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Body surface area-based chemotherapy dosing in lymphoma: Variation across clinician-reported practice, real-world data, and randomized trial reporting

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Short Report

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Abstract

Body surface area (BSA)-based chemotherapy dosing requires decisions regarding calculation formula, weight reassessment, dose rounding, and BSA capping. We hypothesized that these practices vary in routine lymphoma care, that such variation may affect a substantial proportion of patients, and that clinician-reported practice differs from dosing information reported in randomized controlled trials (RCTs). We conducted a multicomponent descriptive study comprising a nationwide survey of Danish hematologists, an anthropometric analysis of 152 consecutive patients with large B-cell lymphoma, and a targeted review of 26 phase II-III lymphoma RCTs published during 2020–2025. Among 53 eligible physicians, 57% reported using a general BSA cap, with additional variation in BSA formula, weight reassessment, dose rounding, and empirical dose adjustment. In the patient cohort, 36% had baseline BSA > 2.0 m^2 and 13% >2.2 m^2; 17% experienced a weight change > 10%, while only 2% had a BSA change > 10%. Overall, 41% of patients had a dose modification, but none were attributed to BSA capping. All RCTs contained a BSA-based treatment component, and no general BSA cap was identified, although BSA formula, weight basis, and reassessment were rarely reported. These findings demonstrate substantial variation in clinician-reported BSA dosing practice, incomplete reporting in contemporary trials, and a notable contrast between frequent self-reported capping and its absence in the separate real-world cohort. The clinical consequences require evaluation using cycle-level dosing and outcome data.

Introduction

Body surface area (BSA) remains the standard basis for dosing cytotoxic agents used in lymphoma, although it is a pragmatic but biologically imprecise proxy for pharmacokinetics and body composition [1–4]. Its application requires several operational decisions, including the choice of BSA formula, frequency of weight reassessment, dose rounding, and whether to apply a BSA cap. These considerations may be particularly relevant in patients with obesity, low body weight, frailty, or fluid retention. Current guidelines recommend full actual-body-weight-based dosing in patients with obesity, especially when treatment is given with curative intent, while allowing dose modification for toxicity or other defined clinical circumstances [5, 6]. Reduced relative dose intensity (RDI) has repeatedly been associated with inferior progression-free survival (PFS) and overall survival (OS) in aggressive lymphoma, particularly large B-cell lymphoma (LBCL) [7–12].

RCTs establish efficacy and safety using predefined dosing schedules and modification rules. The evidence therefore applies most directly to treatment delivered within those frameworks, whereas routine care may apply different approaches to capping, reassessment, rounding, or empirical reduction. Individual deviations may be clinically justified, but their frequency and potential relevance are poorly characterized. Before the consequences of such variation can be studied, its extent and the proportion of patients potentially affected must be defined.

We therefore examined (1) clinician-reported BSA dosing practices, (2) the frequency of anthropometric characteristics that could make these practices relevant in a real-world LBCL cohort, and (3) BSA dosing procedures identifiable in contemporary lymphoma RCTs. The study was designed to characterize a potential trial-to-practice implementation gap rather than to judge individual modifications or test associations with clinical outcomes.

Methods

Study design and clinician survey

This multicomponent descriptive study comprised a nationwide cross-sectional survey, a retrospective anthropometric cohort, and a targeted review of recent RCTs. The three components addressed complementary questions: how clinicians implement BSA-based dosing, how frequently patients have anthropometric characteristics that make variation relevant, and how dosing is specified in influential trials. Danish hematologists, including specialists and residents independently prescribing lymphoma chemotherapy, were invited through the Danish Society of Hematology; one reminder was sent after eight weeks. The questionnaire addressed BSA formula, weight reassessment, capping, dose rounding, and empirical adjustment in patients with obesity, low body weight, frailty, or fluid retention. It characterized general practice without regimen-specific vignettes or systematic distinction by lymphoma subtype, regimen, or treatment intent. Responses were collected in March-April 2026. The study was registered with the data protection authority of Region Zealand (P-2025-20421) and evaluated by the regional ethics committee (EMN-2025-09758).

Real-world anthropometric cohort

We analyzed 152 consecutive patients with LBCL diagnosed at Zealand University Hospital between 2017 and 2021. Eligible patients were adults (≥ 18 years) with histopathologically confirmed, newly diagnosed LBCL treated with curative-intent first-line therapy. Body weight and BSA, calculated using the Mosteller formula, were recorded before chemotherapy. All patients had body weight measured both before and after therapy. Changes in body weight and BSA from initiation to completion of R-CHOP-like therapy were assessed. We determined the proportions with baseline BSA > 2.0 or > 2.2 m^2, corresponding to commonly used capping thresholds, and with changes > 10% in body weight or BSA. This quantified how often capping or reassessment practices could potentially affect calculated doses.

We also recorded whether chemotherapy doses were modified at treatment initiation or during subsequent cycles and the documented reason, categorized as BSA capping, frailty including advanced age, toxicity, weight change, or other reasons. The cohort was not designed or powered to evaluate associations with toxicity, response, or survival.

Randomized trial review

A PubMed search, last updated in January 2026, retrieved 123 adult English-language lymphoma RCT publications from 1 January 2020 through 31 December 2025. We included original phase II-III studies comparing arms containing at least one antineoplastic regimen and using response or survival as a primary endpoint. Non-randomized studies, articles without a chemotherapy-containing comparison, and follow-up reports with primary data published before 2020 were excluded. Full-text assessment was restricted a priori to the ten highest-ranked relevant journals in Journal Citation Reports; the review was therefore targeted rather than systematic. Publications, supplementary materials, and accessible ClinicalTrials.gov records were reviewed for eligibility criteria, dosing approach, BSA formula, weight basis, reassessment, and capping. General BSA caps were distinguished from agent-specific maximum doses such as vincristine capping.

Statistics

Data are presented descriptively as counts and percentages. No inferential analyses were performed, and no sample-size calculation was undertaken for clinical outcomes.

Results

Clinician-reported practice

Among 75 respondents, 53 met the eligibility criteria. Twenty-eight percent had < 5 years, 13% had 5–10 years, and 58% had > 10 years of prescribing experience. The Mosteller formula was used by 66%, the DuBois formula by 23%, and 11% were unaware of the formula used. Weight was reassessed at every course by 36%, while 53% reassessed it when a relevant change was suspected; 4% used only baseline weight. A general BSA cap was reported by 57%: 17% capped at 2.0 m^2, 30% at 2.2 m^2, and 10% used another threshold. Dose rounding of 5–10% was accepted by 55%. Empirical adjustment was reported at least occasionally by 76% for obesity, 34% for underweight/cachexia, 94% for elderly or frail patients, and 57% for edema/ascites (Table 1).

Table 1
Clinician-reported chemotherapy dosing practices among 53 physicians treating patients with lymphoma

Domain	Category	n (%)
BSA formula	Mosteller	35 (66)
	DuBois	12 (23)
	Unknown	6 (11)
Weight	Only at treatment initiation	2 (4)
	Weight reassessed at each chemotherapy cycle	19 (36)
	In case of clinical suspicion of significant weight change	28 (53)
	Other	4 (7)
General BSA capping	No	23 (43)
	≥ 2.0 m²	9 (17)
	≥2.2 m²	16 (30)
	Other	5 (10)
Dose rounding accepted	< 5%	12 (22)
	5–10%	29 (55)
	>10%	2 (4)
	Varying	10 (19)
Dose adjustment in patients with obesity (BMI ≥ 30)	No	13 (24)
	Yes, but rarely	25 (47)
	Yes, often	12 (23)
	Yes, always	3 (6)

Domain	Category	n (%)
Dose adjustment in underweight/cachectic patients (BMI < 18.5)	No	35 (66)
	Yes, but rarely	15 (28)
	Yes, often	1 (2)
	Yes, always	2 (4)
Dose adjustment in elderly or frail patients	No	3 (6)
	Yes, but rarely	5 (9)
	Yes, often	35 (66)
	Yes, always	10 (19)
Dose adjustment in patients with fluid retention (e.g., edema/ascites)	No	23 (43)
	Yes, but rarely	18 (34)
	Yes, often	10 (19)
	Yes, always	2 (4)

Real-world anthropometric data

Among 152 patients, 36% had baseline BSA > 2.0 m² and 13% >2.2 m² (Table 2). Thus, thresholds at which 47% of physicians reported capping were reached by a substantial proportion of the cohort. However, BSA capping was not recorded as the primary reason for dose modification in any patient. Survey respondents and cohort patients were not linked and therefore cannot be directly compared. A BSA change > 10% occurred in 2%, whereas a weight change > 10% occurred in 17%. Dose modifications occurred in 41% of patients, including 5% at treatment initiation and 37% during subsequent cycles; 54% of patients with a weight change > 10% had a dose modification. Distributions of pretreatment BSA and weight and their changes are shown in Fig. 1.

Table 2
Body surface area (BSA; calculated using the Mosteller formula), longitudinal changes in body weight and BSA, and chemotherapy dose modifications in a real-world cohort of 152 patients with newly diagnosed large B-cell lymphoma treated with curative intent

Baseline body size and longitudinal changes	**n (%) or median (IQR)**
Baseline body weight, kg	79.0 (68.8–87.4)
Baseline BSA, m^2	1.9 (1.8–2.1)
Baseline BSA > 2.0 m^2	54 (35.5)
Baseline BSA > 2.2 m^2	19 (12.5)
Change in body weight, %	-2.9 (-7.1-0.0)
Weight loss > 10% from treatment initiation to completion	25 (16.4)
Weight gain > 10% from treatment initiation to completion	1 (0.7)
Change in BSA from treatment initiation to completion, %	-1.5 (-3.6-0.0)
BSA decrease > 10% from treatment initiation to completion	3 (2.0)
BSA increase > 10% from treatment initiation to completion	0
Chemotherapy dose modifications	**n (%)**
Any chemotherapy dose modification	63 (41.4)
Dose modification at treatment initiation	7 (4.6)
Dose modification during subsequent cycles	56 (36.8)
Documented primary reason for dose modification among 63 patients with any dose modification	**n (%)**
BSA capping	0
Frailty/advanced age	8 (12.7)
Weight change	35 (55.6)
Toxicity	20 (31.7)

Randomized trial review

Twenty-six RCTs met the inclusion criteria, including six phase II and 20 phase III trials; 19 evaluated curative-intent and seven palliative treatments across major lymphoma subtypes. All contained at least one BSA-based component, and none used body-composition dosing beyond BSA (Table 3). No general protocol-specified BSA cap was identified, although selected drugs had agent-specific maximum doses.

The BSA formula was not reported in any trial, weight basis was explicit in one, and no trial reported systematic BSA recalculation during treatment.

Table 3
Eligibility criteria and chemotherapy dosing information reported in 26 randomized controlled trials

Variable	Categories	n (%) across trials
Eligibility criteria	Hematologic (ANC/platelets)	26 (100)
	Organ dysfunction	25 (96)
	Age limit	19 (73)
	Performance status	23 (88)
	Other frailty criteria	5 (19)
	Body composition*	0
	Other	14 (54)
Dosing feature	At least one BSA-based component	26 (100)
	Fixed-dose component	1 (4)
	Dose-adjusted component (e.g., DA-EPOCH)	1 (4)
	Body-composition dosing other than BSA*	0
BSA formula	Reported	0
	Not reported	26 (100)
General BSA cap	Identified	0
	Not identified in available sources	26 (100)
Weight basis and reassessment	Actual body weight explicitly reported	1 (4)
	Ideal body weight explicitly reported	0
	Systematic BSA recalculation during therapy reported	0
	Weight basis not reported	25 (96)

**Body-composition criteria included underweight, overweight, obesity, muscle mass, fat mass, and lean body mass.*

Discussion

Our study has three principal findings. First, clinicians reported substantial variation in BSA-based chemotherapy dosing, including calculation, weight reassessment, capping, rounding, and empirical modification. Second, although high BSA values were common in the real-world cohort, no dose

modifications attributable to BSA capping were identified despite frequent clinician-reported use of capping. Third, contemporary RCTs did not report general BSA capping and incompletely described other operational aspects of BSA-based dosing. Together, these findings suggest that stated practice may not translate directly into delivered treatment.

Variation extended beyond capping. Clinicians used different BSA formulas, reassessed weight at different intervals, and applied different rounding and empirical dose-modification practices. This may reflect prescribing systems, institutional conventions, toxicity concerns, or deliberate individualization according to treatment intent, frailty, comorbidity, or previous toxicity. Recent registry data in R-CHOP-treated LBCL further illustrate this complexity: underweight BMI was independently associated with inferior survival, whereas exploratory analyses did not suggest that chemotherapy exposure, including upfront dose reduction, explained this association [13]. Thus, anthropometric characteristics may reflect host vulnerability as well as influence dosing decisions. The survey was designed to characterize variation rather than judge individual decisions.

The real-world cohort provided an unexpected contrast to the survey. Thirty-six percent of patients had BSA > 2.0 m^2 and 13% >2.2 m^2, while 57% of clinicians reported using a general cap. Nevertheless, no dose modification was attributed to BSA capping. Because survey respondents and cohort patients were not linked, and clinicians may use different thresholds or apply capping selectively, this cannot be interpreted as a direct discrepancy between reported and actual prescribing. However, the absence of observed capping despite frequent high BSA suggests that self-reported practice may not reflect how often capping is applied at patient level. Weight changed by > 10% in 17% of patients, whereas BSA changed by > 10% in only 2%, suggesting that reassessment frequency could affect calculated doses in a subset of patients, although the cohort cannot establish effects on RDI or outcomes.

The RCT review provided a contrasting framework. No general BSA cap was identified, consistent with ASCO recommendations to use full actual-body-weight-based cytotoxic chemotherapy dosing, particularly when treatment is given with curative intent [5, 6], and with observational evidence associating reduced R-CHOP dose intensity with inferior survival in patients with LBCL [7–12]. However, the BSA formula, weight basis, reassessment procedure, and dose-rounding approach were generally not reported. Thus, even when nominal doses and formal modification criteria are available, individual dose calculation may not be fully reproducible from trial reports. Interpretation requires caution: trial populations are selected and may differ from patients in whom empirical reductions are considered, absence of reported capping does not prove that it never occurred, and survey-reported capping does not establish systematic application. Our findings therefore identify differences between reported frameworks and observed practice but do not establish undertreatment, inappropriate care, or superiority of one dosing strategy.

Because efficacy and safety evidence is generated within predefined treatment schedules and modification frameworks, variation in routine implementation may represent a potential trial-to-practice gap. Future multicenter studies should link cycle-specific weight and BSA with calculated and

administered doses, capping, rounding, treatment delays, reasons for modification, cumulative RDI, toxicity, response, and survival. More explicit documentation of BSA formula, weight basis, reassessment, capping, and rounding in prescribing systems and trial reports would improve reproducibility and comparison between trial-defined and real-world treatment.

Several limitations should be acknowledged. Practice was self-reported and may differ from actual prescribing. The survey did not use regimen-specific scenarios or systematically distinguish treatment intent. The survey was Danish and the anthropometric cohort single-center, limiting generalizability. The cohort lacked detailed cycle-level dosing and outcome data, the RCT review was targeted rather than systematic, and the three study components were independent and unlinked. Comparisons should therefore be interpreted as complementary observations rather than direct patient-level comparisons.

In conclusion, BSA-based lymphoma chemotherapy dosing varies in routine practice and is incompletely described in contemporary RCTs. Notably, no dose modifications attributable to BSA capping were observed in the real-world cohort despite frequent clinician-reported capping and common BSA values above 2.0 m^2. The clinical consequences remain uncertain and require studies incorporating cycle-level anthropometric, dosing, toxicity, and outcome data.

Declarations

Consent to Participate

declaration: Participation in the physician questionnaire survey was voluntary, and completion of the questionnaire was considered consent to participate. For the retrospective patient cohort, individual informed consent was not required, as the study involved retrospective analysis of existing clinical data without collection of human biological material or any study-related intervention as determined by the Regional Committee on Health Research Ethics for Region Zealand.

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Author Contribution

All authors contributed to the study conception and design. C.S.S. and L.M.P. collected and assembled the data. All authors contributed to data interpretation. C.S.S. drafted the manuscript. All authors critically revised the manuscript, approved the final version, and agreed to be accountable for the work.

Data availability:

The data underlying this study are available from the corresponding author upon reasonable request, subject to applicable data protection regulations.

Ethics approval: The study was evaluated by the regional ethics committee (ID: EMN-2025-09758) and registered with the data protection authority of Region Zealand (record no. P-2025-20421)

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Figures

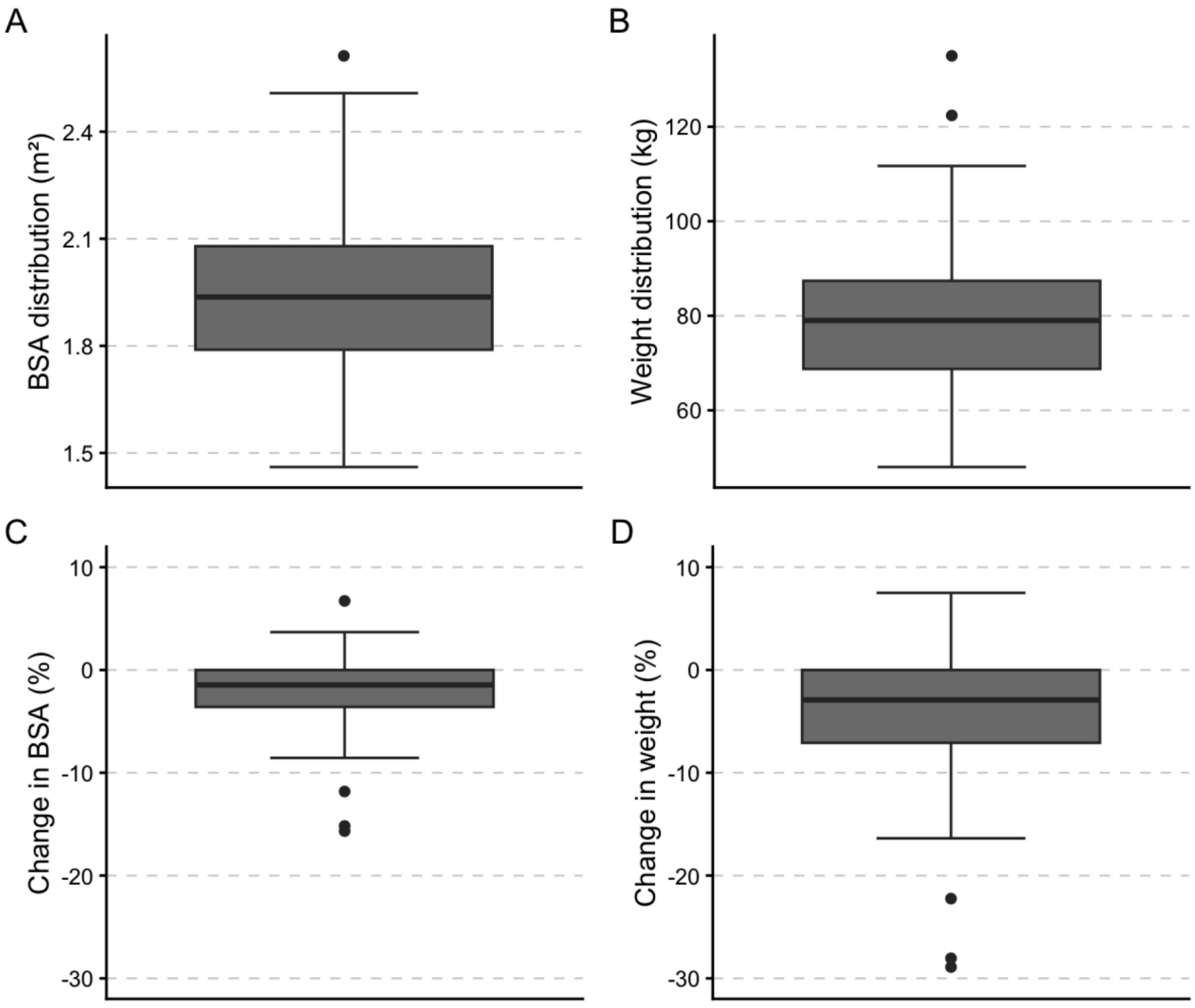


Figure 1

Distribution of pretreatment (A) body surface area (BSA; calculated using the Mosteller formula) and (B) body weight, and changes during treatment in (C) BSA and (D) body weight among 152 consecutive patients with large B-cell lymphoma