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Editorial / Editorial

Evolution of Lung Cancer Management

Evolución del manejo del cáncer de pulmón

Dr. Jorge Moncayo Cervantes

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Lung cancer is the malignant neoplasm with the highest incidence worldwide according to the 2022 Globocan [1]. Of all malignant neoplasms, in men, it ranks first with 15.2%; in women, second with 9.4%, thus becoming a public health problem. Unfortunately, most of the patients are diagnosed at advanced and metastatic stages. The traditional view divided it into two major groups: Non-Small Cell Lung Cancer and Small Cell Lung Cancer. The first included squamous type, adenocarcinoma, and large cells. In this context, the treatment was based on systemic chemotherapy with platinum salts around 1978, and then other drugs such as taxanes, Gemcitabine, and Vinorelbine were added. By the year 2000, the median survival had increased from 4 to 10 months, and the overall survival rate reached only 5% at 5 years [2]. Later, better understanding of molecular biology allowed the discovery of certain genetic anomalies at the cellular level of adenocarcinoma-type tumors, such as mutations, rearrangements, and amplifications, which conferred specific characteristics to their biological behavior and enabled the use of targeted therapies according to the alterations presented.

It is known that there are various receptors at the cell membrane, like tyrosine kinase receptors: a family of enzymes that catalyze the transfer of a phosphate group to a tyrosine amino acid of a protein. This process is called phosphorylation and is involved in intracellular signal transduction, that is, the transmission of information from the outside of the cell to the inside. It triggers various cellular processes such as proliferation, differentiation, maturation, and cell survival.

Recent advances have implicated the role of tyrosine kinases in the pathophysiology of cancer. Although its activity is tightly regulated in normal cells, it can acquire transforming functions due to mutations, overexpressions, autocrine and paracrine stimulation leading to malignancy. The most well-studied mutations are those of the Epidermal Growth Factor Receptor (EGFR), the most frequent being in exon 19. The incidence of the mutation is variable according to different geographical regions, ranging from 16% to 60%. Based on these concepts, drugs that could block all these activities called Tyrosine Kinase Inhibitors (TKI) emerged.

The first generation were Gefitinib and Erlotinib [3-4], whose various randomized clinical trials compared them with first-line chemotherapy. The results in objective response rates (ORR) ranged from 58% to 83% for TKIs and from 15% to 47.3% for chemotherapy. Similarly, progression-free survival (PFS) ranged from 9.2 to 13.7 months vs 4.6 to 6.4 months. There were no differences in overall survival in any of the trials, probably due to the crossover of patients to TKI. It is important to remember that these high rates of objective responses and significant progression-free survival were observed in patients who had mutations, especially those located in exon 19.

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The second generation of TKIs appears with Afatinib [5] in randomized studies versus chemotherapy, results were: ORR ranged from 56% to 67% vs. 23% for TKIs and chemotherapy, and PFS from 13.1 to 6.9 months, respectively. For overall survival, TKI ranged from 31.4 to 33.3 months and chemotherapy from 18.4 to 21.1 months. Likewise, all these positive and significant results were observed in patients with exon 19 mutations. The other TKI is Dacomitinib, whose results regarding ORR and PFS have been similar without impacting overall survival.

The problem with the use of TKIs is Acquired Resistance [6] through various mechanisms, the main one being the T790M mutation in 50 to 70% of cases, and others in small percentages such as MET amplification, HER2: Human Epidermal Growth Factor Receptor 2, small cell lung cancer, and combinations between them.

The third generation is Osimertinib [7] used in patients with this mutation whose results showed a similar ORR, with prolonged PFS and significant improvement in overall survival, especially in the exon 19 subgroup, which reached up to 45.7 months compared to the overall 38.6 months. These results are significantly better than with chemotherapy, achieving PFS of 9 to 14 months, median survivals of 18.6 to 30.5 months, and around 15% at 5 years.

Another important mutation is the ALK rearrangement (Anaplastic Lymphoma Kinase) described in 2007 [8]. EML4 (Echinoderm Microtubule-Associated Protein-Like 4) is the most common fusion gene in this neoplasm, allowing the tumor expression of the oncogenic fusion protein EML4–ALK.

The first-generation TKI inhibitor, Crizotinib, was evaluated in a clinical trial vs. chemotherapy, achieving ORR of 60 to 65%, PFS of 10.9 vs. 7 months, and a 54% survival rate at 2 years. Ceritinib achieves similar ORR and a PFS of 61% at 12 months, and Alectinib achieves an ORR of 93.5%, with a PFS of 27.7 months and a 2-year survival rate of 79%, both second-generation inhibitors.

Immunotherapy has significantly changed the approach to lung cancer treatment. First, because it generates a response that lasts over time due to the generation of immunological memory, allowing for very prolonged responses not achieved with cytotoxic therapies; second, because of its safety profile and relatively fewer side effects.

The immune system has the ability to prevent any damage to the normal cells of our body, for this purpose, it uses checkpoints, which are proteins in immune cells that function as switches that need to be turned on or off to initiate an immune response. Tumor cells use these checkpoints to avoid being destroyed.

In 1992, Tasuku Honjo [9] discovered PD1 (programmed cell death protein 1), a protein expressed on the surface of T cells that usually prevents normal cells from being destroyed, but when blocked, it enhances the immune response against tumor cells.

In 1994, James Allison [9] studied a protein of T lymphocytes, CTLA-4 (cytotoxic T-lymphocyte-associated protein 4), which helps the body keep immune responses under control. CTLA-4 binds to another protein called B7, preventing T cells from destroying other cells, such as cancerous ones.

These discoveries allowed the development of drugs targeting these checkpoints, causing a blockade of their functions, called Checkpoint Inhibitors, which have been divided into two groups: PD1 Inhibitors (Pembrolizumab and Nivolumab) and PD-L1 inhibitors (Atezolizumab and Durvalumab). The other group corresponds to CTLA-4 Inhibitor (Ipilimumab).

Different clinical trials initially used in the second line [10], and then in the first one, have shown promising results when combined [11] and with others such as chemotherapy [12]. This yielded longer long-term survival with 5-year rates of 20%, lower risk of progression compared to chemotherapy, especially in patients with high tumor mutational burden, and significant benefits in patients with specific mutations. These results are even better when the expression of the PD-L1 marker is increased. Consider that the time to response may take several months to assess the efficacy of the therapy. Possible side effects such as fatigue, diarrhea, and skin rashes are manageable, and in some cases, autoimmune reactions can occur.

Recent research is looking for new implicated genes that are useful as biomarkers; for instance, the expression of the ERO1A gene (Endoplasmic Reticulum Oxidoreductase 1 Alpha) [13] identified as a poor prognostic indicator in EGFR gene mutations, and the expression of the non-coding RNA LNX1-AS2 as a poor prognostic indicator for pulmonary adenocarcinoma [14].

Some advances in artificial intelligence (AI) [15] are transforming diagnosis and treatment primarily through the analysis of genomic data and pathological images. DeepGEM, an AI model, predicts genetic mutations quickly and accurately using thousands of tissue sample images, generating mutation maps that improve diagnostic efficiency to guide personalized treatments.

The HPL System [16] histomorphological phenotype learning, classifies tumor phenotypes and associates them with clinical outcomes, achieving 99% accuracy in subtype differentiation, helping to predict recurrences and tumor aggressiveness, and allowing for optimal treatment for patients.

Conclusion: The evolution of lung cancer management has progressed from conventional chemotherapy to targeted therapies based on genetic alterations such as EGFR and ALK. The emergence of tyrosine kinase inhibitors and immunotherapy has significantly improved survival rates. Artificial intelligence emerges as a key tool for personalizing diagnosis and treatment.

1. Abbreviations

EGFR: Epidermal growth factor receptor.

TKI: Tyrosine kinase inhibitor.

ORR: Objective response rate.

PFS: Progression-free survival.

ALK: Anaplastic lymphoma kinase.

CTLA-4: Cytotoxic t-lymphocyte-associated protein 4.

2. Administrative information

2.1 Additional files

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2.3 Author contributions

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3. Statements

3.1 Approval of the ethics committee

Not applicable.

3.2 Consent for publication

Does not apply, as the manuscript does not contain personal data or identifiable patient information.

3.3 Conflict of interest

The author declares no conflict of interest related to the content of this editorial.

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Article / Artículo

Migration of an Implanted Venous Catheter Fragment as an Unexpected Cause of Cough: A Case Report

Migración de fragmento de catéter venoso implantable como causa inesperada de tos: reporte de caso

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ABSTRACT

Introduction: Oncology patients use implantable central venous catheters for long-term venous access. Although generally safe, they may present mechanical complications such as fracture and migration, which can lead to atypical symptoms like chronic cough. **Case report:** We describe a patient with stage IIA infiltrating ductal carcinoma of the breast, Luminal B subtype, who first received neoadjuvant chemotherapy with doxorubicin and cyclophosphamide and then weekly paclitaxel before having a radical mastectomy. She later underwent a radical mastectomy. The central venous catheter, placed for treatment, fractured and migrated with an 11 cm fragment lodged in the right ventricle and atrium. The patient presented with chronic cough as the only symptom. The patient did not receive anticoagulation or undergo prior echocardiography. A right heart catheterization was carried out under neuroleptic sedation and local anaesthesia, successfully retrieving the fragment using a multi-snare loop catheter. **Conclusion:** Fracture and migration of central venous catheters are rare but potentially serious complications that should be considered in patients with nonspecific symptoms such as cough. Retrieval via cardiac catheterization is an effective and safe treatment.

Keywords: Cough, central venous catheter, catheter fracture, high-resolution computed tomography.

RESUMEN

Introducción: Los catéteres venosos centrales implantables se utilizan en pacientes oncológicos para acceso venoso prolongado. Aunque generalmente son seguros, pueden presentar complicaciones mecánicas como fractura y migración, lo que puede generar síntomas atípicos como tos crónica. **Caso clínico:** Se presenta el caso de una paciente con carcinoma ductal infiltrante de mama, estadio IIA, subtipo luminal B, quien recibió quimioterapia neoadyuvante con doxorrubicina y ciclofosfamida, seguida de paclitaxel semanal. Posteriormente, se sometió a mastectomía radical. El catéter venoso central, colocado para el tratamiento, presentó una fractura y migración, con un fragmento de 11 cm alojado en el ventrículo y la aurícula derechos. La paciente se presentó con tos crónica como único síntoma. No recibió anticoagulación ni se le realizó ecocardiografía previa. Se efectuó un cateterismo cardiaco derecho bajo sedación neuroléptica y anestesia local. Se logró la extracción exitosa del fragmento mediante un catéter lazo Multi-Snare®. **Conclusión:** La fractura y migración de catéteres venosos centrales es una complicación infrecuente, pero potencialmente grave, que debe considerarse en pacientes con síntomas inespecíficos como tos. La extracción mediante cateterismo cardiaco es un tratamiento eficaz y seguro.

Palabras Clave: tos, catéter venoso central, fractura de catéter, tomografía computarizada de alta resolución.

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1. Introduction

Totally implantable central venous catheters are widely used in patients requiring long-term venous access, particularly in oncology. These devices consist of a titanium reservoir with a silicone septum and a radiopaque polyurethane catheter with a heparin coating. They offer advantages in terms of safety and comfort but may be associated with complications such as infection, thrombosis, and catheter fracture, the latter being a rare but potentially serious event [1].

In Latin America, data on implantable catheter fractures are limited. In Argentina, Norese et al. reported a fracture and embolization rate of 0.86% in a series of 3,953 cases. No specific data are available for Ecuador, highlighting the importance of documenting such cases [2].

Cough is a common symptom in medical practice with multiple etiologies, ranging from respiratory diseases to gastroesophageal reflux and adverse drug effects [3]. Occasionally, a less recognized but clinically relevant cause is the presence of foreign bodies in the vascular system, such as fractured catheter fragments, which can trigger nonspecific respiratory symptoms [4].

Incidental detection of these fragments through imaging studies, particularly high-resolution computed tomography (HRCT), has been described in the literature as an unexpected finding that requires thorough evaluation and timely intervention to prevent serious complications [2].

The exact pathophysiological mechanism by which catheter fracture causes chronic cough is not fully understood. It has been postulated that migration of catheter fragments to the pulmonary circulation may result in microemboli or local inflammatory reactions that stimulate cough receptors [5].

Pinch-off syndrome, a well-documented cause of implantable catheter fracture, has been identified as a predisposing factor in multiple clinical cases. Management includes early identification via imaging, correction of insertion technique to avoid compression between the first rib and clavicle, and in advanced cases, removal of the affected catheter to prevent serious complications such as fragment migration and pulmonary embolism [6].

This report presents the case of a patient with chronic cough in whom a fractured implantable venous catheter was incidentally identified by CT. This finding underscores the importance of considering unusual causes in the evaluation of persistent symptoms and the need for detailed imaging in cases with no evident etiology.

The objective of this article is to present a clinical case of chronic cough secondary to migration of a fractured implantable central venous catheter fragment, emphasizing the importance of a comprehensive clinical evaluation and imaging studies such as CT for timely diagnosis.

2. Case Report

A 64-year-old female patient, with no personal or family medical history or harmful habits, ECOG performance status 0, was diagnosed with invasive ductal carcinoma of the right breast, stage IIA (T1N0M0), grade II, Luminal B subtype. She received neoadjuvant chemotherapy with doxorubicin and cyclophosphamide (4 cycles), followed by weekly paclitaxel (12 doses). Treatment was completed in January 2024. A right radical mastectomy was performed in February 2024.

On physical examination, vital signs were within normal limits. At the site of the left subclavian implantable venous catheter, no signs of infection were observed. Cardiopulmonary auscultation was normal and painless. The patient reported having had a persistent cough for approximately one month prior to the identification of the catheter fracture. The catheter, inserted on August 25, 2023, had been used exclusively during chemotherapy and maintained adequate patency throughout.

During routine follow-up, a thoracic CT was requested in January 2025 (Figure 1), which revealed a fracture at the upper portion and displacement of the catheter, with an approximately 11 cm fragment lodged in the right atrium and ventricle. This was an incidental finding. The scan also showed scattered micronodules and fibrotic changes in the lung parenchyma.

A comparison with a previous chest X-ray from 2024 confirmed a rupture of the subclavian port catheter (Figure 2).

About one month after the finding, in December 2024, catheter removal was scheduled for January 16, 2025. Right heart catheterization was performed under neuroleptic sedation and local anesthesia, guided by fluoroscopy with contrast (Figure 3).

Access was obtained via the right femoral vein using ultrasound guidance. A Multi-Snare® loop catheter was used to successfully extract the fragment. The procedure was well tolerated, and the patient recovered without immediate complications.

A follow-up echocardiogram on February 14, 2025, showed no structural damage or significant findings. Left ventricular ejection fraction was 65%, with a longitudinal strain of -18% and no thrombi. The patient is currently asymptomatic, with no cough or complications, and continues oncology follow-up with letrozole 2.5 mg/day.

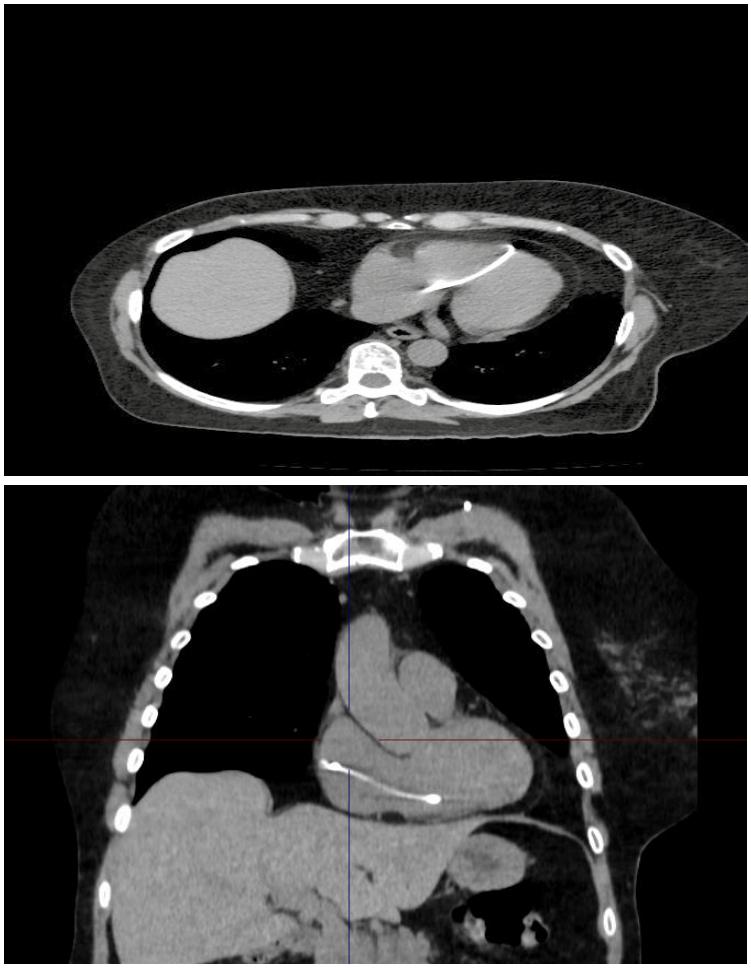
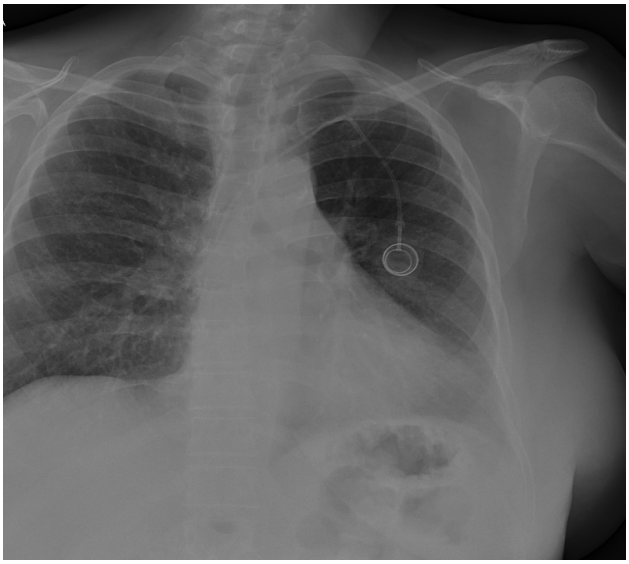


Figure 1. High-resolution chest CT scans showing the reservoir catheter in the right atrium and ventricle. A) Transverse view; B) Sagittal view.
Source: SOLCA Hospital–Guayaquil.

A



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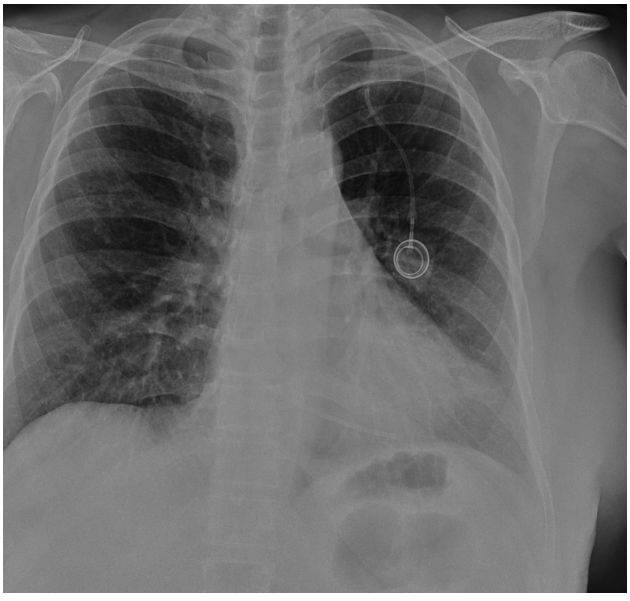

Figure 2. Standard chest X-ray comparison. A) Reservoir catheter in the normal position along the internal jugular vein trajectory; B) The proximal end of the reservoir catheter is located in the right atrium and ventricle.
Source: SOLCA Hospital–Guayaquil.

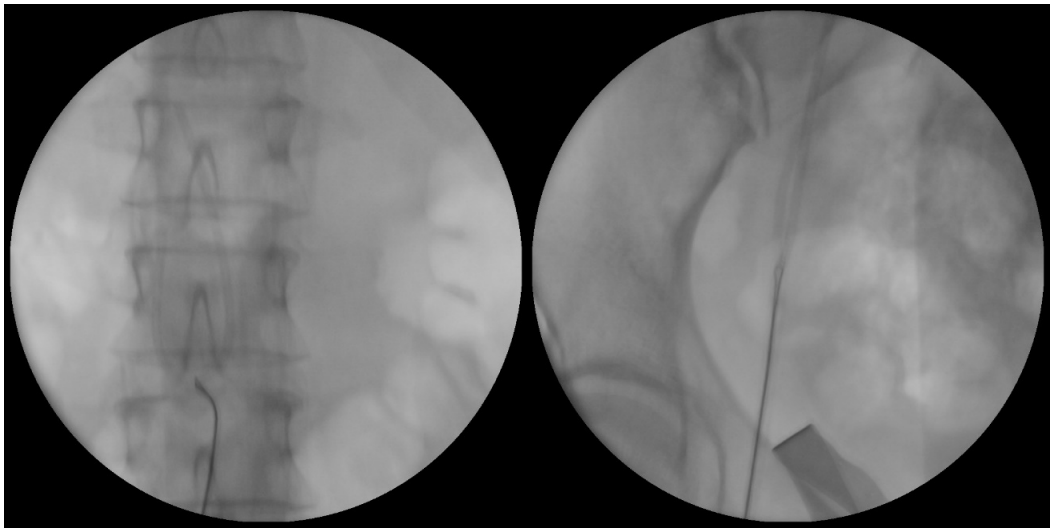

Figure 3. Contrast-enhanced X-ray during reservoir catheter extraction by hemodynamics.
Source: SOLCA Hospital–Guayaquil.

3. Discussion

Totally implantable central venous catheters are commonly used in oncology patients requiring long-term venous access. Despite their safety and convenience, mechanical complications such as catheter fracture and migration can occur. Although infrequent, these complications can have serious consequences including fragment embolization and the onset of chronic cough. In the absence of an apparent cause, such symptoms warrant consideration of less obvious etiologies that may be overlooked in initial evaluations [7,8].

Intravascular migration of implanted medical device fragments, while rare, represents a plausible mechanism [9]. These foreign bodies can cause mechanical irritation of vascular or cardiac structures and may trigger local inflammatory responses capable of sensitizing cough reflex receptors [10]. This highlights the need for thorough clinical and imaging evaluation in patients with a history of prolonged venous catheterization, especially when presenting with persistent atypical respiratory symptoms [9,10].

In our patient, the left subclavian catheter fracture and migration of the fragment into the right atrium and ventricle were incidental findings on thoracic CT performed as part of oncology follow-up. Notably, the patient presented with chronic cough as the only symptom, with no clinical or laboratory evidence suggesting a primary pulmonary cause. This supports the hypothesis that the fragment's contact with cardiac structures may have triggered the cough reflex, as proposed in other clinical reports involving intracardiac catheter migration [11].

Ribeiro et al. [12] described a series of cases in which central venous catheter fragments were incidentally identified through imaging. All were successfully retrieved via percutaneous approach without complications. Although the patients did not exhibit respiratory symptoms, the findings support the efficacy of minimally invasive treatment and highlight the importance of timely diagnosis.

Other reports have described catheter fragments migrating into cardiac chambers or pulmonary vessels being associated with respiratory symptoms, even in the absence of other clinical findings, as noted by Nayeemuddin et al. [13]. They also described successful management of vascular foreign bodies using percutaneous techniques and emphasized the importance of prompt diagnosis. Such studies, like this case, support the need to consider this etiology in patients with implanted devices and unexplained persistent symptoms.

Regarding treatment, percutaneous extraction via cardiac catheterization is an effective and safe option. In this case, the procedure was successful and complication-free, reaffirming previous findings regarding the efficacy of minimally invasive management in such cases [14].

This case underscores the importance of maintaining a high index of suspicion for common symptoms such as cough in patients with indwelling catheters and the need for advanced imaging studies for timely evaluation. Documenting and disseminating such cases contributes to expanding clinical knowledge and improving the management of rare but relevant complications.

4. Conclusion

Fracture and migration of totally implantable central venous catheters is a rare but potentially serious complication that may manifest with nonspecific symptoms such as chronic cough. This clinical case highlights the importance of considering this etiology in patients with implanted devices and unexplained persistent symptoms.

The incidental CT finding, along with successful resolution via cardiac catheterization, reinforces the need for comprehensive clinical evaluation and imaging studies in the diagnostic approach.

Despite the limited literature on this topic, this case aligns with other reports documenting catheter fragment migration as a cause of respiratory symptoms, thus adding further evidence on its presentation and management. Documenting such events helps broaden clinical awareness and supports more precise diagnostic suspicion.

5. Abbreviations

ECOG: Eastern Cooperative Oncology Group.

CT: Computed tomography.

6. Administrative Information

6.1 Additional files

None.

6.2 Acknowledgements

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6.3 Author Contributions

Walter Alexis Encalada Collahuazo**:** conceptualization, original draft writing, investigation, review and editing of the manuscript, and final approval of the manuscript.

6.4 Funding

None.

6.5 Availability of Data and Materials

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

7. Declarations

7.1 Consent for publication

The patient provided written informed consent for the publication of this case report.

7.2 Conflict of Interest

The author declares no conflict of interest.

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Resection of Mandibular Tumor of Odontogenic Myxoma Type, A View on Modern Surgery: Case Report

Diagnóstico y manejo quirúrgico de maxioma odontogénico tempomandibular utilizando CAD/CAM: Reporte de caso

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ABSTRACT

Introduction: Odontogenic myxoma (OM) is a benign, locally invasive neoplasm that affects the maxillomandibular complex and has a high recurrence rate. It accounts for an average of 8.3% of odontogenic tumors. Its clinical course is usually asymptomatic in the early stages; however, it may present with pain, paresthesia, tooth mobility, and limitations in mastication and swallowing in more advanced stages. Diagnosis includes imaging studies such as computed tomography (CT) and magnetic resonance imaging (MRI), which typically reveal multilocular radiolucent lesions described as having a "soap bubble" or "honeycomb" appearance. Due to the asymptomatic nature of the lesion, diagnosis is often delayed. **Case report:** We report the case of a 15-year-old male patient with no relevant medical history, presenting with a space-occupying lesion in the right mandibular body and ramus. Imaging studies raised the diagnostic suspicion of a possible odontogenic myxoma. Histopathological examination revealed a low-grade spindle cell tumor with extensive myxoid transformation, focal atypia, and no necrosis. Given the extension of the tumor, age of the patient, and degree of invasion, a wide surgical resection with safety margins was performed, followed by mandibular reconstruction using a custom-designed prosthesis based on three-dimensional imaging and a vascularized free fibula flap. **Di scussion:** Extensive mandibular myxomas require a multidisciplinary approach and meticulous, individualized preoperative planning aimed at achieving optimal functional, aesthetic, and oncologic outcomes. Conclusion: This case highlights the importance of applying three-dimensional imaging technologies in the reconstructive surgery of complex maxillofacial lesions.

Keywords: Myxoma, imaging, three-dimensional, maxillomandibular neoplasms, case report.

RESUMEN

Introducción: El mixoma odontogénico es una neoplasia benigna, localmente invasiva, que afecta el complejo maxilomandibular y presenta una alta tasa de recurrencia. Representa en promedio el 8,3 % de los tumores odontogénicos. Su curso clínico suele ser asintomático en las etapas tempranas, aunque puede manifestarse con dolor, parestesia, movilidad dental, limitación para masticar y deglutir en etapas avanzadas. El diagnóstico incluye estudios de imagen —tomografía

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axial computarizada y resonancia magnética nuclear—, que evidencian lesiones radiolúcidas multiloculares descritas como "pompas de jabón" o "panal de miel". Debido a la naturaleza asintomática de la lesión, su diagnóstico suele ser tardío. **Presentación del caso:** Se reporta el caso de un paciente masculino de 15 años, sin antecedentes médicos relevantes, con lesión ocupante de espacio en cuerpo y rama mandibular derecha. Los estudios imagenológicos sugirieron la sospecha diagnóstica de posible mixoma odontogénico, y el estudio histopatológico reveló lesión tumoral fusocelular de bajo grado con extensa transformación mixoide y con atipia focal, sin necrosis. Dada la extensión tumoral, la edad del paciente y el grado de invasión, se realizó resección quirúrgica amplia con márgenes de seguridad y reconstrucción mandibular utilizando prótesis diseñada por imagenología tridimensional y colgajo libre de peroné vascularizado. **Discusión:** Los mixomas mandibulares extensos requieren un abordaje multidisciplinario y planificación prequirúrgica meticulosa individualizada, para lograr adecuados resultados funcionales, estéticos y oncológicos. **Conclusiones:** Este caso resalta la importancia de aplicar tecnologías de imagenología tridimensional en la cirugía reconstructiva de lesiones maxilofaciales complejas.

Palabras Clave: mixoma, imagenología tridimensional, neoplasias maxilomandibulares, reporte de caso.

1. Introduction

Odontogenic myxoma (OM) is a benign locally invasive maxillomandibular neoplasm with a high recurrence rate. It primarily affects women in the third and fourth decades of life, although pediatric cases have also been reported. In most cases, it is located in the posterior mandibular region, followed by the incisor area, maxilla, and, in rare cases, the mandibular condyle [1,2].

OM accounts for approximately 2.2% to 17% of odontogenic tumors, with an average frequency of 8.3%. It is the third most common odontogenic tumor, following ameloblastoma and odontoma [3,4]. Its rarity and invasive behavior encourage further research to better understand its biological characteristics and improve clinical management.

Initially asymptomatic, OM can present symptoms such as pain, paresthesia, tooth mobility, and ulceration as it progresses, which can lead to limitations in mastication and swallowing. These manifestations are often associated with bone perforation and soft tissue invasion [5,6].

Diagnosis relies on imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI), which typically reveal multilocular radiolucent lesions described as having a "soap bubble" or "honeycomb" appearance. Less frequently, unilocular images with well-defined or poorly defined borders may be observed. OM may also be associated with an unerupted tooth and, upon cortical bone perforation, may present a peripheral "sunray" appearance—characteristic of bone sarcomas— thus hindering differential diagnosis [3,7,8,9].

Diagnosis is confirmed through histopathological examination. The tumor, of mesenchymal origin, is composed of round, angular, spindle-shaped, and stellate cells in a loose myxoid stroma with scarce collagen fibers. Mesenchymal markers such as vimentin, muscle-specific actin, and, to a lesser extent, the S-100 protein are generally positive. In isolated cases, positivity for CK19, a marker of normal odontogenic epithelium, may be observed [10].

Treatment consists of total surgical resection; however, the surgical approach remains controversial. Some authors suggest enucleation and curettage due to the benign nature of the tumor, while others recommend radical surgery with primary reconstruction because of its high recurrence rate. In this case, managed at Clínica Bonnadona, radical surgery with primary reconstruction supported by CAD/CAM (Computer-Aided Design/Computer-Aided Manufacturing) technology was conducted to ensure comprehensive treatment [11,12].

2. Case Presentation

This case report was prepared in accordance with the SCARE guidelines.

A 15-year-old male patient, with no significant medical, familial, or genetic history, high school graduate, of mixed race, was admitted to our institution presenting a space-occupying lesion located in the right mandibular body and ramus. The patient was hemodynamically stable with no other significant findings on physical examination.

The maxillofacial surgery service requested a biopsy and histopathological identification of the lesion. The report described a low-grade primary spindle cell tumor with extensive odontogenic myxoid changes, focal atypia, and no necrosis. Immunohistochemistry showed focal S100 protein reactivity in tumor cells.

Based on these findings, it was decided to perform a hemimandibulectomy + condylectomy + replacement of the right temporomandibular joint + microvascularized flap + virtual planning of a custom-made prosthesis for the temporomandibular joint, right mandibular body and ramus, and mandibular angle, followed by the placement of a three-dimensional reconstructive plate.

A computed tomography (CT) scan of the paranasal sinuses (PNS) and face in three-dimensional projection was performed, which revealed a large expansile osseous mass in the right mandible, with extension into the soft tissues of the ipsilateral hemiface, apparent involvement of the masseter muscle and the medial pterygoid muscle, and infiltration of the ipsilateral maxillary sinus (Figure 1A).

The tumor margins were defined and projections were made for reconstruction with a vascularized fibula graft and the design of a prosthesis with an occlusal splint to ensure proper mandibular positioning (Figure 1B).

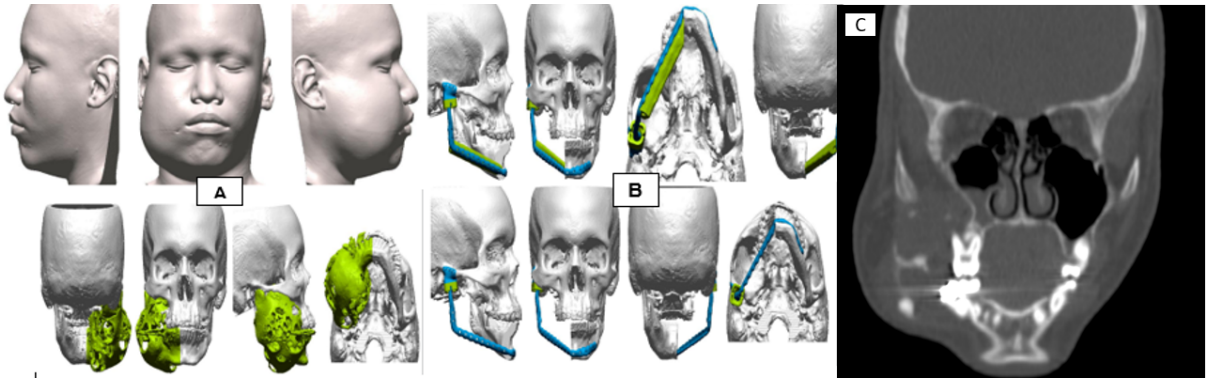

Figure 1. A. Three-dimensional imaging reconstruction of the tumor. **B.** Implant design. **C.** Simple coronal slice of paranasal sinuses (PNS).
Source: Clínica Bonnadona Prevenir, patient case report.

The surgical procedure was performed using a multidisciplinary approach by a highly specialized team composed of an oral and maxillofacial surgeon, a head and neck surgeon, a vascular surgeon, a pediatric surgeon, and a plastic surgeon. All members of the team had more than 15 years of experience in the management of oncologic patients, which allowed for efficient and precise coordination within a single surgical session.

Tracheotomy and gastrostomy were performed under general anesthesia as measures to secure the airway and ensure enteral nutrition. Subsequently, resection of the maxillomandibular neoplasm was carried out through a right submandibular and preauricular approach, extending to the submandibular gland. The ascending ramus of the mandible was approached, and subperiosteal dissection was performed, followed by in bloc resection of the lesion involving the symphysis, body, ramus, and mandibular condyle, ensuring safety margins as per the virtual surgical plan (Figures 2 and 3). Satellite lymph nodes were also resected and sent for pathological examination.

For the reconstruction, a microvascularized osteomyocutaneous flap was positioned and fixed with a mandibular plate on the left mandible and aligned using an occlusal splint. A vascularized fibula graft was harvested (Figure 4A) and transferred as a microvascularized flap to the hemimandibulectomy defect, allowing for the obliteration of the dead space and improved vascularization through an end-to-end microvascular anastomosis between the facial artery and the superior thyroid vein. After confirming adequate perfusion, the surgical wound was closed in layers (Figure 4B), and the procedure was completed without complications. The patient's family was informed that the procedure was well-tolerated with no adverse events, and the patient would be transferred to the pediatric intensive care unit (PICU) as part of the established protocol for this type of surgery.

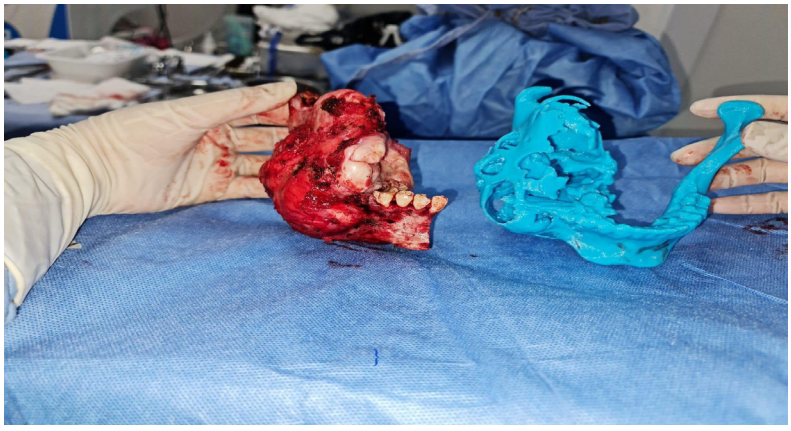

Figure 2. Comparison between the resected tumor and three-dimensional imaging.

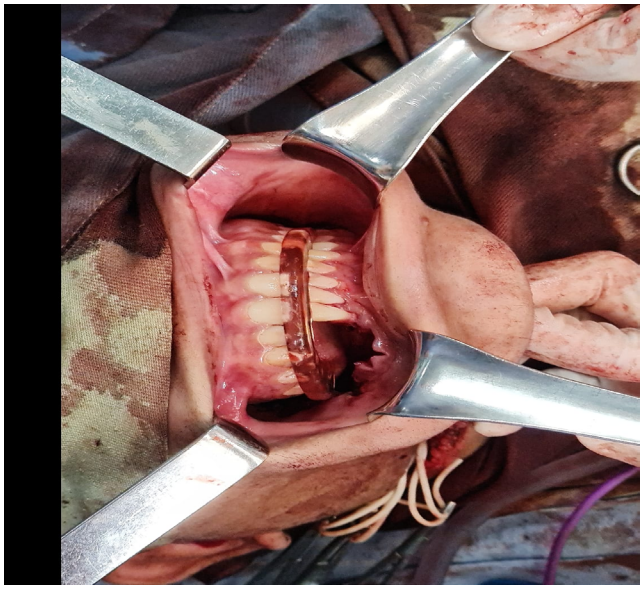

Figure 3. Hemimandibulectomy

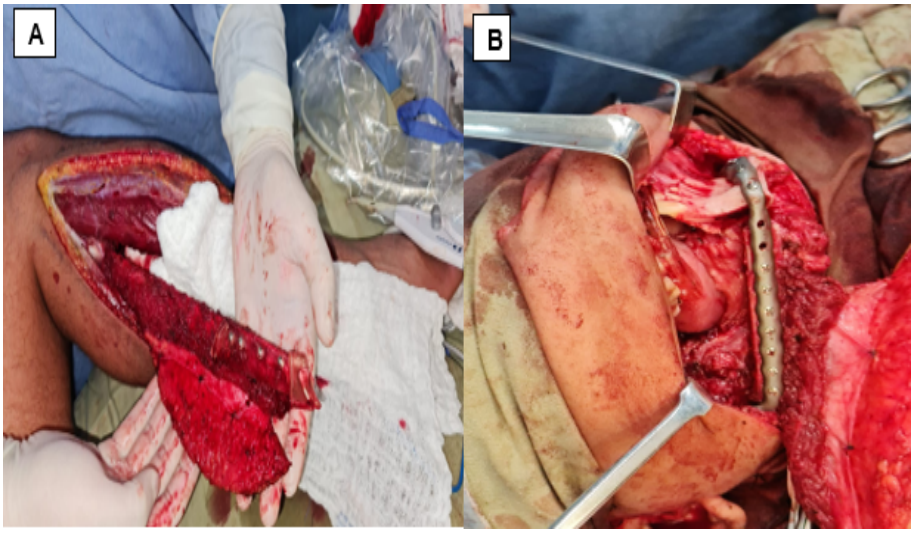

Figure 4 A. Vascularized fibula graft **B.** Fixation of the graft to the mandible.
Source: Clínica Bonnadona Prevenir, patient case report.

During his hospital stay, the patient developed a collection in the right side of the neck, accompanied by febrile spikes and a positive culture for Gram-negative bacteria, which required broad-spectrum antibiotic therapy and surgical reintervention for lavage, debridement, and drainage.

Following clinical improvement, the patient was transferred to the general ward under multidisciplinary management. After an adequate recovery, he was discharged to continue his outpatient rehabilitation.

The outpatient follow-up performed four months post-surgery showed a favorable evolution, with no signs of infection or recurrence (Figures 5B and 5C).

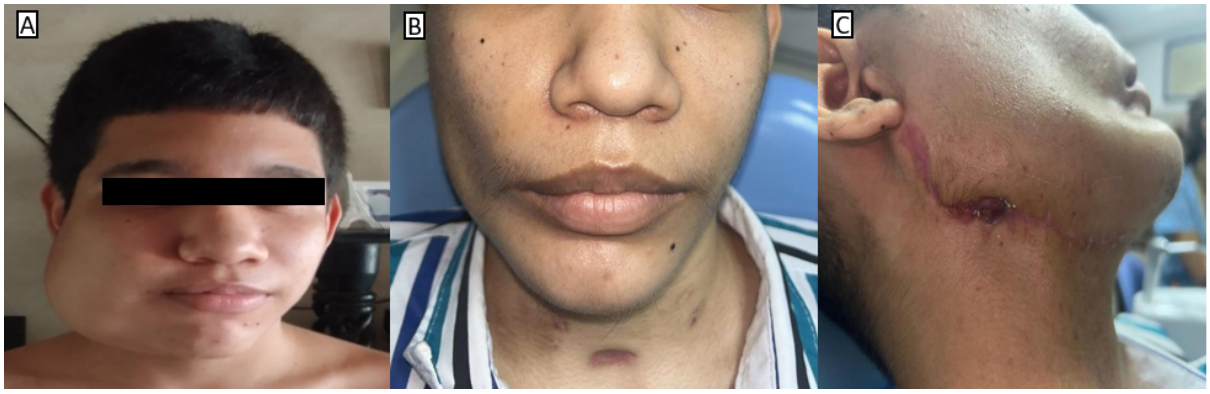

Figure 5 A. Preoperative view **B.** Postoperative result, frontal view **C.** Postoperative result, lateral view
Source: Clínica Bonnadona Prevenir, patient case report.

3. Discussion

Odontogenic myxoma (OM) is a benign, locally invasive odontogenic tumor with a high rate of local recurrence, although it is generally not associated with malignant transformation or metastasis [13]. It is a rare lesion and is scarcely documented in the literature [14]. These maxillomandibular neoplasms are considered radioresistant. Suárez Condez described a case in which radiotherapy was indicated prior to surgical resection, but the poor clinical progression of the disease resulted in the patient's death [15].

The participation of an experienced pathologist is essential because diagnosis can guide the treatment approach, whether surgical or conservative. Additionally, follow-up with imaging studies is crucial to detect early recurrences. In cases of extensive resections, reconstructive procedures should be postponed until a disease-free period is confirmed [13].

Surgical options include conservative management, such as enucleation and curettage—especially in pediatric patients—or non-conservative approaches. Tapia Contreras and colleagues emphasize the importance of considering factors such as age, growth, function, and craniofacial aesthetics when selecting the appropriate treatment [11,12].

Conservative management is associated with a recurrence rate of 19%, compared to 6% in those treated with resection [14]. In radical treatment, vascular grafts or microvascularized flaps using fibula or iliac crest are employed to maintain both aesthetics and functionality [11].

In the case presented here, considering the tumor size, the patient's age, and the degree of invasion, a non-conservative approach was chosen and a complete resection with appropriate safety margins was carried out. Reconstruction was achieved using a custom-designed prosthesis based on three-dimensional imaging and a vascularized fibula graft. The radical treatment resulted in satisfactory aesthetic and functional outcomes, with no evidence of tumor recurrence up to four months postoperatively.

4. Conclusion

Odontogenic myxoma, despite its benign nature, presents a therapeutic challenge due to its infiltrative potential and tendency for recurrence. In this case, the maxillomandibular neoplasm was located in the right mandibular body and ramus and required extensive surgical resection. Through a multidisciplinary approach and meticulous preoperative planning, complete tumor excision was achieved, along with immediate reconstruction using a custom-made prosthesis designed with three-dimensional imaging and a vascularized fibula graft. This therapeutic strategy not only preserved the patient's masticatory function but also successfully restored facial aesthetics. This case highlights the importance of comprehensive assessment and individualized treatment planning to achieve optimal functional, aesthetic, and safe outcomes for each patient.

5. Declarations

5.1 Ethical Considerations

The case report was approved by the Research Ethics Committee of OCBP, with prior consent from the patient's family.

5.2 Conflict of Interest

The authors declare that there are no conflicts of interest related to this case report. All authors independently participated in the development, analysis, and interpretation of the data, as well as in the article writing.

5.3 Funding

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5.4 Disclaimer

The authors assume full responsibility for the opinions and conclusions presented in this article.

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Article / Artículo

Malnutrition Associated with Oncohematological Diseases in Health Institutions in Ecuador

Desnutrición asociada a las enfermedades oncohematológicas en instituciones de salud de Ecuador

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ABSTRACT

Introduction: Malnutrition continues to be a common finding among hospitalized cancer patients in Ecuador. The objective of this study was to determine the magnitude of malnutrition associated with onco-hematological disease in a series of hospitals in the country. **Methodology:** A cross-sectional prevalence study (Ecuadorian Study of Malnutrition in Oncology) was conducted in five hospitals in the provinces of Guayas (3), Manabí (1), and Azuay (1). A total of 390 patients with a confirmed diagnosis of cancer (63.6 % women; 36.4 % men) with a mean age of 55.3 ± 16.5 years were included; 47.2% were ≥ 60 years old. The most common tumor locations were at the kidney and urinary tract, uterus, ovary, prostate, and testicle (18.7%); breast (16.1%); leukemia and lymphoma (15.1%); and large intestine/rectum and anus (15.1%). At the time of the survey, 42.8% pf the OHD patients were receiving chemotherapy. Each participant was interviewed, the Subjective Global Assessment was applied, and anthropometric measurements were taken. All patients classified in categories B (moderate malnutrition/at risk) or C (severe malnutrition) of the survey were considered malnourished. **Results:** The overall prevalence of malnutrition was 49.7% (n = 194); 14.4% (n = 56) corresponded to severe malnutrition (category C). There were no significant associations between nutritional status and age, educational attainment, tumor location, or cytoreductive treatment (p > 0.05). Malnutrition was more common in men than in women. **Conclusions:** Approximately one in two cancer patients hospitalized in Ecuador has some degree of malnutrition, and one in seven has severe malnutrition. These findings highlight the need to establish systematic nutritional screening and dietetic support programs in the country's oncology services.

Keywords: Cancer, malnutrition, nutritional assessment.

RESUMEN

Introducción: La desnutrición continúa siendo un hallazgo frecuente en los pacientes oncológicos hospitalizados en Ecuador. El objetivo de este estudio fue determinar la magnitud de la desnutrición asociada a la enfermedad oncohematológica en una serie de hospitales del país. **Metodología:** Se llevó a cabo un estudio transversal de prevalencia (Estudio Ecuatoriano de Desnutrición en Oncología) en cinco hospitales de las provincias de Guayas (3), Manabí (1) y Azuay (1). Se incluyeron 390 pacientes con diagnóstico confirmado de cáncer (63,6 % mujeres; 36,4 % hombres) con una edad media de 55,3 ± 16,5 años; el 47,2 % tenía ≥ 60 años. Las localizaciones tumorales más frecuentes fueron riñón y vías urinarias, útero, ovario, próstata y testículo (18,7 %); mama (16,1 %); leucemias y linfomas (15,1 %); e intestino grueso/recto y ano (15,1 %). Al momento de la encuesta, el 42,8 % recibía quimioterapia. A cada participante que fue entrevistado se le aplicó la Encuesta Subjetiva Global y se le realizaron mediciones antropométricas. Se consideró desnutrido todo paciente clasificado en las categorías B (desnutrición

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moderada/en riesgo) o C (desnutrición grave) de la encuesta. **Resultados:** La prevalencia global de desnutrición fue del 49,7 % (n = 194); el 14,4 % (n = 56) correspondió a desnutrición grave (categoría C). No se observaron asociaciones significativas entre el estado nutricional y la edad, el nivel educativo, la localización tumoral ni la administración de tratamiento citorreductor (p > 0,05). La desnutrición fue más frecuente en los hombres que en las mujeres. **Conclusiones:** Alrededor de uno de cada dos pacientes oncológicos hospitalizados en Ecuador presenta algún grado de desnutrición y uno de cada siete cursa con desnutrición grave. Estos hallazgos resaltan la necesidad de establecer programas sistemáticos de tamizaje nutricional y soporte dietoterapéutico en los servicios oncológicos del país.

Palabras clave: cáncer, desnutrición, evaluación nutricional.

1. Introduction

Oncohematological disease (OHD) profoundly affects the patient's nutritional status through various biological and suprabiological, endogenous, and exogenous mechanisms that often overlap and intersect [1,2]. The most immediate consequences of malnutrition secondary to OHD include energy-nutrient malnutrition (ENM), deterioration of functional capacity, loss of functional independence and autonomy, and the inability to independently maintain adequate nutritional status through oral food intake [2,3].

It should not be surprising that malnutrition is a prevalent characteristic among patients receiving treatment for OHD [4]. Santana Porbén (2023) has recently reported the current rates of malnutrition associated with OHD in different geographical latitudes [5]. In this regard, it is worth mentioning the ELAN Ecuador Study: the first multicenter, nationwide study was organized in 2014 and revealed malnutrition in more than 5,000 patients treated in hospitals and health centers in 22 out of the 24 provinces. Although malnutrition from all causes reached 37%, researchers noticed that this figure corresponded to 65% among those diagnosed with solid organ cancer, leukemia, and lymphoma [6].

Other studies conducted in Ecuador have revealed the magnitude of malnutrition associated with OHD. Moya and Gallegos (2022) conducted an observational study at the Ecuadorian Social Security Institute (IESS) Hospital in the city of Santo Domingo (Santo Domingo de los Tsáchilas Province) with 114 patients (Men: 51.0%; average age: 69.0 ± 13.6 years) undergoing cancer treatment (men: prostate: 21.1% vs. women: breast: 12.3%) at the institution. According to the SGA—tool used for nutritional screening—malnutrition was present in 34.2% of patients. Interestingly, overweight and obesity predominated in the study series [7]. In a second study, Bajaña et al. (2022) applied a modification of the NUTRIC score to estimate the nutritional status of 176 patients (Women: 64.2%; Average age: 57 ± 6 years) undergoing cancer treatment (Gynecological locations: 25%) upon admission to the intensive care unit (ICU) at SOLCA Guayaquil. The average NUTRIC score was 3.0 ± 0.9. 30.1% of patients received NUTRIC scores ≥ 5 upon admission to the hospital ICU, thus placing them at increased nutritional risk. The NUTRIC score was associated with worse clinical condition upon admission at the ICU, a longer stay there, and a higher in-hospital mortality rate [8].

The Latin American Study on Malnutrition in Oncology was completed in the 2019–2020 biennium as a multicenter, multinational effort by FELANPE aimed primarily at realistically and objectively exposing the frequency of malnutrition among patients undergoing OHD treatment in hospitals and cancer care centers in Latin American countries. Researchers' expectations were met, the DNO LATAM Study revealed a malnutrition rate of 59.1% in 1,842 patients treated at 52 health centers in 10 Latin American countries [9].

The Ecuadorian Group for the Study of Hospital Malnutrition (GEEDH by its Spanish acronym) was in charge of Ecuador's portion in the DNO Study. Therefore, this article presents the results of the DNO Ecuador Study and report on the nutritional status of cancer patients treated in the country's hospitals.

2. Methodology

2.1 Study design

Cross-sectional prevalence survey. The procedures completed during the survey included an interview with the patient, completion of the research forms, performance of the SVA, and collection of anthropometric measurements. The DNO Ecuador Study was conducted between October and November 2019.

2.2 Study location

Health centers and services specializing in the care of patients with OHD affiliated w ith t he Ecuadorian Ministry of Public Health (MSP by its Spanish acronym) and the Ecuadorian Social Security Institute (IESS by its Spanish acronym). The survey procedures were completed in clinical hospitalization wards, intensive care units, bone marrow transplant units, and hospital surgery services. The study was conducted in five hospitals in the provinces of Guayas (3), Manabí (1), and Azuay (1). These hospitals are leading cancer centers in the country.

2.3 Eligibility criteria

Patients of both sexes, aged 18 years or older, who were hospitalized or receiving outpatient care during the study observation window at participating health centers, and who voluntarily consented to participate after reading and signing the informed consent form, were included in the DNO Ecuador Study. Patients who did not complete the procedures prescribed in the design or whose data were not recovered were excluded from the DNO Ecuador Study. The following variables were collected from each patient: sex, age, primary tumor location, and type of treatment.

The sample size was calculated to be 390 patients for infinite populations. Patients were selected using the simple random method from among those who attended the health center for outpatient medical procedures or who were admitted on the day chosen for conducting the study activities.

Patient selection, collection of demographic and clinical data, and administration of the tools were carried out by locally appointed interviewers properly trained in the research procedures. A procedure manual was created to support interviewer teams training and thus guaranteeing the quality of the procedures. The interview with the patient, the completion of the research forms, and the gathering of anthropometric measurements were conducted at the participating oncology units.

2.4 Global Subjective Nutritional Status Survey

The nutritional status of patients was assessed using the GSS (See appendix) and has three categories: A) Well-nourished; B) Moderately malnourished/at risk of malnutrition; and C) Severely malnourished. This is based on weight loss, food intake, functional impairment, persistent gastrointestinal symptoms, metabolic stress, depletion of muscle mass and adipose tissue, and the presence of fluid distribution disorders such as edema and ascites.

As part of the patient's nutritional assessment, height (meters), body weight (kilograms), and Body Mass Index (BMI: kg/m^2) were obtained using internationally accepted procedures described in the DNO Ecuador Study procedures manual. Scales and height meters were checked and calibrated by the institution's technical staff before conducting the study. Serum albumin values (g/L) were also obtained.

2.5 Statistical analysis

Measures of central tendency (mean) and dispersion (standard deviation) were used, and data were presented in absolute frequencies and percentages. Given the size of the study series, it was not necessary to verify the normality of the variables of interest.

The frequency of malnutrition was estimated from the percentage of patients with SGA scores (B + C). It was distributed according to the demographic and clinical characteristics of the subject. The nature and strength of the associations between the frequency of malnutrition (as the main variable of the study), on the one hand, and the demographic and clinical characteristics of the patients surveyed (which acted as covariates), on the other, were evaluated using independence tests based on the chi-square distribution. A p-value <0.05 was considered statistically significant.

2.6 Ethical considerations

Patients participating in the DNO Ecuador Study were asked to sign an informed consent form. To this end, the patient was informed about the purposes of the research and the non-invasive nature of the procedures involved. The patient was guaranteed the right to refuse to participate in the study without compromising the healthcare to which they are entitled.

The patient's personal data was protected by replacing names and surnames and personal identification numbers with appropriate alphanumeric codes. The local study coordinator kept the codes in a secure location for traceability and possible amendments.

Relevant endorsements were obtained after review and approval by the institutional Bioethics, Teaching, and Research Committees. The pro tempore presidency (2019–2021) of the Latin American Federation of Nutritional Therapy, Clinical Nutrition, and Metabolism (FELANPE by its Spanish acronym), and the committees that make up the Governing Board also endorsed the DNO Ecuador Study.

3. Results

Table 1 shows the demographic characteristics of patients examined during the activities of the DNO Ecuador Study. Women outnumbered men. The average age was 55.3 ± 16.5 years. Approximately half of the patients were aged ≥ 60 years. Most patients attained primary and secondary education.

Table 1. Demographic characteristics of patients

Characteristics	Findings [%]
Sex	
· Male	142 [36.4]
· Female	248 [63.6]
Age, years (median, s.d.)	**55,3 ± 16.5**
· < 60	206 [52.8]
· ≥ 60	184 [47.2]
Educational attainment	
· Primary school	110 [28.2]
· Secondary school	127 [32.6]
· Vocational training	42 [10.8]
· Technical education	64 [16.4]
· Undergraduate	47 [12.1]

s.d.: standard deviation

Source: Records from the DNO Ecuador Study

Series size: 390

Table 2 shows the distribution of patients examined during the Ecuador DNO Study according to the participating health center. A total of 390 patients were surveyed in 5 hospitals. Hospitals of the SOLCA network contributed 84.3% of the study series.

Table 2. Distribution of patients by health center

Institution	Province	Finding [%]
"Dr. Abel Gilbert Pontón" Hospital	Guayas	28 [7.2]
"Teodoro Maldonado Carbo" Hospital	Guayas	33 [8.5]
SOLCA Guayaquil	Guayas	260 [66.7]
SOLCA Portoviejo	Manabí	19 [4.9]
SOLCA Cuenca	Azuay	50 [12.8]
All hospitals		390 [100.0]

Source: Records from the DNO Ecuador Study

Series size: 390

Table 3 shows the clinical characteristics of the patients studied. Neoplasms of the kidneys and urinary tract, uterus and ovaries, prostate and testicles (17.8%); breast (16.1%); large intestine, rectum, and anus (15.1%); and leukemias and lymphomas (15.1%) were the most common. One-third of the patients had completed a cytoreductive surgery program as their first line of antineoplastic treatment. Chemotherapy (alone or in combination with radiotherapy) was the most common cytoreductive treatment option. It should be noted that one-fifth of the patients were receiving symptomatic treatment.

Table 3. Clinical characteristics of patients

Characteristics	Findings [%]
Tumor location	
· Breast	63 [16.1]
· Large intestine/Rectum and anus	59 [15.1]
· Head and neck	20 [5.1]
· Leukemia/Lymphoma	59 [15.1]
· Lungs and airways	8 [2.1]
· Esophagus/Stomach/Small intestine	44 [11.3]
· Liver and bile ducts/Pancreas	17 [4.3]
· Kidneys and urinary tract/Uterus/Ovaries/Prostate/Testicles	73 [18.7]
· Other locations	47 [12.1]
Cytoreductive treatment	
· Cytoreductive surgery	118 [30.3]
· Chemotherapy	167 [42.8]
· Chemotherapy + Radiotherapy	18 [4.6]
· Radiotherapy	6 [1.5]
· Hormone therapy	7 [1.8]
· Symptomatic treatment	74 [19.0]

Source: Records from the DNO Ecuador Study
Series size: 390

After applying for the SGA, the following results were obtained: Score A) Well nourished, 50.3%; Score B) Moderately malnourished/at risk of malnutrition, 35.4%; and Score C) Severely malnourished, 14.4%. Thus, malnutrition, estimated from the sum of the SGA scores (B + C), affected 49.8% of the study series.

Finally, Table 4 shows the associations between the nutritional status of patients with OHD, on the one hand, and demographic and clinical characteristics, on the other. Malnutrition was independent of the characteristics of the patient with OHD. A significant influence of sex was found: the prevalence of malnutrition was higher in men (61.3%) than in women (43.1%), with an absolute difference of 18.2% ($p < 0.05$; chi-square test of independence).

Table 4. Distribution of malnutrition by sex, age, educational attainment, location, and treatment.

Characteristics	Findings [%]	
	Malnourished	Well nourished
Frequency	194 [49.7]	196 [50.3]
Sex		
· Male	87 [61.3]	55 [38.7]
· Female	107 [43.1]	141 [56.9]
Age		
· < 60 years	95 [46.1]	111 [53.9]
· ≥ 60 years	99 [53.8]	85 [46.2]
Level of Education		
· Primary school	49 [44.5]	61 [55.5]
· Secondary school	67 [52.8]	60 [47.2]
· Vocational training	34 [53.1]	30 [46.9]
· Technical education	20 [47.6]	22 [52.4]
· Undergraduate	24 [51.1]	23 [48.9]
Tumor location		
· Breast	13 [20.6]	50 [79.4]
· Large intestine/Rectum and anus	38 [64.4]	21 [35.6]
· Head and neck	11 [55.0]	9 [45.0]
· Leukemia/Lymphoma	28 [47.5]	31 [52.5]
· Lungs and airways	4 [50.0]	4 [50.0]
· Esophagus/Stomach/Small intestine	39 [88.6]	5 [11.4]
· Liver and bile ducts/Pancreas	12 [70.6]	5 [29.4]
· Kidneys and urinary tract/Uterus/Ovaries/Prostate/Testicles	35 [47.9]	38 [52.1]
· Other locations	14 [29.8]	33 [70.2]
Cytoreductive treatment		
· Cytoreductive surgery	44 [37.3]	74 [62.7]
· Chemotherapy	88 [52.7]	167 [47.3]
· Chemotherapy + Radiotherapy	10 [55.6]	18 [44.4]
· Radiotherapy	5 [83.3]	6 [16.7]
· Hormone therapy	2 [28.6]	7 [71.4]
· Symptomatic treatment	45 [60.8]	74 [39.2]

Source: Records from the DNO Ecuador Study

Series size: 390

4. Discussion

This paper presents the results of the Ecuador DNO Study, the first research project specifically designed to assess the nutritional status of cancer patients treated in Ecuadorian hospitals. Study findings reveal that approximately half of patients with oncohematological diseases (OHD) are malnourished. This result was predictable considering the negative impact that neoplasms have on the patient's ability to maintain adequate nutritional status through conventional oral intake.

Prior to the DNO Ecuador Study, the ELAN Ecuador Study [6] was the most solid and best-documented source of information on the prevalence of cancer-related malnutrition in the national hospital setting. The results obtained from the present DNO Ecuador Study show a significant reduction in the prevalence

of patients affected by malnutrition compared to previous studies, a finding that deserves particular attention and analysis. Likewise, the prevalence of malnutrition observed in patients with OHD through the DNO Ecuador Study was lower than that reported in the DNO LATAM Study, [9] which reported a prevalence of 59.6%. This difference suggests regional variations in patterns of cancer malnutrition that require further research for a comprehensive understanding.

The variations observed in the prevalence of cancer-related malnutrition require further research to elucidate the underlying factors responsible for these changes, only preliminary hypotheses are possible in the current context. Changes in the prevalence of malnutrition could be attributed to multiple interrelated factors, including seasonal variations in the demographic, clinical, and health characteristics of the study population; a higher representation of young patients could contribute to a lower prevalence of malnutrition due to their better nutritional reserves and capacity for recovery. In addition, the increase in the proportion of neoplasms with less nutritional impact, particularly those in early stages or with specific locations that have less influence on nutritional status, together with the implementation of early detection strategies and the refinement of diagnostic methods, could partly explain these findings. Earlier diagnosis of neoplastic disease, before obvious nutritional alterations become apparent, could result in an apparent reduction in the prevalence of malnutrition in the series studied. This suggests that improved screening systems and greater awareness of the importance of timely diagnosis are changing the nutritional profile of patients at the time of cancer diagnosis [10-11].

The variation observed in the prevalence of cancer malnutrition could also be attributed to the increase in the proportion of overweight or obese patients diagnosed with OHD [12]. Last but not least, the lower rate of cancer-related malnutrition reported in the conclusions of the Ecuador DNO Study could be the first consequence of an increased presence and involvement of nutritionists in the Ecuadorian health system [13].

It is a matter of concern that 50% of cancer patients treated in Ecuadorian hospitals are malnourished. This poor nutritional status adversely affects the response to cytoreductive treatments and increases the risk of complications, including mortality. Therefore, the development and management of nutritional intervention programs that offer comprehensive support to patients and their families during all stages of treatment, including rehabilitation and reintegration into their social environment, is fully justified [14].

Given that advanced age is a risk factor for nutritional deterioration in cancer patients, the DNO Ecuador Study was extended to analyze the determinants of this condition in the OHD cohort [15]. It has been estimated that educational attainment, as an indicator of an individual's socioeconomic status, is associated with an increased risk of malnutrition [16-18].

For years, it has been documented that, depending on the location of the cancer, there is a greater or lesser risk of nutritional deterioration; for instance, diseases of the digestive system present a higher risk of malnutrition [19]. In addition to malnutrition induced by tumor activity, there are nutritional disorders derived from cytoreductive therapies [20].

This study did not find a clear effect of the proposed determinants of nutritional status on the frequency of cancer-associated malnutrition. However, it was noteworthy that men accounted for the largest number of malnourished patients. It was not the objective of the study to explore the causes of the behavior found for one or another determinant. Sex (in the biological sense of the term) is not perceived to influence the behavior of diseases and comorbidities (except those linked to the subject's chromosome makeup), and epidemiological studies are inconsistent on this point [21]. It is more likely that patients' gender influences the behaviors and lifestyles they exhibit and determines the behavior of malnutrition associated with OHD [22-24]. The potential influence of gender on the nutritional status of cancer patients seems to be modulated by the structure and quality of their family, social, and community support networks [25]. Consequently, it is postulated that patients with robust social support have a greater capacity to cope with the adverse effects of neoplastic disease and its cytoreductive treatments.

5. Conclusions

The DNO Ecuador Study has revealed that malnutrition is highly prevalent among patients seen and treated by OHD in the country's hospitals. Tumor locations had an equivalent negative impact on the nutritional status of patients. Interestingly, malnutrition was concentrated among men, thus suggesting that gender-related behaviors and lifestyles have an impact on the nutritional status of OHD patients.

6. Abbreviations

GEEDH (by its Spanish acronym): Ecuadorian Group for the Study of Hospital Malnutrition

OHD: Oncohematological disease

SGA: Subjective Global Assessment

BMI: Body Mass Index

IESS (by its Spanish acronym): Ecuadorian Social Security Institute

MSP (by its Spanish acronym): Ministry of Public Health

ICU: Intensive Care Unit

7. Administrative information

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7.2 Author's Contributions

Dolores Rodríguez Veintimilla designed the DNO Ecuador Study, drafted the work protocol, supervised the execution of the study, the collection of primary data, and the statistical-mathematical analysis of the results, and drafted the final research report.

Mery Guerrero Tapia participated in drafting the work protocol, supervised the training of local interviewers, conducting the study, and collecting primary data, and participated in drafting the final research report. We deeply regret to inform you that the author passed away before the publication of this article.

Marisol Maldonado, Sandra Herrera, and **Alexandra Centeno** wrote the tools included in the Procedures Manual, participated in the training of local interviewers, supervised the execution of the study and the collection of primary data, and helped writing the final research report.

The authors participated in the writing process of this text and approved the final version.

7.3 Funding

No funding was requested to finance this research.

7.4 Availability of data and materials

Those interested can contact the lead author to obtain copies of the procedures used in the study for study and replication purposes.

8. Declarations

8.1 Conflict of interest

The authors declare no conflicts of interest.

8.2 Limitations of the study

The DNO Ecuador Study is a prospective, ongoing epidemiological investigation designed to characterize with increasing precision the magnitude and impact of malnutrition on the clinical course of OHD and response to cytoreductive therapy. The methodology of this study includes the progressive incorporation of new centers, patients, and provinces to improve the representativeness of findings. This report is an initial analysis with data from five hospitals in three provinces of the country.

8.3 Future extensions

This research, as an extension of the DNO Ecuador Study, analyzes the current nutritional support provided to hospitalized cancer patients. A subsequent report will present data on the clinical recognition of malnutrition and the nutritional therapeutic strategies employed in the health centers included in the sample.

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APPENDICES

FEDERACIÓN LATINO AMERICANA DE TERAPIA
FELANPE
NUTRICIONAL, NUTRICION CLINICA Y METABOLISMO

DÍA DE LA NUTRICIÓN EN ONCOLOGÍA
ENCUESTA SUBJETIVA GLOBAL DEL ESTADO NUTRICIONAL
DATOS GENERALES DEL PACIENTE

Hora de inicio

Nombre(s) y Apellidos:			HC:
Edad:	Sexo:	Sala:	Cama:
Fecha:	Talla _____ cm	Peso Actual _____ Kg	

1. Peso

PESO HABITUAL _____ Kg (Coloque 00.00 si desconoce el peso habitual)	Perdió Peso en los últimos 6 meses ☐ Sí ☐ No ☐ Desconoce	Cantidad Perdida _____ Kg
% Pérdida en relación al Peso Habitual _____ %	En las últimas dos semanas: ☐Continúa Perdiendo ☐Estable ☐Aumento ☐Desconoce	

2. Ingesta alimenticia respecto de la habitual

Ingesta Alimenticia respecto de la Habitual ☐ Sin Alteraciones ☐ Hubo alteraciones	
En caso de alteraciones de la ingesta alimenticia:	
Hace cuanto tiempo _____ Días	Para qué tipo de dieta ☐ Dieta habitual, pero en menor cantidad ☐ Dieta líquida ☐ Líquidos parenterales hipocalóricos ☐ Ayuno

3. Síntomas gastrointestinales presentes hace más de 15 días

Síntomas gastrointestinales presentes hace más de 15 días		☐ Sí	☐ No		
Vómitos	☐ Sí	☐ No	Náuseas	☐ Sí	☐ No
Diarreas	☐ Sí	☐ No	Falta de apetito	☐ Sí	☐ No
Disfagia	☐ Sí	☐ No	Dolor abdominal	☐ Sí	☐ No

4. Capacidad funcional

Capacidad Funcional	☐ Conservada	☐ Disminuida
En caso de disminución de la capacidad funcional:		
Hace cuanto tiempo _____ Días	Para qué tipo de actividad ☐ Limitación de la capacidad laboral ☐ Recibe Tratamiento Ambulatorio ☐ Encamado	

5. Diagnóstico principal y su relación con las necesidades nutricionales

Diagnósticos principales	Demandas metabólicas ☐ Habitual ☐ Estrés Bajo ☐ Estrés Moderado ☐ Estrés Elevado

FEDERACIÓN LATINO AMERICANA DE TERAPIA
FELANPE
NUTRICIONAL, NUTRICION CLINICA Y METABOLISMO

DÍA DE LA NUTRICIÓN EN ONCOLOGÍA
ENCUESTA SUBJETIVA GLOBAL DEL ESTADO NUTRICIONAL
EXAMEN FÍSICO

Pérdida de Grasa subcutánea en Triceps y Tórax

☐ Sin Pérdida ☐ Pérdida Leve ☐ Pérdida Moderada ☐ Pérdida Importante

Pérdida de Masa Muscular en Cuadriceps, Deltoides y Temporales

☐ Sin Pérdida ☐ Pérdida Leve ☐ Pérdida Moderada ☐ Pérdida Importante

Edemas en los Tobillos

☐ Ausente ☐ Leve ☐ Moderada ☐ Importante

Edemas en el Sacro

☐ Ausente ☐ Leve ☐ Moderada ☐ Importante

Ascitis

☐ Ausente ☐ Leve ☐ Moderada ☐ Importante

EVALUACION SUBJETIVA GLOBAL

☐ A	Bien nutrido
☐ B	Moderadamente desnutrido/en riesgo de estarlo
☐ C	Gravemente desnutrido

ONCOLOGÍA

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Original article / Artículo original

Mortality from Malignant Neoplasms of Digestive Organs in Ecuador, Period 2019-2023

Mortalidad por neoplasias malignas en órganos digestivos en Ecuador 2019-2023

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ABSTRACT

Introduction: Mortality from malignant neoplasms of the digestive organs is a public health problem with a direct impact on health systems. **Objective:** To determine the mortality caused by malignant tumors of the digestive organs in Ecuador during the years 2019-2023. **Materials and methods:** An observational, descriptive, cross-sectional study was conducted using open data on deaths recorded by INEC between 2019 and 2023. **Results:** According to the ranking of the cumulative mortality rate, the most frequent malignant tumor was stomach cancer (39%), followed by liver and biliary tract cancer (18%), among others, with a 17% increase in colon cancer during the period, with a linear trend R2 of 86% (p: 0.02). A higher age-standardized mortality rate was obtained in men (60.74), mainly in those ≥ 75 years of age. The provinces with the highest mortality rates were Azuay with 200 deaths, followed by Loja with 187 deaths, and Imbabura with 183 deaths per 100,000 inhabitants. **Conclusions:** During the study period, mortality from digestive organ tumors was observed to be among the highest in Ecuador, varying according to sex, age, and province, with malignant neoplasms of the stomach and colon being the most representative.

Keywords: Mortality, malignant neoplasms, digestive organs.

RESUMEN

Introducción: La mortalidad por neoplasias malignas de órganos digestivos constituye un problema de salud pública con un impacto directo en los sistemas de salud. **Objetivo:** Determinar la mortalidad causada por tumores malignos de órganos digestivos en Ecuador durante 2019-2023. **Material y métodos:** Se realizó un estudio con datos abiertos, de diseño observacional, descriptivo y transversal, de las defunciones registradas en el Instituto Nacional de Estadísticas y Censo del Ecuador en el periodo 2019-2023. **Resultados:** Según el *ranking* de la proporción acumulada de mortalidad, se obtuvo que el tumor maligno más frecuente fue el de estómago (39 %), seguido del de hígado y vías biliares (18 %), entre otros, con un incremento en el cáncer de colon del 17 % durante el periodo y con una tendencia lineal R2 del 86 % (p = 0,02). Se obtuvo una tasa estandarizada por edad de la mortalidad mayor en hombres (60,74), principalmente en ≥ 75 años. La provincia con mayor frecuencia fue Azuay con 200 fallecidos, seguida de Loja con 187 fallecidos e Imbabura con 183 fallecidos por

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cada 100 000 habitantes, entre otras provincias. **Conclusiones:** Durante el estudio, se observó que en Ecuador la mortalidad por tumores de órganos digestivos se ha situado en los primeros lugares, con variaciones según el sexo, la edad y las provincias. Las neoplasias malignas de estómago y colon son las más representativas.

Palabras clave: mortalidad, neoplasias malignas, órganos digestivos.

1. Introduction

According to GLOBOCAN estimates, in 2022 there were 4,905,882 new cases of cancer worldwide and an estimated 3,324,774 deaths from this disease [1]. Therefore, cancer is a public health issue because it requires comprehensive management, long-term care, specialized technologies, multidisciplinary staff, among others [2]. Malignant tumors of the digestive organs are considered a major health problem, although their burden is not uniform worldwide. In the US, these tumors account for 18% of cancer cases and 28% of deaths [3] attributed to factors resulting from population aging and changes in lifestyle and living conditions. Thus, it is essential to review the magnitude of this problem [4].

In Latin America, tackling digestive cancer is a major challenge, considering that they are among the leading causes of mortality in different countries. In addition, socioeconomic and environmental differences are reflected in the rates from various regions in each country [5]. For instance, in Cuba, 25.2% of cancer deaths are attributed to malignant tumors of the digestive system [6]. Similarly, in Chile, from 2016 to 2020, digestive oncological pathologies were the most frequent [7]. In Venezuela, between 2015 and 2019, stomach cancer in men had a rate of 10.2, and colon-rectal cancer in women had a rate of 7.1 per 100,000 inhabitants [8].

Furthermore, these types of cancer have a significant economic impact on health systems and rank in the top 10 according to their location in terms of digestive neoplasms, as in Matanzas, Cuba [9].

In Ecuador, there are few studies that show the distribution of these neoplasms and their impact on the population. It was found that, in the period 2020–2022, there were deaths related to these types of cancers and mortality was concentrated in the 70-79 age group (27%), distributed in the provinces of Sierra and Costa, where the highest rates were recorded [10].

The objective of this study is to determine the behavior of mortality caused by malignant tumors of the digestive organs in Ecuador from 2019 to 2023.

2. Materials and Methods

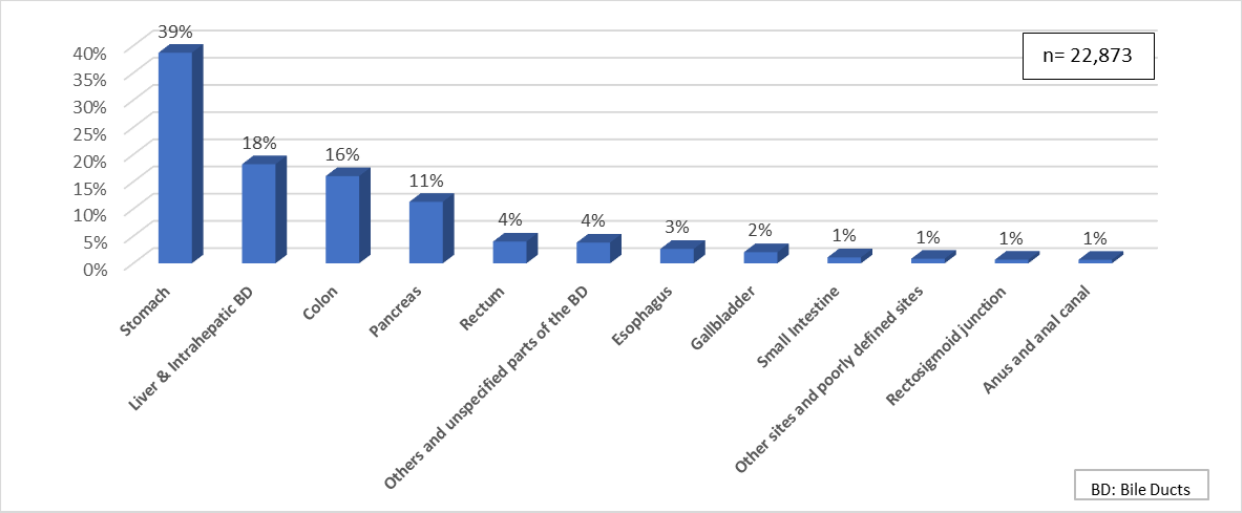
An observational, descriptive, cross-sectional study was conducted. The study population (n= 22,873) includes all deaths from malignant tumors of the digestive organs (codes C15 to C26 according to ICD-10) recorded in Ecuador between 2019 and 2023. Death data were obtained from the National Institute of Statistics and Census of Ecuador (INEC by its acronym in Spanish) in January 2025, when the data had already been validated through the online open database. The following variables were obtained: tumor location, province of residence, age, and sex. A descriptive analysis was performed using frequencies and percentages. To observe temporal changes, the annual behavior was evaluated through online graphs, performing the linear trend test and taking the R2 value, which represents the proportion of variance in the dependent variable that can be explained by the independent variable. Its interpretation indicates that the percentage of variability in the observed data can be explained by the linear relationship between variables. The analysis was performed in Microsoft Excel 2021 (Spanish version) and IBM SPSS Statistics version 29, determining statistical significance with a p-value <0.05.

For this study, anonymized data publicly available on the INEC's open death platform was used. Confidentiality, security, and data protection regulations in force in Ecuador were complied with.

3. Results

Figure 1 shows the ranking of the cumulative proportion of mortality from malignant tumors of the digestive organs in Ecuador from 2019 to 2023. Stomach cancer (C16) was the most frequent with 39%, followed by liver and biliary tract cancer (C22), 18%; colon (C18), 16%; and pancreatic cancer (C25), 11%.

Figure 1. Ranking of cumulative mortality from digestive organ tumors in Ecuador, both sexes, 2019-2023.



Source: Mortality data – INEC

Regarding the mortality trend due to the most common digestive organ tumors between 2019 and 2023, shown in Figure 2, there was a 3% increase in stomach tumors, a 3% decrease in liver and bile duct tumors, and a 0.1% decrease in pancreatic tumors, while colon cancer showed a 17% increase.

In the period 2019-2023, cases of colon cancer showed an upward trend. Linear regression analysis indicated that this trend was statistically significant ($p = 0.023$). The coefficient of determination ($R^2 = 0.86$) showed that 86% of data variability can be explained by the linear relationship between time (years) and the number of cases, thus supporting the consistency of the observed increase.

The age-standardized mortality rate (world population) due to digestive organ tumors by sex shows a rate of 60.74 for men and 42.10 for women per 100,000 inhabitants. They are mainly concentrated in the 75+ age group for men (16.9) and women (11.39). However, most cases are found in both sexes aged 60 and over (Figure 3).

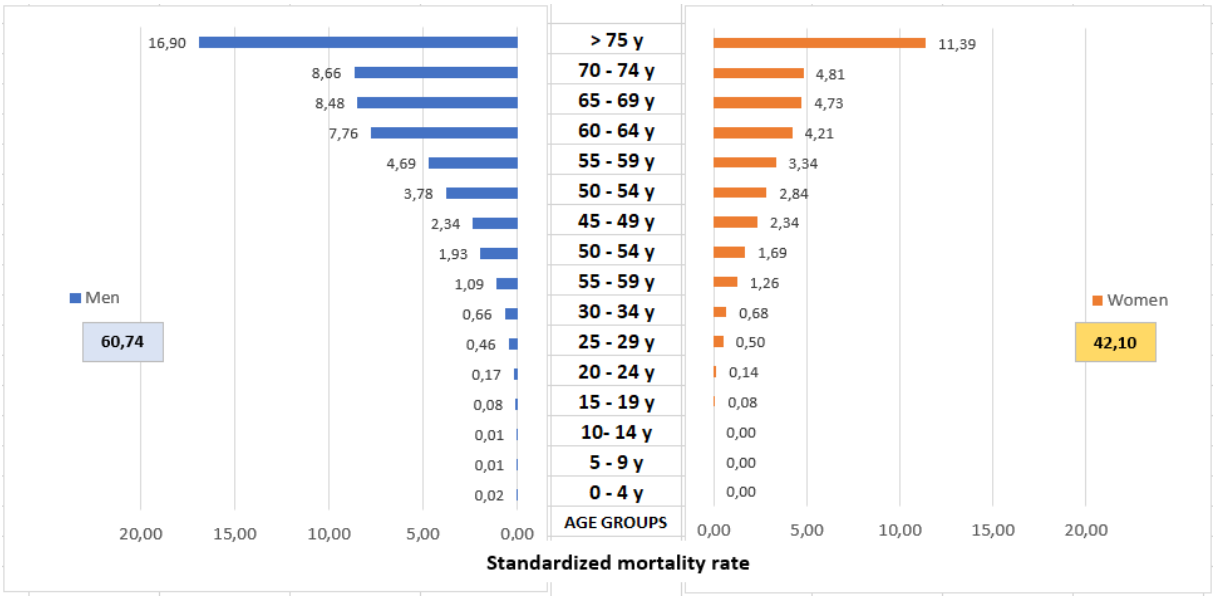
Regarding the place with the highest mortality rate from digestive organ tumors by province of residence, the distribution rate shows that Azuay, with 200 deaths had the highest frequency, followed by Loja with 187 deaths, and Imbabura with 183 deaths per 100,000 inhabitants (Figure 4).

The percentage distribution of mortality by sex was analyzed in the different provinces of Ecuador. In provinces such as Guayas, Manabí, and El Oro, higher mortality was observed in men; while in Pichincha, Azuay, Imbabura, and Chimborazo, mortality was higher in women. In the rest of the provinces, no differences were found in mortality rates between the two sexes (Figure 5).

Figure 2. Mortality trend of the most common malignant tumors of the digestive organs. Ecuador, both sexes, 2019-2023.

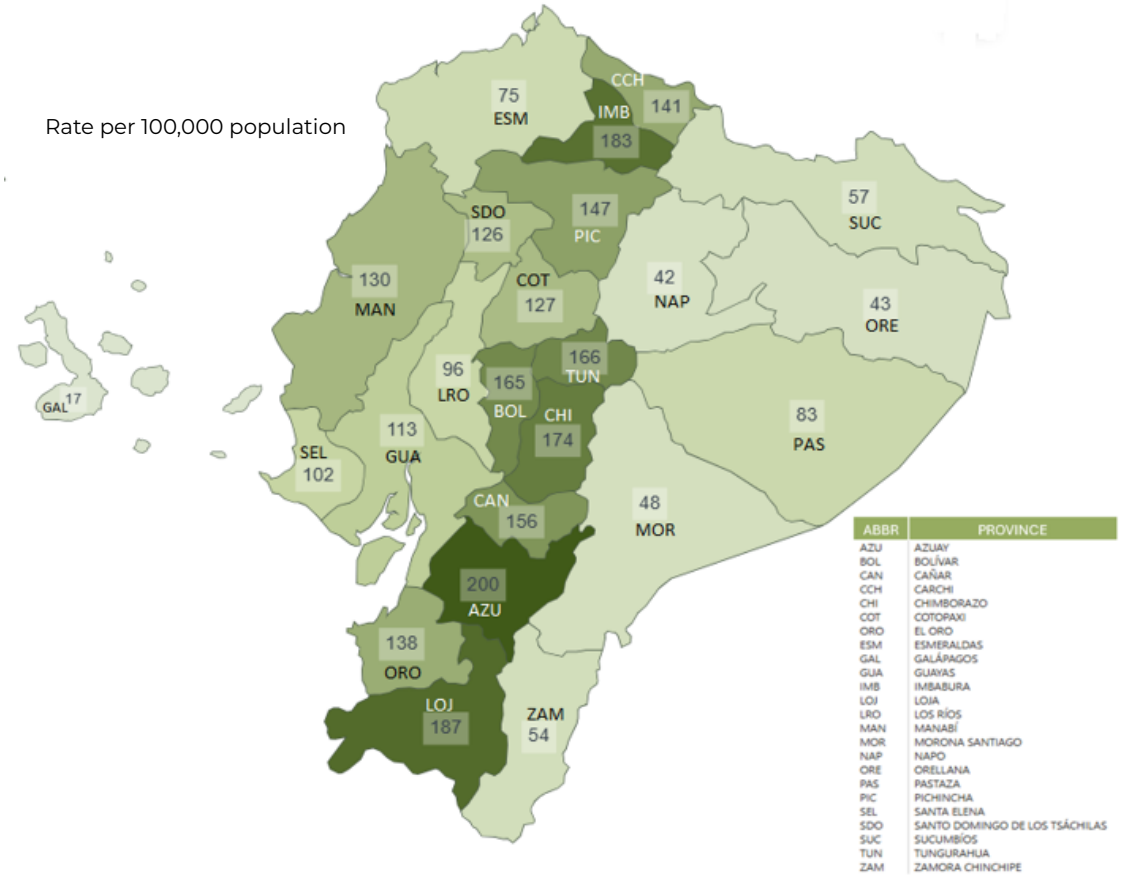
Source: Mortality data – INEC.

Figure 3. Age-standardized mortality rate from malignant tumors of the digestive organs by sex in Ecuador, 2019-2023



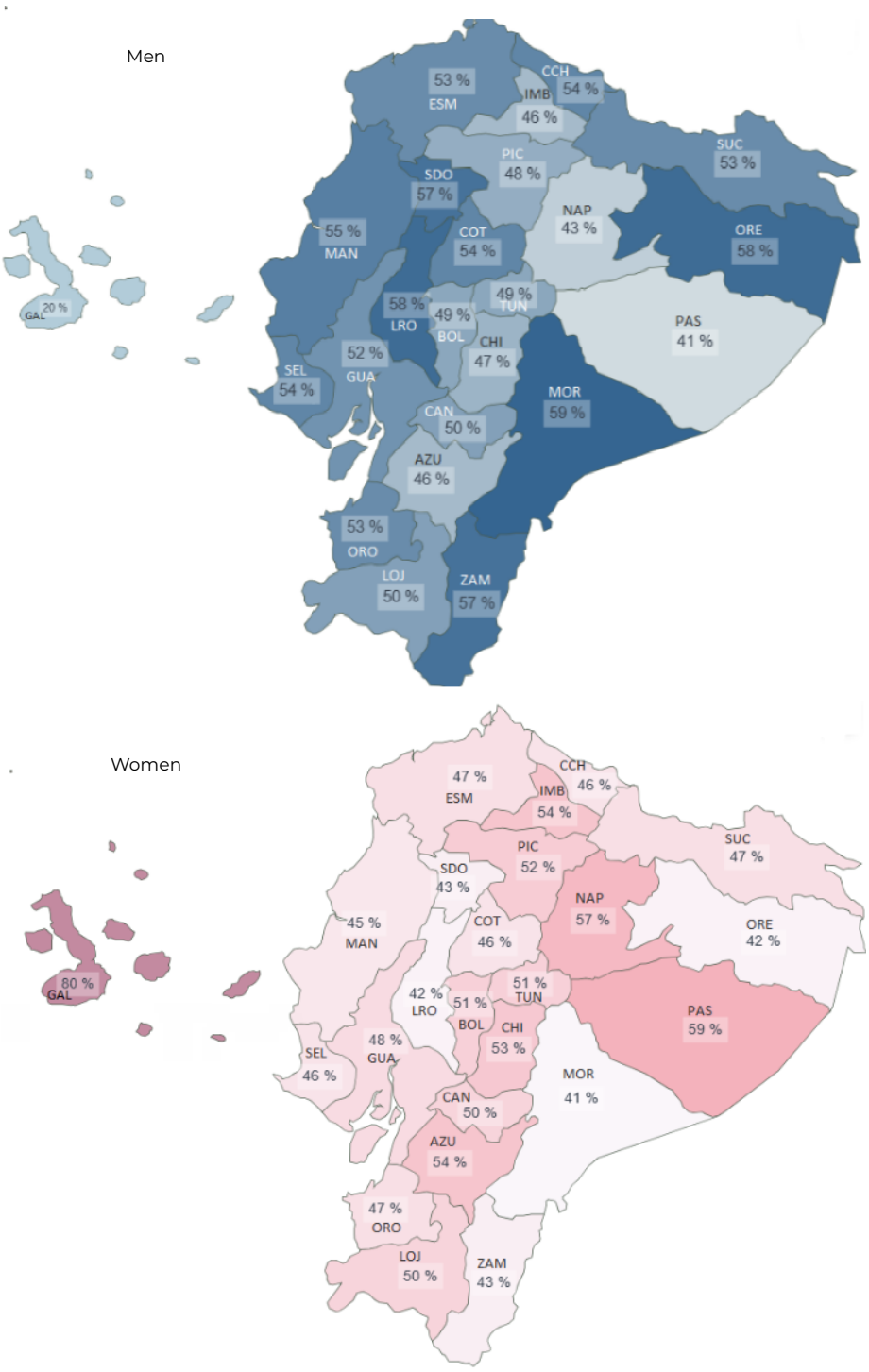
Source: Mortality data – INEC.

Figure 4. Distribution rate of mortality from digestive organ tumors by province in Ecuador, for both sexes, 2019-2023.



Source: Mortality data – INEC.

Figure 5. Percentage distribution of mortality in digestive organ tumors by province and gender in Ecuador. 2019-2023.



Source: Mortality data – INEC.

4. Discussion

In Ecuador, during the period 2019–2023, mortality from malignant tumors of the digestive organs has remained among the leading causes of death, with a sustained trend. Malignant stomach tumors were identified as the most frequent. This finding is consistent with previous studies conducted in Quito and Guayaquil, which reported high mortality rates of up to 80.5% [11,12].

Similar patterns have been described in other Latin American countries, although with epidemiological particularities. In Colombia, for example, a study on mortality trends from digestive tumors showed a more pronounced increase in men between 2002 and 2014 [13]. This trend partially resembles what was observed in our analysis. In contrast, in Colón, Cuba, between 2011 and 2020, there was also a sustained increase in mortality from malignant tumors of the digestive system, but with a predominance of colon cancer (52%), mainly affecting men over 60 years of age [9]. These differences are accentuated when compared with the data collected at Tungurahua, Ecuador, between 2000 and 2014, where the highest mortality was observed in women and malignant stomach tumors were the most common [14].

The variations between countries, and even between provinces within the same territory, probably respond to differences in the distribution of risk factors, eating habits, prevalence of infections such as Helicobacter pylori, access to diagnostic services, availability of timely treatment, and social determinants of health. In the case of Ecuador, the geographical distribution shows higher mortality rates in both coastal and mountain provinces, a pattern that coincides with that described in Chile, where marked differences in mortality rates from digestive tumors have been identified between northern and southern regions, with temporal variations reflecting epidemiological changes between 2002 and 2021 [15].

Taken together, these findings highlight the need for prevention and early detection strategies tailored to the epidemiological and geographical characteristics of each region. They also demonstrate the urgency of public policies that reduce inequalities in access to diagnosis and treatment, with the aim of reducing the burden and mortality associated with these neoplasms in the country.

5. Conclusions

Mortality from digestive organ tumors varies according to sex, age group, and province in Ecuador, with an increase in colon cancer, although the greatest burden of disease continues to be malignant stomach tumors. The findings of this study highlight the need to implement prevention and control measures focused on the most affected provinces and groups.

6. Abbreviations

SOLCA (by its acronym in Spanish): Sociedad de Lucha Contra el Cáncer.

ICD 10: International Statistical Classification of Diseases and Related Health Problems 10th Revision.

INEC (by its acronym in Spanish): Instituto Nacional de Estadística y Censos.

7. Administrative information

7.1 Contribution of the authors

Real J.; Jaramillo L.; Conceptualization, validation, visualization, methodology, project management, writing: review and editing.

Tanca J.; Pacheco L.: Validation, methodology, project management, review.

Real R., Puga G.: Conceptualization, project management, methodology, writing: review and editing.

All authors read and approved the final version of the manuscript.

7.2 Funding

None.

7.3 Availability of data and materials

The data are freely available on the INEC website: https://aplicaciones3.ecuadorencifras.gob.ec/BIINEC-war/index.xhtml

7.4 Declarations

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

7.5 Ethics committee approval

Open or public data was used for this research.

7.6 Conflicts of interest

The authors declare that they have no conflicts of interest.

7.7 Limitations

This study does not explain the causes of mortality from malignant tumors of the digestive organs, but it does provide useful information for identifying their distribution according to location, age, sex, and most affected provinces. These data constitute a baseline for future research to better understand the problem and develop prevention and control strategies appropriate for each region of Ecuador.

7.8 Additional files

None declared by the authors.

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ONCOLOGÍA

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Article / Artículo

Effect of Physical Therapy and Health Education early Intervention on Functional Recovery after Radical Mastectomy: A Systematic Review

Efecto de la intervención temprana de fisioterapia y educación en salud en la recuperación funcional postmastectomía radical: una revisión sistemática

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ABSTRACT

Introduction: Radical mastectomy, used in the treatment of locally advanced breast cancer, is frequently associated with physical and functional sequelae such as lymphedema, pain, limited shoulder mobility, and impaired quality of life. Early intervention through physical therapy and health education has proven to be a key strategy for preventing complications, promoting functional recovery, and improving patient autonomy. **Objective:** The purpose of this study is to analyze the scientific evidence on the benefits of early physical therapy and health education for post-radical mastectomy patients. **Methodology:** A systematic review based on a comprehensive search for information on the effect of early intervention with physical therapy and health education on functional recovery after radical mastectomy. The databases reviewed were: PubMed, Physiotherapy Evidence Database (PEDro), Web of Science, Cochrane, Global Cancer Observatory, and Lilacs; publications correspond to the last 10 years. **Results:** Sixty full- text scientific articles were evaluated, of which 23 met the inclusion criteria related to physical therapy interventions, therapeutic exercises, and health education in post- mastectomy patients. Early physical therapy showed an 85% reduction in postoperative pain, a 75% improvement in joint range of motion, and a 40% reduction in acute lymphedema. Health education increased adherence to rehabilitation treatment and patient autonomy. **Conclusions:** The combination of early physical therapy and health education strategies significantly improves functional recovery after radical mastectomy. Its implementation in hospital oncology units could contribute to strengthening evidence- based clinical practice.

Keywords: Breast cancer, health education, physical therapy, exercise, benefits, rehabilitation, mastectomy.

RESUMEN

Introducción: La mastectomía radical, empleada en el tratamiento del cáncer de mama localmente avanzado, se asocia con frecuencia a secuelas físicas y funcionales como linfedema, dolor, limitación de la movilidad del hombro y deterioro en la calidad de vida. La intervención temprana mediante fisioterapia y educación en salud ha demostrado ser una estrategia clave para prevenir complicaciones, promover la recuperación funcional y mejorar la autonomía de las pacientes. **Objetivo:** El propósito de esta investigación fue analizar la evidencia científica sobre los beneficios de la fisioterapia temprana y la educación en salud para pacientes posmastectomía radical. **Metodología:** Revisión sistemática basada en una búsqueda exhaustiva de información acerca del efecto de la intervención temprana de fisioterapia y educación en salud en la recuperación funcional posmastectomía radical. Las bases de datos revisadas fueron PubMed, Physiotherapy Evidence Database (PEDro), Web of Science, Cochrane, Global Cancer Obervatory y Lilacs, cuyas publicaciones corresponden a los últimos diez años. **Resultados:**

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Se evaluaron 60 artículos científicos a texto completo, de los cuales 23 cumplieron con los criterios de inclusión relacionados con intervenciones de fisioterapia, ejercicios terapéuticos y educación en salud en pacientes posmastectomía. La fisioterapia temprana mostró una reducción del dolor posoperatorio en un 85 %, una mejoría del 75 % en el rango articular y una disminución del linfedema agudo en un 40 %. La educación en salud aumentó el cumplimiento del tratamiento rehabilitador y la autonomía de las pacientes. **Conclusiones:** La combinación de fisioterapia temprana y estrategias educativas en salud mejoran significativamente la recuperación funcional tras una mastectomía radical. Su implementación en unidades oncológicas hospitalarias podría contribuir al fortalecimiento de una práctica clínica basada en la evidencia científica.

Palabras clave: cáncer de mama, educación en salud, fisioterapia, ejercicio, beneficios, rehabilitación, mastectomía.

1. Introduction

Breast cancer is the most common malignancy among women worldwide, with more than 2.2 million new cases in 2022. In Latin America, the high mortality (220,000 deaths) in that same year reflects inequalities in access to diagnosis, treatment, and rehabilitation [1]. In Ecuador, breast cancer is the leading cancer by incidence among women, with 3,903 new cases and more than 12,400 women affected and ranks fourth in cancer-related mortality. This underscores the need to implement protocols tailored to the local context, such as early physiotherapy and postoperative health education [2].

In many cases, radical mastectomy is accompanied by axillary lymph node dissection, which can lead to significant sequelae such as lymphedema, persistent pain, restricted shoulder mobility, and reduced muscle strength. In light of the functional complications associated with radical mastectomy, early physiotherapy and patient education are essential to optimize recovery and prevent long-term sequelae. Starting in the inpatient period, the implementation of therapeutic strategies such as early mobilization and structured patient education has been shown to significantly improve postoperative recovery, reduce risks, and facilitate an effective return to daily-life activities. In this context, progressive exercise protocols have strong scientific support, thus validating their safety and effectiveness in enhancing joint mobility and reducing pain [3].

International evidence, including recommendations from the American Cancer Society, supports the effectiveness of combining early physiotherapy with progressive postoperative exercises to significantly improve mobility, reduce potential surgical side effects, and enhance patient confidence. These interventions enable patients to safely resume their daily activities [4].

Following radical mastectomy, the aim is to provide clear recommendations on self-care, progressive exercises, and lymphedema prevention. These measures not only strengthen the rehabilitation process but also enable patients to identify clinically meaningful warning signs such as muscle weakness, persistent pain, or sudden loss of mobility. This comprehensive approach promotes a safer recovery and reduces the risk of long-term complications [5].

Functional impairments following radical mastectomy are grouped into three main categories: neuromuscular, musculoskeletal, and lymph vascular. Table 1 synthesizes these sequelae and physical therapy modalities most commonly employed to address them, thus providing a clinical frame of reference for the present review [6].

This systematic review is supported by three fundamental reasons. First, from a clinical perspective, there is a need to incorporate safe, effective, and accessible early therapeutic strategies for patients treated in hospital oncology units to improve functional status and quality of life after radical mastectomy. Second, a substantial gap in the regional scientific literature is identified. The available evidence in Latin America and particularly in the national context is limited, which justifies conducting a broad search spanning the last ten years (2015–2025), without excluding seminal studies that may provide relevant data on early advances in this field. Finally, this review has the potential to positively influence local physiotherapy practice. By systematizing existing information, it seeks to facilitate the development of clinical and educational recommendations applicable at both national and international levels and to strengthen the development of oncologic physiotherapy through an evidence-based approach centered on comprehensive care and patient well-being.

Table 1. Main functional sequelae and rehabilitative treatment modalities in women after mastectomy

Functional sequelae	Description	Rehabilitation treatment
Restriction of range of motion (ROM)	Limitation in moving the arm and shoulder on the affected side [7].	Progressive mobility exercises and manual therapy to restore joint range of motion [8].
Lymphedema	Arm edema caused by the accumulation of lymphatic fluid following lymph node removal [9].	Manual lymph drainage, compression bandaging, and specific exercises to stimulate lymph flow [10, 11, 12].
Persistent pain	Chronic pain in the surgical area or shoulder that does not resolve after the initial recovery period [13, 14].	Relaxation techniques, physiotherapy, and electrotherapy to relieve pain [15, 16, 17, 18].
Loss of muscle strength	Weakness in the arm and shoulder muscles due to postsurgical immobility [19, 20].	Specific muscle-strengthening exercises and progressive resistance training [21].
Postural alterations	Changes in posture due to loss of breast tissue or pain-related compensations [22, 23].	Postural training, strengthening of stabilizing muscles, and ergonomic correction [24, 25, 26].

2.Methodology

2.1 Objectives

The general objective of this study was to identify the scientific evidence on the benefits of early physiotherapy and health education for patients after radical mastectomy through a systematic literature review. Specifically, the study aimed to optimize early postmastectomy functional recovery through physiotherapy by evaluating its effects on joint range of motion, muscle strength, and endurance based on evidence-supported protocols; to strengthen self-care and patient self-management after surgery by providing educational tools on complication prevention and techniques to prevent lymphedema; and to design structured physiotherapeutic intervention programs that facilitate functional recovery for improving patients' quality of life.

2.2 Eligibility criteria

Articles published in the last ten years were included. Regarding the population, eligible participants were adult women aged 40–65 years, who had undergone unilateral radical mastectomy (left or right). The intervention was postoperative physiotherapy or rehabilitative treatment. Eligible designs included clinical trials (randomized or nonrandomized), systematic reviews, meta-analyses, and evidence-based clinical practice guidelines. Publications had to be available in full text in English, Spanish, or Portuguese. Studies were considered if they reported outcomes on functional sequelae after radical mastectomy and their therapeutic management.

2.3 Exclusion criteria

We excluded studies that included only medical or surgical interventions without a physical rehabilitation component; those that assessed exclusively aesthetic or reconstructive procedures unrelated to functional recovery; did not analyze functional sequelae after radical mastectomy; lacked a clearly defined study population (e.g., editorials, letters to the editor, or narrative reviews without systematic analysis); and those involving patients with severe comorbidities that could affect functional outcomes, such as active metastases or neuromuscular and cardiovascular diseases.

2.4 Study design

Systematic literature review based on studies published in the last ten years that addressed physiotherapy interventions in women following radical mastectomy.

The PubMed, Physiotherapy Evidence Database (PEDro), Web of Science, Cochrane Library, Global Cancer Observatory, and LILACS databases were used. In addition, Google Scholar was used as an open search engine. These sources enabled the retrieval of scientific articles, systematic reviews, and clinical trials published in English, Spanish, and Portuguese that address early physiotherapy combined with health education strategies in postmastectomy patients.

A systematic search was conducted across the six databases and Google Scholar. The strategy included Spanish- and English-language terms related to "breast cancer," "postmastectomy physiotherapy and rehabilitation," "early mobilization," "biomechanical alterations," and "functional impairments." MeSH/DeCS subject headings and free-text terms were combined using the Boolean operators AND and OR. The search was restricted to the title and abstract fields. After deduplication and application of date and language filters, potentially eligible articles were reviewed in full text for final inclusion.

All articles retrieved from the databases, which met the criteria defined in the search strategy, were imported into the Rayyan QCRI software. This tool streamlined the screening process, thus enabling an efficient selection of relevant studies by marking each record as "included," "excluded," or "maybe."

2.4.1 Population and sample

As part of the systematic search strategy, 130 records were initially identified. After removing duplicates and applying automatic filters in the reference manager, 60 articles continued to the full-text assessment phase. Two independent reviewers screened titles, abstracts, and full texts using the predefined eligibility criteria (oncologic diagnosis, rehabilitative intervention as a principal component, and functional outcomes). From the studies retrieved in the systematic search, 23 articles were selected and thematically classified as follows:

- 10 studies on early postmastectomy physiotherapy.
- 5 studies focused on early mobilization.
- 3 studies on progressive exercises.
- 2 studies specifically addressing lymphedema reduction.
- 3 studies related to health education interventions.

In total, 37 articles were excluded following title, abstract, and full-text assessment. The primary reasons for exclusion were absence of a population with an oncologic diagnosis and lack of rehabilitative intervention as a central component of the study.

2.4.2 Data collection

A detailed analysis was performed to extract publication characteristics, study design, population, intervention details, and outcomes of interest from the 23 studies. Each variable was coded in an electronic data matrix with duplicate verification, and discrepancies were resolved by consensus. The

following clinical parameters were systematized: postoperative pain, muscle strength and endurance, lymphedema, shoulder range of motion, overall function, and treatment adherence. Data quality and consistency were verified prior to tabulation in the results tables, in accordance with the transparency and reproducibility standards of the PRISMA 2020 guideline.

2.4.3 Variables assessed

The following variables were selected to directly assess the clinical effectiveness of physiotherapeutic and educational interventions in post–radical mastectomy patients:

- **Postoperative pain:** Quantified using the Visual Analog Scale (VAS) and the Numeric Rating Scale (NRS) to determine the ability of early physiotherapy to reduce acute or persistent pain after surgery.
- **Muscle strength:** Assessed to identify functional improvements in the muscles of the affected upper limb, as an indicator of motor recovery.
- **Lymphedema:** Measured in terms of volume or symptomatology, to assess the effectiveness of decongestive techniques and self-care strategies.
- **Shoulder range of motion:** Used to determine whether progressive exercises enable the recovery of adequate joint mobility in the operated limb.
- **Muscle endurance:** Assessed to determine whether patients improve their capacity to sustain prolonged physical effort, thereby promoting functional independence.

2.4.4 Secondary Variables

These variables complemented the clinical analysis and helped assess the long-term rehabilitative impact:

- **Functionality:** Assessed in terms of independence in daily-life activities (DLAs), as an overall indicator of postoperative recovery.
- **Adherence to the rehabilitative treatment:** Considered to determine whether combining health education with physiotherapy improves therapeutic continuity and patient engagement in the recovery process.

2.4.5 Synthesis methods

A narrative synthesis was performed, grouping the studies by type of intervention and the clinical outcomes assessed. In particular, we identified relevant studies on the effectiveness of treatments for postmastectomy lymphedema, which evaluated interventions such as combined therapy, exercise, compression, and lymphatic drainage. Classification was conducted independently by three reviewers, and any discrepancies were resolved by consensus or by involving a fourth reviewer.

To prepare the data for synthesis, several conversions and adjustments were performed. When standard deviations were not reported, they were derived from confidence intervals or from the reported standard error. Pain scales were normalized to a 0–10 Visual Analog Scale (VAS) to enable comparison across studies. Conversely, when studies used kilograms as the unit of measurement, data were handled without modification or adjustment. These adaptations allowed for a more homogeneous presentation of the results.

3. Results

To explore potential sources of heterogeneity among the included studies, a subgroup analysis was conducted based on the studies' objectives (assessing benefits, efficacy in terms of the physiotherapeutic

effect, and the resources used to analyze physiotherapeutic mechanisms) and on outcomes that demonstrated greater effectiveness. Meta-regression was not performed due to the limited number of studies with comparable data over the past ten years.

To evaluate the robustness of the findings, sensitivity analyses were conducted focusing on two key aspects: the risk of bias in the included studies and the variability of the analytical models.

First, studies with significant methodological limitations such as small sample sizes, absence of a control group, or limited description of the interventions were identified. Upon excluding these studies from the analysis, the primary outcomes an 85% reduction in postoperative pain, a 75% improvement in range of motion, and a 40% decrease in acute lymphedema remained stable, supporting the consistency of the assembled evidence.

Stacked bar charts were used to compare the effectiveness of different interventions in reducing lymphedema. A nonconventional display (radar chart) was used to simultaneously depict the variables analyzed when assessing the effectiveness of post–radical mastectomy physiotherapy, and a time-trend line chart was employed to visualize postmastectomy recovery trajectories, comparing age groups to identify differences in recovery speed over time. Additionally, a summary table presented the main results of each study, including author, year, type of intervention, sample size, and quantitative outcomes (pain reduction, improvement in range of motion [ROM], and exercises found to be effective in enhancing postoperative recovery).

Additionally, the influence of the type of intervention on outcomes was explored using an alternative grouping model: physiotherapy alone, health education, and a combined approach. Although slight percentage variations were observed between groups, the overall trend confirmed that combining both strategies provides greater benefits for post-radical mastectomy functional recovery. It is noteworthy that these sensitivity analyses were not prespecified in the initial protocol but were applied in an exploratory manner to strengthen the interpretation of the results and reduce the potential impact of methodological biases or heterogeneity across studies.

3.1 Publication bias

Variability in intervention protocols represents a moderate risk of bias, according to the JBI (Joanna Briggs Institute) checklist [27] for randomized controlled trials (RCTs) and quasi-experimental studies. Differences in the timing of physiotherapy initiation (24–48 h vs 72 h postoperative), exercise intensity, and program duration compromise the comparability of outcomes and limit external validity, particularly with respect to recovery of range of motion and lymphedema prevention. The lack of standardization in the description of interventions further reinforces this methodological risk.

It is important to consider geographic representativeness. In this review, a location bias was identified, as most studies originated from Europe and Asia, with limited representation from Latin America. This constraint compromises the generalizability of findings, particularly in contexts with sociocultural and economic differences and varying access to health services.

Publication bias was assessed and the need for a comprehensive literature search stood out. This review acknowledges the possible exclusion of studies with negative or inconclusive results, which may have led to an overestimation of the positive effects of early physiotherapy and health education. The lack of a search of grey literature or clinical trial registries further reinforces this limitation.

Some of the included studies present methodological limitations that increase the risk of bias, according to the JBI checklists appropriate to their design.

These methodological weaknesses include small sample sizes, absence of long-term follow-up, and inadequate control groups, which compromise internal validity and the ability to establish robust causal relationships.

Such weaknesses—assessed using specific items from the JBI checklist (e.g., the adequacy of random allocation, blinding, and the validity of outcome measures)—suggest a moderate-to-high risk of bias affecting the quality of the evidence. Finally, the applicability of results should be evaluated in relation to context. In this review, the transferability of the findings is limited in settings with technological or socioeconomic constraints, which implies a risk of bias in their practical implementation, particularly in resource-limited regions.

3.2 Methodological assessment of certainty

As part of the methodological synthesis, an intervention–mechanism matrix (Table 2) was developed to operationalize postmastectomy physiotherapy techniques and link them to their expected physiological effects. Drawing on the included studies, the most frequently reported interventions were grouped: passive/assisted mobilization; isometric and progressive resistance exercises with an aerobic component; and cryotherapy plus manual lymphatic drainage. Two reviewers independently extracted their operational definitions (mode of application and, when available, dosing parameters), as well as the evidence on mechanisms of action, discrepancies were resolved by consensus. The documented physiological effects were supported by the studies' own results and mechanistic descriptions, as well as by the biological plausibility outlined in the literature cited in Table 2. If terminological heterogeneity was found, concepts were standardized according to conventional physiotherapy usage to enhance reproducibility. This table served as a framework for interpreting the mechanistic coherence of the findings and guiding the discussion of their clinical implementation.

Table 2. Effects of applied physiotherapy techniques

Intervention	Description	Expected physiological effects
Assisted passive mobilizations	Applied to the affected upper limb to preserve shoulder mobility and prevent complications such as axillary web syndrome or a painful shoulder.	• Stimulation of synovial fluid production, improving joint lubrication. • Prevention of adhesions and contractures. • Maintenance of joint range of motion and reduction of stiffness [28].
Isometric, progressive resistance, and aerobic exercises	Implemented progressively to improve muscle tone and endurance.	• Activation of muscle fibers without generating joint movement (isometrics), which enhances strength with minimal risk of injury. • Increase in cardiorespiratory capacity and reduction of fatigue [29].
Cryotherapy and manual lymph drainage (MLD)*	Localized application of cold and manual techniques for the management of postoperative pain and edema.	• Cryotherapy decreases nerve conduction velocity, reducing pain and inflammation [30]. • MLD stimulates lymphangiomotor activity, enhances the reabsorption of interstitial fluid, and promotes endorphin release, improving comfort and reducing the risk of lymphedema [31].

Table 3 presents a sequenced post–radical mastectomy rehabilitation protocol developed from the synthesis of included studies and relevant clinical guidelines. The framework organizes care into time-based phases with their therapeutic objective, interventions, and duration: (i) **inpatient phase (0–72 h),** focused on preventing complications through localized cryotherapy, passive/active-assisted mobilization within the tolerated range, manual lymphatic drainage, and initial patient education; (ii) **early phase (days 3–30),** aimed at pain control and restoration of ROM, with progression from mobilizations to scapular-girdle isometrics and self-care education; (iii) **functional phase (1–3 months),** incorporating progressive strengthening, active mobility, aerobic exercise, and training for daily-life activities (DLAs); and (iv) **maintenance phase (>3 months),** focused on optimizing strength and endurance and preventing side effects through aerobic exercise, progressive resistance training, mobility work, and ongoing education. This protocol proposes individualized progressions according to tolerance, pain, and comorbidities, and serves as a practical framework for clinical implementation and follow-up.

Table 3. Post – radical mastectomy rehabilitation protocol

Phase	Therapeutic objective	Intervention	Duration
Inpatient phase (0–72 h)	Prevention of postoperative complications.	• Cryotherapy to the affected area. • Passive shoulder mobilization within the patient's tolerable range of motion. It is important not to force the joint [32]. • Manual lymphatic drainage to reduce inflammation. • Patient health education on activities to promote improvement.	Days 0-3
Early phase (days 3–30)	Physiotherapy treatment for pain and initial restoration of range of motion (ROM).	• Active–passive or active-assisted mobilization if improvements are observed [33]. • Isometric exercises for the biceps, triceps, shoulders, or scapular girdles. • Patient education on self-massage techniques.	Weeks 1-4
Functional phase (1–3 months)	Progressive strengthening and daily-life activities (DLAs).	• Active mobility exercises • Aerobic exercise. • Progressive resistance/strength training. • Daily-life activities (DLAs) [34]. • Patient health education and recommendations.	Weeks 4-12
Maintenance phase (>3 months)	Optimization of strength and prevention of side effects.	• Aerobic training • Progressive strength/resistance exercises. • Active mobility. • Patient health education and recommendations [35].	From the third month onward

3.3 Study participants

This systematic review presents a summary of 23 articles (Table 4).

Table 4. Description of review results

Author	Year	Title	Objective	Results
Oyuki Flores-León [28]	2023	Musculoskeletal benefits of early physiotherapy in postmastectomy patients	To evaluate the musculoskeletal benefits of early physiotherapy in postmastectomy patients.	Significant benefits in musculoskeletal recovery.
Everton Hiury Lins Mendes [5]	2022	The Role of Physiotherapy in Women Postmastectomy	To analyze the role of physiotherapy in women after mastectomy.	Improvement in quality of life and pain reduction.
Jihee Min [36]	2024	Early implementation of exercise to facilitate recovery after breast cancer surgery: a randomized clinical trial	To facilitate postoperative recovery through early exercise.	Accelerated recovery and improved quality of life.
Ifat Klein [37]	2021	A pilot study evaluating the effect of early physiotherapy on pain and disabilities after breast cancer surgery: a prospective randomized controlled trial	To evaluate the effect of early physiotherapy on postoperative pain and disability.	Significant improvement in pain and musculoskeletal disabilities.
Samantha Karlla Lopes de Almeida Rizzi [3]	2020	Early unrestricted upper-extremity range-of-motion exercises after mastectomy and immediate implant reconstruction are safe and beneficial: a randomized trial	To evaluate the safety and benefits of early unrestricted range-of-motion (ROM) exercises.	Safe and beneficial exercises for recovery.
Priya Kannan [38]	2021	Effectiveness of physiotherapy interventions on quality of life and upper-quadrant pain severity in women with postmastectomy pain syndrome: a systematic review and meta-analysis	To evaluate the effectiveness of physiotherapy interventions on quality of life and pain.	Significant improvement in quality of life and pain reduction.
Claire Davies [31]	2020	Interventions for Breast Cancer–Related Lymphedema: Clinical Practice Guideline of the APTA Academy of Oncologic Physical Therapy	To provide clinical practice guidelines for the management of lymphedema.	Effective guidelines for managing lymphedema.
Jesús Baltasar González Rubino [39]	2023	Effectiveness of physiotherapy for axillary web syndrome after breast cancer: a systematic review and meta-analysis	Evaluate the effectiveness of physical therapy in axillary membrane syndrome.	Significant improvement in mobility and reduction in pain.
Medline Plus [40]	2023	Discharge after mastectomy	Provide information about discharge after mastectomy.	Detailed information about the registration process.
Oncology Section of the American Physical Therapy Association [41]	2023	Lymph node surgery for breast cancer	Provide information about lymph node surgery.	Detailed information about the surgery.

Author	Year	Title	Objective	Results
Oncology Section of the American Physical Therapy Association[42]	2021	Exercises After Breast Cancer Surgery	Provide postoperative exercises for breast cancer.	Effective exercises for post-operative recovery.
Martín Barrientos [43]	2022	Effectiveness of postoperative physiotherapy for breast cancer: a systematic review	Evaluate the effectiveness of postoperative physical therapy treatment.	Significant improvement in postoperative recovery.
Maike Trommer et al. [44]	2023	Exercise interventions for adults with cancer receiving radiotherapy alone	Evaluate interventions withexercises for adults with cancer.	Improved quality of life and reduced pain.
María Gabriela Araya-Medrano [45]	2021	Physiotherapeutic approach to functional disorders of the shoulder joint complex due to oncological treatments for breast cancer	Evaluate the physiotherapeutic approach to functional shoulder disorders.	Improved mobility and reduced pain.
Alexandra Ruan Arcanjo Barbosa et al. [46]	2023	Physiotherapy Resources for Gaining ROM in Women Postoperative from Radical Mastectomy	Evaluate physiotherapy resources to gain ROM in post-operative women.	Significant improvement in mobility.
Mauro Tauda [47]	2025	Strength training and its impact on lymphedema and shoulder mobility after breast cancer surgery: systematic review	Assessing the impact of strength training on lymphedema and shoulder mobility.	Improved mobility and reduction of lymphedema.
L Balance[32]	2023	Return to daily-life activities after breast cancer surgery: a questionnaire-based prospective observational study of patients undergoing mastectomy with or without immediate reconstruction	Assessing the return to daily-life activities after mastectomy.	Improved quality of life and return to daily activities.
Jorge Luis Abreus Mora [48]	2024	Mastectomy and physical exercise	To assess the importance of regular, tailored physical exercise in women who have undergone mastectomy as a strategy to improve prognosis, reduce complications, and enhance quality of life during and after oncologic treatment	Regular physical activity performed with sufficient intensity reduces the risk of tumor recurrence and breast cancer–related mortality, improves quality of life, diminishes treatment-related adverse effects, and mitigates the impact of the toxic triad, thereby improving disease prognosis.
Samantha KLA Rizzi [49]	2021	Limited shoulder range-of-motion exercise protocol for 15 or 30 days after oncoplastic breast-conserving surgery: a randomized clinical trial	To evaluate the limited shoulder range-of-motion exercise protocol.	Improved mobility and reduced pain.

Author	Year	Title	Objective	Results
LB Gomide [50]	2007	Morbidity after breast cancer treatment and physiotherapy performance	The aim of this review is to discuss the main sequelae of CM treatment and the role of the physical therapist in the prevention and treatment of these complications.	Prevention and treatment of lymphedema, scar adhesions, and pulmonary complications can be achieved. In addition, pain reduction and the maintenance of range of motion, muscle strength, and proper posture are integral components of physiotherapy.
Linda A Koehler, Anne H Blaes [51]	**2015**	Movement, function, pain, and postoperative edema in axillary web syndrome	Determine the clinical characteristics of AWS related to movement, function, pain, and postoperative edema, and define the incidence and risk factors for AWS within the first 3 months after breast cancer surgery.	Axillary web syndrome is prevalent after breast/axillary surgery for early-stage breast cancer and may persist beyond 12 weeks. Early consequences include movement restriction; however, the long-term effects of persistent AWS cords remain unknown.
Casassola, Giovana Morin [52]	**2020**	Physiotherapy interventions used in the functional rehabilitation of the upper limb in women after mastectomy	Identify the indicators of functionality and the types of physical therapy interventions used for the evaluation and functional rehabilitation of the upper limb in post-mastectomy women.	The functional indicators reported across the articles were shoulder range of motion, muscle strength, limb volume, pain, functional status, and quality of life. The physiotherapeutic interventions proposed included stretching; joint mobilization; neural mobilization; health education; scar massage; myofascial therapy; conventional decongestive therapy; vibration therapy; acupuncture; active exercise; and muscle strengthening.

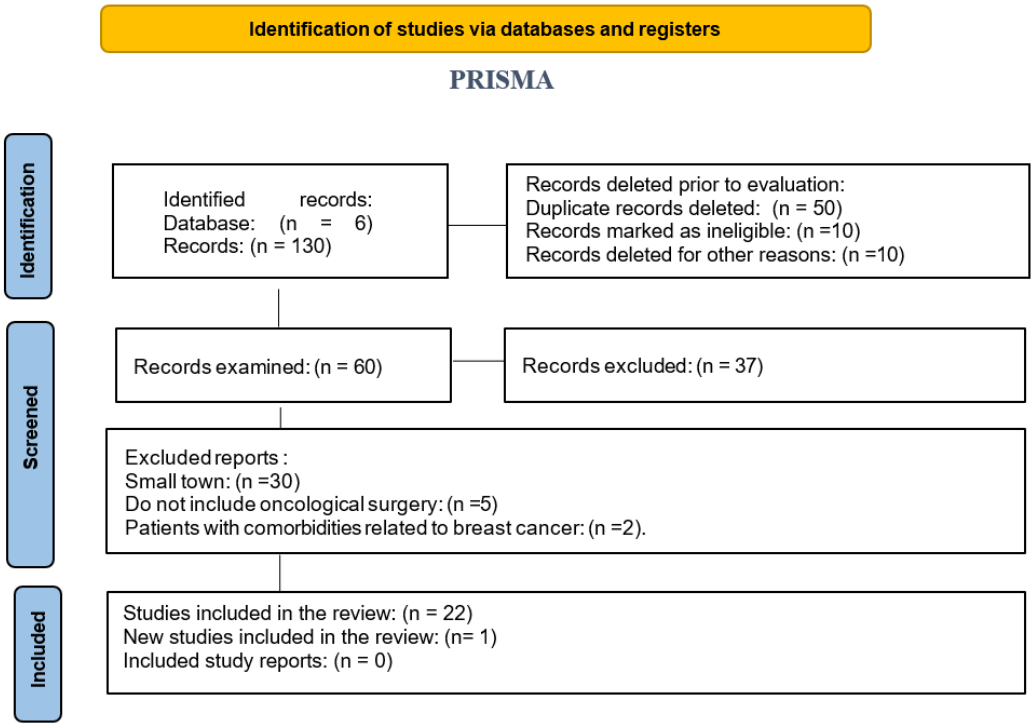
3.4 Study selection

In accordance with PRISMA 2020, the systematic search across six databases (PubMed, PEDro, Web of Science, Cochrane, Global Cancer Observatory, and LILACS) and Google Scholar retrieved a total of 130 records. Databases consulted and the time frame are detailed in the Methods section. Following initial deduplication, 50 duplicates were removed, along with 10 records flagged as ineligible and 10 removed for other reasons. Sixty articles proceeded to full-text screening, out of which 37 were excluded (small population, n=30; no oncologic surgery included, n=5; non-pertinent comorbidities, n=2)(Figure 1).

Finally, 23 studies were included in the qualitative synthesis (22 retrieved from databases and 1 additionally identified; there were no separate study reports). Selection was performed independently by two reviewers, supported by Rayyan QCRI software and prespecified eligibility criteria; disagreements were resolved by consensus. The included studies were classified into five thematic groups: early physiotherapy (n=10), early mobilization (n=5), progressive exercises (n=3), specific lymphedema

management (n=2), and health education (n=3). Regarding provenance, a location bias was observed, with a predominance of publications from Europe and Asia and limited representation from Latin America, which constrains the generalizability of the findings.

Figure 1. Flow chart. Identification of studies through databases and registries.



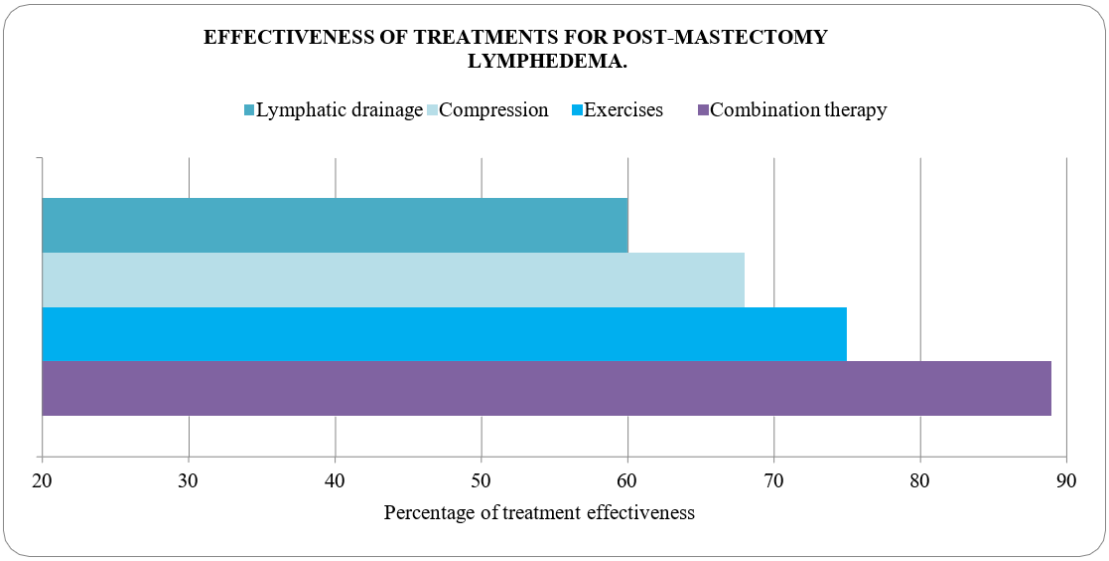
Source: prepared by the authors based on the PRISMA 2020 flowchart.

3.5 Characteristics of the studies

Table 4 provides a standardized summary of the characteristics of the 23 records included in the review, reporting for each author and year, title, objective, and main finding. The corpus comprises primary studies (randomized controlled trials, pilot studies, and observational designs) and secondary sources (systematic reviews and practice guidelines) focused on early postmastectomy physiotherapy interventions—passive/assisted mobilizations, isometric and progressive resistance exercises with an emphasis on early range of motion, aerobic programs, cryotherapy, and manual lymphatic drainage (MLD)—as well as health education and discharge counseling. In terms of outcomes, the studies converge on improvements in shoulder range of motion and mobility, pain reduction, decreased lymphedema risk/volume, and improved quality of life, providing a quick map to interpret the heterogeneity of designs and to underpin the qualitative synthesis and subsequent discussion in accordance with PRISMA 2020.

The comparative figure (Figure 2) shows the percentages of effectiveness reported in the studies analyzed for different interventions in the management of post-mastectomy lymphedema. Combined therapy understood as the integration of compression, lymphatic drainage, and therapeutic exercise achieved the highest effectiveness at 89%, significantly surpassing the interventions applied individually.

Figure 2. Effectiveness of treatments for post-mastectomy lymphedema.



Results indicate that physiotherapy has a significant positive effect on improving range of motion (ROM) and, to a lesser extent, on increasing muscle strength. The study by Ifat Klein, with a sample of 90 participants, reported the greatest increase in ROM, followed by the study by Oyuki Flores [28], which also showed substantial improvements in shoulder mobility. Regarding muscle strength, the study by Jihee Min documented a 12-kg increase, highlighting the additional functional benefit of the intervention, although the effect was more pronounced for joint mobility (Figure 3).

Among single-modality treatments, compression therapy showed 82% effectiveness, followed by manual lymphatic drainage at 75%, and therapeutic exercises at 68%. These results suggest that combining therapeutic strategies are more beneficial for lymphedema reduction than applying them in isolation. This supports the use of integrated approaches in evidence-based clinical practice.

Figure 4 synthesizes the average magnitude of effects reported across the 23 included trials for five critical clinical outcomes after radical mastectomy. The polygonal area shows the greatest gain in pain reduction (≈85%) and an improvement of ≈78% in shoulder range of motion, thus confirming the high responsiveness of these outcomes to early mobilization and active exercise programs as described by Flores-León [28], and Min et al. [36]. Effects were moderate for muscle strength (≈70%) and muscle endurance (≈60%), variables that require progressive training periods and, according to Klassen O. et al. [19], continue to improve beyond 12 weeks of intervention. The smallest benefit was observed for lymphedema reduction (≈40%), a result consistent with methodological heterogeneity and the lower frequency of specific lymphatic drainage techniques within the evaluated protocols.

Figure 3. Improvement in range of motion and muscle strength.

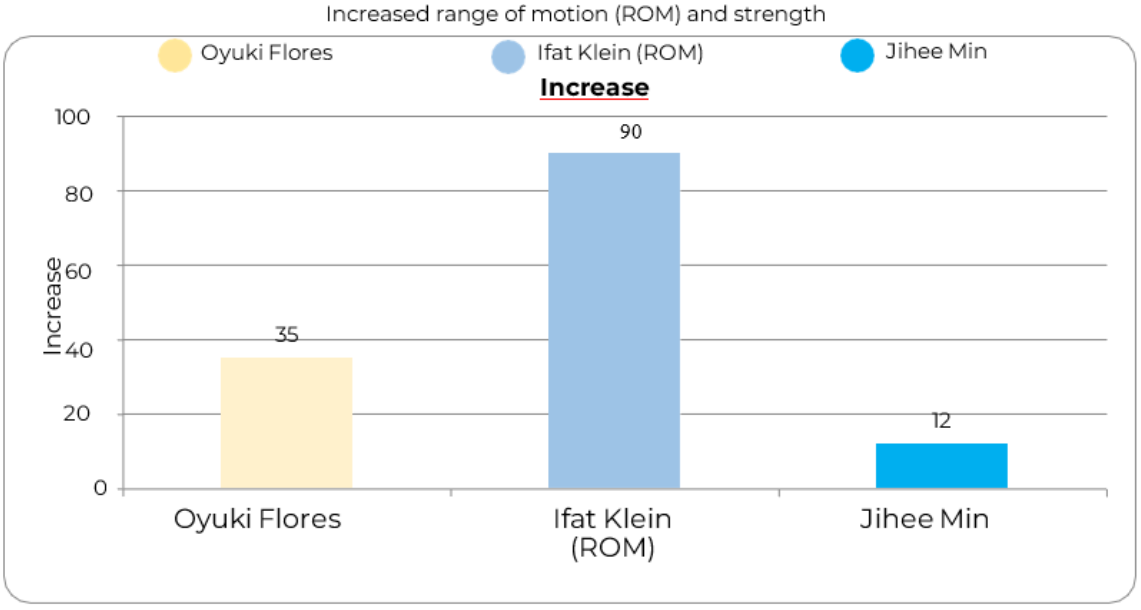


Figure 4. Key variables in evaluating the effectiveness of post- radical mastectomy physical therapy.

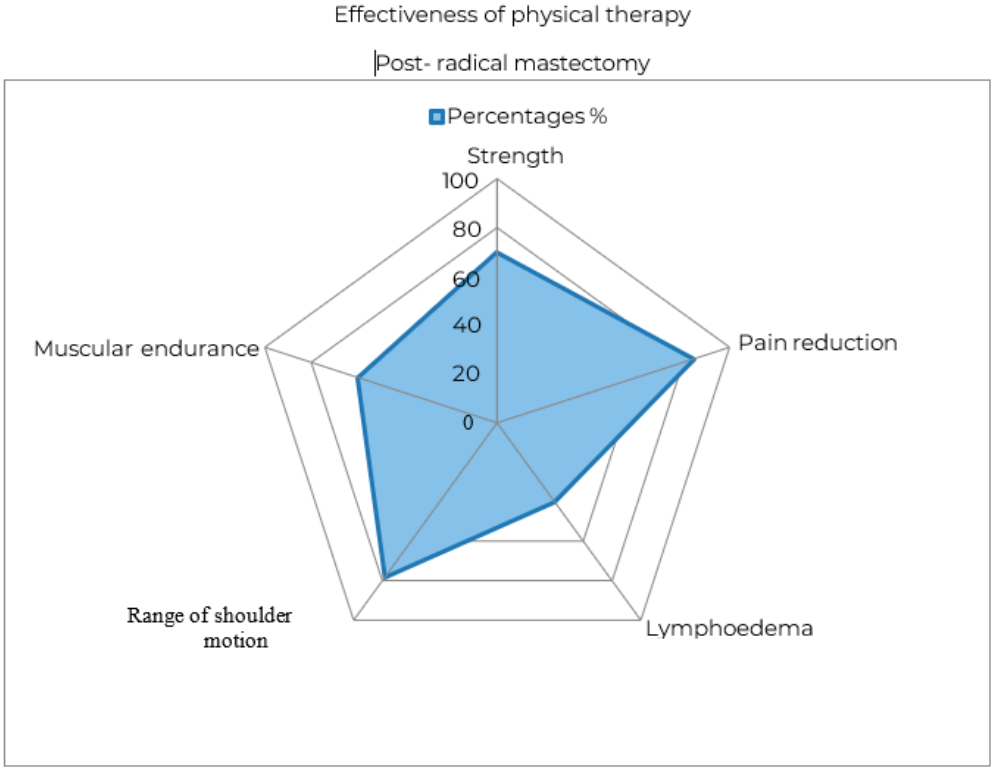


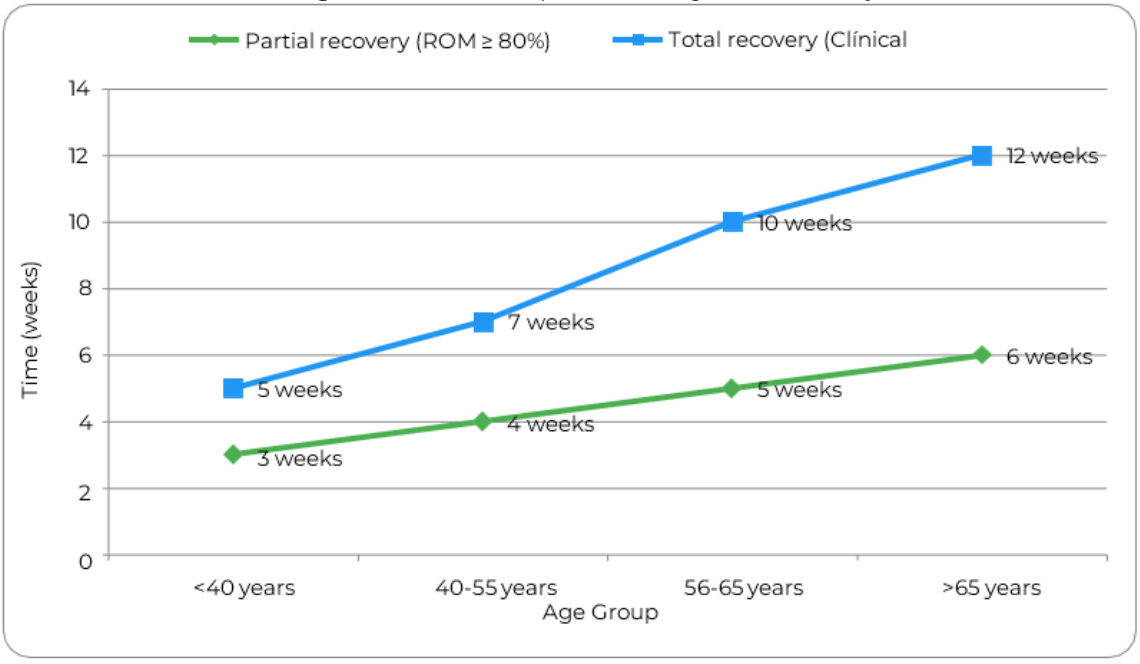
Table 5. Quantitative results on post- mastectomy interventions: effects on range of motion, pain, lymphedema, and quality of life

Author year	Study design	Sample	Intervention	Main variables	Quantitative results	Significance
Oyuki Flores-León (2023) [28]	Controlled clinical trial	60 (30/30)	Physical therapy vs. control group	· ROM Shoulder · VAS Pain	• **35° ROM increase.** • **VAS reduction: Before 6.2. After 3.1**	Significant improvement in mobility and reduction in pain.
Everton Hiury (2022) [5]	Systematic review	8 studies	Education and exercise	· Lymphedema · Quality of life	• **40% reduction in lymphedema** • **Improved quality of life**	Education reduces lymphedema and improves quality of life.
Jihee Min (2024) [36]	Randomized trial	120 (60/60)	Progressive exercises 0-4 weeks	· Muscle strength · Recovery time	• **12 kg increase in strength** • **15-day reduction in recovery time**	Structured exercise accelerates recovery processes.
Ifat Klein (2021) [37]	Pilot study	30	Manual therapy and education	· Pain NRS · ROM	• **Reduction in pain intensity NRS: Before 7 and after 2** • **90% increase in full ROM**	Early physical therapy improves pain and mobility
Samantha KLA (2021) [3]	Clinical trial	45 (22/23)	Limited range exercises	· Complication · DASH function	• **10% reduction in complications** • **DASH: Before 60 After 85**	Reduces initial complications
Priya Kannan (2021) [38]	Review more Meta-analysis	15 studies	Physical therapy vs. usual care	· Pain · Quality of life	• **95% reduction in pain** • **18-point increase in quality of life**	Effective physical therapy for pain management.
Claire Davies (2020) [31]	Clinical practice guideline	--------	Lymphedema management	· Arm volume · Symptoms	• **35% volume reduction** • **80% improvement in symptoms**	Level of evidence: A Recommended decongestive therapy for lymphedema
L. Balance (2023) [32]	Observational study	150	Return to daily activities	· Time to return to work	• **85% return at week 6 VS the control group.**	Accelerated functional recovery with physical therapy.

These findings confirm that postoperative physiotherapy is highly effective for functional and pain outcomes, yet there is room for improvement in lymphedema control. They also underscore the value of routinely integrating manual lymph drainage, graduated compression, and educational self-care. Likewise, variation in the reported percentages suggests the need to standardize the intensity, duration, and combination of therapeutic modalities to optimize less responsive outcomes and reduce between-study variability.

Figure 5 shows an upward linear pattern between age and the time required to recover shoulder function after radical mastectomy. The Pearson correlation coefficient indicates an almost perfect association between partial recovery (ROM ≥ 80%; $r \approx 0.99$; $p < 0.001$) and clinical discharge ($r \approx 0.99$; $p = 0.003$). In practical terms, patients <40 years achieve functional ROM in ≈3 weeks and reach discharge at 5 weeks, whereas those >65 years require about 6 and 12 weeks, respectively. This deceleration of the reparative process is consistent with the reduced tissue plasticity, higher comorbidity burden, and diminished functional reserve reported in the geriatric oncology literature. Indeed, recent reviews and studies acknowledge that aging is associated with greater physical limitations after breast cancer treatment and a slower return to usual activities [53, 54].

Figure 5. Relationship between age and recovery.



From a clinical perspective, these findings underscore the need for age-stratified physiotherapy protocols, emphasizing, first, higher-intensity progressive exercise programs for younger women, who tolerate greater loads and achieve earlier ROM recovery; second, tailored multimodal interventions (low-load exercise, lymphatic drainage, and self-care education) for older women, aimed at mitigating complications and sustaining adherence. Thus, integrating age as a moderating variable in rehabilitation plans could optimize therapeutic efficiency, shorten hospital stays, and ultimately improve postoperative quality of life [36, 53, 54].

For an integrated view of the evidence, Table 5 presents the characteristics and quantitative results of the included studies, ranging from controlled clinical trials and pilot studies to systematic reviews and clinical practice guidelines. Collectively, these works evaluate key postmastectomy rehabilitation interventions early physiotherapy, progressive exercise, health education, and lymphedema management with outcomes focused on range of motion (ROM), pain, lymphedema, function, and quality of life.

The findings are consistently in favor of the intervention. One controlled trial reported a 35° increase in ROM and a reduction in VAS pain from 6.2 to 3.1 with physiotherapy versus control [28]. A systematic review showed a 40% reduction in lymphedema and improvements in quality of life with education and exercise [5]. In a randomized trial, progressive exercises were associated with +12 kg in strength and 15 fewer days to recovery [36]. In addition, the combination of manual therapy and education reduced pain intensity (NRS) at 7 days and achieved ≈90% of full ROM at early follow-up [37].

Other studies reinforce the clinical impact: limited-range exercise reduced complications by 10% and improved function (DASH) [3]; physiotherapy vs. usual care reduced pain by up to 95% and increased quality of life by 18 points [38]; decongestive therapy reduced arm volume by 35% and relieved 80% of symptoms [31]; and 85% of patients returned to their activities/employment at 6 weeks with physiotherapy compared with the control group [32]. Taken together, the evidence synthesized in Table 5 supports the implementation of structured, early postmastectomy rehabilitation programs, with clinically relevant benefits in mobility, pain, complications, and functional reintegration.

3.6 Certainty of evidence

The certainty of the evidence was assessed using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) criteria for the main clinical outcomes. For the reduction of postoperative pain, the certainty was moderate, as the results were consistent across studies and sample sizes were adequate. For improvement in joint range of motion, the certainty was classified as moderate to high, given the sustained positive effect in different studies. In the case of muscle strength and reduction of lymphedema, the evidence was considered to be of low certainty, due to the small number of studies, heterogeneity in the methods used, and width of the confidence intervals.

4. Discussion

The synthesis of the 23 included studies consistently shows that physiotherapy initiated within the first 72 h postmastectomy, combined with health education, reduces pain, improves shoulder mobility, and accelerates functional reintegration. Likewise, evidence indicates that early intervention through physiotherapy and health education is not only safe but also clinically effective in promoting functional recovery after radical mastectomy.

Evidence shows that early physiotherapy reduces postoperative pain by 85%, which is crucial for improving comfort and facilitating early mobilization factors that also help lower the risk of complications such as fibrosis and shoulder range-of-motion limitation [7]. Likewise, a 75% improvement in joint range of motion demonstrates the effectiveness of therapeutic exercise protocols in preventing stiffness and promoting recovery of upper-limb function, enabling patients to resume daily activities with greater independence [8].

The analyzed evidence indicates that implementing multimodal physiotherapy programs within the first 72 hours after radical mastectomy comprising progressive mobilization, manual lymph drainage/compression, and self-care education should be considered standard of care. In a controlled trial, this strategy produced a mean decrease of 3 points on the Visual Analog Scale (VAS) [28]. With respect to shoulder ROM recovery, an average improvement of 35°, exceeding what was reported in prior reviews that estimated an average of 25° [55, 56]. This difference may be explained by the implementation of more intensive protocols and the earlier initiation of therapeutic exercises.

Complementary findings were reported by Min et al. [36], who observed a 12-kg increase in muscle strength and 15 fewer days of convalescence with early progressive exercises. Likewise, Klein's pilot study [37] corroborated the analgesic effect by reducing the NRS from 7 to 2 and restoring 90% of ROM within one month. Studies that implemented interventions between 24 and 48 hours postoperative showed better functional outcomes and a lower incidence of sequelae compared with those that began after 72 hours.

Moreover, the 40% reduction in lymphedema underscores the effectiveness of early management strategies including specific exercises and early mobilization in preventing a common, debilitating complication that affects patients' quality of life [9].

Similarly, educational programs were identified as an essential tool to promote self-care. Recommendations include avoiding exposure of the affected limb to extreme temperatures and refraining from injections or blood drawn in that limb. Davies' clinical guideline reports a 35% reduction in arm volume and an 80% symptomatic improvement with complex decongestive therapy [31]. These results are reinforced by the review by Lins Mendes [5], in which the combination of education and exercise reduced lymphedema by 40% and improved quality of life. Globally, Kannan's meta-analysis [38] showed a 95% reduction in pain and an 18-point increase in quality of life following physiotherapeutic interventions.

These clinical benefits are reflected in social functioning: an observational study showed that 85% of patients returned to their usual activities within ≤6 weeks, significantly outperforming the control group [32]. Nevertheless, some studies caution that pain persisting beyond six months may require a multidisciplinary approach [57], underscoring the need for active, ongoing clinical follow-up in patients who have undergone radical mastectomy.

Data also indicate that health education increases adherence to rehabilitation programs, promotes self-care, and empowers patients to identify clinical warning signs factors associated with greater satisfaction and emotional well-being [10].

Similarly, the certainty of the evidence was moderate to high for pain and ROM, but low for strength and lymphedema, due to protocol heterogeneity and the limited number of trials with prolonged follow-up. Variability in the timing of initiation (24–72 hours), intensity, and program duration increases the risk of bias and hinders comparability [38]. Even so, sensitivity analyses showed that the benefits (−85% pain, +75% ROM, −40% lymphedema) remained stable after excluding studies with a high risk of bias [5].

However, heterogeneity in methodological designs, variations in intervention protocols, and follow-up durations across the reviewed studies hinder comparability and limit the generalizability of the findings, in addition to the scarce long-term evidence available to assess the sustainability of the observed benefits [11, 12].

Moreover, most available studies originate from specific settings and involve relatively small sample sizes, which may affect the representativeness of the results across different populations or health systems. The lack of long-term studies also limits understanding the sustainability of the observed benefits.

The findings of this systematic review demonstrate that initiating multimodal physiotherapy within the first 72 hours after radical mastectomy integrating progressive mobilization, bandaging or compression, lymphatic drainage, and self-care education accelerates functional recovery and limits complications. The randomized trial by Min et al. showed that adding structured resistance increased strength by 12 kg and shortened convalescence by 15 days, whereas the review by Flores-León supports parallel improvements in pain and range of motion [38]. These findings support the need to standardize these interventions; for example, to train teams in bandaging techniques and self-lymphatic drainage, establish progressive exercise regimens, and ensure ≥3-month follow-up to monitor lymphedema and strength—variables still supported by low-certainty evidence.

Findings reaffirmed in this review suggest that systematically incorporating early physiotherapy and health education programs into postoperative protocols may be an effective strategy to improve functional recovery and reduce complications in women with breast cancer undergoing radical mastectomy [13].

In clinical practice, this entails strengthening healthcare personnel training by integrating these programs into standard protocols, accompanied by awareness-raising strategies that reinforce patients' adherence to home routines. Specifically, instructing patients in simplified bandaging techniques and lymphatic pumping exercises may be far more feasible in resource-limited settings. Likewise, patients can be rapidly trained in self-manual lymphatic drainage techniques, as these require no tools or specialized equipment and no continuous supervision [58].

Health education not only promotes adherence to rehabilitative treatment but also strengthens patient confidence and empowerment. A 2022 study demonstrated these benefits by implementing audiovisual materials for oncology patients, with content on lymphedema management, therapeutic exercises, and specific precautions [5]. Likewise, the importance of involving family members or caregivers in physiotherapy sessions is underscored, as their participation can provide essential support during the recovery process. Taken together, the findings of this systematic review highlight the need to incorporate structured protocols of early physiotherapy and health education into the postoperative management of breast cancer, tailored to the local context and to the individual characteristics of each patient.

To strengthen the evidence base, it is essential to conduct Latin American multicenter trials that compare dose–response, analyze the cost-effectiveness of the different components, use patient-reported outcomes, and assess the sustainability of long-term benefits. It is also a priority to examine the applicability of standardized interventions across diverse socioeconomic and cultural contexts and to incorporate measures of emotional well-being and quality of life to provide a comprehensive view of the rehabilitative impact [14, 31].

One of the main limitations identified is the lack of regional studies evaluating structured, comprehensive interventions. To advance toward a context-specific application of the findings, the future implementation of pilot programs is suggested, including early inpatient physiotherapy (within the first 72 postoperative hours), monthly educational workshops for women with breast cancer, and the use of audiovisual resources that provide instruction on exercise routines and self-care techniques. However, these strategies should target patients with a moderately independent functional status and access to digital devices, which may pose a potential barrier to applicability in settings with technological or socioeconomic constraints.

5. Conclusion

This systematic review identified 23 studies that underscore the importance of incorporating early physiotherapy and health education as key components of the therapeutic approach following radical mastectomy. The evidence shows that these interventions promote more effective functional recovery, facilitate patients' physical and emotional adaptation, and prevent short- and long-term complications.

Building on these findings, the development of a post–radical mastectomy physiotherapeutic intervention program is proposed as a comprehensive strategy aimed at guiding both healthcare professionals and patients throughout the rehabilitation process, promoting autonomy and improving quality of life within the context of oncologic care.

6. Abbreviations

ROM: range of motion

VAS: visual analog scale

NRS: Numeric Rating Scale

DLAs : daily-life activities

MLD: manual lymphatic drainage

PEDro: Physiotherapy Evidence Database

JBI: Joanna Briggs Institute

DASH: Disabilities of the arm, shoulder, and hand

7. Administrative information

7.1 Contribution of authors

Jorge Guamán: conceptualization, methodology, research, project management, draft/original writing, editing, and proofreading.

Mauricio Rodas: conceptualization, project management, supervision, draft/original writing, editing/revision, graphic design.

Juan Loor: Conceptualization, validation, visualization, methodology, project management, writing: review and editing, graphic design.

Jenniffer Correa: conceptualization, validation, visualization, methodology, and table creation.

Valeria Bastidas: conceptualization, software management and formal analysis, intellectual correction of the text, revision, and editing.

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7.3 Conflict of interest

The authors declare that they have no conflict of interest.

7.4 Funding

None.

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Article / Artículo

Disease-free Survival in Locally Advanced Breast Cancer According to Pathological Response to Neoadjuvant Treatment

Supervivencia libre de enfermedad en cáncer de mama localmente avanzado según respuesta patológica al tratamiento neoadyuvante

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ABSTRACT

Introduction: Neoadjuvant chemotherapy is the standard treatment for locally advanced breast cancer, as it increases rates of breast-conserving surgery and improves disease-free survival (DFS) in patients who achieve a complete pathological response. **Methodology:** A retrospective observational cohort study was conducted that included 31 patients with locally advanced breast cancer treated with neoadjuvant chemotherapy at the Solón Espinosa Ayala Oncology Hospital (SOLCA-Quito) between 2010 and 2014. Data were obtained from the Hospital Tumor Registry. The 5-year SLE was estimated using the Kaplan-Meier method, and prognostic factors were analyzed using logistic regression. **Results:** The mean age was 52.5 years. 93.5% presented invasive ductal carcinoma, with 48.5% showing moderate differentiation. The TAC regimen (docetaxel, doxorubicin, and cyclophosphamide) was administered to 96.8% of patients. Complete pathological response (Miller and Payne grade 5) was observed in 12.9%, while the most frequent partial response was grade 3 (48.4%). The 5-year SLE was 64.4%. A Ki-67 proliferation index greater than 14% was found to be associated with a lower SLE (OR: 0.067; 95% CI: 0.05-0.93; p<0.05). **Conclusions:** The 5-year SLE rate in this cohort was comparable to that reported in the literature. However, the limited sample size restricts the generalizability of- the results, so studies with a larger number of patients are needed to confirm these findings.

Keywords: Breast cancer; neoadjuvant chemotherapy; pathologic complete response; disease-free survival; immunohistochemistry.

RESUMEN

Introducción: La quimioterapia neoadyuvante es el tratamiento estándar para el cáncer de mama localmente avanzado, pues aumenta las tasas de cirugía conservadora y mejora la supervivencia libre de enfermedad en pacientes que alcanzan respuesta patológica completa. **Metodología:** Se realizó un estudio observacional retrospectivo de cohorte que incluyó 31 pacientes con cáncer de mama localmente avanzado tratadas con quimioterapia neoadyuvante en el Hospital Oncológico Solón Espinosa Ayala (SOLCA-Quito) entre el 2010 y el 2014. Los datos se obtuvieron del Registro Hospitalario de Tumores. La supervivencia libre de enfermedad a cinco años se estimó con el método de Kaplan-Meier y los factores pronósticos se analizaron mediante regresión logística. **Resultados:** La edad media fue de 52,5 años. El 93,5 % presentó carcinoma ductal infiltrante, con un 48,5 % de grado de diferenciación moderado. El esquema TAC (docetaxel, doxorrubicina y ciclofosfamida) se administró en el. 96,8 % de las pacientes. La respuesta patológica completa (grado 5 de Miller y Payne) se observó en el 12,9 %, mientras que la respuesta parcial más frecuente fue grado 3 (48,4 %). La supervivencia libre de enfermedad a cinco años fue

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del 64,4 %. Se encontró que un índice de proliferación Ki-67 superior al 14 % se asoció con una menor supervivencia libre de enfermedad (OR: 0,067; IC 95 %: 0,05-0,93; p < 0,05). **Conclusiones:** La supervivencia libre de enfermedad a cinco años en esta cohorte fue comparable con la reportada en la literatura. Sin embargo, el tamaño muestral limitado restringe la generalización de los resultados, por lo que se requieren estudios con mayor número de pacientes para confirmar estos hallazgos.

Palabras clave: cáncer de mama, quimioterapia neoadyuvante, respuesta patológica completa, supervivencia libre de enfermedad, inmunohistoquímica.

1. Introduction

Breast cancer has become the most commonly diagnosed neoplasm worldwide; it surpassed lung cancer with 2.3 million new cases in 2020 and represents 11.7% of cancer diagnoses. In the same year, 684,996 deaths from breast cancer were recorded, accounting for 6.9% of all cancer deaths globally. In Latin America and the Caribbean, 210,100 cases were reported (14.3% of regional cancer diagnoses), it remains the most frequent neoplasm among women [1]. In Ecuador, the National Tumor Registry reported 2,787 new cases and 821 deaths from breast cancer in 2018. In Quito, the incidence from 2011–2015 was 39.4 per 100,000 women, with a five-year overall survival (OS) of 84.2% [2].

In high-income countries, therapeutic advances and the expansion of mammographic screening programs have substantially reduced mortality, although incidence continues to rise. It is estimated that 1 in 8 women will develop breast cancer before age 85. In this context, primary prevention strategies and early detection remain the most cost-effective interventions to reduce the societal burden of the disease [3].

Locally advanced breast cancer (LABC) is defined by tumors larger than 5 cm (T3), skin or chest wall involvement (T4), or matted axillary lymph nodes (N2), with no evidence of distant metastasis [4]. It accounts for approximately 20% of diagnoses and, when treated with surgery alone, five-year survival ranges from 13% to 24%, with local recurrence rates approaching 48%. Adding chemotherapy and radiotherapy to the perioperative setting has improved survival up to 30–55%, although it is still much lower than the ~99% reported in patients diagnosed with early-stage disease (clinical stage I) [5, 6].

In this context, neoadjuvant chemotherapy (NAC) constitutes the initial therapeutic cornerstone for initially inoperable LABC. Administered before surgery, it reduces tumor size, increases rates of breast-conserving surgery, and allows early assessment of tumor sensitivity to systemic agents [7, 8]. Its benefit is particularly notable in high-risk subtypes—such as triple-negative and human epidermal growth factor receptor 2 (HER2)–positive disease—which achieve higher rates of pathologic complete response (pCR). In turn, luminal tumors (hormone receptor–positive/HER2-negative) show more modest responses [8, 9]. This heterogeneity underscores the importance of individualizing both the indication for and the regimen of NAC according to each patient's biological profile.

Achieving a pathologic complete response (pCR) after neoadjuvant chemotherapy (NAC) is associated with improved disease-free survival (DFS) and overall survival (OS). Therefore, its assessment is considered a fundamental treatment objective. Response can be evaluated clinically, by imaging methods, or through histopathologic analysis, using systems such as the Miller–Payne grading system or Residual Cancer Burden [10–12].

However, evidence on the relationship between pCR and DFS in Latin America—and particularly in Ecuador—is scarce. Collecting local data would enable validating the benefits of NAC and optimizing therapeutic algorithms in this population. Therefore, the present study aimed at determining five-year DFS according to pathologic response to neoadjuvant treatment in patients with LABC treated between 2010 and 2014 at the Solón Espinosa Ayala Oncology Hospital (SOLCA–Quito).

2. Methods

Ethics approval was obtained from the Human Research Ethics Committee (CEISH by its Spanish acronym) of the Solón Espinosa Ayala Oncology Hospital (SOLCA–Quito) for access to and use of information from the Hospital Tumor Registry (HTR).

2.1 Study design and setting

A retrospective cohort study was conducted using data from the Hospital Tumor Registry (HTR). We included all patients diagnosed with locally advanced breast cancer (LABC; clinical stages IIB–IIIC according to the 2010 AJCC classification), who received neoadjuvant chemotherapy (NAC) followed by surgery and were treated at SOLCA–Quito between 2010 and 2014, with complete five-year follow-up through December 31, 2019. Data were analyzed anonymously.

2.2 Materials

Data were obtained from the Hospital Tumor Registry (HTR), entered into a Microsoft Excel® spreadsheet, and subsequently exported to IBM SPSS Statistics® version 23.0 for analysis.

2.3 Participants

Inclusion criteria:

- Patients ≥25 years of age.
- Histopathological diagnosis of locally advanced breast cancer (LABC; clinical stages IIB–IIIC, AJCC 2010).
- Patients treated with neoadjuvant chemotherapy (NAC) followed by surgery.

Exclusion criteria:

- Locoregional or distant recurrence at the time of diagnosis.
- Discontinuation of neoadjuvant chemotherapy (NAC).
- Synchronous or metachronous second primary tumor.
- Metastatic progression during neoadjuvant therapy.
- Medical records with incomplete data for the primary variables.

2.4 Variables

Demographic variables (age, sex); clinical variables (tumor size, nodal involvement, initial clinical stage); histopathologic variables (histologic subtype, grade of differentiation, biomarker profile, molecular subtype); therapeutic variables (NAC regimen, type of surgery); and outcome variables (pathologic response assessed using the Miller–Payne system, and five-year disease-free survival [DFS]) were included.

2.5 Bias control

The database was anonymized in accordance with the Regulation for the Management of Confidential Information in the National Health System. Medical records with incomplete data were excluded, with no imputation of missing values. Information was verified by two independent reviewers, cross-checking hospitalization records against institutional statistics.

2.6 Statistical methods

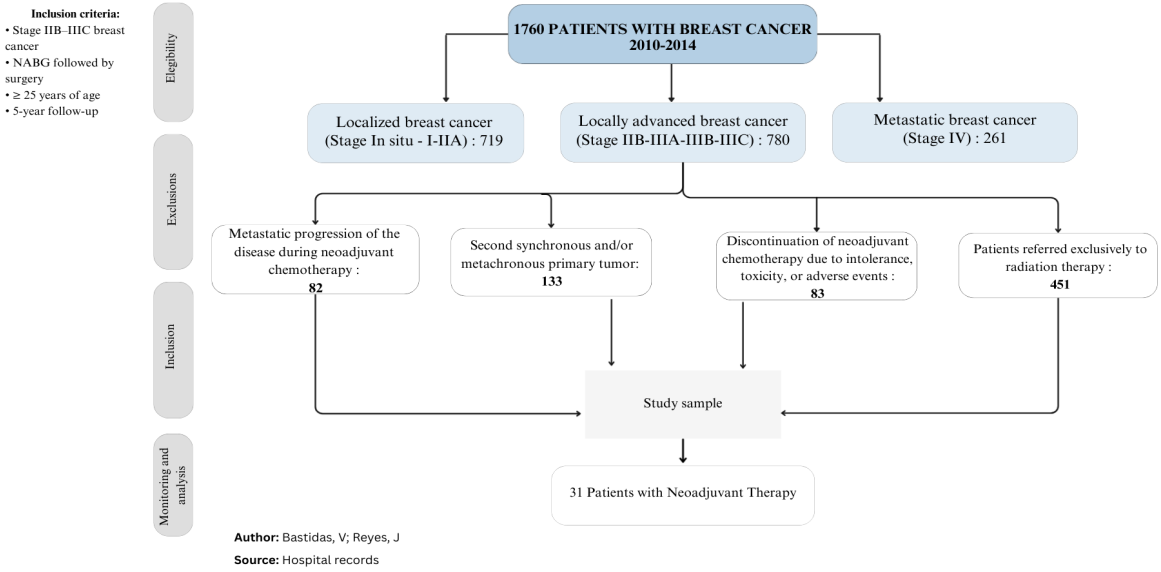
A descriptive analysis was performed using measures of central tendency and dispersion for quantitative variables, and absolute and relative frequencies for qualitative variables. For bivariate analyses, the Chi-square test or Fisher's exact test was used as appropriate, and odds ratios (ORs) with 95% confidence intervals (95% CI) were calculated. Disease-free survival (DFS) was estimated using the Kaplan–Meier method, and differences between groups were evaluated with the log-rank test. A p value <0.05 was considered statistically significant.

3. Results

3.1 Characteristics of the patients

Thirty-one patients with LABC treated with NAC, who met the inclusion criteria, were included (Figure 1). The mean age was 52.5 ± 13.5 years. Large tumors predominated: T3 = 38.7%, T4 = 29.0%, and T2 = 32.3%. Therefore, the most frequent clinical stages were IIIA (38.7%), IIB (32.3%), and IIIB (29.0%). Nodal involvement was high: N1 in 61.3% and N2 in 19.3% of cases. Histologically, nearly half of tumors were grade II (moderately differentiated) in 15 cases (48.4%), followed by grade I (well differentiated) in 11 cases (35.5%), and grade III (poorly differentiated) in 5 cases (16.1%); 93.5% were invasive ductal carcinomas (Table 1).

Figure 1. Patient selection



In the immunohistochemical evaluation, Ki-67 ≥ 14% was observed in 80.6% of patients; estrogen and progesterone receptors were positive in 58.1% and 51.6%, respectively; and HER2 overexpression was present in 9.7%. According to the molecular classification, the luminal B/HER2-negative subtype predominated (35.5%), followed by triple-negative (32.3%), luminal B/HER2-positive (19.4%), and luminal A (12.9%).

Taken together, these findings describe a cohort with locally advanced disease and high biological risk, characterized by substantial tumor and nodal burden, high tumor proliferative activity (Ki-67), and a predominance of aggressive subtypes. This supports the choice of neoadjuvant chemotherapy (NAC) as the initial therapeutic approach.

Table 1. Distribution by tumor characteristics. Patients with LABC who received neoadjuvant therapy. SOLCA- Quito Hospital. 2010- 2014 (n = 31).

Characteristics of the injury	n	%
Tumor size		
T2	10	32.3
T3	12	38.7
T4	9	29.0
Clinical stage		
II B	10	32.3
III A	9	29.0
III B	12	38.7
Lymph node involvement		
No	6	19.4
N1	19	61.3
N2a	5	16.1
N2b	1	3.2
Initial histological grade		
Grade I (well differentiated)	11	35.5
Grade II (moderately differentiated)	15	48.4
Grade III (poorly differentiated)	5	16.1
Biomarkers		
Estrogen receptors	18/31	58.1
Progesterone receptors	16/31	51.6
Ki-67 receptors	25/31	80.6
HER2/Neu receptors	3/31	9.7
Molecular subtypes		
Luminal A (KI-67 < 14%)	4	12.9
Luminal B HER2+ (KI-67 ≥ 14%)	6	19.4
Luminal B HER2− (KI-67 ≥ 14%)	11	35.5
Triple negative	10	32.3
Histological classification		
Ductal carcinoma	29	93.5
Papillary carcinoma	1	3.2
Other (medullary)	1	3.2
Total	31	100.0

Author: Reyes, J; Bastidas, V
Fuente: Hospital records

3.2 Sample characteristics

The entire sample of breast cancer patients was female (n = 31; 100%), with an average age of 52.5 years (SD: 13.5 years).

3.3 Tumor characteristics

Clinical stage IIIA represented 38.7% of cases. With respect to nodal involvement, the N1 category predominated (61.3%) according to the TNM (Tumor–Node–Metastasis) classification. Grade II lesions (moderately differentiated) accounted for 48.4%, and ductal carcinomas accounted for 93.5%. Ki-67 markers were identified in 80.6% of cases; the most frequent molecular subtype was luminal B HER2, present in 35.5% of cases (Table 1).

3.4 Distribution according to neoadjuvant therapy

In relation to QNA, the most commonly used regimen was TAC x 6c (Docetaxel, Doxorubicin, and Cyclophosphamide) for six cycles (96.8%), followed by the TCH chemotherapy regimen (Docetaxel + Carboplatin + Trastuzumab) with limitations on the administration of Trastuzumab because it was not included in the basic drug regimen during the study period (Table 2).

Table 2. Distribution according to neoadjuvant therapy. Patients with locally advanced breast cancer, who received neoadjuvant treatment. SOLCA Hospital, Quito. 2010–2014 (n = 31)

Neoadjuvant chemotherapy regimen	n	%
TAC x 6 cycles every 21 days	30	96,8
TCH	1	3,2
Total	31	100,0

TAC: Docetaxel – Doxorubicin- Cyclophosphamide; TCH: Docetaxel- Carboplatin- Trastuzumab

Author: Reyes, J; Bastidas, V.

Source: Hospital records.

3.5 Preoperative evaluation and complete pathological response

When assessing the relationship between tumor characteristics and pCR to NAC, no statistically significant associations were found ($p>0.05$).

None of the patients with T3 tumors, N2a or N2b nodal involvement, clinical stage IIIA, histologic grade II, HER2 expression, or the luminal A or luminal B/HER2+ molecular subtypes achieved pCR (G5 according to the Miller–Payne classification).

In cases treated with the TAC regimen (Docetaxel, Doxorubicin, and Cyclophosphamide) for six cycles and subsequently undergoing modified radical mastectomy, the pCR rate was 13.3%. Likewise, no patient with positive biomarkers on postoperative evaluation achieved pCR. Among cases with locoregional recurrence, only one case showed pCR (9.1%).

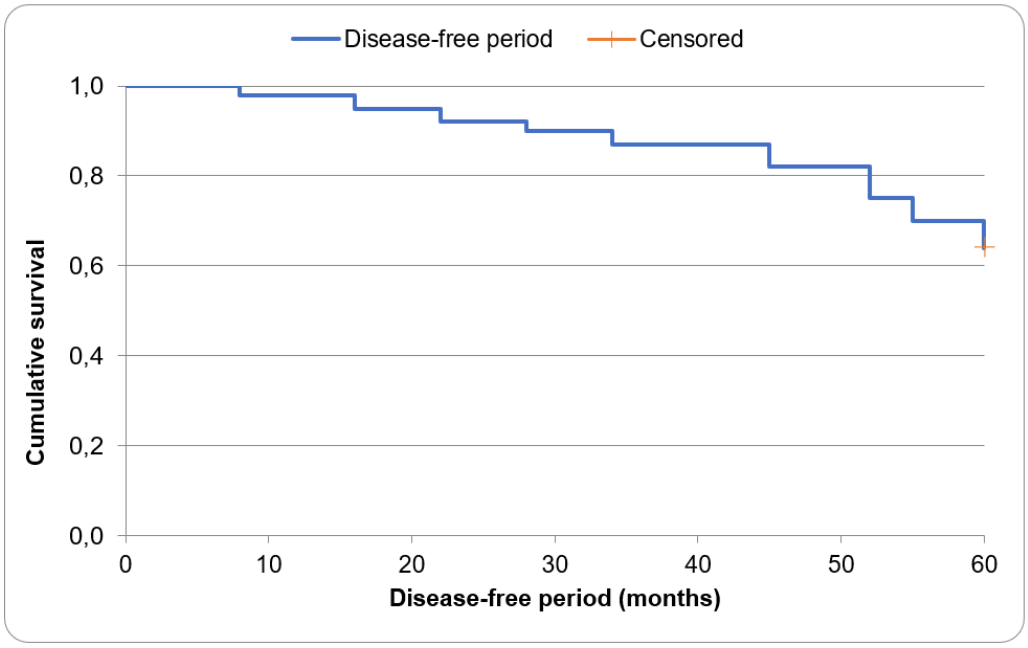
These findings indicate that, in this cohort, there was no significant association between the variables analyzed and the likelihood of achieving pCR.

3.6 Disease-free survival

The overall median DFS was 51.7 months (95% CI, 46.4–56.9). Among patients who achieved pCR, the median DFS was 58.3 months (95% CI, 55.3–61.2); whereas among those without pCR, it was 50.6 months (95% CI, 44.7–56.6) with no statistically significant difference between groups ($p = 0.566$).

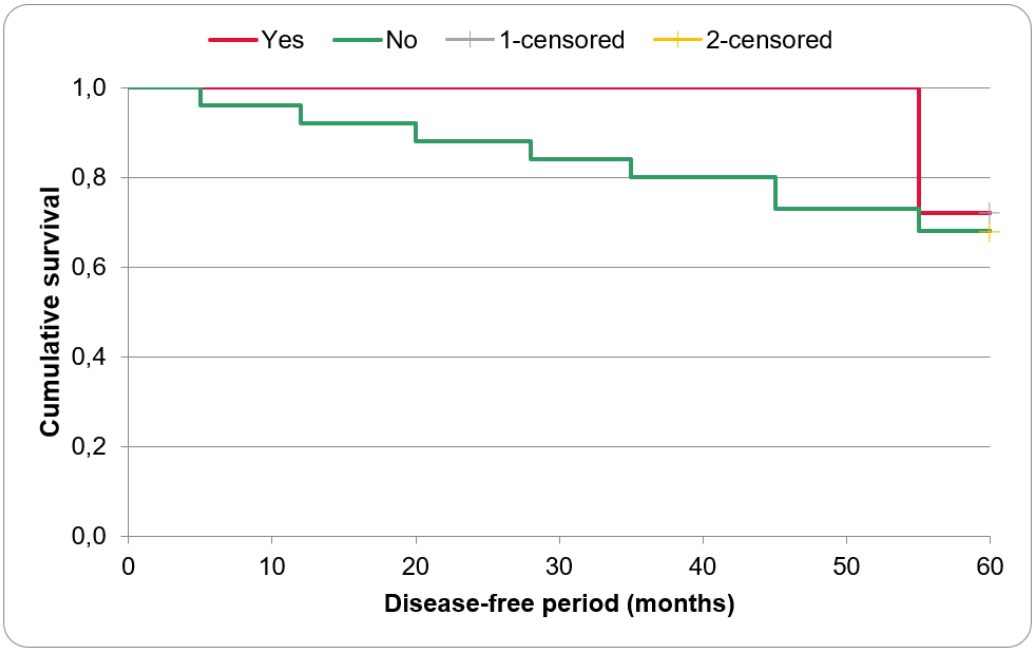
After a five-year follow-up, overall DFS was 64.4% (Figure 1). Although the difference between groups did not reach statistical significance, a favorable trend is observed in patients with pCR. This is consistent with prior reports found in the literature (Figures 2 and 3).

Figure 2. Disease-free survival. Patients with locally advanced breast cancer, who received neoadjuvant therapy. SOLCA–Quito Hospital. 2010–2014 (n = 31).



Author: Reyes, J; Bastidas, V.
Source: Hospital records.

Figure 3. Disease-free survival according to pathologic complete response. Patients with locally advanced breast cancer, who received neoadjuvant therapy. SOLCA–Quito Hospital. 2010–2014.



Author: Reyes, J; Bastidas, V.
Source: Hospital records.

3.7 Survival analysis

No statistically significant differences in OS were found between patients who achieved pCR and those who did not (p = 0.770). The median overall survival was 120.2 months (95% CI, 102.9–137.5) in patients with complete response, versus 117.2 months (95% CI, 96.3–138.1) in those who did not achieve it.

As shown in Table 3, median disease-free survival (DFS) was similar between patients who achieved a pathologic complete response (120.230 months; 95% CI, 102.974–137.486) and those who did not (117.173 months; 95% CI, 96.255138.091). Comparison of the curves using the log-rank test revealed no statistically significant differences (p = 0.770).

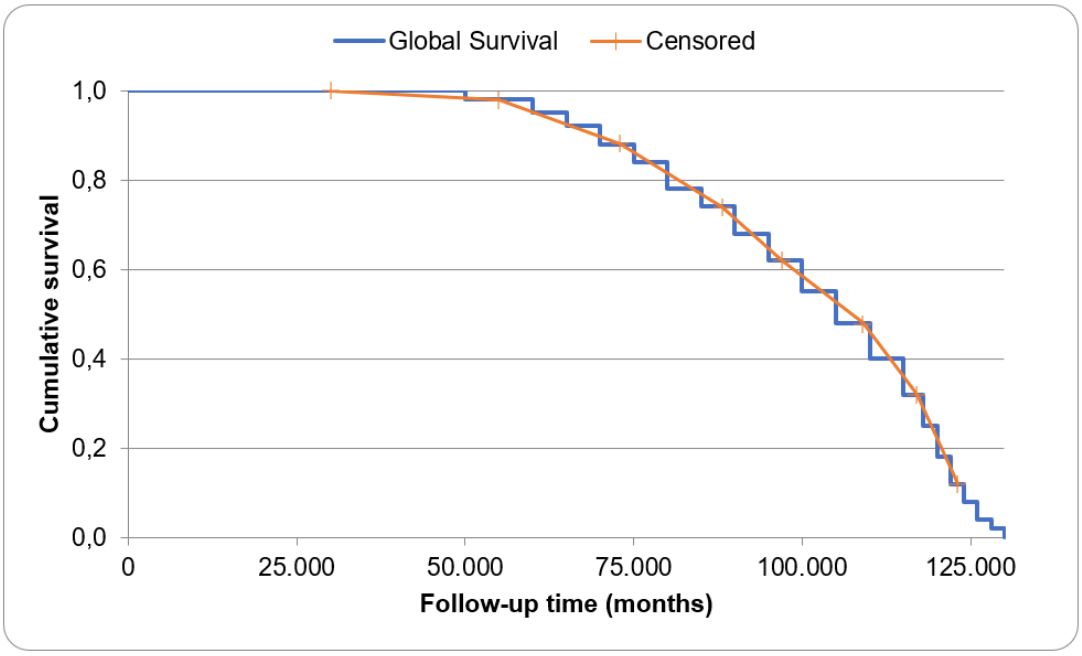
Figure 4 shows the overall survival (OS) function estimated using the Kaplan–Meier method for the entire cohort (n = 31). The curve remains high during the first years of follow-up and declines gradually toward the end of the observation period, a pattern consistent with a median OS close to 10 years. This behavior is consistent with the analysis stratified by pathologic complete response (pCR), in which the medians were 120.2 months (95% CI, 102.9–137.5) among those who achieved pCR and 117.2 months (95% CI, 96.3–138.1) among those who did not, with no significant differences between curves (log-rank p = 0.770). Taken together, the figure summarizes prolonged survival in the series with no detectable effect of pCR on OS.

Table 3. Median survival. Patients with locally advanced breast cancer, who received neoadjuvant therapy. SOLCA–Quito Hospital. 2010–2014 (n = 31).

Complete pathological response	Survival according to complete pathological response (months)			Log Rank
	Median	95 % CI		
		Lower	Higher	
Yes	120.230	102.974	137.486	
No	117.173	96.255	138.091	*p = 770*

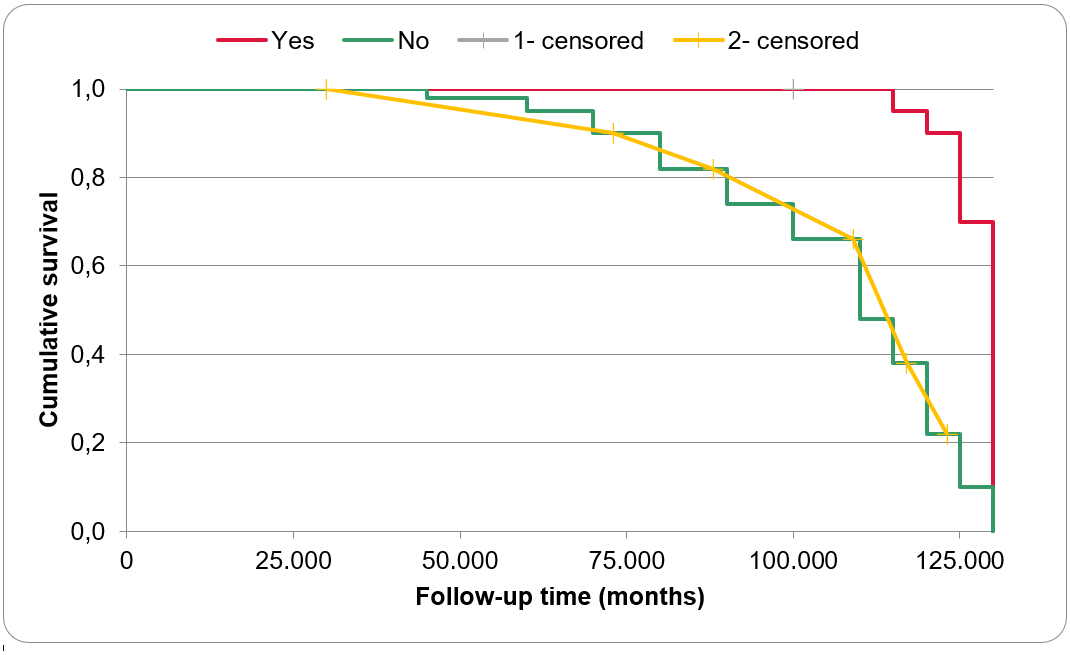
Figure 5 presents the Kaplan–Meier overall survival curves stratified by pathologic complete response (pCR). The trajectory of the pCR group remains slightly higher throughout follow-up, but the separation between curves is limited, and the comparison does not show statistically significant differences (log-rank p = 0.770). In line with the figure, the estimated medians were 120.2 months (95% CI, 102.9–137.5) for those who achieved pCR and 117.2 months (95% CI, 96.3–138.1) for those who did not, suggesting no detectable effect of pCR on OS in this cohort. This result should be interpreted in light of the sample size and the low frequency of pCR (12.9%), factors that may reduce the power to detect modest differences between groups.

Figure 4. Overall survival of patients with locally advanced breast cancer.



Author: Reyes, J; Bastidas, V.
Source: Hospital records.

Figure 5. Survival according to complete pathological response.



Author: Reyes, J; Bastidas, V.
Source: Hospital records.

4. Discussion

In this study, we analyzed a series of 31 cases of LABC treated with NAC, focusing on five-year disease-free survival (DFS) and overall survival (OS). The cohort had a mean age of 52.5 years; tumors were mainly T2 (32.3%) and T3 (38.3%), with stage IIB in 32.3% and N1 nodal involvement in 61.3%. Histologically, moderately differentiated invasive ductal carcinomas predominated. Regarding molecular subtypes, luminal B/HER2-negative with Ki-67 >14% (35.5%) and triple-negative (32.3%) were most frequent. Nevertheless, these features were not associated with chemotherapy response in our cohort, in contrast to Tan et al. [13], who reported these subtypes to be associated with better response and longer DFS.

Tumor size is an important prognostic factor and, by definition, all tumors in LABC are 5 cm or larger. In this case series, tumor size was not associated with response to neoadjuvant therapy, which is likely attributable to the small sample size. In this regard, the study by Dhanushkodi et al. [14] provides evidence that patients with larger tumors have a poorer response to neoadjuvant therapy.

In an international pooled analysis conducted by Cortazar et al. [15], patients who achieved pCR showed better long-term outcomes compared with those who had residual disease at the time of surgery. However, given the small number of cases and the fact that only 12.9% achieved a complete response to neoadjuvant therapy, this association could not be established in our series. Nevertheless, when outcomes in this cohort were analyzed, non-statistically significant differences were observed in both DFS and OS according to response to neoadjuvant therapy.

In this population, a locoregional recurrence rate of 35.5% and a five-year DFS of 64.4% were documented, with an overall median of 51.6 months. Among patients who achieved pCR, the median DFS was 58.3 months, with no statistically significant differences compared with those who did not ($p > 0.05$). These results are comparable to those of Ospino et al. [16], who reported a five-year DFS of 63.3% in a series of 171 cases in Colombia, with age and clinical-stage characteristics similar to those of this cohort. Regarding locoregional recurrence, the rate observed in this study is similar to that reported by Trabulsi et al. [17], who described a 34% recurrence rate in patients treated at a referral center in Saudi Arabia. Likewise, the absence of significant differences in DFS by pathologic response is consistent with Spring et al. [18], who despite demonstrating a favorable trend among patients with complete response note that the magnitude of the benefit remains a matter of debate.

PCR following NAC is recognized as a key prognostic indicator in LABC, as it is associated with better long-term outcomes. In this study, only 12.9% of patients achieved pCR, which limits the ability to demonstrate statistically significant differences in survival. Similar results were described by Dhanushkodi et al. [19], who also observed low pCR rates in cohorts with advanced disease. In turn, Cortazar et al. [15], in a large-scale meta-analysis (CTNeoBC), confirmed that achieving pCR predicts longer DFS and OS. Additionally, Spring et al. [18] reported that although pCR correlates with a lower risk of recurrence and death, the magnitude of this benefit varies by molecular subtype. Moreover, debate persists regarding its absolute prognostic value. Huang et al. [20] demonstrated, in a meta-analysis focused on triple-negative breast cancer (TNBC), that pCR is associated with up to a 76% reduction in the risk of progression or death, thus reinforcing its value as a marker of therapeutic efficacy. Therefore, although no statistically significant differences were found in this cohort, international evidence supports pCR as a robust predictor of better prognosis, underscoring the need for studies with larger sample sizes in our population to confirm this relationship.

With respect to OS, this study found a mean of 120.2 months, which is higher than that reported by Trabulsi et al. [17], who, in a series of 153 LABC cases, described survival of 108 months. This difference is likely explained by their cohort being made up of predominantly young women (<50 years), which was associated with poorer response to neoadjuvant therapy and worse OS.

These results are also consistent with the findings of Spring et al. [19], who determined that pCR to neoadjuvant therapy is associated with better DFS and OS in patients with LABC. According to these authors, the prognostic significance of pCR after NAC remains somewhat controversial. While pCR demonstrates sensitivity to the agents administered in the neoadjuvant setting, the true test of treatment efficacy depends on its ability to predict long-term outcomes of recurrence and death, which varies according to immunohistochemical classification.

Accordingly, Huang et al. [20] found that achieving pCR was associated with a 76% lower risk of progression, recurrence, or death. Moreover, the association between pCR and survival was consistent across clinical trial and real-world settings and was not significantly affected by variation in molecular subtype or the use of adjuvant chemotherapy. According to those investigators, patients with early-stage TNBC, who achieved pCR, had substantially better long-term outcomes than those who did not.

In the multivariable analysis, Ki-67 expression was associated with poorer disease-free survival (DFS). This is consistent with reports by Tan et al. [21], indicating that Ki-67 expression—whether assessed before or after treatment—is associated with poorer DFS, though not with overall survival (OS).

Regarding Ki-67 expression, multiple studies have demonstrated its utility as a prognostic and predictive marker in breast cancer, as it directly reflects the rate of cellular proliferation and correlates with the risk of recurrence and tumor progression. This index is particularly relevant for differentiating between luminal A and luminal B subtypes, with a 14% cutoff commonly used for this biological classification, thereby informing more individualized therapeutic decisions. Likewise, the literature indicates that Ki-67 can predict the magnitude of benefit from chemotherapy, particularly in luminal tumors treated with anthracycline- and taxane-based regimens. Thus, it represents a prognostic factor for survival in hormone receptor–positive patients [22, 23]. Nevertheless, despite its clinical value, controversies persist regarding the standardization of its assessment and the optimal interpretative threshold, underscoring the need for prospective studies and international consensus to strengthen its applicability as a prognostic and predictive tool in routine clinical practice.

The role of Ki-67 as a dynamic marker has attracted interest, as variations in its expression could anticipate changes in tumor growth rate and provide prognostic value in patients who do not achieve pCR. Nevertheless, its clinical utility is controversial because most evidence comes from retrospective studies and lacks robust methodological standardization. In particular, disagreement persists regarding the most appropriate cutoff to define high proliferation, as the values used have been largely arbitrary and heterogeneous across studies. Moreover, literature has focused mainly on Ki-67 assessment in pre- and post-treatment contexts within neoadjuvant settings; to date, there is no consensus on its incorporation into post-surgical therapeutic decision-making [24]. These gaps highlight the need for prospective studies and international consensus to validate its use as a prognostic and predictive tool in LABC.

The results of this study suggest that pCR after NAC in LABC may be associated with better outcomes in terms of DFS and OS; however, given the small sample size and the fact that pCR was achieved in only four cases, this interpretation should be made with caution, as no statistical significance was observed in the analyses performed. This is the primary limitation of this work.

5. Conclusions

The findings of this study reaffirm the importance of NAC in the management of LABC, while highlighting the need to strengthen understanding of its real-world impact on our population. Although statistically significant differences in survival by pathologic response were not demonstrated, there is a trend supporting the prognostic value of complete (pathologic) response (pCR) and of the tumor proliferative index. In this regard, we consider that Ki-67 though not yet established as a standard marker in clinical practice should be prioritized as a complementary tool for prognostic stratification and therapeutic decision-making. Likewise, the low frequency of complete responses observed in this cohort underscores the need to optimize treatment regimens and to explore more effective therapeutic alternatives in high-risk subtypes, such as luminal B and triple-negative tumors. From the authors' perspective, it is essential to promote multicenter studies with larger sample sizes and prolonged follow-up, not only to confirm these observations but also to provide robust evidence to adapt and improve treatment protocols in the local and regional context.

Results should be interpreted with caution due to the small sample size, the retrospective nature of the design, and the absence of analyses stratified by molecular subtype, which limits the generalizability of the findings and reinforces the need for studies with greater statistical power.

6. Abbreviations

HREC: Human Research Ethics Committee (by its Spanish acronym)

LABC: locally advanced breast cancer

TNBC: triple-negative breast cancer

HER2: human epidermal growth factor receptor 2

TNM: Tumor, Node, Metastasis

OR: odds ratios

NAC: neoadjuvant chemotherapy

HTR: Hospital Tumor Registry

pCR: pathologic complete response

OS: overall survival

DFS: disease-free survival

7. Administrative information

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7.2 Contributions from authors

Reyes, J: conceptualization, validation, visualization, methodology, project management, methodology, writing: review and editing

Bastidas, V: conceptualization, visualization, supervision of original draft writing, revision, and editing.

All authors read and approved the final version of the manuscript.

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7.4 Statements

7.4.1 Ethics Committee Approval

The study protocol was approved by the Human Research Ethics Committee (CEISH) of SOLCA Quito, code 059-2021-MSP-VGVS.

7.4.2 Conflict of interest

None declared by the authors.

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