

ONCONET PROJECT, WP1.1: "The environment of cancer disease"

1ST Workshop on Nutrition, diet, physical activity-Cancer for trainees, dietitians, nutritionists, physical activity specialists, nurses and oncologists.

Towards the implementation of personalized complex care project in obese oncologic patients: managing soft evidence issues

- MINUTES -

[Introduction]

Obesity has been associated with an increased incidence and a worse prognosis for most types of cancers by a considerable body of research (JCO, 34:4197, 2016). This mounting evidence has led most experts, researchers and clinicians to recommend weight control and lifestyle interventions with the aim of reducing the risk of recurrence, especially in obese oncologic patients (JCO, 34:646, 2016). Thus, individuals involved in patient follow-up (oncologists, further health professionals, caregivers, family members...) are confronted with a situation that differs from the single presence of either cancer or obesity.

Obese patients face several specific challenges related to diagnosis and treatment of cancer, ranging from a reduced participation in cancer screening programs, lower tumor-marker expression and issues with medical imaging, altered pharmacokinetics and hormone levels and also a higher risk of minor complications after surgery (J Nat Rev Clin Oncol 10:519, 2013). From a management point of view, the concurrence of obesity and cancer requires the instauration of a personalized project complex care (PPCS), to effectively attend these patients.

However, many questions remain about how to perform this follow-up, such as the adequacy of current screening procedures, the actual effect of weight loss and lifestyle interventions on cancer recurrence or death, or how to deal with both health-care professionals and patients preconceptions surrounding cancer and obesity.

[Objectives]

The main objective of this workshop was to foster discussion on existing controversies in the field of nutritional and physical activity interventions in obese oncologic patients that arise either from a weak level of available evidence, which does not allow to develop strong recommendations, or from the implicit conceptions of the patients, care-givers, doctors and other health-care providers involved in the process.

By confronting different points of view on such existing controversies, it is expected to clarify how deal with areas of unclear evidence in practice.

[Methodology]

This event follows an exploratory sequential mixed methods design conducted through group discussion, as described by Creswell (2014). The workshop is organized in four tracks that gather controversial themes about the oncologic patient with obesity.

- Track 1. Nutritional screening of oncologic patients, from theory to practice.
- Track 2. Recommendations on weight loss, physical activity and nutritional changes in obese oncologic patients.
- Track 3. Cancer treatment, obesity and weight loss.
- Track 4. Implicit preconceptions in the care of the oncologic patient with obesity.

Each track is introduced in plenary session by several short presentations offered by professionals from different fields that highlight some existing controversies on the topic. Discussion on the proposed controversies is carried out in four small groups (see group list at the end of this document), with the help of a group facilitator. Each track ends in plenary discussion.

Recommended readings that sustain presentations have been provided by every speaker and are listed in each track's section. An electronic copy of the different documents is available at: <https://www.dropbox.com/sh/07ozwerfbu81g2b/AADSY6kg4vJCRIg0P0GdHyc7a?dl=0>

For a general understanding on the topic, attendants are suggested the following papers:

- American Society of Clinical Oncology position statement on obesity and cancer. Clin Oncol 32:3568-74. 2016.
- Goodwin P & Chlebowski R. Obesity and Cancer: Insights for Clinicians. JCO 34:4197-4202. 2016.

[Topic list]

TRACK 1. NUTRITIONAL SCREENING OF ONCOLOGIC PATIENTS: FROM THEORY TO PRACTICE.

- Inclusive nutritional screening - needed now more than ever. Dr. Carolina Bento, IPOFG, Coimbra, Portugal.
- The role of the nursing service in the nutritional screening of oncologic patients. María Jarana Díaz, OncoHealth Institute, Madrid, Spain.
- Why is it important to perform a nutritional screening in women with endometrial cancer? Dr. Vera Ramos, Centro Hospitalar e Universitário de Coimbra; FMUC, Coimbra, Portugal.

- How is the **nutritional screening** of obese oncologic patients currently performed? What is the level of **awareness of malnutrition risk of obese oncologic patients**? Who is responsible for performing nutritional screenings? Who should be?
- Which level/kind of information is *really* necessary? Are we taking measures that are not giving relevant information? Are there any specific indicators of nutritional status that are not taken into account and should be included? Is **body composition** relevant?
- Are we performing a nutritional screening... at all?
- Will we be capable of an **individualized intervention**, with positive and meaningful influences on outcome? Do we have guidelines on nutrition and physical activity to guide us?
- **Are women aware** of the association between **endometrial cancer and obesity**? **What about Gynecologic Oncologists**, are they trained to discuss and evaluate obese patients?
- **When and what kind of lifestyle interventions** should be discussed with women with endometrial cancer?

Arends et al. Diagnostic Criteria for the Classification of Cancer-Associated Weight Loss. JCO 33:1-38, 2015.

Arends, J. et al. ESPEN expert group recommendations for action against cancer-related malnutrition. Clin. Nutr. 2017. doi:10.1016/j.clnu.2017.06.017

Gioulbasanis, I. et al. Nutritional assessment in overweight and obese patients with metastatic cancer: does it make sense? Ann. Oncol. 26, 217–221, 2015.

Prado, C. M., Cushen, S. J., Orsso, C. E. & Ryan, A. M. Sarcopenia and cachexia in the era of obesity: clinical and nutritional impact. 2015. doi:10.1017/S0029665115004279

Rehnan, Andrew G., et al. "Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies." The Lancet 371:569-57.2017.

Secord, Angeles Alvarez, et al. "Body mass index and mortality in endometrial cancer: A systematic review and meta-analysis." Gynecologic oncology 140: 184-190. 2016

Smits, Anke, et al. Body mass index and the quality of life of endometrial cancer survivors—a systematic review and meta-analysis. Gynecologic oncology 137:180-187.2015

Beavis, Anna L., et al. Almost half of women with endometrial cancer or hyperplasia do not know that obesity affects their cancer risk." Gynecologic oncology reports 13:71. 2015

Beavis, Anna L., Anna Jo Bodurtha Smith, and Amanda Nickles Fader. Lifestyle changes and the risk of developing endometrial and ovarian cancers: opportunities for prevention and management." International journal of women's health 8:151. 2016.

TRACK 2. RECOMMENDATIONS ON WEIGHT LOSS, PHYSICAL ACTIVITY AND NUTRITIONAL CHANGES IN OBESE ONCOLOGIC PATIENTS.

- Precision nutrition for cancer patients. The role of alterations in lipid metabolism. Prof. Dr. Ana Ramirez de Molina, IMDEA, Madrid, Spain.
- Herb-drug Interactions caused by “Weight loss Products” in Oncologic Patients. Prof. Maria Graça Campos, OIPM-FFUC, Coimbra, Portugal.
- The PREDICOP intervention study: the effect of a diet and physical activity intervention in breast cancer survivors. Carlota Castro, ICO Barcelona, Spain.

- Which **molecular alterations** define the differences between **obese and non-obese** cancer patients?
- Does lipid metabolism constitute a target for personalized treatments including targeted nutritional interventions?
- Might nutritional changes include **specific bioactive compounds** (i.e. nutraceuticals) targeting molecular alterations? Is the time for targeted supplements with therapeutic activity as part of an integrative therapeutic approach?
- Obese patients face several challenges related to the solicitations to consume “**Weight loss Products**” and the majority of those can interact with treatment of cancer. Can we prevent these events?
- Chemotherapy and hormonal therapy in obese patients with cancer is affected by some “Natural Products” that can **change pharmacokinetics and hormone levels**. Should we set-up a method to follow up the patient in order to prevent these changes?
- The precision of therapy is crucial for the success of the treatment. Should we be pro-active and give information to patients, specific for each treatment protocol, involving the patient in the solution to prevent the fall of treatment correlated to herb-drug interaction (medicinal plants and food)?
- Are **weight loss recommendations** to obese woman with cancer taking into account the **evidence-based cancer guidelines**? Is it enough to prescribe a low-calorie diet?
- What kind of nutritional advice do we propose? Can be **fasting an option**? What **sort of lifestyle interventions** are more appropriate?
- In the absence of convincing evidence, should care be taken to avoid communicating a belief that weight loss can lower risk of recurrence and death?

References:

Li Z, Kang Y. Lipid Metabolism Fuels Cancer's Spread. *Cell Metab* 25:228-230. 2017.

Sánchez-Martínez R et al. A link between lipid metabolism and epithelial-mesenchymal transition provides a target for colon cancer therapy. *Oncotarget* 6:38719-36. 2016

Mouhid L et al. Improving In Vivo Efficacy of Bioactive Molecules: An Overview of Potentially Antitumor Phytochemicals and Currently Available Lipid-Based Delivery Systems. *J Oncol*. 2017:7351976.

González-Vallinas M et al. Dietary phytochemicals in cancer prevention and therapy: a complementary approach with promising perspectives. *Nutr Rev*. 71:585-99. 2013.

Hager K. K. Healthy Weight Loss for the Cancer Survivor. *J Adv Pract Oncol*. 2014 Jul-Aug; 5(4): 297–300.

Ilana Levy, Samuel Attias, Eran Ben-Arye, Lee Goldstein, Elad Schiff, Adverse events associated with interactions with dietary and herbal supplements among inpatients, *British Journal of Clinical Pharmacology*, 2017, 83, 4, 836

World Cancer Research Fund International/American Institute for Cancer Research. Continuous Update Project Report: Diet, Nutrition, Physical Activity and Breast Cancer. 2017. Available at: wcrf.org/breast-cancer-2017.

Continuous Update Project. Diet, nutrition, physical activity and breast cancer survivors. WCRF 2014.

Buckland G, Travier N, Agudo A. The role of diet, weight control and physical activity in breast cancer survivors. *Breast Cancer Manag*. 3:497-505. 2014.

TRACK 3. TREATMENT ADJUSTMENT, OBESITY AND WEIGHT LOSS.

- Obesity and Cancer treatment effectiveness. Idoia Morilla, ICO Barcelona, Spain
- Adipose tissue, obesity and cancer: a high-risk combination. Dr. Charlotte Vaysse, IPBS, Oncopole, Toulouse, France.
- Chemoresistance in breast cancer. Prof. Catherine Muller, IPBS, Oncopole, Toulouse, France.
- The risky crosstalk of metabolic dysregulation and breast cancer in obesity. Prof. Paulo Matafome, ESTeSC, IBILI, Coimbra, Portugal.
- What about children? Differences between obese and non-obese pediatric oncologic patients. Dr. Nanci Baptista and Dr. Ana Faria, Hospital Pediatrico, Coimbra, Portugal.

- Does obesity influences treatment effectiveness? Do dosages need to be calculated differently? Should current or adjusted weight in order to prevent toxicity while maintaining the maximum effectiveness?
- Does **surrounding adipose tissue** promotes **cancer aggressiveness** in obesity? What are the signals involved?
- Identification of **new pharmacological targets** to treat cancer in obese patients?
- Is **BMI correlated** with **cancer development** in obesity? What are the main triggers for cancer development in obesity?
- Can we identify new markers of diagnosis for cancer development in obesity?
- Is there evidence that **less than full weight-based dosing** compromises **efficacy** in obese patients with cancer?
- If an obese patient experiences **high-grade toxicity**, should chemotherapy doses or schedule be modified differently from modifications used for non-obese patients with cancer?
- Can **weight loss have a negative impact** on treatment?

Rehnan et al. How to Manage the Obese Patient with Cancer. JCO 34:4284, 2016.

Yavas et al. The impact of Body Mass Index on Radiotherapy Technique in patients with early-stage endometrial cancer. A single-center dosimetric study. IJGC 24:1607, 2014.

Tao W & Lagergren J. Clinical management of obese patients with cancer. J Nat Rev Clin Oncol 10:519-533; 2013.

Wang YY et al. Mammary adipocytes stimulate breast cancer invasion through metabolic remodeling of tumor cells. JCI Insight 2: e87489. 2017. doi :10.1172

Laurent V et al. Periprostatic adipose tissue acts as a driving force for the local invasion of prostate cancer in obesity: role of the CCR3/CCL7 axis. Nature Communications, 7:10230. 2016. doi: 10.1038.

Bochet L et al. Adipocyte-Derived Fibroblasts promote tumor progression and contribute to desmoplastic reaction in breast cancer. Cancer Research, 73:5657-68. 2013.

TRACK 4. IMPLICIT PRECONCEPTIONS IN THE CARE OF THE ONCOLOGIC PATIENT WITH OBESITY.

- Implicit preconceptions in the care of the oncologic patient with obesity. The experience of the nursing team at Quiron Salud. Maria Jarana, Madrid.
- Implicit preconceptions in the care of the oncologic patient with obesity. The experience of the nutrition team at IPOFG, Coimbra, Portugal – Dr. Carolina Bento
- Nutritional concerns of breast cancer patients with obesity: experiences from PREDICOP intervention study. Carlota Castro Espin, ICO Barcelona, Spain.
- Physical activity preconceptions in obese oncologic patients. Prof. Fontes Ribeiro, UC, Coimbra, Portugal.

- What are the implicit preconceptions of the **health professionals, patients, family members** that can be influencing the care of the oncologic patient with obesity?
- Is it possible/necessary/desirable to operate on them?

References

Gulland, A. Three in four are unaware of obesity link to cancer, says charity. *BMJ* 354:i4898, 2016.

Poulain, J.P. Perspective socio-anthropologique de la prise en charge de la dénutrition du malade cancéreux. *Bulletin du Cancer* 101:258-263, 2014.

[Program]

Thursday, 07 th Sept 2017		Friday, 08 th Sept 2017		Saturday, 09 th Sept 2017	
		09-09.10h	Day 2 introduction	09-09.10h	Day 3 introduction
		09.10-10.40h	Track 2 presentation & discussion	09.10-10.40h	Track 4 presentation & discussion
		10.40-11.10h	Coffee break	10.40-11.10h	Coffee Break
		11.10-11.45	Track 2 remarks	11.10-11.45h	Track 4 remarks
		11.45-13h	Plenary session: Sociology a dimension to take into account when treating cancer patients with excess weight <i>Prof. Jean-Pierre Poulain</i>	11.45-13h	Plenary discussion: <i>Future lines and recommendations Paula Jakszyn & Elena Carrillo</i>
				13-13.30h	Wrap up & Closing
		13-14h	Lunch	13.30h	Lunch
13.30-14h	Registration	14-15.30h	Track 3 presentations		
14-15h	Opening session <i>Prof. Maria Filomena Botelho, Onconet-Coimbra</i> <i>Prof. Roland Bugat, Onconet PI</i> <i>Collaborating institutions</i>	15.30-16	Coffee break		
15-15.30h	Coffee break	16.30-18h	Track 3 discussion		
15.30-17h	Track 1 presentations & discussion	18-18.30h	Track 3 remarks and Day 2 closing		
17-17.30h	Track 1 remarks and Day 1 closing				
18h	SOCIAL PROGRAM: Visit to University of Coimbra	20h	SOCIAL PROGRAM: Dinner at "República da Saudade"		

[List of participants]

Group 1

Paula Jakszyn, ES, group facilitator
Carolina Bento, PT
Ana Ramirez, ES
Nanci Baptista, PT
Anabela Mota Pinto, PT
Angela Moca, FR
Roland Bugat, FR
Cristiana Fonseca, PT
Inês Zorrinho, PT
Lelita Santos, PT

Group 2

Elena Carrillo, ES, group facilitator
María Jarana, PT
Maria Graça Campos, PT
Catherine Muller, FR
Carla Barbosa, PT
Maria Filomena Botelho, PT
Paula Alves, PT
Ana Paula Leite, PT
Arantza Ibarrola, ES
Jean-Pierre Poulain, FR

Group 3

Carlota Castro, ES, group facilitator
Charlotte Vaysse, FR
Margarida Abrantes, PT
Ana Elisabete Ferreira, PT
Enrique Carrillo, ES
Carlos Freire de Oliveira, PT
Alicia Utrilla, ES
Carlos Fontes Ribeiro, PT
Ana Bela Sarmento, PT
Natália Amaral, PT

Group 4

Patrick Ritz, FR, group facilitator
Idoia Morilla, ES
Paulo Matafome, PT
André Dias Pereira, PT
Salomé Pires, FR
Vera Ramos, PT
Helena Saldanha, PT
Roi Villar, ES
Paula Tavares, PT

[Minutes]

1. Objectives, methodology and Attendances

The main objective of this workshop was to foster discussion on existing controversies in the field of nutritional and physical activity interventions in obese oncologic patients that arise either from a weak level of available evidence, which does not allow to develop strong recommendations, or from the implicit conceptions of the patients, care-givers, doctors and other health-care providers involved in the process.

This three-day event followed an exploratory sequential mixed methods design conducted through group discussion, as described by Creswell (2014). The workshop was organized in four tracks that gathered controversial topics about the oncologic patient with obesity.

- Track 1. Nutritional screening of oncologic patients, from theory to practice.
- Track 2. Recommendations on weight loss, physical activity and nutritional changes in obese oncologic patients.
- Track 3. Cancer treatment, obesity and weight loss.
- Track 4. Implicit preconceptions in the care of the oncologic patient with obesity.

Each track was introduced in plenary session by several short presentations offered by professionals from different fields that highlight some existing controversies on the topic. Discussion on the proposed controversies was initially intended to be carried out in four small groups (see group list at the end of this document), but for richness of discourse purposes, all tracks except track 1 were directly discussed in plenary group.

A total of 46 attendants from different institutions in the participating countries, France, Portugal and Spain. Beyond the ONCONET institutions, professionals and experts from hospitals, governmental institutions and research centers joined the workshop.

The presentations of the meeting can be downloaded from the following [Dropbox folder](#). These minutes do not include all the details of the discussion that arose from the presentation; rather, it focuses on the general messages that are relevant for all attendants, for the achievement of this workshop goals, and for the pursuit of the global ONCONET objectives: (1) to educate general population through knowledge management, (2) to improve the knowledge of health professionals (despite not having all grade A evidence), and (3) to achieve political impact to fill the gap between health agencies and patients.

2. Summary of conclusions.

Through the presentations included in the four tracks and the subsequent discussion, several challenges to the implementation of personalized complex care projects in obese oncologic patient that arise from soft evidence issues were pointed out. We here provide a list of the main questions identified, grouped in four categories: obesity phenotype and risk indicators; knowledge management on obesity, cancer and lifestyle; stakeholder interaction and communication.

- Obesity phenotype and risk indicators:
 - International agencies support that there is a established relationship between obesity (BMI >30) and the incidence of certain types of cancer; and the relationship between obesity and cancer prognosis (overall survival; disease survival; disease-free survival) is suggested on breast, prostate, colon. *HOWEVER*, despite the fact that there is a link between inflammation/metabolic status and obesity, and inflammation/metabolic status and cancer at the molecular and celular level, the relationship between these two entities at the clinical level is not so clear for the different types and stages of cancer and different types of obesity.
 - Differentiation between prevention vs treatment/care is warranted. Both, general population and health professionals need to be aware of the relationship between obesity and cancer at different points.
 - Moreover, the scientific community is mainly using BMI as an obesity indicator, a measure that is not clear in terms of use, cut-offs or interpretations.
 - It does not differentiate between metabolically healthy and unhealthy obesity.
 - Whole body composition should be something to be considered, because of the potential effect of fat distribution and other body compartments (i.e. muscle mass, intracellullar water, extracellullar water).
 - Waist-hip ratio has demonstrated to be a better to reflect visceral adipose tissue.

- Knowledge management on obesity, cancer and lifestyle:
 - There is a general lack of data on the effects of (1) diet; (2) body composition, (3) exercise in obese oncologic patients.
 - Diet is not only relevant in order to lose weight and to prevent sarcopenia and treatment complications. Diet composition may act as an environment modulator for the development and/or evolution of tumors (i.e. fat composition, antioxidants, etc.).
 - The effect of weight loss during cancer treatment is unknown: it might be beneficial, but it might also release toxic substances stored in the adipose tissue.
 - There is not enough knowledge about the right type of exercise for each person, and there has even been posited a paradoxical effect of exercise in cancer. Starting to exercise being sedentary may drive cancer appearance (stress, miokines...), but it has also shown to reduce cancer in its first stages.

- Data about the joined effect of diet and exercise is lacking.
 - Clinical trials on (1) treatment adjustment based on body composition, (2) prognosis depending on lifestyle interventions, body composition, metabolic status, (3) quality of life, (4) connection with other diseases, (5) all the previous according to the cancer stage.
 - Beyond clinical trials, the mere regular pick up of data from the daily practice (BMI, waist to hip ratio, metabolic syndrome and other simple markers) would contribute a lot to the advancement of this field.
- Stakeholder interaction:
- Notwithstanding all the previous considerations about the level of evidence, it is clear that there needs to be a stronger integration-connection between all the agents involved in the prevention and care of cancer on obese individuals. This includes the general population, patients, their relatives, professionals outside hospitals, professionals inside hospitals.
 - Health education is the first requisite for all the above mentioned to be part of the decisions. With that aim, they need to be informed and empowered to make healthy choices. Information only is not enough; behavior change must be the ultimate goal, and to achieve that awareness needs to be gained with regard to both consensus and controversies.
- Communication:
- Communicating soft-evidence issues is a big challenge. How should we proceed taking into account the available evidence (not grade A),
 - how do we communicate obesity as a risk factor?
 - Maybe in terms of prevention it is right to talk about obesity, but from the diagnosis, it might be more informative to refer to metabolic syndrome.
 - What to do when the diagnosis is made?
 - With regard to diet, food has impact beyond the biological dimension, and the diagnosis moment might be a good time to work with it, because of the sensitivity around health.
 - The same can be ascertained in the case of exercise, as long as benefits outweigh risks.
 - Communicating controversies versus providing very simple messages (especially to the patients).

[Organizing Committee]

Prof. Maria Filomena Botelho, University of Coimbra
Prof. Ana Margarida Abrantes, University of Coimbra
Prof. Salomé Pires, University of Coimbra
Dr. Mafalda Laranjo, University of Coimbra

[Scientific Committee]

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Dr. Antonio Agudo Trigueros, ICO Barcelona
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[Administrative support]

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[With the Collaboration of]

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Universitário de Coimbra, PT
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[Venue and contact information]

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