Experimental Hematology & Oncology

CORRESPONDENCE Open Access

Application patterns and outcomes of hematopoietic stem cell transplantation in peripheral T-cell lymphoma patients: a multicenter real-world study in China

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Abstract

The optimal timing and type of hematopoietic stem cell transplantation (HSCT) for treating peripheral T-cell lymphoma (PTCL) remain controversial. This retrospective real-world study investigated the application pattern and outcomes of HSCT in China. The analysis encompassed 408 PTCL patients with a median age of 45.5 years, all of whom received initial adequate therapy at five hospitals. Among patients with nodal PTCL who responded effectively to first-line therapy (the "responders", $n=127$) and subsequently underwent HSCT consolidation ($n=47$, 37.0%), 93.6% received auto-HSCT, while 6.4% underwent allo-HSCT. Front-line auto-HSCT showed potential for long-term disease control in nodal PTCL responders. Among non-nodal PTCL responders ($n=80$) with HSCT ($n=26$, 32.5%), 46.2% underwent allo-HSCT and 53.8% received auto-HSCT. Upfront allo-HSCT provides longer progression-free survival (PFS) for non-nodal PTCL responders, with lower 3-year cumulative incidence of relapse (CIR) (16.7% vs. 56.0%) and comparable non-relapse mortality (NRM) (10.4% vs. 11.0%) compared to auto-HSCT. For patients who achieved remission with second-line salvage regimens, allo-HSCT was the primary choice (82.4%) for non-nodal PTCL, while auto-HSCT was more common (82.4%) in nodal PTCL. Nodal PTCL patients underwent auto-HSCT after ≥ 3 lines of treatment had a higher 3-year CIR (81.0%) compared to those treated in the first (26.0%) or second line (26.0%). Non-nodal PTCL patients underwent allo-HSCT after ≥ 3 lines had a higher 3-year NRM (37.5%) compared to after first (10.4%) or second line treatment (8.5%). These findings highlight distinct HSCT application patterns for PTCL in China, emphasizing the impact of early disease control and upfront consolidative HSCT.

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Keywords Hematopoietic stem cell transplantation, Peripheral T-cell lymphoma, Autologous HSCT, Allogeneic HSCT

To the editor,

Peripheral T-cell lymphoma (PTCL) presents significant treatment challenges due to its heterogeneous nature and generally poor prognosis [1]. Hematopoietic stem cell transplantation (HSCT) offers a potential cure for PTCL. However, the optimal timing and type of transplant, whether autologous (auto-HSCT) or allogeneic (allo-HSCT), are still under debate.

This retrospective, real-world study has been conducted at five HSCT-qualified medical centers in China to investigate the impact of HSCT. After rigorously screening, we further analyzed 408 PTCL patients who had received adequate initial treatment and had confirmed response status (median age: 45.5 years).

Consolidative auto-HSCT after first-line treatment of PTCL has been extensively published [2–6]. However, due to the diverse subtypes of PTCL and the varying patient characteristics across different studies, the conclusions remain controversial. In the present study, auto-HSCT was the preferred HSCT type for 93.6% of nodal PTCL responders (Additional file 1, Table S1), including those with complete remission (CR) or satisfactory partial remission (PR) (Fig. 1A-C; Fig. S1). The progression-free survival (PFS) and overall survival (OS) curves of patients with auto-HSCT reached plateau (Fig. 1D; Fig. S2A), suggesting auto-HSCT may achieve long-lasting response and even cure [2, 5, 6]. The benefit of auto-HSCT consolidation on PFS for nodal-PTCL responders was also observed when excluding ALK+ALCL, also in the PSM cohort (Fig. S2B, Fig. S3A and Table S4).

Previous studies have shown that up-front allo-HSCT in PTCL is associated with a low relapse rate but a high risk of non-relapse mortality (NRM) [7, 8]. In our analysis for non-nodal PTCL who underwent HSCT consolidation ($n=26$; Fig. S1D; Fig. S2C and D), 46.2% of patients underwent allo-HSCT, while 53.8% auto-HSCT (Fig. 1A). Among these patients, those who underwent allo-HSCT demonstrated a more favorable PFS (median PFS: 82.7 months vs. 15.8 months, $P=0.031$; Fig. 1E). Additionally, the 3-year CIR and NRM were 16.7% and 10.4% for the allo-HSCT group, and 56.0% and 11.0% for the auto-HSCT group. The lower NRM was also confirmed in the PSM cohort of non-nodal responders (Fig. S3B and Table S5). These results suggest that upfront allo-HSCT may be associated with a lower CIR while maintaining comparable NRM rates compared to auto-HSCT in non-nodal PTCL patients.

The optimal HSCT consolidation strategy for patients in remission following salvage therapy remains uncertain in the literature [9, 10]. While both auto-HSCT and allo-HSCT are considered viable options, there is a lack of comparative data and varying transplant preferences among centers, influenced by factors such as transplant eligibility, pathological subtypes and disease risk stratification. This study observed a distinct HSCT pattern after second-line treatment, with non-nodal PTCL patients more likely to undergo allo-HSCT (82.4%) and nodal PTCL patients predominantly choosing auto-HSCT (82.4%; Fig. 2A and Table S2). This finding highlights it is challenging to compare the efficacy of auto-HSCT and allo-HSCT after salvage therapy for PTCL, due to the selection propensity in the type of HSCT for different PTCL subtypes.

Our findings also indicate that HSCT performed after ≥3 lines treatment was associated with adverse outcomes (Fig. 2B-E, Fig. S8; Table S3). Specifically, nodal PTCL patients in remission status who underwent auto-HSCT after ≥3 lines showed a significantly higher 3-year CIR at 81.0%, compared to 26.0% in the first line and 26.0% in the second line (Fig. 2D). One possible reason for the reduced effectiveness of later-line auto-HSCT is the resistance to high-dose chemotherapy in patients who failed front-line treatment [11].

For non-nodal patients, the application of allo-HSCT consolidation following ≥3 lines treatment demonstrated a significant increase in 3-year NRM rates, reaching 37.5% in comparison to 10.4% in the first and 8.5% in the second-line treatment, although with a comparable 3-year CIR (Fig. 2E). This finding emphasizes the impact of a heavy treatment history on bone marrow hematopoiesis and immune reconstitution in patients undergoing allo-HSCT, rendering them more vulnerable to complications such as graft-versus-host disease and infections [8, 12].

Overall, our study underscores the distinct HSCT applications for nodal and non-nodal PTCL in China, highlighting the potential drawbacks of consolidative HSCT in later-line treatment. Further research with larger sample sizes is warranted to confirm our findings.

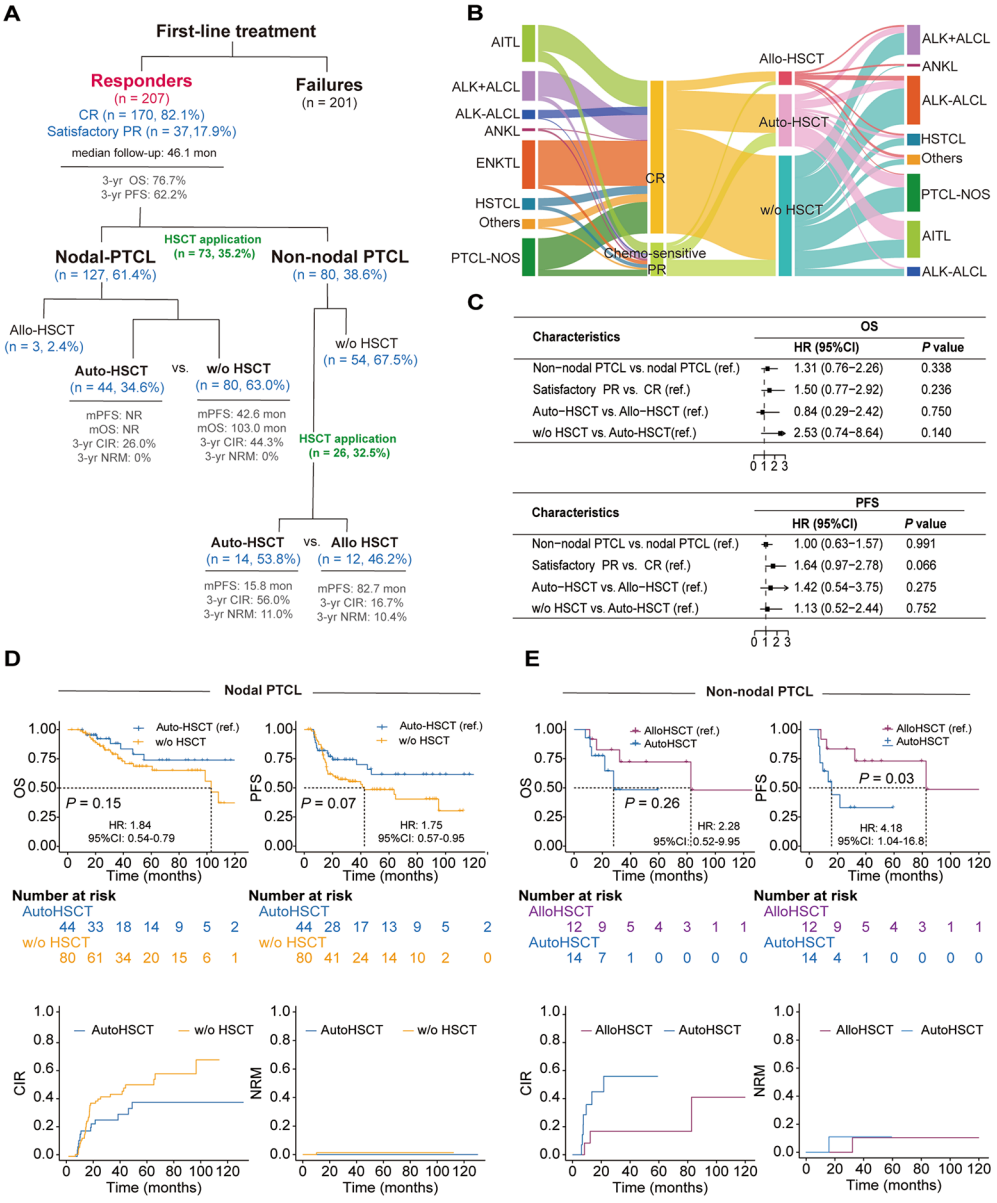

Fig. 1 Flow chart and treatment patterns for patients who responded effectively to first-line treatment. (**A**) Flow chart for patients with PTCL who demonstrated a positive response (responders) to first-line treatment. (**B**) Initial treatment response and subsequent treatment choices in responders. (**C**) Analysis of clinical characteristics impacting progression-free survival (PFS) and overall survival (OS) in responders using a univariate Cox model. (**D**) Outcomes since initial treatment with autologous hematopoietic stem cell transplantation (auto-HSCT) and without HSCT in nodal-PTCL responders. (**E**) Outcomes for non-nodal PTCL responders with auto-HSCT and allogeneic-HSCT (allo-HSCT). For PR patients, if the initial treatment was deemed insufficient by the hematologist and immediate salvage therapy was needed, it was considered unsatisfactory PR. Otherwise, it was classified as satisfactory PR to distinguish between responsive patients and those with primary refractory disease. CIR: Cumulative incidence of relapse; NRM: Non-relapse mortality; w/o: Without; CI: Confidence Interval; AITL: Angioimmunoblastic T-cell lymphoma; ALK-ALCL: Anaplastic lymphoma kinase-negative anaplastic large cell lymphoma; ALK + ALCL: Anaplastic lymphoma kinase-positive anaplastic large cell lymphoma; ANKL: Aggressive NK-cell leukemia; ENKTL: Extranodal NK/T-cell lymphoma, nasal type; HSTCL: Hepatosplenic T-cell lymphoma; PTCL-NOS: Peripheral T-cell lymphoma, not otherwise specified

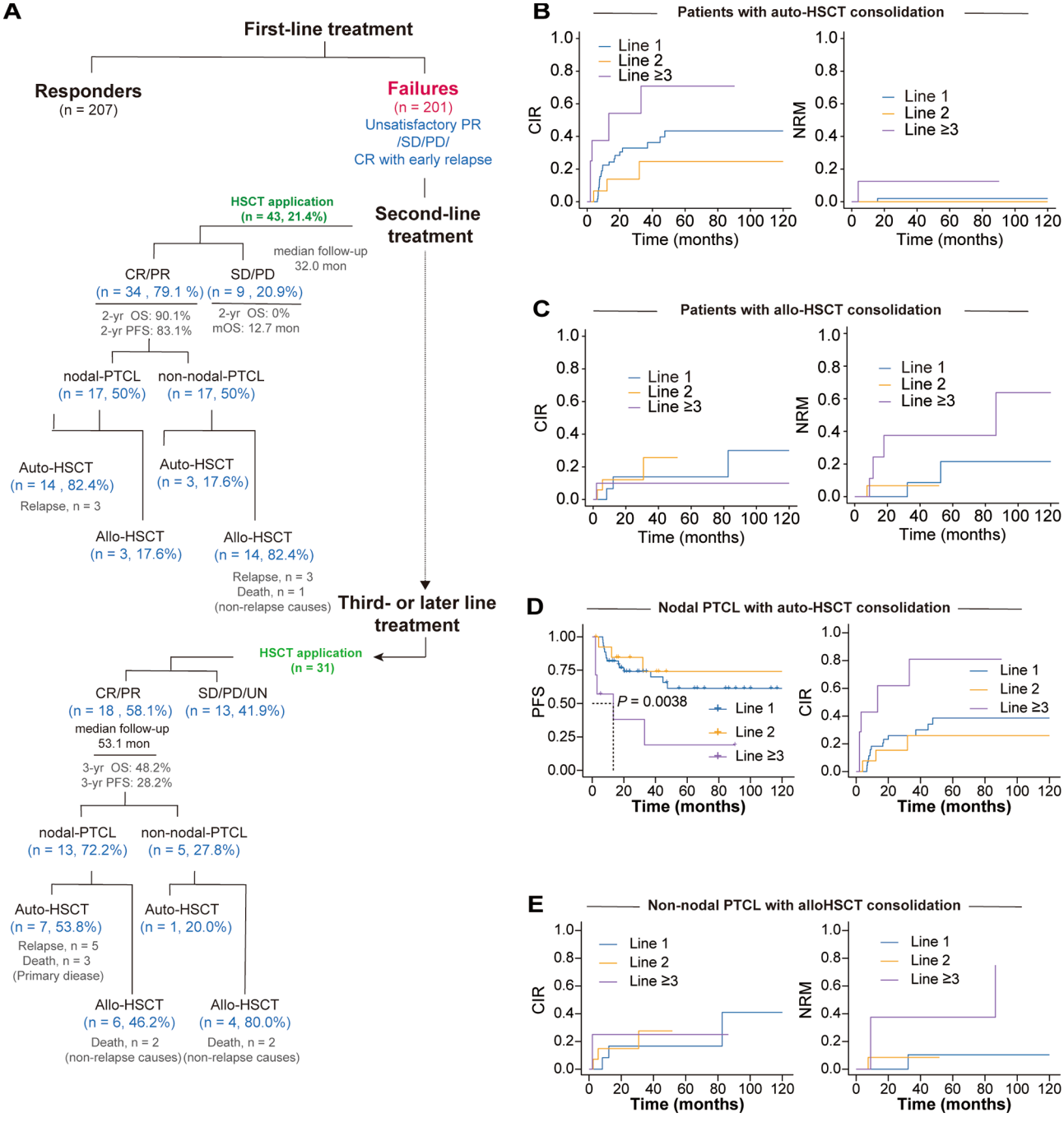

Fig. 2 Flow chart for non-responders and HSCT application outcomes at the different lines. (**A**) Flow chart for patients with PTCL who did not respond effectively to first-line treatment. (**B**) CIR and NRM following auto-HSCT for patients who achieved remission at first-line, second-line, and third-line treatment. (**C**) CIR and NRM following allo-HSCT consolidation for patients in remission at first-line, second-line, and third-line treatment. (**D**) PFS and CIR following auto-HSCT for nodal-PTCL patients with remission status at first-line, second-line, and third- or later-line treatment. (**E**) CIR and NRM following allo-HSCT for non-nodal PTCL patients with remission status at first-line, second-line, and third- or later-line treatment

Abbreviations

HSCT	Hematopoietic Stem Cell Transplantation
Auto-HSCT	Autologous Hematopoietic Stem Cell Transplantation
Allo-HSCT	Allogeneic Hematopoietic Stem Cell Transplantation
ALK + ALCL	Anaplastic Lymphoma Kinase-Positive Anaplastic Large Cell Lymphoma
CIR	Cumulative Incidence of Relapse
NRM	Non-Relapse Mortality
CR	Complete Remission
PR	Partial Remission
SD	Stable Disease
PD	Progressive Disease

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40164-024-00557-9.

Supplementary Material 1

Acknowledgements
We are grateful for the invaluable support provided by all the follow-up patients throughout this study. A special acknowledgment goes to Prof. Hao Zhang and Prof. Xin Du for their continuous support.

Author contributions
EJ, DZ and YL initiated and designed the study. HG collected the data, conducted the statistical analysis and wrote the draft manuscript. ZZ aided in data collection, and was responsible for patient follow-up. JW provided constructive suggestions. All authors corrected and reviewed the manuscript, and consented to publication of the paper.

Funding
This work was supported by the Fundamental Research Funds for the Central Universities Funds (3332023058, and 2023-I2M-C&T-B-108); the Tianjin Natural Science Foundation (23JCZXJC00220 and 23JCZXJC00040); the National Key Research and Development Program of China (2023YFC2508902); the Ministry of Science and Technology of China (2021YFA1101603); National Natural Science Foundation of China [82170217 and 82070192]; the Key Project of Tianjin Natural Science Foundation [20JCZDJC00410]; and the CAMS Innovation Fund for Medical Sciences (CIFMS) [2021-I2M-1-073].

Data availability
The datasets and analysis codes are available on reasonable request to the corresponding author.

Declarations

Ethics approval and consent to participate
This multicenter retrospective study was conducted at five hospitals in China with approval from the Ethics Committee of the Institute of Hematology & Blood Diseases (Approval Number: QTJC2024018-EC-1) and a waiver of informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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Received: 18 May 2024 / Accepted: 12 August 2024
Published online: 24 August 2024

References

1. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016;127(20):2375-90. Epub 20160315. doi: https://doi.org/10.1182/blood-2016-01-643569.
2. Ellin F, Landström J, Jerkeman M, Relander T. Real-world data on prognostic factors and treatment in peripheral T-cell lymphomas: a study from the Swedish Lymphoma Registry. Blood. 2014;124(10):1570-7. Epub 20140708. https://doi.org/10.1182/blood-2014-04-573089 .
3. Fossard G, Broussais F, Coelho I, Bailly S, Nicolas-Virelizier E, Toussaint E, et al. Role of up-front autologous stem-cell transplantation in peripheral T-cell lymphoma for patients in response after induction: an analysis of patients from LYSA centers. Ann Oncol. 2018;29(3):715 – 23. https://doi.org/10.1093/annonc/mdx787.
4. Park SI, Horwitz SM, Foss FM, Pinter-Brown LC, Carson KR, Rosen ST, et al. The role of autologous stem cell transplantation in patients with nodal peripheral T-cell lymphomas in first complete remission: Report from COMPLETE, a prospective, multicenter cohort study. Cancer. 2019;125(9):1507-17. Epub 20190129.https://doi.org/10.1002/cncr.31861.
5. Gao H, Wu M, Hu S, Ding N, Ji X, Mi L, et al. Effect of autologous hematopoietic stem cell transplantation for patients with peripheral T-cell lymphoma in China: A propensity score-matched analysis. Front Oncol. 2022;12:1039888. Epub 20221117. https://doi.org/10.3389/fonc.2022.1039888.
6. Yang P, Cai M, Cao Y, Fan S, Tang W, Ji M, et al. Up-front autologous stem cell transplant in peripheral T-cell lymphoma patients achieving complete response after first-line treatment: A multicentre real-world analysis. Br J Haematol. 2024. Epub 20240125. https://doi.org/10.1111/bjh.19317.
7. Schmitz N, Truemper L, Bouabdallah K, Ziepert M, Leclerc M, Cartron G, et al. A randomized phase 3 trial of autologous vs allogeneic transplantation as part of first-line therapy in poor-risk peripheral T-NHL. Blood. 2021;137(19):2646-56. https://doi.org/10.1182/blood.2020008825.
8. Le Gouill S, Milpied N, Buzyn A, Peffault De Latour R, Vernant J-P, Mohty M, et al. Graft-Versus-Lymphoma Effect for Aggressive T-Cell Lymphomas in Adults: A Study by the Société Française de Greffe de Moëlle et de Thérapie Cellulaire. Journal of Clinical Oncology. 2008;26(14):2264-71. https://doi.org/10.1200/JCO.2007.14.1366.
9. Baek DW, Moon JH, Lee JH, Kang K-W, Lee HS, Eom H-S, et al. Real-world data of long-term survival in patients with T-cell lymphoma who underwent stem cell transplantation. Blood Cancer Journal. 2023;13(1):95. https://doi.org/10.1038/s41408-023-00868-w.
10. Du J, Yu D, Han X, Zhu L, Huang Z. Comparison of Allogeneic Stem Cell Transplant and Autologous Stem Cell Transplant in Refractory or Relapsed Peripheral T-Cell Lymphoma: A Systematic Review and Meta-analysis. JAMA Netw Open. 2021;4(5):e219807. Epub 20210503. https://doi.org/10.1001/jamanetworkopen.2021.9807.
11. Smith SM, Burns LJ, van Besien K, LeRademacher J, He W, Fenske TS, et al. Hematopoietic Cell Transplantation for Systemic Mature T-Cell Non-Hodgkin Lymphoma. Journal of Clinical Oncology. 2013;31(25):3100-9. https://doi.org/10.1200/JCO.2012.46.0188.
12. Ogonek J, Kralj Juric M, Ghimire S, Varanasi PR, Holler E, Greinix H, Weissinger E. Immune Reconstitution after Allogeneic Hematopoietic Stem Cell Transplantation. Front Immunol. 2016;7:507. Epub 20161117. https://doi.org/10.3389/fimmu.2016.00507.

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