Trust the autologous transplant program provided by the doctor and actively cooperate with the treatment" (87%) were the most common reasons for opting for ASCT. Physical condition (73%), side effects (65%), the risk of recurrence (64%), and family burden (48%) were the main reasons for patients to reject ASCT (Figure 4).

Disease relapse and maintenance treatment

As shown in Figure 5, 18% of the total patients relapsed, lower in the TR group than in the non-TR group (14% versus 19%, P>0.05), and 69% of them relapsed once (65% in the TR group and 71% in the non-TR group, P>0.05). Fifty-seven percent of patients received maintenance treatment (64% in the TR group and 54% in the non-TR group, P<0.05), and more than half (56%) of them received lenalidomide (59% in the TR group and 55% in the non-TR group, P>0.05) (Figure 5A-5C).

Information acquisition channels of patients

Forty percent of patients obtained information from other sources in addition to that provided by their doctors and a higher percentage of patients did so in TR group than in non-TR group (52% vs 35%, P<0.01). "Search for information online" and "communication between patients" were the most common information acquisition channels. Compared with the non-TR group, the TR group more favored professional channels such as the hospital websites and other medical professional websites other than Baidu website (Supplementary Figure 1).

Among the forms of continuing education, face-to-face communication with doctors was the most preferred channel for patients (89% for all the patients; 90% for the TR group and 89% for the non-TR group, P>0.05), followed by listening to other patients about their treatment experience (44% for all the patients; 42% for the TR group and 45% for the non-TR group, P>0.05), searching internet for on-line lectures (21% for all the patients, 30% for the TR group and 17% for the non-TR group, P<0.01), communicating via social media WeChat (20% for all the patients; 27% for the TR group and 17% for the non-TR group, P<0.01).

Discussion

Multiple myeloma (MM) affects physical, psychological, and social domains of quality of life. Our results revealed significant difference in socioeconomic status including education levels, occupational status, and annual income between patients who received ASCT and those who did not. Previous studies suggested that individuals with low socioeconomic status are at a higher risk of MM [9, 10]. Socioeconomic status is a strong predictor for survival prognoses in MM as well as other diseases [11–13]. Chan *et al* [9] suggested that the variation in survival between ethnic groups is primarily driven by differences in the levels of socioeconomic deprivation, which is consistent with data from the Surveillance, Epidemiology, and End Results (SEER) Program [14]. Education level is an important factor

in MM patients' demography and is an independent factor affecting survival outcomes [15]. In our study, higher proportion of patients in the TR group had higher levels of education than that in the non-TR group. As expected, patients with higher education had a better economic and occupational status, which might have led them to choose a better and more timely medical treatment.

Almost all patients in our study had medical insurance coverage. Still, the direct out-of-pocket costs were significant and they were generally higher in the TR group than those in the non-TR group. Previous studies have shown that cost of treatment is an important aspect influencing patients' decision in selecting treatment and greatly impacting patients' quality of life [16–18]. Financial hardship may result from direct out-of-pocket costs for treatment, such as nursing and nutrition costs, and other indirect costs, such as travel costs and compensation loss due to inability to work, all of which are expected to influence the patient's choice of transplantation. Eventually, the effectiveness of treatment may be dependent on the patient's ability to cope with the financial burden associated with receiving long-term treatment, as MM tends to be a chronic disease that requires long-term adherence to therapy.

Before treatment, as revealed in our study, doctors mainly communicated to patients about MM as a disease per se, such as "a malignancy with abnormal proliferation of plasma cells", "needs long-term treatment", "is incurable and will relapse in almost all patients", whereas information related to ASCT was less discussed. Although 73% of patients had been recommended by their doctors for ASCT, the communication mainly included "indications", "procedures", and "a standard solution that can prolong survival and improve prognosis". Other aspects of ASCT were less covered, such as "can delay recurrence", "may cost less post transplantation", and "better quality of life", which are expected to be easy to understand if discussed and might increase patients' confidence in the treatment. The patient's desire for "full communication with doctors" was obvious and adequate communication is expected to have a positive influence on patients' choices of transplantation. As in our study, patients with MM are generally older than 55 years upon diagnosis, may be unstable to work, have low levels of education and low income, and lack knowledge of the disease. These unfavorable factors may cause patients to easily lose confidence in treatment when facing high treatment costs and the uncertainty of treatment efficacy. Therefore, it is important for physicians to have adequate and appropriate face-to-face discussion with patients to help them build confidence in treatment.

Our study indicated that the main reasons that patients selected ASCT were "to delay recurrence, improve quality of life, prolong survival" and "trust the treatment provided by doctors", whereas the main reasons that patients rejected this treatment were "worried about physical condition", "risk of relapse", "side effects" and "family burden". Patients with good physical conditions may opt for an intensive treatment, including ASCT to elicit a deeper response, improve quality of life, and achieve long-term remission and potential functional cure. On the other hand, for elderly and frail patients, the priority may be the disease control and maintaining quality of life, dealing with comorbidities and the challenges of polypharmacy, potential treatment-associated toxicities, and functional limitations [19]. Longer-term, less intensive, and more tolerable treatment regimens with treatment convenience and the ability to continue with daily activities are of substantial importance in both the frontline and relapse settings.

Although hematopoietic stem cell transplantations have become a life-saving treatment for patients with hematologic malignancies, the treatment is associated with psychological distress and psychiatric comorbidities, which, in turn, may impact patients' quality of life, function, and recovery [20]. Over the recent years, new treatment strategies have been proposed to address these issues. Some medical centers have carried out various forms of patient education [21, 22]. Researchers have formulated a conceptual framework and key research questions in the educational needs of transplantation patients, caregivers, and families [23]. Consistent with what was revealed in this study that patients' education were often inadequate, it was reported that, in an 18-month formative evaluation of education for patients with MM receiving ASCT, patients and caregivers both expressed anxiety about what to expect during the entire transplant process [25]. Patients often expressed desires to be involved in their treatment decision-making but often are not included in an effective way [26].

The goal of patient education is to guide patients and provide support. Despite the need for improvement in education, there is a lack of published educational materials for patients with MM who are receiving ASCT [25]. Previous studies have indicated that cancer patients prefer to receive their education using multiple modalities, particularly those that allow for active feedback [27, 28]. In our study, face-to-face interview with doctors was the most preferred channel for patients. Other channels included listening to other patients about their treatment experience, searching online for relevant videos and lectures, and communicating via the social media such as WeChat.

Summary

Education levels, occupational status, and annual income were the main factors affecting transplantation therapy choice among patients with MM. It is important for physicians to ensure adequate and appropriate face-to-face discussion with patients and their family members to better educate them and help them build confidence in ASCT. Educational materials are needed for patients who are receiving ASCT to guide them and provide support.

Declarations

Funding

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Authors' contributions

Zhen Cai was responsible for designing the review protocol, interpreting results and giving important guidance to the research. Jingsong He was responsible for designing the review protocol, writing the protocol, conducting the search, screening potentially eligible studies. Li Yang contributed to writing the report, conducting the search, analysing data, and interpreting results. Yang Yang, Yi Zhao, Donghua He,

Xiaoyan Han, Gaofeng Zheng, Wenjun Wu was responsible for data extraction and provided feedback on the report. Songfu Jiang, Ying Lu, Wenbin Qian, Guifang Ouyang, Jianping Lan, Wenda Luo, Huixian Hu, Jianping Shen, Jinwen Huang, Yuemin Kuang, Shenxian Qian, Jiaping Fu, Huifang Jiang, Kang Yu and Huang He was responsible for conducting the search, screening potentially eligible studies, extracting data.

Data Availability

Data available on request.

Code availability Word.

Ethics approval

It is a non-interventional study based on routine data recording. EC was deemed to be unnecessary.

Consent to participate

See above.

Consent for publication

See above.

Conflict of interest

The authors declare no competing interests.

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Table

Table 1 is available in the Supplementary Files section.

Figures

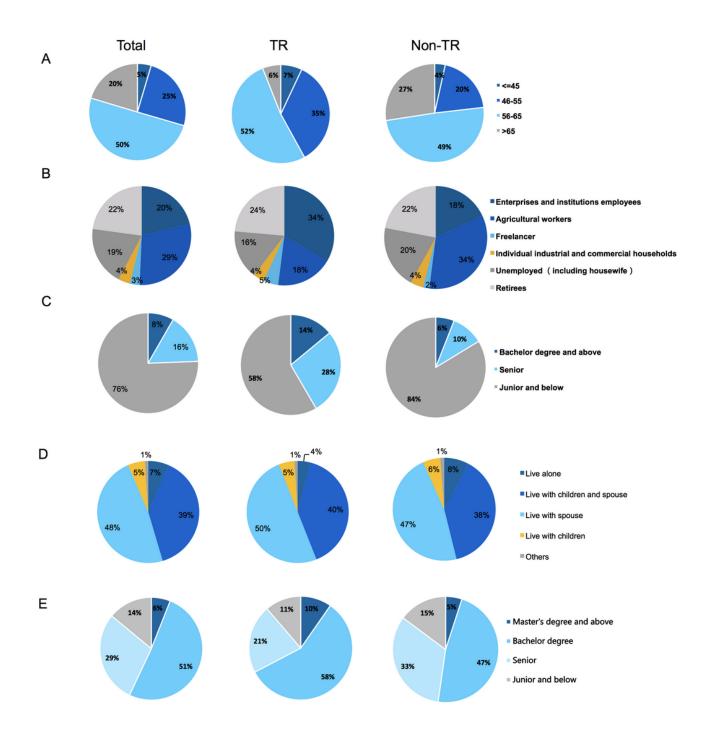


Figure 1

Comparison demographic of patients between MM patients with transplant or not

The proportion of the MM patients in age in the TR group and non-TR groups, 70% were older than 55 years old (A). More than 70% had been working in agriculture or were unemployed, retired, or working as freelancers. Compared to the non-TR group, the TR group had more employees in enterprises and institutions (34% vs 18%, P<0.01) and slightly more retirees (24% vs 22%, P>0.05), but fewer agricultural workers (18% vs 34%, P<0.01) (B). The proportion of patients in the TR group who had bachelor degree and above was larger than that in the non-TR group (14% vs 6%, P<0.01), although the junior high school was the highest level of education among 75% of all the patients in this study (C). Most patients (87%)

lived with their spouses, of which 39% lived also with children (D). Fifty-seven percent of patients' children had a bachelor's degree or above (68% in TR group vs 52% in the non-TR group, P<0.01). (E).

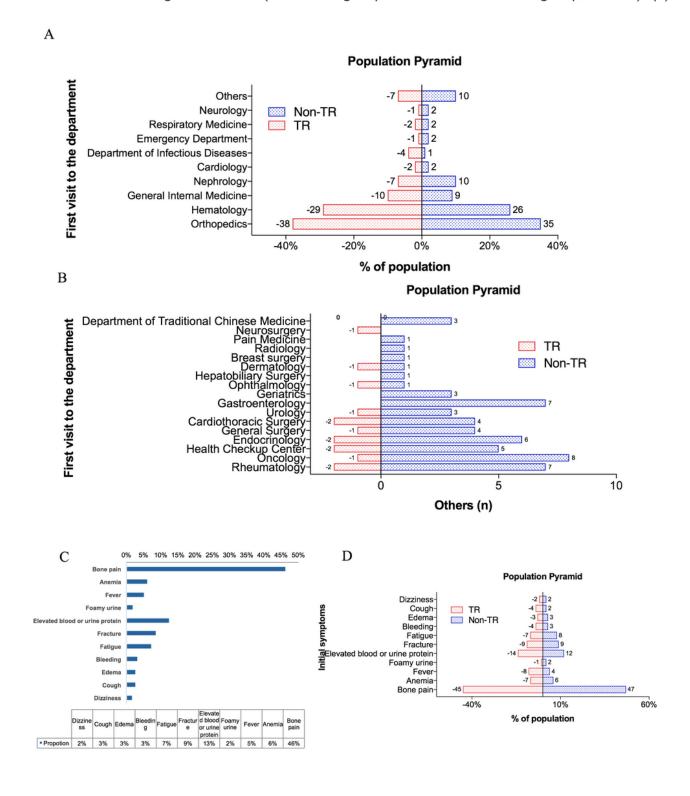


Figure 2

The departments for patients' first visits and the initial symptoms

The most common departments for patients' first visits (A, B) and the initial symptoms of the patients in total (C) and in TR and non-TR groups (D).

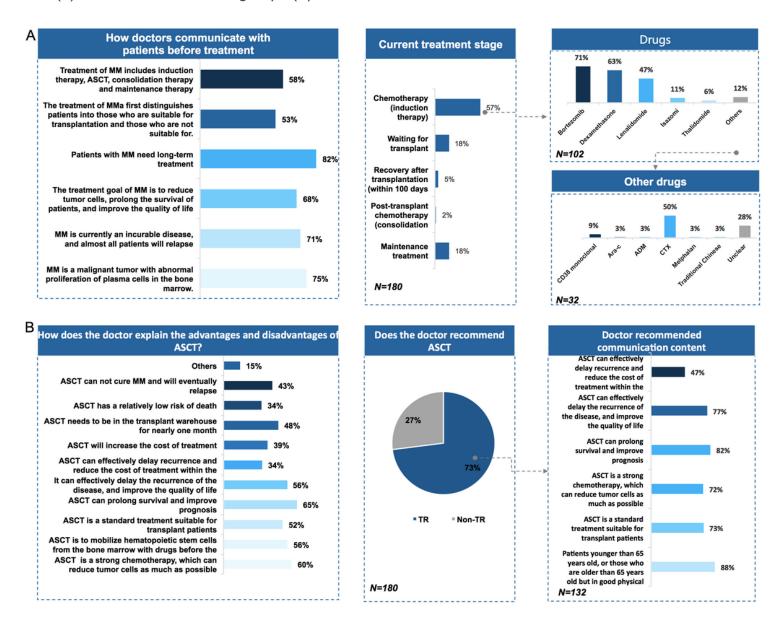


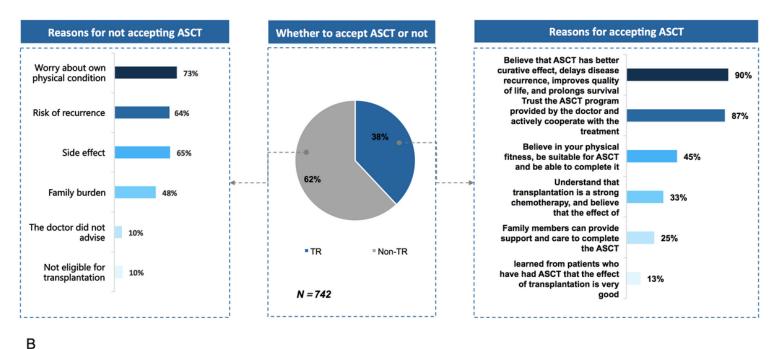
Figure 3

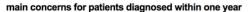
The contents of communication before transplantation between doctors and patients

(A) How patients with multiple myeloma were told by doctors and the treatment programs. Before treatment, more than 70% of patients were told that 1) patients with MM need long-term treatment, 2) MM is a malignant tumor with abnormal proliferation of plasma cells in the bone marrow, 3) MM is currently an incurable disease and will relapse in almost all patients after treatment. Fifty-seven percent of patients were receiving chemotherapy at the time of survey, while the patients under maintenance treatment and waiting for treatment accounted for 18%. Bortezomib (71%) and dexamethasone (63%) were the most commonly used therapeutic drugs. (B) How does the doctor explain the advantages and disadvantages of ASCT to patients. Seventy-three percent of patients were recommended for ASCT by their doctors. One

of the main points that doctors communicated to their patients was that ASCT is a perfered treatment option for patients with good physical status, i.e., patients younger than 65 years old or older than 65 years but in good physical condition, and may prolong survival and improve prognosis.







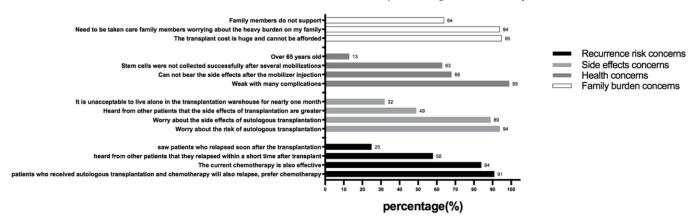


Figure 4

Reasons for choosing or not choosing ASCT and the main concerns of patients

Thirty-eight percent of patients accepted ASCT. "Believe that autologous transplantation has a better curative effect, delays disease recurrence, improves quality of life, and prolongs survival (90%)" and "Trust the autologous transplant program provided by the doctor and actively cooperate with the treatment" (87%) were the most common reasons for opting for ASCT. Physical condition (73%), side effects (65%), and the risk of recurrence (64%), and family burden (48%) were the main reasons for

patients to reject ASCT (A) and the main concerns for patients including recurrence risk, side effects, health and family burden concerns (B).

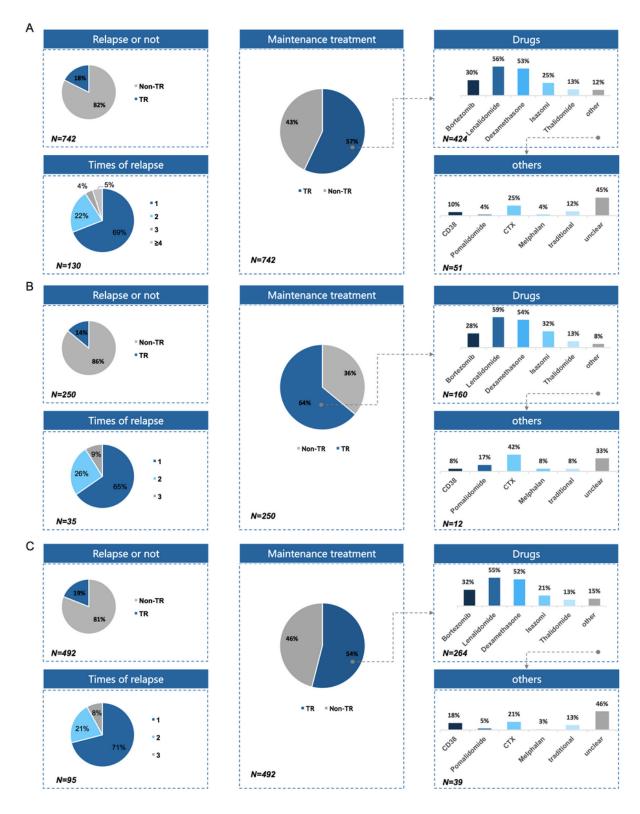


Figure 5

The relapse situation and maintenance treatment of patients in total (A), transplant group (B) and non-transplant group(C).

Eighteen percent of the total patients relapsed, lower in the TR group than in the non-TR group (14% versus 19%, P>0.05), and 69% of them relapsed once (A) (65% in the TR group (B) and 71% in the non-TR group (C), P>0.05). Fifty-seven percent of patients received maintenance treatment (64% in the TR group and 54% in the non-TR group, P<0.05), and more than half (56%) of them received lenalidomide (59% in the TR group and 55% in the non-TR group, P>0.05).

Supplementary Files

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- table1.docx