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Fasting blood glucose is a novel prognostic indicator for extranodal natural killer/T-cell lymphoma, nasal type

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Background: Extranodal natural killer (NK)/T-cell lymphoma, nasal type (ENKTL) is an aggressive disease with poor prognosis, requiring risk stratification. However, the prognosis of ENKTL is not fully defined and needs supplementation. We hypothesised that fasting blood glucose (FBG) may be a new prognostic factor for ENKTL.

Methods: We retrospectively analysed 130 patients newly diagnosed with ENKTL.

Results: Both univariate analysis and multivariate analysis revealed that FBG $>100\,mg\,dl^{-1}$ was associated with a poor outcome. Patients with FBG $>100\,mg\,dl^{-1}$ at diagnosis had more adverse clinical features, achieved lower complete remission rates ($P=0.003$) and had worse overall survival ($P<0.001$) and progression-free survival ($P<0.001$) compared with low-FBG patients. Measurement of FBG was helpful in differentiating between low-risk patients using the International Prognostic Index (IPI) and Prognosis Index for peripheral T-cell lymphoma (PIT) scoring and patients in a different category using the Korean Prognostic Index (KPI) scores with different survival outcomes ($P<0.05$).

Conclusion: Our data suggest that measuring FBG levels at diagnosis is a novel, independent predictor of prognosis in ENKTL and helps to distinguish low-risk patients with poor survival, and this holds true in patients considered low-risk by IPI, PIT and KPI.

Extranodal natural killer (NK)/T-cell lymphoma, nasal type (ENKTL), is a distinct entity of non-Hodgkin's lymphoma in the World Health Organisation (WHO) classification system (Ai *et al*, 2012), which is quite rare in Western populations, but relatively common in East Asia (especially China) and Latin America (Harris *et al*, 1999; Vose *et al*, 2008). ENKTL accounts for 7–10% of all non-Hodgkin lymphomas in Asia and Latin America (Gill *et al*, 2010). ENKTL is an aggressive disease with poor prognosis, as optimal treatment strategies have not been fully defined (Al-Hakeem *et al*, 2007). Therefore, analysis of prognostic factors at the time of diagnosis is important for optimisation of treatment strategies for individual patients. Several potential prognostic factors for survival in patients with ENKTL have been investigated, including regional lymph node involvement (You *et al*, 2004), elevated lactate dehydrogenase (LDH) (Lee *et al*, 2005), poor performance (Lee *et al*, 2005), paranasal extension (Logsdon *et al*, 1997; Li *et al*, 1998), presence of B symptoms (Kim *et al*, 2001), high Epstein–Barr virus (EBV) DNA titres (Au *et al*, 2004) and

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absolute lymphocyte counts (Huang *et al*, 2011). The International Prognostic Index (IPI) has prognostic value in many subtypes of non-Hodgkin's lymphoma, but its value in ENKTL remains controversial (Chim *et al*, 2004). Although most studies demonstrated that the low-risk IPI category was associated with better survival outcome in ENKTL, the distribution of patients in different risk groups was unbalanced (Lee *et al*, 2006). Gallamini *et al* (2004) proposed PIT, the Prognosis Index for peripheral T-cell lymphoma, unspecified (PTCL-U) to identify different outcomes of PTCL-U. Recently, PIT has also been used in other subtypes of T-cell lymphoma and been proven effective (Rodriguez *et al*, 2007). However, the value of PIT to predict the prognosis of ENKTL remains unclear. Given the limitations of the IPI and PIT scoring systems, the Korean Prognostic Index (KPI) and local tumour invasiveness in ENKTL were proposed, and demonstrated better predictive discrimination than the IPI or PIT scoring system (Lee *et al*, 2006). In addition, this model might be further improved by other laboratory data (such as haemoglobin and platelet counts) and pathologic characteristics (Huang *et al*, 2011).

Recent clinical research has suggested that blood glucose levels in cancer patients may be an important prognostic indicator (Richardson and Pollack, 2005; LeRoith *et al*, 2008). Elevated blood glucose levels have been shown to predict shorter survival times in stomach cancer (Zhou *et al*, 2010), lung cancer (Luo *et al*, 2012), pancreatic cancer (Li *et al*, 2011), breast cancer (Erickson *et al*, 2011), colorectal cancer (Meyerhardt *et al*, 2003), endometrial cancer (Friberg *et al*, 2007), cervical cancer (Lee *et al*, 2010) and acute lymphocytic leukaemia (Sonabend *et al*, 2009). To the best of our knowledge, the prognostic value of fasting blood glucose (FBG) has never been studied in patients with ENKTL. In our pilot study, we observed that patients with higher FBG levels had worse outcomes in clinical practice. The objective of this retrospective analysis was to assess whether FBG at diagnosis has prognostic significance in patients with ENKTL, nasal type.

MATERIALS AND METHODS

Patients. We retrospectively reviewed the medical records of 130 newly diagnosed patients with ENKTL between January 2003 and April 2010 at Sun Yat-sen University Cancer Centre, China. The criteria for case inclusion were as follows: (i) pathologically confirmed diagnosis of NK/T-cell lymphoma, based on the WHO Classification of Tumours of Hematopoietic and Lymphoid Tissues; (ii) NK/T-cell type demonstrated by immunohistochemistry, flow cytometry or EBV *in situ* hybridisation; (iii) no previous malignancy or a second primary tumour; (iv) no previous treatment and (v) adequate clinical information and follow-up data. Patients were excluded if: (1) they were negative for EBV by *in situ* hybridisation; (2) they had blasting NK-cell lymphoma/leukaemia; (3) aggressive NK-cell leukaemia; (4) PTCL-U and (5) patients had taken medications that increased FBG before diagnosis. We obtained approval from the Institutional Review Board of Sun Yat-Sen University Cancer Centre. Informed consent for the collection of medical information was provided at the first visit of all patients. All pathologic specimens were reviewed and reclassified by central review according to the WHO criteria for pathologic diagnosis. Antibodies to the following antigens were used for immunophenotype analysis: CD3, CD56, TIA-1, Gram-B, CD45RO, CD20, CD79a, CD30, Ki67 and the anaplastic large cell lymphoma kinase. *In situ* hybridisation was used for the detection of EBV-encoded RNA.

Data collection. The data were collected at diagnosis, including patient demographics, diabetes mellitus (DM) status, height, weight, % body mass index (BMI), FBG, Eastern Cooperative Oncology Group performance status (ECOG PS), primary site, involved sites, systemic B symptoms, complete blood count, serum LDH, biochemical profile, findings of bone marrow examinations and computed tomography scans of the thorax, abdomen and pelvic cavity. ENKTL was classified into two subsets based on the anatomic distribution of the tumour at presentation (Logsdon *et al*, 1997; Rodriguez *et al*, 2007). Upper aerodigestive tract NK/T-cell lymphoma (UNKTL) was defined as a primary tumour involving the nasal cavity, nasopharynx and upper aerodigestive tract. Extraupper aerodigestive tract NK/T-cell lymphoma (EUNKTL) was defined as primary tumours at all sites other than UNKTL sites. All patients were staged using the Ann Arbour staging system (Lamkin *et al*, 2009). Fasting blood glucose was measured when patients had not eaten for at least 8 h, by clinical laboratories using standard quality assurance. According to American Diabetes Association (ADA) criteria, patients were classified into two groups according to the degree of FBG (Luo *et al*, 2012): (1) euglycemic group, those who had FBG concentrations $\leqslant 100\,\mathrm{mg\,dl^{-1}}$ and (2) hyperglycemic group, whose FBG concentrations $>100\,\mathrm{mg\,dl^{-1}}$.

Response criteria. The treatment response was evaluated according to the International Working Group Recommendations for Response Criteria for non-Hodgkin's lymphoma (Cheson *et al*, 1999; Grillo-Lopez *et al*, 2000).

Statistical analyses. Overall survival (OS) was measured from the date of diagnosis to the date of death from any cause or to the date of the last follow-up visit. Progression-free survival (PFS) was calculated from diagnosis to first progression, relapse after response or death from any cause, or to the date of last follow-up. Categorical characteristics were compared by χ^2 test or Fisher's exact test. Overall survival and PFS were estimated using the Kaplan–Meier method. The significance of differences between survival curves was tested using the log-rank test. Significant variables in the univariate analysis were considered as variables for the multivariate analysis of survival. The latter was performed by the Cox regression mode. $P<0.05$ was considered statistically significant, and all *P*-values corresponded to two-sided significance tests. Statistical analysis was performed using SPSS 18.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

Patient characteristics. The clinical characteristics of the 130 patients are shown in Table 1. Men predominated, and the median age was 43 years (range, 11–74). Seventy patients had B symptoms (53.8%) at presentation, and most patients had localised diseases (Ann Arbour stages I, II; $n=100$; 76.9%). In patients with EUNKTL, the primary lesion sites were skin or soft tissue ($n=6$), gastrointestinal tract ($n=4$), adrenal gland ($n=2$) and others ($n=2$). The median FBG at diagnosis was $92.9\,\mathrm{mg\,dl^{-1}}$ (range: 61.0–193.7). Only two patients with FBG $>100\,\mathrm{mg\,dl^{-1}}$ at diagnosis had been diagnosed with DM for >10 years and took insulin daily to control blood glucose. Baseline clinical features of patients with FBG $\leqslant 100\,\mathrm{mg\,dl^{-1}}$ at diagnosis were compared with those of patients with FBG $>100\,\mathrm{mg\,dl^{-1}}$ at diagnosis. No significant between-group difference was observed for age, gender and different groups of IPI, KPI and PIT. In addition, the ratio of hyperglycaemia was not statistically different among BMI, B symptom, Ann Arbour stage, regional lymph node involvement, subtypes and LDH levels (Table 1). Patients with FBG $>100\,\mathrm{mg\,dl^{-1}}$ at diagnosis tended to have worse ECOG PS, a higher chance of having albumin levels $<35\,\mathrm{g\,l^{-1}}$ and thrombocytopenia.

Treatment modalities and response. The primary treatment modalities were as follows: (i) no treatment (8 cases); (ii) chemotherapy alone (80 cases) and (iii) chemotherapy followed

Table 1. Baseline clinical characteristics according to fasting blood glucose (FBG) levels at diagnosis (FBG $\leqslant 100\,mg\,dl^{-1}$ vs FBG $>100\,mg\,dl^{-1}$)

Characteristics	Glucose level $\leqslant 100\,mg\,dl^{-1}$, *n* (%)	Glucose level $>100\,mg\,dl^{-1}$, *n* (%)	*P*-value
No. of patients	94 (72.3)	36 (27.7)	
Diagnosis of diabetes			0.075
Yes	0 (0)	2 (5.6)	
No	94 (100.0)	34 (94.4)	
Age (median (range), years)	43 (11–74)	44 (31–70)	0.802
$\leqslant 60$	80 (85.1)	30 (83.3)	
> 60	14 (14.9)	6 (16.7)	
Gender			0.403
Female	22 (23.4)	6 (16.7)	
Male	72 (76.6)	30 (83.3)	
ECOG PS			0.022
0–1	88 (93.6)	28 (77.8)	
$\geqslant 2$	6 (6.4)	8 (22.2)	
BMI ($kg\,m^{-2}$)[a]			0.595
<18.5	26 (29.5)	6 (20.0)	
18.5–<25	46 (52.3)	18 (60.0)	
$\geqslant 25$	16 (18.2)	6 (20.0)	
Mass			1
<5 cm	82 (87.2)	32 (88.9)	
$\geqslant 5$ cm	12 (12.8)	4 (11.1)	
B symptom			0.586
+	52 (55.3)	18 (50.0)	
−	42 (44.7)	18 (50.0)	
Ann Arbour stage			0.283
I–II	70 (74.5)	30 (83.3)	
III–IV	24 (25.5)	6 (16.7)	
Regional lymph node involvement			0.499
+	48 (51.1)	16 (44.4)	
−	46 (48.9)	20 (55.6)	
Extranodal sites			0.695
<2	66 (70.2)	24 (66.7)	
$\geqslant 2$	28 (29.8)	12 (33.3)	
Bone marrow			0.669
Involvement	4 (4.3)	2 (5.6)	
+	90 (95.7)	34 (94.4)	
−			
Subtypes			1
UNKTL	84 (89.4)	32 (88.9)	
EUNKTL	10 (10.6)	4 (11.1)	
IPI score[b]			0.278
0–1	70 (76.1)	24 (66.7)	
2–5	22 (33.9)	12 (33.3)	
PIT score[b]			0.097
0–1	82 (89.1)	28 (77.8)	
2–4	10 (10.9)	8 (22.2)	
KPI score[b]			0.313
0–1	50 (54.3)	16 (44.4)	
2–4	42 (45.7)	20 (55.6)	
WBC			0.181
$< 4.0\times10^{9}\,l^{-1}$	12 (12.8)	8 (22.2)	
$\geqslant 4.0\times10^{9}\,l^{-1}$	82 (87.2)	28 (77.8)	
ALC			0.886
$< 1.0\times10^{9}\,l^{-1}$	22 (23.4)	8 (22.2)	
$\geqslant 1.0\times10^{9}\,l^{-1}$	72 (76.6)	28 (77.8)	
Haemoglobin			0.604
$< 110\,g\,l^{-1}$	22 (23.4)	10 (27.8)	
$\geqslant 110\,g\,l^{-1}$	72 (76.6)	26 (72.2)	
Platelet counts			0.002
$<150\times10^{9}\,l^{-1}$	6 (6.4)	10 (27.8)	
$\geqslant 150\times10^{9}\,l^{-1}$	88 (93.6)	26 (72.2)	
Total protein			0.153
$< 60\,g\,l^{-1}$	10 (10.6)	8 (22.2)	
$\geqslant 60\,g\,l^{-1}$	84 (89.4)	28 (77.8)	
Albumin			0.043
$< 35\,g\,l^{-1}$	16 (17.0)	12 (33.3)	
$\geqslant 35\,g\,l^{-1}$	78 (83.0)	24 (66.7)	
LDH[b]			0.154
$\leqslant 245\,U\,ml^{-1}$	68 (73.9)	22 (61.1)	
$> 245\,U\,ml^{-1}$	24 (26.1)	14 (38.9)	

Abbreviations: EUNKTL = extraupper aerodigestive tract NK/T-cell lymphoma; ECOG PS = Eastern Cooperative Oncology Group performance status; BMI = body mass index; IPI = International Prognostic Index; PIT = Prognostic Index for Peripheral T-cell lymphoma unspecified; KPI = Korean Prognostic Index; WBC = white blood cell; ALC = absolute lymphocyte count; LDH = lactate dehydrogenase.
[a]Complete information on BMI was available in 118 cases.
[b]Complete information on IPI score, PIT score, KPI score or LDH was available in 128 cases.

Table 2. Treatment of patients according to fasting blood glucose (FBG) levels at diagnosis (FBG $\leqslant 100\,mg\,dl^{-1}$ vs FBG $>100\,mg\,dl^{-1}$)

Treatment	FBG $\leqslant 100\,mg\,dl^{-1}$ (no. of patients)	FBG $>100\,mg\,dl^{-1}$ (no. of patients)	*P*-value
Patient treated	94	36	0.616
No treatment	6	2	
Chemotherapy alone	60	20	
Chemotherapy followed by radiotherapy	28	14	
Anthracyclines used	70	28	0.727
L-asparaginase used	16	4	0.391
Efficacy			0.003
CR unachieved	36	24	
CR achieved	52	10	

Abbreviation: CR = complete remission.

by radiotherapy (42 cases). The regimens of chemotherapy in the initial treatment included: CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone), CHOP-like [(CHOP + L-asparaginase), CHOP + HD-MTX (CHOP + high-dose methotrexate), CHOPE (CHOP + etoposide)], EPOCH (etoposide, doxorubicin, vincristine, cyclophosphamide, prednisone), alternating triple therapy regimen (CHOP-B, IMVP-16 and DHAP), CHOP-B (cyclophosphamide, doxorubicin, vincristine, prednisone and bleomycin), IMVP-16 (ifosfamide, etoposide, methotrexate), DHAP (dexamethasone, cytarabine, cisplatin)], GEMOX (gemcitabine, oxaliplatin), GEMOX + L-asparaginase, SMILE (dexamethasone, methotrexate, ifosfamide, L-asparaginase, etoposide) and vincristine + L-asparaginase + dexamethasone. The treatment details and outcomes are listed in Table 2. No significant difference was observed in the treatment modalities between patients grouped by FBG $\leqslant 100\,mg\,dl^{-1}$ and FBG $>100\,mg\,dl^{-1}$ at diagnosis. In the initial treatment modality, 122 patients (93.8%) were evaluated for treatment responses, and 62 patients (50.8%) achieved complete remission (CR). The rate of CR in the initial treatment was significantly lower in patients with FBG $>100\,mg\,dl^{-1}$ ($P = 0.003$).

Survival and prognostic factors. The median survival time was 31.7 months (95% confidence interval (CI): 21.4–42.0), and the estimated 5-year OS and PFS rate in 130 patients was 51.2% and 30.8%, respectively (Figure 1). At the time of analysis, 78 patients (60.0%) had died because of tumour progression ($n=72$), treatment-related toxicity ($n=2$) and unknown causes ($n=4$). The 5-year estimate for OS was 61.9% for patients with FBG $\leqslant 100\,mg\,dl^{-1}$ and 26.3% for those with FBG $>100\,mg\,dl^{-1}$ ($P<0.001$; Figure 2A). Patients with FBG $>100\,mg\,dl^{-1}$ at diagnosis also had worse 5-year PFS than patients with low FBG at diagnosis (9.8% *vs* 38.8%, $P<0.001$; Figure 2B). Table 3 shows the results of univariate and multivariate analyses of clinical variables considered as predictors of OS and PFS.

The distribution of patients within risk groups based on IPI, PIT and KPI scores is presented in Table 4. Using the IPI and PIT scoring systems, >70% of all cases were in the low-risk category (with no or one adverse factor), but these two prognostic models failed to differentiate between patients with different outcomes in the low-risk group. The KPI model balanced distribution of patients into different risk groups better than the IPI and PIT models. For patients in the low-risk category according to IPI and PIT, FBG at diagnosis could distinguish between those with good outcomes and those with poor outcomes. Patients with FBG $\leqslant 100\,mg\,dl^{-1}$ at diagnosis had better survival than those with FBG $>100\,mg\,dl^{-1}$ (5-year OS of low-risk IPI: 54.3% *vs* 25.0%, $P=0.013$; 5-year OS of low-risk PIT: 51.2% *vs* 21.4%, $P=0.006$). In the KPI prognostic model, FBG also helped to differentiate between patients with different prognosis in the category of no or one risk factor (5-year OS: 72.0% *vs* 37.5%, $P=0.013$) and two or more than two risk factors (5-year OS: 19.0% *vs* 0%, $P=0.046$).

DISCUSSION

Our study identified that FBG $>100\,mg\,dl^{-1}$ was independently associated with poor survival in patients with ENKTL.

The value of hyperglycaemia for prognosis in a range of malignancies was previously investigated (Zhou *et al*, 2010) and demonstrated an inverse relationship between glucose levels and length of survival time in stomach cancer (Zhou *et al*, 2010), lung

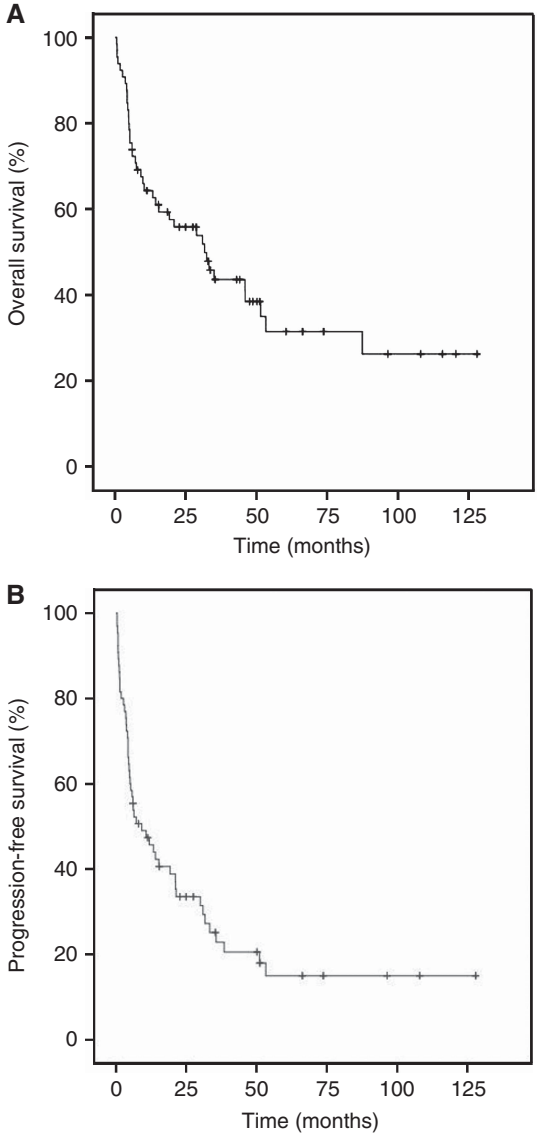

Figure 1. (**A**) Overall survival of 130 patients with extranodal natural killer T-cell lymphoma, nasal type (ENKTL). (**B**) Progression-free survival of 130 patients with ENKTL, nasal type.

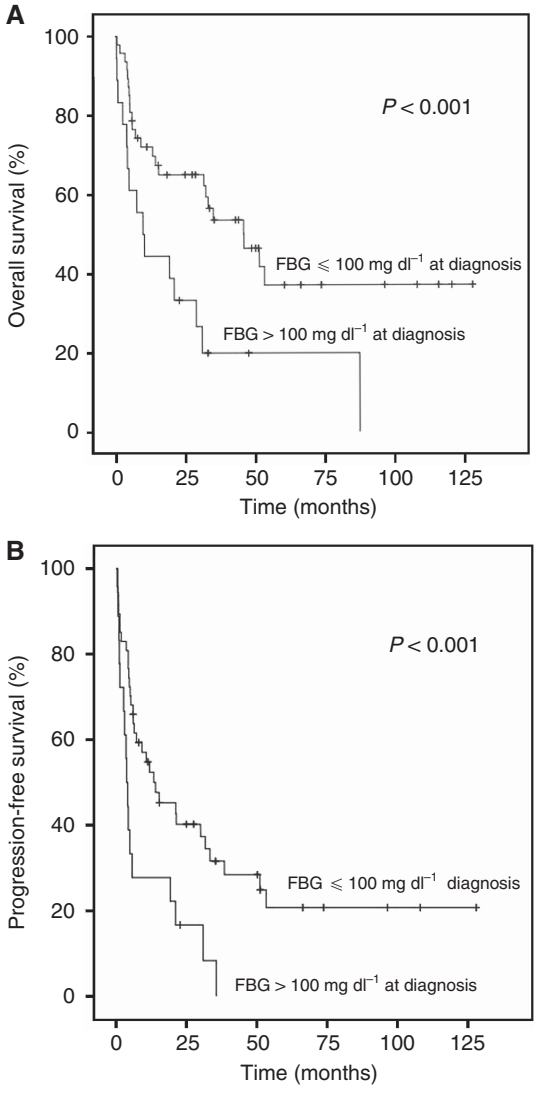

Figure 2. (**A**) Overall survival of patients according to fasting blood glucose (FBG) $\leqslant 100\,mg\,dl^{-1}$ *vs* $>100\,mg\,dl^{-1}$ at diagnosis. (**B**) Progression-free survival of patients according to FBG $\leqslant 100\,mg\,dl^{-1}$ *vs* $>100\,mg\,dl^{-1}$ at diagnosis.

Table 3. Analysis of prognostic factors for OS and PFS in patients

	OS			PFS		
	Univariate analysis	Multivariate analysis		Univariate analysis	Multivariate analysis	
Parameters	***P*-value**	**RR (95% CI)**	***P*-value**	***P*-value**	**RR (95% CI)**	***P*-value**
Age >60 years	0.345			0.408		
Gender, male	0.889			0.764		
BMI	0.101			0.095		
ECOG PS (⩾2)	<0.001			0.004		
B symptoms	0.065			0.016		
Ann Arbour (III–IV)	0.007			0.002		
WBC ($<4.0\times10^9\,l^{-1}$)	<0.001			0.007		
ALC ($<1.0\times10^9\,l^{-1}$)	<0.001			0.002	2.259 (1.374–3.714)	0.001
Haemoglobin ($<110\,g\,l^{-1}$)	0.002			0.06		
Platelet counts ($<150\times10^9\,l^{-1}$)	<0.001			0.002		
Total protein ($<60\,g\,l^{-1}$)	<0.001	5.648 (3.020–10.562)	<0.001	<0.001		
Albumin ($<35\,g\,l^{-1}$)	<0.001			0.012		
Fasting blood glucose level ($>100\,mg\,dl^{-1}$)	<0.001	2.824 (1.745–4.569)	<0.001	<0.001	2.094 (1.321–3.320)	0.002
LDH ($>245\,U\,ml^{-1}$)	<0.001					
Regional lymph node involvement	<0.001			0.003		
Subtype	0.201			0.165		
Bone involvement	<0.001			0.008		
Extranodal sites (⩾2)	<0.001			<0.001	2.562 (1.594–4.116)	<0.001
Mass (⩾5 cm)	0.244			0.819		
IPI (2–5)	<0.001			0.003		
KPI (2–4)	<0.001	2.638 (1.578–4.411)	<0.001	<0.001	2.053 (1.306–3.228)	0.002
PIT (2–4)	<0.001			0.182		

Abbreviations: CI = confidence interval; ALC = absolute lymphocyte count; OS = overall survival; PFS = progression-free survival; BMI = body mass index; ECOG PS = Eastern Cooperative Oncology Group performance status; WBC = white blood cell; LC = lymphocyte count; LDH = lactate dehydrogenase; IPI = International Prognostic Index; KPI = Korean Prognostic Index; PIT = Prognostic Index for Peripheral T-cell lymphoma unspecified.
Cox regression mode was used for statistical analysis. $P<0.05$ was considered statistically significant.

cancer (Luo *et al*, 2012), ovarian carcinoma (Lamkin *et al*, 2009), cervical cancer (Lee *et al*, 2010) and acute lymphocytic leukaemia (Sonabend *et al*, 2009). However, the impact of FBG on the survival of patients with NHL including ENKTL has not been described. To the best of our knowledge, this clinical study is the first to observe that FBG at diagnosis is a prognostic factor of survival in ENKTL, nasal type.

In this study, we divided patients into two groups using a cutoff value of $100\,mg\,dl^{-1}$ FBG based on ADA criteria (Luo *et al*, 2012). Our data demonstrated a notable difference in clinical behaviour between the higher and lower FBG groups. Patients with FBG $>100\,mg\,dl^{-1}$ were more likely to develop adverse clinical features, including poor PS, lower platelet counts and lower albumin levels. In addition, patients with FBG $>100\,mg\,dl^{-1}$ at diagnosis were more likely to achieve a lower rate of CR. Regardless of the association between FBG and other prognostic factors, multivariate analysis showed that FBG at diagnosis was a powerful predictor of OS and PFS in patients with ENKTL, nasal type.

Although ENKTL is a distinctive entity with poor prognosis, >70% of the patients in our study were categorised as low-risk based on IPI and PIT scores. However, FBG at diagnosis separated patients in the low-risk category of IPI and PIT on the basis of survival outcome. When adding FBG at diagnosis to the two models, the low-risk patients were separated on the basis of different survival outcomes with sufficient statistical power. In addition, FBG at diagnosis also separated patients in a different category of KPI score based on the survival outcome.

The biological mechanism by which hyperglycaemia increases mortality risk of patients diagnosed with ENKTL is unclear. Several potential explanations have been proposed for the observed association between hyperglycaemia and increased all-cause mortality in cancer patients (Barone *et al*, 2002). First, cancer patients with hyperglycaemia may have increased tumour cell proliferation and metastatic capacity as a consequence of the physiologic environment of hyperinsulinemia (Richardson and Pollack, 2005). It has been suggested that high insulin or increased free insulin-like growth factor (IGF-1) levels in hyperinsulinemic states can promote cancer cell and tumour growth (Richardson and Pollack, 2005). Second, glucose metabolism of cancer cells is different from normal cells mainly because of a lack of oxygen present in hypoxic tumour conditions. Activation of hypoxia-inducible factor stimulates the expression of glycolytic enzymes and decreases reliance on mitochondrial oxidative phosphorylation in tumour cells, which occurs even under aerobic conditions. Moreover, glucose utilisation of cancer cells is significantly enhanced when compared with normal tissue because of the overexpression of five transmembrane transporters, termed GLUT1-5. GLUT is significantly associated with the likelihood of metastasis and hence poor patient prognosis (Medina and Owen, 2002; Guo *et al*, 2010). Third, the presence of diabetes in cancer patients may have indirect impact on cancer outcome. A study

Table 4. Distribution of patients within risk groups and OS by determined by IPI, KPI and PIT

Prognostic model	No. of patients (%)	5-year OS (%)	*P*-value
IPI score[a]			
0–1	94 (73.4)	46.8	0.003
2–5	34 (26.6)	17.6	
PIT score[a]			
0–1	110 (85.9)	43.6	0.009
2–4	18 (14.1)	11.1	
KPI score[a]			
0–1	66 (51.6)	63.6	< 0.001
2–4	62 (48.4)	12.9	

Abbreviations: OS = overall survival; IPI = International Prognostic Index; KPI = Korean Prognostic Index; PIT = Prognostic Index for Peripheral T-cell lymphoma, unspecified. Differences between survival curves were tested using the log-rank test. $P<0.05$ was considered statistically significant.
[a]Complete information on IPI score, PIT score and KPI score was available in 128 cases.

indicated that cancer patients with pre-existing diabetes were often treated less aggressively than those without diabetes (van de Poll-Franse *et al*, 2007). Thus, differences in cancer treatment between patients with and without diabetes may contribute to increased mortality. However, this proposed hypothesis was not supported by our data, which demonstrated no significant difference in cancer treatment between the two groups. In addition, patients with hyperglycaemia may have a poorer response to cancer treatment (Brunello *et al*, 2011). There is no direct evidence to suggest that glycaemia control can decrease cancer recurrence or cancer mortality, although data may support this hypothesis in breast cancer (Krone and Ely, 2005).

Our study has several strengths including: (1) all patients were newly diagnosed, which ruled out any impact on patients' outcomes by possible disproportionate pretreatment that patients might receive; (2) despite the limited data generally derived from retrospective hospital records review, we were able to collect and adjust for most potential prognostic factors to avoid bias; (3) we measured FBG instead of random blood glucose, and therefore this value could be used to establish a baseline to control values for all patients with the same status. However, our study was also limited in several aspects: (1) our cases included both diabetic and non-diabetic patients and therefore the impact of diabetic status was not accounted for; (2) the findings of this study may be specific to the study sample in Asian populations; (3) this was a retrospective study with a small number of patients. Therefore, a prospective study with a large number of cases is needed to confirm a correlation between FBG and ENKTL prognosis.

In conclusion, this study suggested that FBG at diagnosis is a prognostic indicator of clinical outcome in ENKTL, nasal type and may have important implications for the control of glycaemia in patients with this disease. Further investigation is required to provide a better understanding of the mechanisms underlying the association between blood glucose levels and clinical outcome. Future prospective clinical studies are required to confirm our findings.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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