Effect of Initial Body Mass Index on Survival Outcome of Patients With Acute Leukemia: A Single-Center Retrospective Study

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Abstract

Obesity is associated with an increased occurrence of malignancies. However, the effect of body mass index (BMI) on survival outcome remains controversial in acute leukemia (AL) patients. In this single-institution study, we retrospectively analyzed 531 consecutive AL patients. Preliminary results indicated that an increased BMI (> 25) was associated with a better outcome, which we did not confirm in the validation cohort.

Background: Obesity is associated with an increased risk of mortality from cardiovascular causes and occurrence of malignancies. However, the effect of body mass index (BMI) on survival outcome remains controversial in acute leukemia (AL) patients. **Patients and Methods:** A total of 531 adults with AL who entered clinical trials in our institution between 1994 and 2012 were analyzed retrospectively for the effect of BMI at diagnosis on outcome. The median follow-up was 4.7 years (95% confidence interval [CI], 4.0-5.1). **Results:** BMI had no significant effect on complete response rate, disease-free survival (DFS), or overall survival (OS) in patients from the whole cohort when considering a cutoff value for BMI of 25, and when analyzed according to age, or initial cytogenetics. In T-acute lymphoblastic leukemia (T-ALL) patients with BMI $>$ 25, median DFS was not reached with a 3-year DFS at 76%, and median DFS was 16.1 months with 3-year DFS at 13% for those with BMI $\leq$ 25 ($P = .005$). Median OS was not reached in T-ALL patients with BMI $>$ 25 versus 28.3 months in those with BMI $\leq$ 25 (3-year OS: 78% vs. 41%; $P = .04$). Multivariate analyses confirmed the prognostic value of BMI ($>$ 25 vs. $<$ 25) in T-ALL, but only in terms of DFS (hazard ratio, 0.25; 95% CI, 0.05-0.87; $P = .037$). However, in a validation cohort of 211 T-ALL patients, these results were not confirmed. **Conclusion:** Results from the literature are very heterogeneous and contradictory regarding the effect of BMI on leukemia outcome. Even if nutritional status during chemotherapy courses is critical, these findings provide further evidence that initial body size does not have a major prognostic effect on survival in AL patients.

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Introduction

In developed countries, the advent of our consumer society has been associated with a growing incidence of overweight and obesity worldwide, which became a major health concern. According to the National Center for Health Statistics surveys, the prevalence of a body mass index (BMI) $>$ 30 concerns more than a third of the US population, affecting more specifically people from Hispanic/black communities or with low income, with a trend to progressive increase over time.[1,2] This issue is not limited to the United States of America. In a recent study conducted in 53 countries, members of the Organization for Economic Co-operation and Development (EOCD), highlighted that at 11 years old, 33% of children are at least overweight and 18% of the EOCD global population is considered obese (BMI $\geq$ 30). This represents a major concern because obesity is thought to be responsible for 1% to 10% of actual health expenditures.[3] In fact, obesity is associated with an increased risk of mortality from diabetes mellitus, cardiovascular disease, hypertension, and certain cancers.[4]

Obesity also modifies the pharmacokinetics of numerous drugs and obese patients might be overtreated because of dosage capping based on ideal body weight. However, obesity and risk of cancer is

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associated with a substantial heterogeneity in population-level effects suggesting that different mechanisms are involved in carcinogenesis and likely driven by a specific genetic background. Recent meta-analyses have evidenced a significant association between an increased BMI and the risk to develop certain hematological malignancies including acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL).[5,6] The relationship between obesity and carcinogenesis is not fully established, but seems to provide somehow the inflammatory environment and metabolic disruption for clonal selection.[7] In the context of acute leukemia (AL), adipocytes are present in the bone marrow where they promote leukemia cell survival and resistance to treatment through the production of amino acids, free fatty acids, proinflammatory adipokines, and cytokines.[8]

Despite conflicting results in the literature regarding the effect of BMI on malignancy outcome, obesity seems to increase the risk of treatment-related complications and to adversely affect outcome in pediatric AL.[9,10] In this single-center retrospective study, we aimed to investigate whether BMI, determined at the time of diagnosis, could affect disease outcome in adult patients treated for AL.

Patients and Methods

Data Sources and Patients

A total of 531 consecutive AL patients who entered into clinical trials in our institution (Lyon-Sud University Hospital, France) between 1994 and 2012 were retrospectively analyzed. Our analyses included 343 cases of AML, 146 of ALL (99 B-lineage ALL and 47 T-lineage ALL), and 52 of acute promyelocytic leukemia (APL) (Table 1). Based on data collected at the time of diagnosis, BMI was calculated as weight (kg) divided by the square of height (m). Patients were stratified according to the World Health Organization (WHO) international BMI classification: underweight (BMI $<$ 18.5), normal weight (BMI 18.5 to $<$ 25), overweight (BMI 25 to $<$ 30), and obese (BMI $\geq$ 30). For analyses, patients were also stratified according to a 2-sided (BMI $<$ or $\geq$ 25) classification. Clinical and biological features at baseline and clinical outcome were compared according to both stratifications. Patients for whom weight or height at diagnosis were missing were excluded from analyses.

Treatment Trials

Patients were initially treated according to different clinical trials depending on the leukemia subtype, the period of study, and the patient's age. All protocols were reviewed and approved by the institutional review board of the relevant institution and were conducted in accordance with the Declaration of Helsinki. All participants gave their written informed consent. All patients were given induction chemotherapy. All AML patients were treated with an anthracycline and cytarabine-based induction chemotherapy regimen. All-*trans* retinoic acid was added for patients with APL. All ALL patients received a 4-week 4-drug induction chemotherapy. Imatinib mesylate was added for patients with Philadelphia

Table 1 Demographic and Disease Characteristics of Patients in the 4 BMI Groups

Characteristic	BMI				All Patients (n = 531)
	Underweight (n = 19)	Normal Weight (n = 273)	Overweight (n = 168)	Obese (n = 71)	
Median Age, Years	49.1 (16-78.5)				
Sex					
Male	4 (11)	52 (155)	33 (100)	11 (34)	300
Female	4 (8)	51 (118)	29 (68)	16 (37)	231
AL Subtypes					
AML	3 (12)	48 (164)	34 (115)	15 (52)	343
B-ALL	5 (5)	60 (59)	27 (27)	8 (8)	99
T-ALL	2 (1)	70 (33)	21 (10)	6 (3)	47
APL	2 (1)	33 (17)	40 (21)	25 (13)	52
PS					
0	3 (5)	52 (93)	32 (56)	13 (23)	177
1	4 (9)	53 (121)	29 (67)	14 (33)	230
2	4 (3)	37 (26)	36 (32)	13 (9)	70
3	8 (1)	54 (7)	30 (4)	8 (1)	13
4	0 (0)	67 (6)	22 (2)	11 (1)	9
Karyotype					
Favorable	5 (3)	43 (28)	40 (24)	15 (10)	65
Intermediate	2 (5)	50 (96)	33 (64)	15 (29)	194
Unfavorable	3 (3)	47 (47)	34 (34)	15 (15)	99
MDS/Cancer	3 (2)	67 (31)	33 (22)	17 (12)	67

Data are presented as n (%) except where otherwise stated.
Abbreviations: AL = acute leukemia; AML = acute myeloid leukemia; APL = acute promyelocytic leukemia; B-ALL = B-cell lineage acute lymphoblastic leukemia; BMI = body mass index; MDS = myelodysplastic syndrome; PS = World Health Organization performance status classification; T-ALL = T-cell lineage lymphoblastic leukemia.