Evaluation of Respiratory Functions in Pediatric Oncology Patients Receiving Bleomycin Treatment

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Abstract

Purpose: Bleomycin is a chemotherapeutic agent that causes lung toxicity. Bleomycin is mostly used in the treatment of germ cell tumors(GCT) and Hodgkin Lymphoma(HL) in childhood cancers. In this study, we aimed to detect bleomycin toxicity to the lung in the early period. **Materials and methods:** Pulmonary functions of patients aged 5 years and older who were admitted to the Division of Pediatric Oncology with germ cell tumors and Hodgkin Lymphoma between 2012 and 2022, who received bleomycin treatment and were in remission for at least 6 months were evaluated. The evaluation of respiratory function was based on history, physical examination, posteroanterior chest radiography and pulmonary function test. **Results:** There were 109 patients with GCT and 122 patients with HL. The number of patients with GCT who entered follow-up and lived were 59, those with HL were 89]. The number of patients who received bleomycin treatment, were in remission for at least 6 months and underwent PFTs were 46 for HL and 12 for GCT. There were 21 patients with PFT abnormalities. Of these patients, 3 were diagnosed with GCT and 18 were diagnosed with HL. The type of PFT abnormality in the majority of patients was restrictive disorder. **Conclusion:** The absence of respiratory symptoms in 90% of patients with PFT abnormalities shows the importance of PFT in asymptomatic patients. Patients who have received bleomycin as part of treatment should also be followed-up for late pulmonary toxicity.

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BEP	Bleomycin, cisplatin, etoposide
ABVD	Adriamycin, bleomycin, vinblastine, dacarbazine
GCT	Germ cell tumor
HL	Hodgkin Lymphoma
CT	Computed tomography

BEP	Bleomycin, cisplatin, etoposide
FEV_1	forced expiratory volume in one second
FVC	forced vital capacity
PEF	Peak Expiratory Flow
MEF_{25-75}	mean flow between 25% and 75% of FVC
DLCO	diffusing capacity for carbon monoxide
PFT	pulmonary function test

ABSTRACT

Purpose: Bleomycin is a chemotherapeutic agent that causes lung toxicity. Bleomycin is mostly used in the treatment of germ cell tumors(GCT) and Hodgkin Lymphoma(HL) in childhood cancers. In this study, we aimed to detect bleomycin toxicity to the lung in the early period.

Materials and methods: Pulmonary functions of patients aged 5 years and older who were admitted to the Division of Pediatric Oncology with germ cell tumors and Hodgkin Lymphoma between 2012 and 2022, who received bleomycin treatment and were in remission for at least 6 months were evaluated. The evaluation of respiratory function was based on history, physical examination, posteroanterior chest radiography and pulmonary function test.

Results: There were 109 patients with GCT and 122 patients with HL. The number of patients with GCT who entered follow-up and lived were 59, those with HL were 89]. The number of patients who received bleomycin treatment, were in remission for at least 6 months and underwent PFTs were 46 for HL and 12 for GCT. There were 21 patients with PFT abnormalities. Of these patients, 3 were diagnosed with GCT and 18 were diagnosed with HL. The type of PFT abnormality in the majority of patients was restrictive disorder.

Conclusion: The absence of respiratory symptoms in 90% of patients with PFT abnormalities shows the importance of PFT in asymptomatic patients. Patients who have received bleomycin as part of treatment should also be followed-up for late pulmonary toxicity.

Keywords: lung toxicity, bleomycin, germ cell tumor, Hodgkin Lymphoma, pulmonary function test

INTRODUCTION

Bleomycin is an antibiotic agent obtained from a strain of Streptomyces verticillus in 1966, which shows anti-tumor activity by inducing free radicals and is used in the treatment of HL, GCT and squamous carcinomas in the head and neck region[1,2].

Since bleomycin inactivation is low in the lung, bleomycin-induced toxicity is observed in the lung due to bleomycin accumulation[3]. After oxidative damage caused by bleomycin in the lung, type 1 pneumocytes are destroyed, granulocyte influx begins, and chemotactic factors, elastase, collagenase and myeloperoxidase are released[4]. Vascular and cellular damage develops due to bleomycin accumulation, an inflammatory process begins in the lung parenchyma and growth factors released from macrophages stimulate fibroblasts. Secondary to activated fibroblasts, lung fibrosis eventually develops. Bleomycin toxicity may occur early or late and pulmonary fibrosis usually occurs 1 to 6 months after treatment[5,6]. Early-onset pulmonary toxicity is uncommon, occurs as a hypersensitivity reaction and may develop into interstitial pneumonitis from the first time the drug is administered up to several months after completion of chemotherapy. Early-onset toxicity does not have a clear dose relationship to late-onset toxicity[7].

Interstitial pneumonia, also known as hypersensitivity reaction, may develop at the first dose of chemotherapy or may occur months later. Methotrexate, bleomycin, procarbazine and carmustine are among the agents that cause this picture. In most cases the response to drug withdrawal and steroid treatment is good and normal lung function is restored. [8,9].

Pulmonary toxicity of chemotherapy may develop as inertstitial lung pneumonia in the early period and pulmonary fibrosis in the late period. Toxic effects vary depending on the dose of chemotherapy received, whether radiation therapy is received, the dose rate of radiation, duration, pre-existing lung disease and steroid use[8]. There are different methods used to determine all these findings, such as PFT, chest radiography and CT[10-12].

This study aimed to investigate lung toxicity in pediatric oncology patients using bleomycin as part of the treatment and to detect the lung toxicity of bleomycin in the early period.

MATERIALS and METHODS

This study was conducted on patients diagnosed with HL and GCT who applied to the Pediatric Oncology outpatient clinic of Cukurova University Faculty of Medicine between 2012 and 2022. Ethics Committee of Cukurova University Faculty of Medicine approved the study (meeting no 2, on 2.4.2021).

Patients treated and is being followed-up with a diagnosis of HL or GCT, who are in remission for at least 6 months after completion treatment, who are 5 years old or older (for compliance with PFT), received bleomycin treatment, accepted to enroll into the study and signed an informed consent were included into the study.

231 files of patients diagnosed with HL and GCT were scanned. There were 109 patients diagnosed with GCT and 122 patients diagnosed with HL. 15 of the patients diagnosed with GCT and 17 of the patients with HL were excluded because they were exitus. While 35 of the 94 living patients diagnosed with GHT were excluded from follow-up, 16 of the 105 living patients diagnosed with HL were excluded because they were never followed-up. The number of patients with GCT who were followed-up and alive were 59, that of HL were 89.

The number of patients who received bleomycin treatment, were in remission for at least 6 months and could be reached and underwent PFT were 46 for HL and 12 for GHT and the total number of patients were 58.

All living and reachable patients diagnosed with HL and GCT were prospectively

subjected to PFT and chest radiography. Those with PFT disorders were evaluated as obstructive type, restrictive type and mixed type. Chest radiographs were evaluated as normal or pathological (interstitial fibrosis findings) were present.

Obstructive disorder was defined when FEV1/FVC is decreased (<80%) and/or FEV1 is decreased (<80%), FEF25-75(MEF25-75) is decreased (<70%), FVC is normal, restrictive disorder; situations where FEV1/FVC is normal or increased (> 80%), FVC is decreased (< 80%), mixed disorder; FEV1/FVC decreased (<80%) and FVC decreased (<80%) conditions were considered[13]. In PFT, values are determined as a percentage based on the values in healthy individuals for a certain age, gender, height, body weight and race.

In our study, the bleomycin dose was calculated as units/m^2. Fort the calculation of body surface area [(Body weightx4)+7]/(Body weight + 90) formula was used.

In our study, the abnormalities in the lung functions of GHT and HL patients who were in remission for at least 6 months and who received bleomycin treatment was eveluated by PFT, chest radiography, thorax CT. Bleomycin cumulative dose, chronic respiratory symptoms, RT, height, body weight, stage, histopathological subtype, family history recurrence, and smoking status were also recorded.

The relationship between the patients with PFT disorder and the variables such age at diagnosis, duration of remission, chemotherapy protocols of the patients, whether they received radiotherapy, cumulative dose of bleomycin received, smoking, gender, whether pathology was detected in chest radiography and thorax tomography, presence of symptoms, and histopathological subtype were examined.

Statistical Analysis

When performing statistical analysis, chi square test statistics were used to compare categorical measurements between groups. In comparing numerical measurements between groups, t-test was used in independent groups if the assumptions were met and Mann-Whitney U test was used if the assumptions were not met. Categorical measurements were summarized as numbers and percentages and numerical measurements were summarized as mean and standard deviation (median and minimum-maximum where necessary). IBM SPSS Statistics Version 20.0 package program was used in the statistical analysis of the data. In all tests, the statistical significance level was taken as 0.05.

RESULTS

148 patients who were diagnosed with HLand GCT, were followed-up, who remission for at least 6 months were evaluated in the study.

The number of patients with GCT was 59 (40%) and the number of patients with HL was 89 (60%).

114 of 148 patients (77%) received bleomycin treatment, and 58 patients who were in remission for at least 6 months, were under regular follow-up, and wanted to undergo examination and PFT were included in the study. PFT was performed in 12 patients diagnosed with GCT and in 46 patients diagnosed with HL.

Of the 58 patients who underwent PFT, 7 (12,1%) had cough, 5 (8,6%) had sputum, 8 (13,8%) had shortness of breath, and 4 (6,9%) had wheezing. Among those who underwent PFT, smoking prevalence was 3,4%.

Of the 58 patients who underwent PFT, 37 (63,8%) had normal functions. Obstructive disorder was detected in 3 (5,2%), restrictive disorder in 16 (27,6%), and mixed type disorder in 2 (3,4%).

Of the 58 patients who underwent PFT, 45 (77,6%) received the ABVD (adriamycin, bleomycin, vinblastine, dacarbazine) protocol, 1 (1,7%) received the COPP (cyclophosphamide, oncovin, procarbazine, prednisone)-ABV(adriamycin, bleomycin, vinblastine) protocol, 12 (20,7%) received the BEP(bleomycin, etoposide, cisplatin) protocol, and acute bleomycin toxicity occurred in only 1 (1,7%) was observed in the patient, and bleomycin treatment was discontinued due to unexplained changes in the patient's lung imaging that did not improve despite treatment for metastasis and infection.

When the histopathological subtypes of all 46 HL patients who underwent PFT were examined, there were no patients diagnosed as nodular lymphocyte predominant and classical lymphocyte -depleted, 2 (4.3%) patients were classical lymphocyte-rich, 20 (43,5%) patients were classical nodular sclerosing, 17 (37%) The patient had mixed cellularity, and 7 (15,2%) patients could not be classified. Of the 46 HL patients who underwent PFT, 32 (69,6%) had post-treatment thorax CT scans. 11 (52,2%) had a ground glass appearance on thorax CT, 2 (10,9%) had a nodular lesion, 2 (4,3%) had an infection, 1 (2,2%) had a ground glass appearance. There was elevation of the hemidiaphragm. Of 46 patients diagnosed with HL, PFT was normal in 28 (60.9%), restrictive disorder in 14 (30.4%), obstructive disorder in 3 (6.5%), and mixed in 1 (2.2%) there was a type of disorder. One of the HL patients (2.2%) who underwent PFT was a smoker.

Considering the histolopathological subtypes of all 12 GCT patients who underwent PFT, 1 patient (8,3%) was germinoma, 1 patient (8,3%) was immature teratoma, 6 patients (50%) were yolk sac tumors, 4 patients (33,4%) were mixed. It was classified as a germ cell tumor. 8 of these patients (67%) were girls and 4 (33%) were boys. Only 1 of 12 patients (8,3%) was a smoker. None of the patients had a post-treatment thorax CT. Chest radiography of 11 of 12 patients diagnosed with GCT (91,7%) was normal, and only 1 (8,3%) had interstitial fibrosis. In the PFTs performed on the patients, 2 (16,7%) patients had a restrictive disorder, 1 (8,3%) patient had a mixed type disorder, while 9 (75%) patients had normal PFTs.

Of the 58 patients who underwent PFT, 21 (36,2%) had defective PFT. Of the 21 patients with impaired PFT, 8 (38,1%) were female and 13 (61,9%) were male. Of the PFT disorder patients, 18 (85,7%) were diagnosed with HL and 3 (14,3%) were diagnosed with GCT. Only 1 (4,8%) patient with PFT disorder was a smoker. Among the patients with PFT disorders, 3 (14,3%) had obstructive type disorder, 16 (76,2%) had restrictive type disorder and 2 (9,5%) had mixed type disorder.

Of 21 patients with PFT disorders, 3 (14,3%) received the BEP protocol and 18 (85,7%) received the ABVD protocol. In our study also we found a similar rate with the above mentioned study(The rate of PFT disorder detected in asymptomatic patients was 71%).

The mean height (p=0.05) and body weight (p=0.048) were lower in patients with impaired PFT (Table 1). There was no significant difference between the bleomycin dose and PFT impairment.

DISCUSSION

While the incidence of HL is higher in adolescents and in the male gender,[14,15] in our study, 2/3 of our patients with impaired PFT and diagnosed with HL were under the age of 15, and the gender ratios of these patients were equal between boys and girls.

When looked at according to HL histopathological subtypes, the NSHL subtype of classical HL ranks first in terms of frequency[16] and in our study, it was the most common histopathological subtype in patients who were diagnosed with HL, received bleomycin treatment were in remission for at least 6 months and were also found to have PFT disorder.

Protocols such as ABVD and COPP are used in the treatment of HL[17] but in our study, the chest protocol received by all HL patients with PFT abnormalities was ABVD. COPP treatment is not applied to HL patients Department Pediatric Oncology in Cukurova University Faculty of Medicine.

GHT is rare in childhood with a rate of 2% under the age of 15 and it peaks between the ages of 0-4 and during adolescence[18,19] in our study, 3 patients with impaired PFT were diagnosed with GHT, and 1 of our patients was in the adolescence period while the other 2 were diagnosed under 4 years.

Bleomycin is an antibiotic agent with known lung toxicity and is used as part of the chest protocol in the treatment of HL and GCT[20]. Lung fibrosis develops as a result of cell damage due to bleomycin accumulation, and its effects are seen between 1 and 6 months after treatment[6]. It causes the development of interstitial fibrosis, especially in the lung[7].

In our study, 32 of the 58 patients who received bleomycin treatment and were in remission for at least 6 months and underwent PFT had a thorax CT in the system, and while half of them were associated with interstitial fibrosis, the remaining half were normal.

When the thorax CT and chest radiographs of patients with PFT disorders were examined, the most common finding indicating interstitial fibrosis was the ground glass appearance.

One of the limitations of our study is that thorax CT is more valuable than chest radiography in the diagnosis of interstitial fibrosis and not all of our patients with defective PFTs had thorax CT in the system. None of our patients diagnosed with GCT had a thorax CT in the system. On the other hand, since having a thorax CT scan would create a radiation load for our patients who had primary oncological disease and received multiple CT and RT, chest radiography, which has a much lower radiation load compared to CT, was taken for our patients. On the other hand, it is difficult to evaluate interstitial fibrosis in chest radiographs, and changes in chest radiographs may vary depending on the evaluating physician.

In a study conducted in adults[8,9], lung fibrosis was observed in 10% of patients who received bleomycin over 400 units/m^2, whereas in our study, the highest bleomycin dose taken by our patients with PFT disorders was 160 units/m^2. Although some of our patients received bleomycin at a dose of 80 units/m^2 lung fibrosis findings were detected on chest radiographs. Although some of our patients received doses higher than 80 units/m^2 it was observed that there was no effect on thorax CT and chest radiography. Since our patients did not receive doses as high as 400 units/m^2 of bleomycin a significant relationship between lung fibrosis and cumulative dose of bleomycin may not have been detected.

PFT is performed on children over the age of 5 who can comply, and the age limit reduced the number of patients participating in our study.

When interpreting the PFTs performed in our study, they were categorized into 4 types: normal, obstructive disorder, restrictive disorder and mixed type disorder. Disorders in PFT were detected in 36% of 58 patients who underwent PFT. In a study[21], it was found that 18% of PFT disorders were of restrictive type. In our study, restrictive disorders were found in 27,6% of the patients who underwent PFT. Obstructive disorder was not reported in the same study but in our study obstructive disorder was found in 5,2% and mixed type disorder was found in 3,4%.

When restrictive, obstructive, and mixed type disorders were examined, no significant relationship was found regarding whether or not receiving RT, cumulative dose of bleomycin, smoking, and chronic respiratory symptoms. This may be due to the small number of patients in our study.

In our study, significantly lower FEV1, FVC, FEV1/FVC, PEF, MEF_{25-75} values were found in patients with PFT disorders who received RT to the mediastinum, 6 months and received bleomycin treatment. Another limitation of our study was that DLCO could not be evaluated in PFT. Because low DLCO is considered limit the most sensitive and first sign of PFT disorder that may develop in the future.

In our study, patients diagnosed with GHT who received bleomycin and were in remission for at least 6 months were found to have PFT abnormalities in the absence of clinical and radiological changes, which may be a precursor to bleomycin-induced pulmonary damage in the future.

Two of the patients who received bleomycin treatment, were in remission for at least 6 months, and underwent PFT were smoking. No statistically significant difference was detected between bleomycin and cigarettes. This may be because the number of smokers was low and because our patients were young, not enough time had passed for the effects of smoking to be seen.

The point emphasized by Record E. et al. in their study[22] was that patients without clinical symptoms constituted 2/3 of the study participants and had PFT disorders. In our study, the rate of patients who received bleomycin treatment, were in remission for at least 6 months, and were found to have impaired PFT but were asymptomatic was 71%. The common point between our study and this study was that both rates were very close to each other.

In a study conducted by Conte P. et al.[23], it was stated that drug-induced interstitial lung disease occurs as a result of the use of drugs that cause inflammation and interstitial fibrosis. In our study, only 1 patient developed interstitial lung disease due to acute bleomycin toxicity. Bleomycin treatment was discontinued and prednol was started. This was a similar feature of our study to this study. Our patient was in remission for at least 6 months and PFT was performed and chest radiography was taken. The PFT and chest radiography of our patient, who was in remission, were normal and the patient had no chronic respiratory symptoms. PFT was normal was the aspect of our study that was incompatible with this study.

In a study by Dei-Adomakoh YA et al.[24], they mentioned bleomycin-induced pneumonia in a young Ghanaian male patient with HL. In our study, respiratory symptoms developed in one of our patients while receiving the ABVD protocol, and after the findings of lung metastasis were excluded, bleomycin-induced lung injury was considered and the bleomycin treatment given to our patient was discontinued and prednol treatment was started. Our patient continued her regular follow-up, and in this study, both a chest x-ray and PFT were performed. PFT was normal. Our patient was lucky in terms of survival. In the study mentioned about, even if the patients went into remission, the risk of toxicity-related lung pathologies increased with each relapse due to bleomycin treatment.

In a study conducted by Uzel I et al.[25], bleomycin-induced pneumonia was detected in a patient diagnosed with testicular cancer, developing 2 years after completing the BEP protocol. In our study, PFT disorder and lung pathology were also detected in our patients who completed chemotherapy and were in remission for years.

Conclusion

Clinical findings should be evaluated with PFT and chest radiography in the regular follow-up of patients

who received bleomycin treatment after the diagnosis of HL and GHT and evaluation with PFT should be performed in the annual follow-up of those with abnormalities. Detection of bleomycin-induced lung toxicity in later ages in patients who have received bleomycin treatment shows how important it is to follow-up the patients.

Conflict of interest statement: There is no conflict of interest.

REFERENCES

1. Graves PR, Siddiqui F, Anscher MS, Movsas B. Radiation pulmonary toxicity: from mechanisms to management. *Seminars in radiation oncology* 2010; 20: 201–207.
2. Sikic BI. Biochemical and cellular determinants of bleomycin cytotoxicity. *Cancer Surv* 1986; 5:81-91.
3. Fennell DA, Rudd RM. Pulmonary toxicity and cancer treatment.*Hosp Med* 2004; 65:462-464.
4. Kreisman H, Wolkove N. Pulmonary toxicity of antineoplastic therapy.*Semin Oncol* 1992; 19:508-520.
5. Versluys AB, Bresters D. Pulmonary Complications of Childhood Cancer Treatment. *Paediatr Respir Rev.* 2016; 17:63-70.
6. Sleijfer S. Bleomycin-induced pneumonitis. *Chest* 2001; 120:617-624.
7. Hinson JM, Mckibben AW. Chemotherapy-associated lung injury. In Perry MC Ed. *Chemotherapy Source Book* . 3rd Ed., Baltimore: Williams & Wilkins, 2001;468-476.
8. Liles A, Blatt J, Morris D, et al. Monitoring pulmonary complications in longterm childhood cancer survivors: guidelines for the primary care physician. *Cleve Clin J Med* 2008; 75:531–539.
9. Meadors M, Floyd J, Perry MC. Pulmonary toxicity of chemotherapy.*Semin Oncol.* 2006; 33:98-105.
10. Wit R, Sleijfer S, Kaye SB, et al. Bleomycin and scuba diving: where is the harm. *Lancet Oncol* 2007; 8:954–5.
11. Guner SI, Yanmaz MT, Selvi A, Usul C. Chemotherapy and Radiation Induced Pulmonary Dysfunction in Hodgkin Lymphoma Patients.*Indian J Hematol Blood Transfus.* 2016; 32:431-436.
12. Rossi SE, Erasmus JJ, McAdams HP, Sporn TA, Goodman PC. Pulmonary drug toxicity: radiologic and pathologic manifestations.*Radiographics* 2000; 20:1245-59.
13. Evans SE, Scanlon PD. Current practice in pulmonary funtion testing. Mayo Clin Proc 2003;78:758-763.
14. Pötter R. Paediatric Hodgkin's disease. *Eur J Cancer* 1999; 35:1466-1476.
15. Percy CL, Smith MA, Linet M. Lymphomas and reticuloendothelial neoplasms. In: Ries LA, Smith MA, Gurney JG, et al. Eds. Cancer Incidence and Survival among Children and Adolescents United States SEER Program. National Cancer Institute, Bethesda, 1999:35.
16. Laurent C, et al. Prevalence of Common Non-Hodgkin Lymphomas and Subtypes of Hodgkin Lymphoma by Nodal Site of Involvement: A Systematic Retrospective Review of 938 Cases. *Medicine* 2015, 94:987.
17. Pizzo PA, Poplack DG. *Principles and practice of pediatric oncology.* 7th Ed., Philadelphia: Lippincott Williams & Wilkins, 2015.
18. Ries LAG, Smith MA, Gurney JG, et al. Cancer incidence and survival among children and adolescents: United States SEER Program 1975-1995. National Cancer Institute, SEER Program. Bethesda, 1999.
19. Schneider DT, Calaminus G, Koch S, et al. Epidemiologic analysis of 1,442 children and adolescents registered in the German germ cell tumor protocols. *Pediatr Blood Cancer* 2004; 42:169–175.
20. Abid SH, Malhotra V, Perry MC. Radiation-induced and chemotherapy-induced pulmonary injury. *Curr Opin Oncol* 2001; 13:242–8.
21. Bossi G, Cerveri I,Volpini E, et al. Long-term pulmonary sequelae after treatment of childhood hodgkin's disease. *Ann Oncol* 1997; 1:19-24.
22. Record E, Williamson R, Wasilewski-Masker K, Mertens AC, Meacham LR, Popler J. Analysis of Risk Factors for Abnormal Pulmonary Function in Pediatric Cancer Survivors. *Pediatr Blood Cancer* . 2016; 63:1264-1271.
23. Conte P, Ascierto PA, Patelli G, et al. Drug-induced interstitial lung disease during cancer therapies: expert opinion on diagnosis and treatment. *ESMO Open* 2022; 7:100404.
24. Dei-Adomakoh YA, Afriyie-Mensah JS, Gbadamosi H. Bleomycin-induced pneumonitis in a young

Ghanaian male with Hodgkin's Lymphoma. *Ghana Med J* 2020; 54:279-283.
25. Uzel I, Ozguroglu M, Uzel B, et al. Delayed onset bleomycin-induced pneumonitis. *Urology* 2005; 66:195.

Table 1. Relationship between PFT disorder and height and body weight

	PFT normal	PFT disordered	P
Height (mean±*ss*)	161,4±15,2	151±21,2	0,05
Body weight (mean±*ss*)	61±18,5	49,6±23	0,048

Table 2. Clinical characteristics of patients with PFT disorders

patient	sex	height (cm)	body weight (kg)	age at diagnosis (year)	current age (year)	Diagnosis	Histopathological type	stage	smoking	PFT disorder type	Chemotherapy	Cumulative dose of bleomycin u/m^2	RT histo
1)M.Ç.	M	136	36	4,5	10	HL	mixed cellular	3	no	restrictive	ABVD	80	no
2)A.Ö.	M	151	50	8,5	12,5	HL	rich in lymphocytes	3	no	restrictive	ABVD	160	Abd
3)M.K.	M	122	20	4,5	6,5	HL	nodular sclerosing	2	no	restrictive	ABVD	130	medi
4)H.İ.C.	M	124	21	7	8	HL	unclassifiable	2	no	restrictive	ABVD	120	no
5)K.B.	M	175	98	15	22	HL	nodular sclerosing	2	no	restrictive	ABVD	160	no
6)A.K.	M	169	70	9,5	14,5	HL	unclassifiable	2	no	restrictive	ABVD	120	medi
7)F.K.	M	180	85	6	18	HL	Nodular sclerosing	3	no	restrictive	ABVD	120	cervi
8)F.A.	F	158	60	17	28	HL	Nodular sclerosing	2	yes	obstructive	ABVD	80	no
9)M.H.Y.	M	145	20	3,5	13	HL	mixed cellular	3	no	obstructive	ABVD	120	no
10)A.K.	F	167	50	15	26	HL	Nodular sclerosing	4	no	mixed	ABVD	140	medi
11)C.Ö.	M	176	85	16	22,5	HL	rich in lymphocytes	1	no	restrictive	ABVD	90	no
12)A.K.	F	167	53	16	22	HL	unclassifiable	4	no	obstructive	ABVD	160	no
13)O.Ö.	M	160	61	16	24	HL	Nodular sclerosing	2	no	restrictive	ABVD	160	no
14)E.G.	M	175	65	7	14,5	HL	mixed cellular	3	no	restrictive	ABVD	160	no
15)M.N.	M	126	37	5	7	HL	Nodular sclerosing	3	no	restrictive	ABVD	160	no
16)K.E.	F	130	20	4,5	11,5	HL	Nodular sclerosing	2	no	restrictive	ABVD	160	no
17)N.C.U.	F	157	55	14	16,5	HL	mixed cellular	2	no	restrictive	ABVD	160	medi

patient	sex	height (cm)	body weight (kg)	age at diag-nosis (year)	current age (year)	Diagnosis	Histopathological type	stage	smoking	PFT disor-der type	Chemo therapy	Cumulative dose of bleomycin u/m^2	RT histo
18)M.K.	M	110	30	7	8,5	HL	mixed cellular	4	no	restrictive	ABVD	160	no
19)S.M.	F	165	51	14	23,5	GCT	Yolk sac tumor	1	no	restrictive	BEP	60	no
20)A.Y.	F	151	52	2,5	12,5	GCT	Yolk sac tumor	1	no	restrictive	BEP	120	no
21)E.K.	F	126	24	1,5	7	GCT	Mixed germ cell tumor	1	no	mixed	BEP	135	no