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"Characteristics of Sexual Dysfunction in Patients with Lung Cancer"

LUDICAS Ibero-American Study

Promoter: GECP Foundation
Protocol code: [redacted]

V2.0 of June 7, 2023

[redacted]

1. Project description

Characteristics of Sexual Dysfunction in Patients with Lung Cancer.

2. Promoter and protocol code

Promoter: GECP Foundation

Protocol code: [redacted]

Version: v2.0 of 01 June 2023

3. Principal Investigator and Project Coordinator

[redacted]

4. Qualifications and experience of the team of researchers and, where appropriate, of the person responsible for the medical care of the participants

Since 2020, the CLARIFY project (monitoring of long cancer survivors using artificial intelligence) was initiated at the Puerta de Hierro University Hospital, previously approved by the ethics committee of
investigation of the Puerta de Hierro University Hospital on 09/03/2020 (Minutes no. 5/2020). This research is led by Dr. Mariano Provencio and tells
with the participation of the team of medical oncologists and the staff of the research center of the Puerta de Hierro hospital.

The project was planned to be developed over 3 years until 2023, divided into 3 phases, the two initial phases with the aim of collecting information to identify the clinical, pathological and molecular characteristics of the disease, as well as the acute effects of cancer treatments and the evaluation of their efficacy through the monitoring of the most relevant clinical outcomes such as survival and identification of risk factors for recurrence tumor. While the third phase is aimed at evaluating the long-term effects on the quality of life of patients, including the alteration of sexual function.

Within the third phase of the project, between May 2020 and May 2022, data were obtained from 383 long-term patients survivors of lung, breast and lymphoma cancer. The initial findings obtained on the alterations in the quality of life of these patients showed a high frequency of sexual dysfunction (SD) in this population, influenced by age, type of cancer and type of cancer treatment.

These initial results served as a basis for generating additional hypotheses. They were presented as oral communication at the congress of the Spanish Society of Medical Oncology on October 18, 2022 and accepted to be presented at the poster session of the annual congress of the American Society of Clinical Oncology ASCO on June 5, 2023.

Experience of the group of researchers in projects led by Dr Mariano Provencio:

- IPT-2011-1569-01000. Valorization of oncological biomarkers for the development of diagnostic/prognostic kits for prostate and lung cancer
- PI13/01806. Image Re-Analysis Study and Correlation Between Metabolic Changes Targeted by PET/CT and Known Mutations in Non-Small Cell Lung Cancer (NSCLC)
- PI18/01778. "Predictive Value of Treatment Response of CB2 Expression in Colon Cancer" (Co-PI)
- H2020-SC1-2016-2017 (Personalized Medicine). IASIS. Integration and analysis of heterogeneous big data for precision medicine and suggested treatments for different types of patients.
- RTC-2017-6502-1. INmunoSIGHT- Immunological and molecular characterization in liquid biopsy of patients with lung cancer for immunotherapy.
- H2020-875160 CLARIFY. Cancer Long Survivors Artificial Intelligence Follow up.
- P4 LUCAT. Personalized medicine for lung cancer treatment: using Big Data-driven approaches for decision support.

Experience of the principal investigator:

- H2020-875160 CLARIFY. Cancer Long Survivors Artificial Intelligence Follow up.

- P4LUCAT. Personalized medicine for lung cancer treatment: using Big Data-driven approaches for decision support.

- Author and principal investigator of the national registry of the Colombian Association of Hematology and Oncology ACHO of patients with cancer and Covid 19 infection (ACHOC-C19). 2020-2022.

- Author and principal investigator of the Epidemiological Registry of Malignant Melanoma in Colombia (REMMEC) of the Colombian Association of Hematology and Oncology ACHO. 2021- present.

5. Funding

The financing of the project will be supported by the promoter of the study, the GECP Foundation.

6. Objective and justification of the research based on the most up-to-date review of the available scientific evidence.

Theoretical framework

The population of cancer survivors may suffer long-term alterations secondary to antineoplastic treatments that lead to the deterioration of their quality of life and that include the generation of sexual dysfunction (SD).

Most of the data on SD in cancer patients come from patients with breast cancer, gynecologic neoplasms, and prostate cancer, most of whom receive hormonal cancer treatments and cytotoxic chemotherapy, and have often undergone mutilating cancer surgeries.

There are limited prospective studies carried out with heterogeneous collection instruments, which does not allow obtaining adequate and complete information on the real situation of the problem.

As a source of local data, there is a study to characterize sexual dysfunction in a cohort of cancer survivor patients derived from the European CLARIFY H2020 project (Cancer Long Survivor Artificial Intelligence Follow-Up) that we carried out at the Puerta de Hierro University Hospital from May 2020 to May 2022.
A total of 383 patients were included, distributed according to diagnosis in breast cancer 68.1% (261), lung cancer 26.3% (101) and lymphomas 5.48% (21).
Globally, 69% of men vs. 31% of women reported being sexually active and 76% of women vs. 24% of men had general sexual dissatisfaction.

In our study, the largest sample of patients was women with breast cancer (261), which corresponds to the highest overall frequency reported in the literature of this type of neoplasm.
In relation to the stage, patients with early breast cancer treated and followed up receiving hormonal therapy showed a greater tendency to suffer moderate disorders of the phases of sexual response, while patients with a diagnosis time greater than 5 years showed a tendency to not present alterations. Statistically significant associations were confirmed in patients with metastatic breast cancer to present severe disorders of the phases of sexual response.

Regarding the specific characteristics of patients with lung cancer, which represented a smaller sample size (101), 66.3% (67) were men, the median age was 64 and 61 years in men and women respectively. 45% of women and 41% of men reported being sexually active. The absolute frequency of overall sexual dissatisfaction was 8.8% in men vs. 2.8 in women.
Men showed a tendency to develop severe alterations in the phases of sexual response. On the other hand, a statistically significant association was evidenced for severe sexual response disorders in women. Of these, 35.2% received chemotherapy, 26.4% immunotherapy and 20.5% targeted therapies.

When looking for similar information in the literature, we found previous research in women with lung cancer that supports that 95% of these patients score below the 50th percentile when rating their sexual function and a 2022 study, in which 64% had metastatic disease, and almost half were receiving targeted therapy, finding that 77% reported moderate to severe sexual dysfunction.

Our data obtained in patients with lung cancer, despite representing a small sample size, suggest that SD is an alteration that is significantly affecting the quality of life of this population.

In addition, they suggest that there is a potential role for new cancer treatments such as targeted therapy and immune checkpoint inhibitors in the development of DS, for which there is limited information

Justification

Given the increase in lung cancer survivors and the therapeutic options different from those historically described as associated with DS, added to the fact that the patient profile has changed in recent years, with the male gender remaining the most affected, but with a significant increase in diagnosis in women and younger and non-smoking patients; it is important to characterize SD in this population and determine its severity as well as the associated risk factors and the role of new antineoplastic therapies.
This knowledge will make it possible to propose strategies for approaching and monitoring cancer that help improve the quality of life of these patients during and after cancer treatments.

A study is planned to be carried out with a larger number of patients with lung cancer, including the population of Spain and Latin American countries to obtain a sample of more diverse and heterogeneous characteristics, with clinical, cultural and sociodemographic differences. This will allow us to obtain better and greater data and consequently to define the clinical and treatment factors significantly associated with SD in these individuals and to obtain a more complete view of the reality of the problem.

The results of this research will make it possible to carry out interventions specifically aimed at this population and modify the oncological follow-up guidelines currently in force. Likewise, the information collected will serve as a basis for generating new protocols for a multidisciplinary approach including the participation of psychology and specialists in urology, gynecology and psychiatry.

Additionally, the knowledge obtained will allow to generate education about SD to the entire treating medical team and patients to overcome the barriers that prevent adequately addressing this condition.

7. General Objective

To identify and describe the type, frequency, and severity of SD in patients with lung cancer and to generate targeted clinical approach and oncological follow-up strategies based on specific findings in this population.

8. Secondary Objectives

- Describe the clinical, cultural, and sociodemographic characteristics of the study population.
- To characterize differences in sexual dysfunction in patients with lung cancer according to age, sociodemographic characteristics, region of residence, and type of cancer treatment.
- Identify risk factors for the development and severity of sexual dysfunction.
- To promote education and awareness among the health team on the identification and characteristics of sexual dysfunction in patients with lung cancer.
- To collect information to generate recommendations for the multidisciplinary approach and management of sexual dysfunction during oncological follow-up applicable to current oncology practice.
- To propose education strategies on the management of sexual dysfunction in patients with lung cancer aimed at patients and their families.
- To generate a collaborative network of Ibero-American research.

9. Methods and procedures envisaged, including statistical and other analytical tests

The recruitment will be carried out from July 2023 and will be carried out until December 2023, the analysis of the information will be carried out from January to March 2024.
Clinical and demographic variables (Annex 1) will be collected by the treating oncologists and recorded in an electronic data collection notebook designed for this study, which will be accessed through a personal username and password.

Data anonymization will be ensured for all patients. To this end, they will identify themselves with a numerical code in order to respect the confidentiality of personal data. The patient's initials and medical record number will be separated from the rest of the data and will not be included in the study database.

Measurements of sexual function will be performed through an electronic survey that will be sent to patients who agree to participate in the study and sign the informed consent. This electronic survey will be hosted on an exclusive study platform, which the patient will enter through a user corresponding to the anonymization numerical code and a personal password assigned after signing the informed consent.

The survey will consist of single-choice questions based on two validated questionnaires to explore and diagnose sexual dysfunction in women (FSM) and men (FSH) separately, which have been evaluated and translated into Spanish by a local research group in the Valencian Community and are available for use in the primary care setting in Spain. These instruments were selected because of the possibility of self-administration, their history of efficacy in assessing complete sexual function in the general population, and their low level of complexity. Through this instrument, criteria of the phases of sexual response according to DSM V (FSH) and DSM IV (FSM) will be evaluated, as well as a descriptive parameter of sexual activity. (Appendices 2 and 3)

The information entered by patients will only be visible by the principal investigator, who will have a personal username and password to access the data.

10. Statistical analysis

A descriptive analysis of the variables will be carried out; for the characteristics a univariate analysis. The qualitative variables will be determined with absolute and relative frequencies and the quantitative variables by measures of central tendency and dispersion, with mean and standard deviation for those with normal and median distribution and interquartile range for those with non-normal distribution. Subsequently, an inferential analysis will be performed, with chi2 distribution to evaluate the correlations between the different variables and the main outcomes in the measurement of sexual function.
Possible trends in association between variables and outcomes will be evaluated and the main trends described will be carried out through a multivariate analysis.
Logistic regression analyses will be performed to determine risk factors
Statistical analyses will be carried out using the SPSS Statistics 20 or R program.

11. Full project overview in understandable language

The population of cancer survivors may suffer long-term alterations secondary to antineoplastic treatments that lead to the deterioration of their quality of life and that include the generation of sexual dysfunction (SD). Most of the data on SD in cancer patients come from patients with breast cancer, gynecologic neoplasms, and prostate cancer, most of whom receive hormonal cancer treatments and cytotoxic chemotherapy.

According to data from recent institutional research on the characteristics of SD in cancer survivors, it was documented that patients with lung cancer have a high frequency of DS, which is significantly affecting their quality of life.

Given the increase in survivors of this type of neoplasm and the fact that the patient profile has changed in recent years with a significant increase in diagnosis in women and younger and non-smoking patients; In addition to the fact that cancer treatment is different from that usually related to SD generation, it is of great importance to characterize SD in this population and determine its severity as well as the associated risk factors and the role of new antineoplastic therapies.
This knowledge will make it possible to propose strategies for approaching and monitoring cancer that help improve the quality of life of these patients during and after cancer treatments.
Likewise, the information collected will serve as a basis for generating new protocols for a multidisciplinary approach and will generate education about SD for the entire treating medical team as well as for patients and their families.

12. Participants, Consent and Information

12.1 Justification for the involvement of human beings in the research project

Due to the observational nature of the study, there is no possibility that the study will generate any type of risk in the subjects studied, since it does not imply any change in the patient's care with respect to their normal clinical follow-up. The research protocol will be submitted for approval by the research ethics committees (CEIC) of the participating institutions.

Prior to the commencement of the study, the protocol, clinical information questionnaire, patient information sheet, and informed consent for the study will also be submitted for approval by the Clinical Research Ethics Committee (CEIC). .
Patients who meet all inclusion criteria and give informed consent will be recruited. Each subject invited to participate in the study will be given a written document called a "Patient Information Sheet" that will contain the relevant information necessary for them to decide if they want to participate in the study. The investigator will inform the patient as fully as possible of the details of the study. Participating subjects may withdraw their consent to the use of their data in the analysis at any time, without giving a reason and without incurring any liability or loss.

12.2 Criteria for the inclusion/exclusion of research participants

Inclusion criteria

- Age greater than or equal to 18 years and less than or equal to 70 years.
- Diagnosis of lung cancer stages IB to IV.
- Have received systemic cancer treatment for at least 3 months or be under cancer follow-up after having received systemic therapy for at least 3 months with stable tumor disease or in partial or complete response on imaging.
- ECOG ≤ 2

Exclusion Criteria

- Patients with comorbidities (kidney failure, cardiovascular diseases or similar) not controlled with corresponding medical management.
- Individuals with physical disability or cognitive impairment that prevents them from completing the electronic data collection form.

12.3 Where applicable, method of randomization

Not applicable.

12.4 Study modality: open, single-blind or double-blind

Analytical cross-sectional observational study.

12.5 Deadlines and details of information for potential research participants, including proposed methods for communicating such information.

Not applicable

12.6Documentation, visual or other material to be used in the request for consent, or, in the case of persons unable to consent, for authorisation to participate in the research

1. Patient information sheet that will contain the relevant and necessary information for the patient to decide if they want to participate in the study. (Annex 4)

2. Informed consent (Annex 5), which each researcher must explain to the patient as completely as possible, specifying in understandable language the characteristics of the research project.

12.7 Provisions to ensure respect for the privacy of research participants and to ensure the confidentiality of personal data

The study will be conducted in accordance with the Good Clinical Practice (GCP) Standards.
The confidentiality of the data will be guaranteed in accordance with the provisions of Organic Law 3/2018, of 5 December, on the Protection of Personal Data and guarantee of digital rights and will separate personal clinical data in accordance with current legislation (Law 14/2007, of 3 July, on biomedical research).
All patients' data will be anonymized. To this end, the patient will be identified by means of a numerical code in order to respect the confidentiality of the patients' personal data. The patient's initials and medical record number will be separated from the rest of the data, not included in the study database.
Access to personal information will be restricted to the study investigators, the HUPHM clinical research ethics committee and specialized personnel authorized to verify the data and procedures of the study, always maintaining the confidentiality of the latter in accordance with current legislation.
The informed consent will be written in Spanish and in understandable language.

Subjects participating in the study may withdraw their consent to the use of their data in the analysis at any time, without giving a reason and without incurring any liability or loss.

12.8 Forecasts for the processing of information that may be generated during research and of relevance to the present or future health of participants and members of their families

The results of this research will serve as prospective local evidence of larger sample size on the characteristics of sexual dysfunction in the growing population of lung cancer survivors, who present a specific patient and treatment profile that is different from that of other cancer populations.
This information will make it possible to define the clinical and treatment factors significantly associated with SD in these individuals and to obtain a more complete view of the reality of the problem.

The data obtained will facilitate the implementation of interventions specifically aimed at this population and propose modifications to the oncological follow-up guidelines currently in force. Likewise, the information collected will serve as a basis for generating new protocols for a multidisciplinary approach, including psychology and specialists in urology, gynecology and psychiatry.

Additionally, education about SD can be generated for the entire treating medical team and for patients and their families to help overcome the barriers that prevent adequately addressing this condition and improve quality of life.

12.9 Other Information

The source of the clinical information of the patients, as well as of the pathological data, will be in all cases the patient's medical history.

The information collected will be entered into the database and will be protected with an individual username and password for each researcher.