

Article

Elevated Fasting Glucose in Patients with Lymphoma: A Real-World Observational Study

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Abstract

Background/Objectives: Patients with lymphoma are at increased risk of dysglycemia due to disease-related and treatment-associated metabolic alterations. This study aimed to characterize fasting capillary glucose patterns in patients with lymphoma undergoing routine capillary fasting blood glucose assessment before fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT). **Materials and Methods:** Consecutive patients with lymphoma undergoing clinically indicated FDG PET/CT at the University Hospital Zurich were included. Capillary fasting blood glucose (cFBG) was measured before tracer administration and categorized according to American Diabetes Association fasting glucose thresholds. Additional analyses were performed in patients examined before 11:00 AM and in patients without known diabetes mellitus. Multivariable linear regression was used to identify factors associated with cFBG. **Results:** The cohort included 210 consecutive patients with lymphoma (median age 64 years, IQR 48–73; 44% female, 92/210; median BMI 24 kg/m², IQR 22–28). Known diabetes mellitus was present in 12% (25/210). Median cFBG was 104 mg/dL (IQR 95–115; 5.8 mmol/L, IQR 5.3–6.4). Overall, 64% (135/210) had cFBG values above the normal range (≥ 100 mg/dL; ≥ 5.6 mmol/L). Among patients examined before 11:00 AM, this proportion was 69% (81/117). After excluding patients with known diabetes mellitus, 60% (111/185) had cFBG values above the normal range, and 7% (13/185) had values ≥ 126 mg/dL (≥ 7.0 mmol/L). In multivariable analysis, BMI and regular exercise were independently associated with cFBG. **Conclusions:** Almost two-thirds of patients with lymphoma undergoing FDG PET/CT had cFBG values above the normal range, including 60% of those without known diabetes mellitus. These findings highlight the need for improved dysglycemia screening and management in lymphoma care.



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1. Introduction

Patients with malignancies are at increased risk of developing new-onset diabetes mellitus or hyperglycemia, irrespective of a pre-existing diagnosis of diabetes. Diabetes is common among patients with cancer, likely reflecting shared metabolic, inflammatory, and

lifestyle-related risk factors [1–3]. In addition to patient-related factors, oncologic therapies may further impair glycemic regulation, with corticosteroids, chemotherapy, targeted treatments, and selected immunotherapies all potentially contributing to dysglycemia in patients with or without pre-existing diabetes [3–5].

This issue is particularly relevant in patients with hematologic malignancies, including lymphoma. Hyperglycemia has been described as a frequent metabolic complication during treatment of hematologic cancers, and patients with lymphoma may be especially vulnerable because many standard treatment regimens include high-dose glucocorticoids [6–8]. In patients with lymphoma treated with CHOP (Cyclophosphamide, Hydroxydaunorubicin, Oncovin, Prednisone)-based chemotherapy, glucocorticoid-induced diabetes mellitus has been specifically reported, underscoring the clinical relevance of treatment-associated dysglycemia in this population [8]. In addition, metabolic disturbances may persist beyond active treatment in survivors of hematologic malignancies [9].

Dysglycemia is clinically relevant because it may complicate oncologic care and adversely affect patient outcomes. During chemotherapy, hyperglycemia has been reported in approximately 10–30% of patients with malignancies and has been associated with increased infection risk, treatment-related complications, and mortality [1,4,7]. Suboptimal glycemic control may also interfere with planned therapy, including the need for treatment modifications in vulnerable patients [1,3]. Beyond acute complications, the coexistence of cancer and diabetes is associated with increased symptom burden and worse patient-reported outcomes, highlighting the broader clinical impact of dysglycemia in oncologic populations [3,10].

Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography is routinely used for staging and response assessment in FDG-avid lymphomas and is also performed in selected follow-up settings [11]. Because fasting glucose assessment is routinely performed before tracer administration, this setting provides a pragmatic opportunity to characterize glycemic status in an unselected oncologic population. Thus, the current study was designed to systematically assess capillary fasting blood glucose status in consecutive patients with lymphoma undergoing clinically indicated FDG PET/CT at different stages of care.

2. Materials and Methods

2.1. Study Design and Setting

This retrospective observational study of consecutive patients was conducted at the University Hospital Zurich. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Cantonal Ethics Committee Zurich (Kantonale Ethikkommission Zürich; BASEC No. 2023-02276). Written informed consent for the scientific use of clinical data was obtained from all patients.

2.2. Study Population

Consecutive adult patients with lymphoma undergoing clinically indicated oncologic fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography between June 2023 and December 2024 were included. If a patient underwent more than one FDG PET/CT examination during the study period, only the earliest examination was included in the analysis. Patients were identified using lymphoma-related ICD-10 codes, including Hodgkin lymphoma (C81), follicular lymphoma (C82, including C82.9), non-follicular lymphoma (C83), mature T/NK-cell lymphoma (C84), other or unspecified non-Hodgkin lymphoma (C85), and malignant immunoproliferative diseases (C88). Active lymphoma was defined based on FDG PET/CT results. Clinical and demographic informa-

tion was obtained from the institutional electronic health record and from standardized patient questionnaires completed at the time of examination.

2.3. Capillary Fasting Blood Glucose Measurements and Definitions

As part of routine clinical practice, patients were instructed to fast before FDG PET/CT. Patients scheduled for afternoon examinations were instructed to fast for at least 4 h before imaging, whereas patients scheduled for morning examinations were assumed to have fasted overnight. Before tracer administration, fasting status was confirmed by trained nursing staff, and capillary fasting blood glucose was measured using the Accu-Chek® Inform II device (Roche Diagnostics, Switzerland). The Accu-Chek® Inform II has demonstrated strong agreement with laboratory glucose measurements, with reported concordance and intraclass correlation coefficients of approximately 0.95 or higher. When deviations occur, reported values tend to be lower than the laboratory reference method, with an average negative bias of approximately 5–10% [12–14].

For the present study, capillary fasting blood glucose values were categorized according to American Diabetes Association criteria: normal fasting glucose, <100 mg/dL (<5.6 mmol/L); impaired fasting glucose, 100–125 mg/dL (5.6–6.9 mmol/L); and fasting glucose in the diabetes range, ≥ 126 mg/dL (≥ 7.0 mmol/L). In addition, values ≥ 200 mg/dL (≥ 11.1 mmol/L), corresponding to the random glucose threshold for diabetes, were recorded separately. Importantly, capillary fasting blood glucose was used as a screening measure only. Formal diagnosis of diabetes mellitus requires confirmatory testing, including venous fasting plasma glucose measurement after at least 8 h of fasting, according to current guidelines [15]. Known diabetes mellitus was defined based on documentation in the medical record, use of glucose-lowering medication, or patient self-report.

Because abdominal adiposity, particularly visceral fat, is closely linked to insulin resistance and glucose metabolism, visceral and subcutaneous fat thickness were assessed as pragmatic CT-derived markers of abdominal fat distribution. Abdominal visceral and subcutaneous fat thickness were assessed on CT images in a standardized manner as pragmatic surrogate measures of abdominal fat distribution. Visceral fat thickness was measured as the distance between the inner surface of the anterior abdominal wall and the anterior aortic wall at the level of the aortic bifurcation [16]. Subcutaneous fat thickness was measured as the distance between the skin and the outer surface of the anterior abdominal wall at the same anatomical level [16].

Regular exercise was based on patient self-report at the time of examination. Information on exercise type, intensity, duration, or frequency was not available.

2.4. Statistical Analysis

Continuous variables are presented as median and interquartile range, and categorical variables are presented as frequencies and percentages. Comparisons between groups were performed using the Mann–Whitney U test, Kruskal–Wallis test, or Fisher’s exact test, as appropriate. Confidence intervals for proportions were calculated as exact binomial 95% confidence intervals. Spearman’s rank correlation was used to assess associations between continuous or ordinal variables.

Multivariable linear regression was performed to identify independent predictors of capillary fasting blood glucose. Variables were eligible for inclusion in the multivariable model if they showed an association with capillary fasting blood glucose in univariable analysis at a threshold of $p < 0.20$. Analyses were performed as complete-case analyses. Continuous predictor variables were log-transformed where appropriate to reduce skewness and mitigate heteroscedasticity. Model adequacy was assessed using residual diagnostics, evaluation of linearity, and checks for multicollinearity.

Three sensitivity analyses were performed. First, analyses were repeated in patients examined before 11:00 AM, representing patients most likely to have fasted for at least 8 h. Second, analyses were repeated after exclusion of patients with known diabetes mellitus. Third, capillary fasting blood glucose values were multiplied by a correction factor of 1.08 to account for the reported negative bias of the Accu-Chek® Inform II compared with laboratory reference methods [12–14]. All statistical tests were two-sided, and $p < 0.05$ was considered statistically significant. Statistical analyses were performed using R.

3. Results

A total of 210 consecutive patients with lymphoma undergoing clinically indicated FDG PET/CT were included. The median age was 64 years (IQR 48–73), 44% of patients were female (92/210), and 12% had known diabetes mellitus (25/210). The most frequent lymphoma-related ICD group was non-follicular lymphoma (C83; 34%, 71/210), followed by other or unspecified non-Hodgkin lymphoma (C85; 19%, 40/210), follicular lymphoma (C82, including C82.9; 19%, 39/210), Hodgkin lymphoma (C81; 15%, 32/210), mature T/NK-cell lymphoma (C84; 10%, 20/210), and malignant immunoproliferative diseases (C88; 4%, 8/210). Overall, 51% (109/210) of the patients had active lymphoma.

Median capillary fasting blood glucose was 104 mg/dL (IQR 95–115), corresponding to 5.8 mmol/L (IQR 5.3–6.4). Overall, 36% of patients had cFBG values <100 mg/dL (<5.6 mmol/L; 75/210), 51% had values between 100 and 125 mg/dL (5.6–6.9 mmol/L; 107/210), and 13% had values ≥ 126 mg/dL (≥ 7.0 mmol/L; 28/210). Thus, 64% of the cohort (135/210) had cFBG values above the normal range, defined as ≥ 100 mg/dL (≥ 5.6 mmol/L). One patient had a cFBG value ≥ 200 mg/dL (≥ 11.1 mmol/L). The distribution of cFBG values is shown in Figure 1.

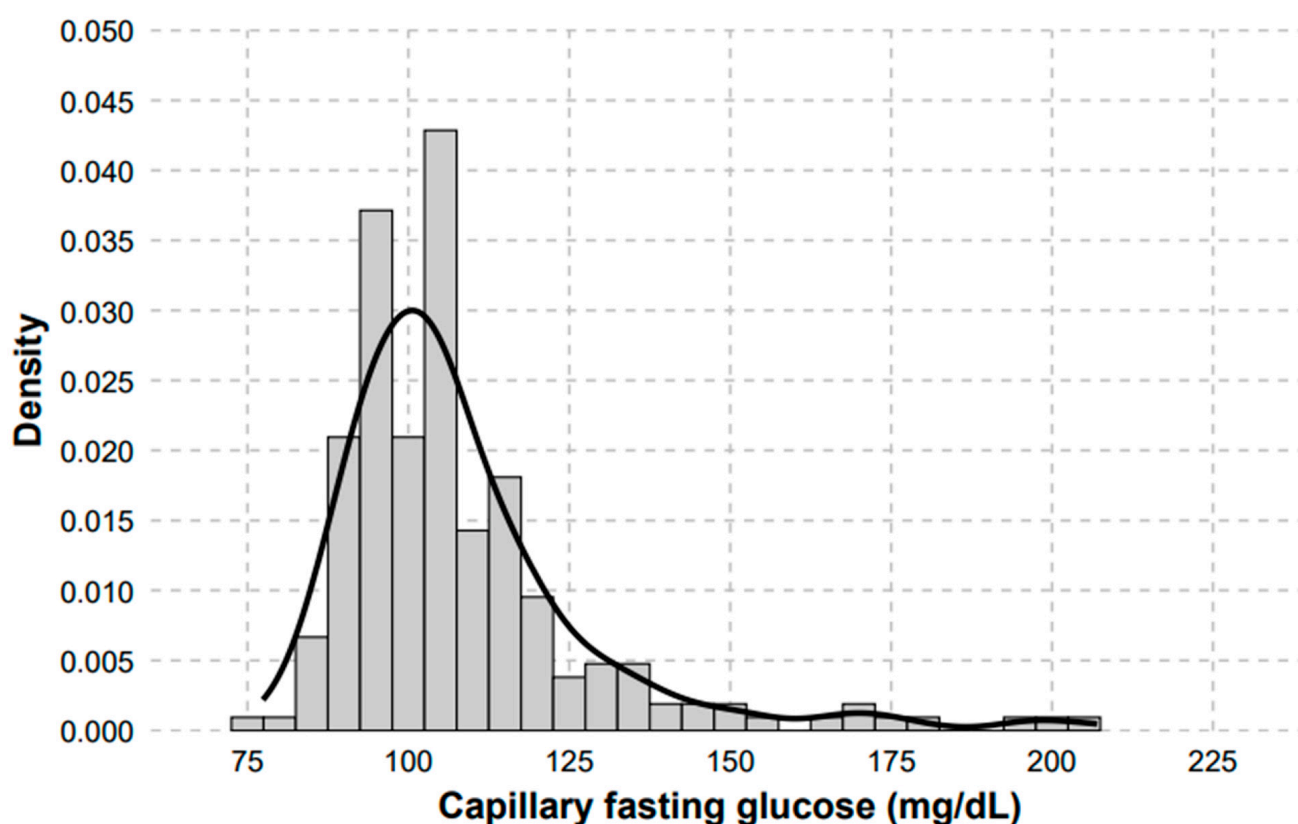


Figure 1. Distribution of capillary fasting glucose (cFBG). Histogram of capillary fasting glucose with overlaid kernel density estimate. The y-axis represents probability density (area under curve = 1).

Baseline characteristics stratified by cFBG category are shown in Table 1.

Table 1. Patient characteristics stratified by capillary fasting glucose levels.

	Overall, N = 210	<100 mg/dL (<5.6 mmol/L), N = 75, 36%	100–125 mg/dL (5.6–6.9 mmol/L), N = 107, 51%	≥126 mg/dL (≥7.0 mmol/L), N = 28, 13%	p-Value
Capillary FBG [IQR], mg/dL	104 [95, 115]	94 [90, 95]	106 [104, 113]	140 [131, 165]	<0.001
mmol/L	5.8 [5.3, 6.4]	5.2 [5.0, 5.3]	5.9 [5.8, 6.3]	7.8 [7.3, 9.2]	
Female, %	92 (44)	31 (41)	53 (50)	8 (29)	0.119
Age [IQR], years	64 [48, 73]	64 [48, 73]	64 [48, 73]	64 [48, 73]	0.028
BMI [IQR], kg/m ²	24 [22, 28]	23 [21, 26]	24 [22, 28]	26 [23, 31]	0.013
<18	5 (2%)	4 (5%)	1 (0%)	0	
18–25	109 (51%)	41 (54%)	57 (53%)	11 (39%)	
25–30	66 (31%)	24 (32%)	33 (30%)	9 (32%)	
30–35	25 (11%)	6 (8%)	13 (12%)	6 (21%)	
35–40	2 (1%)	0	2 (1)	0	
>40	3 (1%)	0	1 (0)	2 (7%)	
Ever smoker, %	98 (46%)	32 (42%)	52 (48%)	14 (50%)	0.681
Known diabetes mellitus, %	25 (12%)	1 (1%)	9 (8%)	15 (53%)	<0.001
Hypertension, %	78 (37%)	20 (26%)	44 (41%)	14 (50%)	0.044
Regular exercise, %	88 (41%)	37 (49%)	46 (43%)	5 (17%)	0.015
Active lymphoma, %	109 (51%)	43 (57%)	47 (43%)	19 (67%)	0.039
Subcutaneous fat [IQR], mm	23 [18, 30]	22 [17, 28]	25 [19, 32]	21 [17, 27]	0.160
Visceral fat (IQR), mm	52 [36, 70]	45 [35, 58]	55 [36, 70]	69 [49, 94]	0.004

BMI—body mass index, FBG—fasting blood glucose, IQR—inter-quartile-range.

Patients with cFBG values ≥126 mg/dL had a higher median BMI than patients with normal cFBG values (26 kg/m² [IQR 23–31] vs. 23 kg/m² [IQR 21–26]; $p = 0.013$). Known diabetes mellitus, hypertension, active lymphoma, and visceral fat thickness were more frequent or higher in patients with higher cFBG categories, whereas regular exercise was less frequent. Sex, smoking status, and subcutaneous fat thickness did not differ significantly across cFBG categories.

Among 117 patients examined before 11:00 AM, median cFBG was 104 mg/dL (IQR 97–113), corresponding to 5.8 mmol/L (IQR 5.4–6.3). In this subgroup, 69% of patients (81/117) had cFBG values ≥100 mg/dL (≥5.6 mmol/L), 9% (11/117) had values ≥126 mg/dL (≥7.0 mmol/L), and none had values ≥200 mg/dL (≥11.1 mmol/L). Among patients examined after 11:00 AM, the corresponding proportions were 58% (54/93) and 18% (17/93) for the ≥100 mg/dL and ≥126 mg/dL thresholds, respectively. The difference in cFBG between patients examined before and after 11:00 AM did not reach statistical significance ($p = 0.413$; Figure 2).

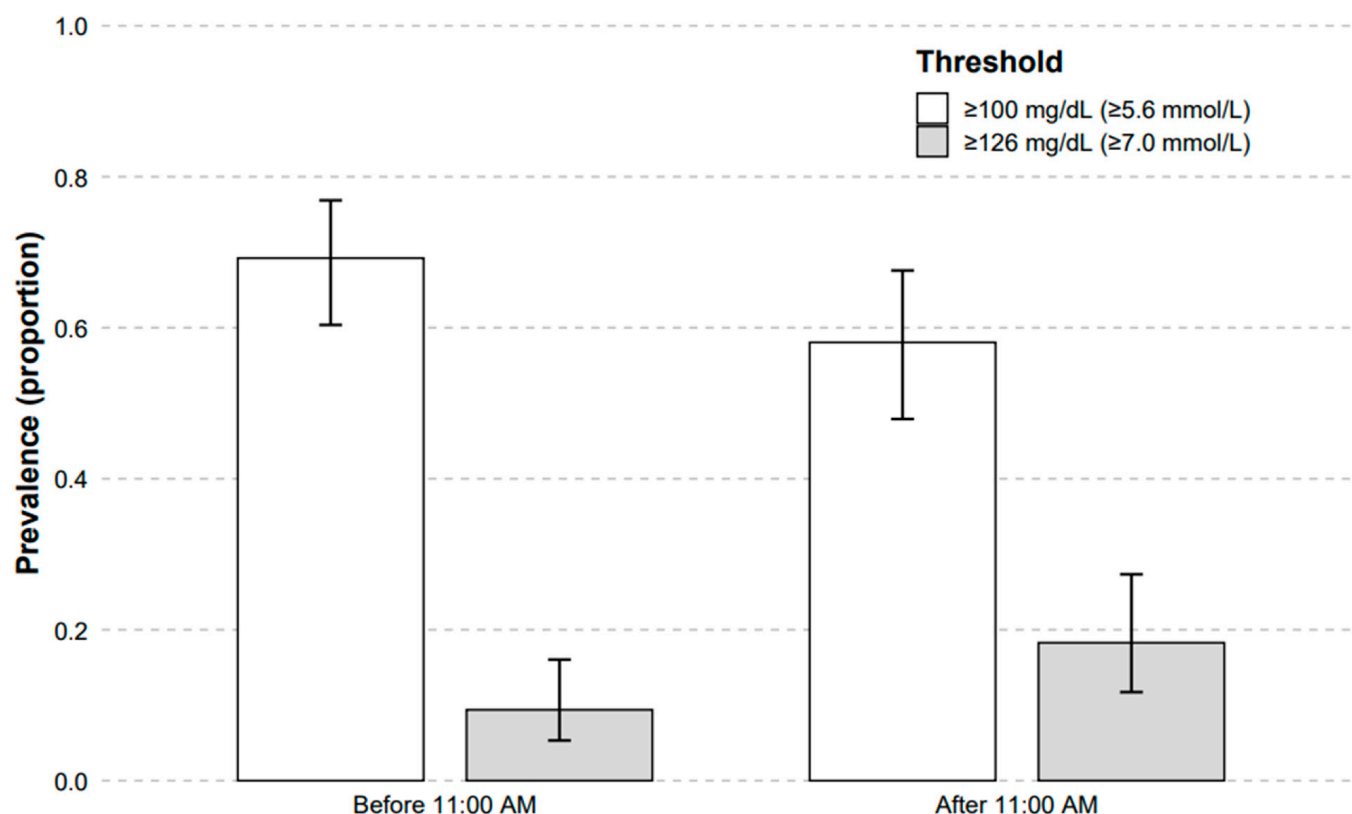


Figure 2. Prevalence of elevated capillary fasting glucose by time of examination. Bars indicate prevalence; error bars represent Wilson 95% confidence intervals. Patterned fills distinguish thresholds. The difference in capillary FBG between early and later assessments did not reach statistical significance ($p = 0.413$).

After applying an upward correction factor of 1.08 to account for the reported negative bias of capillary point-of-care glucose measurements, corrected cFBG values ≥ 126 mg/dL (≥ 7.0 mmol/L) were observed in 23% of patients in the overall cohort (48/210) and in 22% of patients examined before 11:00 AM (26/117).

After excluding the 25 patients with known diabetes mellitus, median cFBG was 103 mg/dL (IQR 95–113), corresponding to 5.7 mmol/L (IQR 5.3–6.1). Within this subgroup, 60% of patients (111/185) had cFBG values ≥ 100 mg/dL (≥ 5.6 mmol/L), and 7% (13/185) had values ≥ 126 mg/dL (≥ 7.0 mmol/L), compatible with possible previously unrecognized diabetes. After application of the correction factor, 16% of patients without known diabetes mellitus (29/185) had corrected cFBG values ≥ 126 mg/dL (≥ 7.0 mmol/L).

In subgroup analyses, elevated cFBG was observed in 62.5% (20/32) of patients with Hodgkin lymphoma and 64.6% (115/178) of patients with non-Hodgkin lymphoma, as well as in 60.6% (66/109) of patients with active lymphoma and 68.3% (69/101) without active lymphoma. These findings were broadly consistent with the overall cohort and support the main observation that elevated fasting glucose was common across clinical subgroups.

In univariable linear regression, age, BMI, hypertension, regular exercise, and visceral fat thickness were associated with cFBG, whereas sex, active lymphoma, smoking status, and subcutaneous fat thickness were not. Associations between clinical variables, abdominal fat measures, physical exercise, and cFBG are shown in Table 2.

Table 2. Linear regression analysis for the prediction of capillary fasting glucose.

	Univariate Coefficient (95% CI), <i>p</i> -Value	Multivariate Coefficient (95% CI), <i>p</i> -Value
Male	−1.7 (−7.2 to 3.9), 0.546	
Age, years	9.8 (2.7 to 16.9), 0.007	8.5 (−0.8 to 18.0), 0.074
Active lymphoma	2.4 (−3.1 to 7.9), 0.389	
BMI, kg/m ²	24.6 (9.4 to 39.8), 0.002	19.9 (0.2 to 39.5), 0.047
Ever smoker	2.3 (−3.2 to 7.8), 0.409	
Hypertension	9.0 (3.4 to 14.6), 0.002	5.3 (−0.6 to 11.2), 0.080
Regular exercise	−5.8 (−11.3 to −0.2), 0.039	−6.3 (−12.0 to −0.6), 0.030
Subcutaneous fat, mm	2.2 (−4.4 to 8.8), 0.516	
Visceral fat, mm	10.9 (5.1 to 16.7), <0.001	3.1 (−3.9 to 10.2), 0.383

BMI—body mass index.

In multivariable linear regression, BMI remained independently associated with higher cFBG (coefficient 19.9, 95% CI 0.2 to 39.5; $p = 0.047$), whereas regular exercise was independently associated with lower cFBG (coefficient −6.3, 95% CI −12.0 to −0.6; $p = 0.030$). Age ($p = 0.074$), hypertension ($p = 0.080$), and visceral fat thickness ($p = 0.383$) were not independently associated with cFBG in the multivariable model.

4. Discussion

This study assessed glycemic status in consecutive patients with lymphoma who underwent standardized cFBG assessment before clinically indicated FDG PET/CT. We report three major findings. First, nearly two-thirds of patients had cFBG values above the normal range, and this finding remained consistent in the sensitivity analysis restricted to patients examined before 11:00 AM. Second, among patients without known diabetes mellitus, elevated cFBG was detected in 60%, and 7% had values ≥ 126 mg/dL (≥ 7.0 mmol/L), a level that corresponds to the fasting plasma glucose threshold for diabetes but requires confirmatory venous testing for diagnosis. When applying an adjustment to account for reported capillary-venous bias [12–14], 16% of patients without known diabetes had corrected cFBG values ≥ 126 mg/dL in this sensitivity analysis. Third, BMI and regular exercise were independently associated with cFBG, whereas age, hypertension, and visceral fat thickness were not independent predictors in multivariable analysis.

These findings support previous observations that dysglycemia is common among patients with cancer, including those with hematologic malignancies. Hyperglycemia has been described as a frequent metabolic complication in hematologic cancers, particularly in the context of systemic therapy, glucocorticoid exposure, and treatment-related stress [4,6,7]. This is especially relevant in lymphoma, where glucocorticoids are part of many commonly used treatment regimens. In patients treated with CHOP-based chemotherapy, glucocorticoid-induced diabetes mellitus has been specifically reported [8]. The present study adds to this literature by showing that abnormal fasting glucose values are frequently detectable during routine clinical imaging, including in patients without previously known diabetes. These data are also consistent with related real-world oncology cohorts undergoing FDG PET/CT, including melanoma and lung cancer patients [17,18].

The association between BMI and higher cFBG is consistent with the known relationship between adiposity and insulin resistance. In patients with hematologic malignancies, BMI may be particularly relevant because hematologic cancers have been reported to strengthen the association between BMI and insulin resistance among cancer survivors [9].

Regular exercise was associated with lower cFBG, in line with evidence that physical activity and exercise interventions may improve glucose metabolism in cancer survivors [19,20]. Other traditional risk factors, including age, hypertension, and visceral fat thickness, were not independently associated with cFBG. This may reflect the influence of lymphoma-related factors, treatment exposure, systemic inflammation, acute illness, or stress-related metabolic changes, which may reduce the apparent contribution of conventional metabolic risk factors [1,4,7].

From a clinical perspective, the high prevalence of elevated cFBG is relevant. Hyperglycemia in cancer patients has been associated with infectious complications, treatment-related morbidity, and adverse clinical outcomes [1,4,7]. In addition, the coexistence of cancer and diabetes is associated with increased symptom burden and worse patient-reported outcomes [3,10]. Although a single capillary fasting glucose measurement cannot establish a formal diagnosis of diabetes or distinguish transient stress-, treatment-, or illness-related hyperglycemia from persistent metabolic dysfunction, abnormal values obtained during routine FDG PET/CT preparation may help identify patients who warrant confirmatory metabolic assessment and follow-up, particularly those without known diabetes.

Glycemic status is also relevant in the FDG PET/CT workflow, because elevated circulating glucose may affect FDG uptake and standardized uptake value measurements. Current FDG PET/CT procedure standards recommend fasting before tracer injection and generally allow imaging when pre-injection glucose remains below 200 mg/dL (11.1 mmol/L) [21]. This threshold is appropriate for imaging feasibility but is higher than glucose values used to flag possible dysglycemia in clinical care. Thus, routine pre-imaging glucose measurement may serve both procedural and clinical purposes. In the present cohort, FDG PET/CT imaging was performed according to current procedure standards and only after pre-injection glucose values were within accepted limits. Therefore, elevated cFBG was unlikely to have compromised routine image acquisition or diagnostic interpretation.

Several limitations should be acknowledged. First, this was a retrospective single-center study conducted at a tertiary care hospital, which limits generalizability and precludes causal inference. Second, while useful for screening, the analysis relied solely on capillary point-of-care glucose measurements rather than venous fasting plasma glucose or HbA1c. Although all measurements were performed by trained staff using a standardized device, capillary values may differ from venous plasma glucose and are subject to measurement variability. Therefore, cFBG values should be interpreted as screening values rather than diagnostic measurements. Third, the study reflects real-world fasting conditions in the FDG PET/CT setting, and not all patients necessarily fulfilled the 8 h fasting requirement used for formal diabetes testing. To address this, we performed a sensitivity analysis in patients examined before 11:00 AM, representing those most likely to have fasted overnight. Fourth, the cohort included patients with different lymphoma entities, disease phases, and treatment histories. Detailed information on recent corticosteroid exposure, chemotherapy timing, immunotherapy, acute illness, nutritional status, and longitudinal metabolic follow-up was not available and may have influenced cFBG values. Fifth, visceral and subcutaneous fat distribution was estimated using standardized linear CT measurements at the level of the aortic bifurcation. Although practical, area- or volume-based segmentation would provide a more precise assessment of body fat distribution.

5. Conclusions

Elevated fasting glucose values are common in patients with lymphoma undergoing clinically indicated FDG PET/CT, including in patients without previously known diabetes mellitus. Although capillary fasting glucose cannot replace formal diagnostic testing, rou-

tine pre-imaging glucose assessment may help identify patients who warrant confirmatory metabolic evaluation. Therefore, elevated pre-imaging glucose values should be considered not only in relation to imaging feasibility but should also be communicated to the treating oncologist and incorporated into standardized follow-up pathways where appropriate. These findings support increased awareness of dysglycemia in lymphoma care and the integration of glucose follow-up into oncologic workflows.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The raw data supporting the conclusions of this article may be made available by the authors on request.

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