

The assessment of anorexia in patients with cancer: cut-off values for the FAACT–A/CS and the VAS for appetite

S. Blauwhoff-Buskermolen^{1,2} · C. Ruijgrok¹ · R. W. Ostelo^{3,4} · H. C. W. de Vet³ · H. M. W. Verheul² · M. A. E. de van der Schueren^{1,5} · J. A. E. Langius^{1,6}

Received: 23 March 2015 / Accepted: 16 June 2015

© The Author(s) 2015. This article is published with open access at Springerlink.com

Abstract

Purpose Anorexia is a frequently observed symptom in patients with cancer and is associated with limited food intake and decreased quality of life. Diagnostic instruments such as the Anorexia/Cachexia Subscale (A/CS) of the Functional Assessment of Anorexia/Cachexia Therapy (FAACT) questionnaire and the visual analog scale (VAS) for appetite have been recommended in the assessment of anorexia, but validated cut-off values are lacking. This study aimed to obtain cut-off values of these instruments for the assessment of anorexia in patients with cancer.

Methods The FAACT–A/CS and the VAS for appetite were administered to patients with cancer before start of

chemotherapy. As reference standard for anorexia, two external criteria were used: (1) a cut-off value of ≥ 2 on the anorexia symptom scale of the EORTC QLQ C-30 and (2) the question “Do you experience a decreased appetite?” (yes/no). ROC curves were used to examine the optimal cut-off values for the FAACT–A/CS and VAS.

Results A total of 273 patients (58 % male; 64.0 ± 10.6 years) were included. The median score on the FAACT–A/CS was 38 (IQR 32–42) points and 77 (IQR 47–93) points on the VAS. Considering both external criteria, the optimal cut-off value for the FAACT–A/CS was ≤ 37 (sensitivity (se) 80 %, specificity (sp) 81 %, positive predictive value (PV⁺) 79 %, negative predictive value (PV[−]) 82 %) and for the VAS was ≤ 70 (se 76 %, sp 83 %, PV⁺ 80 %, PV[−] 79 %).

Conclusions For the assessment of anorexia in patients with cancer, our study suggests cut-off values of ≤ 37 for the FAACT–A/CS and ≤ 70 for the VAS. Future studies should confirm our findings in other patient samples.

✉ S. Blauwhoff-Buskermolen
s.buskermolen@vumc.nl

¹ Department of Nutrition and Dietetics, Internal Medicine, VU University Medical Center, P.O. Box 7057, 1007 MB Amsterdam, The Netherlands

² Department of Medical Oncology, VU University Medical Center, Amsterdam, The Netherlands

³ Department of Epidemiology and Biostatistics and the EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands

⁴ Department of Health Sciences, VU University, Amsterdam, The Netherlands

⁵ Faculty of Health and Social Studies, Department of Nutrition, Sports and Health, HAN University of Applied Sciences, Nijmegen, The Netherlands

⁶ Faculty of Health, Nutrition and Sport, The Hague University of Applied Sciences, The Hague, The Netherlands

Keywords Anorexia · Cancer · Cut-off values · Questionnaire · Appetite

Abbreviations

EORTC QLQ C-30	European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire
FAACT–A/CS	Functional Assessment of Anorexia/Cachexia Therapy Anorexia/Cachexia Subscale
PV ⁺	Positive predictive value
PV [−]	Negative predictive value
ROC	Receiver operating characteristic
Se	Sensitivity

Sp Specificity
VAS Visual analog scale

Introduction

Anorexia—defined as a loss of appetite—is a symptom with a high prevalence but often neglected in patients with cancer [1]. In advanced cancer, anorexia is the 4th most common symptom after pain, fatigue, and weakness [2].

The prognosis of patients with cancer is adversely affected by the presence of anorexia as it limits food intake and, in combination with cancer cachexia, it induces muscle wasting and weight loss, eventually leading to increased morbidity and mortality [1]. Anorexia is also inversely associated to quality of life, independent of other symptoms [3].

There are several causes for a decreased appetite in patients with cancer. For example, to be diagnosed with cancer may result in distress and reduced desire to eat [4]. Furthermore, an active tumor causes an inflammatory response and changes in hypothalamic function which have impacts on appetite [1, 5]. Moreover, anti-tumor treatments such as chemotherapy or radiotherapy may negatively affect appetite [6].

In order to diagnose anorexia, it is important to have valid and reliable instruments. For clinical practice, a yes/no question (“do you experience a decreased appetite”) or anorexia symptom scale of the quality of life questionnaire of the EORTC [7] can be used. More recently, two instruments have been proposed to diagnose anorexia in the definition of cancer cachexia: the Anorexia/Cachexia Subscale (A/CS) of the Functional Assessment of Anorexia/Cachexia Therapy (FAACT) questionnaire [8] and the visual analog scale (VAS) for appetite but validated cut-off values for these two instruments are lacking [9, 1]. For example, for the FAACT–A/CS, a cut-off value of ≤ 24 has been advised to assess anorexia [9] based on the fact that it is the half of the maximum score than can be obtained. However, as only few patients were diagnosed with anorexia when using this cut-off value [10], the special interest group “Cachexia-Anorexia in Chronic Wasting Diseases” from the European Society for Clinical Nutrition and Metabolism (ESPEN) consented to a higher cut-off value of ≤ 30 during its meeting in 2011. However, both proposed cut-off values have not been validated. For the VAS for appetite, studies have used cut-off values of < 50 [11] and < 70 [12], but objective support is also lacking for these cut-off values.

Therefore, the aim of this study was to provide empirical evidence for cut-off values for the FAACT–A/CS and the VAS to assess anorexia in patients with cancer.

Materials and methods

Participants

This cross-sectional study consisted of patients with advanced cancer scheduled for a new chemotherapy treatment. Adult patients with diagnosis of breast/colorectal/lung/prostate cancer were invited to enter the study before start of treatment with chemotherapy. Patients who had received chemotherapy during the last month and those with insufficient command of the Dutch language were excluded. The patients were recruited from October 2011 to March 2014 from the departments of Medical Oncology and Pulmonology at the VU University Medical Center in Amsterdam, The Netherlands. The research protocol was approved by the Medical Research and Ethics Committee and informed consent was obtained from all participants.

Measures of anorexia

In order to examine anorexia, patients were asked to fill out the FAACT–A/CS (4th version, Dutch) and the VAS for appetite before start of chemotherapy treatment. These instruments were presented to the patients on paper and assistance was offered if required. Both instruments were filled out based on the patients’ experience regarding their appetite during the last 7 days.

The 12 items of the FAACT–A/CS [8] were scored on a five-point Likert scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, and 4 = very much) (Fig. 1). The scores of negatively worded items were reversed. The sum score ranges from 0 to 48, whereby a lower score indicates less appetite. For scoring the FAACT–A/CS, the FACIT manual was applied [13].

The VAS for appetite is a 100-mm line in which the extremities were anchored by “I had no appetite at all” (0 mm) and “My appetite was very good” (100 mm) (Fig. 2). The VAS score for anorexia was obtained by measuring the distance in millimeter from the anchor “I had no appetite at all” to the point drawn by the patient. Again, lower scores point to less appetite.

External criteria for anorexia assessment

At present, no gold standard exists to diagnose anorexia in patients with cancer. Therefore, two external criteria with high face validity were used as reference method in order to determine the optimal cut-off values of the FAACT–A/CS and the VAS. The first external criterion was the anorexia symptom scale of the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ)-C30 (3rd version) [7] which consists of one item that assesses appetite: “Have you lacked appetite?” The responses are scaled on a four-point Likert scale (1 = not at all, 2 = a

Fig. 1 The Anorexia/Cachexia Subscale of the FAACT questionnaire [13]

FAACT (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

<u>ADDITIONAL CONCERNS</u>		Not at all	A little bit	Some-what	Quite a bit	Very much
06	I have a good appetite.....	0	1	2	3	4
ACT1	The amount I eat is sufficient to meet my needs.....	0	1	2	3	4
ACT2	I am worried about my weight.....	0	1	2	3	4
ACT3	Most food tastes unpleasant to me.....	0	1	2	3	4
ACT4	I am concerned about how thin I look.....	0	1	2	3	4
ACT6	My interest in food drops as soon as I try to eat.....	0	1	2	3	4
ACT7	I have difficulty eating rich or "heavy" foods.....	0	1	2	3	4
ACT9	My family or friends are pressuring me to eat.....	0	1	2	3	4
02	I have been vomiting.....	0	1	2	3	4
ACT10	When I eat, I seem to get full quickly.....	0	1	2	3	4
ACT11	I have pain in my stomach area.....	0	1	2	3	4
ACT13	My general health is improving.....	0	1	2	3	4

little, 3 = quite a bit, and 4 = very much). A cut-off value of ≥ 2 on the anorexia symptom scale was used to assess anorexia, because the response option "a little" indicates that patients experience their appetite to be different from normal (in contrast to the response option "not at all"). The second external criterion which was used in order to assess anorexia is a frequently asked question in clinical practice: "Did you have a decreased appetite during the last month?" The response option for this question was dichotomous: yes/no.

Statistical analysis

Descriptive statistics were used to describe the patient population regarding their age, sex, and type of cancer. Means and standard deviations or medians and interquartile range were calculated for quantitative patient characteristics as well as for the scores of the FAACT-A/CS and the VAS for appetite. Absolute numbers and frequencies were presented for nominal data.

In order to examine the optimal cut-off values for the FAACT-A/CS and the VAS for appetite, receiver operating characteristic (ROC) curves were assessed with the two

external criteria as reference standard. In these ROC plots, the true positive rate (sensitivity) was plotted against the false positive rate (1-specificity) over a range of cut-off values. Perfect discrimination of a test is obtained when the ROC curve passes through the upper left corner (100 % sensitivity, 100 % specificity). The optimal cut-off values for the FAACT-A/CS and the VAS for appetite were determined by the overall smallest percentage of false positives and false negatives. The sensitivity and specificity for these cut-off values were obtained by the ROC curves analysis. In addition, the positive and negative predictive values were calculated. Due to the use of two external criteria, two cut-off values were obtained for both instruments. The cut-off value corresponding with the highest predictive value was chosen.

The analyses were carried out using SPSS software, version 20 (2011, IBM Corporation, Armonk, NY, USA).

Results

Three hundred and fourteen patients were invited to participate in this study and 273 patients participated (Fig. 3). The

Fig. 2 The visual analog scale (VAS) for appetite

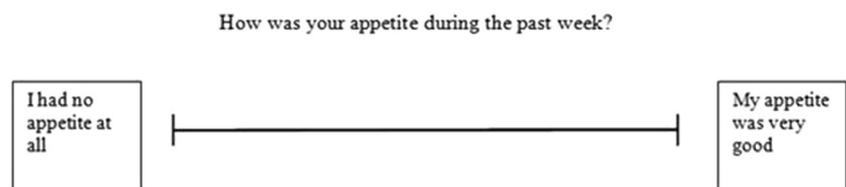
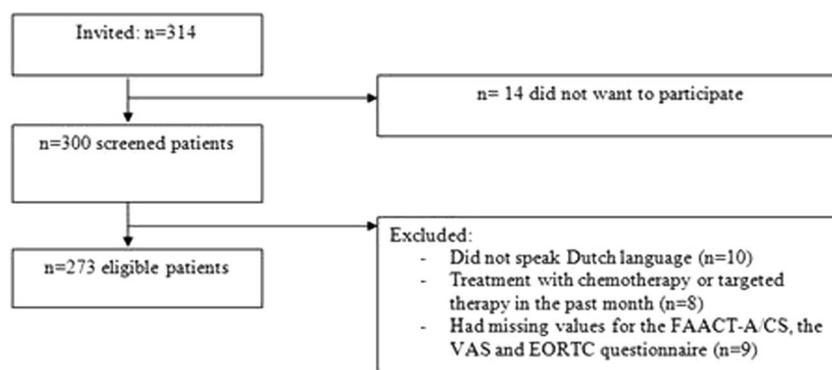


Fig. 3 Flowchart



participants had a mean age of 64.0 ± 10.6 years; 58 % of the patients were male and the most common type of cancer in this study population was lung cancer (Table 1).

The median score on the FAACT–A/CS was 38 (IQR 32–42) points and 77 (IQR 47–93) points on the VAS for appetite. The median scores of the FAACT–A/CS and the VAS for the different response categories of both external criteria are presented in Table 2. A gradual decline in the median scores of the FAACT–A/CS and the VAS was noticeable for the response options “not at all” to “very much” of the anorexia symptom scale of the EORTC QLQ C-30. Comparing the two external criteria shows that the median score was 41 points for the FAACT–A/CS for the option “not at all” of the anorexia symptom scale of the EORTC QLQ C-30 and also for the option “no” of the clinical practice question. For the VAS, the median score was 90 points for “not at all” on the EORTC QLQ C-30 compared to 88 points for “no” of the clinical

practice question (Table 2). Median scores on the FAACT–A/CS were different in patients with breast cancer (lower, 34 points (IQR 30–39)) and colorectal cancer (higher, 40 (IQR 36–43)) compared to patients with prostate and lung cancer (38 (IQR 32–41) and 37 (IQR 30–41) respectively). This was also the case for VAS scores: breast cancer (lower, 51 (IQR 41–78), colorectal cancer (higher, 87 (IQR 64–96) compared to prostate cancer and lung cancer (73 (IQR 48–92 and 72 (IQR 41–91), respectively).

The optimal cut-off values for the FAACT–A/CS were ≤ 37 and ≤ 38 according to the external criteria EORTC QLQ C-30 and the decreased appetite question, respectively. For the VAS for appetite, the optimal cut-off values were ≤ 70 and ≤ 72 according to the external criteria EORTC QLQ C-30 and the decreased appetite question, respectively. The cut-off values of ≤ 37 on the FAACT–A/CS and ≤ 70 on the VAS had the highest predictive values (Table 3); therefore, these cut-off values are suggested for the assessment of anorexia in patients with cancer. The sensitivity, specificity, positive predictive value (PV⁺), and negative predictive value.

(PV[−]) for these cut-off values are presented in Table 3.

Table 1 Patient characteristics ($n = 273$)

Characteristic	Number (%)
Male/female ratio	158/115 (58/42)
Age in years	64.0 ± 10.6^a
Cancer type	
Breast (stage IV)	34 (13)
Prostate (stage IV)	50 (18)
Colon/rectal (stage IV)	78 (29)
Lung (stage II–IV)	111 (41)
Treatment line	
1st line	205 (75)
2nd line	41 (15)
Higher than 2nd line	27 (10)
Treatment in 6 months before inclusion	
Surgery	39 (14)
Chemotherapy	51 (19)
Targeted therapy	22 (8)
Hormonal therapy	58 (21)
Presence of brain metastases	24 (9)

^a Data presented as mean \pm SD

Discussion

The results of this study reveal that using two external criteria, the optimal cut-off value to assess anorexia is ≤ 37 for the FAACT–A/CS and ≤ 70 for the VAS for appetite. This indicates that the currently used cut-off values for the FAACT–A/CS and the VAS for appetite are too low, leaving many persons with a lack of appetite undetected. The obtained cut-off value of ≤ 37 for the FAACT–A/CS is substantially higher than the currently used cut-off value of ≤ 24 [9] and even higher than the more recently proposed cut-off value of ≤ 30 . This suggests that dividing the maximum attainable sum score of 48 points by half is inappropriate to examine anorexia in patients with cancer. In another study in patients with lung cancer, mean scores of the FAACT–A/CS were higher in patients with weight loss (37.2 ± 6.5) compared to patients without weight loss (33.1 ± 7.7 , $p = 0.01$) [14], but in both groups,

Table 2 Median scores of the FAACT–A/CS and the VAS for appetite for the response categories of the external criteria

External criteria	FAACT–A/CS (0–48) median (IQR)	VAS for appetite (0–100) median (IQR)
EORTC QLQ C-30: “Have you lacked appetite?”		
Not at all (<i>n</i> = 141)	41 (38–43)	90 (77–96)
A little (<i>n</i> = 74)	36 (33–38)	62 (42–80)
Quite a bit (<i>n</i> = 33)	29 (25–33)	41 (29–50)
Very much (<i>n</i> = 20)	22 (17–26)	8 (3–23)
“Did you have a decreased appetite during the last month?”		
No (<i>n</i> = 153)	41 (37–43)	88 (73–96)
Yes (<i>n</i> = 115)	33 (27–37)	49 (33–72)

FAACT functional assessment of anorexia/cachexia therapy, A/CS Anorexia/Cachexia Subscale, VAS visual analog scale, EORTC QLQ European Organization for Research and Treatment of Cancer Quality of Life questionnaire

mean scores were >30. For the VAS for appetite, the proposed cut-off value of <70 [12] corresponds with the findings in our study, which implies that the cut-off value of <50 [11] might underestimate the prevalence of anorexia in patients with cancer.

In order to examine the cut-off values for the FAACT–A/CS and the VAS for appetite to assess anorexia in patients with cancer, the optimal cut-off values were calculated using ROC curves and defining the optimal cut-off point as the point with the smallest summed percentages of misclassification. This implies that the false negative classifications (missed patients with loss of appetite) and false positive misclassifications (patients unjustly classified as having loss of appetite) were appreciated equally.

We made use of two external criteria because a gold standard to assess anorexia is lacking. Studies that assessed anorexia instruments have usually looked at correlations with food intake [15, 16], performance status [8], and functional and clinical outcomes [16]; however, there may be a lot of confounding factors using these variables. For example, food intake may not only be hampered due to anorexia but also due to dysphagia or chewing problems. Correlation between food

intake and desire to eat was low according to Parker et al [15]: Pearson’s *r* was 0.38 at the highest. Arezzo di Trifiletti et al. [16] found no significant correlation between VAS appetite and food intake and VAS appetite and body weight and a low correlation between the FAACT and food intake (*r* = 0.46) and FAACT and BMI (*r* = 0.40). We have chosen the EORTC QLQ C-30 as an external criterion for its availability of reference values for the anorexia symptom scale in a general, healthy population from Germany, Norway, Austria, Denmark, and the USA [17]. Of the 7802 healthy subjects, 86 % scored “not at all,” 10 % “a little,” 3 % “quite a bit,” and 1 % “very much.” It is debatable what should be considered a loss of appetite. According to our opinion, patients who indicate that they have lacked their appetite “a little” imply that they have at least some problems with their appetite. This idea was supported by the reference values of the general population because 86 % of healthy subjects indicated no problems with appetite at all. Therefore, a cut-off value of ≥ 2 on the anorexia symptom scale of the EORTC QLQ C-30 was used in this study to assess anorexia. However, when one would consider a cut-off value of ≥ 3 (“quite a bit” and “very much”), the optimal cut-off values would be ≤ 34 for the FAACT–A/CS and ≤ 59 for the VAS for appetite in our study population. These cut-off values are lower than the cut-off values we propose (≤ 37 for the FAACT–A/CS and ≤ 70 for the VAS for appetite), but still higher than those currently used. As second external criteria, we used the question “Did you have a decreased appetite during the last month,” since it is frequently used in clinical practice and easy for patients to answer. Our study showed that the optimal cut-off values for the FAACT–A/CS and the VAS were comparable for the two external criteria we used.

We here present for the first time cut-off values for the FAACT–A/CS and the VAS for appetite, two instruments recommended for the assessment of anorexia in the diagnosis of the cancer anorexia-cachexia syndrome [9]. This study indicates that the optimal cut-off values for assessing anorexia in

Table 3 Cut-off values of the FAACT–A/CS and the VAS for appetite with their corresponding sensitivity, specificity, and predictive values

	Se (%)	Sp (%)	PV ⁺ (%)	PV [–] (%)
FAACT–A/CS $\leq 37^a$	80	81	79	82
FAACT–A/CS $\leq 38^b$	85	69	67	86
VAS $\leq 70^a$	76	83	80	79
VAS $\leq 72^b$	76	76	70	81

FAACT–A/CS Anorexia/Cachexia Subscale (A/CS) of the Functional Assessment of Anorexia/Cachexia Therapy, VAS visual analog scale, Se sensitivity, Sp specificity, PV⁺ positive predictive value, PV[–] negative predictive value

^a Determined by external criterion EORTC QLQ C-30

^b Determined by external criterion decreased appetite question

patients with cancer might be higher (≤ 37 for the FAACT–A/CS and ≤ 70 for the VAS for appetite) than the currently used cut-off values (≤ 24 or ≤ 30 for the FAACT–A/CS and < 50 for the VAS for appetite). Future studies should confirm our findings in other patient samples.

Conflict of interest MS: Member of the Nutricia Advanced Medical Nutrition Oncology Advisory Board. All remaining authors have declared no conflicts of interest.

Funding sources This study did not receive external funding.

Author contributions SB, CR, RO, HCV, and JL designed and conducted the study. SB and CR participated in data collection and analysis. SB, CR, RO, HCV, HMV, MS, and JL participated in data interpretation and manuscript writing. All authors read and approved the final manuscript.

Open Access This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits any noncommercial use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

References

- Laviano A, Meguid MM, Rossi-Fanelli F (2003) Cancer anorexia: clinical implications, pathogenesis, and therapeutic strategies. *Lancet Oncol* 4:686–694
- Walsh D, Donnelly S, Rybicki L (2000) The symptoms of advanced cancer: relationship to age, gender, and performance status in 1000 patients. *Support Care Cancer* 8:175–179
- Lis CG, Gupta D, Grutsch JF (2009) Can anorexia predict patient satisfaction with quality of life in advanced cancer? *Support Care Cancer* 17:129–135
- Holland JC, Rowland J, Plumb M (1977) Psychological aspects of anorexia in cancer patients. *Cancer Res* 37:2425–2428
- Argiles JM, Busquets S, Toledo M, Lopez-Soriano FJ (2009) The role of cytokines in cancer cachexia. *Curr Opin Support Palliat Care* 3:263–268
- von Meyenfeldt M (2005) Cancer-associated malnutrition: an introduction. *Eur J Oncol Nurs* 9(Suppl 2):S35–S38
- Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JC (1993) The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 85:365–376
- Ribaudo JM, Cella D, Hahn EA, Lloyd SR, Tchekmedyian NS, Von Roenn J, Leslie WT (2000) Re-validation and shortening of the Functional Assessment of Anorexia/Cachexia Therapy (FAACT) questionnaire. *Qual Life Res* 9:1137–1146
- Muscaritoli M, Anker SD, Argiles J, Aversa Z, Bauer JM, Biolo G, Boirie Y, Bosaeus I, Cederholm T, Costelli P, Fearon KC, Laviano A, Maggio M, Rossi Fanelli F, Schneider SM, Schols A, Sieber CC (2010) Consensus definition of sarcopenia, cachexia and pre-cachexia: joint document elaborated by special interest groups (SIG) “cachexia-anorexia in chronic wasting diseases” and “nutrition in geriatrics”. *Clin Nutr* 29:154–159
- Laviano A, Sanchez-Lara K, Gioulbasanis I, Ronzani G, Rossi-Fanelli F (2011) The ESPEN anorexia score is a reliable tool to quantitatively and qualitatively assess appetite in unselected cancer patients. *Clin Nutr Suppl* 40
- van der Meij BS, Schoonbeek CP, Smit EF, Muscaritoli M, van Leeuwen PAM, Langius JAE (2013) Pre-cachexia and cachexia at diagnosis of stage III non-small-cell lung carcinoma: an exploratory study comparing two consensus-based frameworks. *Br J Nutr* 109: 2231–2239
- Blum D, Omlin A, Fearon K, Baracos V, Radbruch L, Kaasa S, Strasser F (2010) Evolving classification systems for cancer cachexia: ready for clinical practice? *Support Care Cancer* 18:273–279
- Cella DF (1997) FACIT Manual: Manual of the Functional Assessment of Chronic Illness Therapy (FACIT) scales.
- LeBlanc T, Samsa G, Wolf S, Locke S, Cella D, Abernethy A (2015) Validation and real-world assessment of the Functional Assessment of Anorexia-Cachexia Therapy (FAACT) scale in patients with advanced non-small cell lung cancer and the cancer anorexia-cachexia syndrome (CACS). *Support Care Cancer*:
- Parker BA, Sturm K, MacIntosh CG, Feinle C, Horowitz M, Chapman IM (2004) Relation between food intake and visual analogue scale ratings of appetite and other sensations in healthy older and young subjects. *Eur J Clin Nutr* 58:212–218
- Arezzo di Trifiletti A, Misino P, Giannantoni P, Giannantoni B, Cascino A, Fazi L, Rossi Fanelli F, Laviano A (2013) Comparison of the performance of four different tools in diagnosing disease-associated anorexia and their relationship with nutritional, functional and clinical outcome measures in hospitalized patients. *Clin Nutr* 32:527–532
- Scott NW, Fayers PM, Aaronson NK, Bottomley A, Graeff de A, Groenvold M, et al (2008) EORTC QLQ C-30 reference values.