Original Study

Consolidative Radiotherapy After Autologous Stem Cell Transplantation for Relapsed or Refractory Diffuse Large B-cell Lymphoma

Brendan G. Coutu,[1] Christopher T. Wilke,[1] Jianling Yuan,[1] Qing Cao,[2] Matthew R. Vernon,[3] Chung Lee,[1] Veronika Bachanova,[2] Kathryn E. Dusenbery[1]

Abstract

Patients with relapsed or refractory diffuse large B-cell lymphoma undergoing autologous bone marrow transplantation benefited from consolidative involved-field radiotherapy (IFRT). All patients who underwent consolidative IFRT had improved locoregional control. Additionally, patients with enlarged lymphadenopathy had an improved locoregional control, disease-free survival, and overall survival at the 2-year evaluation.

Introduction: We evaluated the role of consolidative radiotherapy (RT) for patients undergoing high-dose chemotherapy (HDC) and autologous stem cell transplantation (ASCT) for relapsed or refractory diffuse large B-cell lymphoma (DLBCL). **Materials and Methods:** We reviewed the medical records of 72 consecutive patients who had undergone ASCT for relapsed or refractory DLBCL at our institution from 2006 to 2014. Pretransplant conditioning consisted of HDC and total body irradiation. Of the 72 patients, 13 received post-transplant consolidative RT at the discretion of the consulted radiation oncologist. **Results:** Consolidative RT was associated with significantly improved 2-year locoregional control (LRC) (92% vs. 68%; $P = .04$). However, no difference was seen in either the 2-year progression-free survival (PFS) (69% vs. 54%; $P = .25$) or overall survival (OS) (85% vs. 59%; $P = .44$). Analysis of the subgroup of 19 patients with persistent residual masses $\geq$ 2 cm on post-transplant imaging demonstrated a significant improvement in LRC (100% vs. 36%; $P < .01$), PFS (88% vs. 27%; $P = .01$), and OS (100% vs. 45%; $P = .02$) with consolidative RT. **Conclusion:** The use of consolidative RT after HDC and ASCT for relapsed or refractory DLBCL appears to significantly improve LRC. For patients with masses $\geq$ 2 cm after ASCT, improved 2-year PFS and OS were seen. Prospective trials are needed to further identify the patients who would derive the most benefit from consolidative RT in the ASCT setting.

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Introduction

Diffuse large B-cell lymphoma (DLBCL) accounts for 40% of all newly diagnosed cases of non-Hodgkin lymphoma.[1] Conventional combination chemotherapy can induce a complete response (CR) in ~60% of patients. However, some patients will present with primary refractory disease and, among patients who achieve an initial CR, a significant proportion will develop a relapse. After the conclusion of the Parma Study Group trial, high-dose chemotherapy (HDC) combined with autologous stem cell transplantation (ASCT) became the standard salvage approach for relapsed or refractory DLBCL.[2] However, only 40% to 50% of patients with chemotherapy-sensitive relapse and 30% of those with primary refractory disease will achieve long-term progression-free survival (PFS) after ASCT. The patterns of failure in the patients with recurrence despite HDC-ASCT have largely been within the sites of previous disease involvement.[3,4] This has generated increased interest in the use of consolidative involved-field radiotherapy (IFRT) with the hope of improving post-ASCT outcomes.[2,4-6]

To the best of our knowledge, no high-quality prospective randomized trials have directly addressed the utility of consolidative IFRT. Thus, the benefit of RT in the transplant setting has often

[1]Department of Radiation Oncology
[2]Blood and Marrow, Transplant Program, University of Minnesota, Minneapolis, MN
[3]Department of Radiation Oncology, Southwestern Vermont Medical Center, Bennington, VT

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Address for correspondence: Kathryn E. Dusenbery, MD, Department of Radiation Oncology, University of Minnesota, 420 Delaware Street, Minneapolis, MN 55455
E-mail contact: dusen001@umn.edu

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Table 1 Patient Characteristics

Characteristic	Consolidative IFRT (n = 13)	Observation (n = 59)	*P* Value
Sex			.16
Male	10 (77)	33 (56)	
Female	3 (23)	26 (44)	
Age at transplantation (y)			.58
30-39	0 (0)	3 (5)	
40-49	2 (15)	10 (17)	
50-59	7 (54)	21 (36)	
60-75	4 (31)	25 (42)	
B symptoms	1 (8)	28 (47)	<.01[a]
Previous consolidative IFRT	2 (15)	12 (20)	.68
Disease state			.73
Primary refractory disease	2 (15)	7 (12)	
Relapsed disease	11 (85)	52 (88)	
Involved sites of disease			.90
Head and neck	5 (38)	31 (53)	
Axilla	4 (31)	14 (34)	
Mediastinum	4 (31)	19 (32)	
Abdomen	9 (69)	32 (54)	
Pelvis	5 (38)	25 (42)	
Stage at relapse			.88
I	1 (8)	3 (5)	
II	2 (15)	6 (10)	
III	4 (31)	16 (27)	
IV	6 (46)	34 (58)	
Transplant conditioning regimen			.59
TBI	11 (85)	53 (90)	
Other	2 (15)	6 (10)	
Era of transplantation			.71
<2010	3 (23)	11 (19)	
≥2010	10 (77)	48 (81)	
Tumor size ≥2 cm			<.01[a]
Before ASCT	9 (69)	15 (25)	
After ASCT	8 (62)	11 (19)	
Pretransplant Deauville score			.17
<4	5 (38)	35 (59)	
≥4	8 (62)	24 (41)	
Median follow-up duration (days)	763	742	.13

Data presented as n (%).
Abbreviations: ASCT = autologous stem cell transplantation; IFRT = involved-field radiotherapy; TBI = total body irradiation.
[a]Statistically significant.

been extrapolated from single institutional retrospective series. A review of these data, however, demonstrated conflicting information regarding the use of consolidative IFRT and its role for patients undergoing ASCT for relapsed or refractory disease.

We examined the clinical efficacy of consolidative IFRT in a group of patients who had undergone ASCT at our institution for relapsed or refractory DLBCL. We report the results of a retrospective analysis of 72 patients who had undergone HDC and ASCT in accordance with a single institutional protocol at the University of Minnesota (UMN).

Materials and Methods

Patients

We reviewed the medical records of 72 consecutive patients who had undergone HDC and ASCT for relapsed or refractory DLBCL (43 males and 29 females) at the UMN according to a single institutional protocol from 2006 to 2014. This institutional protocol provided stringent inclusion criteria for patients to undergo ASCT for relapsed or refractory DLBCL, including age < 75 years, Karnofsky performance score > 80%, and no serious organ