ORIGINAL ARTICLE

Korean J Intern Med 2019;34:894-901
https://doi.org/10.3904/kjim.2017.174

KJIM

Costs and clinical outcomes of patients with diffuse large B-cell lymphoma in first remission: role of PET/CT surveillance

Koung Jin Suh[1], Ki Hwan Kim[2], Ryul Kim[3], Ja Min Byun[2], Miso Kim[3], Jin Hyun Park[2], Bhumsuk Keam[3], Tae Min Kim[3], Jin-Soo Kim[2], In Sil Choi[2], and Dae Seog Heo[3]

[1]Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam; [2]Department of Internal Medicine, Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul; [3]Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea

Received: May 6, 2017
Revised : September 30, 2017
Accepted: October 27, 2017

Correspondence to
Ki Hwan Kim, M.D.
Department of Internal Medicine, Seoul Metropolitan Government Seoul National University Boramae Medical Center, 20 Boramae-ro 5-gil, Dongjak-gu, Seoul 07061, Korea
Tel: +82-2-870-2229
Fax: +82-2-831-0714
E-mail: floresta405@gmail.com

In Sil Choi, M.D.
Department of Internal Medicine, Seoul Metropolitan Government Seoul National University Boramae Medical Center, 20 Boramae-ro 5-gil, Dongjak-gu, Seoul 07061, Korea
Tel: +82-2-870-2229
Fax: +82-2-831-0714
E-mail: hmoischoi@hanmail.net

Background/Aims: The role of [18F]-fluorodeoxyglucose positron emission tomography-computed tomography (PET/CT) in patients with diffuse large B-cell lymphoma (DLBCL) in first remission is unclear.

Methods: Medical costs within the first 3 years of treatment completion and clinical outcomes of 118 patients with DLBCL in first remission with and without surveillance PET/CT (PET/CT [+] group [n = 76] and PET/CT [–] group [n = 42], respectively) were retrospectively analyzed.

Results: In a propensity matched cohort with adjustment for International Prognostic Index risk and relapse, the PET/CT (+) group was shown to have similar medical costs as the PET/CT (–) group. Relapse-free survival (RFS) and overall survival (OS) were comparable between the two groups (median RFS not reached [NR] for both groups, $p = 0.133$; median OS NR, $p = 0.542$). Among 76 patients with surveillance PET/CT, 31 (40.8%) had findings suggestive of recurrence and 16 of these (51.6%) were later confirmed to have recurrent disease. Fifteen patients (48.4%) were confirmed to not have recurrence after follow-up CT or PET/CT evaluation (n = 10) and biopsy (n = 4). None of the patients with negative PET/CT findings had disease recurrence. Sensitivity, specificity, positive predictive value, and negative predictive value of PET/CT for detection of recurrence were 1, 0.75, 0.52, and 1, respectively.

Conclusions: Surveillance PET/CT resulted in similar clinical outcomes and medical costs compared to no surveillance PET/CT. Approximately half of patients with PET/CT findings of recurrence had no recurrence after follow-up imaging and biopsy, which would not have been carried out if PET/CT had not been performed in the first place.

Keywords: Lymphoma, large B-cell, diffuse; Positron emission tomography computed tomography; Costs and cost analysis; Sensitivity and specificity; Survival

INTRODUCTION

The prognosis of patients with diffuse large B-cell lymphoma (DLBCL) has been significantly improved after the introduction of CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), and even more with

pISSN 1226-3303
eISSN 2005-6648
http://www.kjim.org

the introduction of rituximab into the treatment regimen [1-4]. However, the improvement in treatment results with rituximab in the first-line treatment has been reported to adversely affect treatment outcomes when these patients recur [5]. Therefore, for patients with complete remission (CR) after treatment with rituximab, the importance of early diagnosis and treatment of disease recurrence has increased.

[18F]-fluorodeoxyglucose positron emission tomography-computed tomography (PET/CT) is a useful tool for the diagnosis and prognostication of DLBCL, as well as for evaluation of treatment response [6]. The usefulness of PET/CT follow-up to detect relapses after CR has been demonstrated [5,7]. However, whether this early detection of recurrence found by PET/CT surveillance leads to any survival benefit has not been proven yet. Moreover, considering the characteristics of DLBCL with its high cure rate, there is concern that tracking all patients with PET/CT will lead to an increase in medical costs [8].

In this study, we aimed to evaluate the role of PET/CT in patients with DLBCL in first remission along with an analysis of its effects on clinical outcomes and medical costs.

METHODS

Study design and patient population

A retrospective study of patients diagnosed with DLBCL at Seoul National University Hospital (SNUH) and Seoul National University Boramae Medical Center (SNU-BMC) was conducted. Costs incurred specifically for DLBCL from the date of CR after completion of standard chemotherapy through the subsequent 3 years were calculated. Patients newly diagnosed with DLBCL between January 2005 and January 2015 were eligible for inclusion. The Institutioanl Review Board at SNUH and SNU-BMC approved this study (IRB No.26-2014-98), and it was conducted in accordance with the Declaration of Helsinki. Written informed consent was not acquired because it was a retrospective study. All patients' records/information were anonymized and deidentified prior to analysis.

Cost definitions and data sources

Costs consisted of the following two components: inpatient and outpatient costs. These data were retrieved from the institutional accounting system. Costs related to emergency room visits were regarded as inpatient costs. Costs of prescription drugs sold in the hospital pharmacy were included in the cost analysis. However, costs of drugs bought outside the hospital could not be included due to insufficient data. The proportion of medical expenses not covered by the National Health Insurance Service was determined to evaluate the economic burden on patients and the government separately. All cost estimates are represented according to the annual exchange rate in 2016 (1,189.50 Korean won = 1 US dollar).

The duration of follow-up was defined from the date of diagnosis to the end of follow-up at our institution. Relapse-free survival (RFS) was measured from the date of diagnosis to either the date of disease recurrence or death. The overall survival (OS) was defined as the interval from the date of diagnosis to death.

Statistical analysis

The *t* test was performed to evaluate the association between clinicopathological variables and undergoing surveillance PET/CT. Both hospitals in this study used the same PET/CT scan (Briograph mCT 40, Siemens Medical Solutions, Knoxville, TN, USA) for examination. RFS and OS were calculated using the Kaplan-Meier method, and the values were compared using the log-rank test. Costs were compared between variables by using the *t* test and analysis of variance, as appropriate. We used multivariate analysis with backward stepwise multiple linear regression to analyze clinicopathological factors as well as PET/CT surveillance that may have been associated with costs. p values of < 0.05 were considered significant. All analyses of data collected through February 2017 were performed by using SPSS software version 21 (IBM Co., Armonk, NY, USA) and GraphPad Prism 5 (GraphPad Software Inc., La Jolla, CA, USA).

RESULTS

Patient characteristics

Characteristics of 118 patients diagnosed with DLBCL are summarized in Table 1. A total of 76 patients (64.4%) received PET/CT surveillance after achieving CR (here-

Table 1. Patient characteristics

Characteristic	PET-CT (–)	PET-CT (+)	*p* value
No. of patients	42 (35.6)	76 (64.4)	
Age, yr	57 (29–85)	59 (23–82)	0.524
Sex			0.738
Male	24 (57.1)	41 (53.9)	
Female	18 (42.9)	35 (46.1)	
ECOG PS			0.022
0	17 (40.5)	12 (15.8)	
1	21 (50.0)	52 (68.4)	
2	4 (9.5)	10 (13.2)	
3	0	12 (2.6)	
LDH, IU/mL	210.5 (99–5,110)	216.0 (125–3,742)	0.481
Extranodal involvement			0.240
No	33 (78.6)	52 (68.4)	
Yes	9 (21.4)	24 (31.6)	
Stage			0.456
1	13 (31.0)	14 (18.4)	
2	14 (33.3)	27 (35.5)	
3	6 (14.3)	13 (17.1)	
4	9 (21.4)	22 (28.9)	
IPI risk			0.671
Low	24 (57.1)	36 (47.4)	
Low-intermediate	9 (21.4)	16 (21.1)	
High-intermediate	3 (7.1)	9 (11.8)	
High	6 (14.3)	15 (19.7)	
Treatment			0.125
R-CHOP	40 (95.2)	76 (100.0)	
R-EPOCH	2 (4.8)	0	
Duration of follow-up, mon	32 (7–135)	54 (11–133)	< 0.001

Values are presented as number (%) or median (range).
PET-CT, positron emission tomography-computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; IPI, International Prognostic Index; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone; R-EPOCH, rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin.

after, PET/CT [+] group), whereas 42 patients (35.6%) did not (hereafter, PET/CT [–] group). The median age was 57 years in the PET/CT (–) group and 59 years in the PET/CT (+). The PET-CT (+) group was more likely to have poor performance status; however, stage and International Prognostic Index (IPI) risk were similar between the groups. Most of the patients received the R-CHOP regimen for their initial treatment. The median follow-up was 31.8 months for the PET/CT (–) group and 49.6 months for the PET/CT (+) group, respectively (p = 0.021).

Univariate and multivariate analysis of medical costs

Data on the outpatient number of clinic visits and admission, and costs by follow-up PET/CT are described in detail in Table 2. When the follow-up duration was

https://doi.org/10.3904/kjim.2017.174

Table 2. Univariate analysis for medical costs during the first 3 years after achieving complete response

Subject	PET-CT (–) (n = 42)	PET-CT (+) (n = 76)	*p* value
Duration of follow-up, mon	28 (3–36)	36 (6–36)	< 0.001
Relapse	3 (7.1)	16 (21.1)	0.049
Outpatient visits			
No. of visits	14 (4–103)	25 (6–57)	< 0.001
Costs	2,256,327 (214,178–38,923,231)	4,959,357 (1,021,569–10,941,483)	0.021
Hospitalization			
No. of hospitalization	0 (0–15)	0 (0–14)	0.691
Costs	0 (0–91,291,439)	0 (0–6,440,852)	0.862
Total costs	2,499,689 (340,094–130,214,670)	5,229,901 (1,596,393–71,140,025)	0.755
Total costs paid by patients[a]	326,819 (64,540–108,837,381)	636,100 (176,051–33,422,478)	0.460

Values are presented as median (range) or number (%). Statistical significance test was done by independent *t* test.
PET-CT, positron emission tomography-computed tomography.
[a]Costs that were not reimbursed by the National Health Insurance Service; thus, paid by the patients. Costs are stated in Korean won.

Table 3. Results of multivariate linear regression models analyzing total medical costs

Variables[a]	B	SE	*p* value
Age	–185,986	101,263	0.069
Relapse	11,618,666	4,320,967	0.008

Adjusted R^2 = 0.403, F = 14.140.
SE, standard error.
[a]Other variables in the model included International Prognostic Index risk score, and positron emission tomography-computed tomography follow-up.

limited to the first 3 years after achieving a CR for the medical cost comparison, the median duration of follow-up was longer in the PET-CT (+) group compared with the PET-CT (–) group (36 months [range, 6 to 36] vs. 28 months [range, 3 to 36], $p < 0.001$). Accordingly, the number of outpatient visits and associated costs were also higher in the PET/CT (+) group. There was no statistically significant difference in the number of hospitalizations and any associated costs between the two groups. Within 3 years, the total medical costs were 2,499,689 won for the PET/CT (–) group and 5,229,901 won for the PET/CT (+) group, respectively ($p = 0.755$). There was no significant difference in costs paid by patients (326,819 for the PET/CT [–] group vs. 636,100 for the PET/CT [+] group, $p = 0.460$).

In univariate analyses, factors associated with higher medical costs were relapse ($p < 0.001$) and IPI risk ($p = 0.003$; low risk vs. high-intermediate risk, $p = 0.003$; low-intermediate risk vs. high-intermediate risk, $p = 0.012$). Older age was associated with lower medical costs, but statistical significance was not reached (NR, $p = 0.071$). PET/CT surveillance and duration of follow-up were not associated with medical costs ($p = 0.755$ and $p = 0.639$, respectively). In the multivariate analysis, relapse was the only factor associated with medical costs ($p = 0.008$) (Table 3). Older age was associated with lower costs, but statistical significance was NR ($p = 0.069$).

Characteristics and medical costs of patients who received regular follow-up PET/CT and who did not received any follow-up PET/CT

To more accurately analyze the medical costs of a group that routinely performed, PET/CT, we limited our analysis to patients who regularly performed PET/CT and patients who never performed PET/CT (n = 77). Baseline characteristics of these patients are described in Sup-

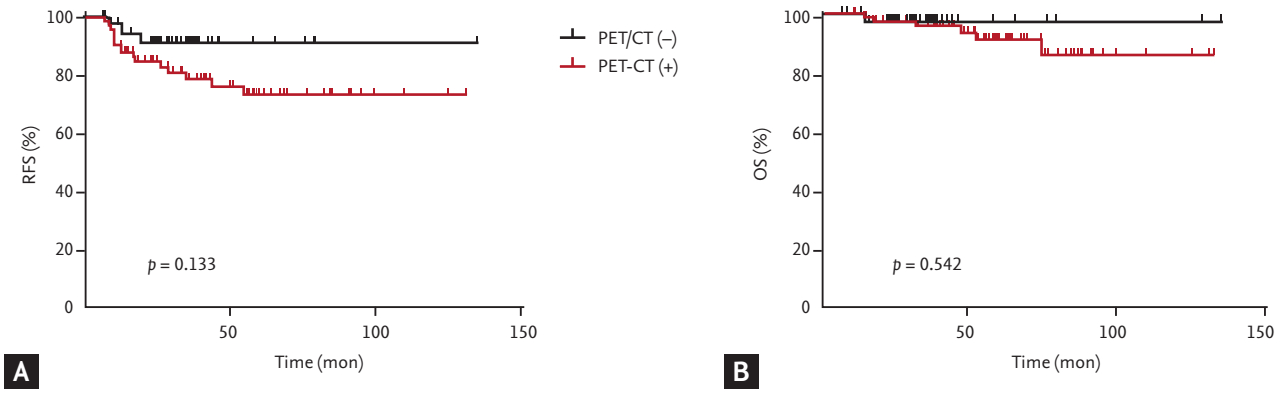

Figure 1. Kaplan-Meier plots of (A) relapse-free survival (RFS) and (B) overall survival (OS) based on follow-up positron emission tomography-computed tomography (PET/CT).

plementary Table 1. There was no significant difference in age, sex, stage, IPI risk, and treatment between the groups. Follow-up duration was longer in regular PET/CT surveillance group, and accordingly, number of outpatient visits was higher in regular PET/CT surveillance group. However, there was no significant difference in in the medical costs associated with outpatient visits. There was no statistically significant difference in the number of hospitalizations and any associated costs between the two groups (Supplementary Table 2).

Propensity score matching

We used propensity score matching to analyze the effects of follow-up PET/CT on the costs. In order to minimize the bias caused by nonrandom allocation to follow-up PET/CT, we developed a matching scheme that included variables that were shown to be associated with costs. We included the following domains: age, IPI risk, and relapse. We then used propensity score matching to match 41 patients (96.7% of the relevant group) in the PET/CT (–) group and 41 patients (53.9% of the relevant group) in the PET/CT (+) group. With the exception of follow-up duration, there were no significant differences in age, ECOG PS, IPI risk, or relapse (Table 4). In this propensity-matched cohort, the number of outpatient clinic visits were significantly higher in the PET/CT (+) group compared with the PET/CT (–) group (median number of visits, 27 vs. 14, $p = 0.003$). Costs associated with outpatient clinic visits and hospitalization were numerically higher in the PET/CT (+) group, although statistical significance was NR ($p = 0.077$ and $p = 0.535$, respectively) (Table 4).

Clinical outcomes

Median RFS and OS were similar between the PET/CT (+) group and PET/CT (–) group (median RFS and OS NR for both groups, $p = 0.133$ and $p = 0.542$, respectively) (Fig. 1). A factor associated with both RFS and OS was IPI risk (median RFS NR for all subgroups, mean RFS 122.1 months for IPI low risk patients, 91.4 months for low-intermediate risk patients, 90.2 months for high-intermediate risk patients, and 57.4 months for high risk patients, $p = 0.008$; median OS NR for all subgroups, median OS 129.1 months for IPI low risk patients, 106.3 months for IPI low-intermediate risk patients, 122.8 months for high-intermediate risk patients, and 74.7 months for high risk patients, $p = 0.022$). Poor performance status was associated with shorter OS (median NR, mean OS 127.9 months for ECOG PS 0 to 1 patients vs. 73.6 months for ECOG PS 2 to 3 patients, $p = 0.007$).

Results of PET/CT and subsequent evaluations

Among 76 patients with follow-up PET/CT, 31 patients (40.8%) had findings suggestive of recurrence. Sixteen of these patients (51.6%) were confirmed to have recurrent disease at the time of PET/CT without further evaluation (n = 2; maximal standardized uptake value [SUVmax], 17.3 and 4.2, respectively), after follow-up CT evaluation (n = 3; SUVmax 2.5, 23.7, and 32.4), after follow-up PET/CT evaluation (n = 1; SUVmax, 5.3), and after biopsy with or without follow-up CT evaluation (n = 10; median SUVmax, 8.2; range, 3.1 to 15.9).

Fifteen patients (48.4%) had positive PET/CT findings yet were confirmed to have no recurrence without further evaluation (n = 1; SUVmax, 0.0), after follow-up

https://doi.org/10.3904/kjim.2017.174

Table 4. Patient characteristics and medical costs during the first 3 years after achieving complete response of propensity-score matched cohort (n = 82)

Subject	PET-CT (–) (n = 41)	PET-CT (+) (n = 41)	*p* value
Age	56 (29–85)	58 (23–82)	
ECOG	0 (0–1)	0 (0–1)	
IPI risk			
Low	24 (50)	24 (50)	1.000
Low-intermediate	9 (50)	5 (50)	
High-intermediate	2 (50)	2 (50)	
High	6 (50)	6 (50)	
FU duration	28 (3–36)	36 (7–36)	0.002
Relapse	3 (7.3)	3 (7.3)	1.000
Outpatient clinic			
No. of visits	14 (4–103)	27 (6–45)	0.003
Costs	2,270,235 (214,178–38,923,231)	4,818,810 (2,005,402–7,646,772)	0.077
Hospitalization			
No. of hospitalization	0 (0–15)	0 (0–8)	0.539
Costs	0 (0–91,291,439)	0 (0–6,440,852)	0.535
Total costs	2,461,140 (340,094–130,214,670)	5,591,534 (2,005,402–71,140,025)	0.930
Total costs paid by patients[a]	306,155 (64,540–108,837,381)	636,100 (176,823–33,422,478)	0.509

Values are presented as median (range) or number (%). Statistical significance test was done by independent *t* test.
PET-CT, positron emission tomography-computed tomography; ECOG. Eastern Cooperative Oncology Group; IPI, International Prognostic Index; FU, follow-up.
[a]Costs that were not reimbursed by the National Health Insurance Service; thus, paid by the patients. Costs are stated in Korean won.

CT evaluation (n = 9; median SUVmax, 4.07; range, 1.5 to 4.9), after follow-up PET/CT evaluation (n = 1; SUVmax, 6.4), and after biopsy with or without follow-up CT evaluation (n = 4; SUVmax, 4.3, 5.2, 5.8, and 9.9). None of the patients with negative PET/CT findings (n = 45) had disease recurrence. Sensitivity and specificity of PET/CT for detection of recurrences were 1 and 0.75, respectively, and positive and negative predictive values for PET/CT in detection of recurrences were 0.52 and 1, respectively.

DISCUSSION

In this study, we demonstrated that surveillance PET/CT resulted in similar clinical outcomes and medical costs compared to no surveillance PET/CT. Moreover, due to its low specificity and positive predictive value, approximately half of patients with PET/CT findings of recurrence were found to have no evidence of disease after followup imaging and occasionally biopsy, which would not have been carried out if PET/CT had not been performed in the first place.

Routine surveillance imaging in first remission is a common practice; however, the clinical utility of serial imaging in asymptomatic patients remains questionable [9,10]. The role of PET/CT in surveillance of patients with DLBCL in first remission remains even more unclear. PET/CT is useful for detecting recurrence and re-staging since it can discriminate residual cancer against fibrosis or necrosis following treatment. However, PET/CT has a risk of false negative results due to partial volume effects or suppression of metabolism after chemotherapy, as well as false positive results due to inflammatory changes [11]. Patient anxiety associated with imaging and false-positive results is also a problem to consider.

Despite this uncertainty, nearly 50% of patients receive at least one PET/CT during surveillance [9]. Simi-

larly, in our study of 118 patients, 64.4% of patients had at least one PET/CT during their follow-up, in opposition to consensus guidelines that question the role of routine PET/CT during follow-up of asymptomatic patients [12-14].

Considering the prevalence of tests in the absence of validation of the usefulness of PET/CT, many investigators continue their efforts to find a subset of patients who could benefit from PET/CT follow-up with minimization of radiation burden and cost. Petrausch et al. [8] recommended surveillance PET/CT only in patients < 60 years with clinical signs of relapse and in all patients > 60 years.

Cost as well as clinical utility are also important issues, since cost is not only a burden to the patient but also a burden to the state. Huntington et al. [15] undertook a cost-effective analysis comparing three strategies: routine clinical follow-up without serial imaging, routine follow-up with CT scans every 6 months for 2 years, or routine follow-up with PET/CT every 6 months for 2 years. In this analysis, 2 years of routine PET/CT were associated with little survival benefit compared with clinical follow-up (life-years gained, 0.04 years) and with substantial costs (incremental cost-effectiveness ratios of $168,750/quality-adjusted life years). In our small-scale study, PET/CT surveillance did not show an increase in overall medical costs. However, since there is a significant association between outpatient visits and related costs, it is anticipated that surveillance PET/CT in all patients will result in ineffective increases in medical costs. If a cost-effectiveness analysis had been performed in our study, the results for our patients would have been similar.

Our study has limitations. It was a retrospective analysis, and performing PET/CT scan was a matter of a physician discretion, which might have led to selection bias. In addition, cost-effectiveness was not analyzed and only a simple cost-analysis was performed. We calculated costs related to hospital admission and outpatient visits from the accounting system of SNUH and SNU-BMC, but patients may have visited other hospitals and incurred additional costs related to the disease, which were not captured. Moreover, cost comparisons with other countries are difficult because of different healthcare systems and reimbursement policies of the governments.

Despite these limitations, our study is the first attempt in Korea to better understand the role and cost of PET/CT surveillance in patients with DLBCL in first remission. More than 60% of DLBCL patients in first remission in two tertiary hospitals in Korea had PET/CT at least one time during their follow-up. Although PET/CT surveillance was not associated with significantly increased costs in our group of patients, there was no evidence of any survival benefit from PET/CT surveillance either. Moreover, a significant proportion of patients had to undergo additional imaging and biopsy due to false positive results of PET/CT. The role of routine surveillance PET/CT in DLBCL patients with first remission has not been elucidated yet. To confirm our results and establish the role of PET/CT in DLBCL in first remission, larger studies with a cost-effective analysis and quality-of-life measures addressing imaging-associated patient anxiety should also be considered.

KEY MESSAGE

1. Surveillance positron emission tomography-computed tomography (PET/CT) in diffuse large B-cell lymphoma (DLBCL) patients in first complete remission resulted in similar clinical outcomes and medical costs compared to no surveillance PET/CT.
2. Due to its low positive predictive value of 0.52, significant proportion of patients had to undergo additional imaging and biopsy due to false positive results of PET/CT.
3. The role of routine surveillance PET/CT in DLBCL remains unclear.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Held G, Schubert J, Reiser M, Pfreundschuh M; German High-Grade Non-Hodgkin-Lymphoma Study Group. Dose-intensified treatment of advanced-stage diffuse large B-cell lymphomas. Semin Hematol 2006;43:221-229.

https://doi.org/10.3904/kjim.2017.174

2. Sehn LH, Donaldson J, Chhanabhai M, et al. Introduction of combined CHOP plus rituximab therapy dramatically improved outcome of diffuse large B-cell lymphoma in British Columbia. J Clin Oncol 2005;23:5027-5033.
3. Pfreundschuh M, Kuhnt E, Trumper L, et al. CHOP-like chemotherapy with or without rituximab in young patients with good-prognosis diffuse large-B-cell lymphoma: 6-year results of an open-label randomised study of the MabThera International Trial (MInT) Group. Lancet Oncol 2011;12:1013-1022.
4. Feugier P, Van Hoof A, Sebban C, et al. Long-term results of the R-CHOP study in the treatment of elderly patients with diffuse large B-cell lymphoma: a study by the Groupe d'Etude des Lymphomes de l'Adulte. J Clin Oncol 2005;23:4117-4126.
5. Hagberg H, Gisselbrecht C; CORAL study group. Randomised phase III study of R-ICE versus R-DHAP in relapsed patients with CD20 diffuse large B-cell lymphoma (DLBCL) followed by high-dose therapy and a second randomisation to maintenance treatment with rituximab or not: an update of the CORAL study. Ann Oncol 2006;17 Suppl 4:iv31-iv32.
6. Johnson SA, Kumar A, Matasar MJ, Schoder H, Rademaker J. Imaging for staging and response assessment in lymphoma. Radiology 2015;276:323-338.
7. Zinzani PL, Stefoni V, Tani M, et al. Role of [18F]fluorodeoxyglucose positron emission tomography scan in the follow-up of lymphoma. J Clin Oncol 2009;27:1781-1787.
8. Petrausch U, Samaras P, Haile SR, et al. Risk-adapted FDG-PET/CT-based follow-up in patients with diffuse large B-cell lymphoma after first-line therapy. Ann Oncol 2010;21:1694-1698.
9. Abel GA, Vanderplas A, Rodriguez MA, et al. High rates of surveillance imaging for treated diffuse large B-cell lymphoma: findings from a large national database. Leuk Lymphoma 2012;53:1113-1116.
10. Thompson CA, Ghesquieres H, Maurer MJ, et al. Utility of routine post-therapy surveillance imaging in diffuse large B-cell lymphoma. J Clin Oncol 2014;32:3506-3512.
11. Long NM, Smith CS. Causes and imaging features of false positives and false negatives on F-PET/CT in oncologic imaging. Insights Imaging 2011;2:679-698.
12. Zelenetz AD, Gordon LI, Wierda WG, et al. Non-Hodgkin's lymphomas, version 2.2014. J Natl Compr Canc Netw 2014;12:916-946.
13. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. J Clin Oncol 2014;32:3059-3068.
14. Tilly H, Gomes da Silva M, Vitolo U, et al. Diffuse large B-cell lymphoma (DLBCL): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2015;26 Suppl 5:v116-v125.
15. Huntington SF, Svoboda J, Doshi JA. Cost-effectiveness analysis of routine surveillance imaging of patients with diffuse large B-cell lymphoma in first remission. J Clin Oncol 2015;33:1467-1474.

Supplementary Table 1. Baseline characteristics of patients who received regular follow-up PET-CT and who did not (n = 77)

Characteristic	PET-CT (–)	PET-CT (+)	*p* value
No. of patients	42 (54.5)	35 (45.5)	
Age, yr	57 (29–85)	55 (30–82)	0.633
Sex			0.616
Male	24 (57.1)	18 (51.4)	
Female	18 (42.9)	17 (48.6)	
ECOG PS			0.001
0	17 (40.5)	1 (2.9)	
1	21 (50.0)	29 (82.9)	
2	4 (9.5)	5 (14.3)	
LDH, IU/mL	210.5 (99–5,110)	235.0 (131–3,742)	0.989
Extranodal involvement			0.129
No	33 (78.6)	22 (62.9)	
Yes	9 (21.4)	13 (37.1)	
Stage			0.625
1	13 (31.0)	8 (22.9)	
2	14 (33.3)	10 (28.6)	
3	6 (14.3)	5 (14.3)	
4	9 (21.4)	12 (34.3)	
IPI risk			0.614
Low	24 (57.1)	16 (45.7)	
Low-intermediate	9 (21.4)	7 (20.0)	
High-intermediate	3 (7.1)	5 (14.3)	
High	6 (14.3)	7 (20.0)	
Treatment			0.191
R-CHOP	40 (95.2)	35 (100)	
R-EPOCH	2 (4.8)	0	
Duration of follow-up, mon	32 (7–135)	58 (11–131)	0.002

Values are presented as number (%) or median (range).
PET-CT, positron emission tomography-computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; IPI, International Prognostic Index; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone; R-EPOCH, rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin.

https://doi.org/10.3904/kjim.2017.174

Supplementary Table 2. Univariate analysis for medical costs during the first 3 years after achieving complete response in patients who received regular follow-up PET-CT and who did not (n = 77)

Subjects	PET-CT (–) (n = 42)	PET-CT (+) (n = 35)	*p* value
Duration of follow-up, mon	28 (3–36)	36 (6–36)	< 0.001
Relapse	3 (7.1)	6 (17.1)	0.286
Outpatient visits			
No. of visits	14 (4–103)	26 (6–56)	0.003
Costs	2,256,327 (214,178–38,923,231)	5,443,348 (1,021,569–7,646,772)	0.061
Hospitalization			
No. of hospitalization	0 (0–15)	0 (0–7)	0.624
Costs	0 (0–91,291,439)	0 (0–32,311,317)	0.260
Total costs	2,499,689 (340,094–130,214,670)	5,624,649 (2,005,402–39,468,247)	0.690
Total costs paid by patients[a]	326,819 (64,540–108,837,381)	709,808 (176,823–4,938,925)	0.405

Values are presented as median (range) or number (%). Statistical significance test was done by independent *t* test.
PET-CT, positron emission tomography-computed tomography.
[a]Costs that were not reimbursed by the National Health Insurance Service; thus, paid by the patients. Costs are stated in Korean won.