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Editorial / Editorial

Smoking: a bad habit that makes people sick

El tabaquismo, un mal hábito que enferma

Dr. Fernando Cano Pazmiño*

Pneumology Service SOLCA - Guayaquil, Member of ATS, ACCP, ALAT, ERS and SETET Staff Clinic, Guayaquil, Ecuador

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According to the Royal Spanish Academy, a habit is defined as a special way of behavior or conduct acquired by repetition of equal or similar actions or originated by instinctive tendency [1]. They can be beneficial or harmful to our health. Smoking is considered a harmful habit that generates addiction and causes disease.

Smoking can be defined as a chronic and addictive, easily preventable inflammatory illness that shortens people's lives and causes disabilities. It can result in premature death, especially for long-term smokers, due to the development of chronic, irreversible diseases.

According to the Pan-American Health Organization, there are 1.3 billion tobacco users in the world. It kills 8 million people every year, out of whom 7 million are active smokers and one million are passive. The life expectancy of smokers is 10 years shorter compared to non-smokers. Tobacco-related mortality in the Americas is 24% from cancer and 45% from chronic respiratory diseases. Tobacco is the only legal consumer product that kills half its users; they will die from related diseases, losing an average of 10 to 15 years of life. Children and adolescents who use electronic cigarettes are at least twice as likely to smoke cigarettes later in life [2].

By 2020, the prevalence of tobacco use among teenagers aged 13 to 15 in the Americas was 11.3%. As of 2016, the prevalence of tobacco use among adolescents in Ecuador was 4.60%. In 2017, the prevalence of tobacco consumption among adults in the Americas was 15.2%, the highest among men. The good news is that the trend of tobacco consumption is declining in people aged 15 and over [3]. However, the consumption of electronic cigarettes is different; among children aged 13 to 15, the rates have doubled and even tripled in the last 5 years.

To understand how smoking causes non-communicable and carcinogenic respiratory diseases, it is necessary to know that cigarette smoke is an aerosol resulting from incomplete combustion of tobacco composed of more than 7000 substances that are pharmacologically active, cytotoxic, and mutagenic. Seventy of them are recognized as carcinogens, responsible for 30% of cancers. The cigarette has a main smoke stream and a lateral one. The main, which is 95% gaseous, contains billions of particles with a size of 0.2 to 0.5 microns and are therefore breathable. Moreover, the high concentrations of reactive free radicals in each inhalation has effects on

* **Corresponding Author:** Dr. Fernando Cano Pazmiño, fcano50@icloud.com

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the respiratory system (4). Thus, the two main effects produced by tobacco smoke on the respiratory tract and that generate diseases are the induction of inflammation and carcinogenic mutagenic, assisted by infections by alteration of mucociliary clearance, giving rise to pathologies such as Chronic obstructive pulmonary disease (COPD), emphysema, chronic bronchitis, asthma, interstitial lung diseases, pulmonary fibrosis, and lung cancer [4].

What about the e-cigarette or vaping? Initially proposed as an alternative and safer measure than cigarettes or tobacco both by consumption and method of quitting smoking, current evidence indicates that this is not the case. Both the World Health Organization and the consensus or guidelines of the Respiratory Scientific Societies indicate that there is no scientific evidence to demonstrate that e-cigarettes are safe, as they can promote the development of obstructive airway diseases, severe inflammatory lung diseases such as EVALI (E-cigarette or Vaping use-Associated Lung Injury), and because their toxic chemicals released in the steam can cause cancer. Nor is there any scientific evidence to indicate that e-cigarettes are an effective method for smoking cessation and instead increase tobacco consumption because of their nicotine content, which we know is an addictive substance; in many cases, smokers end up consuming both products [5,6].

So, how can we help smokers? The answer is tobacco cessation, which is a program that combines psychological support with pharmacological support. Logically, it is not 100% effective because there are individual or genetic factors of greater or lesser sensitivity in people who modify their response to scientifically established methods to quit smoking [7].

The statement published by the ALAT (Latin American Thorax Association) "emphasizes the importance of strengthening the control of tobacco and electronic cigarettes in Latin America, by implementing stricter regulations, educating the community, increasing taxes, promoting smoking cessation, including new therapeutic options such as Cytisine, and continuing to combat the influence of the tobacco industry in formulating health policies" [8].

Then, it is possible to conclude that smoking is a chronic addictive disease that can give rise to high morbimortality non-curative pathologies with high-cost management. While it is true that there is a decrease in tobacco consumption in young people and adults, the same is not the case with the use of e-cigarettes or vaping, which is increasing in children, adolescents, and young people who have not previously smoked, thus increasing the risks to their health.

1. Abbreviations

COPD: Chronic obstructive pulmonary disease

EVALI: E-cigarette or vaping use-associated lung injury

ALAT: Latin American Thorax Association

2. Administrative information

2.1. Additional Files

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The author declares that he has no conflicts of interest.

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Article / Artículo

Further exploring the SPIKES protocol from the perspective of oncology patients in terms of personality traits Prospective questionnaire-based study

Análisis del protocolo SPIKES desde la perspectiva del paciente oncológico Estudio prospectivo basado en cuestionarios

Irene Solana López*, Manuel Meilan Uzcategui, Elia Martínez Moreno, Ignacio Juez Martel, David Gutiérrez Abad, Elena Lahoz León, Olga Mateo Rodríguez, Jaime Martínez Moreno, Carlos de Zea Luque, Ana Manuela Martín Fernández de Soignie, Fátima Escalona Martín, Isabel Santana Gómez and Juan Antonio Guerra Martínez

Servicio de Oncología Médica, Hospital Universitario de Fuenlabrada, Madrid (Spain)

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ABSTRACT
Background: Establishing adequate communication is part of the therapeutic process and of the integral approach to the oncology patient. The SPIKES protocol defines a series of general recommendations aimed at facilitating this process. To date, there is no questionnaire that makes it possible to personalize the communication of bad news in a systematized way. Some studies support the hypothesis that personality influences the communicative modes; therefore, the aim of this work is to try to establish nuances in the SPIKES protocol based on personality traits. **Methods:** Single-center, observational, prospective, descriptive and correlational study, conducted on a sample of 51 oncology patients based on a personality questionnaire and a communication questionnaire (based on the SPIKES protocol). **Results:** The scores recorded in all domains of the communication questionnaire were high. There was no significant correlation with the personality questionnaire domains. **Conclusions:** There are certain needs tending towards universality in the communication of bad news that the SPIKES protocol adequately reflects; it can be considered the gold standard. However, it is not possible to establish nuances in it according to personality traits based on the results of this work. In the strategy phase, attention should be paid to life and family planning in the context of oncologic disease.

Keywords: SPIKES protocol, communication of bad news, psycho-oncology, individualized medicine, physician-patient relations.

RESUMEN
Introducción: Establecer una adecuada comunicación forma parte del proceso terapéutico y del abordaje integral del paciente oncológico. El protocolo SPIKES emite una serie de recomendaciones generales destinadas a facilitar este proceso. No existe hasta la fecha un cuestionario que permita personalizar de una manera sistematizada la comunicación de malas noticias. Existen estudios que apoyan la hipótesis de que la personalidad influye en los modos comunicativos. Por ello, el objetivo de este trabajo fue intentar establecer matices en el protocolo SPIKES con base en los rasgos de personalidad.
Materiales y métodos: Estudio unicéntrico, observacional, prospectivo, descriptivo y correlacional, realizado sobre una muestra de 51 pacientes oncológicos con base en un cuestionario de personalidad y un cuestionario de comunicación, el cual se basa a su vez en el protocolo SPIKES. **Resultados:** Las puntuaciones registradas en todos los dominios del cuestionario de

*** Corresponding Author:** Irene Solana López, irene.solana@salud.madrid.org

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comunicación fueron elevadas. Ninguna correlación con los dominios del cuestionario de personalidad resultó significativa. **Conclusiones:** Existen determinadas necesidades tendentes a la universalidad en torno a la comunicación de malas noticias que el protocolo SPIKES recoge adecuadamente, por lo que puede considerarse el *gold standard*. No se pueden establecer matices en este cuestionario en función de los rasgos de personalidad con base en los resultados de este trabajo. En la fase de estrategia, conviene prestar atención a la planificación vital y familiar en el seno de la enfermedad oncológica.

Palabras Clave: protocolo SPIKES, comunicación de malas noticias, psicooncología, medicina personalizada, relación médico-paciente.

1. Introduction

The SPIKES protocol is currently considered the gold standard to communicate sensitive clinical information in Oncology. This protocol consists of six steps or domains that are developed cyclically, namely: "S", Setting; "P", Perception; "I", Invitation; "K", Knowledge; "E": Empathy and Emotions; and "S", Strategy and Summary. Its authors issued a series of general recommendations for executing each step, laying the foundations for the good outcome of the communicative act [1].

The SPIKES protocol was developed by the Canadian oncologist and psychologist R. Buckman, M. D. and the psychiatrist W. F. Baile, M. D. It was first published in 2000 in the journal The Oncologist. It arose from the need to facilitate the communication of bad news in the oncology field [1].

After conducting a survey of oncologists attending the 1998 annual meeting of the American Society of Clinical Oncology (ASCO), which assessed the attitudes and practices of attendees regarding the communication of bad news, the authors relied on their clinical experience and a review of the literature published in 1985 to create the protocol [2]. It is, therefore, designed from the perspective of oncologists, which remains unchanged to date [1].

In 2020, Von Blanckenburg, P. et al. attempted to turn the SPIKES protocol around by applying it from the patient's perspective. This resulted in the creation of a scale called "MABBAN" that would allow to know the patients' opinion about the items of the SPIKES protocol. However, this scale has not been implemented in daily clinical practice, partly due to its length and the time availability in our clinics [3].

In the field of palliative care, the concept of "Shared Care Planning" (SCP) is emerging strongly in recent years [4, 5].

Shared Care Planning is the process by which healthcare professionals promote and accompany the patient in reflecting on his/her illness based on their own scale of values and priorities to make the most appropriate care decisions adapted to each stage of their illness [4, 5].

This process, which comes from palliative medicine but would be beneficial to extend to the field of Oncology, requires the generation of a therapeutic bond based on trust, where communication is postulated as a fundamental element [6].

Numerous investigations in the field of psycho-oncology and language psychology are being carried out to individualize the SCP process as much as possible.

There is a communicative model applicable to SCP, called the "DICS model" (dominant, influyent, sincere and conscious) that establishes four communicative modes through personality patterns, and issues recommendations for adapting discourse based on them. Its basis is related to the idea that certain personality traits (which are identifiable) establish patterns in the emission of language —both internal (of the individual with him/herself) and external (of the individual with the environment). In turn, this has an impact on how the individual needs to receive the message to enhance its understanding [7]. In other words, by identifying the predominant personality traits, healthcare personnel could adapt their discourse or communicative mode to enhance and facilitate the exchange of information.

The four communicative domains are [7]:

1) Analytical people (rational and introverted, characterized by orientation to following rules, processes and procedures).
2) Dominant people (rational and extroverted, characterized by orientation to challenges and achievement of results).

3) Influenceable people (extroverted and emotional, characterized by orientation towards dealing with, interacting, and influencing other people).
4) Secure people (emotional and introverted, oriented to staying in the current situation).

Based on the applicability of this model, the question of the current validity of the SPIKES protocol emerges, should it be revised and adapted to different personality patterns?

In the field of personality trait identification, Cook-Briggs, K. and Briggs-Myers, I., authors of the Myers-Briggs personality questionnaire, argued that personality could be broadly delimited on the basis of eight traits grouped into four opposing categories. Thus, personality would be defined by the combination of four of the following traits: introversion-extroversion, realism-intuition, thinking-foresight, feeling-spontaneity, and judgment-perception [8].

The design of these categories was the product of twenty years of research by the authors and was carried out with the following interpretative sense [8]:

1) The introversion-extroversion category explores where and how the individual directs his/her attention and energy.
2) The realism-intuition category explores how information is preferred to be dealt with.
3) The thinking-feeling category explores how the individual makes decisions.
4) The judgment-perception category explores the interaction with the outside world.

Although the Myers-Briggs questionnaire is not exempt from criticism regarding its ability to categorize personality, and many authors argue that it is a simplistic model that fails to adequately systematize the complexity that personality entails, other authors and studies have relied on this questionnaire in an attempt to relate personality traits to language [9]. For example, Lee C. et al. found significant correlations between responses on the Myers-Briggs questionnaire and language use in a sample of 80 Korean students [10]. In another study, Keh S., et al. employed algorithms based on this questionnaire to design of artificial language (chat-bots) [11].

With the aim of identifying personality patterns to establish nuances in the application of the SPIKES protocol, the Medical Oncology Service of the University Hospital of Fuenlabrada designed and validated two questionnaires:

1) The first, on personality, based on the Myers-Briggs questionnaire [8].
2) The second, on patient wishes and perceptions regarding the communication of sensitive clinical information, based on the MABBAN scale [3] and the SPIKES protocol [1].

2. Materials and methods

Single-center, observational, prospective, descriptive and correlational study, based on questionnaires and performed on a cohort of oncology patients with tumors of digestive origin and unknown origin. Patients were selected in order of arrival at the first oncology consultation until completing a sample size of N=51 from October 2022 to March 2023. They had to meet the following inclusion criteria: 1) Over 18 years of age; 2) Colorectal, pancreatic, gastric, biliary, and biliary tumors of unknown origin; 3) Any staging at diagnosis; 4) In neoadjuvant, adjuvant or first line treatment of unresectable disease (locally advanced or metastatic); 5) Signed informed consent for participation in the study and publication of data. The Ethics Committee of the Hospital Universitario de Fuenlabrada approved the study.

Two questionnaires were designed, linguistically adapted, and validated. The first was a personality questionnaire based on the Myers-Briggs questionnaire [8]. The second, on patient wishes and perceptions regarding the communication of sensitive clinical information, was based on the MABBAN scale [3] and the SPIKES protocol [1]. As part of the strategy phase of this second questionnaire, questions

aimed at exploring the patients' desire regarding the oncologist's intervention aimed at normalization of the disease in the nuclear family were included, which is unusual since this area is not contemplated as part of the recommendations specified in the SPIKES protocol [1]. It should also be noted that the "perception" and "invitation" steps of the SPIKES protocol were merged into one domain in our questionnaire. The questionnaires (as well as the statistical validation analysis) can be found in the supplementary material associated with this article.

The questionnaires were designed according to the closed-question model with a Likert-type scale from 1 to 5. The responses were collected, anonymized by means of a 6-digit identification code on Google forms.

In addition, the following data were recorded for each patient: age, sex, educational level, field of study, type of tumor diagnosed, tumor stage at diagnosis, metastatic CNS involvement at diagnosis, previous contact with an oncology service (due to previous oncologic process or due to oncologic disease in the family nucleus) and previous psychiatric pathology.

Firstly, a descriptive analysis of the overall sample and the responses to the questionnaires was performed using the IBM-SPSS version 25.0 program.

The scores of the questionnaires were grouped a posteriori into percentages by domains (Questionnaire 1: extroversion/introversion, realism/intuition, foresight/spontaneous, true to one's ideas/ complacent. Questionnaire 2: environment, perception/invitation, knowledge, emotions, strategy), based on the following formula:

$$x = \frac{(\sum(\textit{puntuación preguntas del dominio}) - \sum(\textit{puntuación contrapreguntas del dominio}))}{(\textit{Puntuación máxima obtenible}) \times 100}$$

Therefore, a scale from 100% (maximum score in the questions) to -100% (maximum score in the counter-questions) was used, with 0% representing people with mixed personality traits or indifference in the items of the SPIKES protocol.

The percentages by domain were correlated, secondly, using Spearman's test for nonparametric distribution, based on the results obtained in the Kolmogorov-Smirnov test.

3. Results

A sample of 51 oncologic patients was recruited (60.8% men, 39.2% women; mean age 62±10 years; 60.8% with basic education, 21.6% medium, 10% higher; 7.8% with a history of anxious-depressive pathology). All had gastrointestinal tumors or tumors of unknown origin (17.6% localized, 37.3% locally advanced, 45.1% metastatic). None of the patients had CNS metastases at diagnosis. At the time of recruitment, 29 patients (56.9%) were in first-line treatment, 17 (33.3%) in adjuvant, and 5 (9.8%) in neoadjuvant. Finally, 23.5% (12 patients) had had previous contact with the Oncology Service because of a personal oncologic history, 37.3% (19 patients) because of oncologic disease in the family nucleus. The remaining 39.2% (20 patients) had never visited an oncology department.

In the personality questionnaire, the study population was considered predominantly extroverted (51% of the patients), realistic (54.8%), and farsighted (49%). About 30% of the patients considered that their personality presented mixed traits: extroversion-introversion (29.4%), realism-intuition (39.2%), foresight-spontaneity (33.3%). In the fourth domain, however, 49% of the patients considered that they presented mixed traits between fidelity to their own ideas and complacency towards those close to them. Thirty-three percent defined themselves as "complacent".

In the questionnaire of wishes and perceptions regarding the communication of sensitive clinical information, most patients scored high on all items of the SPIKES protocol. More than 50% of patients scored 78.3% in the "environment" domain, 23.6% in the "perception-invitation" domain, 64.7% in the "knowledge" domain, 86.2% in the "emotions" domain, and 76.4% in the "strategy" domain.

Two patients (3.9% of the total number of patients) scored negatively (between -33.3% and -0.1%) in each domain ("environment", "emotions", "knowledge", "strategy"); except in the domain "perception-

invitation", where 4 (7.8%) scored between -33.3% and -0.1% and 2 (3.9%) scored between -100% and -33.3%. Likewise, for 4 patients (7.8%) the domain "perception-invitation" was indifferent (score: 0%) and for 1 patient (2%), the domain "knowledge" as well.

The correlations between the domains of the personality questionnaire and the domains of the questionnaire based on the SPIKES protocol were not significant ($p>0.05$). No correlation was found between the baseline traits of the study population and the responses in the questionnaires ($p>0.05$). It should be noted that no correlation was found between disease staging at diagnosis and the results obtained in the questionnaires.

An exploratory sub-analysis of correlation was performed between the domains of the personality questionnaire and the individual questions of questionnaire 2. Correlation was observed between the degree of foresight and the questions environment 1: "I would like the oncologist to inform me in a quiet environment without interruptions" (Spearman correlation coefficient (rs)=0.34, $p=0.02$) and environment 2: "I would like the same oncologist to always inform me" (rs=0.27, $p=0.05$). A correlation was also observed between the degree of spontaneity and the questions emotions 2: "I appreciate that the oncologist pauses during the information process and respects my silences" (rs= -0.39, $p=0.004$) and emotions 3: "I would like the oncologist to ask me openly about my emotions. After that, I will decide whether I want to share them or not" (rs= -0.29, $p=0.003$). Likewise, it should be noted that no correlation was found between the personality domains and the questions related to the normalization of the disease in the family nucleus.

4. Discussion

Effective communication between patients, family members, and healthcare personnel is crucial to provide comprehensive care and improve the quality of life of patients [12]. It allows early detection and addressing fear and anxiety, as well as accompanying in other psycho-spiritual issues inherent to serious and chronic diseases, such as oncologic disease. It has been shown that effective communication improves acceptance and adaptation to the disease [13, 14]. In addition, it can enhance SCP and decrease rates of pathological grief [4, 15].

Although there are multiple assessment questionnaires available for the oncologic process, such as nutrition screening, scales for elderly patients, psychological health questionnaires, etc., there is no questionnaire formally implemented in clinical practice that allows the process of communicating bad news to be adapted to the individual needs and wishes of each patient [15, 16].

Based on the hypothesis that personality influences language modes, this paper has attempted to find nuances in the six steps of the SPIKES protocol, without success. This may be related to the following points:

First, the personality traits of the patients in our sample were relatively homogeneous and tended toward extroversion, realism, foresight, and neutrality with respect to complacency versus fidelity to one's own ideas. Moreover, the statistical analysis was performed on the basis of 4 personality domains (in turn based on the 8 opposing traits) and not on the basis of the 16 personality categories defined by Myers-Briggs and arising from the different combinations of the 8 traits. This analysis was thus performed for reasons of sample size, sample representativeness and statistical power [8].

Secondly, the domains of the second questionnaire (which in turn correlated with the steps of the SPIKES protocol [1]) were generally positively assessed, with a very small percentage of patients (as described in the results section) scoring indifferent or negative. These results lead us to conclude in favor of the tendency towards the universality of certain needs regarding the communication of bad news, and we can affirm that the SPIKES protocol covers them adequately [1].

The fundamental success of this protocol consists of issuing a series of general guidelines that leave room for the individual interpersonal art of the healthcare professional involved in the act of communication. Thus, its generality makes it adaptable to the different personalities of both the patients and the healthcare professionals. Furthermore, the protocol is designed in such a way that the previous step guarantees the correct development of the following step. Therefore, it starts from the simplest (seeking a serene environment) to the most complex (communicating the information and setting out a strategy) but not before having asked what information and how much information the patient wants to know and having validated the emotions that arise around the process of communicating bad news [1].

Although we have not achieved our main objective —which was to design an algorithm that would allow us to individualize, through personality traits, the process of communicating sensitive clinical information— there are some noteworthy findings.

First, we explored patients' views on addressing the family sphere as part of the strategy phase. This was done through two questions (and their respective counter-questions) as follows: "*I wish the oncologist would help me to normalize my disease in the nuclear family*" and "*I wish to be taught tools to normalize the oncologic disease with my children*". In both questions, the median score (collected as a Likert Scale from 1 to 5) was 4 CI95% (3.6-4). Therefore, those of us who practice in the field of oncology should pay attention more frequently to this area, which sometimes tends to be relegated to the background by the therapeutic strategy and purely clinical aspects. Achieving an adequate understanding and acceptance of the disease by the family facilitates the accompaniment and support of the patient by those close to him or her, results in better rates of therapeutic compliance, favors earlier detection of complications and generates greater emotional well-being, which in turn influences physical well-being [16].

Secondly, when the analysis of the strategy phase is broken down by questions, we found two clear blocks. The first is called the "Therapeutic planning block" and is made up of two questions (one on the desire to receive therapeutic information and the other on the desire to participate in clinical decision-making). The second, called "Life planning block" is made up of three questions (the two previously mentioned on the family sphere and a third one aimed at planning for other life circumstances). We grouped the score obtained in these blocks from 0% to 100%. In the therapeutic planning block, 43.1% scored between 75%-100%. However, in the life planning block, 78.4% were in this score range, which is almost double the number of patients. These results lead to the conclusion that there is a predominant concern among patients regarding the collateral consequences that their disease may have on their daily lives [12]. This concern is above (in many cases) the concern for the more purely clinical issues of the disease, according to the results of our work.

This work deals with a subjective field of study. This subjectivity makes it difficult to systematize the object of study, and it can be said that this is the main limitation of this work. However, primary importance should be given to the reduction of emotional impact and comprehensive support, paying attention to the patient's social environment, which is perceived positively by patients in terms of quality of care [12, 16].

5. Conclusions

Establishing effective communication is part of the therapeutic process and the comprehensive approach to the oncology patient. The high scores recorded in all domains of our Patient Perceptions and Wishes Questionnaire regarding the communication of bad news support that the SPIKES protocol remains, to date, the gold standard in this area. Nuances in it cannot be standardized on the basis of personality traits based on the results of this work. Within the strategy phase, 78.4% of the patients participating in this study scored between 75-100% in the so-called "Life Planning Block", reflecting a high level of concern for the impact of the disease on the family nucleus; the fact that the oncologist tries to help in this area is perceived positively in terms of quality of care.

6. Abbreviations

ASCO: American Society of Clinical Oncology

CNS: Central nervous system

SCP: Shared Care Planning

CSN: Central Nervous System

7. Administrative information

7.1 Additional Files

None declared by the authors

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7.3. Author contributions

Conceptualization, visualization, methodology, project management, and writing, proofreading and editing: Irene Solana López, Manuel Meilan Uzcategui, Elia Martínez Moreno. **Edition:** Ignacio Juez Martel, David Gutiérrez Abad, Elena Lahoz León, Olga Mateo Rodríguez, Jaime Martínez Moreno, Carlos de Zea Luque, Ana Manuela Martín Fernández de Soignie, Fátima Escalona Martín, Isabel Santana Gómez, Juan Antonio Guerra Martínez. All authors read and approved the final version of the manuscript.

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7.5. Availability of data and materials

Data and materials are available upon request from the corresponding author. No other materials are reported.

7.6. Statements

7.6.1. Ethics committee approval

The study received approval from the Research Ethics Committee (CEI) of the University Hospital of Fuenlabrada.

7.6.2 Conflicts of interest

The authors declare no conflicts of interest.

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Annexes

Anexo 1. Diseño de los cuestionarios

Se diseñó un primer cuestionario exploratorio de rasgos de personalidad, basado en la interpretación que el cuestionario de Myers-Briggs hace de los ocho rasgos contrapuestos por pares que, para estos autores, definen los dieciséis tipos de personalidad.

Se diseñó un segundo cuestionario, basado en el cuestionario MABBAN, que a su vez está basado en el protocolo SPIKES, para indagar en los deseos de los pacientes respecto a la comunicación de malas noticias durante el proceso oncológico.

Todos los cuestionarios se diseñaron según el modelo de pregunta cerrada y respuesta en forma de escala tipo Likert del 1 al 5. Tanto el cuestionario 1 como el cuestionario 2 se diseñaron en forma de pregunta y contrapregunta para mejorar la validez interna.

Fase de corrección de los cuestionarios preliminares

La versiones preliminares de los cuestionarios fueron evaluadas y corregidas por cuatro personas de diferente edad y diferente perfil académico: un filólogo y graduado superior en música menor de 30 años; un oncólogo, experto en comunicación clínica y humanización del proceso oncológico de entre 40-60 años; una doctora en economía y gestión de la innovación del mismo rango de edad; y una ama de casa con estudios básicos también de entre 40-60 años.

Se indagó en la corrección lingüística del cuestionario, la neutralidad en el modo de formular las preguntas, se hizo hincapié en que ninguna pregunta resultase hiriente o comprometida y se reformuló la versión preliminar para mejorar la compresión.

Fase de validación de los cuestionarios definitivos

Una vez establecido el diseño definitivo de los cuestionarios, se procedió a la fase de validación. Para ello, los cuestionarios fueron transferidos a un formulario de Google que se ofreció a una muestra poblacional aleatoria y variada, no necesariamente oncológica, en cuanto a criterios de edad, género, nivel de estudios, rama de estudios y lengua materna. Esta muestra incluyó a 115 voluntarios.

Se detectó un error de compresión en las preguntas 3 y 4 del cuestionario 2 relativo al paréntesis "(independientemente de si yo acepto o rechazo)". Algunos encuestados interpretaron erróneamente que el oncólogo iba a dejar pasar a la familia en el momento de la información o iba a informar a la familia aunque el paciente rechazara. Por ello, se simplificó lingüísticamente en la versión final; se eliminó el paréntesis y resultó de la siguiente forma:

- Cuestionario 2. Pregunta n.º 3: deseo que el oncólogo me ofrezca estar acompañado por mis familiares durante el proceso de información. Tras el ofrecimiento, yo decidiré si lo acepto o lo rechazo.
- Cuestionario 2. Pregunta n.º 4: deseo que el oncólogo se ofrezca a informar a mis familiares cuando estos no pueden asistir. Tras el ofrecimiento, yo decidiré si lo acepto o lo rechazo.

Por extensión se reformuló también la pregunta 14 del cuestionario 2, ya que la redacción era similar. Se eliminó el paréntesis "(independientemente de si quiero compartirlas o no)" y resultó de la siguiente forma:

- Cuestionario 2. Pregunta n.º 14: deseo que el oncólogo me pregunte abiertamente acerca de mis emociones. Tras ello, yo decidiré si quiero compartirlas o no.

Previo al análisis estadístico para la validación del cuestionario se recodificaron las contrapreguntas en escala Likert inversa.

Sobre las respuestas registradas empleando el programa IBM-SPSS, se realizó un análisis de fiabilidad y reproducibilidad (consistencia interna y estabilidad test-retest) y de validez del instrumento (validez de constructo, discriminante y criterio).

Análisis de consistencia interna

1. Cuestionario 1 (personalidad)

Alfa de Cronbach global para el cuestionario 1 = 0,731. No aumenta significativamente al eliminar preguntas.

Alfa de Cronbach por dimensiones (subgrupos de ítems):

1. Extrovertido/introvertido = 0,809. No aumenta al eliminar preguntas.
2. Realista/intuitivo = 0,619. Aumenta al eliminar la pregunta n.º 14 de forma no significativa a 0,650.
3. Previsor/espontáneo = 0,795. Aumenta de forma no significativa al eliminar la pregunta n.º 7 a 0,816.
4. Fiel a las ideas propias/complaciente = 0,580. Aumenta de forma no significativa a 0,595 al eliminar la pregunta n.º 21.

Dado que la eliminación de preguntas no aumenta de forma significativa la validez interna del cuestionario por dimensiones y la validez interna global es adecuada, no se realizan modificaciones en la versión definitiva del cuestionario n.º 1.

2. Cuestionario 2 (deseos)

Alfa de Cronbach global para el cuestionario 2 = 0,930. No aumenta significativamente al eliminar preguntas.

Alfa de Cronbach por dimensiones (subgrupos de ítems):

1. Importancia del entorno = 0,667. Aumenta al eliminar la pregunta n.º 4 de forma no significativa a 0,694.
2. Importancia de la percepción/invitación = 0,636. No aumenta al eliminar ítems.
3. Importancia del conocimiento = 0,723. No aumenta al eliminar ítems.
4. Importancia de las emociones = 0,881. No aumenta de forma significativa al eliminar ítems.
5. Importancia de la estrategia = 0,863. Aumenta de forma no significativa al eliminar la pregunta n.º 18 a 0,864.

Dado que la eliminación de preguntas no aumenta de forma significativa la validez interna del cuestionario por dimensiones y la validez interna global es adecuada, no se realizan modificaciones en la versión definitiva del cuestionario n.º 2.

Análisis de validez de constructo

1. Cuestionario 1 (personalidad)

Prueba KMO = 0,643; prueba de esfericidad de Bartlett significativa (p = 0,000).

Agrupa los ítems en cuatro componentes que explican el 52 % de la varianza:

- Componente 1 (15,4 % de la varianza): compuesto por los ítems que valoran la espontaneidad (preguntas n.º 18, 19 y 20) y se contraponen en la matriz a las preguntas que valoran la previsión (preguntas n.º 7, 8 y 9), diseñadas las unas como contrapreguntas de las otras.

- Componente 2 (12,7 % de la varianza): compuesto por los ítems que valoran la introversión (preguntas n.° 12 y 13) y se contraponen en la matriz a las preguntas que valoran la extroversión (preguntas n.° 1 y 2), diseñadas las unas como contrapreguntas de las otras.
- Componente 3 (12,2 % de la varianza): compuesto por los ítems que valoran el realismo (preguntas n.° 3, 4, 5 y 6) y se contraponen en la matriz a las preguntas que valoran el carácter intuitivo (preguntas n.° 14, 15, 16 y 17), diseñadas las unas como contrapreguntas de las otras.
- Componente 4 (11,7 % de la varianza): compuesto por los ítems que valoran la personalidad complaciente (preguntas n.° 21 y 22) y se contraponen en la matriz a las preguntas que valoran la fidelidad a las ideas propias (preguntas n.° 10 y 11), diseñadas las unas como contrapreguntas de las otras.

2. Cuestionario 2 (deseos)

   Prueba KMO = 0,797; prueba de esfericidad de Bartlett significativa (p = 0,000).

   Agrupa los ítems en cinco componentes que explican el 55,9 % de la varianza:

- Componente 1 (21,7 % de la varianza): compuesto por los ítems que en contra de la fase de estrategia (preguntas n.° 28-42) y se contraponen en la matriz a las preguntas que sí valoran la fase de estrategia (preguntas n.° 17-21), diseñadas las unas como contrapreguntas de las otras.
- Componente 2 (12,9 % de la varianza): compuesto por los ítems que valoran la fase de emociones (preguntas n.° 12-16) y se contraponen en la matriz a las preguntas en contra de la fase de emociones (preguntas n.° 33-37), diseñadas las unas como contrapreguntas de las otras.
- Componente 3 (10,0 % de la varianza): compuesto por los ítems que valoran la fase de conocimiento (preguntas n.° 8-11) y se contraponen en la matriz a las preguntas que en contra de la fase de conocimiento (preguntas n.° 29-32), diseñadas las unas como contrapreguntas de las otras.
- Componente 4 (6,8 % de la varianza): compuesto por los ítems que valoran la fase de entorno (preguntas n.° 1-4) y se contraponen en la matriz a las preguntas que en contra de la fase de entorno (preguntas n.° 22-25), diseñadas las unas como contrapreguntas de las otras.
- Componente 5 (4,3 % de la varianza): compuesto por los ítems que valoran la fase de percepción/incitación (preguntas n.° 5-7) y se contraponen en la matriz a las preguntas que en contra de la fase de percepción/incitación (preguntas n.° 26-28), diseñadas las unas como contrapreguntas de las otras.

Análisis de validez discriminante

En el diseño de los cuestionarios no hay ninguna variable establecida como discriminante. Por el contrario, la prueba piloto se ejecutó en personas aleatorias de diferente edad, nivel de estudios, rama de estudios y lengua materna. Ninguno reportó ausencia de compresión del cuestionario o dificultades en su realización.

Dado que se encuentra firmemente establecido que las vivencias personales, relacionadas a su vez con las diferencias de edad, el nivel de estudios o la rama de estudios, pueden forjar rasgos de la personalidad y la hipótesis del estudio es que estos a su vez influyen en la manera en la que deseamos que las malas noticias nos sean comunicadas, no es válido realizar en esta fase un análisis discriminante empleando dichas variables, sino que formará parte del análisis de resultados definitivo.

Se realizó un análisis de validez discriminante por lengua materna, empleando la prueba U de Mann-Whitney, y no se encontraron diferencias significativas (p > 0,05) en el porcentaje de puntuación de los diferentes dominios de los cuestionarios 1, 2 y 3.

Análisis de validez de criterio

No existe ningún cuestionario *gold standar* con el cual ejecutar el análisis de validez de criterio.

Análisis de validez de reproducibilidad

Para el análisis de reproducibilidad, se seleccionó aleatoriamente a un 10 % de la muestra (11 personas) que repitieron el cuestionario con cierto margen temporal (7 días) tras la realización del primer intento.

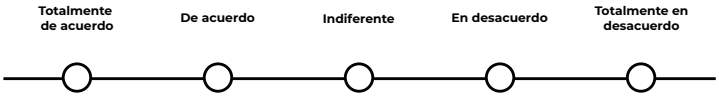
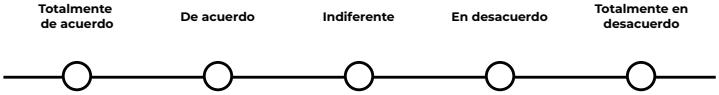
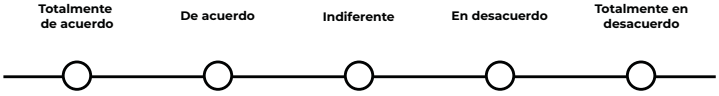
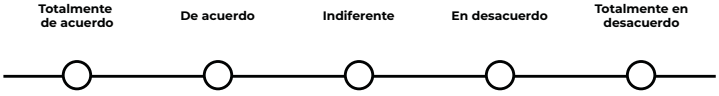
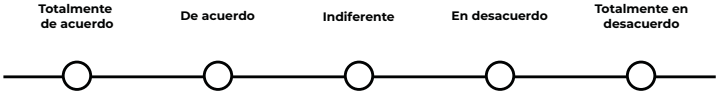
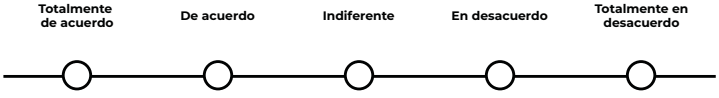
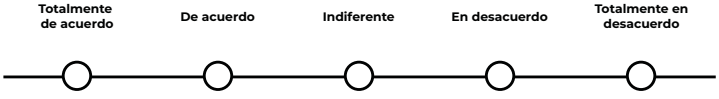
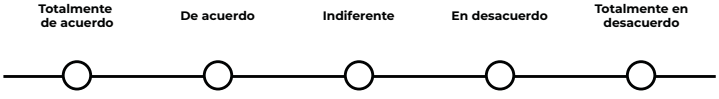
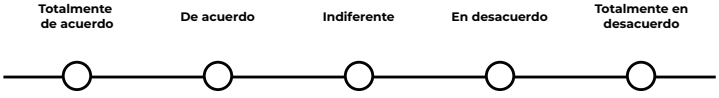
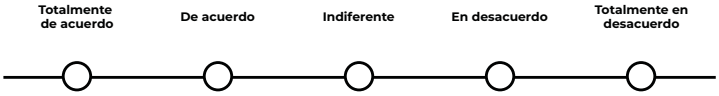
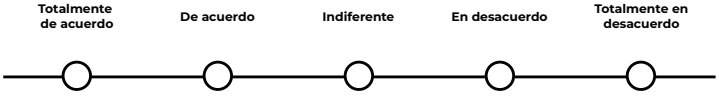
Para ejecutar el análisis de reproducibilidad mediante el coeficiente de correlación intraclase para medidas únicas, se calcularon los porcentajes de puntuación para cada uno de los dominios de los tres cuestionarios. Así mismo, se calculó la puntuación total en cada cuestionario obtenida como la suma del porcentaje obtenido en cada dominio. Se concluyó que la estabilidad test-retest era adecuada.

Cuestionario (Q) y Dominio (D)	Coeficiente correlación intraclase	IC 95 %
(Q)1 (D)Extroversión	0,92	0,73-0,97
(Q)1 (D)Realismo	0,90	0,67-0,97
(Q)1 (D)Previsión	0,98	0,95-0.99
(Q)1 (D)Fidelidad ideas propias	0,83	0,52-0,95
(Q)1 (D)Introversión	0,80	0,41-0,94
(Q)1 (D)Intuición	0,93	0,72-0,98
(Q)1 (D)Espontaneidad	0,91	0,69-0,97
(Q)1 (D)Complacencia	0,67	0,15-0,90
(Q)1 Puntuación total	0,82	0,48-0,95
(Q)2 (D)Entorno	0,92	0,74-0,97
(Q)2 (D)Percepción/Invitación	0,80	0,42-0,94
(Q)2 (D)Conocimiento	0,73	0,30-0,91
(Q)2 (D)Emociones	0,86	0,54-0,96
(Q)2 (D)Estrategia	0,91	0,73-0,97
(Q)2 (D)NO Entorno	0,68	0,19-0,90
(Q)2 (D)NO Percepción/Invitación	0,94	0,60-0,98
(Q)2 (D)NO conocimiento	0,74	0,29-0,92
(Q)2 (D) NO emociones	0,74	0,31-0,92
(Q)2 (D) NO estrategia	0,75	0,30-0,92
(Q)2 Puntuación total	0,66	0,16-0,89
(Q)3 (D)Evaluación	0,93	0,77-0,98
(Q)3 (D)Emociones negativas	0,90	0,69-0,97
(Q)3 Puntuación total	0,91	0,71-0,97

Anexo 2. Cuestionarios

CUESTIONARIO 1. CUESTIONARIO DE PERSONALIDAD

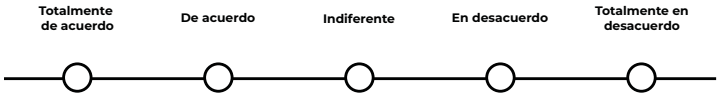
	Totalmente de acuerdo	De acuerdo	Indiferente	En desacuerdo	Totalmente en desacuerdo
1. Me considero una persona extrovertida, habladora.	○	○	○	○	○
2. Me gusta elaborar y compartir mis ideas con otros.	○	○	○	○	○
3. Soy realista, prefiero ver las cosas tal y como son.	○	○	○	○	○
4. Soy minucioso/a, a menudo me fijo en detalles concretos.	○	○	○	○	○
5. Soy práctico/a, no me gustan las ideas que no tienen una aplicación.	○	○	○	○	○
6. Cuando describo mis circunstancias, lo hago de forma detallada y ajustada objetivamente a la realidad.	○	○	○	○	○
7. Me gusta tener soluciones preestablecidas para mis problemas.	○	○	○	○	○
8. Necesito trazar planes detallados, sabiendo qué voy a hacer en cada paso, sin dejar espacio a la improvisación.	○	○	○	○	○
9. Prefiero conocer todas las variables que puedan interferir en mi plan y tener soluciones anticipadas planeadas para ellas.	○	○	○	○	○
10. Cuando tomo decisiones, lo hago priorizando mi escala de valores. Doy menos importancia a la opinión de los demás.	○	○	○	○	○
11. Es más importante que mis decisiones estén perfectamente argumentadas y tengan un sentido lógico que contar con la aprobación de los demás.	○	○	○	○	○

12. Me considero una persona tímida y reservada.	
13. Soy introspectivo/a, no comparto mis ideas con otros.	
14. Me gusta hacerme una idea general de la situación, sin entrar mucho en detalles.	
15. Tiendo a especular con las posibilidades de lo que podrá ser en vez de centrarme en el ahora.	
16. Me gusta perderme en mis pensamientos y abstraerme, aunque no saque conclusiones prácticas.	
17. Cuando describo las circunstancias, tiendo a darle un toque poético, emocional y narrativo.	
18. Dejo mis problemas fluir: las soluciones llegarán por sí solas.	
19. Mis planes son espontáneos y se modifican sobre la marcha.	
20. Soy flexible. No me preocupo sobre las variables que puedan interferir en mi plan. Si se presentan, ya veremos.	
21. Cuando tomo decisiones, me gusta consensuarlas con mis seres queridos.	
22. Priorizo complacer a la mayoría de los implicados, aunque eso suponga modificar mi decisión inicial.	

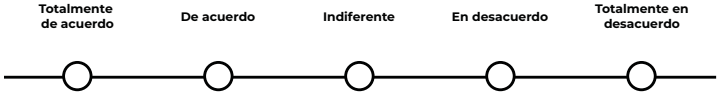
CUESTIONARIO 2. CUESTIONARIO DE DESEOS SOBRE EL PROCESO DE COMUNICACIÓN RELATIVO A LA INFORMACIÓN CLÍNICA EN ONCOLOGÍA

	Totalmente de acuerdo	De acuerdo	Indiferente	En desacuerdo	Totalmente en desacuerdo
1. Deseo que el oncólogo me informe en un ambiente tranquilo y sin interrupciones.	○	○	○	○	○
2. Deseo que me informe siempre el mismo oncólogo.	○	○	○	○	○
3. Deseo que el oncólogo me ofrezca estar acompañado por mis familiares durante el proceso de información. Tras el ofrecimiento, yo decidiré si lo acepto o lo rechazo.	○	○	○	○	○
4. Deseo que el oncólogo se ofrezca a informar a mis familiares cuando estos no pueden asistir. Tras el ofrecimiento, yo decidiré si lo acepto o lo rechazo.	○	○	○	○	○
5. Deseo que el oncólogo me pregunte hasta dónde quiero saber.	○	○	○	○	○
6. Deseo que el oncólogo me pregunte qué información he comprendido hasta la fecha para que, sobre eso, me pueda realizar las aclaraciones necesarias.	○	○	○	○	○
7. Prefiero que el oncólogo me cuente la información con suavidad, sin anticipar desde el inicio que lo que trae son malas noticias.	○	○	○	○	○
8. Deseo que el oncólogo comparta la información clínica conmigo con claridad, utilizando frases sencillas.	○	○	○	○	○
9. Deseo que el oncólogo priorice las ideas más importantes y modere la cantidad de información que me da.	○	○	○	○	○
10. Deseo que el oncólogo se asegure de que he entendido lo que me explica correctamente (aunque ello suponga que yo tenga que repetir al médico la información que me acaba de dar).	○	○	○	○	○
11. Deseo que el oncólogo emplee un lenguaje sencillo exento de tecnicismos.	○	○	○	○	○
12. Deseo que el oncólogo se muestre empático y se preocupe por mis sentimientos.	○	○	○	○	○
13. Agradezco que el oncólogo haga pausas durante el proceso de información y respete mis silencios.	○	○	○	○	○
14. Deseo que el oncólogo me pregunte abiertamente acerca de mis emociones. Tras ello, yo decidiré si quiero compartirlas o no.	○	○	○	○	○

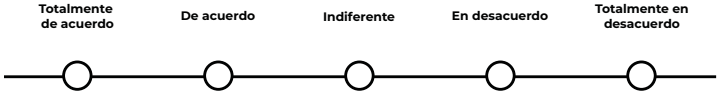
15. Deseo que el oncólogo me ponga una mano en el hombro si lo cree necesario.



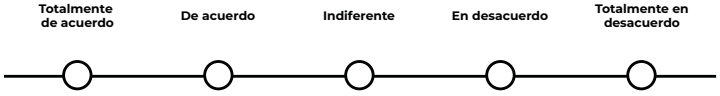
16. Deseo que el oncólogo me mire a los ojos mientras me da la información.



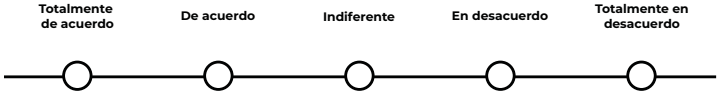
17. Deseo ser informado acerca de las diferentes opciones terapéuticas.



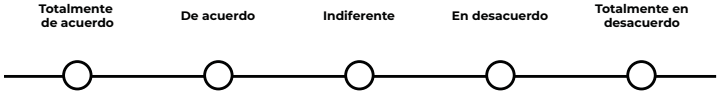
18. Deseo participar en la toma de decisiones respecto al tratamiento.



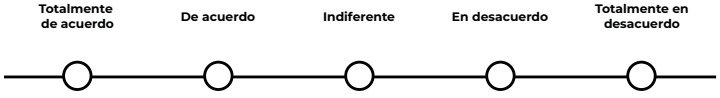
19. Deseo conocer los efectos de mi enfermedad oncológica sobre mis circunstancias vitales y que el oncólogo me ayude a encontrar soluciones.



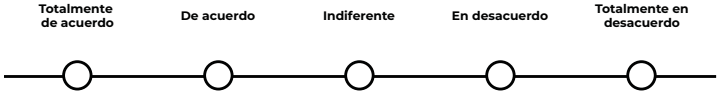
20. Deseo que el oncólogo me ayude a normalizar mi enfermedad en el núcleo familiar.



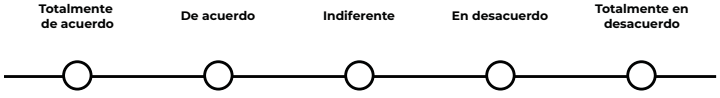
21. Deseo que me enseñen herramientas para normalizar la enfermedad oncológica con mis hijos.



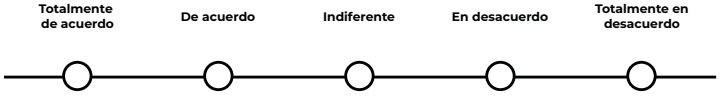
22. Cualquier lugar me parece bien para ser informado, incluso delante de otros pacientes. La enfermedad no es algo que ocultar.



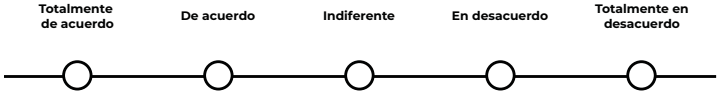
23. Me es indiferente qué oncólogo me informe, siempre y cuando conozca bien mi caso.



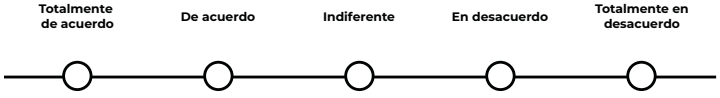
24. El dueño de la información sobre mi enfermedad soy yo. Por ello me molesta que el oncólogo me pregunte si deseo que mis familiares estén presentes en el momento de la información.



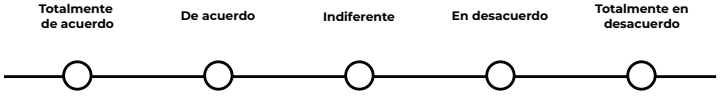
25. Me molesta que el oncólogo se ofrezca a llamar a mis familiares. Me hace sentir que duda de mi capacidad para comprender la información que me da.



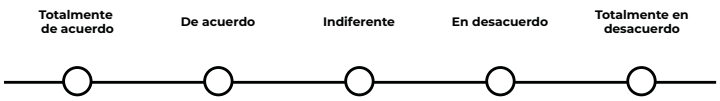
26. Es el oncólogo quien debe considerar cuánta información debe proporcionarme. No quiero que me pregunte cuánto deseo saber.

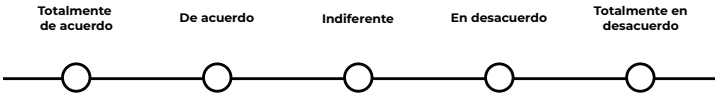
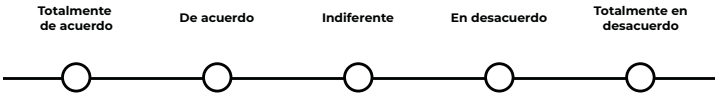
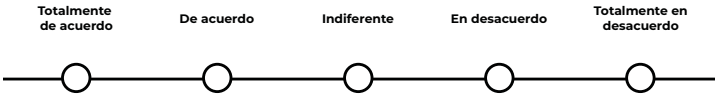
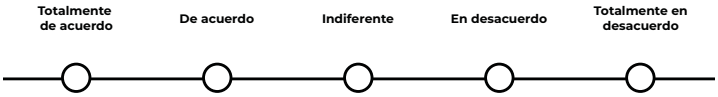
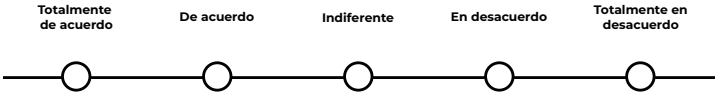
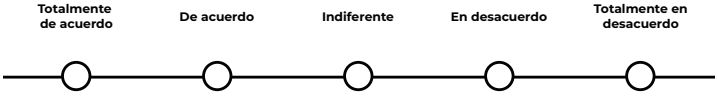
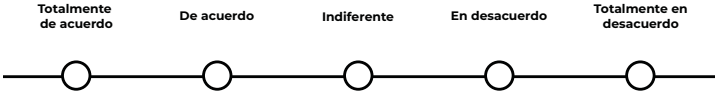
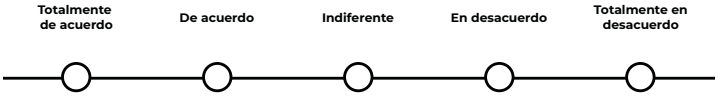
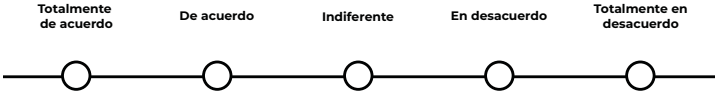
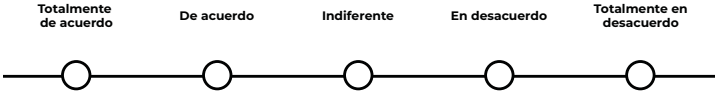
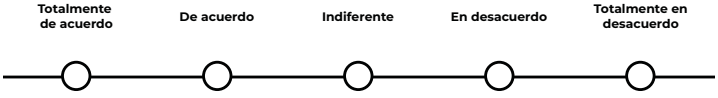
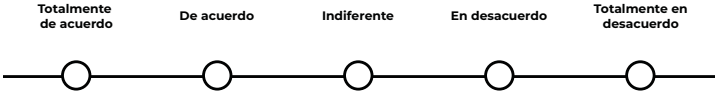
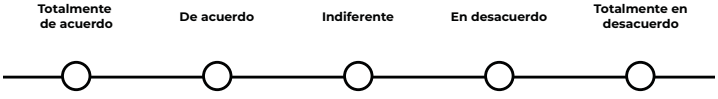
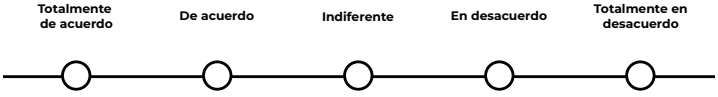


27. Que el oncólogo me pregunte qué sé hasta la fecha (para desde ahí completar la información) me parece un examen innecesario.



28. Prefiero que el oncólogo sea directo y me diga desde el inicio del encuentro que me tiene que dar malas noticias.



29. Me gusta que el oncólogo sea técnico cuando me informa. Que emplee las palabras que mejor definen mi proceso, aunque yo no entienda ese lenguaje. Ya buscaré lo que significan.	
30. Deseo que el oncólogo me informe con frases elaboradas que encadenen varias ideas para seguir mejor el razonamiento.	
31. Deseo que el oncólogo me informe absolutamente todo primero y no le quede nada por decirme. No tiene que protegerme dándome la información de manera progresiva.	
32. No deseo que el oncólogo me pregunte lo que he entendido porque me incomoda tener que explicarle al médico la información.	
33. La empatía no es una cualidad que desee en mi oncólogo. Con que sea bueno científicamente me vale.	
34. Me incomoda que el oncólogo haga pausas durante el proceso de información. No quiero dar pie a silencios.	
35. No deseo que el oncólogo me pregunte por mis emociones. Para mí son algo privado.	
36. No deseo contacto físico del oncólogo, independientemente de cuáles sean mis emociones.	
37. No deseo contacto visual con el oncólogo, me hace sentir incómodo.	
38. No deseo ser informado acerca de las diferentes opciones terapéuticas. Es el oncólogo el que debe decidir cuál es la mejor.	
39. No deseo participar en la toma de decisiones, prefiero que decida unilateralmente el oncólogo.	
40. No deseo conocer las repercusiones de mi enfermedad oncológica en mi vida diaria. No es algo que me preocupe.	
41. El oncólogo no debe preguntar por mi vida familiar ni preocuparse de cómo afecta mi enfermedad oncológica a mis allegados.	
42. No deseo ayuda del oncólogo para exponer mi situación oncológica a mis hijos.	

ONCOLOGÍA

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Article / Artículo

Survival in patients with stage IV breast cancer with systemic and surgical management

Supervivencia en pacientes con cáncer de mama estadio IV con manejo sistémico y quirúrgico

Fernanda Bravo[1], Elsa Vásquez[2], Arnon Oviedo[3], Fernando Herazo[4] and Javier Cuello[4]

1 Hospital Universitario San José, Popayán, Cauca
2 Departamento de Investigación de la Universidad CES, Medellín, Colombia
3 Clínica Nuevo Milenium, Tegucigalpa , Honduras
4 Departamento de Oncología Clínica de la Fundación Colombiana de Cancerología Clínica Vida, Medellín, Colombia

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ABSTRACT

Introduction: Systemic therapy is the standard treatment in patients with metastatic breast cancer at debut. However, combined therapy (systemic therapy plus local/locoregional surgery) is under investigation to determine if it offers additional benefit on oncologic outcomes. Randomized clinical trials (RCTs) have yielded contradictory reports regarding overall survival (OS), while retrospective studies show a favorable impact. This investigation aims to describe the OS and progression-free survival (PFS) of patients with metastatic breast cancer at debut, treated with systemic therapy only or combined therapy. **Materials and method:** A retrospective cohort study of patients with metastatic breast cancer at the debut treated in a specialized cancer care center in Colombia. Two groups were evaluated: EST vs CT, i.e., systemic therapy and breast surgery, respectively. The primary outcomes were PFS and OS, calculated using Kaplan-Meier survival functions and adjusted for confounding variables with Cox models. **Results:** 174 patients received EST, and 88 patients received CT. Median follow-up was 58.38 months; PFS was 38.56 months in the EST group vs 72.25 months in the CT group. OS was 42.4 months (95% CI 33.23-51.56) in the EST group vs. 82.33 (95% CI 62.1-102.55) in the CT group; both results were statistically significant for the surgical group. **Conclusion:** In patients with metastatic breast carcinoma at debut, OS and PFS were better in those treated with CT than in those managed with EST.

Keywords: Breast neoplasms, surgery, survival, therapeutics.

RESUMEN

Introducción: El manejo sistémico es el pilar del tratamiento en las pacientes con cáncer de mama metastásico al debut. Sin embargo, la terapia conjunta (sistémica con cirugía local/locorregional) es objeto de investigación para determinar si ofrece un beneficio adicional en los resultados oncológicos. Los ensayos clínicos aleatorizados tienen reportes contradictorios en cuanto a supervivencia global, mientras que los estudios retrospectivos muestran un impacto favorable. Esta investigación tuvo como objetivo describir la supervivencia global y la supervivencia libre de progresión de pacientes con carcinoma de mama metastásico al debut, tratadas con terapia sistémica exclusiva o terapia conjunta. **Materiales y método:** Estudio retrospectivo de una cohorte de pacientes con carcinoma de mama metastásico al debut de una clínica de referencia oncológica. Se evaluaron dos grupos de manejo: con terapia sistémica exclusiva vs. terapia conjunta. Los resultados principales evaluados fueron la supervivencia libre de progresión y la supervivencia global, calculados mediante las funciones de supervivencia de Kaplan-Meier y ajustados a las variables confusoras con modelos de Cox. **Resultados:** Recibieron terapia sistémica exclusiva 174 pacientes y 88 pacientes, terapia conjunta. La mediana de seguimiento fue de 58,38 meses; la supervivencia libre de progresión fue de 38,56 meses en el grupo de terapia sistémica exclusiva vs. 72,25 meses para el grupo de terapia conjunta. La supervivencia global fue de 42,4 meses (IC

*** Corresponding Author:** Fernanda Bravo, ferxi34@unicauca.edu.co

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95 % 33,23-51,56) en terapia sistémica exclusiva vs. 82,33 (IC 95 % 62,1-102,55) en terapia conjunta, ambos resultados estadísticamente significativos para el grupo quirúrgico. **Conclusión:** En pacientes con carcinoma de mama metastásico al debut, la supervivencia global y la supervivencia libre de progresión fueron mejores en los tratados con terapia conjunta que en los manejados con terapia sistémica exclusiva.

Palabras Clave: cáncer de mama, cirugía, supervivencia, tratamiento.

1. Introduction

It is estimated that 3-8% of patients diagnosed with breast cancer may be diagnosed with metastatic disease [1]. The standard treatment for these cases is systemic therapy with significantly improved OS and PFS, especially in patients with positive hormone receptors and/or HER2 [2,3].

Surgery has been conceived as a therapeutic approach aimed at relieving symptoms and preventing complications associated with the local progression of the disease [3]. However, it has also been suggested that it has a beneficial effect in prolonging patient OS through various mechanisms such as reduction of tumor load, elimination of cancer stem cells, reversal of tumor-induced immunosuppression, reduction in clonal heterogeneity, discontinuation of primary tumor self-seeding, interruption of multidirectional tumor cell movement between primary and distant tumor sites, and decrease in tumor promoter activities mediated by cancer stem cells [4].

As a result, the combined use of systemic therapy and surgical management in patients with stage IV breast cancer has been investigated. RCTs report contradictory results in terms of OS for those receiving both therapies [3,5-7], while retrospective studies, resulting from real-life experiences, show an improvement in this parameter [3,8-12]. It provides relevant evidence in therapeutic decision-making.

Our research aims to describe the OS and PFS of patients with early-stage IV breast cancer, who received CT and EST at a specialized cancer care center in Medellín - Colombia.

2. Methods

An observational retrospective cohort study was carried out using information from Fundación Colombiana de Cancerología Clínica Vida (FCCCV) database in Medellín, between 2013 and 2021. Data collection was carried out from 1 October 2022 to 15 January 2023. Data of individuals who met the inclusion criteria were recorded, so the sample corresponded to the total number of patients.

2.1. Patients

The inclusion criteria were: 1) Patients over 18 years of age with infiltrating stage IV breast cancer at diagnosis; 2) Histological confirmation of primary disease; 3) Clinical or imaging confirmation for metastatic disease; 4) Management with systemic therapy only and/or local or regional surgery, considering any type of breast or axillary surgery. 270 patients met the criteria and were reviewed. Exclusion criteria were considered as follows: medical histories with more than 10% of the data lost, stage IV disease by progression, pregnancy, lactation, metachronous breast cancer, and breast cancer as second primary.

2.2. Variables

The primary result was OS calculated from the start of treatment to the last follow-up or death from any cause. PFS was a secondary outcome calculated from the start of treatment to the date of last follow-up or at which progress was documented.

Variables were evaluated in two groups of patients: exclusive systemic therapy and combined therapy (systemic treatment plus breast and/or axillary surgery). Characteristics of individuals at the time of diagnosis were collected in both groups: age, menopausal status, and body mass index (BMI). The characteristics of the tumor were also recorded: histological type and grade molecular subtype,

tumor size, clinical and pathological classification of regional nodules according to TNM classification [13], site and number of metastases, date, and site of first progression.

The date of diagnosis was the one described in the first study that documented the disease remotely; if this information was not available, the date of the biopsy report; and, if none of the previous were available, the data provided in the institution's database. The date of progression of the disease for the first study was recorded. Finally, the cutoff date for assessing the OS was 8 January 2023 via the Adres platform (www.adres.gov.co/consulte-su-ep).

2.3. Statistical methods

A univariate analysis was carried out to characterize the study population. In the case of quantitative variables, the Kolmogorov-Smirnov normality test was applied to determine whether they presented averages or medians. Qualitative variables were determined using absolute and relative frequencies. Median survival was calculated using the Kaplan Meier curve.

For bivariate analysis, survival associations with each factor were calculated independently; for qualitative variables, chi square of independence; for quantitative variables, student's t-test or Mann-Whitney U test (quantitative – qualitative). The differences in covariable survival were calculated using the Logrank test.

A multivariate analysis was performed to measure the association between covariables and the event occurrence time using a Cox regression. A p value less than 0.05 was considered statistically significant.

As a sensitivity analysis of the possible effect of confounding by indication, a Propensity Score analysis was performed using a logistic regression model, estimating the expected effect throughout the sample. The probability difference is presented with its respective confidence interval.

All analyses were carried out by the STATA software version 16.1.

3. Results

A total of 270 patients met the inclusion criteria, eight cases with unknown start date were excluded, thus obtaining a final group of 262 patients: 174 receiving EST, and 88 receiving CT.

Characteristics of the disease are presented in Table 2. CT patients showed significantly more oligometastases and inflammatory tumors, while EST patients had significantly higher bone, pleural, liver metastases, and T4b tumors. The other characteristics were balanced.

Table 1. Demographic characteristics

Characteristic	Systemic treatment (N = 174)	Systemic + surgical treatment (N = 88)	P
Age, average ± Standard deviation	56.6 (13,4)	56.3 (14)	0.17
Menopausal status			
Premenopausal	48 (27.6)	26 (29.5)	0.77
Postmenopausal	122 (70.1)	61 (69.3)	
Unknown	4 (2.3)	1 (1.1)	
Body mass index			
Low weight:<18.5	18 (10.3)	6 (6.8)	0.19
Normal: 18.5 – 24.9	74 (42.5)	27 (30.7)	
Overweight25 – 29.9	45 (25.9)	29 (33)	
Obesity: > 30	17 (9.8)	14 (15.9)	
Unknown	20 (11.5)	12 (13.6)	

Table 2.

Characteristics	Systemic treatment (N = 174)	Systemic + surgical treatment (N = 88)	P
Laterality			
Unilateral	165 (94.8)	83 (94.3)	0.53
Bilateral	9 (5.2)	5 (5.7)	
Histological type			
Infiltrating ductal carcinoma	144 (82.8)	81 (92)	0.26
Infiltrating lobular carcinoma	13 (7.5)	5 (5.7)	
Mixed	2 (1.1)	0	
Other	5 (2.9)	0	
Occult carcinoma	3 (1.7)	0	
Unknown	7 (4)	2 (2.3)	
Histological grade			
1	17 (9.8)	8 (9.1)	0.15
2	73 (42)	32 (36.4)	
3	65 (37.4)	35 (39.8)	
Occult carcinoma	6 (3.4)	0	
Unknown	13 (7.5)	13 (14.8)	
ER status			
Positive	131 (75.3)	60 (68.2)	0.45
Negative	42 (24.1)	27 (30.7)	
Unknown	1 (0.6)	1 (1.1)	
PR status			
Positive	108 (62.1)	50 (56.8)	0.7
Negative	64 (36.8)	37 (42)	
Unknown	2 (1.1)	1 (1.1)	
Her 2 status			
Positive	34 (19.5)	19 (21.6)	0.82
Negative	138 (79.3)	68 (77.3)	
Equivocal, not FISH	1 (0.6)	0	
Unknown	1 (0.6)	1 (1.1)	
Ki 67, median + IQR	36.4 + 22	38.7 + 25.3	0.70
Subtype IHC			
Luminal A	30 (17.2)	15 (17)	0.16
Luminal B	85 (48.9)	31 (35.2)	
Triple negative	25 (14.4)	20 (22.7)	
Luminal-HER2	18 (10.3)	13 (14.8)	
HER2 positive	16 (9.2)	8 (9.1)	
Unknown	0	1 (1.1)	
Number of metastases			
<4	18 (10.3)	32 (36.4)	<0.001
>4	155 (89.1)	54 (61.4)	
Unknown	1 (0.6)	2 (2.3)	

Table 2. (Continued)

Metastatic site			
Bone	123 (70.7)	51 (58)	0.02
No	51 (29.3)	37 (42)	
Lung	59 (33.9)	27 (30.7)	0.35
No	115 (66.1)	61 (69.3)	
Liver	39 (22.4)	6 (6.8)	0.001
No	135 (77.6)	82 (93.2)	
NCS	6 (3.4)	2 (2.3)	0.46
No	168 (96.6)	86 (97.7)	
Distance	49 (28.2)	22 (25)	0.34
No	125 (71.8)	66 (75)	
Pleural	19 (10.9)	4 (4.5)	0.06
No	155 (89.1)	84 (95.5)	
Other	19 (10.9)	3 (13.6)	0.02
No	155 (89.1)	865 (96.6)	
Tumor size			
T1	4 (2.3)	2 (2.3)	0.02
T2	32 (18.4)	14 (15.9)	
T3	19 (10.9)	13 (14.8)	
T4a	2 (1.1)	5 (5.7)	
T4b	80 (46)	34 (38.6)	
T4C	5 (2.9)	3 (3.4)	
T4d	17 (9.8)	17 (19.3)	
TX	9 (5.2)	0	
Unknown	6 (3.4)	0	
Focality			
Unifocal	157 (90.2)	81 (92)	0.17
Multifocal	7 (4)	3 (3.4)	
Multicentric	3 (1.7)	2 (2.3)	
Multifocal and multicentric	0	2 (2.3)	
Occult	5 (2.9)	0	
Unknown	2 (1.1)	0	
Clinical N			
N1	58 (33.3)	29 (33.3)	0.16
N2	58 (33.3)	28 (31.8)	
N3	29 (16.7)	24 (27.3)	
N0	14 (8)	6 (6.8)	
Nx	8 (4.6)	0	
Unknown	7 (4.1)	1 (1.1)	

When evaluating the treatment characteristics, significant differences between groups were found in almost all the variables. Thus, CT patients presented significantly higher requirements for cytotoxic therapy, polychemotherapy, and the use of Anthracycline drugs with taxans. While patients with EST received significantly more endocrine therapy with aromatase inhibitors (AI) and the combination of AI with cyclin-dependent kinase inhibitor (CDKI). Radiation therapy was administered significantly more in the CT group. There were no differences between the groups regarding the use of anti-Her therapy and suppression of ovarian function. (Table 3).

Characteristics of surgical treatment are presented in Table 4.

Table 3. Characteristics of the treatment

Characteristics	Systemic treatment (N = 174)	Systemic + surgical treatment (N = 88)	P
Cytotoxic therapy			
Monochemotherapy	61 (35.1)	20 (22.7)	0.002
Polychemotherapy	70 (40.2)	56 (63.6)	
No CT/do not accept	43 (24.7)	12 (13.6)	
Chemotherapy drug			
Taxans	53 (30.5)	13 (14.8)	0.001
Anthracyclines	14 (8)	2 (2.3)	
Platinum	0	1 (1.1)	
Capecitabine	1 (0.6)	1 (1.1)	
Taxans and platinum	10 (5.7)	7 (8)	
Taxans y Anthracyclines	38 (21.8)	40 (45.5)	
Taxans and others	6 (3.4)	3 (3.4)	
Antracyclic and others	2 (1.1)	1 (1.1)	
Platinum and others	1 (0.6)	0	
Taxans, anthracyclines and platinum	3 (1.7)	3 (3.4)	
Others	3 (1.7)	6 (6.8)	
Do not require	43 (24.7)	11 (12.5)	
Endocrine Therapy			
Tamoxifen	16 (9.2)	17 (19.3)	0.01
Aromatase inhibitor	60 (34.5)	26 (29.5)	
Fulvestrant	4 (2.3)	5 (5.7)	
Cycline and aromatase inhibitor	37 (21.3)	6 (6.8)	
Cycline and fulvestrant inhibitor	2 (1.1)	0	
Fulvestran anastrozole	1 (0.6)	0	
Do not receive	11 (6.3)	4 (4.5)	
Do not require	43 (24.7)	30 (34.1)	
Suppression of ovarian function			
Surgical	19 (10.9)	7 (8)	0.47
Medicine	6 (3.4)	6 (6.8)	
Radiotherapy	3 (1.7)	3 (3.4)	
Do not receive	8 (4.6)	2 (2.3)	
Do not require	138 (79.3)	70 (79.5)	

Table 3. Characteristics of the treatment (Continued)

Anti HER2 Therapy			
Trastuzumab	10 (5.7)	10 (11.4)	0.4
Pertuzumab	2 (1.1)	0	
Tratuzumab + Pertuzumab	25 (14.4)	12 (13.6)	
Do not receive	1 (0.6)	0	
Do not require	136 (78.2)	66 (75)	
Locoregional radiotherapy			
Breast	7 (4)	2 (2.3)	<0.001
Breast and locoregional nodules	5 (2.9)	6 (6.8)	
Rib cage	0	8 (9.1)	
Rib cage and y locoregional nodules	0	9 (10.2)	
Axial	1 (0.6)	1 (1.1)	
Do not receive	156 (89.7)	35 (39.8)	
Unknown	5 (2.9)	27 (30.7)	
Radiotherapy to metastasis			
Yes	70 (40.2)	21 (23.9)	0.04
No	102 (58.6)	67 (76.1)	
Unknown	2 (1.2)	0	

Table 4. Surgical and systemic treatment characteristics

Characteristics	**Systemic + surgical treatment (N = 88)**
Average N positive by pathology	5.3 + 6.2
First management	
Systemic	78 (88.6)
Surgical	10 (11.4)
Cause of surgery	
Hygienic	24 (27.3)
Systemic but non-local response, albeit stable	21 (23.9)
Complete clinical response	11 (12.5)
No systemic or local response	1 (1.1)
Stable systemic disease and local progression	1 (1.1)
Others	10 (11.4)
Unknown	20 (22.7)
Type of Surgery	
Modified radical mastectomy	71 (80.7)
Simple mastectomy	2 (2.3)
Conservative surgery and axillary dissection	10 (11.4)
Conservative surgery	1 (1.1)
Conservative surgery and sentinel ganglion biopsy	2 (2.3)
Axillary dissection	2 (2.2)

4. Survival Analysis

The 262 patients provided a total of 6910.92 months of follow-up with an average of 58.38 months (range 48.6 - 68 months) and a median of 36.17 months (95% CI 26.91-45,42).

4.2. Progression-free survival

114 progression events occurred, 85 in the EST group and 29 in the CT group. The average PFS in the EST group was 38.56 months (range 29.89–47.24); while for the CT group it was 72.25 (rang 60.92.83.37), i.e., a statistically significant result (p<0.001) (Figure 1A).

PFS at the year of diagnosis was 79.6% (95% CI 72.2–85.2%) and 90.2% (95 % CI 81.4–95%); at 5 years of age 11.5% (4.6–21.8% CI 95%) and 54.6% (30.8–67.9%) for EST vs. CT, respectively.

4.3. Overall survival

118 deaths occurred, 92 in the EST group and 26 in the CT group. The median OS for the entire population was 48.63 months (95% CI 40.43-56.82): for the EST group, it was 42.4 months (93% CI 95% 33, 23-51.56); and for the CT group, 82.33 (95 % CI 62.1-102.55), i.e., a statistically significant difference (p<0.001) (Figure 1B).

OS at the year of diagnosis was 85.7% (CI 95 %: 79.4-90,2%) and 96.4% (CI 95%: 89.1-98.8%). After 5 years of follow up, OS was 30% with 95% CI 20.8-39.7% and 59.9% with 95% CI 44.5-72.2% for the EST group and the CT group, respectively.

4.4. Confounding Factor Adjustment

Based on the results of the study and data from the literature, we considered as confounding variables for adjustment: age, menopausal status, tumor size, site of metastasis, number of metastases, status of hormone and HER2 receptors, molecular subtype, cytotoxic and endocrine systemic management.

The PFS shows an unadjusted analysis with HR 0.34 CI 95 % 0.22-0.52 (p<0.001) and the OS of 0.33 CI 95% 0.21–0.52 (p <0.001) (Table 5).

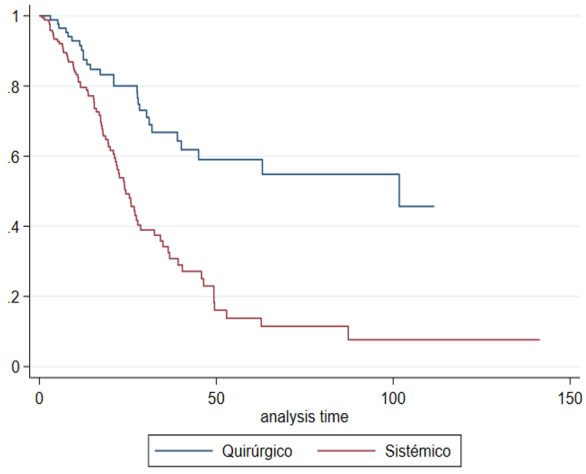

Fig. 1A. Progression free survival according to treatment group

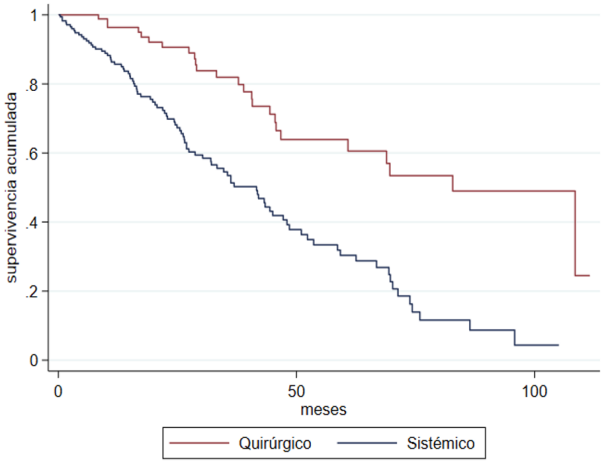

Fig. 1B. overall survival according to treatment group

The adjusted results can be seen in Table 6, showing that for both PFS and OS there is a statistically significant association in favor of CT. In the adjusted estimates, PFS showed a significant association with triple-negative subtype, the presence of liver metastasis and tumor size, T4b being of higher risk. Although T4a, T4d, and Tx showed significant results, the patient group for each of these categories was small and the confidence intervals wide. The same occurred with endocrine management and the use of CDKI and fulvestrant. As for the clinical staging of the nodules, confidence intervals for these categories were also wide.

In the adjusted estimates for OS, significant associations were found in luminal B subtypes, triple-negative, and tumor staging; however, when reviewing the confidence intervals, they were all very wide.

When the sensitivity analysis is carried out by the propensity score considering the characteristics that differed significantly between the groups by indication of treatment (pre-T, number of metastases, and site of the metastasis), the adjusted progression-free survival curves (Figure 2A) and global (Figure 2B) are drawn, and the significant difference in favor of joint management in terms of OS and PFS continues to be observed.

Table 5. Crude analysis of progression free survival and overall survival

	Observed estimate					
	Progression free survival			**Overall survival**		
	HR	CI95%	P value	HR	CI95%	P value
Type of treatment						
Systemic	Ref.			Ref		
Surgical + systemic	0.34	0.22 - 0.52	<0.001	0.33	0.21 - 0.52	<0.001

Table 6. Adjusted analysis of Progression free survival and Overall Survival

	Adjusted estimates							
	Progression free survival				**Overall survival**			
	HR	**CI95%**		**P value**	**HR**	**CI95%**		**P value**
Type of treatment								
Systemic	Ref.				Ref.			
Surgical + systemic	0.28	0.16 - 0.5	<0.001		0.23	0.13 - 0.43		<0.001
Molecular Subtype								
Her 2	Ref.				Ref.			
Luminal A	1.3	0.2	9.4	0.814	6.8	1.0	48.3	0.056
Luminal B	4.5	0.7	29.3	0.116	29.7	4.7	189.0	<0.001
Triple negative	3.5	1.3	9.1	0.010	13.3	4.9	36.1	<0.001
Luminal - Her 2	2.6	0.4	16.6	0.313	3.9	0.6	23.6	0.138
Liver Metastasis								
No	Ref.				Ref.			
Yes	2.2	1.2	4.0	0.009	1.6	0.9	2.7	0.078
Number of metastasis								
1-3 metastasis	Ref.				Ref.			
> 4 metastasis	2.4	1.2	4.8	0.016	1.7	0.9	3.3	0.117
Ct stage								
T1	Ref.				Ref.			
T2	5.2	1.4	19.5	0.015	6.3	1.2	33.3	0.030
T3	4.3	0.9	19.3	0.059	8.9	1.6	50.8	0.014
T4a	9.3	1.3	67.1	0.027	62.3	8.4	461.6	<0.001
T4b	4.7	1.2	18.2	0.023	10.8	2.1	56.7	0.005
T4c	34.2	5.6	207.9	<0.001	61.2	8.6	434.9	<0.001
T4d	4.5	1.2	17.9	0.030	10.7	2.0	57.6	0.006
Tx	15.1	2.1	108.4	0.007	4.2	0.3	51.4	0.263

Table 6. Adjusted analysis of Progression free survival and Overall Survival (Continued)

Cn stage								
Nx	Ref.				Ref.			
N1	8.8	1.7	47.1	0.011	1.3	0.3	6.1	0.774
N2	14.3	2.7	76.4	0.002	2.1	0.4	10.1	0.359
N3	20.1	3.5	114.0	0.001	1.8	0.3	9.1	0.487
N0	7.8	1.2	50.3	0.032	1.4	0.2	7.9	0.704
Type of chemotherapy								
Polychemotherapy	Ref.				Ref.			
Monochemotherapy	1.6	1.0	2.7	0.057	1.6	1.0	2.7	0.067
Did not receive	1.1	0.6	2.3	0.700	1.8	0.9	3.4	0.077
Initial endocrine therapy								
AI+ CDKI	Ref.				Ref.			
Tamoxifen	2.5	1.0	6.6	0.060	1.3	0.5	3.7	0.622
AI	2.3	1.0	5.3	0.052	1.8	0.8	4.2	0.176
Fulvestrant	3.5	1.0	11.9	0.042	2.7	0.8	9.2	0.111
CDKI +Fulvestrant	17.8	3.2	97.9	0.001	NE			
Fulvestrant + AI	NE				NE			

NE: Non estimable; Ref. reference category; AI: aromatase inhibitor; CDKI: Cyclin-dependent kinase inhibitors

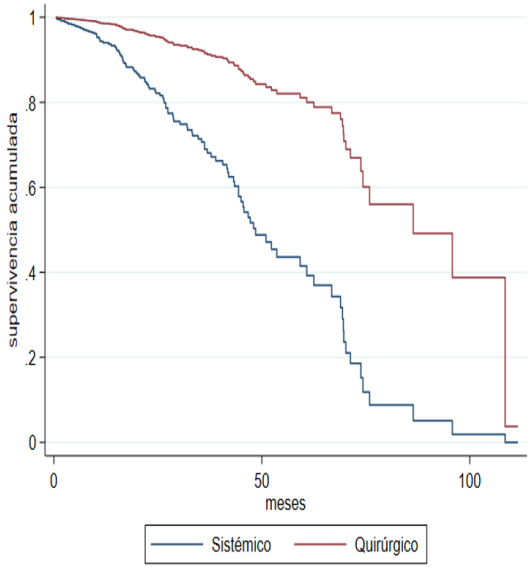

Fig. 2A. Adjusted Overall Survival

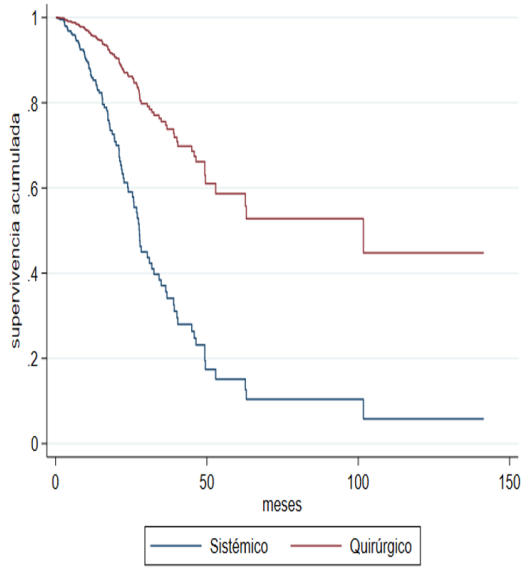

Fig. 2B. Adjusted Progression-Free Survival

5. Discussion

Stage IV breast cancer is a heterogeneous and incurable disease, its management is aimed at prolonging survival and palliation of symptoms, systemic therapy being the main pillar. However, multiple studies have been conducted to assess whether CT offers any additional benefit in oncological outcomes. The present study looked at this group of patients as well as those treated with EST.

Our study population had an average age of 56 years and a predominance of menopausal patients, consistent with what is in the literature. Nationally, Diaz and Cols had an average age of 58.8 years and a 62.9% postmenopausal [14]. And international studies, in general, report an average age of >50 years [1, 6-9, 15-18] and most menopausal patients [5, 7, 12, 17].

The main type of carcinoma in our cohort was the infiltrating subtype, moderate to high grade, hormone-positive, ductal, which is consistent with the global literature [6-9,11,14,17-19]. However, the triple negative subgroup, which has the lowest occurrence in various studies [6,7,12], took the second place in our cohort. Both in the literature and in our study, tumors were mainly classified at stage T4 [6, 8, 11, 14,16, 20]. Although, Soran and Cols [6] and Thomas and Colls [18] reported a higher frequency of small T2 stage tumors in their clinical trials.

Most of our patients received EST as in many of the retrospective studies [8, 11, 16-18]; this is supported by research results showing that surgical treatment is not associated with a higher rate of OS [1, 7, 12, 19]. It is important to note the clinical trial E2108 [7], where they randomized 256 patients to EST and CT, allowed the use of contemporary systemic therapies and showed the absence of effect on OS; thus, a better locoregional control in the CT group.

Our research showed that there were better results in OS and PFS in patients with CT, even after adjusting confounding variables. This is consistent with the findings of several retrospective descriptive studies and even an RCT [6, 8, 11, 12, 14-19]. The survival benefits of locoregional surgery in stage IV patients are supported in multiple hypotheses: some studies suggest that index lesion may behave as a reservoir of sick stem cells and removing it would decrease the likelihood of developing new sites of distant disease [21]. Resection of the primary tumor can increase angiogenesis by sensitizing it to chemotherapy and facilitating the entry of the drug into cancer cells [22,23]. Removing necrotic and tumor tissue eliminates chemoresistant tissues, restores host immunocompetence, and reduces growth of metastases [24, 25] thus resulting in increased patient survival [26]. Although there is the hypothesis that surgery in this group of patients may stimulate the progression of the disease by increased release of local growth factors [27], these can accelerate the proliferation of circulating tumor cells in peripheral blood and affect the OS and PFS [24, 25, 28-30].

In several studies [6, 8, 14, 17] including ours, hormone receptor status was as an independent prognosis factor, suggesting that tumor biology is important in survival. In contrast, there are also reports where sub-group tests of the hormone receptor status or HER2 show no benefit in OS [7].

Polymetastatic disease characterized our population as in a previous Colombian study [14] and in the RCT [1,6,7]. The metastatic pattern, both in number and location of distant disease, has also been identified as an independent and significant variable for patient survival outcomes [6,9-12,15,17]. Soran and Cols [6] identified that patients with solitary bone metastasis undergoing surgery had a significant benefit in OS compared to those who did not undergo surgery, although in their multivariate analysis, that association proved to be marginal. Rapiti and Cols [10] informed that the surgical effect on survival was not different for patients with bone metastases vs. other sites; however, after stratification, they observed a positive effect of surgery with negative margins in those who had bone metastases exclusively. Moreover, there are also studies where survival did not differ according to the treatment independent of the metastasis pattern [1, 7, 12]. For instance, Badwe and Cols [1] concluded that surgical management had no impact on patient survival, but also did not identify any subgroup of patients likely to benefit from locoregional treatment. Our study found a significant association, with worse PFS, in those patients who had liver metastases and metastasis number >4, whereas OS showed no association with these variables.

As in the literature, the most widely used systemic treatment in our population was chemotherapy [1-9, 12,15-18, 20]. Non-administration of systemic therapy, when indicated, occurs in some retrospective studies [8, 9, 14, 16, 17], including at the Tata Memorial Hospital in India [1]. In the RCT, treatment with taxans and antiHER2 was limited to only a small number of patients, thereby affecting their survival results. This is not our case, the patients received almost entirely the indicated therapies, allowing us to observe the real impact of local control on the patient's survival with protocol management.

Due to the retrospective nature of the study, one of its limitations is the lack of randomization and thus the possible bias of selection for the treatment groups, this would explain the beneficial effect in OS and PFS in patients receiving CT. Retrospective studies showed that patients who underwent surgery had better prognostic characteristics [30-33] and some had responded to systemic treatment, which could then be the causes of better survival and not the surgical procedure itself [12]. In our study, patients undergoing surgery had a higher tumor load; it was also observed that when grouping surgical indications, most of them presented a complete or partial response to systemic therapy, leading us to consider that the benefit would be associated with systemic treatment. Similarly, the sample size is low, which does not allow us to establish a clinical recommendation.

As for the clinical records, some patients lacked information about their management, most evident in the early years. However, those were excluded so that they did not affect the results

6. Conclusion

In patients with metastatic breast cancer at debut, the additional benefit that locoregional surgical management can offer is controversial. The higher quality RCT argues that locoregional control does not offer a better OS, while retrospective studies, resulting from real-life experiences, like our research, report a benefit with surgical management.

7. Abbreviations

RCTs: Randomized clinical trials

OS: overall survival

PFS: progression-free survival

EST: exclusive systemic therapy

CT: combined therapy (systemic and local/locoregional surgery).

FCCCV: Fundación Colombiana de Cancerología Clínica Vida

AI: aromatase inhibitors

CDKIs: cyclin-dependent kinases inhibitors

8. Administrative information

8.1. Additional Files

None declared by the authors

8.2. Acknowledgments

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8.3. Author contributions

FERNANDA XIMENA BRAVO: Conceptualization, validation, visualization, methodology, project management, writing: review and editing. **ELSA MARIA VÁSQUEZ TRESPALACIOS:** Conceptualization, validation, visualization, methodology, project management, writing: review and editing. **ARNON OVIEDO:** Conceptualization, validation, visualization, methodology, project management, writing: review and editing. **FERNANDO HERAZO MAYA:** Conceptualization, validation, visualization,

methodology, project management, writing: review and editing. **JAVIER MAURICIO CUELLO LÓPEZ:** Conceptualization, validation, visualization, methodology, project management, writing: review and editing. All authors read and approved the final version of the manuscript

8.4. Financing

The study was funded with the resources of each researcher.

8.5. Availability of data and materials

Data and materials are available upon request from the corresponding author. No other materials are reported.

8.6. Statements

8.6.1. Ethics committee approval

The protocol of this study was approved by the institutional committee of ethics of research in human beings of University CES (code Acta283Proy004) and Fundación Colombiana de Cancerología Clínica Vida. Since this is a retrospective study without any intervention in the care of the patients, no consent was required. Patient data were guaranteed to be anonymous and confidential.

8.6.2. Conflicts of interest

The authors declare that they have no conflict of interest.

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Article / Artículo

Epidemiological characterization of Hodgkin lymphoma in patients treated at the SOLCA - Guayaquil Hospital

Caracterización epidemiológica del Linfoma de Hodgkin en pacientes atendidos en el hospital de SOLCA - Guayaquil

Jhony Joe Real Cotto[1] *, Diego Ulises García Gamboa[2] and Juan Carlos Garcés Santos[2]

1 Universidad Católica Santiago de Guayaquil, Posgrado de Cuidados Paliativos, Guayaquil, Ecuador.
2 Hospital SOLCA – Guayaquil.

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ABSTRACT
Introduction: Hodgkin lymphoma is a disease in which malignant cells form in the lymphatic system; its presence in the population has been increasing in recent years. **Objective:** Epidemiological characterization of the Hodgkin lymphomas treated at the SOLCA - Guayaquil hospital during the period 2010–2021. **Material and methods:** A study was carried out with open data from a cross-sectional observational descriptive design of the new cases of Hodgkin Lymphoma diagnosed and treated at the SOLCA - Guayaquil hospital between 2010 and 2021. **Results:** Hodgkin lymphoma care at the SOLCA - Guayaquil Hospital went from 4% in 2010 to 12% in 2021. Hodgkin lymphoma with nodular sclerosis was mostly observed in men; however, by age group, it was more frequent in men between 0 and 19 years old (37.7%) and in women between 20 and 29 years old (45.3%) from the Guayas province. **Conclusions:** During this period, Hodgkin lymphoma has garnered more attention due to an increase in nodular sclerosis cases observed in men aged 0 to 19 and women aged 20 to 39, which aligns with the standard behavior of this disease.

Keywords: Hodgkin lymphoma, hematologic neoplasms, epidemiology.

RESUMEN
Introducción: El linfoma de Hodgkin es una enfermedad en la que se forman células malignas en el sistema linfático y que en los últimos años ha venido aumentando su presencia en la población. **Objetivo:** Caracterizar epidemiológicamente los linfomas de Hodgkin atendidos en el hospital de SOLCA - Guayaquil durante el periodo 2010-2021. **Materiales y métodos:** Se realizó un estudio de datos abiertos de diseño observacional, descriptivo, de corte transversal, de casos nuevos atendidos con linfoma de Hodgkin diagnosticados en el hospital de SOLCA Guayaquil, entre 2010 y 2021. Resultados: Las atenciones del linfoma de Hodgkin en el hospital de SOLCA Guayaquil fueron del 4 % en el 2010 y del 12 % en el 2021. Se tuvo sobre todo el linfoma de Hodgkin con esclerosis nodular, en hombres; los grupos etarios más frecuentes fueron hombres entre 0 y 19 años (37,7 %) y mujeres entre 20 y 29 años (45,3 %), procedentes de la provincia del Guayas. **Conclusiones:** Durante este periodo incrementaron las atenciones por linfoma de Hodgkin, en las que se observó más la esclerosis nodular en los pacientes, en hombres de 0 a 19 años y en mujeres de 20 a 39 años, similar al estándar de comportamiento de esta enfermedad.

Palabras Clave: Linfoma de Hodgkin, neoplasias hematológicas, epidemiología.

*** Corresponding Author:** Jhony Joe Real Cotto, realcottoj@gmail.com

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1. Introduction

Hodgkin lymphoma (HL) is a lymphoid tissue neoplasm. The damaged tissue comprises mono- and multinucleated cells surrounded by non-neoplastic inflammatory cells. Two histopathological subtypes are recognized: Classic and Nodular Lymphocytic Predominance [1] occurring in individuals of all ages; however, there are two peaks of occurrence (adolescents and over 60 years of age) and a slight predominance in men. HL accounts for about 10% of all lymphomas and 0.5% of all cancers in the United States of America [2]. The incidence has remained unchanged in recent decades. In 2020, there were 83,087 new cases registered worldwide per year, out of which 7091 cases corresponded to South America [3].

The overall incidence, age of occurrence, and even survival vary in different geographic areas [4,5,6], and the incidence of subtypes is affected by geography and socioeconomic factors [5]. Although the specific causes of these discrepancies are unknown, describing HL's epidemiological characteristics helps to clarify this behavior. Reports from Latin America have shown a lower incidence at an earlier age of onset and lower survival compared to Caucasian populations [4,7,8]. In Ecuador, the clinicopathological characteristics of adult HL were described in 2007; and are contrasted the epidemiological data of this study are compared with data from the last 11 years [6,9,10].

This study provides the epidemiological characteristics of patients diagnosed with HL treated at a national referral cancer center from 2010 to 2021. In addition, we describe the local incidence, trends over time, age characteristics, place of origin, and distribution based on histopathological subtypes to help clarify geographical differences and determine a baseline for future research.

2. Material and methods

A cross-sectional descriptive observational design study was carried out at the SOLCA (Sociedad de Lucha Contra el Cancer), Guayaquil. This is a private non-profit oncology institution for public benefit. It has comprehensive and partial agreements for the provision of services with different institutions of the Ecuadorian Network of Comprehensive Health Care (RPIS) and has been established as a reference center at the national level.

The study included patients of all ages with a diagnosis of HL, who were treated between 2010 and 2021, constituting the total population. Data were obtained from the institution's hospital tumor registry, identified by the ICD 10 coding: C81 (HL). Patients who lacked the necessary epidemiological information were excluded.

The demographic variables were sex, age at diagnosis, histopathological subtype, and province of origin. For data analysis, Microsoft Office 2010 Excel spreadsheets, SPSS v.29 license were used. Descriptive statistics were used to summarize the study variables, reported in frequencies and percentages. Continuous variables such as age are reported with medians and ranges. A trend analysis was performed to assess the annual percentage, and the most common types of neoplasms in both sexes in 2021 were identified to determine the incidence of HL.

Regarding ethical aspects, the study was carried out with open data and was authorized by the research committee of SOLCA Guayaquil.

3. Results

Of the different types of neoplasms treated at the SOLCA Hospital in 2021, HL is in 16th place in frequency, corresponding to 1.67% of the total cases (Fig. 1).

We obtained 870 patients with ICD 10 C81 from the hospital registry; 646 patients with a diagnosis of HL, treated between 2010 and 2021, were included in the study. We excluded cases whose complete data were not available (Fig. 2).

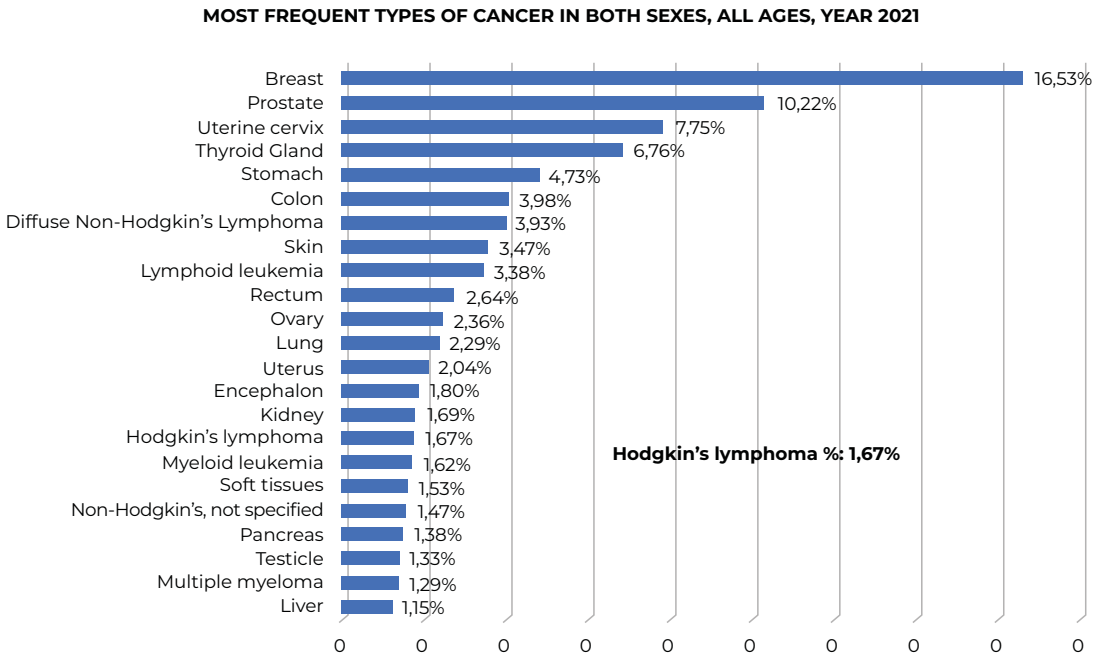


Figure 1. Most frequent types of cancer in the SOLCA - Guayaquil hospital, period 2021.

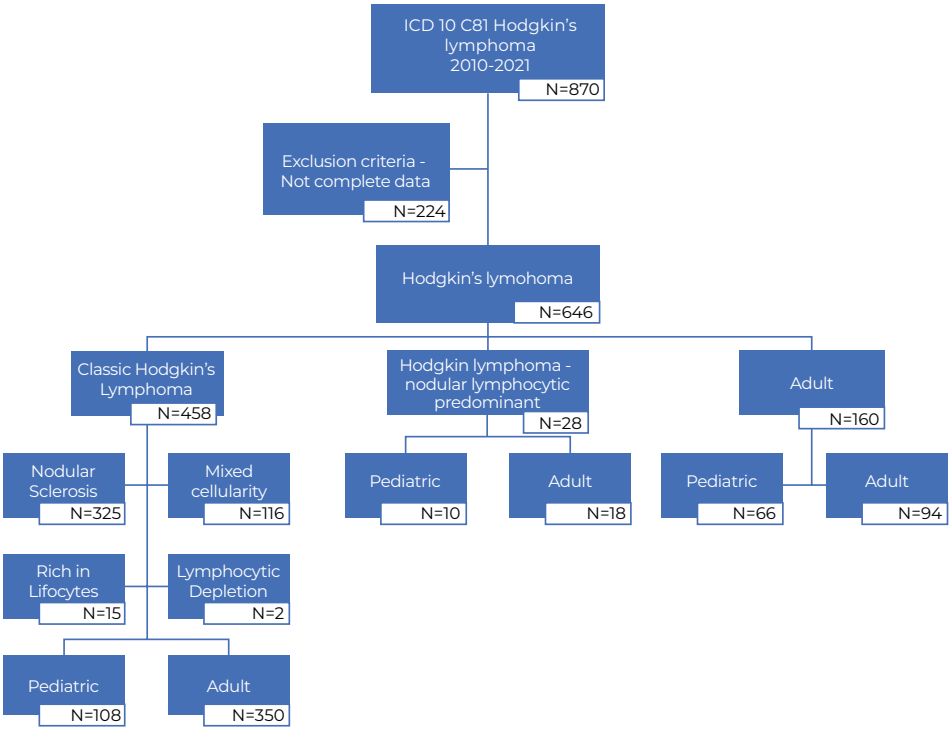


Figure 2. Flow diagram.
Source: SOLCA Hospital - Guayaquil

Table 1 shows the epidemiological characteristics of the patients treated for Hodgkin lymphoma according to histological subtype, sex, age of occurrence, and the three central provinces of origin (see complete map in Fig. 3).

Figure 4 illustrates the trend in the care of HL patients at the SOLCA - Guayaquil hospital during the study period, distinguishing between patients who received partial care through any service, and those who received specific oncological treatment at the institution.

Table 1. Clinical and demographic characteristics of patients with Hodgkin lymphoma treated at SOLCA - Guayaquil hospital.

Characteristics		**N**	**%**
	Total	**646**	**100**
Histological subtype	Hodgkin lymphoma (classic)		
	Nodular sclerosis	325	50,3
	Mixed Cellularity	116	18,0
	Rich in Lymphocytes	15	2,3
	Lymphocytic depletion	2	0,3
	Nodular lymphocyte-predominant Hodgkin lymphoma	28	4.3
	Hodgkin lymphoma, unspecified subtype	160	24.8
Gender	Male	371	57.4
	Female	275	42.6
Median age in years (range)	27 (2-95)		
Age of occurrence	Adults	462	71.52
	Pediatric*	184	28.48
Province	Guayas	375	58.05
	Manabí	77	11.92
	Los Ríos	57	8.82
	Other 15 provinces	137	21.20

* Pediatric: age up to 17 years old.

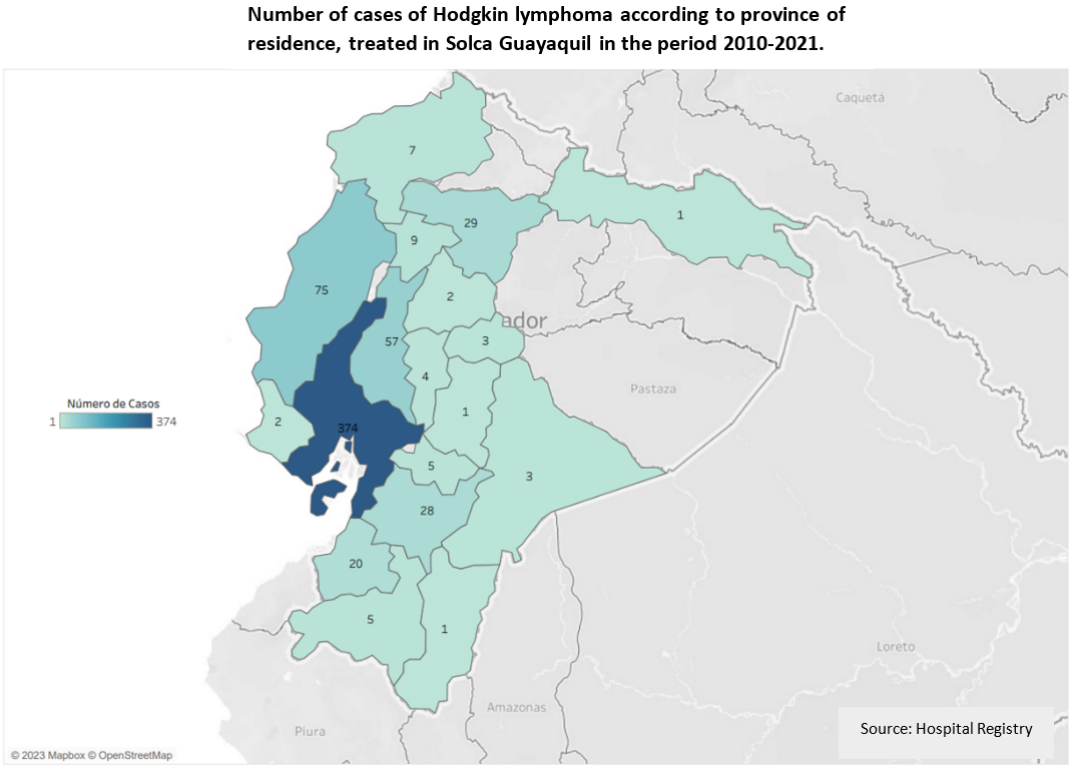
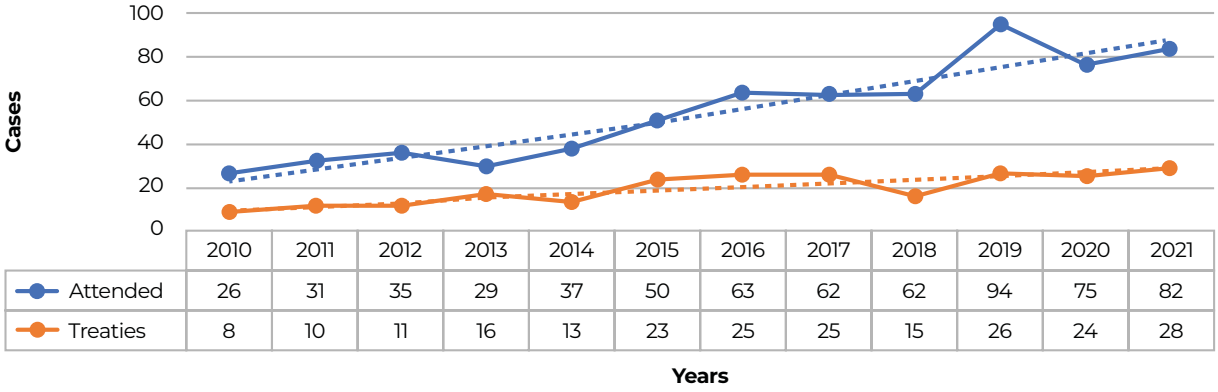


Figure 3. Origin of cases of HL lymphoma in the SOLCA - Guayaquil hospital.

The median age of disease occurrence was 26 years, with a greater number of patients diagnosed in adulthood. Within the epidemiological characteristics of age group and sex in patients with Hodgkin lymphoma, the highest proportion was observed in men in the group of 0–19 years, with 37.7%; while in women it was the group from 20–29 years, with 45.5% (Fig. 5).



	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Attended	26	31	35	29	37	50	63	62	62	94	75	82
Treaties	8	10	11	16	13	23	25	25	15	26	24	28

Figure 4. Trend of patients treated for Hodgkin lymphoma at the SOLCA - Guayaquil hospital, 2010 – 2021.

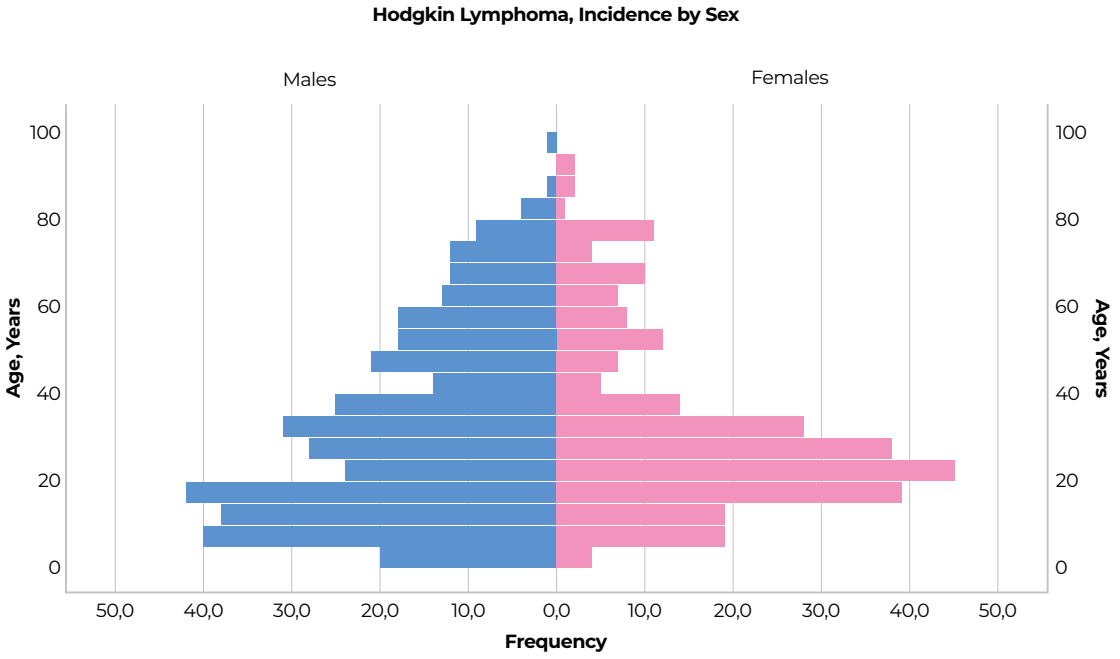


Figure 5. Incidence according to sex and age.
Source: SOLCA - Guayaquil.

4. Discussion

In this study, the proportion of Hodgkin lymphoma in 2021 and its behavior between 2010 and 2021 were obtained. It should be noted that the SOLCA - Guayaquil Hospital is a reference institution for cancer patients and provides services to the public and private health network. The most frequent province of origin was Guayas, with approximately three out of every five patients. A percentage increase in care has been observed annually since 2010 with 4.0%, 2016 with 9.8%, and 2021 with 12.7%. The highest proportion was recorded in 2019 with 14.6%. This may be due to greater health coverage and better public policies.

Furthermore, Hodgkin lymphoma with nodular sclerosis was the most frequent with 50.3%. This figure is maintained over time in the institution as shown by the 10-year study carried out from 1998 to 2007, which reports a frequency of 51.4% for this histological subtype [11]. Likewise, at the Comandante Pinares hospital in the period 2007-2017, nodular sclerosis subtype was the most frequent with 35.3% of cases mostly in men [12]. Also, this research aligns with the findings of the Institute of Hematology and Immunology of Cuba, which found that Hodgkin lymphoma with nodular sclerosis was the most common type of lymphoma in men, representing 64% of cases [9]. Similarly, the AD study in the State of Pará, Brazil, showed that nodular sclerosis was the most common type in men 64% [13]. In the same way, the HL study in western Paraná, Brazil, showed that the nodular sclerosis type was the most frequent in men (64.6%) [14].

In addition, the higher proportion observed in men in the 0-19 years age group is very similar to that of the HL study in western Paraná, Brazil, which indicated they were mostly men (52%) older than 10 years (75%) with a diagnosis of nodular sclerosis (48%) [15].

5. Conclusions

Hodgkin lymphoma with nodular sclerosis is the most common type Hodgkin lymphoma in patients treated at the SOLCA - Guayaquil hospital during this study period, particularly in men from 0 to 19 years of age and women from 20 to 39 years of age. This situation is similar to the world literature on the behavior pattern of this disease.

6. Limitations

While this study could not explain the incidence of Hodgkin lymphoma in Guayaquil, it provided valuable information on the distribution by age, sex, and other aspects of the disease. The results open the door to further research to better understand the incidence of Hodgkin lymphoma in the city and to develop more effective prevention and control strategies.

7. Abbreviations

HL: Hodgkin lymphoma

SOLCA: Sociedad de Lucha Contra el Cáncer

RPIS: Red Pública Integral de Salud

ICD 10: International Classification of Diseases

8. Administrative information

8.1. Additional Files

None stated by the authors

8.2. Authors contribution

Diego García Gamboa: Validation, methodology, project management, review. **Jhony Real Cotto:** Conceptualization, project administration, methodology, script: review and edition. **Juan Garcés Santos:** Conceptualization, validation and review. All authors read and approved the final version of the manuscript.

8.3. Financing

None.

8.4. Availability of data and materials

Data are available upon request to the corresponding author. No other materials are reported.

8.5. Statements

This manuscript has not been previously published, nor is it currently under editorial review for publication in another journal.

8.5.1. Ethics committee approval

Open or public data were used for this research.

8.5.2. Conflicts of interest

The authors declare no conflict of interest.

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Article / Artículo

Calcifying fibrous pseudotumor of the neck in a teenager female patient: case report

Pseudotumor fibroso calcificante de cuello en una paciente adolescente: reporte de caso

Marco Fabricio Bombón[1,2] and Emilio Criollo Vargas[1]

1 Head, Neck and Otorhinolaryngology Surgery Service. SOLCA – Guayaquil, Ecuador.
2 Postgraduate in Surgery, SOLCA - Guayaquil. Espiritu Santo University of Specialties, Guayaquil, Ecuador.

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ABSTRACT
Introduction: Calcifying fibrous pseudotumor is a benign soft tissue tumor, appearing mainly in children and young adults between 20 and 30 years of age, still without a clear and defined etiology. It has a variable body distribution, being relatively uncommon in the neck. **Case report:** We present the case of a 17-year-old teenager female patient with a fast-growing neck tumor; its manifestation was moderate localized pain, excessive snoring, and progressive respiratory distress. **Treatment:** Complete resection of the tumor located in the hypopharynx was performed, which confirmed the histopathological and immunohistochemical diagnosis of calcifying fibrous pseudotumor. **Conclusion:** Calcifying fibrous pseudotumor of the neck is a benign pathology, rare, with non-specific symptoms, and most probably by the tumor compressing the surrounding tissues. Surgical resolution remains the gold standard for treatment. The prognosis after resection is good in the long term, with low recurrence rates. The diagnostic and therapeutic approach in this teenage patient is discussed compared to that described in the literature.

Keywords: Calcifying fibrous pseudotumor, psammomatoid calcifications, benign neck tumor, cervical tumor, teenager.

RESUMEN
Introducción: El pseudotumor fibroso calcificante es un tumor benigno de tejidos blandos que aparece principalmente en niños y adultos jóvenes entre 20 y 30 años de edad, aún sin una etiología clara y definida. De distribución corporal variable, siendo relativamente poco común en el cuello. **Caso clínico:** Se presenta el caso de una paciente adolescente de 17 años con tumor en el cuello de rápido crecimiento que se manifestó con dolor moderado localizado, ronquido excesivo y dificultad respiratoria progresiva. **Tratamiento:** Se realiza resección completa del tumor localizado en hipofaringe, la cual confirma el diagnóstico histopatológico e inmunohistoquímico de pseudotumor fibroso calcificante. **Conclusión:** El pseudotumor fibroso calcificante de cuello es una patología benigna rara, con síntomas inespecíficos y muy probablemente, inducida porque el tumor comprime los tejidos circundantes. La resolución quirúrgica sigue siendo el Gold estándar (GS) en cuanto al tratamiento. El pronóstico postresección es bueno a largo plazo, con tasas bajas de recurrencias. Se discute la aproximación diagnóstica y terapéutica en un paciente adolescente comparado con lo descrito en la literatura.

Palabras Clave: DeCS: Pseudotumor fibroso calcificante, calcificaciones psamomatoides, tumor benigno del cuello, tumor cervical, adolescente.

*** Corresponding Author:** Marco Fabricio Bombón, fabri.bombonpm@gmail.com

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1. Introduction

Calcifying fibrous pseudotumor is a rare benign soft tissue tumor with distinctive histologic features [1]. It is characterized histologically by abundant collagenized tissue, with a focal lymphoplasmacytic infiltrate and psammomatous and dystrophic calcifications [2]. It is more frequent in children and young adults [3]. They are found in numerous body sites, most often in the gastrointestinal tract or subcutaneous soft tissue; however, they are relatively uncommon in the neck [1]. The cause and pathologic mechanisms are unknown [3]. In most cases a single lesion is described, although there are cases of multiple lesions. Its diagnostic approach is clinical and by imaging. It is necessary to have a histopathological specimen to confirm the diagnosis [4]. The aim of this article is to report the case of a calcifying fibrous pseudotumor in the neck of a teenager patient.

2. Case Report

We present the case of a 17-year-old teenager female, with no significant pathologic history, who presented an apparent neck tumor causing moderate pain, excessive snoring for about 4 months and that was worse in recent weeks accompanied by progressive respiratory distress. No neurological or digestive symptoms or signs were evidenced. The patient initially underwent a CT scan of the face and neck, without a definitive diagnosis, which reported paratracheal and retrotracheal tumor with calcifications inside, displacing and partially obliterating the larynx and trachea with regular contours measuring 4 x 11 cm.

On physical examination, there was an increase in cervical volume occupying the entire central topography of the neck, soft to palpation. The oropharynx was palpable bulging, totally compromised by a hard tumor.

2.1. Diagnostic workshop

The patient was evaluated by the Head and Neck Surgery Department, under the presumptive diagnosis of tumor of uncertain behavior of the neck, some complementary examinations were requested, including paraclinical laboratory studies, nasofibrolaryngoscopy, CT of the face, neck, thorax, and ultrasound-guided cytopuncture of cervical tumor.

In the paraclinical laboratory studies, it was evidenced that the hemogram, blood biochemistry, coagulation times performed in the Clinical Laboratory Department of SOLCA-Guayaquil, all stayed in normal parameters.

The nasofibrolaryngoscopy showed tumor of nasopharynx limit with oropharynx, which occupies the entire oropharynx and reaches the hypopharynx, thus displacing the larynx towards the anterior. Due to the size of the mass, it is not possible to access the supraglottis.

The report of the CT of the face and neck with intravenous contrast identifies tumor lesion of defined contours, heterogeneous with soft tissue density and irregular calcifications inside, measuring 69 mm in its major axis in axial plane and 117 mm in its major axis in sagittal plane, with no enhancement after intravenous contrast. On its former margin it contacts and compresses the pharynx, larynx, esophagus and thyroid gland, predominantly in the left lobe. Its later margin involves the prevertebral space, without apparent infiltration of vertebral foramina or bony structures, its lateral margins contact and displace the carotid and jugular veins, without causing infiltration of them. Permeable nasopharynx, with preserved morphology, oropharynx occluded almost completely by the described tumor lesion, no cervical adenopathies are observed (Figure 1).

Chest CT reports: cervical prevertebral tumor lesion, extending to the thoracic operculum, displacing the thyroid anteriorly without infiltrating it and deforming the posterior wall of the trachea, compressing the esophagus.

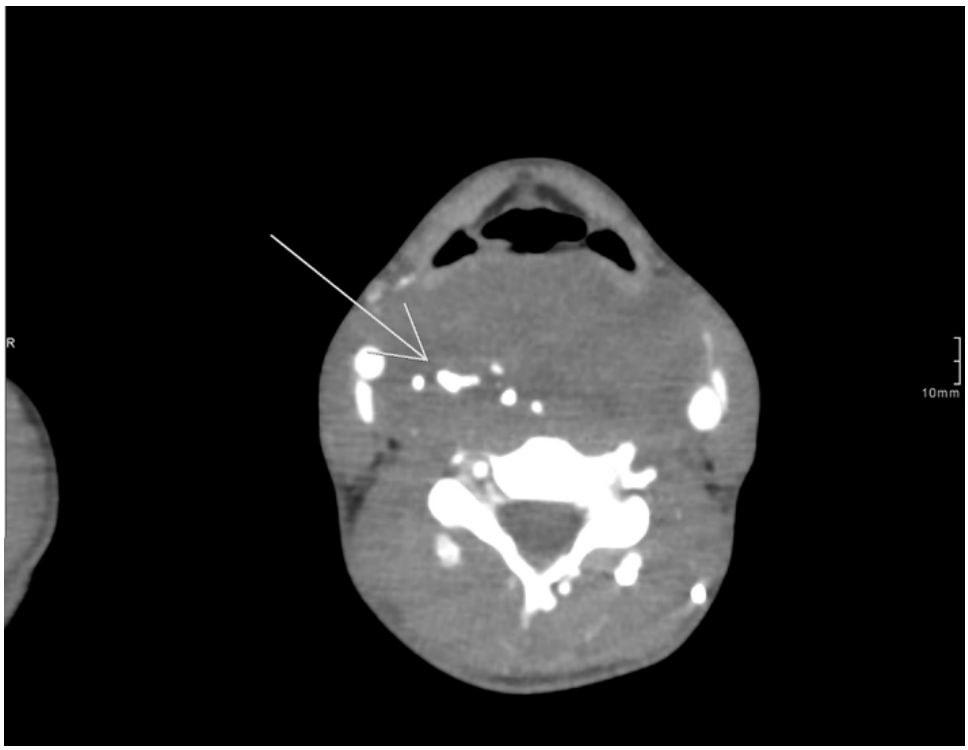

Figure 1. Axial CT scan of face and neck with intravenous contrast with evidence of tumor lesion of defined contours, heterogeneous with soft tissue density and calcifications inside, no enhancement after intravenous contrast.
Source: Department of Radiology and Imaging. SOLCA - Guayaquil

Ultrasound-guided cytopuncture of cervical tumor was neither assessable nor conclusive, since the sample consisted exclusively of erythrocytes with traces of hemolysis and scattered leukocytes. Subsequently, the patient was evaluated with the results of complementary examinations and when the patient did not have a conclusive pathological or cytological result and presented the initial symptoms with apparent exacerbation of the clinical picture (respiratory distress); it was decided to perform open tracheostomy + incisional biopsy of the oropharynx, as a prophylactic measure in case of a probable obstructive picture in the short or medium term.

The procedure is performed without apparent complications and the biopsy result reports paucicellular fibroblastic/myofibroblastic proliferation with spindle cells without significant atypia immersed in a dense collagenous matrix, accompanied by sporadic lymphocytes and scarce psammomatous calcifications. No areas of necrosis, anaplasia or elevated mitotic activity suggestive of malignancy are identified. The findings are suggestive of calcifying fibrous pseudotumor. Immunohistochemical findings rule out fibromatosis and KI:67 demonstrates a very low cell proliferation index.

In this context, the present case is evaluated and reviewed by the skin, sarcoma and soft tissue committee; subsequently by the pathology committee, who after a thorough and exhaustive analysis recommend increasing the immunohistochemical tests, which are detailed in Table 2.

The IHC tests confirmed the diagnosis of calcifying fibrous pseudotumor, with IgG4 positivity. Therefore, in view of the results, surgical resection was decided as the only treatment option. A face, neck and thorax MRI with contrast was requested to complement the imaging findings previously described and in order to define the morphological and anatomical characteristics of the lesion and its relationship with adjacent structures, as well as for the selection of the best surgical technique (Figure 2).

Table 2. Immunohistochemical findings. Source: Department of Pathology.

IHQ Test	Result
B CATENINA	Negative
SOX 10	Focal positivity in myofibroblasts
KI 67	1 %
ANTI-ALPHA SMOOTH MUSCLE ACTIN 1A4	Positive perivascular and in myofibroblasts
S 100	Negative
SYNAPTOPHYSIN	Negative
CHROMOGRANIN	Negative
CD-117	Negative
CD-34	Positive

Source: Departamento de Patología. SOLCA - Guayaquil

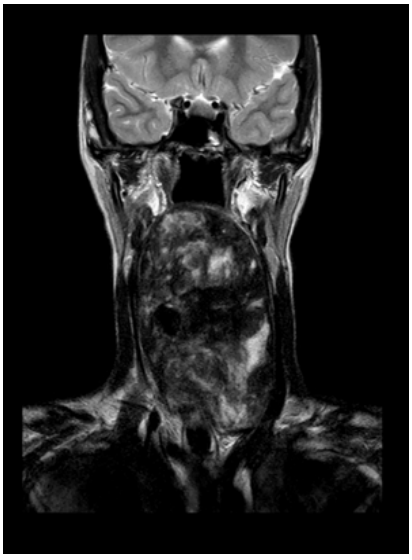

Figure 2. Simple and with contrast axial MRI of face and neck with evidence of extraluminal solid tumor mass in the oropharynx and hypopharynx space, which secondarily obliterates the lumen.
Source: Department of Radiology and Imaging. SOLCA - Guayaquil

The MRI of the face and neck reports: tumor lesion of solid aspect in the space of the oropharynx and hypopharynx, measuring 112 x 66 x 37 mm in its major axes, which secondarily obliterates its light in relation to its histopathological diagnosis of fibrous pseudotumor. Cervical adenopathies of probably inflammatory characteristics in levels I, II, and III there are adenopathies of preserved morphology, the largest measuring 8 mm. Inflammatory process in maxillary sinuses, sphenoidal and ethmoidal cells.

2.2. Treatment and evolution

The patient underwent an exploratory cervicotomy + left lateral dissection + tumor excision; the surgical procedure lasted 4 hours, with an approximate bleeding of 600 ml. A bilateral enlarged cervical incision was performed, finding intraoperatively a tumor in the hypopharynx region, with oval macroscopic characteristics, smooth surface, measuring approximately 8 x 10 cm (Figure 3). In addition, during the surgery, a left cervical lymph node level III, yellowish brown of elastic consistency, measuring 1.2 x 1 cm was isolated; left lateral dissection was performed. The vascular and nervous structures, such as parathyroid and recurrent laryngeal nerve were preserved.

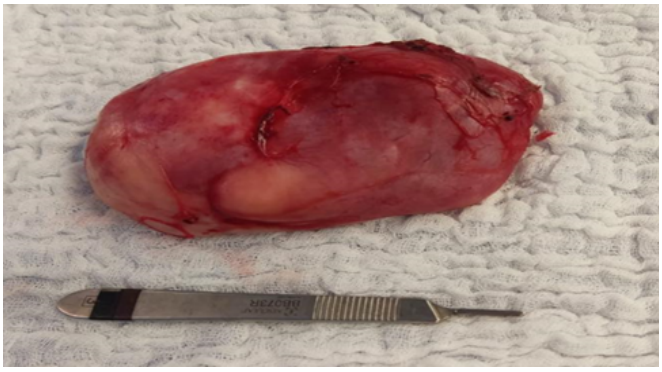

Figure 3. Intraperitoneal findings of hypopharyngeal tumor excision. Source: Solca-Guayaquil. Source: SOLCA - Guayaquil.

The pathology and immunohistochemical report of the surgical specimen indicated calcifying fibrous tumor.

The pathology study of the resected cervical lymph node revealed lymph node with sinusoidal histiocytosis, negative for malignancy.

Total excision of the calcifying fibrous pseudotumor of the hypopharynx was performed, without intraoperative complications, and there were no complications in the postoperative period. The patient was discharged 72 hours after surgery, with little bleeding due to the drains placed during surgery, which were removed after medical discharge, maintaining the tracheostomy, which was functional and in good condition. After the first week, the patient attended outpatient control in the Head and Neck area, where functioning tracheostomy, surgical wound in good healing process, no signs of infection, with relative improvement of the initial symptomatology were observed. Nasofibroscopy was performed and it reported good mobility of both cords. Respiratory exercises were indicated for eventual decannulation. The following week a successful decannulation was performed. Finally, an appointment was made for subsequent controls with results showing a sealed scar and no tumor recurrence. As this type of tumor is benign, the patient does not receive specific oncologic adjuvant treatment.

3. Discussion

The current WHO classification, since 2002, uses the term "calcifying fibrous tumor or pseudotumor" to describe a rare benign mesenchymal lesion [1,14]. Currently, the pathogenesis is uncertain. Possible etiologies include previous infection, trauma or surgical intervention [2].

This type of lesion is characterized by having a defined boundary, lacking a capsule and presenting a wide range of sizes. Microscopically, they present densely hyalinized hypocellular collagen with psammoma or dystrophic calcification and mononuclear inflammatory infiltrate [3,14]. It has been described mainly in children and young adults between 20 and 30 years of age, with little predisposition in women, even without a well-defined cause [4,5].

Calcifying fibrous pseudotumor has been documented in various anatomic locations, such as serosal surfaces, solid and tubular organs, and soft tissues [6]. The most frequently involved sites are the stomach (18%), small intestine (8.7%), pleura (9.9%), neck (6.2%), peritoneum (6.8%), mediastinum (5%), and mesentery (5%) [7]. In this context, there are very few neck cases reported in the literature, as most studies are sporadic case reports, with little or no symptomatology [1].

Patients usually have no specific symptoms, and when they have, these are atypical and most likely induced by the tumor compressing surrounding tissues. Tumors are often detected incidentally during imaging examinations or surgery [8].

Laboratory examination proved to be not so helpful in the diagnosis of calcifying fibrous pseudotumor [5]. The diagnosis is morphologic; therefore, immunohistochemistry could be of use in the differential diagnosis. The spindle cells are strongly and diffusely positive for Vimentin and Factor XIIIa and rarely positive for smooth muscle actin (SMA). Fibrous tumor immunoreactivity for CD34 has

been variably reported in the literature. An IgG:IgG4 ratio has been described in the plasma population, thus suggesting a potential association between IgG4-related disease [7,9].

The treatment of choice and best outcome for calcifying fibrous pseudotumor is surgical removal. Scientists agree that this type of tumor should be removed at the time of diagnosis. Few recurrences and no related deaths are reported [9]. However, other investigators suggest treatment with corticosteroids, but excision of radical tumors by surgery is the main method of treatment because postoperative histopathology and immunohistochemistry allow a definitive diagnosis to be obtained [10,12]. There are 2 types of excision recommended in the literature: open surgical excision and endoscopic excision. Open surgical resection or excision was performed in most cases; laparoscopic or minimally invasive surgery was also used in some cases [9,11]. CT and MRI provide a three-dimensional reconstruction of the lesion and define the morphologic features and their relationship to adjacent structures, which is important for surgical planning [1]. However, while imaging can play an important role in the diagnosis of many lesions, in this type of tumor particularly, the final diagnosis depends on the microscopic examination of the tissue performed in the histopathology study [1,5].

Cases of malignant transformation have not been reported in the literature [13]. Globally, studies have identified that in most cases no recurrences or metastases were observed, except in a few patients, including pediatric patients under 3 years of age, where there was a small recurrence within their follow-up period [15]. The prognosis is usually good with minimal associated morbidity and no reported mortality [13,15].

It is important to determine that the final and definitive diagnosis of calcifying fibrous pseudotumor is made among several similar entities, such as fibromatosis, synovial sarcoma, desmoplastic fibroblastoma, tendon sheath fibroma; exclusively with histological and immunohistochemical studies. Other studies dedicated to the identification of the exact pathogenesis of the tumor and evaluation of the age distribution of occurrence should also be performed to avoid misdiagnosis and unnecessary treatment [15].

4. Conclusions

Calcifying fibrous pseudotumor is a rare pathology, very difficult to diagnose, especially in teenager patients, such as the one in our clinical case. Symptomatology is nonspecific and the location variable, surgical management remains the cornerstone of treatment, with low recurrence rates and has a good long-term prognosis.

This particular case highlights the importance of considering calcifying fibrous pseudotumor as an entity to be taken into account when demonstrating cervical tumors under study, especially in teenager patients with non-specific symptoms. At present, since there are few cases described in the literature, appropriate diagnostic and therapeutic approach will allow proposing, evaluating, and following up future clinical cases as multicenter studies because these are huge opportunities for future medical research

5. Abreviaturas

IHC: Immunohistochemistry.

CT: Computed Axial Tomography

MRI: Magnetic Resonance Imaging

6. Administrative Information

6.1. Additional files

None declared by the authors.

6.2. Acknowledgments

We thank the patient and her family, who agreed to the dissemination of this scientific work.

6.3. Authors' contributions

Marco Fabricio Bombón Caizaluisa: Conceptualization, data curation, formal analysis, acquisition of funds, research, writing - original draft. **Emilio José Criollo Vargas:** Conceptualization, data curation, formal analysis. All authors read and approved the final version of the manuscript.

6.4. Funding

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6.5. Availability of data and materials

Data are available upon request from the corresponding author. No other materials are reported.

6.6. Statements

6.6.1. Informed consent

The patient's legal guardians gave written informed consent for publication of this case report and accompanying images. The Editor-in-Chief of this journal keeps a copy of the written consent for review.

6.6.2. Conflicts of Interest

The authors declare no conflicts of competence or interest

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Case Report / Caso Clínico

Gastric Schwannoma: A Case Report

Schwannoma gástrico. Reporte de un caso

Darío Montes N.[1], Nixon Cevallos R[2] and Rubén Montes N[3]

1 Gastroenterology Department, SOLCA Núcleo Machala, El Oro, Ecuador.
2 Oncology Department, SOLCA Núcleo Machala, El Oro, Ecuador.
3 Internal Medicine Department, Dr. León Becerra Camacho General Hospital, Milagro, Guayas, Ecuador.

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ABSTRACT
Introduction: Schwannomas are benign, slow-growing, Mesenchymal Tumors (MT) that originate in the Schwann cells of the nerves of the Meiisner and Auebarch plexuses. Although they can appear in any location, they are rare in the gastrointestinal tract (GIT). **Case report:** Our case is the presentation of a gastric Schawnnoma with favorable evolution and a good prognosis after a complete resection. **Conclusion:** It is relevant to present this to keep it in mind in the differential diagnosis of subepithelial gastric tumors.

Keywords: Gastric Schwannoma, Gastrointestinal stromal tumors, Immunohistochemistry.

RESUMEN
Introducción: Los schwannomas son tumores mesenquimatosos benignos de crecimiento lento, se originan en las células de Schwann de los nervios de los plexos Meiisner y Auebarch. Aunque pueden aparecer en cualquier localización, son poco frecuentes en el tracto gastrointestinal. **Caso clínico:** Nuestro caso es la presentación de un schawnnoma gástrico con evolución favorable y buen pronóstico tras su resección completa. **Conclusión:** La importancia de presentarlo radica en tenerlo presente en el diagnóstico diferencial de los tumores gástricos subepiteliales.

Palabras Clave: Schwannoma gástrico, Tumores del estroma gastrointestinal, Inmunohistoquímica.

*** Corresponding Author:** Darío Javier Montes Nájera, javiermontesn89@gmail.com

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1. Clinical case

A 61-year-old female with a medical history of type 2 diabetes mellitus treated with hypoglycemic agents. No family history of cancer. She presents dyspepsia with clinical symptoms of postprandial distress syndrome, evolving for one year without alarm signs. No abnormalities were found in her lower digestive tract and hepatobiliary system. Physical examination: Good general condition. Abdomen: Soft, depressible, not painful, no masses, no visceromegaly, and the rest of the physical examination showed no irregularities.

In the blood tests, no deviations were observed.

(Figure 1). Computed Tomography (CT) of the Abdomen and Pelvis, there is evidence of thickening of the gastric antrum wall associated with an exophytic growth tumor, measuring 79 x 84 x 88 mm. Enlarged lymph nodes are observed in the hepatic hilar region, celiac trunk, and peripheral areas

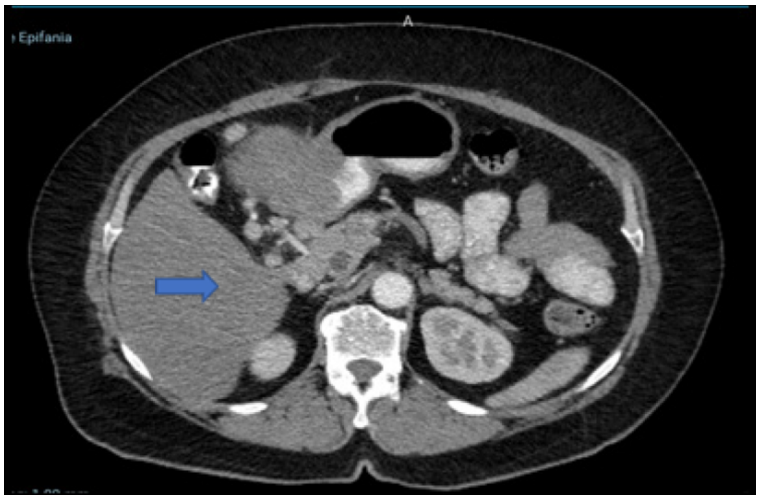

Figure 1. Computed tomography (CT) abdomen-pelvis
Source: Hospital SOLCA Núcleo Machala

Upper Endoscopy (EGD): At the level of the antrum, on the greater curvature, there is a 4 cm subepithelial lesion covered with mucosa, suggesting a Gastrointestinal Stromal Tumor (GISTs) based on its appearance (Figure 2).

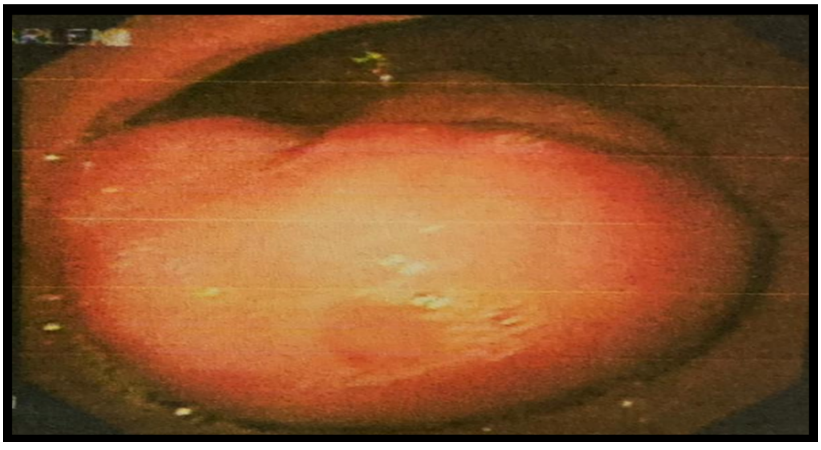

Figure 2. Subepithelial lesion in the antrum, seen on upper endoscopy
Source: Hospital SOLCA Núcleo Machala

An endoscopic ultrasound was performed: In the antrum, a hypoechoic lesion measuring 3 x 4 cm originates in the fourth layer (muscularis propria). It appeared heterogeneous with anechoic areas inside and irregular contours. A 19 G ACQUIRE needle puncture of the lesion is performed for pathological examination (Figure 3).

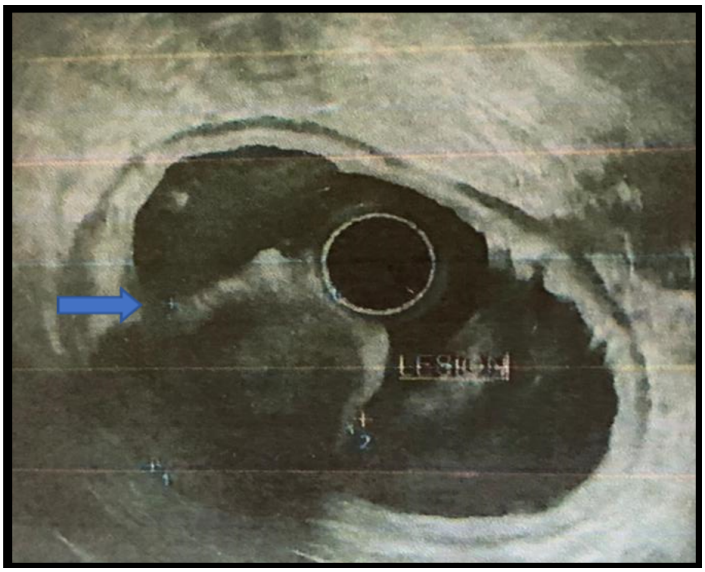

Figure 3. Subepithelial lesion in the antrum, seen on endoscopic ultrasound
Source: IECED GUAYAQUIL (Instituto Ecuatoriano de Enfermedades Digestivas)

The histopathological report describes infiltration of polymorphonuclear neutrophils and mononuclear leukocytes, as well as a fragment of smooth muscle with a neoplastic appearance formed by smooth, fusiform, bipolar muscle fibers with oval nuclei that preserve the nucleocytoplasmic ratio. Immunohistochemistry (IHC) reveals S100 positivity and desmid positivity, while Smooth Muscle Actin, CD34, and CD117 (c-Kit) are negative. This establishes the diagnosis of Gastric Schwannoma (GS).

As definitive treatment, open surgery is performed: Subtotal gastrectomy. Anatomopathological report: Gastric Schwannoma with perigastric lymph nodes showing reactive follicular hyperplasia. In the 24-month follow-up, the patient remains asymptomatic regarding digestive symptoms.

2. Discussion

Gastrointestinal subepithelial tumors are divided into 3 main groups: Neurogenic (schwannomas, neurofibromas), myogenic (leiomyomas and leiomyosarcomas), and GISTs. Differential diagnosis is crucial as they differ in prognosis [3].

Schwannomas are slow-growing benign mesenchymal tumors that originate from Schwann cells of the Meissner and Auerbach plexuses. They are uncommon. Their most common location in the gastrointestinal tract is the stomach (at the greater curvature and antrum), followed by the colon and rectum [3, 5].

Gastric Schwannomas are rare, having a frequency of 0.2% among all gastric tumors, 6.3% of mesenchymal gastric tumors, and 4% of benign gastric tumors. They are more prevalent in women, with a male-to-female ratio of 1:3 and an average age at diagnosis of 57 years [6,12].

The clinical presentation of Gastric Schwannomas can vary greatly. Most are asymptomatic and are diagnosed incidentally. Symptomatic patients often present with abdominal pain, followed by upper gastrointestinal bleeding. Less frequently, they may present with a palpable abdominal mass (3%), loss of appetite (anorexia) (3%), or dyspepsia (1.8%) [6].

Upper Endoscopy (EGD) and the biopsies obtained from it have low yield.4 They often reveal sessile subepithelial tumors covered with mucosa of normal appearance and exophytic growth.7 Endoscopic ultrasound identifies a hypoechoic lesion, either homogeneous or heterogeneous, often with a marginal halo, located in the fourth layer and sometimes in the third layer. Fine-Needle Aspiration (FNA) is the initial diagnostic method, providing a diagnosis in 85.2% of cases. However, in instances where the obtained tissue is insufficient or nonspecific, core needle biopsy may yield better results [3, 8].

Another diagnostic tool used is contrast-enhanced CT, which shows a heterogeneously hypervascular tumor that enhances with contrast, with areas of necrosis. However, radiological findings are nonspecific and are often described as gastrointestinal stromal tumor [7, 13].

Histologically, Gastric Schwannomas are encapsulated tumors containing abundant spindle cells with a prominent lymphoid aggregation characterized by Antoni A and Antoni B areas. Shah AS et al 9. demonstrated that the diagnosis can only be confirmed based on immunohistochemistry (IHC), where GS shows positivity for S-100, vimentin, and glial fibrillary acidic protein, and negativity for CD117 and Smooth Muscle Actin (SMA) [3, 9, 10, 15].

Regarding treatment, surgery is the only curative treatment for GS, and the specific type of procedure depends on the size and location of the lesion. Both conventional and laparoscopic techniques have shown satisfactory results. Lymph node resection is not necessary as SMA rarely presents lymphatic spread or malignant transformation. Endoscopic options are not viable in most cases as the lesion usually arises from the Auerbach plexus, and growths tend to involve the entire muscular layer. The recurrence rate is very rare, so surveillance is not required [7, 10, 14].

3. Conclusions

Schwannomas are benign, slow-growing, mesenchymal tumors that originate in the Schwann cells of the nerves of the Meiisner and Auebarch plexuses. They are uncommon in the gastrointestinal tract. They should be taken into consideration in the differential diagnosis of subepithelial lesions detected during endoscopy.

4. Abbreviations

MT: Mesenchymal Tumors

GIT: Gastrointestinal Tract

CT: Computed Tomography

GIST: Gastrointestinal Stromal Tumors

IHC : Immunohistochemistry

GS: Gastric Schwannomas

SMA: Smooth Muscle Actin

EGD: Esophagogastroduodenoscopy

5. Administrative information

5.1. Additional Files

None declared by the authors

5.2. Acknowledgments

None.

5.3. Author contributions

Conceptualization, methodology, project administration, supervision and writing-draft/original: Darío Montes N. Formal analysis, visualization, writing – review and editing: Nixon Cevallos R. Investigation and validation: Rubén Montes N. All the authors read and approved.

5.4. Funding

The authors did not receive any funding for this research.

5.5. Availability of data and materials

The data are available upon request to the corresponding author.

5.6. Statements

5.6.1. Consent for publication

Written informed consent for the present study was obtained from the patient.

5.6.2 Conflicts of Interest

The authors declare no conflicts of interest.

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