Cancer Care Ontario

Action Cancer Ontario

POSITION STATEMENT TO ADDRESS USE OF HEIGHT AND WEIGHT IN THE BEST EQUATION TO CALCULATE BODY SURFACE AREA IN ORDER TO MINIMIZE CALCULATION ERRORS

INTRODUCTION

Systems to facilitate electronic prescribing have been widely implemented to improve patient safety in clinical practice. This also applies to oncology practice, as there are clinical decision making tools embedded in Systemic Treatment Computerized Physician Order Entry (ST-CPOE) systems, such as OPIS, developed and supported by Cancer Care Ontario (CCO)[1]. An example is the calculation of body surface area (BSA) used in the dosing of chemotherapy agents based on mg/m^2. The chosen equation varies amongst institutions with the top three being the Dubois & Dubois[2], Mosteller[3] and Gehan & George [4] equations. Use of BSA equations other than the Mosteller equation has led to errors in calculation of BSA[5], specifically where height and weight are transposed, leading to inaccurate dosing of chemotherapy with serious consequences. The use of height and weight in these BSA equations can pose additional problems where units used in practice are inconsistent (inches and cm; pounds and kg).

Apart from errors with use of height and weight in BSA equations, further debate arises regarding which weight value (actual, adjusted or ideal body weight) should be used to calculate BSA and chemotherapy doses for obese patients. It is believed that as the pharmacokinetics of chemotherapeutic agents are altered in obese patients[6,7], this patient population may become exposed to excessive chemotherapeutic toxicity should full-weight doses be given. As a result of this paradigm, dose reductions (i.e. doses based on adjusted or ideal body weight, as well as arbitrarily capping the BSA) for these patients are often implemented in clinical practice. However, this philosophy in practice may lead to under dosing, which may potentially compromise the effectiveness of chemotherapy for treatment of malignancies in these patients.

The main focus of this document will address how height and weight should be determined and reported using the best equation to determine BSA in order to reduce the likelihood of calculation error. Due to a lack of evidence, patients with edema and anasarca will not be included in these recommendations.

POSITION STATEMENT

- BSA values should be determined using only the **Mosteller equation** to reduce the risk of BSA calculation and dosing errors
  - **Height** should be consistently reported in **centimeters (cm)**
  - **Weight** should be consistently reported in **kilograms (kg)**
    - **When calculating BSA and/or doses in patients who are obese, it is recommended that actual body weight be used, especially where treatment intent is curative**
      - **Exceptions:** treatment of leukemia, drugs with fixed dosing (e.g. vincristine, bleomycin in certain regimens), dosing of carboplatin where the preferred dosing method is by area-under-the-curve (AUC)

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POSITION STATEMENT (continued)

  - Caution should be used in morbidly obese (BMI > 40 kg/m^2) and obese patients with comorbidities (BMI > 35 kg/m^2) as data is limited
- Considerations for changes in ST-CPOE systems related to BSA:
  - The Mosteller BSA formula should be chosen as the system default BSA formula, which should be set at a hospital, not individual user, level
  - ST-CPOE users should work with system vendors to design screen layouts and workflow to reduce the risk of BSA calculation errors

QUESTIONS

Calculation of Body surface Area

1. Which body surface area calculation equation should be used to prevent incidence of incorrect dosing of chemotherapy?

Calculation of Doses in Obese Patients

2. Which body weight (lean, adjusted or actual) should be used to calculate BSA in the obese patient population to ensure efficacy without increasing toxicity?
3. Does full-weight dosing increase the risk for toxicity in obese patients?

RECOMMENDATIONS

Calculation of Body Surface Area: Use of Height and Weight

The ideal equation for calculating BSA should remove the risk or calculation error should the values for height and weight be transposed inadvertently. It can be seen from Table 1 that the Mosteller equation can fulfill this requirement, as compared with the other two equations noted earlier:

Table 1: Mosteller equation to eliminate the risk of calculating an erroneous BSA and either underdosing (Dubois and Dubois) or overdosing (Gehan and George) the patient.

Patient ht/wt	Mosteller	Dubois & Dubois	Gehan & George
Ht=166cm **Wt=74kg** BMI = 26.9	1.847 m^2	1.819 m^2	1.865 m^2
Ht=74cm **Wt=166kg** BMI = 303.1	1.847 m^2	1.428 m^2 (would result in underdosing)	2.009 m^2 (would result in overdosing)

Of the current list of BSA formulae that may be used, the Mosteller equation appears to also be less complex to use. (Please see Appendix for actual equations)

Although the Mosteller formula does not create dosing errors secondary to transposed height and weight values, if a weight-based drug is ordered using these transposed values, a dosing error will result. Examples of these agents include bevacizumab, cetuximab, panitumumab and trastuzumab. Hence other safeguards should be evaluated, such as work flow changes, in order to ensure accurate height and weight entry. Height and weight measurements should be consistently reported and entered in centimeters (cm) and kilograms (kg) respectively to align with the units in the equation for calculation of BSA and subsequently chemotherapeutic doses.

Dosing of chemotherapy in obese patients: Issues of Weight used in Calculation of BSA and Dose

Obesity is becoming an epidemic in North America. As such, we may expect to see a higher prevalence of obese patients in oncology practice. Many institutions fear that using actual body weight may expose this patient population to greater chemotherapy toxicity. Therefore, ideal or adjusted body weight may be substituted for the actual body weight in the equations to calculate BSA, or a BSA cap may be arbitrarily chosen such that patients with BSAs exceeding this threshold would only receive the maximum established dose[8]. These are examples of measures to help reduce toxicity, however, there is little evidence supporting this philosophy in practice. Although there are concerns with respect to safety, another important factor to consider is whether or not obese patients would be treated effectively. Notably, obesity may be considered a factor for a poorer prognosis in cancer[9], a factor that strengthens the argument that the effectiveness of chemotherapy needs to be maintained. Because of the potential to compromise the effectiveness of chemotherapy with dose reductions, there is support to use full weight-based dosing (using actual weight) in practice for this patient population to achieve optimal outcomes, especially if the intent is curative[10,11,13].

Opportunities in ST-CPOE Systems: Modifications of Workflow

Current CPOE systems incorporate alerts, which provide a second pause for the prescriber to recheck the height and weight values before submitting the order. However, prescribers may suffer “alert fatigue” due to the high frequency and apparent redundancy of these alerts. As a result, errors may be more easily overlooked over time as many of these alerts become automatically overridden. There are a number of opportunities to re-evaluate the ST-CPOE systems and to improve its function. This can include assessment of the tolerance levels established in the CPOE system for heights and weights that are recognized as “out of range” by the system and of how accurate data may be transferred electronically within the patient profile. Audits may be conducted to evaluate degree of alert fatigue and vulnerabilities of the system itself. Other non-prescribing members can also play a role in confirming and verifying that the data entered into the ST-CPOE system is correct.

Additional Considerations

1. Since electronic systems are not readily available to accurately determine the height and weight of a patient, only trained staff with a routine role in performing this work (such as nurses) should perform this task. Errors may arise when other individuals (such as volunteers) who do not perform this task routinely and who may not be knowledgeable about the rationale and meaning of the results are asked to determine the patient’s height and weight.
2. The person who obtains the height and weight of the patient is different than the person ordering the chemotherapy medications. This allows for a second “check” to be implemented and reduces confirmation bias.

METHODS

A literature search was conducted using the following databases: Embase (1947 to August 2012) and Medline (1946 to August 2012; via PubMed). Search terms included: "body surface area", "body surface area equation", "obesity", "chemotherapy", "dosing" and "dose". The ASCO guideline, *Appropriate chemotherapy dosing for obese adult patients with cancer: American Society of Clinical Oncology Clinical Practice Guideline*, **was** also included in assessment of evidence.

KEY EVIDENCE

Choice of Equation for Calculating BSA to Minimize Adverse Incidents

1. **Vu T. Standardization of Body Surface Area. Journal of Oncology Pharmacy Practice 2002;8(2-3):49-54[12].**
   The author provided a rationale for use of the Mosteller equation as opposed to other equations to calculate body surface area. In comparison with other formulae, it was established that the Mosteller equation was among the top three with respect to accuracy in predicting measured BSA values. This equation is therefore perceived to be more accurate than most equations that were developed. Based on current evidence, it is recommended that the Mosteller equation be incorporated in practice based on its accuracy, ease of use and lower likelihood of yielding under- or overdosing of patients should the values be entered incorrectly on the CPOE system.

Use of Actual Body Weight in Obese Patients for Calculating BSA: Balancing Efficacy and Toxicity

1. **Griggs JJ et al. Appropriate chemotherapy dosing for obese adult patients with cancer: American Society of Clinical Oncology Clinical Practice Guideline. Journal of Clinical Oncology 2012;30(13): 1553-1561[13].**

   This guideline provides recommendations for dosing of cytotoxic agents in obese patients. It is recommended that all obese patients should be given full weight-based doses, *especially* if the intent of treatment is to cure. It should be noted that a majority of the data is derived from patients diagnosed with breast, ovarian, colon and lung cancers – all solid tumors. There is currently less data in obese patients with hematologic malignancies. From the data gathered, there appears to be a trend that obese patients given full weight-based doses were at no greater risk for experiencing toxicity or were associated with experiencing less toxicity compared to non-obese patients; much of the evidence surrounds the risk of myelotoxicity. Limiting the dose of chemotherapy in this patient population may adversely affect their overall survival. There is stronger evidence indicating that patients who are underdosed (ie. less than 85% of the full dose), are subject to worsening of their disease free survival and overall survival.

2. **Chambers P et al. Chemotherapy dose reductions in obese patients with colorectal cancer. Annals of Oncology 2012;23:748-753[14].**

   A total of 4781 patients with colorectal cancer were assessed in a retrospective cohort analysis who were initially enrolled in 3 large Medical Research Council trials known as FOCUS[15], FOCUS 2[16] and COIN[17]. Patients received varying combinations and frequencies of 5-fluorouracil, capecitabine, irinotecan and oxaliplatin. Patients were categorized by their body mass index (BMI) as normal, overweight or obese.

Seventeen percent of all patients included in this analysis received an empiric dose reduction of their chemotherapy. Overall the authors demonstrated a trend that patients who were more overweight experienced less toxicity and that there were no significant differences in risk for toxicity between obese and non-obese patients. Additionally, it was determined that obese patients who received full doses of chemotherapy had a slightly improved overall survival at 2 years and a significantly improved progression free survival at 1 year compared to those who received lower adjusted doses.

SUMMARY

- BSA values should be determined using ONLY the **Mosteller equation** to reduce the risk of BSA calculation and dosing errors
  - **Height** should ONLY be reported in **centimeters (cm)**
  - **Weight** should ONLY be reported in **kilograms (kg)**
    - **When calculating BSA and/or doses in patients who are obese, it is recommended that actual body weight be used, especially where treatment intent is curative**
      - **Exceptions:** treatment of leukemia, drugs with fixed dosing (e.g. vincristine, bleomycin in certain regimens), dosing of carboplatin where the preferred dosing method is by area-under-the-curve (AUC)
      - Caution should be used in morbidly obese (BMI > 40 kg/m^2) and obese patients with comorbidities (BMI > 35 kg/m^2) as data is limited
- Opportunities for changes in CPOE system and current workflow practices
  - Encourage non-prescribing individuals to enter height and weight information to avoid confirmation bias
  - Only trained staff (e.g. nurses) who routinely perform this task should obtain height and weight information
  - Design workflow to facilitate electronic transfer of data from one “source of truth”
  - Evaluate the tolerance levels set in the CPOE system for “out of range” heights and weights to ensure they are relevant to current clinical practice. The above may help to reduce the frequency of alerts from the system and therefore reduction of “alert fatigue”
  - Maintain audit logs to evaluate for alert fatigue and system vulnerabilities

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APPENDIX

Table 1: Comparison of formulae to calculate body surface area.

Equation	Formula
Mosteller[3]	$BSA\ (m^2) = \sqrt{\frac{(Height\ (cm) \times\ Weight\ (kg)}{3600}}$
Dubois and Dubois[2]	$BSA\ (m^2) = 0.007184\ \times Height(cm)^{0.725}\ \times Weight(kg)^{0.425}$
Boyd[16]	$BSA\ (m^2) = 0.0003207\ \times Height(cm)^{0.3} \times Weight(grams)^{(0.7285-(0.0188\times LOG(grams))}$
Gehan and George[4]	$BSA(m^2) = 0.0235\ \times Height\ (cm)^{0.42246} \times Weight(kg)^{0.51456}$
Haycock[17]	$BSA(m^2) = 0.024265\ \times Height\ (cm)^{0.3964} \times Weight(kg)^{0.5378}$