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RESEARCH ARTICLE

Dosing of chemotherapy in obese and cachectic patients: results of a national survey

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Abstract *Background* It is not unusual to find obese and cachectic patients in the hematology oncology setting. However, information on dosage in these groups is scarce. *Objective* The objectives of our study were to explore the dosing strategies applied in the treatment of obese and cachectic cancer patients and to determine whether these strategies are applied in clinical trials. *Setting* Members of the Spanish Group for the Development of Hematology–Oncology Pharmacy (GEDEFO). *Methods* We invited all cancer hospital pharmacists to participate in a survey. *Main outcome measure* Descriptive statistics of the dosing strategies approaches. *Results* We invited 159 eligible hospitals to participate, and 38 responded to the survey. A total of 50 surveys were received: different strategies were applied by different physicians from the same hospital and by hematology and oncology departments. Body mass index was used to define obesity and cachexia in 40 and 30 % of the cases, respectively. Capping the body surface area (BSA) was the approach most commonly followed (64.1 %) in obese patients, whereas no specific approach was adopted in cachectic patients. In hematology patients, the BSA calculation was based on ideal body weight or adjusted body weight in 16.0 % of cases (n = 2) and 50.0 % of cases (n = 6), respectively; in oncology patients, use of adjusted or ideal body weight was negligible. Actual body weight was the main approach in obese patients (35 surveys) and cachectic patients (48 surveys). Creatinine clearance was assessed mainly using the Cockcroft and Gault equation (around 76.0 % of responses). As for clinical trials, 64.1 % of the respondents (n = 25 hospitals) considered the criteria from each clinical trial individually. *Conclusions* Dose adjustments are more frequent in obese patients than in cachectic patients. In cancer oncology patients, dose is adjusted mainly by hematology and hematopoietic cell transplant teams. Capping BSA is the most frequent strategy, followed by calculating actual body weight.

Keywords Cachectic patients · Chemotherapy dosing · Extreme-weight · National survey · Obese patients · Spain

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Impact of findings on practice

- Although body mass index (BMI) is well known to define obesity or cachexia, is not routinely evaluated before chemotherapy dosing.
- Chemotherapy dosing among obese patients is more probably adjusted when compared to cachectic patients. This may lead to overdosing or underdosing patients on chemotherapy and enhancing toxicity or decreasing survival rates.
- It is important to ensure training and consensus among the professionals caring for hematology–oncology

patients in Spain in order to achieve the optimal clinical outcomes in obese and cachectic patients.

Introduction

In recent years, the frequency of obesity has increased globally in developing countries. In 2008, 1 in every three adults in the world was overweight and one in every nine was obese [1]. In the United States, overweight and obesity were reported to affect 65 and 30 % of the population, respectively [2]. In contrast, about 50 % of cancer patients develop cachexia, the prevalence of which is higher in patients with tumors of the gastrointestinal tract and lung [3].

In this setting, standardization of chemotherapy dosing in obese and cachectic patients is becoming increasingly important, as this population is usually excluded from clinical trials. Recently, the most current guidelines of the American Society of Clinical Oncology (ASCO) on appropriate chemotherapy dosing for obese adult patients with cancer recommend chemotherapy dosing based on full weight [4]. However, practice pattern surveys have demonstrated that chemotherapy doses in obese patients are frequently insufficient, even at the start of the treatment [5–7], and that this could lead to a decrease in survival rates [7]. Information on chemotherapy dosing in low-weight patients is scarce.

Aim of the study

The objectives of this study were to explore the prescription patterns and approaches applied in obese and cachectic patients in Spanish cancer hospitals and to determine whether these strategies are also applied in clinical trials.

Ethical approval

According to the Spanish law, no ethical approval was required for this study.

Methods

In May 2012, we invited all cancer hospital pharmacists who were members of the Spanish Group for the Development of Hematology–Oncology Pharmacy (GEDEFO) to participate in our survey. The survey was anonymous, and each completed survey received was assigned an identification number.

Survey design

The survey was an independent, pharmacist-driven project designed by two hospital pharmacists. An evaluation was undertaken by the members of the Steering Committee of GEDEFO to ensure that all relevant aspects of the survey were correctly presented and understood. Modifications were made based on the feedback (Electronic Supplementary Material 1).

The survey was divided into five sections:

- Section 1: demographic data for the hospitals [number of beds, private or public practice, and scope (general, cancer, or regional)] and the daily activity of the oncology department (availability of oncology, hematology, and bone marrow transplantation services, number of intravenous cytostatic drugs prepared per month, and number of ongoing clinical trials in oncology–hematology per year).
- Section 2: general considerations in chemotherapy dosing, namely, method used to calculate renal function, adjusted body weight, and body surface area (BSA) and whether dose adjustments were made in amputees.
- Sections 3 and 4 asked for the following issues in obese and cachectic patients respectively: use of BMI to determine obesity or cachexia, BMI cutoffs, weight used to calculate adjusted body weight, calculation of creatinine clearance (CrCl), specific cutoff for BSA, or limitations of CrCl in the Calvert formula. Furthermore, pharmacists were asked whether the same criteria were used for hydrophilic and lipophilic drugs and for patients receiving curative and palliative treatment.
- Section 5: determination of whether dosing in obese and cachectic patients in clinical trials followed the same criteria as in general practice or whether the different criteria established in each clinical trial were taken into consideration.

Each question had 3–5 options and some questions had an "other" option to enable a free text response to be drafted if none of the answers were applicable for the pharmacist. A hospital could have filled out more than one survey if different strategies were carried out by the oncology, hematology, and bone marrow transplant (BMT) teams or if strategies varied between physicians in the same hospital.

Statistical methods

The results were analyzed using descriptive statistics and expressed as the median and range.

Table 1 Demographic characteristics

Number of beds (*n*)	
≤99	1
100–199	6
200–499	18
≥500	13
Functional dependency (*n*)	
Public health system	30
Other public services (e.g., administration, prison)	4
Private health system	2
Public–private health system	2
Scope of hospitals (*n*)	
General	33
Cancer	1
Regional	3
Others	1
Medical specialties (*n*)	
Oncology	2
Hematology	0
Hematology–oncology	23
Hematology–oncology + bone marrow transplant	13
Number of chemotherapy treatments/year [median (range)]	1,200 (120–6,550)
Number of ongoing clinical trials/year [median (range)]	13 (0–150)
Number of respondents in different groups (n surveys)	
OHT	20
HT	12
O	18

BMT bone marrow transplantation, *OHT* surveys where oncology/hematology/BMT strategies are the same, *HT* surveys where hematology/BMT strategies are the same, *O* survey of oncology strategies

Results

Demographic characteristics

Of the 159 hospitals invited to participate, 38 returned 50 surveys (response rate of 23.8 %). One survey was considered ineligible because it was from a pediatric hospital. Demographic characteristics are summarized in Table 1.

Chemotherapy dosing: general considerations

Creatinine clearance was estimated during each cycle of therapy in 22 hospitals (57.9 %), while in nine hospitals (23.7 %) it was only estimated in the case of a variation in the serum creatinine value. Adjusted body weight was not calculated in 17 hospitals (44.7 %), and, where it was calculated (31.6 %), different methods were used (James, Hume, Bauer and Winter, and Devine methods), while nine hospitals did not respond. The most frequently used method to calculate BSA was the Dubois–Dubois method (71.1 %, $n = 27$), followed by the Mosteller formula in 23.7 % ($n = 9$). In approximately half of the hospitals (44.7 %), amputations were taken into consideration when BSA was calculated.

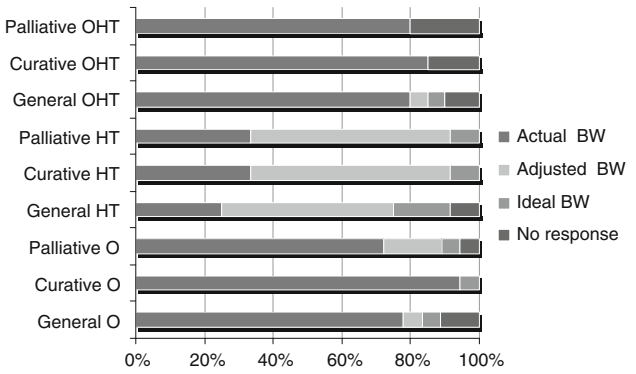

Fig. 1 Body weight used to calculate BSA for general patients and in palliative or curative treatments. *BSA* body surface area; *OHT* surveys where oncology/hematology/BMT strategies are the same; *HT* surveys where hematology/BMT strategies are the same; *O* survey of oncology strategies; *BW* body weight

The results of the survey (50 responses) were analyzed by dividing the responses into three groups: (1) surveys where the oncologic/hematologic/BMT strategies were the same (20 responses from 20 hospitals, OHT group); (2) surveys taking into account only hematologic and BMT strategies (12 surveys from 6 hospitals, HT group); (3) surveys taking into account only oncologic dosing strategies (18 surveys from 18 hospitals, O group). Different strategies were used by different physicians in the OHT group.

Chemotherapy dosing in obese patients

Definition of obese patient

In 40.0 % ($n = 20$) of the surveys, BMI was used to determine whether a patient was obese, the most frequent cutoff being >30–32.9 (15 responses). In 46.0 % of the surveys ($n = 23$), BMI was not taken into consideration for the adjusted body weight calculation. However, the BMI from which the adjusted body weight was calculated differed between the groups: for the OHT and O groups, the cutoff was ≥35 (3 and 2 surveys, respectively), while in the HT group the cutoff was >30 (4 surveys). The nonresponse rate was 28.0 % ($n = 14$).

BSA-based chemotherapy dosing

BSA was capped at 2–2.2 m^2 in 14 responses (70.0 %) in the OHT group, 6 responses (50.0 %) in the HT group, and

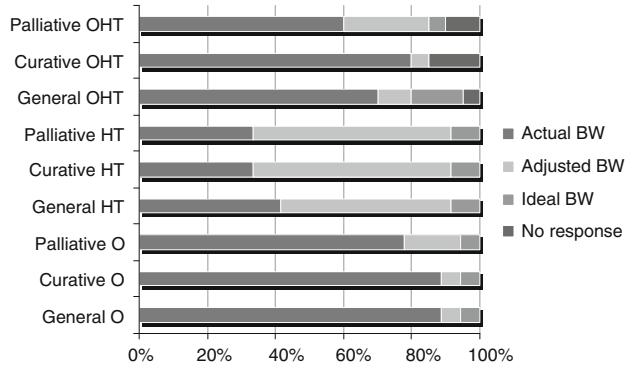

Fig. 2 Body weights used to calculate chemotherapy dosing. *OHT* surveys where oncology/hematology/BMT strategies are the same; *HT* surveys where hematology/BMT strategies are the same; *O* survey of oncology strategies; *BW* body weight

13 responses (72.2 %) in the O group. In Fig. 1 shows the different approaches used to calculate BSA for general patients and in palliative or curative treatments. Pharmacists were asked if they used the same criteria for lipophilic and hydrophilic drugs; 100 % replied that they did.

Body weight-based chemotherapy dosing

Maximum body weight was not taken into consideration in 90.0 % of the responses ($n = 45$). In the four cases (8 %) where it was considered, the cutoff values were 100 kg (one case) and 120 kg (three cases). Overall, use of actual body weight was more frequent (Fig. 2). The same criteria were taken into consideration for lipophilic and hydrophilic drugs in 96.0 % of the respondents ($n = 48$).

Estimation of creatinine clearance in obese patients

The Cockcroft-Gault equation was used by 80.0 % of the OHT group ($n = 16$), 41.7 % of the HT group ($n = 5$), and 88.9 % of the O group ($n = 16$). The modification of diet in renal disease (MDRD) equation was used in 10.0 % of the OHT group ($n = 2$) and 8.3 % of the HT group ($n = 1$), and the 24-h urine collection method was used in only 16.7 % of the HT group ($n = 2$). Actual body weight was used by 84.0 % of the respondents ($n = 42$), followed by adjusted body weight in 12 % ($n = 6$). Overall, only 16.0 % of the respondents capped the CrCl value: 120 mL/min in one case, 125 mL/min in five cases, 150 mL/min in one case, and 200 mL/min in one case.

Chemotherapy dosing in cachectic patients

Definition of cachectic patient

BMI was used to define cachexia by 30.0 % of the respondents ($n = 15$), the most common cutoff being ≤ 16 in 18 responses (36.0 %), followed by 17–18 in 12 % ($n = 6$), and 16–16.99 in 10 % ($n = 5$).

BSA-based chemotherapy dosing

Body surface area was calculated using actual body weight in most cases: 95.0 % of the OHT group ($n = 19$), 100.0 % of the HT group ($n = 12$), and 94.4 % of the O group ($n = 17$). BSA was not limited to a minimum value in 100 % of the respondents ($n = 50$). The same approach was used in palliative and curative treatment, with an overall rate of 98.0 % ($n = 49$) and 96.0 % ($n = 48$) (BSA was calculated using actual body weight). The same criteria were used for hydrophilic and lipophilic drugs.

Body weight-based chemotherapy dosing

Body weight was not capped in 96 % of the respondents ($n = 48$). In the two surveys that stated a minimum body weight, the values were 30 and 40 kg. In all groups, body weight–based chemotherapy dosing involved actual body weight: 95.0 % for the OHT group ($n = 19$), 100 % for the HT group ($n = 12$), and 94.4 % for the O group ($n = 17$). Actual body weight was also used in all groups for curative and palliative care, with an overall rate of 94.0 % ($n = 47$) and 96.0 % ($n = 48$), respectively. The same criteria were taken into consideration for hydrophilic and lipophilic drugs.

Estimation of creatinine clearance in cachectic patients

Creatinine clearance was capped by 20 % of the respondents (n = 10). Cutoff values were 120 mL/min ($n = 2$), 125 mL/min ($n = 2$), and 150 mL/min ($n = 1$). Serum creatinine values were capped at 0.6 mg/dL ($n = 2$). No response was given in three cases. The Calvert formula was not used in three surveys. The method most commonly used to estimate CrCl was the Cockcroft and Gault equation in 80.0 % of the OHT group ($n = 16$), 41.7 % of the HT group ($n = 5$), and 83.3 % ($n = 15$) of the O group. No body weight correction approach was applied at the time of the CrCl calculation in 84.0 % ($n = 42$) of cases.

Clinical trial dosing

Of the 39 hospitals that responded to the survey, 64.1 % considered the criteria from each clinical trial individually ($n = 25$), 15.4 % used clinical practice criteria ($n = 6$), and 5.1 % used a mixed approach (clinical practice and clinical trials) ($n = 2$). Six hospitals did not respond, because they did not perform clinical trials.

Discussion

Our survey, which was performed in several hospitals and in different specialties, showed the wide variety of approaches used to calculate chemotherapy dosing in cachectic and obese patients. We provide the first overview of practical dosing strategies in cachectic patients.

One of our more remarkable findings was the low percentage of respondents who used BMI to class a patient as obese or cachectic (40 and 30 %, respectively). However, most respondents agreed on the BMI cutoff value for obesity (>30–32.9), but not for cachexia (≤16, 36 %; 17–18, 12 %; 16–16.99, 10 %; no response, 42 %). Only half of the hospitals calculated adjusted body weight, and no consensus was observed in the method of calculation, although no single method is considered superior to the others [4]. These results were similar to those of a survey including 52 BMT institutions where no single method was used to calculate chemotherapy dosing in more than 30 % of units [8]. The method most commonly used to calculate BSA among the respondents was the Dubois and Dubois formula (71.1 %).

Our results show that dose adjustments are more frequent in obese patients than in cachectic patients. Routine dose reductions in obese patients are not uncommon, probably because of the fear of overdosing and toxicity in this population. However, the most recent ASCO guidelines on appropriate chemotherapy dosing for obese adult patients with cancer recommend full weight-based chemotherapy doses to be used, particularly when the goal of treatment is cure, although data supporting this strategy in advanced disease remains limited [4]. Up to 40 % of obese patients receive limited chemotherapy doses not based on actual body weight [4]. The approach most frequently used by the respondents to our survey was to cap BSA at 2–2.2 m^2 instead of calculating adjusted body weight. This observation correlates with the findings of an Australian survey of 188 oncologists, where 50.8 % of the respondents capped BSA at 2.0 m^2, 22.1 % used ideal body weight, and 6.1 % routinely used actual body weight [5]. In contrast, the respondents to our survey tended to use adjusted body weight more than ideal body weight. In both cases patients were inappropriately underdosed, but the impact on clinical outcomes would be less if adjusted body weight is used rather than ideal body weight.

We were unable to find firm evidence of the unwillingness to base the dose on full body weight and potential increased toxicity. In a study involving 949 patients with endometrial cancer, of whom 33.2 % were obese and 10.2 % were morbidly obese, those with a higher BMI had less grade 3/4 toxicity than patients whose weight was normal, although this difference disappeared for obese patients receiving ≥95 % of the calculated dose [9]. In a retrospective study of 96,672 women receiving adjuvant chemotherapy for breast cancer, 37 % of the severely obese women had a first-cycle dose reduction of 10 % or more, compared with 20 % of obese women, 11 % of overweight women, and 9 % of women with a healthy weight. Furthermore, the likelihood of being admitted to hospital for febrile neutropenia was lower in obese and severely obese patients than in women with a healthy weight (OR 0.61, 0.83, and 1.0 respectively) [6]. In a retrospective trial conducted in 4,856 patients with colorectal cancer, of whom 45 % had normal weight, 37 % were overweight and 18 % were obese; a significant association was found between increasing weight and the proportion of dose reduction (6 % for normal weight, 17 % for overweight, and 55 % for obesity). No differences were found when toxicity rates were compared between obese patients with reduced doses and those with full doses (16 and 17 %, respectively [10]). In another retrospective study, obese patients receiving full weight-based adjuvant chemotherapy dosing for breast cancer (cyclophosphamide, doxorubicin, and fluorouracil) experienced no increase in grade 3/4 adverse events when compared with non-obese patients [11]. In several studies, obesity was associated with a lower incidence of severe toxicity, which in turn was probably associated with dose capping, thus potentially contributing to poorer survival outcomes [12–16], as also shown in the recent review by Hourdequin et al. [17]. These results indicate that a substantial percentage of patients may be inappropriately underdosed. Our findings demonstrate a greater tendency to use adjusted body weight or ideal body weight in the HT group (50 %) than in the O and OHT groups (30 %); furthermore, adjusted body weight is calculated at lower BMI values in the HT group than in the OHT and O groups (>30 and >35). These findings could be due to the fact that the HT group includes patients undergoing bone marrow transplantation, which requires high doses of chemotherapy. Therefore, a greater fear of overdosing and the pharmacokinetic changes resulting from high-dose chemotherapy could explain the increase in dose adjustments in this group. The pharmacokinetic changes associated with high chemotherapy doses include the following: non-linear elimination kinetics when metabolism is saturated or necessary substrates are depleted; alteration of volume of distribution when protein binding is saturated and drug clearance is modified; and increased volume of distribution with lipophilic agents, as the drug will distribute into the adipose tissue, again leading to altered clearance [18, 19]. However, given that data on the need for dose adjustment and survival rates are inconsistent, no firm conclusions can be drawn [18].

Another area of interest is chemotherapy dosing based on BSA, where no differences were found between palliative and curative care. However, in body weight-based

dosing in palliative care, use of adjusted body weight increased by 20 and 11.2 % in the OHT and O groups, respectively, compared with curative treatment. Different preferences for chemotherapy dosing in specific populations have been shown elsewhere. In the Australian survey [5], clinicians more frequently used actual body weight in adjuvant therapy (84.5 %) than in the treatment of metastatic disease (71 %) [5].

More homogeneous dosing methods were observed with cachectic patients. Almost 100 % of respondents used actual body weight, and no differences where found between dosing for palliative treatment and dosing for curative treatment. In contrast with obese patients, the same approaches were used when chemotherapy dosing is based on BSA or body weight. However, in this group, BSA was not capped, and only two respondents reported having limited body weight (to 30 and 40 kg). The lack of data on chemotherapy dosing in patients with low BMI is disturbing, given that 50 % of patients with cancer have or will develop cachexia [3]. A retrospective study of 4,288 patients with colorectal cancer found that fewer chemotherapy courses were initiated in underweight patients than in normal-weight patients and that underweight patients were more likely than normal-weight patients to receive a lower fluorouracil dose than planned [20]. In contrast, a study including patients with colorectal cancer found that no dose reductions were made in underweight patients, although rates of grade 3–4 diarrhea, leukopenia, and stomatitis were higher in underweight patients than in normal-weight patients [12]. Furthermore, no association was found between BMI and overall survival or progression-free survival in 1,067 patients with ovarian cancer of whom 59 had a BMI < 18. In this group, no differences based on BMI were found in the dose intensity of taxane agents and carboplatin [21]. Even though dosing data in underweight patients are scarce, evidence supports that using actual body weight for chemotherapy dosage is appropriate.

Most of our respondents used the same approach for lipophilic and hydrophilic drugs in both obese and cachectic patients. This result is particularly interesting, given that dosing restrictions are applied for some antimicrobial drugs. However, few data from sufficiently powered trials have been reported on the influence of obesity, morbid obesity, and cachexia on the pharmacokinetics of most anticancer drugs. The pharmacokinetics of the same anticancer drugs may be altered in obese patients, since most cytostatic agents are metabolized by the liver, where accumulation of fat can alter hepatic blood flow and thus affect clearance [18]. In addition, lipophilic drugs can accumulate in the adipose tissue of obese patients, leading to decreased relative hepatic and renal blood flow and increased drug binding to plasma proteins. However, obese and cachectic patients are excluded from pharmacokinetic studies and from most clinical trials. Therefore, in most manufacturer product information dosing guidelines for these groups of patients are not included, only finding in some cases the maximum dose tolerated. The results of retrospective analyses and observational studies suggest that dose restrictions in obese patients may lead to a decrease in disease-free survival and overall survival rates, although data are scarce in cachectic patients [14–16]. Since no validated methods have been developed to correlate drug clearance with the degree of obesity, changes in drug dosing according to pharmacokinetic characteristics are not currently recommended [4].

Only 16.0 and 20.0 % of the respondents capped CrCl in obese and cachectic patients, respectively. Therefore, CrCl was generally not limited in the Calvert formula, an approach that could result in overdosing in obese patients. According to the ASCO guidelines [4], the glomerular filtration rate used in the Calvert formula should not exceed 125 mL/min [4]. However, the study by Eckart et al. concluded that although lean body mass was the best weight descriptor in underweight and normal-weight patients and adjusted-ideal body weight was the best weight descriptor for calculating CrCl in the Cockcroft–Gault formula in overweight and obese patients, the correlation with carboplatin clearance should be called into question. The authors recommend administering a flat dose of carboplatin in all categories in order to reduce this bias [22].

As for chemotherapy dosing in obese and cachectic patients in clinical trials, most respondents take into account the specifications of each trial. Nowadays, electronic prescribing is mainly used to reduce prescription and validation errors. Some electronic prescribing technologies may not meet the specific criteria of each clinical trial, thus accounting for the fact that 21.1 % of the respondents used the same approaches as in general practice or a mixture between clinical trial criteria and general practice.

The low response rate in our study (<25 %) could lead to a potential bias in the results, since maybe only those pharmacists who were more concerned about chemotherapy dosing strategies in specific populations responded to the survey. In addition, the survey did not ask whether chemotherapy was prescribed using electronic prescribing technologies, which usually have standard criteria for capping BSA, or when adjusted body weight was calculated automatically. We surveyed chemotherapy dosing practice, and it is possible that respondents indicated a more conservative approach. Nevertheless, the survey was anonymous to encourage participants to report actual practice.

Conclusion

Our study shows that dose adjustment is more frequent in obese patients than in cachectic patients. Capping BSA is the most common strategy, followed by calculating adjusted body weight. Chemotherapy doses are more frequently adjusted in obese patients by hematology and BMT teams. It is important to ensure training and consensus among the professionals caring for oncology–hematology patients in Spain in order to achieve optimal clinical outcomes in obese and cachectic patients. However, the discrepancies recorded in our results indicate that further studies and guidelines are needed in this setting due to the potential impact on free survival.

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Conflicts of interest Authors have no conflict of interest to declare.

References

1. Stevens GA, Singh GM, Lu Y, Danaei G, Lin JK, Finucane MM, et al. National, regional, and global trends in adult overweight and obesity prevalences. Popul Health Metr. 2012;10(1):22.
2. Modesitt SC, Van Nagell JR Jr. The impact of obesity on the incidence and treatment of gynecologic cancers: a review. Obstet Gynecol Surv. 2005;60(10):683–92.
3. Muscaritoli M, Bossola M, Aversa Z, Bellantone R, Rossi Fanelli F. Prevention and treatment of cancer cachexia: new insights into an old problem. Eur J Cancer. 2006;42(1):31–41.
4. Griggs JJ, Mangu PB, Anderson H, Balaban EP, Dignam JJ, Hryniuk WM, et al. Appropriate chemotherapy dosing for obese adult patients with cancer: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2012;30(13):1553–61.
5. Field KM, Kosmider S, Jefford M, Michael M, Jennens R, Green M, et al. Chemotherapy dosing strategies in the obese, elderly, and thin patient: results of a nationwide survey. J Oncol Pract. 2008;4(3):108–13.
6. Griggs JJ, Sorbero ME, Lyman GH. Undertreatment of obese women receiving breast cancer chemotherapy. Arch Intern Med. 2005;165(11):1267–73.
7. Lyman GH. Weight-based chemotherapy dosing in obese patients with cancer: back to the future. J Oncol Pract. 2012;8(4):e62–4.
8. Grigg A, Harun MH, Szer J. Variability in determination of body weight used for dosing busulphan and cyclophosphamide in adult patients: results of an international survey. Leuk Lymphoma. 1997;25(5–6):487–91.
9. Modesitt SC, Tian C, Kryscio R, Thigpen JT, Randall ME, Gallion HH, et al. Impact of body mass index on treatment outcomes in endometrial cancer patients receiving doxorubicin and cisplatin: a Gynecologic Oncology Group study. Gynecol Oncol. 2007;105(1):59–65.
10. Chambers P, Daniels SH, Thompson LC, Stephens RJ. Chemotherapy dose reductions in obese patients with colorectal cancer. Ann Oncol. 2012;23(3):748–53.
11. Rosner GL, Hargis JB, Hollis DR, Budman DR, Weiss RB, Henderson IC, et al. Relationship between toxicity and obesity in women receiving adjuvant chemotherapy for breast cancer: results from cancer and leukemia group B study 8541. J Clin Oncol. 1996;14(11):3000–8.
12. Meyerhardt JA, Tepper JE, Niedzwiecki D, Hollis DR, McCollum AD, Brady D, et al. Impact of body mass index on outcomes and treatment-related toxicity in patients with stage II and III rectal cancer: findings from Intergroup Trial 0114. J Clin Oncol. 2004;22(4):648–57.
13. Poikonen P, Blomqvist C, Joensuu H. Effect of obesity on the leukocyte nadir in women treated with adjuvant cyclophosphamide, methotrexate, and fluorouracil dosed according to body surface area. Acta Oncol. 2001;40(1):67–71.
14. Wright JD, Tian C, Mutch DG, Herzog TJ, Nagao S, Fujiwara K, et al. Carboplatin dosing in obese women with ovarian cancer: a Gynecologic Oncology Group study. Gynecol Oncol. 2008;109(3):353–8.
15. Lopes-Serrao MD, Ussery SM, Hall RG, Shah SR. Evaluation of chemotherapy-induced severe myelosuppression incidence in obese patients with capped dosing. J Oncol Pract. 2011;7(1):13–7.
16. Abdah-Bortnyak R, Tsalic M, Haim N. Actual body weight for determining doses of chemotherapy in obese cancer patients: evaluation of treatment tolerability. Med Oncol. 2003;20(4):363–8.
17. Hourdequin KC, Schpero WL, McKenna DR, Piazik BL, Larson RJ. Toxic effect of chemotherapy dosing using actual body weight in obese versus normal-weight patients: a systematic review and meta-analysis. Ann Oncol. 2013;24(12):2952–62.
18. Navarro WH. Impact of obesity in the setting of high-dose chemotherapy. Bone Marrow Transplant. 2003;31(11):961–6.
19. Vogl DT, Wang T, Perez WS, Stadtmauer EA, Heitjan DF, Lazarus HM, et al. Effect of obesity on outcomes after autologous hematopoietic stem cell transplantation for multiple myeloma. Biol Blood Marrow Transplant. 2011;17(12):1765–74.
20. Dignam JJ, Polite BN, Yothers G, Raich P, Colangelo L, O'Connell MJ, et al. Body mass index and outcomes in patients who receive adjuvant chemotherapy for colon cancer. J Natl Cancer Inst. 2006;98(22):1647–54.
21. Barrett SV, Paul J, Hay A, Vasey PA, Kaye SB, Glasspool RM, et al. Does body mass index affect progression-free or overall survival in patients with ovarian cancer? Results from SCOTROC I trial. Ann Oncol. 2008;19(5):898–902.
22. Ekhart C, Rodenhuis S, Schellens JH, Beijnen JH, Huitema AD. Carboplatin dosing in overweight and obese patients with normal renal function, does weight matter? Cancer Chemother Pharmacol. 2009;64(1):115–22.