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A call to action: can radiology lead the healthcare transformation?

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This Editorial is inspired by the recent consensus statement by Linda Moy et al.¹ published in Radiology, “Call to Action: Accelerating AI-Driven Transformation in Medical Imaging and the Broader Health Care System.” More than 3.6 billion imaging studies are performed worldwide each year – X-rays, ultrasounds, computed tomographies, and magnetic resonance imaging scans, among others. Each captures more information than initially sought, yet clinicians typically use it only once to answer a specific clinical question. At the same time, the demand for imaging studies can exceed the capacity of many health systems: there are more patients, more chronic diseases, more indications for imaging, and fewer personnel available to acquire and interpret studies in a timely manner. The paradox is that we have never been able to see so much inside the human body, and it has never been so complex to process everything we see. Recently, the International Society for Strategic Studies in Radiology (IS3R) issued a Consensus Statement,¹ presenting an ambitious proposal to redesign the healthcare system around artificial intelligence (AI), and issuing a call to action with an impact on radiology, hospitals, and healthcare.

Radiology has been at the forefront of medical digitalization for decades. It was the first specialty to work with digital data, connect equipment, files, and reports, and, more recently, share information through digital networks. For these reasons, it became the natural laboratory for AI in clinical practice. However, adopting AI as a working tool is not enough. It must be shown that AI increases hospital productivity, reduces staff burnout, improves patient experience, and enhances healthcare efficiency. In a 2024 quality survey by the company KLAS,² more than half of participants reported using AI

in at least one imaging case, up from 16% in 2018; AI adoption increased threefold. In many cases, AI was used as a second reader to identify findings, prioritize studies, or add alerts to the worklist. However, this can lead to alert fatigue, and the benefit is not always clear, especially in terms of saving time, improving report quality, or justifying costs with return on investment and increased efficiency, since it creates another window, another notification, and another decision the radiologist must process.

For years, AI in radiology focused primarily on abnormalities, aiming not to miss anything and flagging everything. As a result, false-positive findings increased, and biopsies, additional imaging, costs, and patient anxiety rose, with no benefit. The IS3R consensus proposes reversing this approach: teaching AI to recognize what is normal, stable, or does not require action. In a retrospective study³ of 1,529 patients, AI autonomously reported 28% of normal chest X-rays, with greater than 99% sensitivity for detecting abnormalities; this accounted for about 8% of all imaging studies. In mammography, the Massai study⁴ found AI detection rates comparable to conventional dual reading, with a 44% reduction in workload.

The IS3R consensus states that medical AI can be highly valuable, not necessarily for difficult diagnoses, but for reducing friction: making an appointment available earlier, performing a shorter imaging study, spending less time searching for history, starting the report with a useful draft, or including a recommendation for the patient. When these improvements add up, efficiency increases. Multimodal AI models, called agentic, combine text and image data, so they can initiate segmentation without the radiologist’s prompting, organize

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information, flag critical findings, retrieve background information, and generate a first draft of the report.

The IS3R consensus proposes opportunistic screening, that is, using all the data already present in the images. Transformation happens when we stop treating each imaging study as a photograph with a single purpose. For example, a chest CT ordered for a specific cardio-pulmonary indication also provides extensive information about the bones, muscles, and blood vessels. Automated analysis in the same study can estimate bone density, body composition, or vascular calcifications and, for example, diagnose osteoporosis, sarcopenia, anemia, or coronary heart disease, without another study or added radiation dose. The possibilities for opportunistic screening are enormous given the more than 3.6 billion imaging studies performed each year, yet much of the information shown in the images goes unused because radiology reports refer only to findings related to the clinician's request. If all imaging findings are combined with the clinical record and, in the future, with molecular and genomic information, radiology can move from simply describing images to diagnosing previously unknown diseases or predicting disease development. This is a fundamental transformation of the radiology paradigm.

The IS3R consensus compares the challenge of opportunistic screening to widespread use of the internet. Networks expanded when they adopted a standard, a common foundation. Health care needs its own operational equivalent: shared rules that let data circulate without losing meaning, security, or traceability. All data must remain high quality from collection through file completion. Continuous vigilance is required, with a model that performs well during evaluation and avoids protocols or equipment changes, which in computer science is known as model drift. One thing is the original system, and another is how it evolves, degenerating with use and with changes introduced for which the system was not trained. Biases may relate to problem definition, patient selection, data classification, outcome measurement, or a different clinical context.

Before buying an AI-based solution, these five questions should be answered:¹ what specific problem does it solve? What task does it eliminate, or how much time does it save? In other words, what is gained? Does it truly apply to my setting and circumstances? How will quality, bias, safety, and return-on-investment be measured? Who has the authority to approve, monitor, pause, or withdraw AI? If these five questions cannot be answered, AI implementation is not viable, likely because of infrastructure limitations.

AI-based opportunistic screening requires a new model and infrastructure to enable reliable data exchange among imaging equipment, PACS, and reporting systems. The value of opportunistic screening depends on selecting actionable findings, validating who benefits from the intervention, and ensuring real follow-up. It does not mean turning every variation in the images into a disease, because that can lead to overdiagnosis and a cascade of unnecessary or even harmful studies or treatments. More data is better only when it leads to better decisions.

The IS3R consensus does not portray the radiologist as an inevitable victim of automation; quite the opposite, it presents the radiologist as a potential administrator of a diagnostic data center. The radiologist can manage all data, including images, medical history, and molecular biomarkers, to support prevention, risk prediction, and personalized treatment through precision medicine. This implies a shift in the radiologist's professional identity. The radiologist's value is based not only on interpreting images, but also on deciding what information matters, how to integrate it, and what action to take. This fact requires leadership, quality standards, workflow design, and technology evaluation. It also requires accepting that some habits, protocols, and models, both personal and systemic, will change.

In conclusion, the IS3R proposes that radiologists lead this redesign under two fundamental conditions.¹ First, AI solutions must be reliable and continuously monitored in the real world. Second, AI must replace specific tasks to deliver meaningful value; for example, making it easier to get an appointment, shortening an imaging study, making reports more understandable to the doctor and the patient, preventing a recommendation from being lost in the system or the file, enabling an image to produce more useful information without exposing the patient to radiation again, and demonstrating that the improvements are safe, equitable, and sustainable. Radiology was one of the first medical specialties to go digital, and it now has the opportunity to become something more: the AI-based entry point for redesigning healthcare around the value of data and around the patient. *This is the call to action!*

The Mexican Federation of Radiology and Imaging (FMRI), through its official journal, JMEXFRI, proudly joins this call to action and invites the Mexican and Latin American radiology community to take an active role in shaping the transformation of medical imaging, speaking with a Latin American voice.

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Ethical considerations

Protection of human subjects and animals. The author declares that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. This article does not involve personal patient

data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

Declaration on the use of artificial intelligence.

The author declares that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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Writing original research articles as a method of scientific knowledge discovery: a practical guide

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ABSTRACT

The knowledge and skills required to write and publish scientific articles are neither innate nor spontaneous. This In-Depth Review provides the theoretical and conceptual foundation and practical skills needed to write and publish original research articles (ORAs), based on the textbook “Guía de Redacción de Artículos Originales en Ciencias de la Salud.” Like radiological image interpretation, scientific writing requires practice and training. The first step is to read the journal’s Instructions for Authors. Drafting an ORA begins with the Results section, presented with Tables, Figures, and Text. The mnemonic “DECIR” (Describe, Emphasize, Complete, Interpret, and Resume) is used for writing the Text of the Results section. Once you identify the main result from the data, define the Key Message as the interpretation of that main result that provides new knowledge, adds to existing but insufficient knowledge, or offers a new interpretation of what is known. The Key Message determines the content of all sections. Write the Introduction based on what is known and unknown about the Key Message. The Materials and Methods section should provide enough information not only to understand the results but also to allow other researchers to replicate the study. Organizing the paragraphs helps you write the Discussion in a minimum of five and a maximum of seven paragraphs. Compare the study results with those of other authors using the mnemonic KNOWS: Knowledge prevalent, New findings, Other published research studies, Wise reasoning, and Scientific posture. The Abstract presents the most important ideas from the ORA sections directly related to the Key Message. The Title should provide specific and engaging information related to the Key Message, in the fewest words (mnemonic PreCISE). Cited references must highlight the importance of the ORA and support its publication. In JMeXFRI, only artificial intelligence (AI)-assisted editing is acceptable. This guide is intended for submitting ORAs to the Journal of the Mexican Federation of Radiology and Imaging (JMeXFRI) (www.jmexfri.com), but it may also be useful for all health science disciplines.

Keywords: Original research articles. Scientific writing. Practical guide. Scientific writing workshop. Radiology. Knowledge discovery.

INTRODUCTION

The original research article (ORA) is the main vehicle for communicating health science¹. However, many research studies do not result in a published original article. The importance of writing cannot be overlooked: scientific writing is a necessary skill for health

science personnel who conduct research; the quality of an ORA depends not only on the characteristics of the research study, but also on the efficiency of the scientific writing^{1,2}.

This In-Depth Review is based on the book, “Guía de Redacción de Artículos Originales en Ciencias de la Salud”, originally published in Spanish¹. This book offers

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an efficient methodology for scientific writing, especially for those new to publishing or still inexperienced. It also provides useful information for authors who have already published and want to improve their scientific writing skills. Even scientific writing experts will find new or familiar concepts in this Guide, presented in a different approach that helps them write more efficiently. This In-Depth Review provides the theoretical and conceptual foundation, as well as the practical skills, needed to write and publish original research articles (ORAs). This guide is intended for ORA submissions to the Journal of the Mexican Federation of Radiology and Imaging (JMeXFRI) (www.jmexfri.com), but it is equally applicable to all health sciences.

WRITING ORIGINAL RESEARCH ARTICLES CAN BE EASY

Many health professionals postpone writing a scientific article because they believe they must present a manuscript that fully satisfies the reader in the first draft. This is a mistake: what matters is writing when you have something to say: new knowledge, adds to existing but insufficient knowledge, or a new interpretation of what is known based on the results of a research study. The goal is not to write well in the first version of the manuscript, but to write. There are no good writers, only good rewriters.

Scientific writing is not difficult; what is difficult to overcome is the habit of not writing. Research is a complex process that requires talented, academically oriented professionals³. Writing an ORA means overcoming the fear of criticism, letting go of the fantasy of saying everything you know, and transforming research data into novel or relevant scientific knowledge¹. Writing an ORA can be difficult because it depends entirely on the author: it requires focusing on the journal's audience and stepping outside oneself to put oneself in the readers' shoes. Writing forces us to organize our thoughts and requires effort. Two fundamental qualities of a writer are a "passion for reading" and a "passion for writing"⁴. Table 1 presents seventeen strategies for successful scientific writing¹.

The author(s) should not seek perfection, because if writing is delayed until the results are perfect, the ORA may never be published^{5,6}. The author(s) determine an ORA's quality, and the best way to achieve an optimal version is to collaborate with one or two co-authors who share knowledge of the subject and an interest in publishing the research study. This activity can be carried out efficiently in the Scientific Writing Workshop

(SWW) – sponsored by the *Federación Mexicana de Radiología e Imagen* – which optimizes the writing and publication of ORAs in the JMeXFRI². The collaborative writing team consists of a radiologist, a resident, and a scientific writing editor, who is also the author of the textbook¹. In the SWW, just over 100 scientific articles published in JMeXFRI over the past five years have guided the writing and publishing process using the textbook "*Guía de Redacción de Artículos Originales en Ciencias de la Salud*"¹.

THE FIRST STEP: READ THE JMEXFRI AUTHORS INSTRUCTIONS

A common mistake authors make is not reading the Instructions for Authors⁷. The importance of this document cannot be overstated. The Instructions for Authors make writing and revising the manuscript and, if the manuscript is accepted, the editorial process more efficient. The Instructions for Authors are freely accessible on the journal's website (<https://www.jmexfri.com/>). The manuscript must adhere to the JMeXFRI Instructions, which also provide the journal's editorial and ethical policies, define the style of scientific articles eligible for publication, and optimize the editorial process in terms of the time and effort required by editors and reviewers.

The JMeXFRI, the official journal of the Federación Mexicana de Radiología e Imagen, communicates scientific knowledge, technological developments, and innovations in Diagnosis and Therapeutic Imaging with a global impact. The journal is published quarterly in American English and in digital format, featuring original articles on the basic and clinical aspects of modern radiology in an international context. The first issue was published in the first quarter of 2022. JMeXFRI publishes the following manuscript types: Full Research Articles, Brief Research Articles, Pictorial Essays, Technical Notes, In-Depth Reviews, Case Reports, Images in Radiology, and Editorials⁷.

All manuscripts submitted to JMeXFRI undergo a rigorous, double-blind peer-review process based on the "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals" of the International Committee of Medical Journal Editors (<http://www.icmje.org>)⁸ and the Committee for Publication Ethics (COPE) (<http://publicationethics.org/resources/code-conduct>). All manuscripts submitted to JMeXFRI undergo screening with iThenticate (Turnitin), which identifies similarities with previously published or publicly available material.

Table 1. Seventeen strategies for successful scientific writing of ORAs

Description
• Consider your task responsibly: what you publish will help other health professionals and the community in general. • Keep in mind that your goal is to convey a clear Key Message, not to impress. • Be authentic; avoid pompous language and unnecessary words. • Schedule specific times for writing in your daily agenda. • Before you start, make sure you have a computer in good condition. • Follow this practical guide and JMeXFRI Instructions for Authors. • Do not think about writing – write. • Divide scientific writing into several subtasks. • Change the subtask when you feel you are falling into a rut or feel “stuck.” • Stay with the task as long as possible when you feel you are writing fluently and enjoying it (i.e., when you feel “inspired”). • Plan your time and space so they are conducive to writing; for example, being alone at a time when you are not receiving phone calls. • Plan a period of mental induction (“mental computer warm-up”): it is suggested that you read two or more articles or book chapters that address the topic you will be writing about. • Write every day, even if it is just a little: “practice makes perfect.” • Avoid starting other major projects while writing a manuscript; if you occupy your mind with other tasks, it takes a long time to reconnect. • Because writing is a solitary activity, balance it with group activities, such as scientific writing workshops. • Preserve your initial enthusiasm. • Remember: you are writing a piece of the puzzle of universal scientific knowledge.

JMeXFRI: Journal of the Mexican Federation of Radiology and Imaging; ORAs: original research articles.

STRUCTURE AND CONTENT OF THE ORIGINAL RESEARCH ARTICLE

The JMeXFRI publishes Full (3,000-word) and Brief (2,000-word) ORAs⁷. Their structure and content are similar, differing only in text length and the number of Tables, Figures, and References (Table 2). The ORA follows a conventional, well-known structure with several components: Title, Abstract, Introduction, Materials and Methods, Results, Discussion, References, and Ethical Statements. Acknowledgments are optional. The JMeXFRI audience should be considered from the start of writing an ORA. This practical guide presents the recommended ORA writing sequence: begin with the Results section, followed by the Introduction, Materials and Methods, and Discussion sections as part of a dynamic process (Figure 1). Write the Abstract, Title, and References last. Supplemental material is optional. Figure 2 summarizes the characteristics and content of each section in the recommended sequence for writing an ORA. Authors whose native language is not English are advised to seek professional English-language editing services,⁷ before submitting their manuscript. A certificate from a professional English-language editor must be included with the submission.

ANATOMY OF THE RESULTS

The “Results” section, which presents the study’s findings with Tables, Figures, and Text based on data analysis, is written first. Mastery of the research topic and a robust statistical analysis supporting the results are essential requirements. Tables and figures allow authors to organize, compare, and contrast data clearly and concisely in logical order. They support a dynamic process that continues even after the manuscript is submitted to the journal, when peer review comments and corrections are received.

Numerical data become the research study results through author analysis and interpretation. The recommendation for identifying the main result is simple: it is the novel or relevant knowledge (adds to existing but insufficient knowledge or a new interpretation of what is known) the research study provides, solidly supported by the methodological design and statistical analysis. The interpretation of the main result is the Key Message. This process is key to identifying new knowledge, knowledge that adds to prior knowledge, or a new interpretation of what is already known, not only confirming what is already known in relation to prior knowledge that constitutes the main result of the research study (Table 3). Other important data

Table 2. Structure and content of ORAs comparing Full and Brief Research Articles published in JMeXFRI

Section	Full Research Article Maximum: 3,000 words	Brief Research Article Maximum: 2,000 words
Abstract	Maximum 250 words ^a	Maximum 200 words ^b
Introduction	300 to 500 words	200 to 300 words
Materials and Methods	800 to 1,000 words	400 to 600 words
Results	700 to 800 words	400 to 600 words
Tables	Maximum 6	Maximum 2
Figures	Maximum 8	Maximum 4
Discussion	800 to 1,000 words	600 to 800 words
References	Maximum 30	Maximum 15

^aStructured; ^bUnstructured. JMeXFRI: Journal of the Mexican Federation of Radiology and Imaging; ORAs: original research articles.

accompanying the main result are presented as secondary results. The length of the section depends on the results presented. Some results may be more appropriately presented as a figure; if the data are self-explanatory, a Table is sufficient.

Table characteristics and content

Tables display numerical results in a concise, orderly way so their meaning is clear. Tables must be presented as editable text and sent as a separate file containing all tables. Number tables with Arabic numerals (e.g., Table 1, Table 2). Include a title that describes the information. Horizontal lines should be double-spaced with no borders (see examples in published JMeXFRI articles). Avoid vertical lines. Use a heading for each column of the table. Abbreviations must be described in the Table footer. Footnotes should appear below the body of the table and include *p*-values and other statistical data.

Figure characteristics and content

Figures include images and graphs. Images consist of all imaging modalities, photographs, anatomical specimens, histologic microphotographs, diagrams, drawings, and schematics. Graphs are graphical representations of numerical data, usually presented as bar and line graphs, and they use color. A 11- or 12-point Arial or Helvetica font should be used. Avoid effects such as shading or letter outlines.

Graphs may be created in PowerPoint or Excel. Distinguish between images and graphs, as the

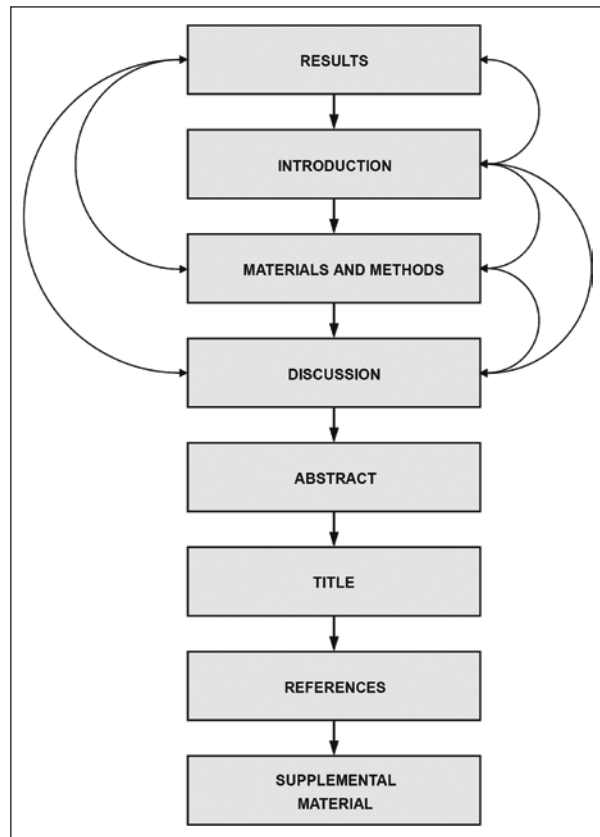


Figure 1. This practical guide presents the recommended sequence for writing an ORA: begin with the Results section, then write the Introduction, Materials and Methods, and Discussion as part of a dynamic process. Write the Abstract, Title, and References last. Supplemental material is optional.

ORA: original research article.

requirements for each differ. Figures that contain images must be in PNG, TIFF, or BMP format. Color or gray-scale (halftone) images require a resolution of at least 300 dpi, preferably 600 dpi. Do not use screen captures or photographs of screens for images or graphs. Export all images directly to the final format from the imaging equipment or a valid DICOM viewer. Color artwork should be submitted as RGB (8 bits per channel).

Each Figure can contain several images (maximum 9 per Figure) or graphs. Figures with multiple panels (images or graphs) should be labeled with capital letters for each image (A, B, C) in the upper left margin (see examples in published JMeXFRI articles). The size of the capital letters in all images of the Figures should be the same. We recommend an Arial or Helvetica 14-point font. For Figures with two or more images, there must be a thin white line between images (see examples in published JMeXFRI articles).

SECTION	CHARACTERISTICS AND CONTENT
RESULTS	Presented in Tables, Figures, and Text, the writing in the simple past tense using the mnemonic DECIR: Describe, Emphasize, Complete, Interpret and Resume. The main result interpretation is the Key Message – which is defined as providing new knowledge, adding to existing but insufficient knowledge, or offering a new interpretation of what is known.
INTRODUCTION	Contextualize what is known and what is not known in relation to the Key Message and establish the aim(s). It is written in one, two, or three paragraphs. References cited in the Introduction and Discussion sections must highlight the importance of the ORA and support its publication.
MATERIALS AND METHODS	What and how was done? Use the simple past tense and include information on how the data were collected, organized, and analyzed. Describe the resources (human and materials) and procedures (methods) used to achieve the aim(s) such as study design, population, site and period of study, inclusion and exclusion criteria, ethical aspects, variables, imaging method(s), and procedures. End with a last paragraph under the subtitle Statistical analysis.
DISCUSSION	Discuss the main and secondary results and Key Message in the context of prevailing scientific knowledge. Write a minimum of five or a maximum of seven paragraphs. The present, simple past, and present perfect tenses are used with passive voice. Use the mnemonic KNOWS: Knowledge prevalent (K), new knowledge (N), Other studies (O), Wise reasoning (W), and Scientific posture (S). In the penultimate paragraph, state strengths and limitations, and in the final paragraph, the Conclusion.
ABSTRACT	It can be structured or unstructured. Using past tense and passive voice. The Introduction is a sentence about what is not known, little known or unknown in relation to the Key Message and states the aim(s). The Materials and Methods provide enough information how the data were collected, organized, and analyzed. Results present numerical data related to the Key Message. The Conclusion is written as a sentence that is the Key Message.
TITLE	Present the Key Message, emphasizing novel or relevant scientific knowledge. Use the mnemonic PreClse. The complete, long title should include an imaging modality and disease(s) in a maximum of 18 words. Include one or more of the following elements related to the Key Message: study design, imaging modality, main result, and/or conclusion.
REFERENCES	References are cited in the text using the corresponding numbers from the final list, which provides complete reference information in a modified Vancouver format. The correct formatting of different types of References must be based on the book Citing Medicine (https://www.ncbi.nlm.nih.gov/books/NBK7256/). Journal names should be abbreviated according to the "List of Abbreviations of Words for Titles" (https://www.ncbi.nlm.nih.gov/nlmcatalog/journals).

Figure 2. Summary of the characteristics and content of each section in the recommended ORA writing sequence.

ORA: original research article.

Identify relevant elements in figures with grayscale or color arrows, arrowheads, dotted arrows, asterisks, or dashed arrows, as appropriate. These indicators must be proportional to the image size. Use white markers on a dark background or black signaling on a light background. We recommend using a colored frame that contrasts with the arrow color.

Submit each appropriately numbered figure in a separate file in the original format in which it was created. All imaging modalities described in the manuscript must be illustrated. Adjustments to brightness, contrast, or color balance are acceptable as long as they do not obscure or remove visible information from the original image. If non-linear adjustments are used, they should be indicated in the caption. Images should not be enlarged, darkened, moved, removed, or have elements added. Fraudulent manipulation is unacceptable and violates scientific ethics.

The figure legends should be included in the manuscript after the references, with the subtitle Figure Legends. Begin with the term "Figure" and the corresponding number, followed by a clear, complete interpretation, independent of the manuscript text. The units of the x- and y-axes should be specified for all coordinate graphs. Define all abbreviations used in each

figure and indicate the units. The font for the legend can be 12-point, double-spaced Arial or Helvetica (similar to the manuscript). Describe the abbreviations used in Figures in the legend footer. Do not use superscript letters or numbers to indicate abbreviations. Show case presentations as individual images for each patient; the legend should include age, sex, plane, imaging modality, and whether contrast was used.

Permission must be obtained to reproduce previously published Tables or Figures in digital format. In some cases, a reproduction permission fee applies. Proof of permission must be provided when submitting the manuscript to JMeXFRI.

Text characteristics and content

The Text of the Results section must be written after the Tables and Figures are prepared so the text clearly, simply, and precisely complements the data. Use simple, direct wording so readers fully understand the research study findings. Do not repeat the same data in identical form in Tables, Figures, and Text. Use sub-headings in this section as appropriate (see examples of JMeXFRI published articles). We recommend writing

Table 3. Differences between the main and secondary results of ORAs

Description	
Main result	The data obtained from the analysis and interpretation of the results that provides new knowledge, adds to existing but insufficient knowledge or a new interpretation of what is known. Methodological procedures and analyses, including sample size, are congruent, complete, and robust, solidly supporting the data results. The interpretation of the main result becomes the Key Message of ORAs.
Secondary results	The information obtained from the analysis and interpretation of the data that provides interesting knowledge, is probably previously known, or complements what is known and reported by other authors. The data are preliminary. Often the sample size is insufficient, or the methodological design is not appropriate to establish definitive conclusions. The description of the secondary results is explicit in the Results section and in the Discussion. The secondary results can become the main result and the main message of another ORA.

ORAs: original research articles.

Table 4. DECIR mnemonic for writing the Text of Results section of ORAs

Definitions
D: describe the characteristics of the data in the Tables and Figures.
E: emphasize the relevant data in Tables and Figures.
C: complete information that is not included in Tables and Figures.
I: interpret the meaning of the data in Tables and Figures.
R: resume data in the Tables and Figures.

ORAs: original research articles.

the Results section in the simple past tense. Avoid first-person expressions. Cite Tables and Figures in the Text in consecutive numerical order and in the order in which they appear in the manuscript.

Mnemonic DECIR

Use DECIR, the mnemonic for Describe, Emphasize, Complete, Interpret, and Resume, to write the text for the data presented in Tables and/or Figures and to systematize the wording of the text (Table 4). The order of the mnemonic components is flexible and does not follow a fixed sequence (for example, DDCCIRIED). One or more components of the mnemonic DECIR can also be included in a single sentence. For example: Describe, Interpret, and Emphasize (DIE) one or more data points; the Text is more complete and clear when two or more components are integrated.

Begin with the study population's characteristics. In the first paragraph, include the number of participants and, if possible, describe the reasons for excluding cases. In comparative longitudinal studies, present the baseline characteristics of the study subjects and include important characteristics of the study population. When a sentence begins with a numeral, spell it out in words – for example, two hundred and ten instead of 210.

Ensure that the numerical data in the Tables and the manuscript are identical. Avoid verbal expressions that indicate qualitative estimates, such as rare, infrequent, occasional, often, commonly, usually, etc.; use numbers when presenting the results. For example, instead of using the term “uncommon,” use a number such as 5% for greater accuracy. Explicitly state the numerical data with statistical significance reported in the Tables and/or Figures. The numbers in Tables and/or Figures, and described in the text, must be identical. Avoid redundant text; do not repeat all the numerical data or information presented in Tables and/or Figures. A common error is to present all data from the Tables and/or Figures in the Text. Do not include information about Materials and Methods or discuss the results.

KEY MESSAGE: THE CORE OF THE ORIGINAL RESEARCH ARTICLE

Writing an ORA means that the research study data have been analyzed within a specific, robust research study and that an expert has conducted the statistical analysis. When the main result and its interpretation define the Key Message – defined as providing new knowledge, adding to existing but insufficient knowledge, or offering a new interpretation of what is known – write and submit the ORA for publication.

The moment to define the Key Message may arise in an academic session or while preparing a conference presentation, whether a talk or a poster. Table 5 presents the characteristics of the Key Message. The author of an ORA must be clear about how the Key Message fits into prevailing scientific knowledge. In the text of the Results section, the Key Message that readers should derive from the data in the tables and/or figures and text must be explicit; it should never be left to the reader's

Table 5. Characteristics of the Key Message of ORAs

Description
Interpretation of the main result that provides new knowledge, adds to existing but insufficient knowledge, or offers a new interpretation of what is known.
Written as a clear and precise sentence or statement.
Has a direct relationship with the Tables, Figures, and Text in the Results section.
Serves as the central topic of the Title, Abstract, Introduction, Materials and Methods, Results, Discussion, and References.

ORAs: original research article.

imagination. Correctly defining the Key Message, based on the data analysis, is a personal process that depends on the skills of the most experienced author with the greatest mastery of the subject matter.

ANATOMY OF THE INTRODUCTION

This section contextualizes what is known and what is not known in relation to the Key Message and establishes the aim(s) of the ORA. Write the Introduction after the Results section and after defining the Key Message of the research study. The Introduction should be written in one, two, or three paragraphs. There is no rule for deciding whether to write one, two, or three paragraphs; this depends on the information the authors choose to present. This section introduces the study topic directly related to the Key Message. We must resist the temptation to include everything we consider important or interesting on the subject. A well-written Introduction gains credibility with well-informed readers, demonstrates that the author is an expert on the subject, and guides less informed readers to understand the Key Message. Readers will continue reading the article if the Introduction convinces them of the study's importance and the wording is clear and simple.

Introduction characteristics and content

The Key Message determines the content of the Introduction and the information from the literature to be cited. Include only references directly related to the Key Message. The recommended verb tenses in the Introduction are simple present, present perfect, and simple past. Abbreviations should be defined the first time they are used.

- **What is known:** the Introduction must present the prevailing or updated knowledge (state of the art) of the subject related to the Key Message. The

information must be sufficient and based on high-quality scientific publications. Authors must be clear about what readers need to know to understand the Key Message. The length of the “what is known” information varies depending on the context of the subject of research study.

- **What is not known:** about the topic of study related to the Key Message is usually expressed in two or three sentences.
- **Aim(s):** the Key Message determines the aim of the ORA. Describe it in the simple past tense, using an infinitive verb, in the last sentence of the Introduction, regardless of whether it has one, two, or three paragraphs. A single aim is usually written, although depending on the Key Message, some authors prefer to write more than one, and occasionally, the hypothesis may be presented instead of the aim.

Reference style

The references cited in the Introduction and Discussion should highlight the importance of the ORA and support its publication. Citations should be carefully selected. The reference list reflects the scientific rigor, ethics, and even the authors' personality. References allow the author to develop a solid argument about what is known and unknown regarding the topic related to the Key Message of the study. The temptation to include a large number of citations in the Introduction to impress the editor should be resisted. Not all sentences in the Introduction need to be cited; prevailing knowledge that is widely accepted does not need to be attributed. It is important to ensure that you are not citing an invalid article or an author accused of scientific malpractice; this can easily be verified (<http://www.ncbi.nlm.nih.gov/pubmed/>).

When writing the text related to References, one of three elements can be highlighted: the information from the cited article, the author being cited

(prominent text vs. prominent author), or the writer's ideas. During the process of writing the ORA and up to the final version (which will be sent to the JMeXFRI journal), it is recommended that, in the drafts, citations be identified using the author's first surname; this allows authors to add or remove references without renumbering the list. These surnames should be replaced by consecutive numbers once the final version is ready for journal submission. Citations are numbered according to the order in which they appear in the Text, including Tables or Figures with citations. These numbers must coincide exactly with the corresponding numbers in the reference list at the end of the ORA. If the author(s) has previously published on the topic, they can refer to relevant findings without stating that it is a self-citation.

Words and phrases to link and contextualize ideas

The Text of the Introduction should flow logically in relation to the Key Message and clearly identify what is known and what is not known. Grammatical conjunctions, words, and phrases serve as connectors; they help achieve logical progression and contextualization of ideas and highlight the research study's importance.

- **Connectors to link ideas:** Moreover,... As it turned out,... Consequently,... Indeed,... In contrast,... Nevertheless,... but few data exist on,... Hence,... Therefore,... On the other hand,... However,... Moreover,... and Furthermore.
- **Connectors to contextualize ideas:** At present,... Currently,... It is presently unclear,... It is currently uncertain,... It is increasingly recognized that,... On the basis of,... In recent years,... In previous studies,... Interestingly,... it is a recommended practice,... it is a standard practice,... There is little information about,... Current guidelines advise against,... Few studies have assessed,... It has been proposed,... It is recommended that,... It has been reported.

Frequent errors in the Introduction include excessive review of the topic, inclusion of results, Tables, Figures, methodological information, a conclusion, and a scarce or excessive number of references. Do not use many abbreviations because they cause confusion; use only those that are strictly necessary.

ANATOMY OF THE MATERIALS AND METHODS

This section describes the resources (human and material) and procedures (methods) used to achieve the research study aim(s). It should include information on how the data were collected, organized, and analyzed. Provide enough information not only to understand the results in relation to the Key Message, but also to allow other researchers to repeat the study and obtain similar results.

The length of the section varies and depends on the novelty (originality) of the data. When the techniques are new or not well known, provide a detailed description of the procedures; when you use a known technique with modifications, cite it and describe the changes. In contrast, when a standard technique is used without modifications, cite it only. For commercial kits, it is sufficient to specify the name and manufacturer (including city and country).

Materials and Methods characteristics and content

Describe what was done (not what was found) in an orderly manner, chronological sequence using the past tense. Include subsections with subheadings to present the information clearly and help the readers locate relevant paragraphs easily; for example: study development and variables, definitions, image acquisition and analysis protocol, and statistical analysis. Describe the study design and procedures in sufficient detail to make the text comprehensible; list participant characteristics and inclusion, exclusion, and elimination criteria.

Describe the equipment by name and manufacturer, and specify the city, state, and country. For imaging studies, describe the sequences in detail; for example, for magnetic resonance imaging, specify the repetition time (TR) and echo time (TE). For computed tomography, indicate if contrast was used, and specify the plane, slice thickness, and slice interval. Use generic names for devices, drugs, and products. Measurements should be in international units.

Describe how informed consent was obtained. Observational, retrospective studies that use information from routine clinical care may not require informed consent. Indicate that the study was approved by a Research Ethics Committee and a Research Committee, and that approval was obtained from a Biosafety Committee if the nature of the study requires it. For

clinical trials, include the protocol registration number (e.g., www.clinicaltrials.gov).

The validity of the Results depends on the procedures described in the Materials and Methods section. All data presented in the Results should have corresponding information in the Materials and Methods section with the technical details necessary to interpret the findings. References in the Materials and Methods section are scarce. They are used mainly to cite specific previously published methods.

Statistical analysis

It must be described in the last paragraph. A statistical expert should perform the analysis and specify which statistical tests were used on what data. Describe the statistical program, including version, manufacturer, city, state, and country. See JMeXFRI Instructions for Authors for complete information.

International guidelines are currently available according to the study design. Consult the reporting guidelines: randomized trials (CONSORT); observational studies (STROBE); diagnostic/prognostic studies (STARD); systematic reviews (PRISMA); case reports (CARE); survey studies (CROSS), among other available guidelines at www.equator-network.org

Errors in Materials and Methods can be critical because the soundness of an investigation largely depends on the methods used. Common errors include not describing the study population, not reporting the number of patients recruited, providing an insufficient description of unknown methods without citation, using ambiguous definitions of variables, performing inadequate statistical analysis, or including data from the Results, Discussion, and Conclusion.

ANATOMY OF THE DISCUSSION

This section discusses the main and secondary Results and Key Message in the context of prevailing scientific knowledge. The Discussion can be the most difficult section to write when you are a novice scientific writer. This section usually does not include Tables or Figures unless they are relevant, and no subsections are required.

Discussion characteristics and content

Organizing the paragraph content helps you write the Discussion. Write a minimum of five and a maximum of seven paragraphs (Table 5) (see examples of

JMeXFRI published articles). The length or amount of data (Results) presented in the ORA should be considered when choosing the number of paragraphs. Use the simple present, simple past, and present perfect tenses. The passive voice is frequently used.

The Discussion compares data presented in the Results section with other published studies related to the Key Message. The wording must be clear and direct. Repeating text, in identical format, from sections of the manuscript that precede the Discussion, particularly the Results, should be avoided. Unlike the Results, which describe what was found, the Discussion compares the results in the context of what is known, what is not known, and the novel or relevant scientific knowledge provided by the research study (Key Message). Emphasize what is new and relevant. Reference style follows the same recommendations described in the Introduction section.

First paragraph: Key Message

The Discussion should start with the main result directly related to the aim of the research study, describe the Key Message, and explain its relevance in the context of global knowledge. The wording of the main result should not repeat what is in the Results section. Numerical data are usually not repeated; it is sufficient to interpret them in text.

The statement “This is the first study...” strongly attracts attention and is recommended only when an extensive and exhaustive literature review has been carried out to ensure that no one has previously published the findings that support the Key Message, based on sound methodology and robust statistical analysis. In the first paragraph, avoid text that is not related to the Key Message. References should not be included.

Mnemonic KNOWS

In the second, third, fourth, and fifth paragraphs, depending on whether the Discussion is written in five, six, or seven paragraphs, the Results of the research study should be compared with those of other authors, based on the mnemonic KNOWS, which stands for: Knowledge prevalent, New findings, Other published studies, Wise reasoning, and Scientific posture (Table 6) (see examples of JMeXFRI published articles). The sequence of the KNOWS elements is flexible; for example, they can be combined in different orders, and some components are often

Table 6. Structure and content of the Discussion in relation to the number of paragraphs in an ORA

Paragraph	5 paragraphs	6 paragraphs	7 paragraphs
First	Key Message	Key Message	Key Message
Second	Main result	Main result	Main result
Third	Secondary result	Main or secondary result	Main result
Fourth	Strengths and limitations	Secondary result	Secondary result
Fifth	Conclusion	Strengths and limitations	Secondary result
Sixth		Conclusion	Strengths and limitations
Seventh			Conclusion

ORA: original research article.

repeated in the same paragraph (e.g., KKNNOOWS or KOONWS). All components of this mnemonic must be present, even if they are described only once in each paragraph.

Second and third paragraphs: main result

In a six- or seven-paragraph Discussion, these paragraphs compare the main result with publications by the most important authors; in a five-paragraph Discussion only the second paragraph compares the main result. Always use the mnemonic KNOWS. The first sentence(s) should be K (Knowledge prevalent) and the last sentence(s) should be W (Wise reasoning) and S (Scientific posture).

Make explicit the relationship between the main result obtained in the research study and that reported by other authors, supported by solid arguments. Other authors who previously published in relation to the Key Message should be cited. It is also appropriate to group citations from several authors. The same publications may be cited in the Introduction and Discussion sections, although there should never be an identical sentence.

Highlight the relevant results of the cited studies (population, number of subjects, imaging modality, and numerical results), always related to the Key Message, as well as the authors' interpretation of these results. Quantitative comparisons are preferable to purely qualitative ones. When the authors' results differ from previous publications, present the results (numerical data) and describe the differences; maintain impartiality when explaining them from the authors' position. Data that do not match should never be hidden or altered.

Fourth and fifth paragraphs: secondary results

In the fourth of a six-paragraph Discussion, or in the fourth and fifth paragraphs of a seven-paragraph Discussion, the secondary result(s) are described. These findings are not directly related to the study's Key Message, but they offer interesting data and complement the study topic. Secondary results often generate hypotheses for future research. Secondary results should also be compared with the most relevant studies, previously published by other authors or by the same author. Always use the mnemonic KNOWS. Follow the same drafting recommendations for the second and third paragraphs of the Discussion, including the structure of the first and last sentences in those paragraphs.

Penultimate paragraph: strengths and limitations

In the penultimate paragraph, explicitly recognize the study's strengths and limitations to interpret the results and the impact of the Key Message. Use the following characteristics to determine strengths and weaknesses: study design, sample size, population type(s), imaging methods, procedures, and laboratory tests. This paragraph should begin with strengths and briefly describe what, in the authors' opinion, are the strengths of the ORA. No research is perfect, and limitations in study results should not discourage authors. The text on a study's limitations is usually longer than the text on its strengths. You do not need to offer excuses for unexpected results. Any biases that influenced the results should be honestly acknowledged and any inconsistencies explained. Identify the study's weaknesses and indicate whether an inconsistency in the design or method could have affected or invalidated any results. Editors, reviewers, or readers may doubt a study's results if they find inconsistencies the authors have not explicitly described. If the limitations involve serious methodological errors that affect the robustness of the results, the research study should not be published.

Last paragraph: conclusion

In the last paragraph, use the single-word subtitle Conclusion. Draw a conclusion based on the main result and Key Message and include recommendations for applying the research results and/or the need for future studies. Do not present a conclusion that is

insufficiently supported by the data. References are usually not included; when they are, there are typically only one or two. If possible, clearly identify any new hypotheses that arise from the research study.

Errors to avoid in the wording of the Discussion include: overinterpretation of results; underinterpretation of results; text unrelated to the main or secondary results; weak argumentation in relation to the Key Message; excessively long text; confusing wording; repetition of text from other sections; data not presented in the Results; a conclusion not supported by the results; insufficient References; References of poor scientific quality; and references unrelated to the Key Message.

ANATOMY OF THE ABSTRACT

The purpose is to present the most important ideas from the ORA sections. Write the Abstract after completing the Introduction, Materials and Methods, Results, and Discussion sections. It should briefly summarize the content of the ORA. It is the only section included in multiple databases.

Abstract characteristics and content

The Abstract must provide the necessary and sufficient information to maintain the interest of readers initially attracted by the Title, to whom the Key Message is addressed. It must be informative, directly related to the Key Message, and written in the past tense and passive voice. Define abbreviations when they are used for the first time. Tables, Figures, and References are not included.

A structured format is used in a Full Research article, with a maximum of 250 words, and the subheadings of the sections of the article are included: Introduction, Materials and Methods, Results, and Conclusion, which replaces the Discussion (Table 7). In the Brief Research Article, write an unstructured abstract without subtitles, with a maximum of 200 words. The Introduction is a sentence about what is not known or is little known in relation to the Key Message. The last sentence of the Introduction states the study aim. The Materials and Methods section includes only information related to the Key Message, including population characteristics, imaging methods, and relevant statistical analyses. Include the study design. The Results describe the number of subjects included in the study and present numerical data related to the Key Message. Include significance

Table 7. KNOWS mnemonic for writing the second, third, fourth, and fifth paragraphs based on the paragraph numbering of the Discussion in ORAs

Definition
K: knowledge, prevailing scientific knowledge.
N: new findings about the main or secondary results of the research study.
O: other published studies.
W: wise reasoning in the interpretation of the main result presented as the Key Message, or of secondary results.
S: scientific posture: impact of the new or relevant knowledge and/or the author's recommendations.

ORAs: original research articles.

values and specific relevant results of the statistical analysis. The Conclusion in the Abstract is written as a sentence that is the Key Message and presents the new or relevant knowledge that the research study provides. A second statement may be included, particularly related to the impact or recommendations.

Keywords represent the main concepts in the ORA that facilitate identification and database retrieval. Include 4 to 6 words Medical Subject Headings (MeSH) terms from the Index Medicus/Medline, available at: <https://www.ncbi.nlm.nih.gov/mesh>.

ANATOMY OF THE TITLE

The Title presents the Key Message, emphasizing novel or relevant scientific knowledge. The Title is the first element that attracts readers' attention to the Key Message. The complete, long title should include an imaging modality and disease(s). The long title may contain a maximum of 18 words, including articles, prepositions, and conjunctions. Insert a short title of 45 characters, including spaces. The short title appears in the header of the published article (see examples of JMeXFRI published articles). You can write the title once the Key Message is defined and modify it while writing the different sections of the manuscript, and even before submission.

Title-specific elements

The Title must be informative and engaging. Use a colon (:) or a hyphen (-) to separate the first part of the Title from an add-on, subheading, or explanation. The Topic (T) being studied should always be included, along with one or more of the following elements related to the Key Message: study design, imaging modality,

main result, and/or conclusion. The mnemonic PreCISE describes the requirements for writing the title: PREeminence of the words highlighting the novelty of the Key Message; Clarity in form and style; Informative regarding the content of the research study; and concISE while including as much relevant information as possible. The title can be a sentence, a question, or a substantive phrase, but you should avoid writing a list of adjectives and/or nouns that presents the Key Message in a confusing way. Including a subtitle is recommended when a long sentence is required. Abbreviations of imaging modalities that are widely known to JMeXFRI readers may be used.

SUPPLEMENTARY INFORMATION

If the authors consider it useful to include additional material on technical details or laboratory procedures, and to avoid an excessive number of Tables, Figures, or References in the main text, this material will be published in digital form as supplementary information on the journal's website. Supplementary material should be numbered, e.g., Table S1, S2; Figure S1, S2; Formula/Equation S1, S2.

REFERENCES

Cite references in the text using the corresponding number in the final list, which provides complete reference information in a modified Vancouver format (see examples in JMeXFRI). A maximum of 30 references is allowed in a Full Research Article and 15 in a Brief Research Article. List references in the order in which they are first mentioned in the text. Before and during writing the ORA, conduct several literature reviews to ensure the authors master the prevailing knowledge on the topic they are addressing.

The format of different Reference types are based on Citing Medicine: The NLM Style Guide for Authors, Editors, and Publishers [Internet]. 2nd ed. (<https://www.ncbi.nlm.nih.gov/books/NBK7256/>). Journal names should be abbreviated according to the "List of Title Word Abbreviations" (<https://www.ncbi.nlm.nih.gov/nlmcatalog/journals>).

Cite references in the text with superscript Arabic numerals, consecutively and in the order of first appearance. Insert the reference number before the final punctuation mark, comma, semicolon, or colon. Reference numbers in Tables and/or Figures must also be given in the order in which they appear. Only published articles should be cited; authors are responsible

for the accuracy of references. For citations with 7 or more authors, list only the first 6 followed by "et al." after the sixth author's name; for 6 or fewer authors, list all authors. Include the Digital Object Identifier (doi) in the reference list. Common errors in References include omitting necessary citations and including too many references.

AUTHORSHIP AND ACKNOWLEDGMENTS

To be listed as an author, a participant must meet all four International Committee of Medical Journal Editors (ICMJE) requirements⁸: substantial contributions to the conception or design of the research study, or the acquisition, analysis, or interpretation of data; drafting the manuscript or revising it critically for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the ORA, ensuring that questions related to the accuracy or integrity of any part are appropriately investigated and resolved.

The order of authors depends on each author's contribution and must be agreed upon before writing begins. Before submitting the article, all authors should agree on the order in which their names will appear in the ORA. List the main author first, followed by the others in descending order by contribution. Include the given name(s), surname(s), and affiliation(s) of the author(s). Indicate where the work was performed, including department, institution, city, state, and country. Only one given name will be published in full; if you have several, please choose which one. Surnames, if more than one, will be separated by a hyphen. Write names, surnames, departments, institutions, cities, and countries without accents. Indicate affiliations in lower-case, superscript, immediately following the author's name and preceding the appropriate affiliation. Provide the 16-digit Open Researcher and Contributor ID (ORCID) of all authors. Include the conflict-of-interest statement of all authors. <https://www.permayer.com/formulario-responsabilidades/#>

A Corresponding Author must also be specified in the manuscript; this person has direct contact with the editorial office of the journal and, therefore, assumes primary responsibility for the writing and publication of the ORA. The Corresponding Author is usually the main author. See the Instructions for Authors for all documents accompanying the manuscript that should be sent: <https://publisher.jmexfri.permayer.com>

Contributions from anyone who does not meet the criteria for authorship should be listed, with permission

Table 8. Elements of the Abstract and their correspondence with the content of the ORA sections

ORA section	Content
Introduction	What is not known related to the Key Message and the aim(s) of the research study
Materials and Methods	Characteristics of the research study, imaging examination, procedures, and statistical analysis mainly related to the Key Message
Results	Only text with relevant data and numerical information mainly related to the Key Message
Conclusion	Main result and Key Message

ORA: original research article.

from the contributor, in an Acknowledgments section. Examples include: The authors thank,... We are deeply indebted to,... We are grateful to,... The authors wish to acknowledge,... We thank.

GUIDELINES FOR THE USE OF ARTIFICIAL INTELLIGENCE IN WRITING AND PUBLISHING ORIGINAL RESEARCH ARTICLES IN JMEXFRI

The use of artificial intelligence (AI) tools and large language models (LLMs) has become common in scientific publishing, particularly for AI-assisted editing, AI-assisted writing, AI-generated scientific content, AI-assisted data analysis, and AI-generated images. However, these uses pose significant risks to validity, confidentiality, transparency, and accuracy in scientific publishing⁹. Because AI can generate incorrect, incomplete, or biased text and images, humans are ultimately responsible for reviewing and ensuring the accuracy of any content generated with AI assistance. According to the International Committee of Medical Journal Editors⁹, ORA-authors should adhere to the following principles when using AI/LLMs:

- AI-assisted technologies should not be cited as an author.
- Because AI tools may incorporate information from sources without proper attribution (including copyrighted material), humans are responsible for citing appropriate sources, obtaining permission when necessary, and ensuring that plagiarism has not occurred when using AI-generated content.
- Authors should be transparent in their use of AI tools at any stage of the editorial process, including manuscript preparation, editing, and review. When AI is used, users should disclose which tool was used, and for what purpose.
- Authors should be able to declare that their paper contains no plagiarism, including in-text and images

produced by AI. Humans must ensure appropriate attribution of all quoted material, including full citations. Citing AI-generated material as the primary source is not acceptable.

- Non-disclosure of AI use may require corrective action and may be construed as misconduct in some circumstances.

Only AI-assisted editing is acceptable in JMeXFRI. Authors who use this technology should describe, in the cover letter and in the appropriate section of the submitted manuscript, how they used AI-assisted tools. A published example in JMeXFRI is: The authors declare that the content was human-generated, but MSCoPilot was used for punctuation and grammar editing¹⁰. Another published example in JMeXFRI is: The author declares that an AI tool (Apple) was used for orthographic and stylistic corrections of the manuscript¹¹.

ONLINE SUBMISSION, REVISION OF THE GALLEY PROOF, AND EDITING OF THE ORIGINAL SCIENTIFIC ARTICLE

The sections of the ORA-final version submitted should appear in the following order: Title, Abstract, Introduction, Materials and Methods, Results, Discussion, Acknowledgments, Ethical Disclosures, References, and Figure Legends. Tables and Figures should be submitted as individual files; the same applies to supplemental material. See the JMeXFRI Instructions for Authors for details and accompanying documents. Submissions of ORAs to JMeXFRI must be made entirely online at the following website: <https://publisher.jmexfri.permayer.com>. which guides authors step by step through the file upload process. All correspondence, including notification of the editor's decision and requests for revisions, is sent via email, so paper documents are not required. The corresponding author will receive information about the manuscript peer review process at the provided email address.

Revising the galley proof is important because it allows you to correct writing and editing errors and

produce the final version of the ORA. Errors can occur in any section, including Tables and Figures. These errors can come from various sources, but they mainly originate in the authors' writing or during journal editing. Errors will always be found in the galley proof. At least two authors should review the galley proof. It is advisable to print the galley proof, read it carefully, and mark any errors. All numerical data and percentages in the Text, Tables, and Figures must be verified. Review the References, pay special attention to grammatical errors, and check punctuation and spacing. Editors may include questions or concerns about the manuscript that arise during editing. Usually, the publisher asks the corresponding author to return the corrected digital galley proof within 48 to 72 hours.

Together with the ORA, a Graphical Abstract is published. It is a visual representation that concisely summarizes the Key Message, results, and imaging findings. The Graphical Abstracts Committee of JMeXFRI creates it. Publication of ORAs in JMeXFRI (www.jmexfri.com) is free of charge for authors, and all published articles are open access.

CONCLUSION

The ORA is a masterpiece of intellectual art: writing means rethinking and reformulating what is known. When the authors decide to write after conducting research, a passion for reading and writing, along with many hours of hard work, are required. When writing an ORA, authors must believe that what they write and publish matters because it provides new knowledge, adds to existing but insufficient knowledge, or offers a new interpretation of what is known through the Key Message, the essence of an ORA. Writing ORAs requires a structured method and strict adherence to specific principles. Always write with the readers in mind. The authors must follow the JMeXFRI Instructions for Authors, which are based on the journal's editorial and ethical policies. This practical guide presents the recommended sequence for writing an ORA: begin with the Results section, followed by the Introduction, Materials and Methods, and Discussion sections, treating it as a dynamic process. The Abstract and Title are written last. There are no shortcuts to developing scientific article-writing skills. You must go through writing, reading, rereading, and rewriting. This activity can be carried out efficiently in the SWW to optimize the writing and publication of ORAs in JMeXFRI. The collaborative writing team consists of a radiologist, a resident, and the scientific writing editor. When you write

scientific articles, you think differently: "Radiologists who research, write, and publish... teach well and interpret better."

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Conflicts of interest

The author discloses no potential conflicts of interest.

Ethical considerations

Protection of human subjects and animals. Not applicable.

Confidentiality, informed consent, and ethical approval. The author declares no ethical responsibilities because no confidential information was presented.

Declaration on the use of artificial intelligence. The author declares that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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Detection of anemia based on blood attenuation cutoff value of combined cardiovascular structures using non-contrast chest CT

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ABSTRACT

Introduction: Low blood attenuation, measured in Hounsfield units (HU) on non-contrast chest computed tomography (CT), has been proposed as an imaging marker of anemia. This study evaluated the correlation between blood attenuation (HU) on non-contrast chest CT and serum hemoglobin levels, and determined the optimal HU cutoff value, based on a combined assessment of multiple cardiovascular structures, for detecting anemia in adult patients. **Material and methods:** This case-control study included adult patients who underwent non-contrast chest CT and a complete blood count within 24 hours. A region of interest (ROI) was defined in five cardiovascular structures – the ascending aorta, aortic arch, descending aorta, and the left and right ventricles – to measure blood attenuation. Correlation analyses and ROC curves were calculated to assess performance metrics for each structure and for the combined cardiovascular structures. **Results:** Eighty-eight patients were included: 44 with anemia and 44 controls with normal serum hemoglobin. Mean hemoglobin levels were 9.5 ± 1.7 and 13.7 ± 1.3 g/dL, respectively ($p < 0.001$). A significant positive correlation was observed between blood attenuation and serum hemoglobin across all cardiovascular structures (Spearman's $\rho = 0.697$ - 0.817 ; $p < 0.001$). In the ROC curve analysis, a blood attenuation cutoff ≤ 38.0 HU in at least three of five cardiovascular structures showed high diagnostic performance for detecting anemia, with sensitivities of 77.3% to 86.4%, specificities of 93.2% to 100%, and accuracies of 71.6% to 85.2%. Moreover, diagnostic performance increased progressively with anemia severity. **Conclusions:** A cutoff value ≤ 38 HU based on combined blood attenuation measurements in at least three of five cardiovascular structures on non-contrast chest CT is a simple and reliable method for detecting anemia; the diagnostic performance of this cutoff value increases in direct proportion to anemia severity.

Keywords: Anemia. Chest tomography. Cardiovascular structures. Hemoglobin. Diagnostic imaging.

INTRODUCTION

Anemia is a public health problem and the most common hematologic disorder worldwide (24%). It is most prevalent among women, children, and older adults^{1,2}. In Mexico, the 2022 Continuous National Health and Nutrition Survey reported a prevalence of 15.8% among women aged 20 to 49 years, 10.1% among adolescents, and 10.3% among older adults³. The gold standard for diagnosing anemia is the serum hemoglobin

level measured in a complete blood count¹. Anemia is associated with functional impairment and increased morbidity and mortality across a wide range of acute and chronic diseases⁴. Qualitative findings such as the aortic ring sign and the hyperdense interventricular septum sign^{5,6}, together with blood attenuation measurements allow incidental detection of anemia on non-contrast chest computed tomography (CT). A reduction in erythrocyte concentration decreases blood attenuation measured in Hounsfield units (HU),

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resulting in blood hypoattenuation on chest CT^{5,7-11}. Reduced blood attenuation significantly correlates with lower serum hemoglobin levels^{5,9,11}.

No consensus exists regarding the optimal cardiovascular structure for measuring blood attenuation, the number of structures to evaluate, or the blood attenuation cutoff for detecting anemia on non-contrast chest CT. Furthermore, differences in image acquisition and analysis protocols for non-contrast chest CT have led to variability in proposed cutoff values for detecting anemia (range, 30 to 40 HU) depending on the anatomical structure and the population studied^{9,11-16}. Several studies have evaluated a single cardiovascular structure and reported variable sensitivity for anemia detection, depending on the structure and study population^{5,9,13,17,18}. In contrast, other reports have evaluated between two and seven cardiovascular structures,^{9,14,17,18} demonstrating that combining measurements improves diagnostic performance for detecting anemia^{9,11,13-16}.

Previous studies have shown that combining blood attenuation measurements from multiple cardiovascular structures (the thoracic aorta, the ventricles, and the inferior vena cava) improves diagnostic performance^{9,14,15,19-21}. However, most studies have been conducted in Asian populations,^{9,14,16-18,21,22} European populations,^{5,7,12,13,23} or American populations⁸, with limited evidence in Latin American populations²⁴ and, particularly, in Mexican patients²⁵. This study evaluated the correlation between blood attenuation (HU) on non-contrast chest CT and serum hemoglobin levels and determined the optimal HU cutoff for detecting anemia based on a combined assessment of multiple cardiovascular structures in adult patients.

MATERIAL AND METHODS

This case-control study was conducted from December 2023 to August 2024 at the Diagnostic and Therapeutic Imaging Service of Regional General Hospital No. 1 of the Instituto Mexicano del Seguro Social in Tijuana, Baja California, Mexico. Eligible patients were older than 18 years, referred by their treating physicians for a non-contrast chest CT scan, and all had a complete blood count performed within 24 hours before or after the imaging examination. Patients with a history of recent blood transfusion, hematologic disease, a contrast-enhanced imaging examination, or factors that would limit the evaluation of cardiovascular structures, such as metallic devices, severe aortic calcification, or significant mediastinal

displacement, were excluded. Because this was a retrospective study using information obtained during medical care, informed consent was waived. The study was approved by the institutional Research and Ethics Committee.

Study development and variables

Variables included age, sex, and hemoglobin level measured within 24 hours before or after the non-contrast chest CT scan. The following five cardiovascular structures were evaluated: the ascending aorta, aortic arch, descending aorta, and the left and right ventricles. Cases were patients with anemia, classified by serum hemoglobin concentration as mild (women: 11.0-11.9 g/dL; men: 11.0-12.9 g/dL), moderate (8.0-10.9 g/dL), or severe (< 8.0 g/dL). Controls were patients with normal hemoglobin levels, classified as non-anemic.

Image acquisition and analysis protocol

Non-contrast chest scans were performed on a 16-slice BrightSpeed® multidetector CT scanner (GE Healthcare, Milwaukee, WI, USA). Patients were positioned supine with sustained deep inspiration. Images were acquired from the lung apex to the base at 120 kVp, with automatic current modulation (Auto mA), a 512 × 512 matrix, and 2-mm axial slices. Blood attenuation was assessed using a standardized mediastinal window (width 200 HU; level 75 HU) and measured within a circular region of interest (ROI) of approximately 1.5 cm², carefully positioned at the center of the vascular lumen or ventricle, at an adequate distance from the walls to avoid partial-volume effects. Blood attenuation was recorded in HU.

The ROI was placed on five cardiovascular structures: the ascending aorta (approximately 1 cm above the valvular plane), the aortic arch (middle portion), the descending thoracic aorta (approximately 1 cm below the carina), the left ventricle, and the right ventricle. The area of greatest diameter within the visible blood pool was selected. Two independent HU measurements were obtained for each structure, and the mean blood attenuation value was recorded. If the difference between the two measurements exceeded 5 HU, the procedure was repeated, and a new measurement was recorded.

During ROI placement, we excluded the vascular wall, calcified or non-calcified atherosclerotic plaques, mural thrombi, papillary muscles, trabeculations, heart

Table 1. Characteristics of control patients without anemia and cases with anemia

Description	Total (n = 88)	Control patients without anemia (n = 44)	Case patients with anemia (n = 44)	p
Sex, n (%)				0.828
Women	53 (60.2)	26 (59.1)	27 (61.4)	
Men	35 (39.8)	18 (40.9)	17 (38.6)	
Age, years, mean $\pm$ SD (min-max)	49.0 $\pm$ 14.4 (18-74)	49.0 $\pm$ 15.0 (18-74)	49.0 $\pm$ 13.9 (22-68)	0.997
Serum hemoglobin, g/dL, mean $\pm$ SD (min-max)	11.6 $\pm$ 2.5 (6.3-16.8)	13.7 $\pm$ 1.3 (12.2-16.8)	9.5 $\pm$ 1.7 (6.3-11.7)	< 0.001

SD: standard deviation.

valves, and areas affected by beam hardening, motion, prosthetic material, or partial volume to ensure that measurements reflected only intraluminal blood. All measurements were performed by a radiology and imaging resident (LGA) with prior training in the measurement methodology, under the direct supervision of a board-certified radiologist (ORG) with 6 years of experience.

Statistical analysis

Quantitative variables are presented as means $\pm$ standard deviation (SD). Normality of continuous variables was assessed using the Shapiro-Wilk test. Categorical variables are presented as absolute frequencies and percentages. Blood attenuation values between patients with and without anemia were compared with the Mann-Whitney U test. The various degrees of anemia severity were evaluated with the Kruskal-Wallis test and Dunn's post hoc comparisons. The chi-square test was used to assess the association between non-contrast chest CT findings and anemia. The association between hemoglobin and blood attenuation was determined using Spearman's correlation coefficient. We evaluated the diagnostic performance of non-contrast chest CT for detecting anemia using receiver operating characteristic (ROC) curves and calculated the area under the curve (AUC). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio, negative likelihood ratio, and diagnostic accuracy were calculated with 95% confidence intervals, and a p -value < 0.05 was considered significant. Statistical analyses were performed using Jamovi software version 2.6 (The Jamovi Project, Sydney, Australia) and the Rj add-on, based on the R statistical environment (R Core Team, Vienna, Austria).

RESULTS

Eighty-eight patients were included: 53 women (60.2%) and 35 men (39.8%), with a mean age of 49.0 ± 14.4 years (Table 1); 44 cases with anemia and 44 controls with normal hemoglobin levels. The mean serum hemoglobin level was 9.5 ± 1.7 g/dL and 13.7 ± 1.3 g/dL, respectively ($p < 0.001$). Among the cases, severe anemia was the most frequent ($n = 21$, 47.7%), followed by moderate anemia ($n = 16$, 33.3%).

Comparison of blood attenuation on non-contrast chest CT in patients without anemia and cases with anemia

Blood attenuation values (HU) in the five cardiovascular structures – the ascending aorta, aortic arch, descending aorta, and the left and right ventricles – were significantly lower in patients with anemia than in control patients with normal hemoglobin ($p < 0.001$), with large effect sizes across all evaluated structures (Cohen's $d = 1.4$ to 2.0) (Table 2). The largest mean differences were observed in the descending aorta (14.8 HU) and the aortic arch (14.4 HU).

Spearman correlation between serum hemoglobin level and blood attenuation values on non-contrast chest CT by cardiovascular structure

There was a significant positive correlation between serum hemoglobin and blood attenuation across all five cardiovascular structures (Figure 1). The strongest correlations were observed in the ascending aorta ($\rho = 0.817$; 95% CI: 0.733-0.877), the aortic arch ($\rho = 0.802$; 95% CI: 0.713-0.866), and the descending aorta ($\rho = 0.742$; 95% CI: 0.630-0.823). The ventricles showed

Table 2. Comparison of blood attenuation values on non-contrast chest CT between cases with anemia and control patients without anemia

Cardiovascular structure	Mean	SD	Min	Max	CV %	Mean difference (95% CI)	p	Cohen's d
Ascending aorta, HU								
Anemia ^a cases	29.5	8.2	14.0	45.0	27.9	13.4 (11-17)	< 0.001	2.0
Non-anemia controls	42.9	4.7	33.0	55.0	10.9			
Aortic arch, HU								
Anemia cases	28.4	8.0	15.0	42.0	28.4	14.4 (11-18)	< 0.001	1.9
Non-anemia controls	42.8	6.9	28.0	58.0	16.2			
Descending aorta, HU								
Anemia cases	27.7	9.4	14.0	48.0	33.9	14.8 (11-20)	< 0.001	1.5
Non-anemia controls	42.5	10.2	20.0	65.0	24.0			
Left ventricle, HU								
Anemia cases	30.8	10.0	12.0	46.0	32.6	11.7 (7-15)	< 0.001	1.5
Non-anemia controls	42.5	4.9	32.0	50.0	11.5			
Right ventricle, HU								
Anemia cases	33.7	11.3	13.0	59.0	33.5	11.6 (8-16)	< 0.001	1.4
Non-anemia controls	45.3	4.1	40.0	57.0	9.1			

^aPatients were classified as anemic according to sex-specific hemoglobin thresholds; women ≤ 11.9 g/dL, men ≤ 12.9 g/dL. CI: confidence interval; CV: coefficient of variation; CT: computed tomography; HU: Hounsfield units; SD: standard deviation.

moderate-to-strong positive correlations: left ventricle ($\rho = 0.701$; 95% CI: 0.576-0.794) and right ventricle ($\rho = 0.697$; 95% CI: 0.571-0.791).

Comparison of blood attenuation values in cardiovascular structures between control patients without anemia and cases with anemia using non-contrast chest CT

Blood attenuation decreased significantly in direct correlation with anemia severity across the five cardiovascular structures ($p < 0.001$) (Table 3). Severe anemia had significantly lower blood attenuation values (range, 24.7 HU to 29.0 HU) than mild (range, 40.7 HU to 44.1 HU) or moderate anemia (range, 26.9 HU to 36.1 HU) across the five cardiovascular structures ($p < 0.001$). The greatest difference in blood attenuation was observed between control patients without anemia and those with severe anemia, particularly in the ascending (42.9 HU vs. 24.7 HU) and descending aorta (42.5 HU vs. 25.7 HU).

Diagnostic performance of blood attenuation for anemia detection according to cardiovascular structure and in at least three combinations of five cardiovascular structures on non-contrast chest CT

ROC analysis showed different blood attenuation values for the five cardiovascular structures (range

32.5 HU to 39.5 HU) (Figure 2). In the ascending aorta, the cutoff was 39.5 HU; in the aortic arch, 33.5 HU; in the descending aorta, 32.5 HU; and in the left and right ventricles, 35.0 HU and 39.5 HU, respectively. The AUC was > 0.800 in all cardiovascular structures. Using the criterion of hypoattenuation in ≥ 3 of 5 cardiovascular structures on non-contrast chest CT, we evaluated combined blood attenuation cutoff values ranging from ≤ 30.0 HU to ≤ 42.0 HU (Table 4). Blood attenuation values of ≤ 32.0 HU and ≤ 38.0 HU showed the best overall performance, with an accuracy of 85.2% for both, and Youden indices of 0.705 and 0.695. We selected a cutoff value of ≤ 38.0 HU because it showed higher sensitivity (77.3% vs. 70.5%) while maintaining high specificity (93.2%) and diagnostic accuracy (85.2%).

Diagnostic performance of blood attenuation value ≤ 38 HU for anemia detection by cardiovascular structure on non-contrast chest CT

The cutoff value of ≤ 38.0 HU showed good diagnostic performance across the five cardiovascular structures (Table 5). The descending aorta had the highest sensitivity (86.4%), followed by the aortic arch (81.8%) and the ascending aorta (77.3%). In contrast, the right ventricle showed the highest specificity (100%) and positive predictive value (100%), while the ascending

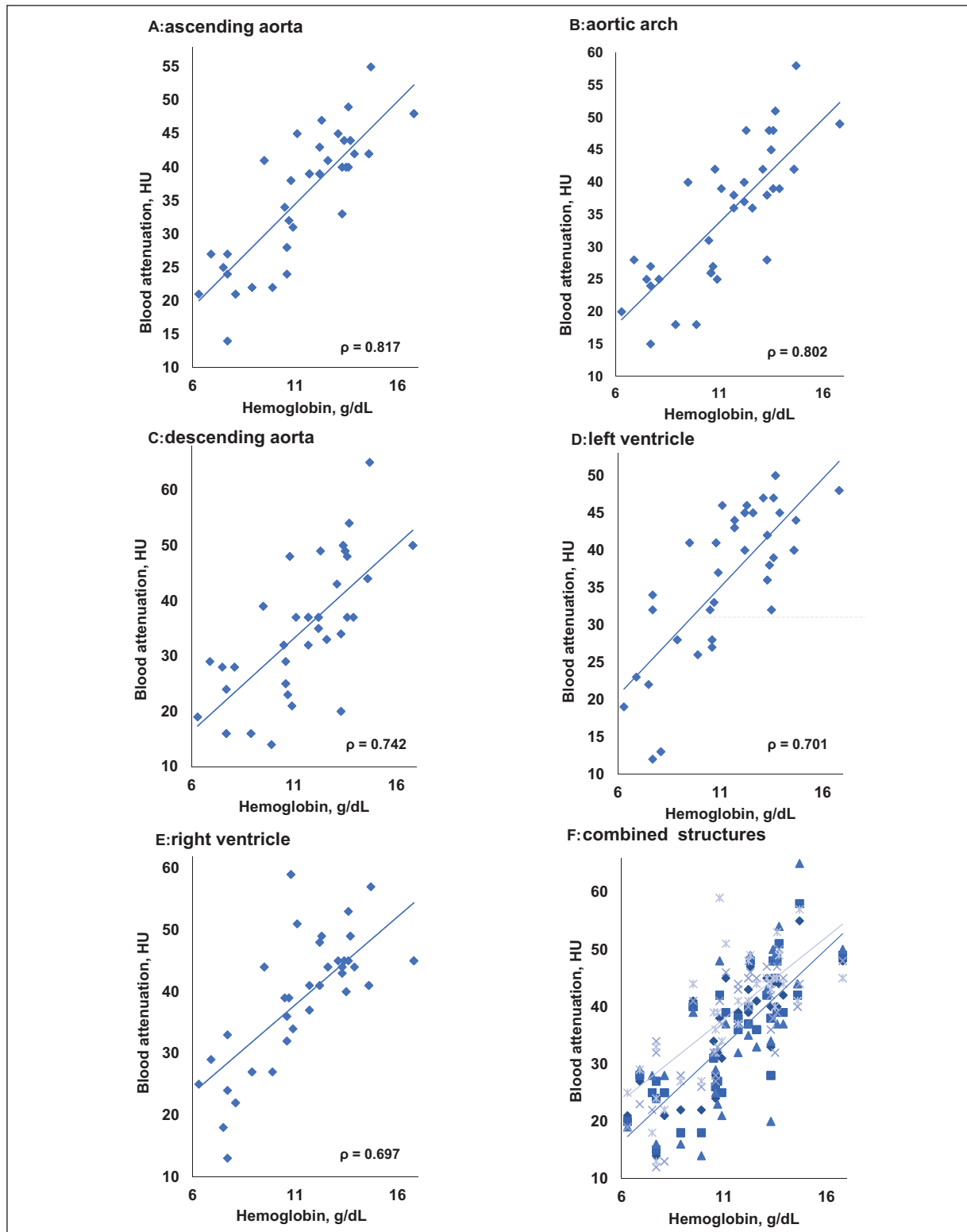


Figure 1. Spearman correlation between serum hemoglobin levels and blood attenuation values in cardiovascular structures on non-contrast chest CT. Scatter plots show the correlation in the **A:** ascending aorta, **B:** aortic arch, **C:** descending thoracic aorta, **D:** left ventricle, and **E:** right ventricle. **F:** combined scatter plot of all five cardiovascular structures. A significant positive correlation between serum hemoglobin levels and blood attenuation values was observed in all structures (Spearman's ρ ranged from 0.697 to 0.817; $p < 0.001$), indicating a progressive decrease in blood attenuation directly related to decreasing hemoglobin levels.

CT: computed tomography.

Table 3. Comparison of blood attenuation values between control patients without anemia and anemia cases according to severity^a in cardiovascular structures using non-contrast chest CT

Cardiovascular structure	No anemia control patients (n = 44)	Cases		
		Mild anemia (n = 7)	Moderate anemia (n = 16)	Severe anemia (n = 21)
Ascending aorta, HU, mean $\pm$ SD	42.9 $\pm$ 4.7	40.7 $\pm$ 2.9	30.8 $\pm$ 6.4	24.7 $\pm$ 6.6
Aortic arch, HU, mean $\pm$ SD	42.8 $\pm$ 6.9	37.7 $\pm$ 1.3	28.2 $\pm$ 6.8	25.4 $\pm$ 8.0
Descending aorta, HU, mean $\pm$ SD	42.5 $\pm$ 10.2	35.6 $\pm$ 2.4	26.9 $\pm$ 7.9	25.7 $\pm$ 10.7
Left ventricle, HU, mean $\pm$ SD	42.5 $\pm$ 4.9	44.1 $\pm$ 1.3	32.3 $\pm$ 5.6	25.2 $\pm$ 9.8
Right ventricle, HU, mean $\pm$ SD	45.3 $\pm$ 4.1	42.1 $\pm$ 6.3	36.1 $\pm$ 5.5	29.0 $\pm$ 13.7

^aMild: women 11-11.9 g/dL, men 11-12.9 g/dL; moderate 8-10.9 g/dL; severe < 8 g/dL. The global comparisons were statistically significant ($p < 0.001$). CT: computed tomography; HU: Hounsfield units; SD: standard deviation.

aorta achieved a specificity of 93.2% and a positive predictive value of 91.9%. The positive likelihood ratio was highest for the ascending aorta ($LR+ = 11.3$), indicating excellent performance in detecting anemia with a cutoff value of ≤ 38.0 HU. The highest diagnostic accuracy was observed in the ascending aorta (85.2%) and the right ventricle (84.1%). These findings indicate that aortic structures, particularly the ascending aorta, offer the best balance among sensitivity, specificity, and overall diagnostic accuracy for detecting anemia on non-contrast chest CT.

Diagnostic performance of a blood attenuation value ≤ 38 HU in at least 3 of 5 cardiovascular structures on non-contrast chest CT in relation to anemia severity

Sensitivity increased progressively with anemia severity (Table 6). Sensitivity was 42.9% for mild anemia, 81.2% for moderate anemia, and 85.7% for severe anemia. Diagnostic accuracy increased from 68.0% in mild anemia to 87.2% and 89.4% in moderate and severe anemia, respectively. The evaluation of the five cardiovascular structures showed the best overall performance in cases of severe anemia. The ascending aorta had a sensitivity of 77.3%, a specificity and a PPV of 91.9%, with a diagnostic accuracy of 85.2%. The aortic arch and descending aorta had sensitivities of 81.8% and 86.4%, respectively, and specificities of 72.7% and 56.8%, respectively. Meanwhile, the right ventricle had a sensitivity of 68.2% and a specificity of 100%. Ventricular structures showed lower sensitivity than aortic structures; however, they maintained high specificity (77.5-100%) and a PPV (77.5%, and 100%).

Furthermore, diagnostic performance of at least three of five cardiovascular structures with blood attenuation values ≤ 38 HU showed the highest sensitivity (85.7%) and accuracy (89.4%) in severe anemia.

Figure 3 shows a non-contrast chest CT of a 34-year-old man without anemia (hemoglobin, 14.2 g/dL). Blood attenuation across the five cardiovascular structures ranged from 36.9 HU to 42.7 HU. Only one of the five structures showed an attenuation below the 38 HU cutoff. Therefore, this patient was correctly classified as non-anemic based on blood attenuation on non-contrast chest CT. Figure 4 shows a non-contrast chest CT of a 57-year-old woman with mild anemia (hemoglobin, 11.3 g/dL). Blood attenuation was below 38 HU in two of the five cardiovascular structures evaluated. Therefore, the patient was classified as non-anemic, indicating a false-negative result and illustrating the low sensitivity of non-contrast CT for detecting mild anemia.

Figure 5 shows a non-contrast chest CT in a 33-year-old woman with moderate anemia (hemoglobin, 9.3 g/dL). Blood attenuation ≤ 38 HU was found on non-contrast chest CT in all five cardiovascular structures. Therefore, the patient was correctly classified as anemic. Figure 6 shows a non-contrast chest CT in a 19-year-old woman with moderate anemia (hemoglobin, 8.1 g/dL). On non-contrast chest CT, blood attenuation ≤ 38 HU was observed in all five cardiovascular structures. The patient was correctly classified as anemic. Figure 7 shows a non-contrast chest CT in an 18-year-old man with severe anemia (hemoglobin, 6.5 g/dL). On non-contrast chest CT, blood attenuation ≤ 38 HU was observed in all five cardiovascular structures. The patient was correctly classified as anemic.

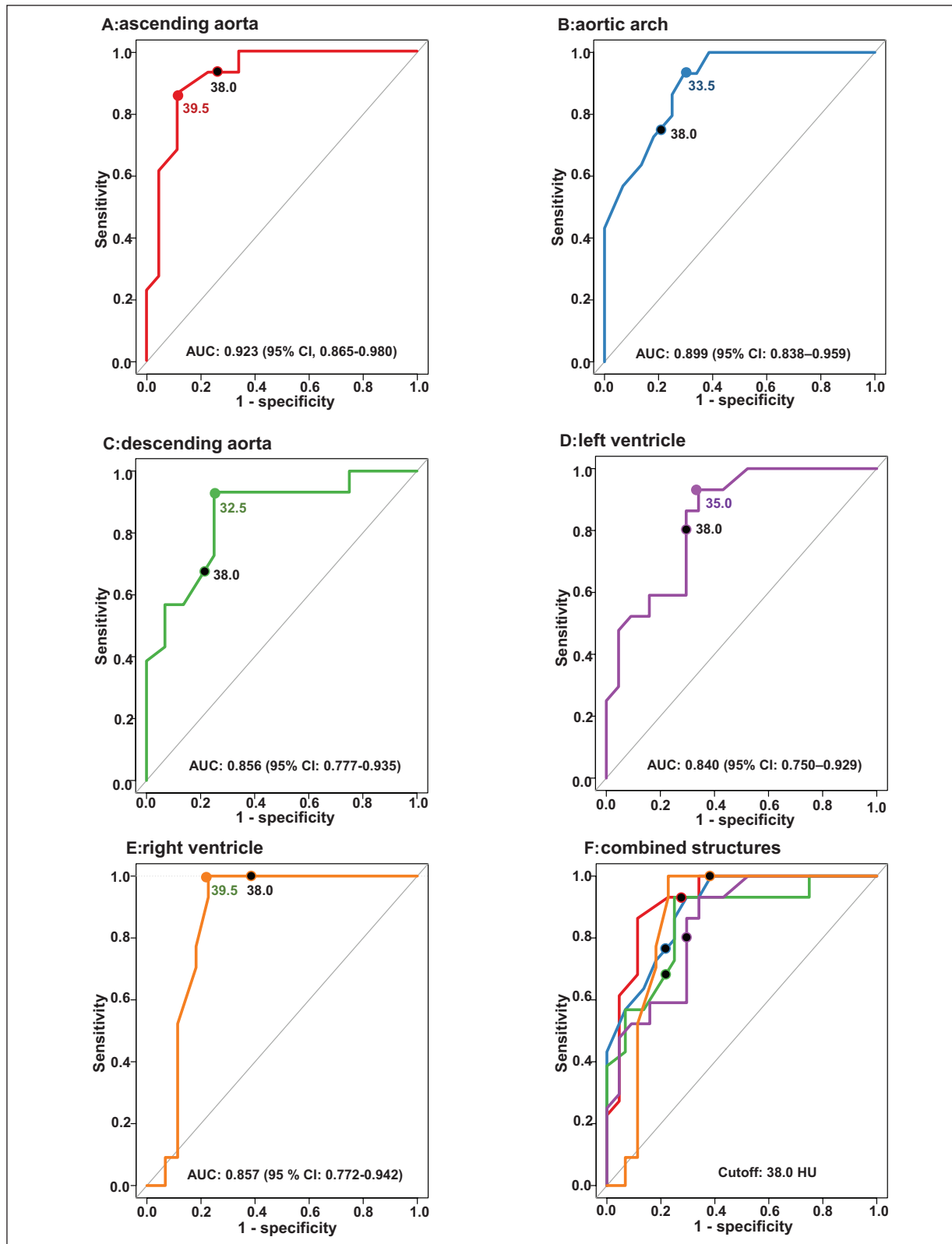


Figure 2. ROC curves showing the diagnostic performance of non-contrast chest CT for detecting anemia based on cutoff values for each cardiovascular structure and the combined optimal blood attenuation threshold of 38 HU in at least three of the five cardiovascular structures. The diagnostic performance of blood attenuation for anemia detection showed an AUC greater than 0.800 in all cardiovascular structures. AUC: area under the curve; CT: computed tomography; HU: Hounsfield units; ROC: receiver operating characteristic.

Table 4. Diagnostic performance of the comparison of different blood attenuation values in at least 3 of 5 cardiovascular structures for detecting anemia on non-contrast chest CT

HU value	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Accuracy % (95% CI)
≤ 30.0	56.8 (41.0-71.7)	100 (92.0-100)	100 (86.3-100)	69.8 (58.0-80.0)	78.4 (68.4-86.5)
≤ 32.0	70.5 (54.8-83.2)	100 (92.0-100)	100 (88.8-100)	77.2 (65.6-86.3)	85.2 (76.1-91.9)
≤ 34.0	70.5 (54.8-83.2)	93.2 (81.3-98.6)	91.2 (76.3-98.1)	75.9 (63.6-85.5)	81.8 (72.2-89.2)
≤ 36.0	70.5 (54.8-83.2)	93.2 (81.3-98.6)	91.2 (76.3-98.1)	75.9 (63.6-85.5)	81.8 (72.2-89.2)
≤ 38.0	77.3 (62.2-88.5)	93.2 (81.3-98.6)	91.9 (78.1-98.3)	80.4 (67.6-89.8)	85.2 (76.1-91.9)
≤ 40.0	81.8 (67.3-91.8)	68.2 (52.4-81.4)	72.0 (57.5-83.8)	78.9 (62.7-90.4)	75.0 (64.6-83.6)
≤ 42.0	95.5 (84.5-99.4)	47.7 (32.5-63.3)	64.6 (51.8-76.1)	91.3 (72.0-98.9)	71.6 (61.0-80.7)

CI: confidence interval; CT: computed tomography; HU: Hounsfield units; NPV: negative predictive value; PPV: positive predictive value.

Table 5. Diagnostic performance of blood attenuation ≤ 38 HU for detecting anemia^a according to cardiovascular structure on non-contrast chest CT

Cardiovascular structure	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	LR+ (95% CI)	LR- (95% CI)	Accuracy % (95% CI)
Ascending aorta	77.3 (62.2-88.5)	93.2 (81.3-98.6)	91.9 (79.0-97.1)	80.4 (70.3-87.7)	11.3 (3.8-34.2)	0.2 (0.1-0.4)	85.2 (76.1-91.9)
Aortic arch	81.8 (67.3-91.8)	72.7 (57.2-85.0)	75.0 (64.5-83.2)	80.0 (67.6-88.5)	3.0 (1.8-5.0)	0.2 (0.1-0.5)	77.3 (67.1-85.5)
Descending aorta	86.4 (72.6-94.8)	56.8 (41.0-71.6)	66.7 (58.2-74.1)	80.6 (65.5-90.1)	2.0 (1.4-2.9)	0.2 (0.1-0.5)	71.6 (61.0-80.7)
Left ventricle	70.4 (54.8-83.2)	79.5 (64.7-90.2)	77.5 (65.1-86.4)	72.9 (62.5-81.3)	3.4 (1.9-6.4)	0.4 (0.2-0.6)	75.0 (64.6-83.6)
Right ventricle	68.2 (52.4-81.4)	100 (92.0-100)	100 (88.4-100)	75.9 (67.1-82.9)	NE	0.3 (0.2-0.5)	84.1 (75.7-91.0)

^aPatients were classified as anemic according to sex-specific hemoglobin thresholds: women ≤ 11.9 g/dL, men ≤ 12.9 g/dL. CI: confidence interval; CT: computed tomography; LR-: negative likelihood ratio; LR+: positive likelihood ratio; NE: not estimable (could not be estimated because specificity was 100%), resulting in the absence of false-positive results. NPV: negative predictive value; PPV: positive predictive value.

DISCUSSION

This study showed that blood attenuation ≤ 38 HU in at least three of five cardiovascular structures (ascending aorta, aortic arch, descending thoracic aorta, left ventricle, or right ventricle) on non-contrast chest CT has high diagnostic performance for detecting anemia in adult patients. Combined evaluation of several cardiovascular structures on non-contrast chest CT, performed for any medical indication, detects incidental anemia without additional scans, contrast administration, or increased radiation dose.

Available evidence indicates that CT diagnostic performance in detecting anemia varies with the cardiovascular structure analyzed. Furthermore, several authors have proposed assessing multiple structures or combining blood attenuation values with qualitative criteria to

improve diagnostic performance when measuring a single anatomical structure^{5,9,13,14,16,18}. Damodaran Kumar et al.¹⁶, in a prospective cross-sectional study of 225 patients in India, assessed blood attenuation in the aortic arch, ascending aorta, descending aorta, and main pulmonary artery on non-contrast chest CT. A blood attenuation cutoff < 37 HU in the aortic arch showed the highest diagnostic performance for detecting anemia (AUC = 0.953, sensitivity 84.8% and specificity 90.0%). The authors concluded that measuring blood attenuation across multiple structures on non-contrast chest CT is a reliable, noninvasive method for detecting anemia and estimating its severity. Abbasi et al.¹⁴, in a retrospective cohort of 325 Iranian patients, analyzed seven cardiovascular structures – ascending aorta, aortic arch, descending thoracic aorta, main pulmonary artery, inferior vena cava, and the right and left

Table 6. Diagnostic performance of blood attenuation ≤ 38 HU in at least 3 of 5 cardiovascular structures according to anemia severity on non-contrast chest CT

Description	Sensitivity, % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	LR+ (95% CI)	LR- (95% CI)	Accuracy % (95% CI)
Anemia (all severities)	77.3 (62.2-88.5)	93.2 (81.3-98.6)	91.9 (79.0-97.2)	80.4 (70.3-87.7)	11.3 (3.8-34.2)	0.2 (0.1-0.4)	85.2 (76.1-91.9)
Mild anemia	42.9 (9.9-81.6)	93.2 (81.3-98.6)	86.3 (61.1-96.2)	62.0 (46.1-75.7)	6.3 (1.6-25.2)	0.6 (0.3-1.2)	68.0 (53.5-80.4)
Moderate anemia	81.2 (54.3-95.9)	93.2 (81.3-98.6)	92.3 (79.6-97.3)	83.2 (64.1-93.2)	11.9 (3.9-36.4)	0.2 (0.1-0.6)	87.2 (76.1-94.4)
Severe anemia	85.7 (63.7-96.9)	93.2 (81.3-98.6)	92.6 (80.6-97.4)	86.7 (69.5-94.9)	12.6 (4.2-38.0)	0.15 (0.05-0.4)	89.4 (79.3-95.7)

^aMild: women, 11-11.9 g/dL, men, 11-12.9 g/dL. Moderate: 8-10.9 g/dL. Severe < 8 g/dL. CI: confidence interval; CT: computed tomography; LR-: negative likelihood ratio; LR+: positive likelihood ratio; NPV: negative predictive value; PPV: positive predictive value.

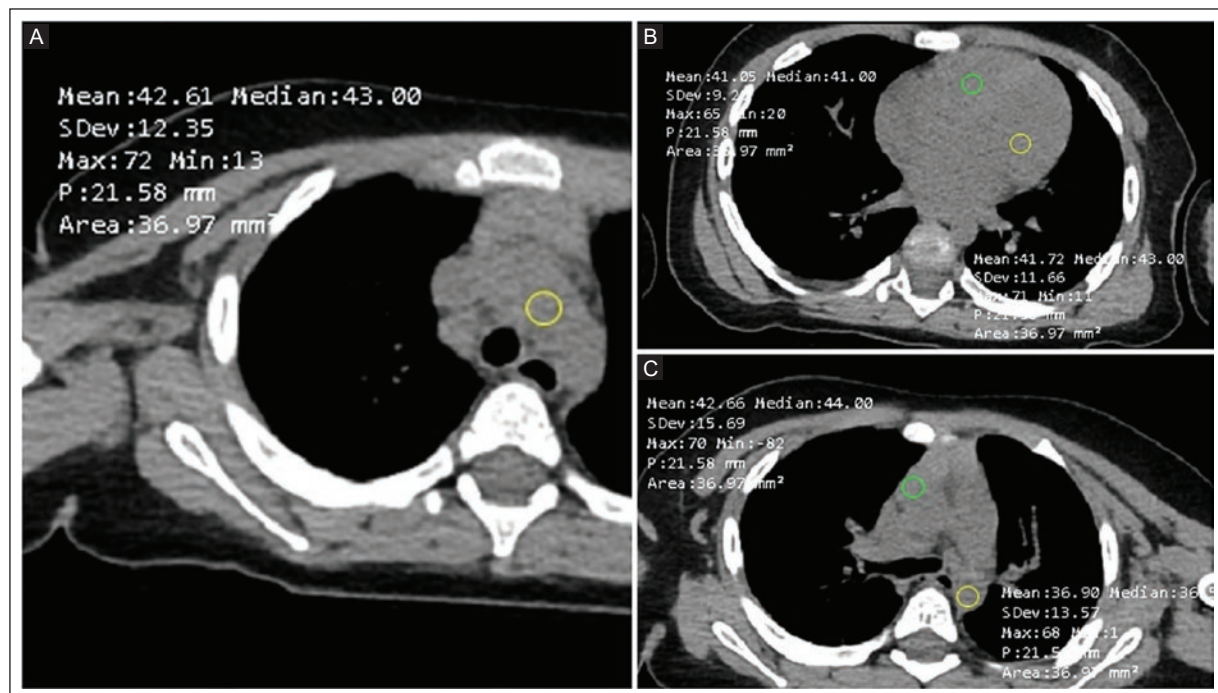


Figure 3. Non-contrast chest CT in a 34-year-old man without anemia (hemoglobin, 14.2 g/dL). **A:** axial view with an ROI (yellow circle) placed centrally within the lumen of the aortic arch, avoiding the vessel wall. The mean blood attenuation was 42.6 HU. **B:** axial view with ROIs placed centrally within the blood pool of the right ventricle (green circle), showing a mean attenuation of 41.0 HU, and in the left ventricle (yellow circle), with a mean attenuation of 41.7 HU. Care was taken to avoid including the papillary muscles, trabeculations, and the ventricular wall. **C:** axial view with an ROI placed in the ascending aorta (green circle) showing a mean attenuation of 42.7 HU, and a second ROI in the descending aorta (yellow circle) with a mean attenuation of 36.9 HU. Both ROIs were placed centrally within the vascular lumen avoiding the aortic wall. Blood attenuation values across the five cardiovascular structures ranged from 36.9 HU to 42.7 HU. Only one of the five structures showed an attenuation value below the 38 HU cutoff. Therefore, this patient was correctly classified as non-anemic based on the blood attenuation values on non-contrast chest CT.

CT: computed tomography; HU: Hounsfield units; ROI: region of interest.

ventricles – using non-contrast chest CT. Combined blood attenuation measurements in various cardiovascular structures provided a reliable method for detecting anemia using non-contrast chest CT. Ayvat Öcal et al.¹⁸ evaluated three cardiovascular structures – ascending

aorta, descending aorta, and the left ventricle – with non-contrast chest CT in a retrospective study of 150 Turkish patients. Using ROC analysis, they identified blood attenuation cutoff values of ≤ 37 HU for the ascending aorta, ≤ 33 HU for the descending aorta, and

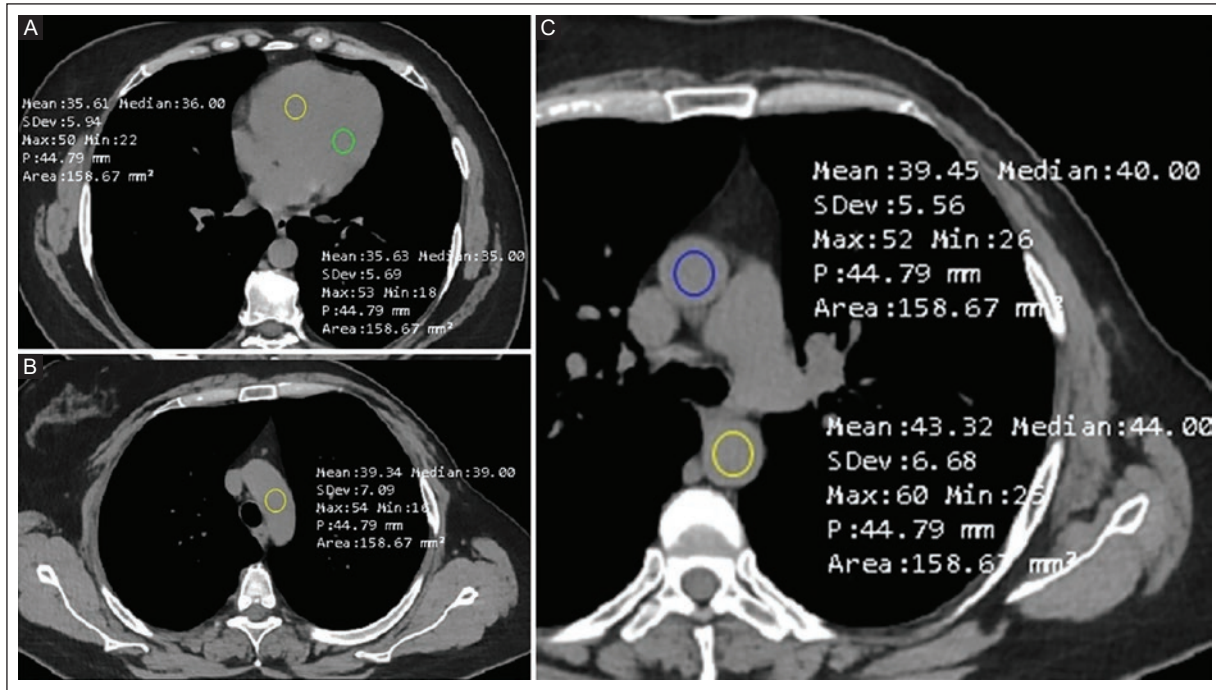


Figure 4. Non-contrast chest CT in a 57-year-old woman with mild anemia (hemoglobin 11.3 g/dL). **A:** axial view with ROIs placed centrally within the blood pool of the left ventricle (yellow circle), showing a mean blood attenuation of 35.6 HU, and the right ventricle (green circle), with a mean attenuation of 35.6 HU. Care was taken to avoid the ventricular wall, papillary muscles, and trabeculations. **B:** axial view with an ROI placed centrally within the lumen of the aortic arch (yellow circle), avoiding the vessel wall. The measured mean blood attenuation was 39.3 HU. **C:** axial view with an ROI placed in the ascending aorta (blue circle) showing a mean blood attenuation of 39.4 HU, and a second ROI placed in the descending aorta (yellow circle) with a mean attenuation of 43.3 HU. Both measurements are from the central vascular lumen avoiding the aortic wall and image artifacts. Blood attenuation values were below the 38 HU cutoff in two of five evaluated cardiovascular structures. Therefore, this patient was classified as non-anemic, despite mild anemia representing a false-negative result. This case demonstrates the low sensitivity of non-contrast CT for detecting mild anemia.

CT: computed tomography; HU: Hounsfield units; ROI: region of interest.

≤ 38 HU for the left ventricle. Combining two or more positive tomographic criteria (aortic ring sign, hyperdense interventricular septum sign, or blood attenuation ≤ 38 HU in the left ventricle) improved diagnostic performance for identifying patients with a hemoglobin < 10 g/dL, with a sensitivity of 81.1%, a specificity of 85.8%, and an accuracy of 84.6%. Our study demonstrated that combining blood attenuation values ≤ 38 HU in three or more cardiovascular structures improved diagnostic performance for identifying anemia, with a sensitivity of 77.3%, a specificity of 93.2%, and an accuracy of 85.2%. Differences in blood attenuation cutoffs reported in other studies likely reflect differences in the populations analyzed, the structures evaluated, and the criteria used to define anemia. Despite variations in specific cutoffs, the studies agree that no single cardiovascular structure consistently provides the best diagnostic performance for detecting anemia on non-contrast chest CT. Our main contribution is the combined assessment of at least three of five cardiovascular structures with blood attenuation values

≤ 38 HU for detecting anemia, which yields high specificity and good accuracy. This suggests that combining multiple measurements provides a more robust evaluation than relying on a single measurement in one cardiovascular structure.

Blood attenuation on non-contrast chest CT has shown a positive correlation with serum hemoglobin^{5,9,10,11}. This association has been demonstrated in different populations by evaluating various cardiovascular structures, including the thoracic aorta, ventricular cavities, interventricular septum, and great vessels^{9,11,14}. In our study, positive correlations were found in all five cardiovascular structures ($\rho = 0.697$ - 0.817 ; $p < 0.001$), with the ascending aorta showing the strongest association with serum hemoglobin ($\rho = 0.817$). Our findings confirm that blood attenuation on non-contrast CT is a reliable quantitative biomarker of serum hemoglobin. The consistency of this association across all evaluated cardiovascular structures establishes blood attenuation as a tool for detecting anemia during routine chest CT interpretation.

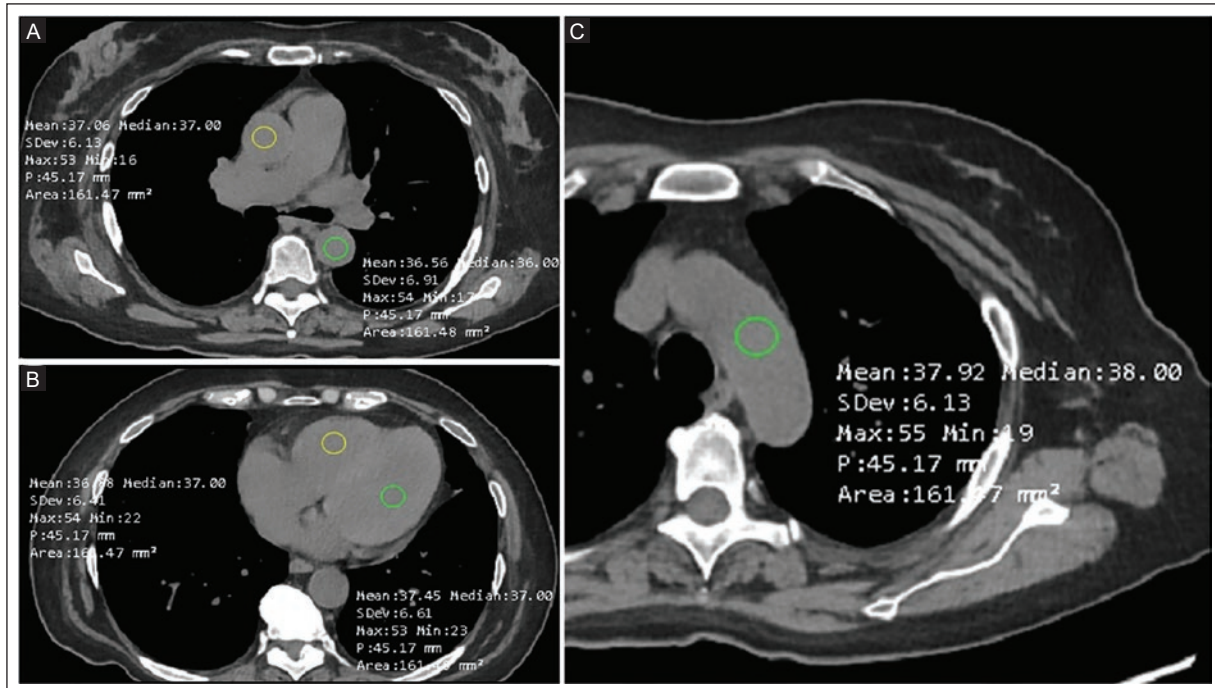


Figure 5. Non-contrast chest CT in a 33-year-old woman with moderate anemia (hemoglobin 9.3 g/dL). **A:** axial view with ROIs placed centrally within the lumen of the ascending aorta (yellow circle), showing a mean blood attenuation of 37.0 HU, and the descending aorta (green circle), with a mean attenuation of 36.5 HU. Both ROIs were carefully placed to avoid the aortic wall. **B:** axial view with ROIs placed centrally within the blood pool of the right ventricle (yellow circle), showing a mean blood attenuation of 36.9 HU, and in the left ventricle (green circle) with a mean attenuation of 37.4 HU. Care was taken to avoid the ventricular wall, papillary muscles, trabeculations, and image artifacts. **C:** axial view with an ROI (green circle) placed centrally within the lumen of the aortic arch, avoiding the vessel wall. The measured mean blood attenuation was 37.9 HU. Blood attenuation values ≤ 38 HU were found on non-contrast chest CT in all five cardiovascular structures. Therefore, the patient was correctly classified as anemic.

CT: computed tomography; HU: Hounsfield units; ROI: region of interest.

Anemia severity has been linked to the diagnostic performance of non-contrast chest CT for detecting anemia^{5,10,13,14,18}. Damodaran Kumar et al.¹⁶ estimated anemia severity based on blood attenuation in multiple structures on non-contrast chest CT. In a retrospective single-center study of 522 German patients, Zopfs et al.¹³ evaluated contrast-enhanced spectral chest CT examinations from which virtual non-contrast reconstructions were obtained. Blood attenuation values from three ROIs, two in the left ventricle and one in the descending aorta, were compared with the serum hemoglobin level. A cutoff of 33.6 HU for men and 32.7 HU for women detected severe anemia with sensitivities of 78% and 100%, and specificities of 87% and 79%, respectively. The authors concluded that contrast-free virtual reconstructions allow reliable estimation of serum hemoglobin levels and anemia detection, with diagnostic performance directly correlating with increasing anemia severity. In our study, blood attenuation values progressively decreased with increasing severity of serum hemoglobin reduction. Severe anemia had significantly lower blood

attenuation values (range 24.7 HU to 29.0 HU) than mild (range 40.7 HU to 44.1 HU) or moderate anemia (range 26.9 HU to 36.1 HU) in the five cardiovascular structures ($p < 0.001$). Furthermore, diagnostic performance using at least three of five cardiovascular structures with blood attenuation values ≤ 38 HU showed the highest sensitivity (85.7%) and accuracy (89.4%) in cases of severe anemia. These findings support the biological plausibility of blood attenuation as an indirect marker of serum hemoglobin concentration and explain how the diagnostic performance of non-contrast chest CT increases as anemia severity increases.

This study has several strengths. First, it simultaneously evaluated five cardiovascular structures using a standardized measurement protocol. From a clinical standpoint, this criterion does not require additional scans, contrast administration, or additional radiation exposure, as it uses information obtained from non-contrast chest CT scans performed for any indication. Measuring the five regions of interest adds about five minutes to routine interpretation time; this increase

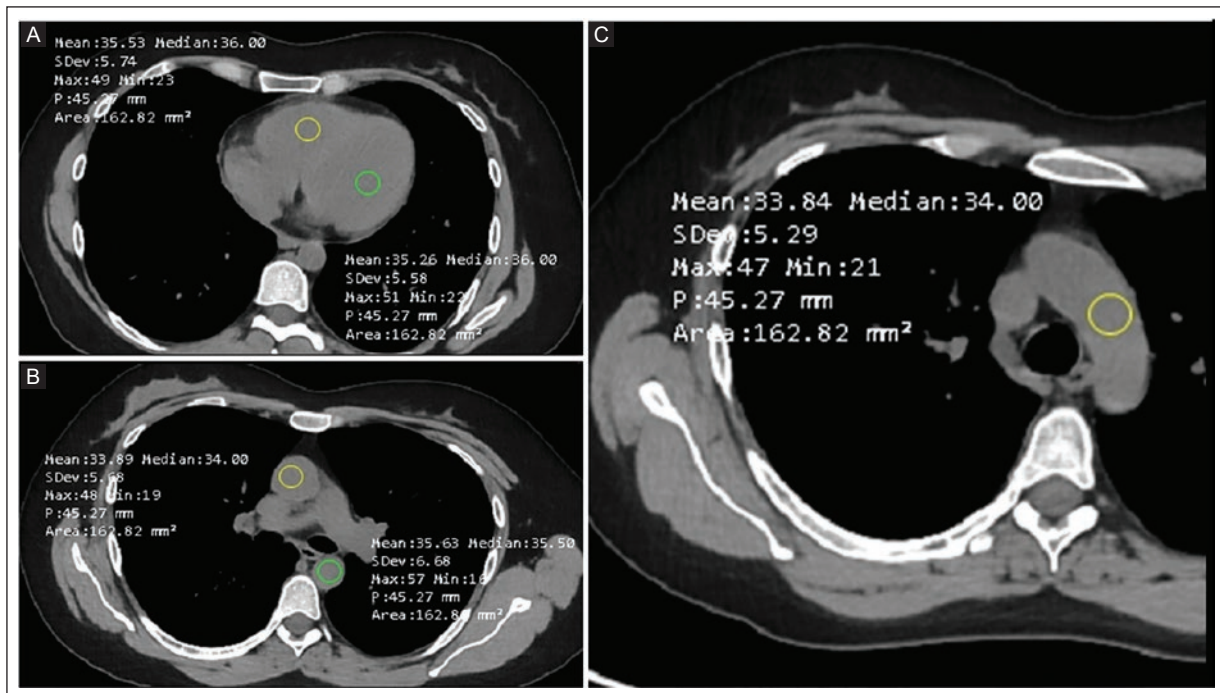


Figure 6. Non-contrast chest CT in a 19-year-old woman with moderate anemia (hemoglobin 8.1 g/dL). **A:** axial view with ROIs placed centrally within the blood pool of the right ventricle (yellow circle), showing a mean blood attenuation of 35.5 HU, and the left ventricle (green circle), with a mean attenuation of 35.3 HU. The ROIs were carefully placed to avoid the ventricular wall, papillary muscles, and trabeculations. **B:** axial view with ROIs placed centrally within the lumen of the ascending aorta (yellow circle), showing a mean blood attenuation of 33.8 HU, and the descending aorta (green circle), with a mean attenuation of 35.6 HU. Both measurements avoided the aortic wall. **C:** axial view with an ROI (yellow circle) placed centrally within the lumen of the aortic arch, avoiding the vessel wall. The measured mean blood attenuation was 33.8 HU. Blood attenuation values ≤ 38 HU were found on non-contrast chest CT in all five cardiovascular structures. The patient was correctly classified as anemic.

CT: computed tomography; HU: Hounsfield units; ROI: region of interest.

could be offset by the potential to incidentally identify patients with anemia, enabling timelier and more comprehensive clinical evaluation. This study has several limitations. Its retrospective design and a single-center cohort limit the generalizability of the results. The sample size was small, particularly in the mild anemia subgroup. Interobserver agreement of the blood attenuation measurements was not assessed. These measurements require external validation in larger, multicenter populations with different clinical characteristics before routine implementation can be recommended.

CONCLUSION

Blood attenuation values ≤ 38 HU on non-contrast chest CT in at least three of five cardiovascular structures – the ascending aorta, aortic arch, descending aorta, and the left and right ventricles – showed high specificity and good overall diagnostic performance for detecting anemia in adult patients. Prospective, multicenter studies with larger cohorts are needed to

validate the proposed blood attenuation cutoff, evaluate interobserver agreement, and determine its impact on incidental detection of anemia and clinical decision-making in different clinical settings.

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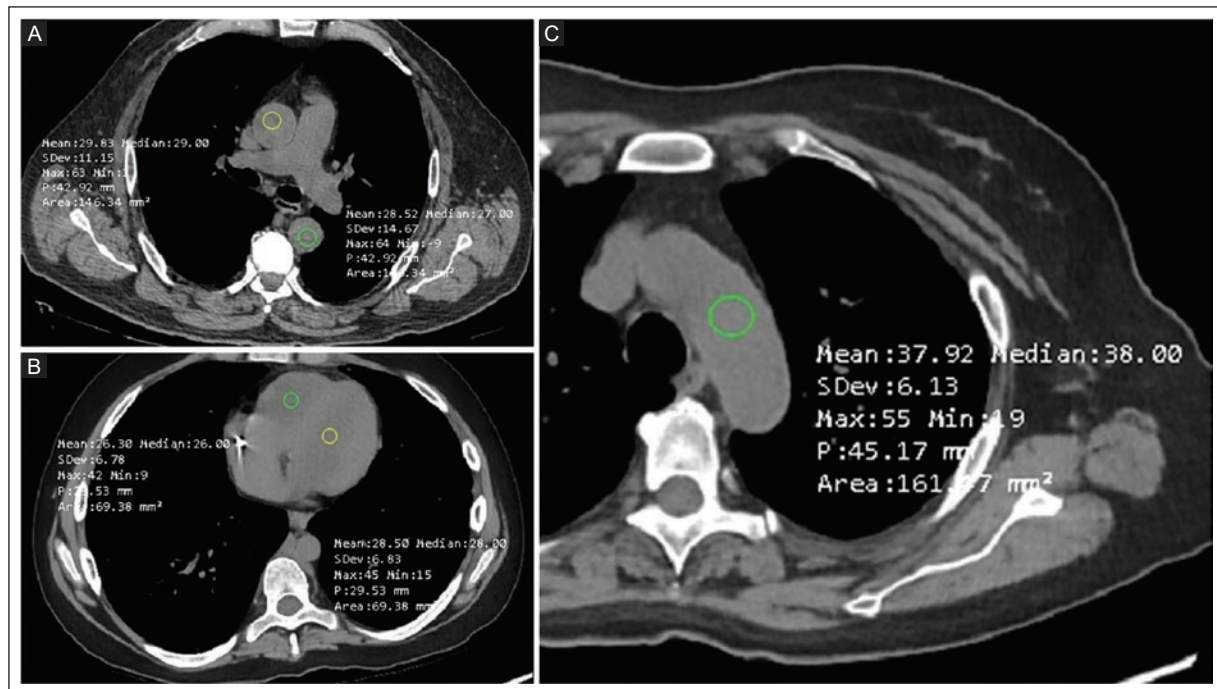


Figure 7. Non-contrast chest CT in an 18-year-old man with severe anemia (hemoglobin, 6.5 g/dL). **A:** axial view with ROIs placed centrally within the lumen of the ascending aorta (yellow circle), showing a mean blood attenuation of 29.8 HU, and the descending aorta (green circle), with a mean attenuation of 28.5 HU. Both ROIs were carefully placed within the vascular lumen avoiding the aortic wall. **B:** axial view with ROIs placed centrally within the blood pool of the right ventricle (green circle), showing a mean blood attenuation of 26.3 HU, and the left ventricle (yellow circle), with a mean attenuation of 28.5 HU. Care was taken to avoid the ventricular wall, papillary muscles, and trabeculations. **C:** axial view with an ROI (yellow circle) placed centrally within the lumen of the aortic arch, avoiding the vessel wall. The measured mean blood attenuation was 37.9 HU. Blood attenuation values ≤ 38 HU were found on non-contrast chest CT in all five cardiovascular structures. The patient was correctly classified as anemic.

CT: computed tomography; HU: Hounsfield units; ROI: region of interest.

Conflict of Interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the World Medical Association and the Declaration of Helsinki (1964) and subsequent amendments.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely collected and anonymized clinical data; therefore, individual informed consent was not required. Relevant ethical recommendations have been followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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MRI findings and clinical manifestations in adult Mexican patients with myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD)

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ABSTRACT

Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an inflammatory demyelinating disorder of the central nervous system. The clinical and imaging characteristics of MOGAD in the Mexican population remain unknown. This study describes the clinical manifestations and magnetic resonance imaging (MRI) findings of the brain, optic nerve, and spinal cord in adult Mexican patients with MOGAD. **Material and methods:** This cross-sectional study included adult patients with suspected MOGAD who were evaluated at a national Mexican referral center. Demographic data, clinical manifestations, anti-MOG antibody status, and MRI findings of the brain, optic nerve, and spinal cord were reviewed. Descriptive statistics were calculated. **Results:** Twenty patients with MOGAD were included. All patients had a positive anti-MOG antibody. Decreased visual acuity and pain with eye movements were the most common clinical manifestations, occurring in 15 (75.0%) patients, while optic nerve abnormalities on MRI were identified in 16 (80.0%) patients. The predominant MRI findings were longitudinally extensive T2 hyperintensity involving the anterior or intraorbital optic nerve in 15 (75.0%) patients, bilateral involvement in 10 (50.0%) patients, and perineural enhancement in 6 (30.0%) patients. Brain lesions were observed in 5 (25.0%) of 20 patients, predominantly presenting as fluffy cortical and infratentorial T2/FLAIR hyperintensities. Spinal cord lesions were identified in 4 (20.0%) patients, mainly as short-segment cervical and thoracic lesions, with conus medullaris involvement in 2 (10.0%) patients. **Conclusion:** In patients with MOGAD, optic neuritis was the predominant clinical and imaging phenotype. Brain and spinal cord involvement was less frequent and exhibited characteristic MRI patterns. These findings represent the first description of the clinical and MRI features of MOGAD in a Mexican cohort and support the recognition of characteristic imaging patterns.

Keywords: Central nervous system diseases. Demyelinating diseases. Magnetic resonance imaging. Myelin oligodendrocyte glycoprotein. Optic neuritis.

INTRODUCTION

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an inflammatory demyelinating disorder of the central nervous system. It is recognized as a distinct clinical entity separate from multiple sclerosis (MS) and aquaporin-4 antibody-associated neuromyelitis optica spectrum disorder

(AQP4-IgG NMOSD)¹. MOGAD most commonly presents with optic neuritis, myelitis, acute disseminated encephalomyelitis (ADEM), cortical encephalitis, and brainstem and cerebellar syndromes². The diagnosis of MOGAD has been enabled by the detection of anti-MOG antibodies and by clinical phenotype criteria, and characteristic clinical and imaging findings².

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Magnetic resonance imaging (MRI) is critical for characterizing and diagnosing MOGAD. The 2023 International MOGAD Diagnostic Criteria are based on characteristic imaging patterns². These findings include longitudinally extensive, bilateral, or enhancing optic neuritis; poorly defined hyperintense brain lesions on T2/FLAIR with cortical or infratentorial predominance; and myelitis with longitudinally extensive lesions, conus medullaris involvement, or predominant gray-matter involvement, as represented by the “H” sign.

Optic neuritis is the most common clinical and imaging manifestation of MOGAD, whereas involvement of the brain and spinal cord is heterogeneous and less common, with distinctive imaging patterns that differentiate this disease from other demyelinating disorders^{3,4}. Evidence regarding the clinical and imaging features of MOGAD in the Latin American population is limited¹. This study describes the clinical features and MRI findings of the brain, optic nerve, and spinal cord in Mexican adult patients with MOGAD.

MATERIAL AND METHODS

This cross-sectional study was conducted from January 2016 to December 2024 at the Departamento de Neuroimagen, Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suarez, in Mexico City, Mexico. Patients with at least one central demyelinating clinical event, such as optic neuritis, transverse myelitis, acute disseminated encephalomyelitis, brainstem or cerebellar syndromes, and/or cerebral cortical encephalitis, and with an anti-MOG test result were included. Patients with a diagnosis of demyelinating disease other than MOGAD, without an anti-MOG test, or with incomplete MRI studies were excluded. Informed consent was not required to analyze and publish data collected during routine medical care. The institutional research and ethics committee approved the study.

Study development and variables

Demographic and clinical data were obtained from the electronic health record. These included age, sex, anti-MOG result, history of COVID-19 vaccination, recent infectious prodrome, initial clinical presentation, specific neurological symptoms, and clinical course at the initial hospital evaluation. A recent infectious or vaccination history was defined as systemic symptoms suggestive of infection or receipt of vaccination within 30 days before the onset of the demyelinating clinical

event; starting in 2021, prior COVID-19 vaccination was recorded.

At the initial hospital evaluation, the clinical course was classified as relapsing if one or more suggestive demyelinating events occurred before the first visit, or as monophasic if no prior events were documented.

Anti-MOG antibodies were determined using the commercial anti-MOG IIFT kit (Euroimmun, Lübeck, Germany). This assay detects IgG antibodies to oligodendrocyte myelin glycoprotein using MOG-transfected EU90 cells and non-transfected control cells. Serum or plasma samples were evaluated by fluorescence microscopy. Qualitative assessment was reported as follows: a negative result, with no reaction at 1:10, was interpreted as no antibodies to MOG in the serum/plasma sample. A positive reaction at 1:10 was indicative of MOGAD⁵.

Definition

MOGAD is a disease associated with antibodies to myelin oligodendrocyte glycoprotein. It is an inflammatory disorder characterized by immune-mediated demyelinating attacks of the CNS that affect the brain, optic nerve, and spinal cord, and is associated with a positive MOG-IgG test. Criteria A, B, and C proposed by the International MOGAD Panel must be met to establish the diagnosis²: (A) a major demyelinating clinical event: optic neuritis, myelitis, ADEM, monofocal or polyfocal brain deficits, brainstem or cerebellar deficits, or cerebral cortical encephalitis, frequently with seizures; (B) a positive MOG-IgG test. Clinical or MRI abnormalities supporting the diagnosis of MOGAD, such as optic neuritis, myelitis, brain, brainstem, or cerebral syndrome; and (C) exclusion of other diagnoses.

Image acquisition and analysis protocol

MRI of the brain, orbits, and spine was performed using a SIGNA™ Explorer 1.5T (GE HealthCare, Chicago, IL, USA) or a MAGNETOM Skyra 3.0T (Siemens Medical Solutions, Erlangen, Germany). Structural MRI with SWI (susceptibility-weighted imaging)/SWAN (susceptibility-weighted angiography) was performed in all patients.

The brain MRI protocol included T1-weighted images with contrast, T2, FLAIR (fluid-attenuated inversion recovery), SWI, and DWI (diffusion-weighted imaging). Orbital MRI included contrast-enhanced and fat-suppressed sequences. Spinal MRI included T2 and STIR (short tau inversion recovery) sequences.

Table 1. Clinical characteristics of adult Mexican patients with MOGAD at initial consultation

#	Sex	Age, years	Vertigo syndrome	Epilepsy	Headache	Ataxia	Area postrema syndrome	Decreased visual acuity and eye pain	Pyramidal syndrome	LL weakness	Urinary incontinence
1	F	33	Absent	Absent	Absent	Absent	Absent	Present	Absent	Absent	Absent
2	F	19	Absent	Absent	Absent	Absent	Absent	Present	Absent	Absent	Absent
3	M	53	Absent	Absent	Absent	Absent	Absent	Present	Absent	Absent	Absent
4	F	39	Absent	Absent	Absent	Absent	Absent	Present	Absent	Absent	Absent
5	F	65	Absent	Absent	Absent	Absent	Absent	Present	Absent	Absent	Absent
6	F	42	Absent	Absent	Absent	Absent	Absent	Present	Absent	Absent	Absent
7	F	51	Absent	Absent	Absent	Absent	Absent	Present	Absent	Absent	Absent
8	F	25	Absent	Absent	Absent	Absent	Present	Present	Absent	Present	Absent
9	F	26	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Present	Present
10	M	26	Absent	Absent	Absent	Absent	Absent	Present	Absent	Absent	Absent
11	M	19	Absent	Present	Absent	Absent	Absent	Present	Absent	Absent	Absent
12	M	44	Absent	Absent	Present	Absent	Absent	Present	Absent	Absent	Absent
13	M	43	Absent	Absent	Absent	Absent	Absent	Present	Absent	Absent	Absent
14	M	41	Absent	Absent	Absent	Absent	Absent	Present	Absent	Absent	Absent
15	F	26	Present	Absent	Absent	Absent	Absent	Present	Present	Absent	Absent
16	F	43	Present	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
17	F	21	Present	Present	Absent	Present	Absent	Absent	Absent	Absent	Absent
18	M	33	Absent	Absent	Present	Present	Absent	Absent	Present	Absent	Absent
19	F	45	Absent	Absent	Absent	Absent	Absent	Present	Absent	Absent	Absent
20	F	48	Absent	Absent	Absent	Absent	Absent	Present	Absent	Absent	Absent

F: female; M: male; LL: lower limbs; MOGAD: myelin oligodendrocyte glycoprotein antibody-associated disease.

MRIs performed within 30 days of symptom onset were analyzed⁶. MRI findings were grouped into three anatomical sites (brain, optic nerve, and spinal cord) according to criteria proposed by the International MOGAD Panel². MRIs were evaluated by a neuroradiologist (RRS) with 4 years of experience.

Statistical analysis

Numerical variables are summarized using measures of central tendency and dispersion (standard deviation). Categorical variables are presented as absolute frequencies and percentages. Excel software (Microsoft Corp., Seattle, WA, USA) was used for the analysis.

RESULTS

Thirty-eight patients with clinical suspicion of MOGAD were evaluated. Twenty were anti-MOG antibody-positive: 13 (65.0%) women and 7 (35.0%) men, with a mean age of 37.1 ± 12.6 years. Two patients (10.0%) had a history of COVID-19 vaccination, and

3 (15.0%) had an infectious prodrome. At initial evaluation, 13 patients (65.0%) had a monophasic course, and 7 (35.0%) had a relapsing course.

Clinical characteristics at initial consultation in patients with MOGAD

The most common reasons for initial consultation were decreased visual acuity and pain with ocular movement (Table 1). Epilepsy, headache, lower-limb weakness, and pyramidal syndrome were less common.

Table 2 shows the frequency of clinical characteristics at initial consultation by anatomical distribution. Brain involvement presented as vertiginous syndrome in three patients (15.0%), followed by epilepsy, headache, or ataxia in two patients (10.0%). In patients with optic nerve involvement, decreased visual acuity and pain with ocular movement were observed in 15 patients (75.0%). In the spinal cord, lower-limb weakness or pyramidal syndrome was reported in 2 patients (10.0%), and urinary incontinence in 1 patient (5.0%).

Table 2. Frequency of clinical characteristics at the initial consultation in adult Mexican patients with MOGAD

Description	n (%)
Brain involvement	
Vertigo syndrome	3 (15.0)
Epilepsy	2 (10.0)
Headache	2 (10.0)
Ataxia	2 (10.0)
Area postrema syndrome	1 (5.0)
Optic nerve involvement	
Decreased visual acuity and eye pain	15 (75.0)
Spinal cord involvement	
Pyramidal syndrome	2 (10.0)
LL weakness	2 (10.0)
Urinary incontinence	1 (5.0)

LL: lower limb; MOGAD: myelin oligodendrocyte glycoprotein antibody-associated disease; MRI: magnetic resonance imaging.

MRI findings involving the brain, optic nerve, and/or spinal cord in patients with MOGAD

MRI showed abnormalities in 19 (95.0%) of 20 patients with MOGAD (Table 3). In the brain, poorly defined, swollen hyperintensities were found in both supratentorial and infratentorial white matter, with some extending into the cortex. Long-segment, bilateral hyperintensities of the anterior portion of the optic nerve predominated. In the spinal cord, the most common finding was short-segment hyperintensity, mainly in the cervical and thoracic segments, with involvement of the conus medullaris.

Table 4 shows the frequency of MRI findings involving the brain, optic nerve, and/or spinal cord in adult patients with MOGAD. Brain involvement was observed in 5 (25.0%) patients. The most common features were fluffy, ill-defined, large hyperintense cortical lesions involving the midbrain, cerebellum, and middle cerebellar peduncles. Parenchymal and meningeal enhancement were observed in 3 (15.0%) and 2 (10.0%) patients, respectively. The optic nerve was the most frequently affected site, with involvement in 16 (80.0%) of 20 patients with MOGAD. Longitudinally extensive hyperintensity and hyperintensity of the anterior segment of the optic nerve were observed in 15 (75.0%) patients. Only 2 (10.0%) cases showed optic disc protrusion. Bilateral optic nerve involvement was observed in 10 (50.0%) patients, and perineural enhancement in 6 (30.0%) cases. Spinal cord lesions were identified

in 4 (20.0%) patients, with short-segment hyperintensity, especially at the cervical and thoracic segments, as the most common pattern. Only 2 (10.0%) patients had hyperintensity in the conus medullaris, and none had the “H” sign.

Some patients had hyperintense lesions in more than one anatomical site: the brain and optic nerve were involved in 2 (10.0%) patients; 3 (15.0%) patients had optic nerve and spinal cord involvement; brain and spinal cord involvement occurred in 2 (10.0%) patients; and 1 (5.0%) patient had involvement of all three target anatomical sites (brain, optic nerve, and spinal cord).

Figures 1, 2, and 3 show representative findings from case 15, including fluffy supra- and infratentorial brain lesions, cortical involvement, variable enhancement patterns, extensive optic nerve involvement, and short-segment hyperintensities in the cervicothoracic spinal cord. Figure 4 corresponds to case 17 and shows cortical hyperintensity with nodular enhancement and infratentorial fluffy lesions with multiple nodular enhancements.

DISCUSSION

In our study, optic neuritis was the most common clinical and imaging abnormality in adult patients with MOGAD, characterized primarily by longitudinally extensive, bilateral involvement with perineural enhancement and optic nerve edema. In contrast, brain and spinal cord abnormalities were less frequent. This is the first study of Mexican patients that systematically characterizes MRI findings in adults with MOGAD. Our results expand knowledge of the disease's imaging spectrum in Latin America and confirm the usefulness of MRI in recognizing characteristic patterns.

Optic neuritis is the most common and characteristic clinical phenotype of MOGAD^{3,4,7,8}. MRI findings have been incorporated into the international diagnostic criteria for MOGAD². Ramanathan et al.⁹ evaluated 50 patients with a clinical episode of optic neuritis; 19 were positive for anti-MOG antibodies. MRI showed bilateral optic neuritis in 16 (84%) of 19 patients with MOGAD, with longitudinally extensive hyperintensity in 18 (95%). The intraorbital segment was the most commonly affected (n = 10, 53%), and optic nerve head edema was observed in 17 (89%). Pestchanker et al.¹ retrospectively evaluated a cohort of 144 patients from Latin American countries that did not include Mexico, who had an episode of demyelinating disease of the central nervous system and were positive for anti-MOG. Coronal, axial, and sagittal MRIs were acquired with 1.5T or 3.0T scanners. MRI protocols and scans were

Table 3. Brain, optic nerve, and spinal cord MRI Findings in adult Mexican patients with MOGAD

#	Brain	Optic nerve	Spinal cord	MRI findings
1	Absent	Present	Absent	STIR hyperintensity of the bilateral intraorbital and intracanalicular segments.
2	Absent	Present	Absent	STIR hyperintensity of the right intraorbital and intracanalicular segments.
3	Absent	Present	Absent	STIR hyperintensity and bilateral intraorbital segment enhancement.
4	Absent	Present	Absent	STIR Bilateral intraorbital segment STIR hyperintensity with perineural enhancement.
5	Absent	Present	Absent	STIR hyperintensity of the bilateral intraorbital and intracanalicular segments with perineural enhancement.
6	Present	Present	Absent	Supratentorial cortical hyperintensities on FLAIR associated with nodular parenchymal enhancement. STIR hyperintensity in the right intraorbital, intracanalicular, and intracranial segments.
7	Absent	Present	Absent	STIR hyperintensity and enhancement of the right intraorbital segment.
8	Absent	Present	Present	Hyperintensity and atrophy of the left intraorbital segment. Long-segment hyperintensities in the cervical spinal cord, without enhancement.
9	Present	Absent	Present	Subcortical and left periventricular hyperintensity, and periaqueductal gray matter hyperintensity. Short-segment T2 hyperintensity (D3–D4) is observed in the spinal cord.
10	Absent	Present	Absent	Hyperintensity on STIR and intraocular and intraorbital segment enhancement, as well as protrusion of the papilla on the left side with perineural enhancement.
11	Absent	Present	Absent	STIR hyperintensity and bilateral intraorbital segment enhancement.
12	Absent	Present	Absent	STIR hyperintensity of the left intraorbital segment
13	Absent	Present	Absent	STIR hyperintensity of the right intraorbital segment.
14	Absent	Present	Absent	STIR hyperintensity and right intraorbital and intracanalicular and left intraorbital, intracanalicular, and intracranial segment enhancement.
15	Present	Present	Present	STIR hyperintensity of the right intraorbital and intracanalicular segments. In the brain, multiple poorly defined, “fluffy” hyperintense lesions on FLAIR, both supra- and infratentorial, with contrast enhancement. In the cervical and thoracic spinal cord, short-segment hyperintensities with enhancement on T1-weighted with contrast images.
16	Absent	Absent	Absent	No MRI abnormalities identified
17	Present	Absent	Absent	FLAIR hyperintensities, poorly defined, “fluffy” type, with enhancement, predominantly infratentorial, associated with meningeal enhancement.
18	Present	Absent	Absent	FLAIR hyperintensities, poorly defined, supratentorial, and in the pons, peduncle, and brainstem, associated with meningeal enhancement.
19	Absent	Present	Present	STIR hyperintensity in the intracanalicular and intraorbital segments of the bilateral optic nerves with perineural enhancement; T2 hyperintensities at the cervical level and in the conus medullaris.
20	Absent	Present	Absent	STIR hyperintensity in the intracanalicular and intraorbital segments of the bilateral optic nerves.

FLAIR: fluid-attenuated inversion recovery; MOGAD: myelin oligodendrocyte glycoprotein antibody-associated disease; MRI: magnetic resonance imaging. STIR: short tau inversion recovery.

not standardized across centers; the minimum sequence set included T2-weighted images, FLAIR, and T1-weighted pre- and post-contrast images of the brain, fat-suppressed sequences of the orbits, and STIR plus T1 with contrast of the spinal cord. The MRIs were reviewed by at least one of the authors (neurologists/neuroimmunologists) and a radiologist, all experts in demyelinating diseases. Among 129 patients with MRI, perineural involvement ($n = 52$, 40.3%), longitudinal involvement ($n = 48$, 37.2%), and bilateral optic nerve involvement ($n = 43$, 33.3%) were observed. The authors concluded that optic nerve involvement – bilateral involvement, longitudinally extensive lesions,

and perineural enhancement – are the most consistent MRI features, whereas brain and spinal cord lesions showed greater variability. Comparable results were found in our study. The optic nerve was the most frequently affected site ($n = 16$, 80.0%) among 20 patients with MOGAD, characterized by longitudinally extensive hyperintensity and hyperintensity of the anterior segment of the optic nerve ($n = 15$, 75.0%), bilateral involvement ($n = 10$, 50%), and perineural enhancement ($n = 6$, 30.0%). The optic nerve is the target organ in adult MOGAD, with extensive involvement of the anterior segments and perineural enhancement, findings that are highly suggestive of this entity^{3,4,7,8,10}.

Table 4. Frequency of brain, optic nerve and/or spinal cord MRI findings in adult Mexican patients with MOGAD

Description	n (%)
Brain, (n = 5)	
Supratentorial poorly defined “fluffy” lesions	5 (25.0)
Large, poorly defined brainstem hyperintensities	3 (15.0)
Hyperintensity of the area postrema	1 (5.0)
Large, poorly defined hyperintensities in the middle cerebellar peduncles	3 (15.0)
Large, poorly defined cerebellum hyperintensities	3 (15.0)
Periventricular hyperintensities	3 (15.0)
Cortical hyperintensities	4 (20.0)
Parenchymal enhancement	3 (15.0)
Meningeal enhancement	2 (10.0)
Optic nerve, (n = 16)	
Longitudinally extensive hyperintensity	15 (75.0)
Anterior segment hyperintensity ^a	15 (75.0)
Bilateral optic nerve hyperintensity	10 (50.0)
Posterior segment hyperintensity ^b	3 (15.0)
Nerve enhancement	3 (15.0)
Perineural/optic nerve sheath enhancement	6 (30.0)
Papillitis/optic disc protrusion	2 (10.0)
Spinal cord, (n = 4)	
Longitudinally extensive transverse myelitis ^c	1 (5.0)
Short segment hyperintensities ^d	3 (15.0)
Cervical hyperintensities	2 (10.0)
Thoracic hyperintensities	2 (10.0)
Hyperintensity of the conus medullaris	2 (10.0)
Spinal cord enhancement	1 (5.0)

One patient did not show any MRI abnormality. No patient had an H sign. ^aIntraorbital and/or intracanalicular segment; ^bChiasm and/or intracranial segment; ^c≥ 3 vertebral segments; ^d< 3 vertebral segments. MOGAD: myelin oligodendrocyte glycoprotein antibody-associated disease; MRI: magnetic resonance imaging.

Brain and spinal cord involvement is less common and heterogeneous in MOGAD. Brain lesions typically involve the white matter, cerebral cortex, brainstem, and cerebellum, appearing as poorly defined hyperintense areas on T2/FLAIR sequences. Spinal cord lesions are classically characterized by longitudinally extensive myelitis, conus medullaris involvement, or predominant gray-matter involvement with the characteristic “H” sign, although short-segment lesions can also be observed^{4,11}. These manifestations are included in the imaging spectrum recognized by the International MOGAD Diagnostic Criteria and represent supportive findings for diagnosis, particularly in patients whose initial phenotype does not correspond to optic neuritis¹². Likewise, Shahriari et al.¹³ reported that although brain and spinal cord involvement occurs less frequently than optic nerve involvement, recognition of these imaging patterns is essential to establish the differential

diagnosis with other demyelinating disorders and to guide timely clinical management. Similarly, in our cohort, brain and spinal cord involvement was considerably less frequent than optic neuritis. Brain lesions were characteristically seen as fluffy hyperintensities with cortical and infratentorial involvement; parenchymal and meningeal enhancement were also seen. Spinal cord lesions were characterized by short-segment hyperintensity, most common at the cervical and thoracic levels, with less frequent hyperintensity in the conus medullaris. Unlike most cohorts, where longitudinally extensive spinal cord lesions predominate, our study showed a higher frequency of short-segment lesions. Cobo-Calvo et al.¹⁴ conducted a retrospective multicenter cohort study in France of adults with an acute clinical demyelinating CNS episode lasting at least 24 hours and positive anti-MOG antibodies. There were 197 patients with MOGAD. MRI included axial and sagittal images of the brain and spinal cord using contrast-enhanced T1, T2, FLAIR, and T1-weighted sequences. Only 49 patients with MOGAD showed MRI abnormalities, with thalamic lesions (n = 9, 18.37%), pontine lesions (n = 17, 34.69%), cortical involvement (n = 8, 16.3%), and leptomeningeal enhancement (n = 3, 6.1%). Lesions in the thalamus and pons were more frequent in patients with anti-MOG antibodies. Brain and spinal cord MRI abnormalities were detected in 1 of 4 patients with MOGAD. Although brain lesions have a heterogeneous distribution, most published series report a predominance of infratentorial involvement, particularly in the brainstem and cerebellum, a finding that aligns with the observations in our cohort. In contrast, spinal cord lesions also showed a variable distribution, underscoring the radiological heterogeneity of MOGAD. Taken together, our findings align with the available evidence and confirm that, although brain and spinal cord involvement is part of the clinical-radiological spectrum of MOGAD, its frequency is considerably lower than that of optic neuritis, which is the predominant disease phenotype¹⁴⁻¹⁶.

The clinical spectrum of MOGAD is broad and heterogeneous; however, recent evidence consistently shows that optic neuritis is the predominant clinical manifestation, typically presenting with acute visual loss, pain with eye movements, and bilateral involvement in a significant proportion of patients. Myelitis is the second most common phenotype. It presents with lower-limb weakness, sensory disturbances, sphincter dysfunction, and, in some cases, conus medullaris involvement. Less commonly, encephalitis or encephalomyelitis occurs,

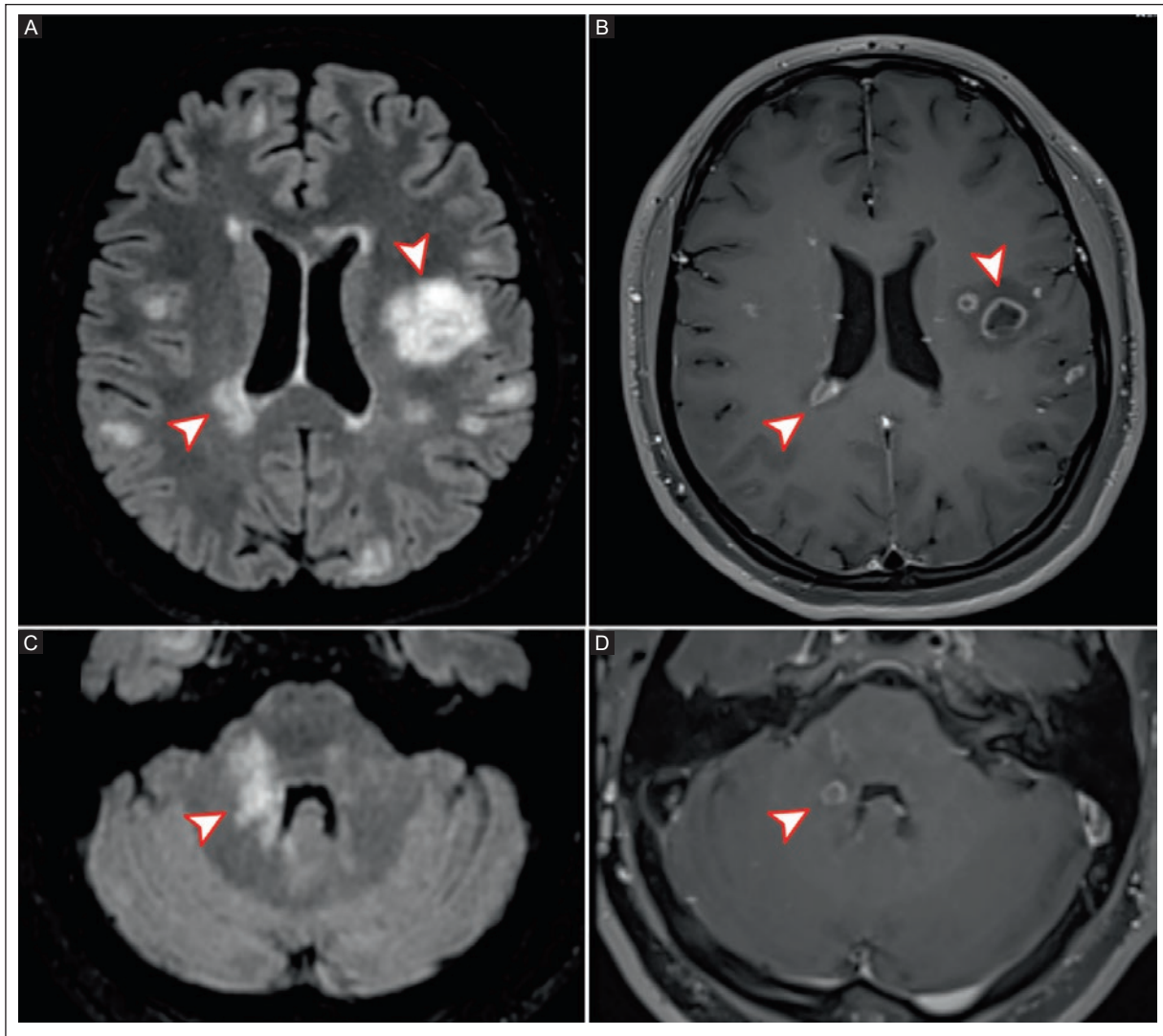


Figure 1. Brain MRI of an anti-MOG antibody-positive woman (case 15) presenting with vertigo, bilateral pyramidal syndrome, decreased visual acuity, and right eye pain. **A:** axial FLAIR image shows diffuse, fluffy supratentorial hyperintense lesions in the periventricular and subcortical white matter (arrowheads). **B:** axial contrast-enhanced T1-weighted image shows multiple supratentorial lesions with complete and incomplete ring enhancement (arrowheads). **C:** axial FLAIR image shows infratentorial involvement, with a fluffy, hyperintense lesion in the pons and the right middle cerebellar peduncle (arrowhead). **D:** axial contrast-enhanced T1-weighted image shows ring enhancement of the lesion involving the right pons and middle cerebellar peduncle (arrowhead).

FLAIR: fluid-attenuated inversion recovery; MOG: myelin oligodendrocyte glycoprotein; MRI: magnetic resonance imaging.

characterized by headache, seizures, altered consciousness, and focal neurologic deficits, as well as brainstem and cerebellar syndromes, including diplopia, vertigo, ataxia, dysarthria, and other signs of cranial nerve dysfunction^{4,8,11,17}. In our cohort, the most frequent clinical manifestations involving the brain were epilepsy or headache, observed in 2 patients (10.0%). At the optic nerve level, decreased visual acuity and pain with eye movements were present in 15 patients (75.0%). In the spinal cord, lower-limb weakness or pyramidal syndrome were the most frequent manifestations, observed in 2 patients (10.0%). Cobo-Calvo et al.¹⁴ evaluated 197 patients with

MOGAD; the most frequent phenotype was optic neuritis in 60.9% of patients, and 50 (41.7%) cases were bilateral. Myelitis occurred in 22.3%, and 7.6% developed optic neuritis and myelitis simultaneously. Only 8 patients (4.1%) developed an isolated brainstem syndrome, 5 (2.5%) had an isolated encephalopathic syndrome, 4 (2.0%) had a brainstem syndrome accompanied by encephalopathy, and 1 (0.5%) had optic neuritis with a brainstem syndrome. Other less frequent accompanying symptoms at baseline were neuropathic pain (7.6%), fever (9.0%), and area postrema symptoms (2.1%), and 2 patients (1.4%) developed seizures. Jurynczyk et al.³

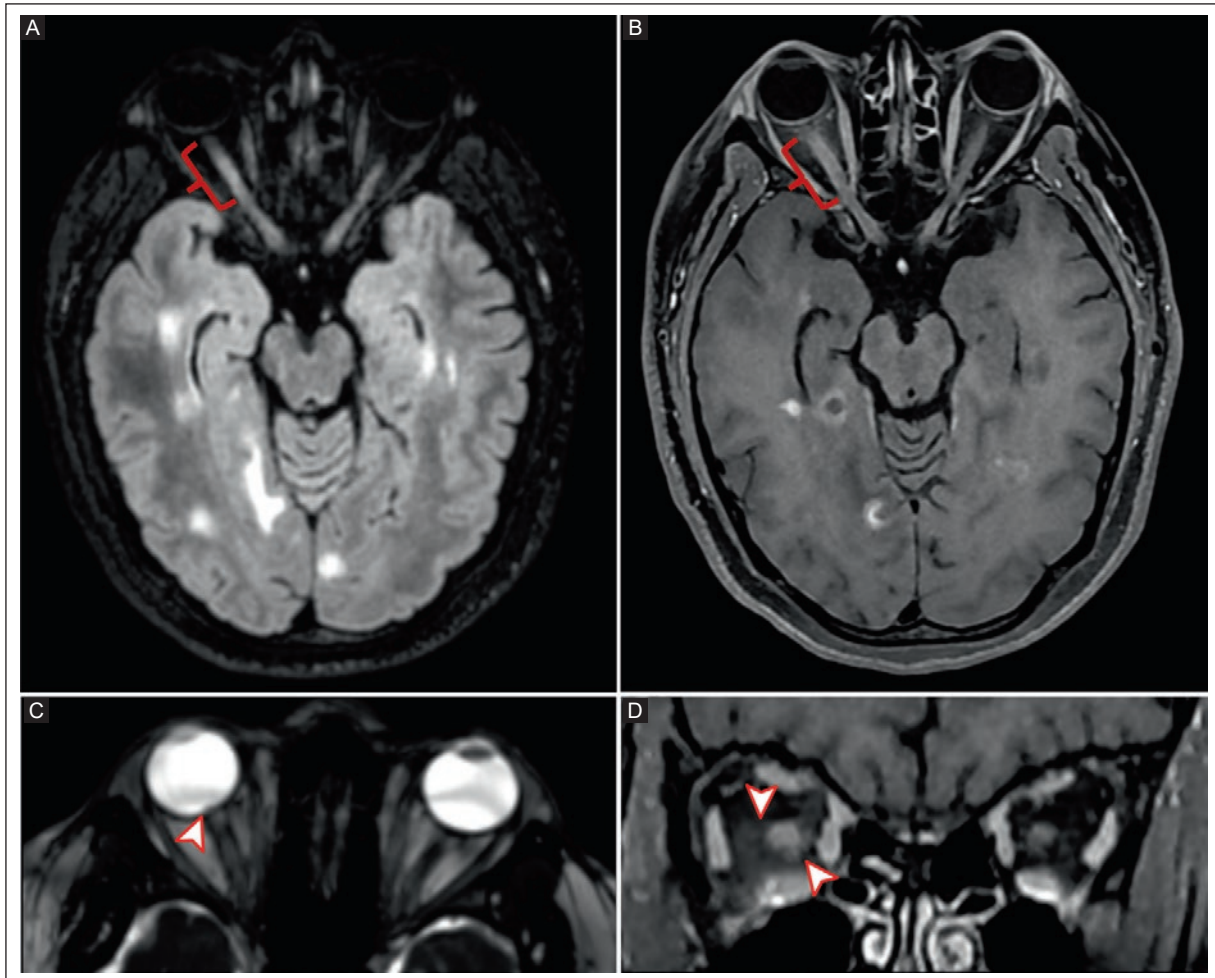


Figure 2. Orbital MRI of an anti-MOG antibody-positive woman (case 15) presenting with vertigo, bilateral pyramidal syndrome, decreased visual acuity, and right eye pain. **A:** axial FLAIR image shows a bracket delineating the extent of a hyperintense signal along the right optic nerve, consistent with longitudinally extensive optic neuritis. **B:** axial, fat-suppressed, contrast-enhanced T1-weighted image shows enhancement of the right optic nerve, with associated perineural enhancement. The bracket delineates the longitudinal extent of optic nerve involvement. **C:** axial FIESTA image shows protrusion of the right optic disc into the posterior globe (arrowhead). **D:** a coronal fat-suppressed, contrast-enhanced T1-weighted image shows increased signal and perineural fat enhancement around the right optic nerve, consistent with optic perineuritis (arrowheads).

FIESTA: fast imaging employing steady-state acquisition; FLAIR: fluid-attenuated inversion recovery; MOG: myelin oligodendrocyte glycoprotein; MRI: magnetic resonance imaging.

in the United Kingdom reported a retrospective observational cohort of 252 patients with MOGAD. Among these patients, 139 (55%) had optic neuritis, and 60 (24%) had bilateral neuritis. Forty-five (18%) had only transverse myelitis, 35 (14%) had longitudinally extensive myelitis, and 10 (4%) had short-segment myelitis. Only 23 (9%) had optic neuritis and myelitis simultaneously. Regarding brain involvement, 45 patients (18%) had acute disseminated encephalomyelitis. MOGAD presents a distinctive clinical phenotype, characterized mainly by recurrent optic neuritis and a better functional prognosis than other demyelinating diseases. Optic neuritis is the predominant clinical manifestation of MOGAD,

frequently occurring bilaterally, while myelitis is the second most common phenotype. In contrast, brainstem syndromes, encephalopathy, and other neurologic manifestations such as seizures or area postrema symptoms are rare, confirming that MOGAD has a broad clinical spectrum, but a clear predominance of optic nerve involvement^{3,14}.

The main strengths of this study are the inclusion of patients who met international MOGAD diagnostic criteria, the comprehensive characterization of clinical manifestations, and systematic MRI evaluation of the brain, optic nerves, and spinal cord. The use of an imaging protocol and the interpretation of studies by a

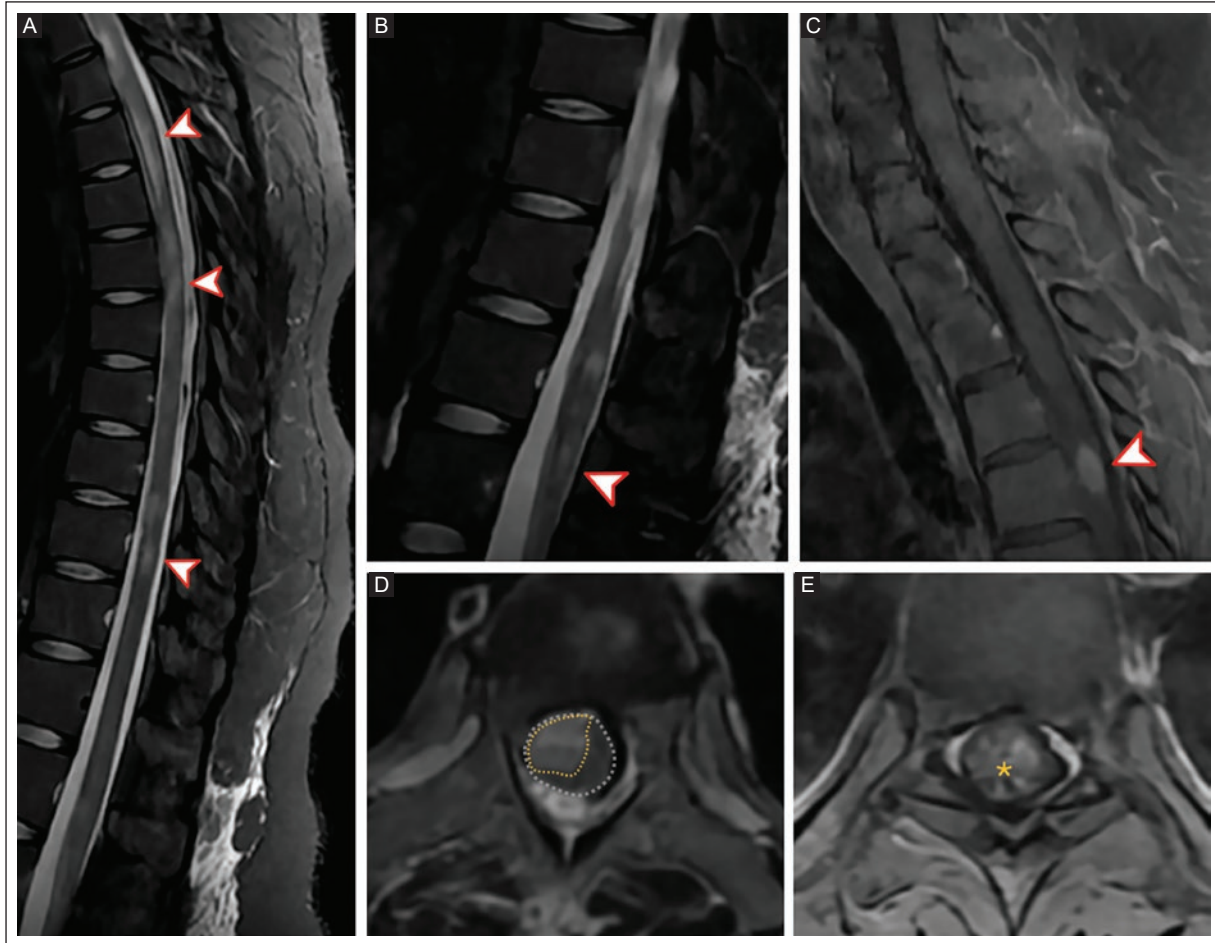


Figure 3. Spine MRI of an anti-MOG antibody-positive woman (case 15) presenting with vertigo, bilateral pyramidal syndrome, decreased visual acuity, and right eye pain. **A:** sagittal STIR image of the cervicothoracic spine shows multiple short-segment hyperintense spinal cord lesions (arrowheads). **B:** sagittal STIR image shows additional short-segment spinal cord lesions involving the conus medullaris (arrowhead). **C:** sagittal contrast-enhanced T1-weighted image shows focal enhancement of a cervical spinal cord lesion, consistent with active inflammation (arrowhead). **D:** axial T2-weighted image shows a spinal cord lesion occupying more than 50% of the axial cross-sectional area (yellow dotted line) and involving the central gray matter and peripheral white matter. The white dotted line outlines the cross-sectional area of the spinal cord. **E:** axial contrast-enhanced T1-weighted image shows enhancement of the spinal cord lesion, consistent with active inflammation (asterisk).

MRI: magnetic resonance imaging; MOG: myelin oligodendrocyte glycoprotein; STIR: short tau inversion recovery.

neuroradiologist allowed a detailed and consistent assessment of the clinical and imaging spectrum of patients with MOGAD. However, the study has some limitations. Its retrospective design and small sample size limit the generalizability of its results and the feasibility of inferential statistical analyses.

CONCLUSION

In this cohort of Mexican adult patients with MOGAD, optic neuritis was the predominant clinical and imaging feature, characterized by longitudinally extensive bilateral involvement and perineural enhancement. Brain and spinal cord lesions were less frequent and

heterogeneous in distribution. These findings confirm that MRI plays a fundamental role in identifying characteristic MOGAD patterns and is a useful tool for diagnosing and differentiating MOGAD from other inflammatory demyelinating diseases of the central nervous system. Prospective multicenter studies with larger patient cohorts are recommended to validate these findings, evaluate the clinical course, and assess their impact on early diagnosis, prognosis, and management.

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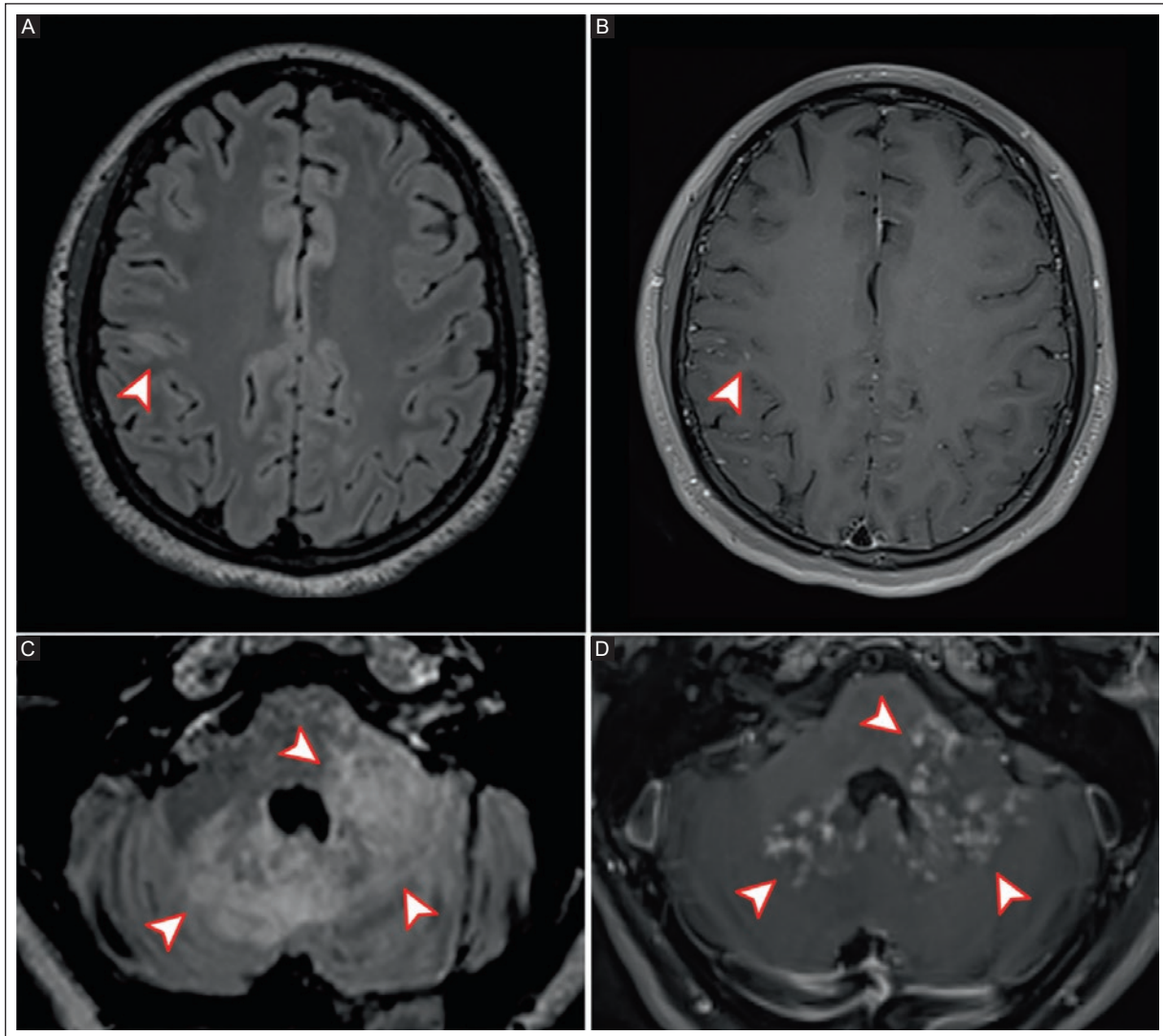


Figure 4. Brain MRI of an anti-MOG antibody-positive woman (case 17), presenting with recurrent vertigo syndrome and ataxia followed by the onset of epileptic seizures. **A:** axial FLAIR image shows a hyperintense lesion involving the cortex and subcortical white matter of the right superior parietal lobule (arrowhead). **B:** axial contrast-enhanced T1-weighted image shows nodular enhancement of the lesion in the right superior parietal lobule (arrowhead). **C:** axial FLAIR image shows predominant infratentorial involvement, with multiple fluffy hyperintense lesions in the left middle cerebellar peduncle and cerebellar hemispheres (arrowheads). **D:** axial contrast-enhanced T1-weighted image shows multiple nodular enhancing infratentorial lesions (arrowheads).

FLAIR: fluid-attenuated inversion recovery; MOG: myelin oligodendrocyte glycoprotein; MRI: magnetic resonance imaging.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the World Medical Association and the Declaration of Helsinki (1964) and subsequent amendments.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, Informed consent was not required for this observational study of information collected during routine clinical care.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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Differentiating malignant from benign breast lesions with type 2 or 3 kinetic curves using an apparent diffusion coefficient cutoff value on MRI

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ABSTRACT

Introduction: A low apparent diffusion coefficient (ADC) value is associated with breast lesions suspected of malignancy. This study aimed to determine the optimal ADC cutoff value to differentiate malignant from benign breast lesions with kinetic curve types 2 or 3 on breast magnetic resonance imaging (MRI). **Material and methods:** This cross-sectional study included women with breast lesions classified as Breast Imaging Reporting and Data System (BI-RADS) category 4 or 5. ADC was measured using diffusion-weighted imaging (DWI) MRI, and the kinetic curve was assessed with dynamic contrast-enhanced (DCE) MRI. A receiver operating characteristic (ROC) curve was used to determine the optimal ADC cutoff for differentiating malignant from benign breast lesions. Histopathological diagnosis of the breast lesion served as the gold standard. **Results:** A total of 65 women with breast lesions exhibiting kinetic curve types 2 or 3 were included. An optimal ADC cutoff of $\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$ differentiated malignant from benign lesions, yielding a sensitivity of 88.5% (95% CI, 76.6-95.6), a specificity of 84.6% (95% CI, 54.6-98.1), a PPV of 95.8% (95% CI, 85.7-99.5), a NPV of 64.7% (95% CI, 38.3-85.8), and an accuracy of 87.7% (95% CI, 77.2-94.5). The accuracy of kinetic curve types 2 and 3 alone ranged from 49.2% to 50.8%, indicating limited diagnostic performance for each kinetic curve type and significantly lower accuracy than that of the optimal ADC cutoff value (87.7%) for predicting malignant breast lesions. **Conclusion:** The optimal ADC value of $\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$ demonstrated high diagnostic performance in differentiating malignant from benign breast lesions in patients with kinetic curve types 2 or 3. Incorporating it into clinical practice provides a quantitative parameter that complements the qualitative interpretation of the kinetic curve.

Keywords: Breast neoplasms. Contrast medium. Diffusion magnetic resonance imaging. Magnetic resonance imaging.

INTRODUCTION

Magnetic resonance imaging (MRI) of the breast integrates diffusion-weighted imaging (DWI), which provides information on tissue microstructure and cellular-ity by using the apparent diffusion coefficient (ADC), and dynamic contrast-enhanced MRI (DCE-MRI), which characterizes the kinetic behavior of enhancement^{1,2}.

In general, malignant lesions show greater diffusion restriction and lower ADC values than benign lesions. A meta-analysis of 13,847 breast lesions reported a mean ADC of $1.03 \times 10^{-3} \text{ mm}^2/\text{s}$ in malignant lesions compared with $1.5 \times 10^{-3} \text{ mm}^2/\text{s}$ in benign lesions. ADC performance is independent of magnetic field strength, the b-values used, and the measurement method³. Breast MRI also provides complementary information

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for characterizing lesions suspected of malignancy by integrating morphological, functional, and kinetic descriptors⁴. Kinetic analysis classifies late enhancement behavior as persistent (type 1 curve), plateau (type 2), and washout (type 3). However, interpreting these patterns in isolation has limited specificity because they overlap between benign and malignant lesions^{4,5}.

Lesions with a type 2 kinetic curve represent the primary scenario of overlap between benign and malignant lesions, whereas the type 3 curve does not fully resolve the ambiguity, as it occurs in more than half (57.4%) of malignant breast lesions⁵. ADC values have shown high diagnostic performance across populations for malignant breast lesions, with sensitivity and specificity greater than 94% and an area under the curve (AUC) of 0.981⁶. In another study, sensitivity was 96%, specificity 71%, and the AUC 0.858⁷.

The diagnostic performance of ADC has been reported for lesions with a type 2 curve, with an optimal cutoff of $1.0 \times 10^{-3} \text{ mm}^2/\text{s}$ ⁸, and for lesions with a type 3 curve, with an optimal cutoff of $0.89 \times 10^{-3} \text{ mm}^2/\text{s}$ ⁹. To the best of our knowledge, the diagnostic performance of a single ADC cutoff across both curve types (2 and 3) has not been evaluated. This study aimed to evaluate the diagnostic performance of ADC, using an optimal cutoff that differentiates malignant from benign breast lesions in patients with a type 2 or type 3 kinetic curve on MRI.

MATERIAL AND METHODS

This retrospective cross-sectional study was conducted from January 2015 to August 2024 at the *Centro Medico ABC* (American British Cowdray), *Observatorio* and *Santa Fe* campuses, in Mexico City, Mexico. The study included women aged 18 years or older with BI-RADS category 4 or 5 breast lesions who had undergone DWI-MRI and DCE-MRI and had a biopsy for histopathological confirmation. Patients with a history of neoadjuvant chemotherapy were excluded. Because this was a retrospective study using information obtained during medical care, informed consent was not required. The study was approved by the institutional Local Research and Ethics Committee.

Study development and variables

The following variables were obtained from the clinical records: age, family history of breast cancer, hormonal status, hormone replacement therapy use, and breast

density. Histopathological results of the breast biopsy and MRI findings – signal intensity on T1, T2, and Tau inversion recovery with short Tau inversion time (TIRM/STIR), and kinetic curve type – were recorded.

Image acquisition and analysis protocol

Breast MRI was performed on a MAGNETOM Skyra 3.0T scanner (Siemens, Erlangen, Germany) using an 18-channel dedicated phased-array breast coil. Axial DWI sequences were acquired using spin-echo echo-planar imaging with b values of 50 and 800 s/mm² and fat saturation. ADC values were obtained by placing a region of interest (ROI) of at least 2 mm² within lesions with or without diffusion restriction, while avoiding cystic regions, areas of necrosis, hematomas, fatty tissue, and artifacts.

Subsequently, DCE-MRI sequences were acquired after intravenous administration of gadolinium contrast medium (Bayer AG, Leverkusen, Germany) at 0.1 mmol/kg body weight and a flow rate of 3.5 mL/s. Axial T1-weighted sequences with fat suppression were obtained before contrast administration and in six acquisitions after contrast administration, at 60-second intervals (60, 120, 180, 240, 300, and 360 seconds). An ROI was placed at the site of greatest enhancement. Signal-time intensity curves were generated and classified according to contrast medium behavior into three types: persistent curve (type 1), defined by a continuous increase in contrast uptake > 10% in the late phase; plateau (type 2), defined by no change in signal strength, remaining horizontal; and washout (type 3), defined by a decrease in uptake > 10% after the peak.

Statistical analysis

Quantitative variables with a normal distribution are described using means and standard deviation (SD); variables with a non-normal distribution are described as medians and interquartile range. Qualitative variables are presented using absolute frequencies and percentages. The Receiver Operating Characteristic (ROC) curve was used to determine the optimal ADC cutoff value, and Youden's J-index and area under the curve (AUC) were calculated. The association between the type of kinetic curve and histopathological diagnosis was evaluated using the chi-square test. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy, positive likelihood ratio, negative likelihood ratio, and

false-positive and false-negative results for ADC and for type 2 and type 3 curves were calculated. SPSS v29.0 (IBM Corp., Armonk, NY, USA) was used for the analysis.

RESULTS

We included 65 women with 65 BI-RADS category 4 or 5 breast lesions and kinetic curve types 2 or 3. The mean age was 49.3 ± 12.5 years (Table 1). Heterogeneous fibroglandular tissue was the predominant pattern in 43.1% of patients ($n = 28$), followed by scattered fibroglandular tissue in 41.5% ($n = 27$). The mean ADC value was $1.006 \pm 0.350 \times 10^{-3} \text{ mm}^2/\text{s}$. The left breast was most affected, accounting for 55.4% of cases ($n = 36$). The predominant finding was an irregular mass in 58.5% ($n = 38$) followed by non-mass enhancement in 26.2% ($n = 17$). The mean maximum diameter was $28.0 \pm 21.1 \text{ mm}$.

Histopathologic diagnosis of malignant or benign breast lesions with a type 2 or 3 kinetic curve

Of 52 malignant breast lesions (80.0%), 13 (25.0%) were BI-RADS 4 and 39 (75.0%) were BI-RADS 5 (Table 2). A type 2 kinetic curve was observed in 29 (55.8%) and a type 3 in 23 (44.2%) of the 52 malignant lesions. There was a significant association between the BI-RADS 5 category and a histopathologic diagnosis of malignancy ($p < 0.001$). The most frequent malignant diagnoses were invasive ductal carcinoma ($n = 34$, 65.4%) and invasive lobular carcinoma ($n = 15$, 28.8%). There were 13 (20.0%) benign lesions, of which 12 (92.3%) were BI-RADS 4 and 1 (7.7%) was BI-RADS 5. A type 2 kinetic curve was found in 9 (69.2%) and a type 3 kinetic curve in 4 (30.8%) of the 13 benign breast lesions. There were no significant differences between malignant and benign breast lesions with type 2 or 3 kinetic curves ($p = 0.38$).

Diagnostic performance of the optimal ADC cutoff value with type 2 or 3 kinetic curve for differentiating malignant breast lesions

ROC analysis showed an ADC cutoff of $\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$ for differentiating malignant from benign breast lesions with type 2 or 3 kinetic curves (AUC, 0.956; 95% CI, 0.907-1.000) (Figure 1). An ADC of $\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$ correctly classified 46 (88.5%) of

Table 1. Clinical and MRI data of women with breast lesions with a type 2 or 3 kinetic curve

Description	(n = 65)
Age (years), mean $\pm$ SD	49.3 $\pm$ 12.5
Relative with a history of breast cancer, n (%)	
Mother	5 (7.7)
Sister	3 (4.6)
Grandmother	4 (6.2)
Other	3 (4.6)
None	50 (76.9)
Hormonal status, n (%)	
Premenopausal	38 (58.5)
Menopausal	27 (41.5)
Hormone replacement therapy, n (%)	
Yes	6 (9.2)
No	59 (90.8)
Amount of fibroglandular tissue on MRI, n (%)	
Almost entirely fatty	5 (7.7)
Scattered fibroglandular tissue	27 (41.5)
Heterogeneous fibroglandular tissue	28 (43.1)
Extreme fibroglandular tissue	5 (7.7)
ADC $\times 10^{-3} \text{ mm}^2/\text{s}$, mean $\pm$ SD	1.006 $\pm$ 0.350

ADC: apparent diffusion coefficient; MRI: magnetic resonance imaging; SD: standard deviation.

Table 2. Histopathologic diagnosis of malignant and benign breast lesions with a type 2 or 3 kinetic curve

Description	Parameter	Type 2/3 kinetic curves
Malignant breast lesion, n (%)	52 (80.0)	29 (55.8)/23 (44.2)
Invasive ductal carcinoma, n	34	18/16
Invasive lobular carcinoma, n	15	9/6
Ductal carcinoma in situ, n	1	1/0
Invasive mucinous carcinoma, n	1	0/1
Invasive tubular carcinoma, n	1	1/0
Benign breast lesion, n (%)	13 (20.0)	9 (69.2)/4 (30.8)
Xanthogranulomatous mastitis, n	4	4/0
Complex fibroadenoma with sclerosing adenosis, n	2	2/0
Usual ductal hyperplasia, n	2	1/1
Fibroadenomatous hyperplasia, n	1	1/0
Fibroadenoma, n	1	0/1
Lymph node with hyperplasia, n	1	0/1
Flat epithelial atypia, n	1	1/0
Hyperplasia with atypia, n	1	0/1

the 52 malignant lesions (true positive) and 11 of the 13 benign lesions (true negative) with a sensitivity of 88.5% (95% CI, 76.6-95.6), a specificity of 84.6% (95% CI, 54.6-98.1), and an accuracy of 87.7% (95% CI, 77.2-94.5) for predicting malignant breast lesions (Table 3). In comparison, the isolated type 2 kinetic curve, independent of the ADC, showed a sensitivity of 55.8%, a specificity of 30.8%, and an accuracy of 50.8%, while the isolated type 3 kinetic curve showed a sensitivity of 44.2%, a specificity of 69.2%, and an accuracy of 49.2%. The accuracy of kinetic curves 2 and 3 ranged from 49.2% to 50.8%, indicating limited diagnostic performance of each curve type. It was significantly lower than the optimal ADC cutoff (87.7%) for predicting malignant breast lesions.

Figure 2 shows the breast MRI of a 64-year-old woman with an irregular mass, an ADC of $0.764 \times 10^{-3} \text{ mm}^2/\text{s}$, and a type 2 kinetic curve. The histopathologic diagnosis was invasive ductal breast carcinoma. This patient's ADC ($\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$) was consistent with the optimal cutoff for predicting malignancy. Figure 3 shows the breast MRI of a 41-year-old woman with irregular, heterogeneous mass lesions, an ADC of $0.619 \times 10^{-3} \text{ mm}^2/\text{s}$, and a type 3 kinetic curve. The histopathologic diagnosis was invasive ductal carcinoma of the right breast. This patient's ADC ($\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$) was consistent with the optimal cutoff for predicting malignancy.

Diagnostic performance of the optimal ADC cutoff with type 2 or 3 kinetic curve for differentiating benign breast lesions

To differentiate benign breast lesions, an ADC value of $> 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$ showed a sensitivity of 84.6%, a specificity of 88.5%, and an accuracy of 87.7% (Table 4). However, six malignant lesions had ADC values below the cutoff, three with a type 2 kinetic curve and three with a type 3 kinetic curve. In contrast, the isolated type 2 kinetic curve showed a sensitivity of 69.2%, a specificity of 44.2%, and an accuracy of 49.2%. The type 3 kinetic curve showed a sensitivity of 30.8%, a specificity of 55.8%, and an accuracy of 50.8%. The accuracy of kinetic curves 2 and 3 ranged from 49.2% to 50.8%, indicating the limited diagnostic performance of each kinetic curve, which was significantly lower than the optimal ADC (87.7%) for predicting benign breast lesions.

Figure 4 shows a breast MRI of a 23-year-old woman with a palpable lump. The ADC was $1.806 \times 10^{-3} \text{ mm}^2/\text{s}$,

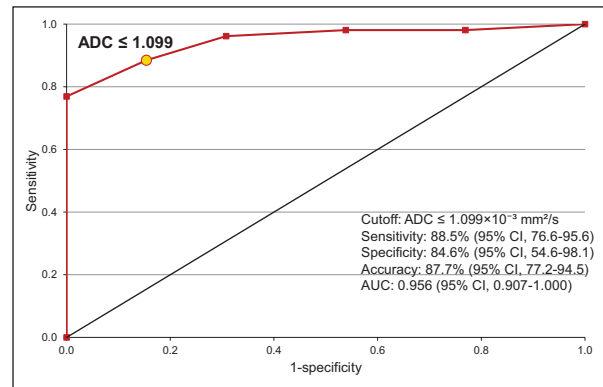


Figure 1. The ROC curve identified an optimal ADC cutoff of $\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$, with a sensitivity of 88.5%, a specificity of 84.6%, and an accuracy of 87.7% for differentiating malignant from benign breast lesions in women with type 2 or 3 kinetic curves. The AUC was 0.956 (95% CI, 0.907-1.000).

ADC: apparent diffusion coefficient; AUC: area under the curve; DCE-MRI: dynamic contrast-enhanced magnetic resonance imaging; CI: confidence interval; MRI: magnetic resonance imaging; ROC: receiver operating characteristic.

with a type 2 kinetic curve. The histopathologic diagnosis was complex fibroadenoma with sclerosing adenosis. This patient's ADC ($> 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$) was consistent with the optimal cutoff for predicting benignity. Figure 5 shows the breast MRI of a 39-year-old woman with a palpable lump. The ADC was $1.605 \times 10^{-3} \text{ mm}^2/\text{s}$, with a type 3 kinetic curve. The histopathologic diagnosis was fibroadenoma. This patient's ADC ($> 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$) corresponded with the optimal cutoff for predicting benignity. Angiogenesis and capillary permeability of dense fibrovascular stroma can simulate malignancy on the kinetic curve, but the ADC showed higher accuracy than kinetic assessment for defining breast lesion benignity.

Figure 6 shows a breast MRI of a 63-year-old woman diagnosed with encephalitis who underwent a PET/CT scan (not shown) that revealed an incidental finding in the left breast. Mammography and breast ultrasound were performed with no conclusive findings (not shown). A breast MRI was requested as a complementary examination. The ADC was $1.614 \times 10^{-3} \text{ mm}^2/\text{s}$, with a type 3 kinetic curve. The histopathologic diagnosis was usual ductal hyperplasia. Angiogenesis and capillary permeability of dense fibrovascular stroma can simulate malignancy on the kinetic curve, but the ADC ($> 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$), consistent with the optimal cutoff, showed greater accuracy than the kinetic curve or PET/CT for predicting benignity.

Table 3. Diagnostic performance of the optimal ADC cutoff ($\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$) alone in the overall cohort and type 2 and 3 kinetic curves alone for differentiating malignant breast lesions^a

Description	Optimal ADC cutoff ($\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$)	Type 2 kinetic curve alone	Type 3 kinetic curve alone
Sensitivity, % (95% CI)	88.5 (76.6-95.6)	55.8 (41.3-69.5)	44.2 (30.5-58.7)
Specificity, % (95% CI)	84.6 (54.6-98.1)	30.8 (9.1-61.4)	69.2 (38.6-90.9)
Positive likelihood ratio (95% CI)	5.75 (1.60-20.65)	0.81 (0.52-1.25)	1.44 (0.60-3.43)
Negative likelihood ratio (95% CI)	0.14 (0.06-0.30)	1.44 (0.60-3.43)	0.81 (0.52-1.25)
PPV, % (95% CI)	95.8 (85.7-99.5)	76.3 (67.6-83.3)	85.2 (70.7-93.2)
NPV, % (95% CI)	64.7 (38.3-85.8)	14.8 (6.8-29.3)	23.7 (16.7-32.4)
Accuracy, % (95% CI)	87.7 (77.2-94.5)	50.8 (38.1-63.4)	49.2 (36.6-61.9)

^aHistopathologic diagnosis was confirmed. ADC: apparent diffusion coefficient; CI: confidence interval; NPV: negative predictive value; PPV: positive predictive value.

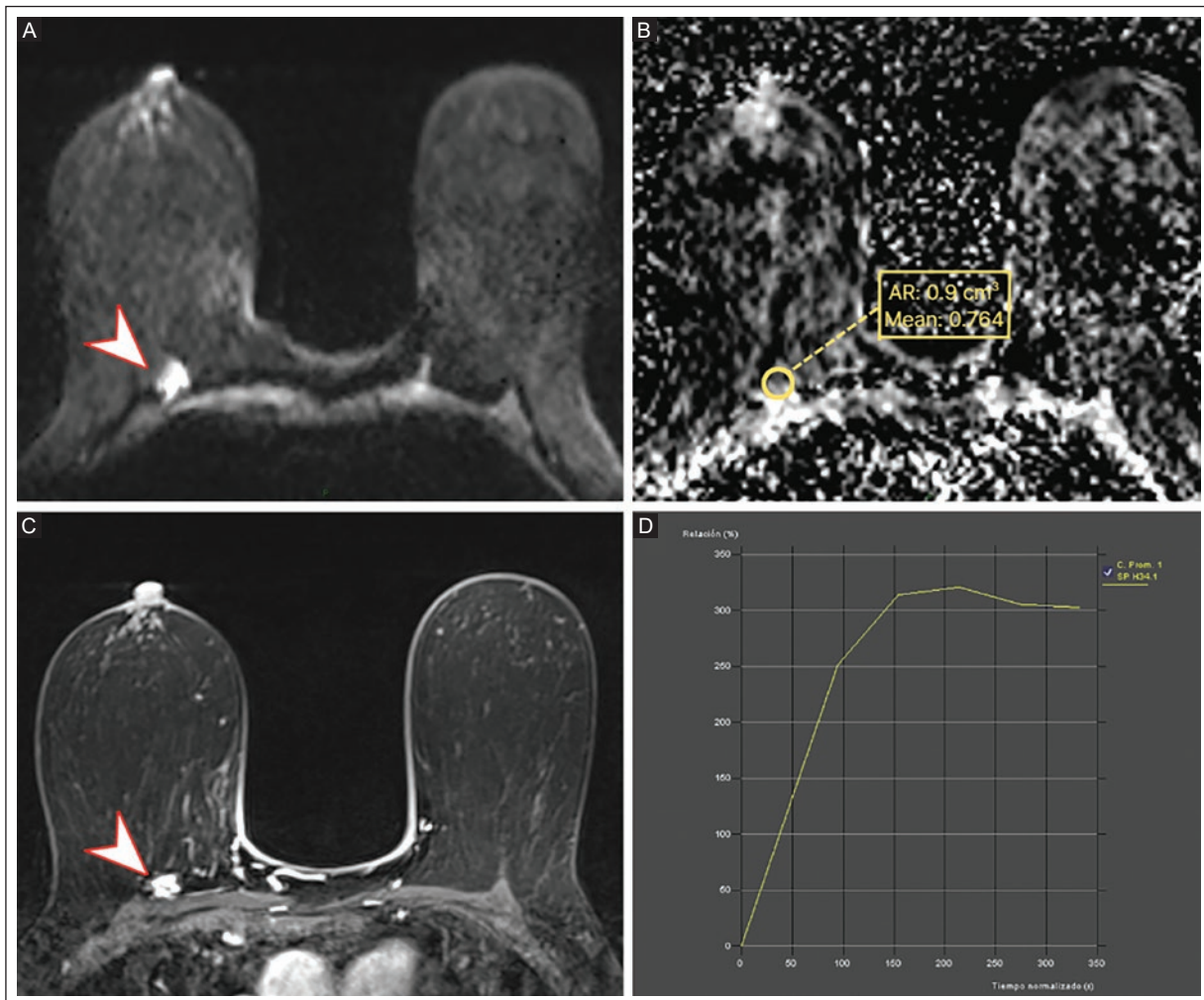


Figure 2. Breast MRI of a 64-year-old woman with an irregular mass at the junction of the upper quadrants of the right breast, classified as BI-RADS 4c. **A:** axial DWI sequence of the right breast shows an irregular hyperintense mass with restricted diffusion (arrowhead). **B:** ADC map shows a hypointense mass. The ROI shows an ADC of $0.764 \times 10^{-3} \text{ mm}^2/\text{s}$ (circle). **C:** first post-contrast T1-weighted sequence shows homogeneous enhancement of the mass (arrowhead). **D:** kinetic curve of DCE-MRI shows a plateau pattern (type 2). The histopathologic diagnosis was an invasive ductal breast carcinoma. This patient's ADC ($\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$) was consistent with the optimal cutoff for predicting malignancy.

ADC: apparent diffusion coefficient; BI-RADS: Breast Imaging Reporting and Data System; DCE-MRI: dynamic contrast-enhanced magnetic resonance imaging; DWI: diffusion-weighted imaging; MRI: magnetic resonance imaging; ROI: region of interest.

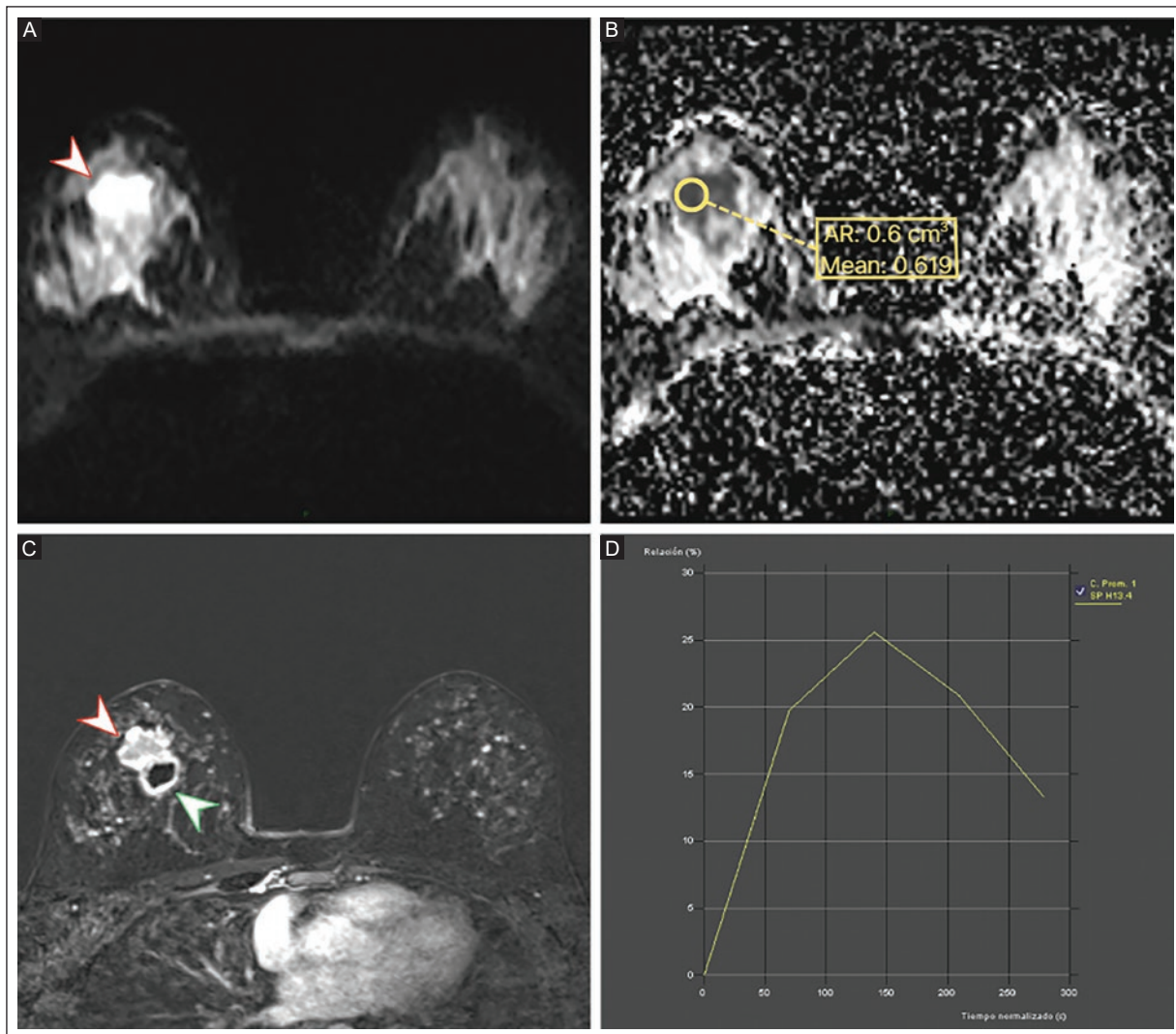


Figure 3. Breast MRI of a 41-year-old woman with an irregular, heterogeneous mass with indistinct margins at the junction of the inferior quadrants of the right breast, classified as BI-RADS 4c. **A:** axial DWI sequence of the right breast shows a hyperintense irregular mass with restricted diffusion (arrowhead). **B:** ADC map shows a hypointense mass. The ROI shows an ADC of $0.619 \times 10^{-3} \text{ mm}^2/\text{s}$ (circle). **C:** first post-contrast T1-weighted sequence shows an irregular mass with heterogeneous enhancement (red arrowhead) and a hypointense area suggestive of necrotic tissue (green arrowhead). **D:** kinetic curve of DCE-MRI shows a washout pattern (type 3). The histopathologic diagnosis was invasive ductal carcinoma of the right breast. This patient's ADC ($\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$) was consistent with the optimal cutoff for predicting malignancy.

ADC: apparent diffusion coefficient; BI-RADS: Breast Imaging Reporting and Data System; DWI: diffusion-weighted imaging; DCE-MRI: dynamic contrast enhanced magnetic resonance imaging; MRI: magnetic resonance imaging; ROI: region of interest.

DISCUSSION

In this study, the optimal ADC cutoff ($\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$) showed high diagnostic performance for differentiating malignant from benign breast lesions in patients with type 2 or 3 kinetic curves. A single ADC cutoff was useful for distinguishing malignant from benign lesions in patients with suspected malignant breast lesions who had a type 2 or 3 kinetic curve. This finding represents the scenario with the greatest overlap between benign

and malignant lesions. ADC complements the qualitative interpretation of the kinetic curve in clinical practice.

ADC is a useful quantitative parameter for characterizing breast lesions suspicious for malignancy, using a cutoff derived from ROC analysis that incorporates diffusion into the morphological and kinetic evaluation of MRI¹⁰. El Khoully et al.¹⁰ reported a cross-sectional study of 93 American women. An ADC of $1.600 \times 10^{-3} \text{ mm}^2/\text{s}$ showed a sensitivity of 91.7% and a specificity of 72% (AUC 0.82) for differentiating malignancy in 101

Table 4. Diagnostic performance of $> 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$ as the optimal ADC cutoff value alone in the overall cohort, and type 2 and type 3 kinetic curves alone for differentiating benign breast lesions^a

Description	Optimal ADC cutoff ($> 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$)	Type 2 kinetic curve alone	Type 3 kinetic curve alone
Sensitivity, % (95% CI)	84.6 (54.6-98.1)	69.2 (38.6-90.9)	30.8 (9.1-61.4)
Specificity, % (95% CI)	88.5 (76.6-95.6)	44.2 (30.5-58.7)	55.8 (41.3-69.5)
Positive likelihood ratio (95% CI)	7.33 (3.34-16.12)	1.24 (0.80-1.92)	0.70 (0.29-1.66)
Negative likelihood ratio (95% CI)	0.17 (0.05-0.62)	0.70 (0.29-1.66)	1.24 (0.80-1.92)
PPV, % (95% CI)	64.7 (38.3-85.8)	23.7 (16.7-32.4)	14.8 (6.8-29.3)
NPV, % (95% CI)	95.8 (85.7-99.5)	85.2 (70.7-93.2)	76.3 (67.6-83.3)
Accuracy, % (95% CI)	87.7 (77.2-94.5)	49.2 (36.6-61.9)	50.8 (38.1-63.4)

^aHistopathologic diagnosis was confirmed. ADC: apparent diffusion coefficient; CI: confidence interval; NPV: negative predictive value; PPV: positive predictive value.

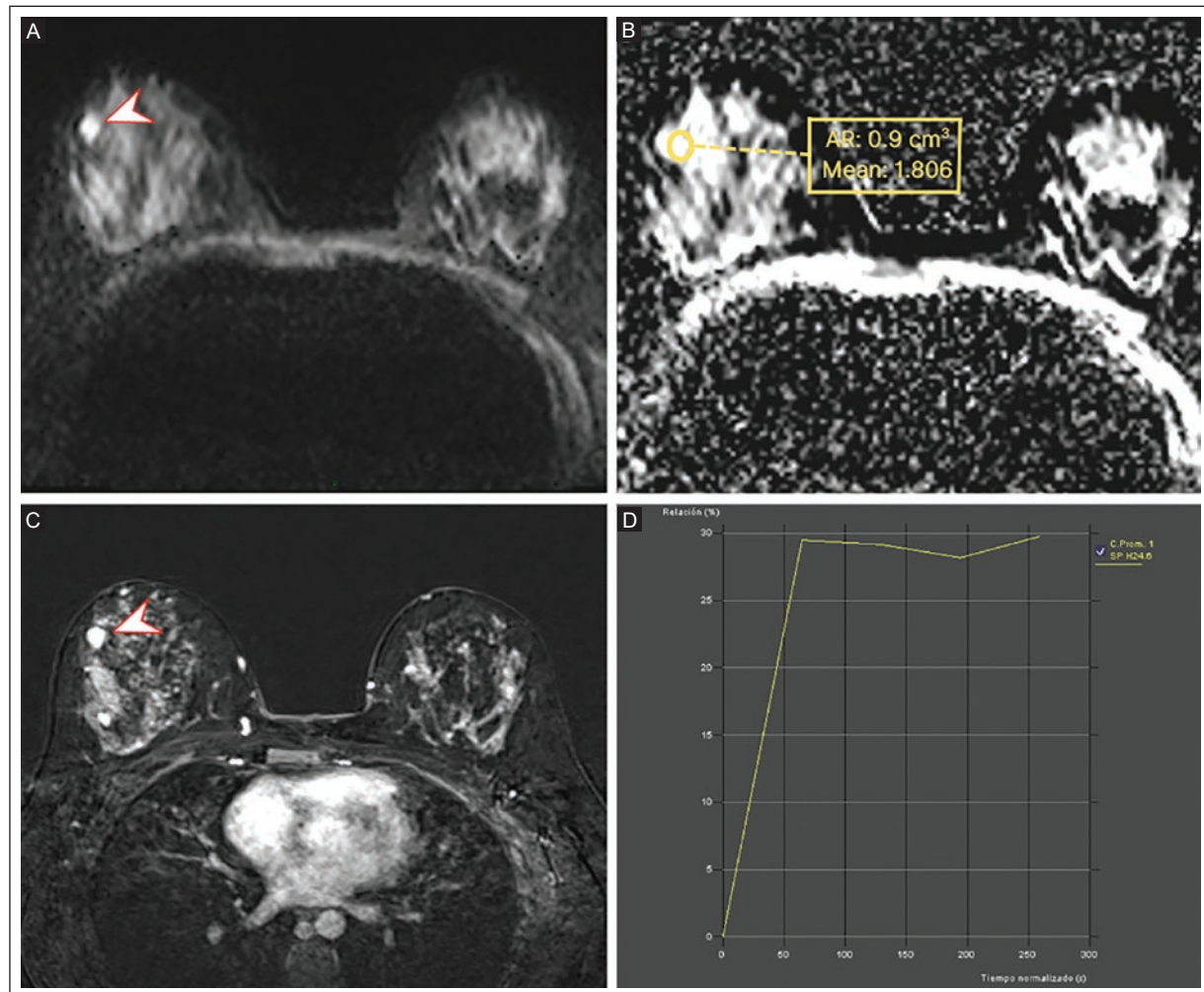


Figure 4. Breast MRI of a 23-year-old woman with a palpable lump, classified as BI-RADS 4a. She underwent gene evaluation due to a family history of breast cancer. **A:** axial DWI sequence of the right breast shows a hyperintense oval mass with no restricted diffusion (arrowhead). **B:** ADC map shows a hyperintense mass. The ROI shows an ADC of $1.806 \times 10^{-3} \text{ mm}^2/\text{s}$ (circle). **C:** first post-contrast T1-weighted sequence shows an oval mass with homogeneous enhancement (arrowhead). **D:** kinetic curve of DCE-MRI shows a plateau pattern (type 2). The histopathologic diagnosis was complex fibroadenoma with sclerosing adenosis. This patient's ADC ($> 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$) was consistent with the optimal cutoff for predicting benignity.

ADC: apparent diffusion coefficient; BI-RADS: Breast Imaging Reporting and Data System; DWI: diffusion-weighted imaging; DCE-MRI: dynamic contrast-enhanced magnetic resonance imaging; MRI: magnetic resonance imaging; ROI: region of interest.

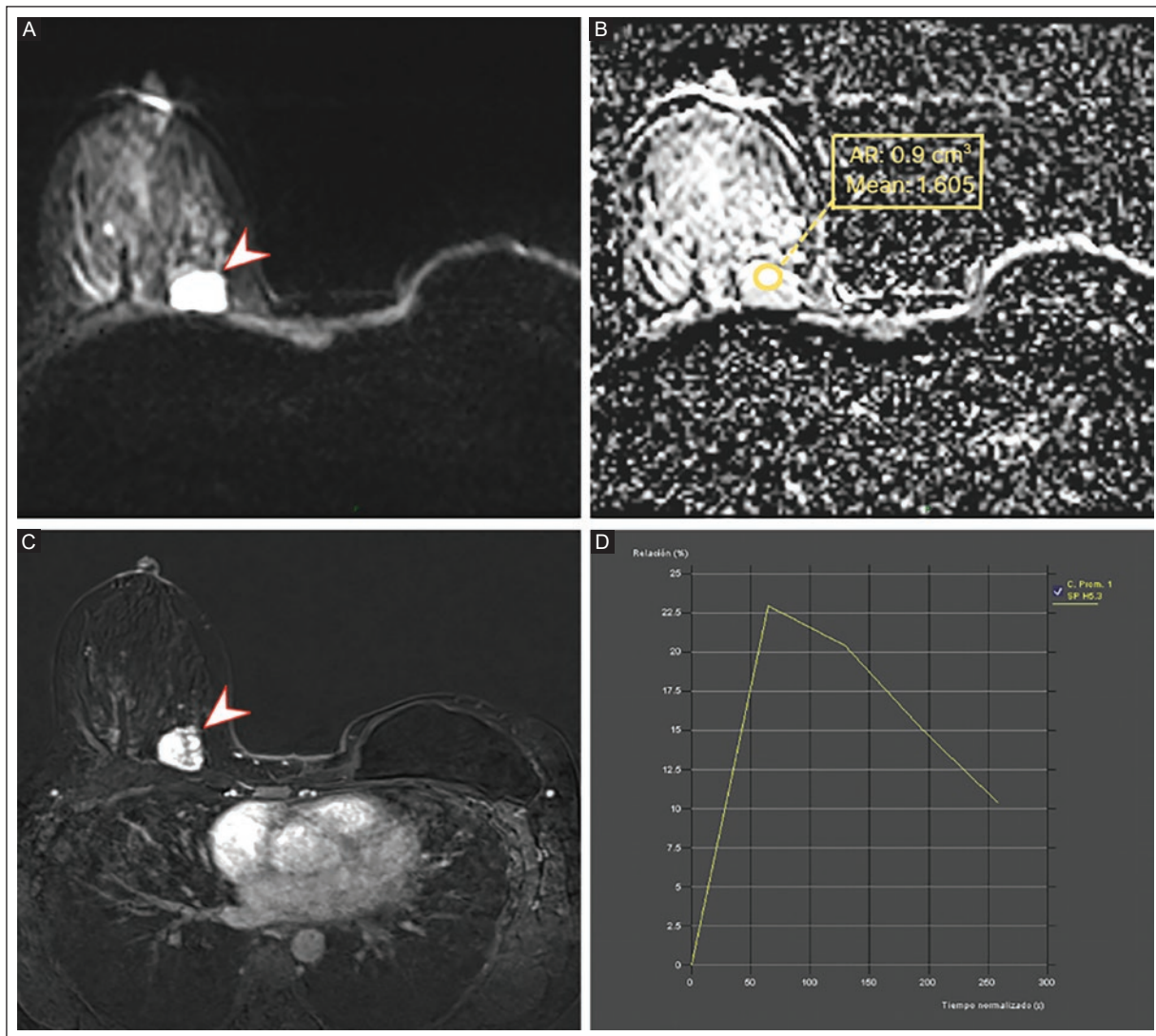


Figure 5. Breast MRI of a 39-year-old woman with a palpable lump at the junction of the inner quadrants of the right breast, classified as BI-RADS 4b. **A:** axial DWI sequence of the right breast shows a hyperintense oval mass with no restricted diffusion (arrowhead). **B:** ADC map with a hyperintense mass. ROI with an ADC value of $1.605 \times 10^{-3} \text{ mm}^2/\text{s}$ (circle). **C:** first post-contrast T1-weighted sequence shows an oval mass with heterogeneous enhancement (arrowhead). **D:** kinetic curve of DCE-MRI shows a washout pattern (type 3). The histopathologic diagnosis was fibroadenoma. Angiogenesis and capillary permeability of dense fibrovascular stroma can simulate malignancy on the kinetic curve. This patient's ADC ($> 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$) was consistent with the optimal cutoff for predicting benignity.

ADC: apparent diffusion coefficient; DWI: diffusion-weighted imaging; BI-RADS: Breast Imaging Reporting and Data System; DCE-MRI: dynamic contrast-enhanced magnetic resonance imaging; MRI: magnetic resonance imaging; ROI: region of interest.

breast lesions. Ulu Öztürk et al.⁸, in a cross-sectional study of 107 breast lesions in 97 Turkish women with a type 2 kinetic curve, reported that an ADC cutoff of $1.000 \times 10^{-3} \text{ mm}^2/\text{s}$ showed a sensitivity of 80% and a specificity of 97% for differentiating malignancy. Tezcan et al.⁹, in a Turkish cross-sectional study of 116 breast lesions with a type 3 kinetic curve, found that an ADC cutoff of $0.89 \times 10^{-3} \text{ mm}^2/\text{s}$ showed a sensitivity of 92%, a specificity of 95%, and an AUC of 0.97 for differentiating malignancy. Youn et al.¹¹ reported in a

cross-sectional study of 240 breast lesions (63 malignant and 177 benign) that a single ADC cutoff of $1.530 \times 10^{-3} \text{ mm}^2/\text{s}$ exhibited similar performance between the screening and diagnosis of malignancy, with no significant difference in sensitivity (88.5% and 94.6%; $p = 0.40$) or reduction in biopsy indication (16.7% and 15.2%; $p = 0.78$). In our study, the optimal ADC cutoff ($\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$) differentiated malignant and benign lesions with a sensitivity of 88.5%, a specificity of 84.6%, an accuracy of 87.7%, and an AUC of 0.956.

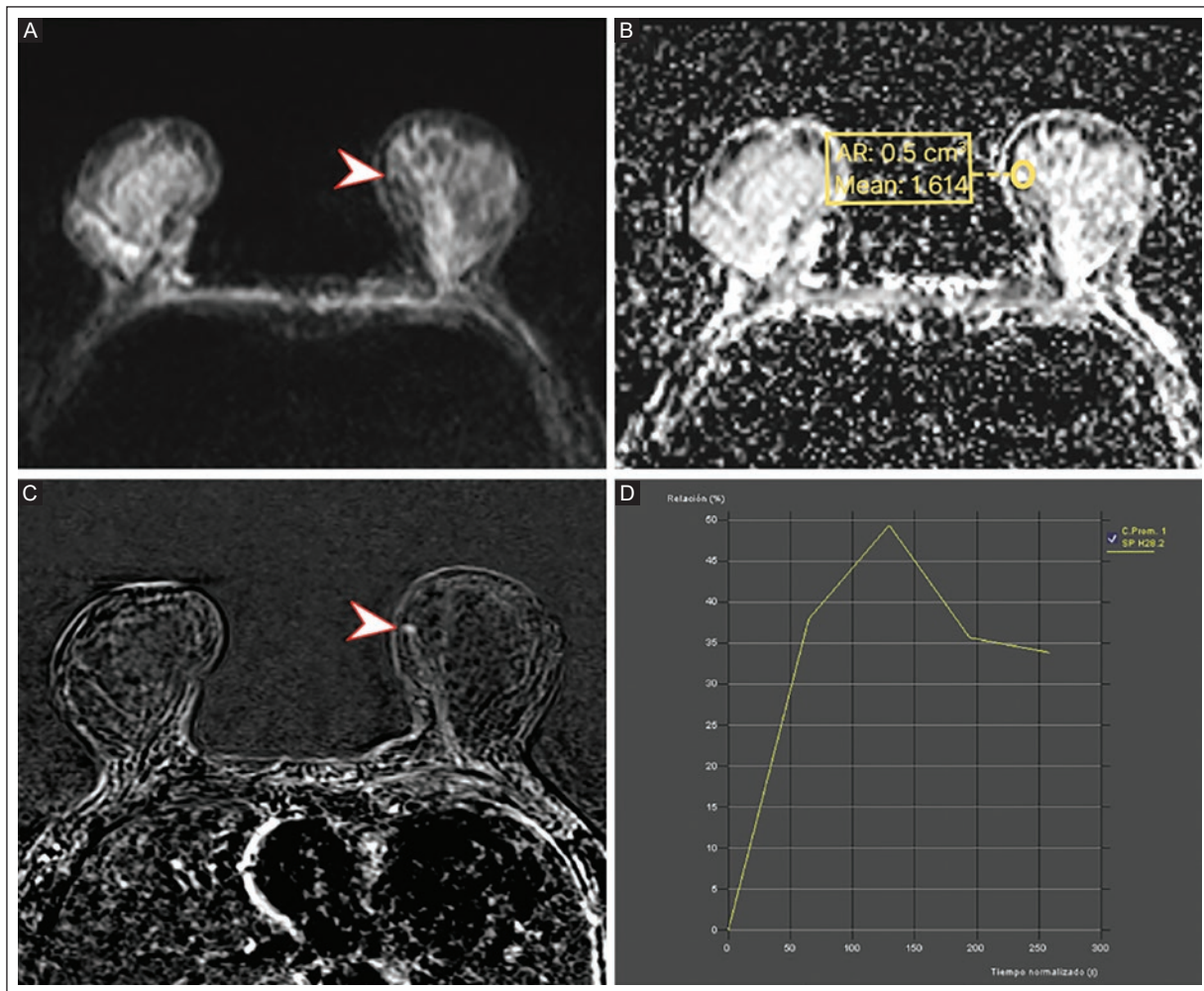


Figure 6. A 63-year-old woman diagnosed with encephalitis underwent a PET/CT scan (not shown), which revealed an incidental finding in the left breast. Mammography and breast ultrasound were performed with no conclusive findings (not shown). The case was categorized as BI-RADS 0, and a breast MRI was requested as a complementary examination. **A:** axial DWI sequence of the breast MRI shows an isointense oval mass with circumscribed margins and no restricted diffusion (arrowhead). **B:** ADC map shows a hyperintense mass. ROI shows an ADC of $1.614 \times 10^{-3} \text{ mm}^2/\text{s}$ (circle). **C:** first post-contrast T1-weighted sequence shows an oval mass with homogeneous enhancement (arrowhead). **D:** kinetic curve of DCE-MRI shows a washout pattern (type 3). The histopathologic diagnosis was usual ductal hyperplasia. This patient's ADC ($> 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$), consistent with the optimal cutoff, showed greater accuracy than the kinetic curve or PET/CT for predicting benignity.

ADC: apparent diffusion coefficient; BI-RADS: Breast Imaging Reporting and Data System; DWI: diffusion-weighted imaging; DCE-MRI: dynamic contrast-enhanced magnetic resonance imaging; MRI: magnetic resonance imaging; PET/CT: positron emission tomography/computed tomography; ROI: region of interest.

Diagnostic performance was comparable to or superior to that reported in populations with a type 2 kinetic curve⁸ and a type 3 curve⁹ and higher than that reported in a population including both curve types¹⁰, suggesting that the ADC is an independent parameter from the kinetic pattern of breast tissue. Our results suggest that a single ADC cutoff of $\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$, independent of kinetic curve type (2 or 3), is useful for differentiating malignant from benign lesions.

ADC has been proposed for reclassifying suspicious lesions on DCE-MRI as benign, in order to reduce unnecessary biopsies without missing malignant breast

lesions¹². Baltzer et al.¹², in a German cross-sectional study of 150 breast lesions (73 malignant and 77 benign), reported that an ADC $> 1.400 \times 10^{-3} \text{ mm}^2/\text{s}$ showed a sensitivity of 100%, and a specificity of 80.5% for predicting benign breast lesions. Fujiwara et al.⁷, in a Japanese, single-center cross-sectional study of 519 breast masses (47 benign, 472 malignant), reported that an ADC of $1.015 \times 10^{-3} \text{ mm}^2/\text{s}$ showed a sensitivity of 96%, a specificity of 71%, and an AUC of 0.858 in differentiating benign and malignant lesions. In our study, an ADC $> 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$ differentiated benign and malignant lesions with a sensitivity of

84.6%, a specificity of 88.5%, and an accuracy of 87.7%. Our optimal ADC ($> 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$) performed better specificity than that reported by Fujiwara et al.⁷ (71%) and was comparable to the report by Baltzer et al.¹² (80.5%). However, unlike these studies, which integrated the kinetic curve type into their analysis, our study assessed only the diagnostic performance of the ADC for benign lesions, independent of the kinetic curve type, to reclassify benignity, even in the subgroup with type 3 kinetic curves, which have the highest diagnostic ambiguity. The optimal ADC that we propose may be useful in reducing unnecessary biopsies, independent of kinetic curve evaluation.

The kinetic curve alone has limited discriminative capacity because of overlapping enhancement patterns between benign and malignant lesions, particularly for the type 2 curve⁵. Kul et al.¹³, in a cross-sectional study of 84 Turkish women, reported that the combined evaluation of morphology on breast MRI and type 1, 2, or 3 kinetic curves showed a sensitivity of 97.9% and a specificity of 75.7% for predicting malignant lesions, whereas an ADC of $0.920 \times 10^{-3} \text{ mm}^2/\text{s}$, regardless of curve type, showed a sensitivity of 91.5% and an increased specificity of 86.5%. In our study, type 2 and 3 kinetic curves, independent of ADC value, showed low diagnostic accuracy (49.2% to 50.8%) for differentiating malignancy from benignity, in contrast to the optimal ADC value, which showed an accuracy of 87.7%. The diagnostic ambiguity of kinetic curve assessment, particularly for the type 2 curve, can be resolved by combining it with an evaluation of the optimal ADC.

The strengths of our study are a standardized image acquisition protocol and histopathological confirmation as the reference standard for all evaluated breast lesions. The limitations include its retrospective design, small sample size, and single-center setting, which limit generalization to other equipment or protocols. In addition, the proposed optimal ADC cutoff was not validated in an independent cohort.

CONCLUSION

The optimal ADC cutoff ($\leq 1.099 \times 10^{-3} \text{ mm}^2/\text{s}$) showed high diagnostic performance for differentiating malignant breast lesions from benign lesions, regardless of kinetic curve type (2 or 3). The proposed optimal ADC value should be validated in multicenter studies with larger patient populations before its clinical application is considered.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the World Medical Association and the Declaration of Helsinki (1964) and subsequent amendments.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely collected and anonymized clinical data; therefore, individual informed consent was not required. Relevant ethical recommendations have been followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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Percutaneous transhepatic cholangioscopy reveals epithelial changes in the biliary tract induced by drainage catheters

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ABSTRACT

Percutaneous transhepatic cholangioscopy (PTC) is an endoscopic technique that directly visualizes the biliary epithelium and enables targeted biopsy acquisition to evaluate indeterminate biliary lesions and manage benign and malignant biliary diseases. Its diagnostic and therapeutic applications continue to expand. This case series describes PTC-observed epithelial changes associated with biliary drainage catheters and their histopathologic correlation in four patients with benign biliary disease. Device dwell times ranged from 21 to 390 days. PTC demonstrated diffuse mucosal erythema, marked hyperemia, villous-like papillary projections, and exophytic polypoid granulation tissue in areas of biliary device contact. Targeted biopsies revealed acute and chronic inflammation, exuberant granulation tissue, and subepithelial fibrosis with no evidence of atypia or dysplasia, providing histopathologic correlation with the PTC findings. These changes suggest that exposure to biliary drainage devices may be associated with localized epithelial abnormalities. PTC enabled direct assessment of the biliary epithelium and targeted tissue sampling, allowing endoscopic findings to be correlated with microscopic histopathologic alterations. This approach helps evaluate biliary mucosal abnormalities and characterize epithelial changes associated with indwelling biliary devices. Combining cholangioscopy visualization with histologic assessment may improve understanding of device-related mucosal responses and help distinguish reactive changes from lesions that require further diagnostic evaluation and management.

Keywords: Percutaneous transhepatic cholangioscopy. Biliary drainage. Biliary epithelium. Benign biliary disease.

INTRODUCTION

Minimally invasive management of benign biliary disease, including strictures secondary to surgical injury, bilioenteric anastomotic strictures, and complex lithiasis, often relies on prolonged use of biliary drainage catheters¹. Maintaining biliary duct patency promotes progressive biliary tract remodeling² and avoids complex surgical interventions². However, foreign bodies within the biliary tract may induce local changes due to mechanical friction, bacterial colonization, biofilm formation, and persistent inflammation^{1,3,4}.

Conventional imaging modalities such as cholangiography, computed tomography, and magnetic resonance imaging allow assessment of duct patency and detection of strictures or lithiasis but are limited in their ability to evaluate the biliary epithelium in detail⁵⁻⁷. In this context, percutaneous transhepatic cholangioscopy (PTC), an endoscopic technique that enables direct intraluminal visualization of the biliary epithelium, allows detailed mucosal assessment, targeted biopsy acquisition, and therapeutic interventions such as electrohydraulic lithotripsy (EHL), which fragments biliary stones with

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high-energy hydraulic shock waves under direct endoscopic visualization^{5,8-10}. Although the lithogenic effect of biliary devices has been described, the morphologic changes induced in the biliary epithelium have been poorly characterized, particularly through direct evaluation^{1,3,9,10}. This case series of four patients with benign biliary disease describes biliary epithelial changes associated with exposure to biliary drainage catheters, evaluated by PTC and histopathology.

MATERIAL AND METHODS

This case series was conducted in the Department of Interventional Radiology and Endovascular Therapy at Hospital General de Mexico “Dr. Eduardo Liceaga” in Mexico City, Mexico, from January 2022 to December 2025. The study included four adult patients with benign biliary disease who received biliary drainage catheters. Data were obtained during routine medical care; therefore, informed consent was waived. The study was approved by the institutional Ethics and Research Committee.

Study development and variables

Information from clinical records included the following variables: sex, age, clinical diagnosis, type of biliary device, device exposure time (days), PTC findings, and histopathology report. Resolve® biliary drainage catheters (Merit Medical, South Jordan, UT, USA) were used for biliary drainage. Device dwell time was defined as the cumulative interval from biliary device placement to PTC.

Imaging acquisition and analysis protocol

All procedures were performed under sterile conditions with continuous fluoroscopic guidance in an angiography suite using a digital fluoroscopy system (Artis with PURE® technology, Siemens Healthineers, Forchheim, Germany). Percutaneous biliary access was obtained and previously placed biliary drainage catheters were removed. An initial cholangiogram was performed to assess biliary anatomy, residual strictures, filling defects, and ductal wall irregularities.

PTC examination was subsequently performed using a digital cholangioscope (SpyGlass™ Discover, Boston Scientific, Marlborough, MA, USA) with an outer diameter of 10.8 Fr, a working length of 65 cm, a 1.2-mm working channel, and four-way deflection. The cholangioscope was introduced through the percutaneous

access under continuous saline irrigation to optimize visualization. A systematic evaluation of the intrahepatic and extrahepatic bile ducts was performed, with particular attention to areas of prolonged contact with biliary drainage catheters. The biliary epithelium was systematically assessed for color, surface architecture, hyperemia, mucosal irregularity, mural thickening, papillary projections, and polypoid lesions. Targeted biopsies were obtained under direct endoscopic visualization with biopsy forceps. Cholangioscopy findings were documented with digital photographs and correlated with histopathology results.

Biliary stones requiring fragmentation were treated under direct endoscopic visualization using EHL (AUTOLITH® Touch System), which generates high-energy hydraulic shock waves to fragment stones unamenable to conventional extraction techniques with a single-use bipolar EHL probe compatible with SpyGlass™ (Northgate Technologies Inc., Boston Scientific, Marlborough, MA, USA). Stone fragments were subsequently extracted under fluoroscopic and cholangiographic guidance until complete ductal clearance and satisfactory biliary patency were confirmed. An interventional radiologist (CSR) with 5 years of experience in percutaneous biliary interventions performed all procedures.

RESULTS

Clinical diagnoses, biliary devices, device dwell times, PTC findings, and histopathologic findings of four patients are presented below.

Case 1

A 52-year-old woman with left hepatolithiasis and large choledocholithiasis underwent management with an internal-external (mixed) percutaneous transhepatic biliary drainage catheter with side holes, positioned for external and duodenal drainage after two failed endoscopic retrograde cholangiopancreatography (ERCP) attempts; device dwell time was 218 days. Percutaneous and intraprocedural cholangiography demonstrated filling defects in the left hepatic duct and common bile duct, consistent with hepatolithiasis and choledocholithiasis (Figures 1A, B). PTC revealed diffuse mucosal erythema, marked hyperemia, and friable, villous-like papillary projections over a nodular base in the distal common bile duct (Figures 1C, D). Histopathology of targeted biopsies showed ulcerated mucosa with acute

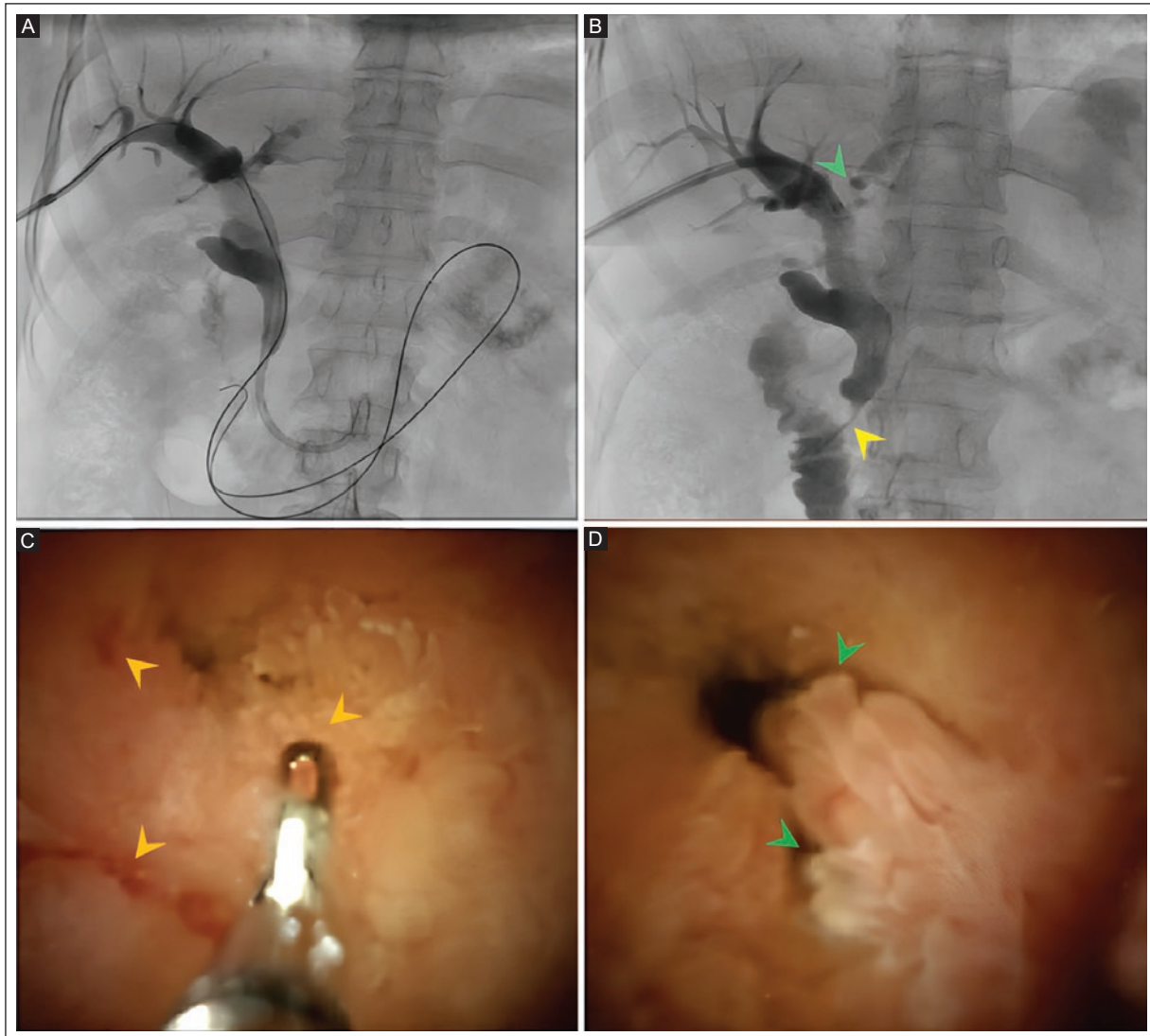


Figure 1. A 52-year-old woman with left hepatolithiasis and a large choledocholithiasis, managed with an internal-external (mixed) percutaneous transhepatic biliary catheter; the device dwell time was 218 days. **A:** percutaneous cholangiography and **B:** intraprocedural cholangiography during PTC showing ductal dilation with filling defects in the left hepatic duct (green arrowhead) and the distal common bile duct (orange arrowhead). **C:** PTC visualization during targeted tissue sampling with biopsy forceps (*SpyBite*) shows diffuse mucosal erythema, marked hyperemia, and friability over a nodular mucosal base (orange arrowheads). **D:** detailed PTC view reveals abnormal surface architecture with friable, villous-like papillary mucosal projections (green arrowheads) and surrounding erythema at the site of chronic catheter contact.

PTC: percutaneous transhepatic cholangioscopy.

inflammation, superficial bacterial colonization, recent hemorrhage, and subepithelial fibrosis.

Case 2

A 31-year-old woman with a surgical bile duct injury managed with hepaticojejunostomy and associated bilateral hepatolithiasis underwent bilateral percutaneous biliary drainage catheter placement; device dwell time was 210 days. Transhepatic cholangiography

demonstrated filling defects in both hepatic ducts (Figures 2A, B). PTC revealed a well-circumscribed, exophytic, whitish polypoid mass at the hepatic duct confluence (anastomotic site) and focal mucosal denudation in the left hepatic duct (Figures 2C, D). After targeted polypectomy and biopsy, histopathologic examination confirmed polypoid granulation tissue with mixed acute and chronic inflammatory infiltrates at the hepaticojejunostomy site and exuberant granulation tissue within the left hepatic duct, with no evidence of malignancy.

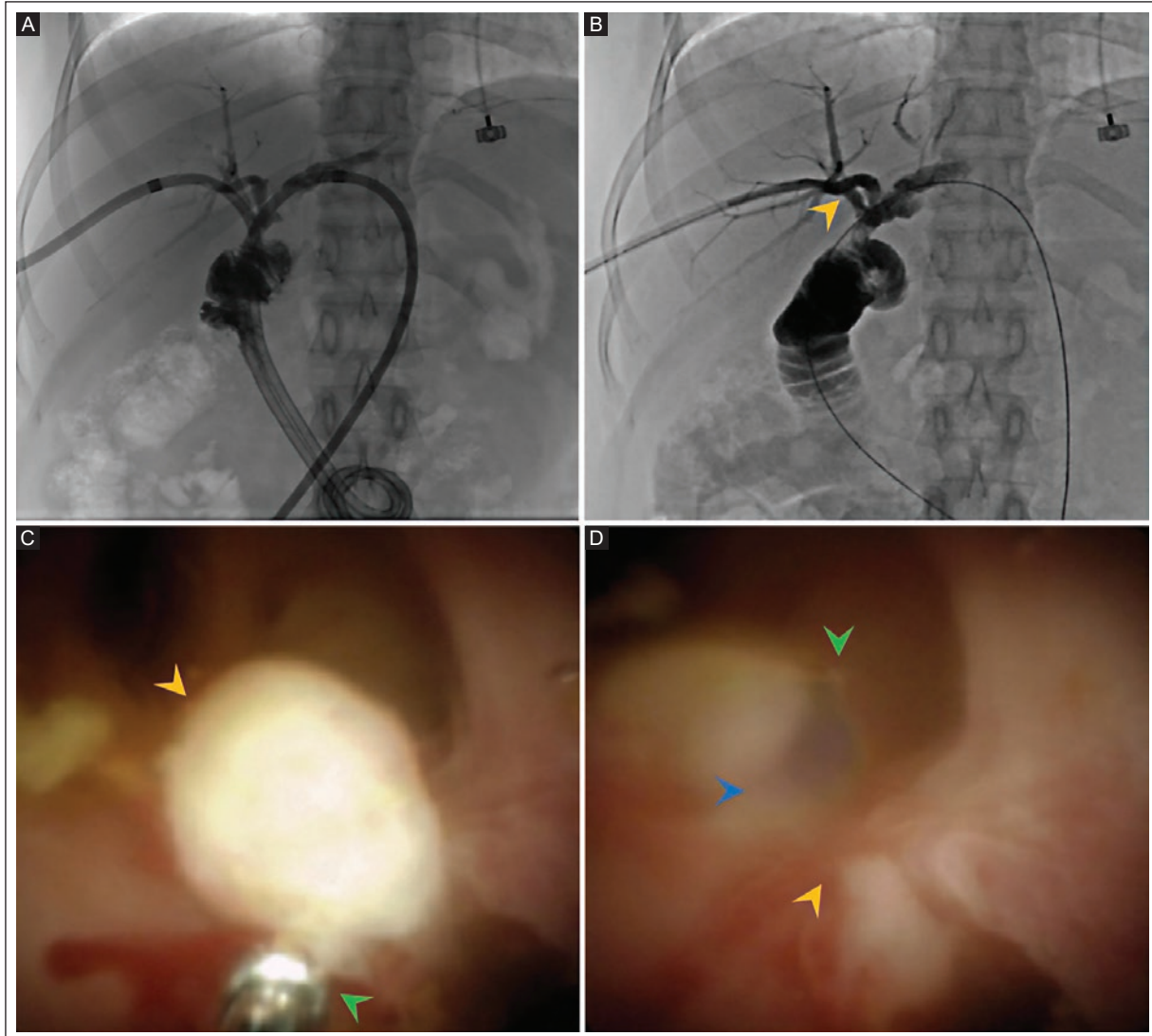


Figure 2. A 31-year-old woman with postsurgical biliary injury after hepaticojunostomy and bilateral hepatolithiasis, treated with bilateral percutaneous biliary catheters; the dwell time of the catheters was 210 days. **A:** percutaneous cholangiography and **B:** intraprocedural cholangiography during PTC, showing the use of an EHL probe for stone fragmentation (orange arrowhead). **C:** PTC image at the hepatic duct confluence shows a well-circumscribed, exophytic, whitish polypoid mass (orange arrowhead) at the site of chronic catheter contact, identified during targeted polypectomy and tissue sampling with endoscopic forceps (*SpyBite*) (green arrowhead). **D:** Post-polypectomy PTC evaluation of the left hepatic duct mucosa shows localized mucosal denudation (orange arrowhead), marginal hyperemia (green arrowhead) and altered endoluminal contours (blue arrowhead).

EHL: electrohydraulic lithotripsy; PTC: percutaneous transhepatic cholangioscopy.

Case 3

A 49-year-old man with prior cholecystectomy and recurrent biliary obstruction, previously managed endoscopically without improvement, underwent internal-external percutaneous transhepatic biliary drainage; the device dwell time was 390 days. Percutaneous cholangiography showed persistent ductal dilation and irregular filling defects in the left intrahepatic biliary tract (Figures 3A, B). PTC demonstrated diffuse mucosal erythema, marked hyperemia, and villous-like papillary

mucosal hyperplasia with a fine nodular surface architecture (Figures 3C, D). Histopathologic examination showed mild mixed acute and chronic inflammatory infiltrates and stromal edema, corresponding to the endoluminal papillary mucosa observed on PTC, with no evidence of cellular atypia or dysplasia.

Case 4

A 35-year-old man with left hepatolithiasis, multiple failed ERCP attempts, and a history of recurrent

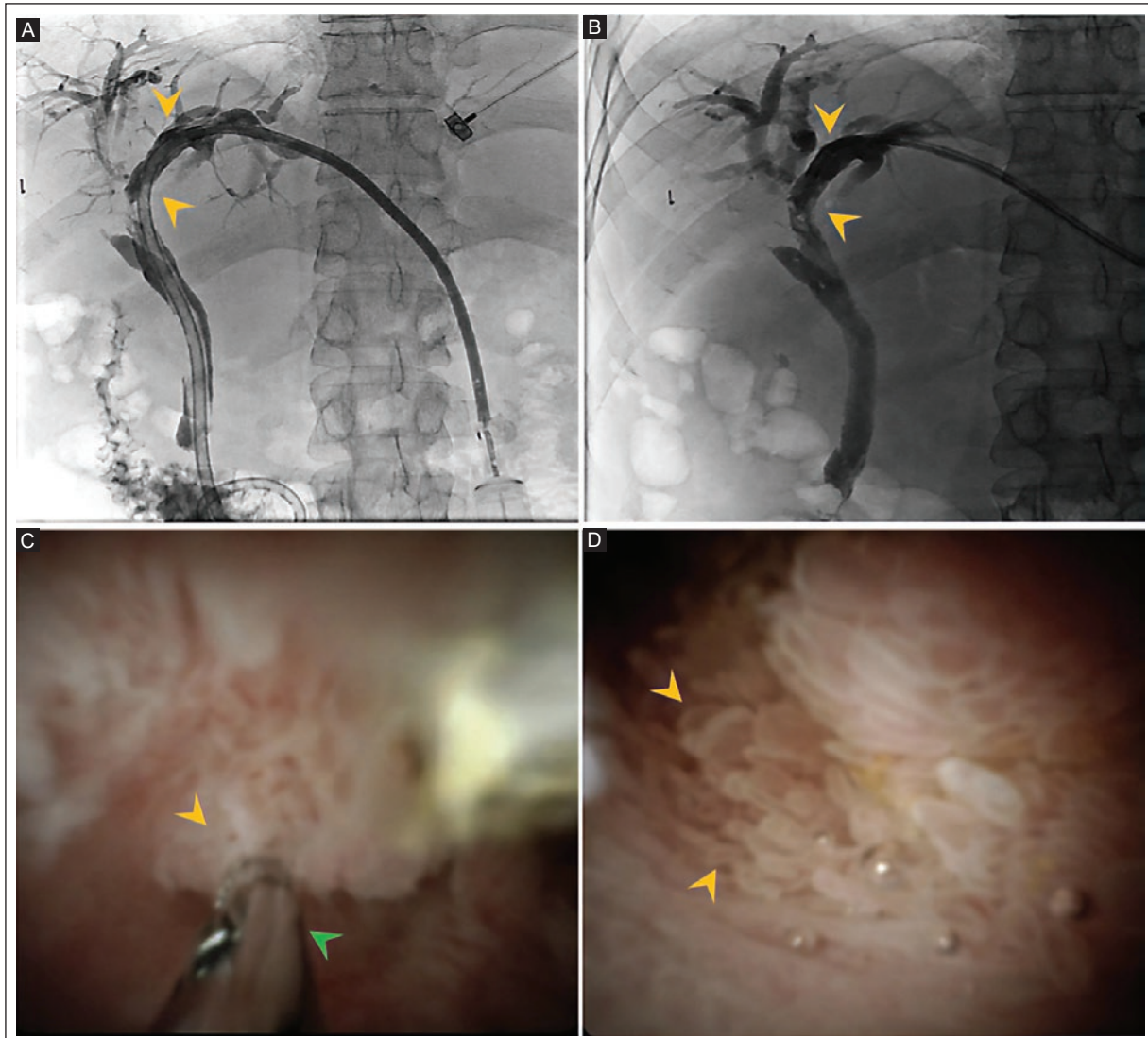


Figure 3. A 49-year-old man with recurrent post-cholecystectomy biliary obstruction managed with an internal-external (mixed) percutaneous biliary catheter; the catheter dwell time was 390 days. **A:** percutaneous cholangiography, and **B:** intraprocedural percutaneous cholangiography during PTC, showing post-cholecystectomy biliary anatomy, with persistent dilation and irregular filling defects in the left intrahepatic biliary tract (orange arrowheads). **C:** direct PTC visualization shows diffuse mucosal erythema, hyperemia, and highly friable, villous-like papillary projections at the catheter contact site (orange arrowhead), captured during targeted tissue sampling with endoscopic forceps (*SpyBite*) (green arrowhead). **D:** high-magnification endoluminal PTC view highlighting prominent villous-like papillary mucosal hyperplasia with a fine nodular surface architecture (orange arrowheads), induced by chronic mechanical device contact.

PTC: percutaneous transhepatic cholangioscopy.

cholangitis was managed with a percutaneous biliary drainage catheter with a dwell time of 21 days. Fluoroscopic imaging showed obstructive left hepatolithiasis (Figures 4A, B). PTC with EHL stone fragmentation and a targeted biopsy of an irregular, hyperemic mucosal area in the distal common bile duct were performed (Figures 4C, D). Histopathologic examination of the targeted biopsy demonstrated nonspecific chronic inflammatory changes with irregular surface architecture, correlating with the irregular hyperemic mucosal

appearance observed on PTC, with no evidence of atypia. Given the patient's history of recurrent cholangitis, these findings could not be attributed solely to device exposure.

DISCUSSION

In this case series, PTC consistently identified mucosal abnormalities in the biliary epithelium of four patients with biliary percutaneous drainage catheters.

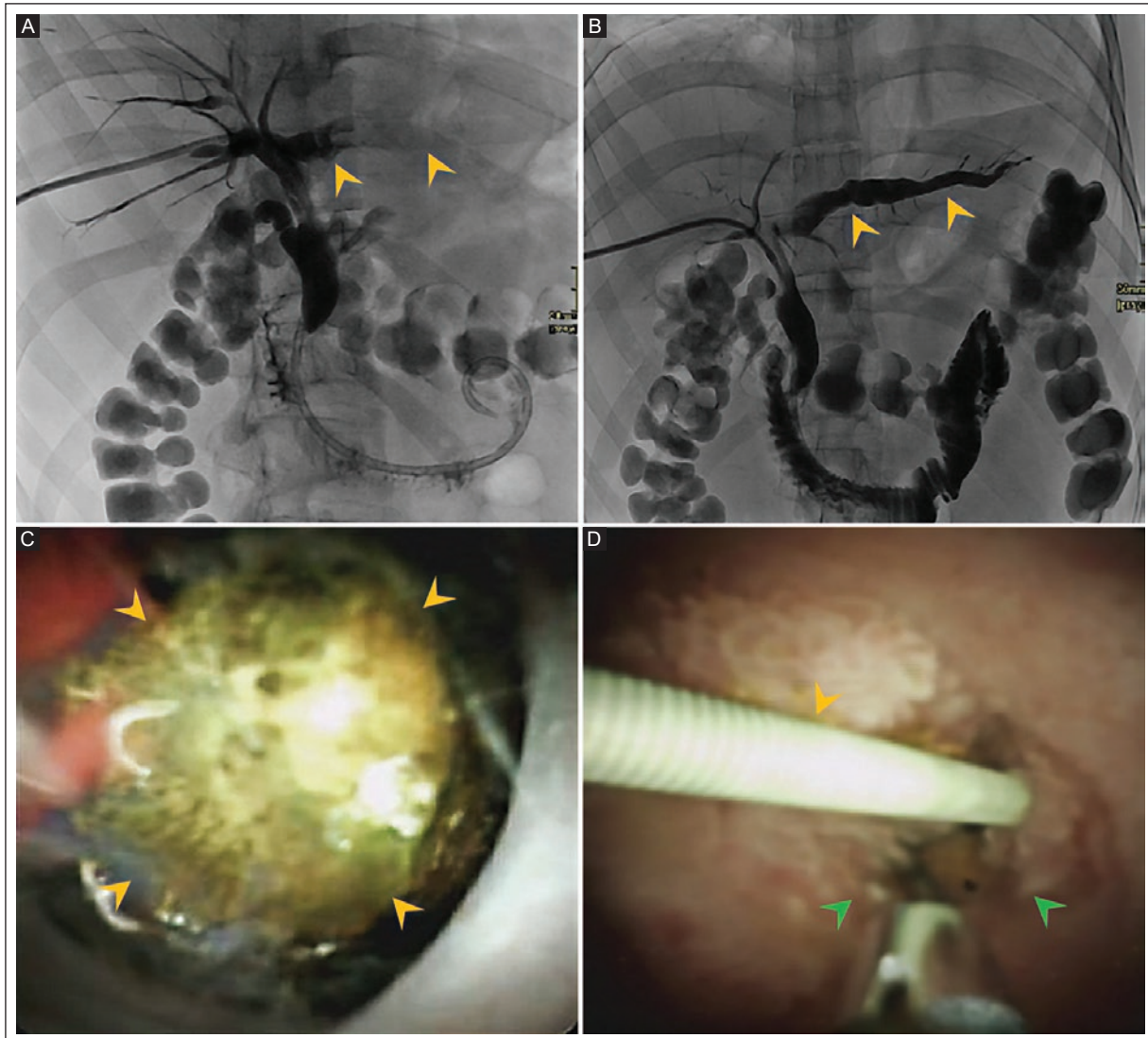


Figure 4. A 35-year-old man with left hepatolithiasis and recurrent cholangitis, managed with a percutaneous transhepatic biliary drainage catheter; the device dwell time was 21 days. **A-B:** percutaneous cholangiography images demonstrating obstructive left hepatolithiasis, with the percutaneous drainage catheter in place (orange arrowheads). **C:** PTC visualization shows a large, impacted, dark-pigmented biliary calculus (orange arrowheads) causing partial luminal occlusion and surrounding hyperemic ductal mucosa. **D:** PTC view during application of an EHL probe (orange arrowhead) under direct endoscopic control for stone fragmentation, with targeted biopsy sampling of an irregular, erythematous mucosal segment in the distal common bile duct (green arrowheads).

EHL: electrohydraulic lithotripsy; PTC: percutaneous transhepatic cholangioscopy.

Histopathologic examination revealed chronic inflammation and subepithelial fibrosis with no evidence of dysplasia or malignancy, confirming the reactive, non-neoplastic nature of these abnormalities. These findings demonstrate that contact with biliary devices induces epithelial mucosal alterations. Direct endoluminal visualization and targeted biopsy sampling via PTC allow precise characterization of these device-induced epithelial changes.

The biliary epithelium undergoes tissue remodeling in response to mechanical irritation, foreign body

reactions, and local bacterial colonization, with endobiliary devices promoting persistent inflammation, mucosal erosion, and reactive tissue changes^{1,3,4,9,10}. Contact with synthetic catheter materials disrupts tight junction integrity in the cholangiocyte layer, triggering a sustained cascade of pro-inflammatory cytokines, fibroblast recruitment, and extracellular matrix deposition^{5,9}. In our case series, direct PTC examination showed papillary projections and hyperemic, irregular mucosal changes associated with biliary device dwell times ranging from 21 to 390 days. Histopathologic examination

demonstrated granulation tissue, chronic inflammatory infiltrate, and subepithelial fibrosis. Notably, even in the patient with a short exposure time of 21 days, mucosal alterations were already present, highlighting the rapid onset of tissue reactivity after catheter insertion. Alabraba et al.¹¹ demonstrated the feasibility of PTC and lithotripsy for duct clearance, noting that surgical sutures and indwelling devices promote cholestasis and foreign body reactions. Similarly, Ghazle et al.¹² reported ultrasound wall thickening secondary to stent-induced cholangitis (dwell time 9 days to 5 months), whereas Hausegger et al.¹³ observed complete mucosal denudation followed by submucosal inflammation and fibrogranulomatous incorporation without mucosal hyperplasia in malignant biliary obstructions. The difference between our findings and those of Hausegger et al.¹³ likely stems from differences in underlying pathophysiology, as our study evaluated benign biliary conditions, in which cellular regenerative capacity and proliferative response remain preserved. Furthermore, prolonged catheter indwelling and bacterial biofilm formation serve as a continuous nidus for low-grade infection, exacerbating stromal hyperplasia and mural remodeling^{9,10,14}. Contact with biliary devices appears to trigger a continuous spectrum of benign epithelial hyperplasia and stromal fibrosis that must be distinguished from true biliary ductal pathology.

Transhepatic cholangiography, computed tomography, and magnetic resonance imaging have limited ability to characterize mucosal abnormalities in patients with chronic biliary interventions who show nonspecific ductal wall irregularities, mural thickening, or filling defects^{6,7,14}. Our findings highlight that chronic mechanical contact and biofilm formation from indwelling catheters induce benign, reactive mucosal changes, such as villous-like papillary hyperplasia and polypoid granulation tissue, that can mimic ductal pathology. In this context, PTC plays a crucial diagnostic and therapeutic role. By moving beyond mere catheter exchange or fluoroscopic intervention, the interventional radiologist uses high-definition endoluminal visualization and targeted biopsy to definitively rule out dysplasia, preventing misdiagnosis and avoiding unnecessary, high-risk surgical resections. In our case series, targeted biopsies obtained under direct PTC visualization successfully ruled out dysplasia or malignancy in all cases with marked papillary changes. As highlighted by Alabraba et al.¹¹ and Ren et al.¹⁴, percutaneous endobiliary intervention offers a safe, practical, and highly effective alternative for ductal management, stricture recanalization, and stone clearance when conventional ERCP is unfeasible

because of surgically altered anatomy or severe luminal narrowing. PTC provides a direct endoluminal approach that overcomes standard imaging limitations by combining interventional radiology access with high-definition endoscopic visualization, enabling high-resolution mucosal assessment, targeted tissue sampling, and complex therapeutic procedures such as EHL or laser lithotripsy under direct vision^{5,8,14}. Precise differentiation among retained lithiasis, fibrinous debris, and reactive papillary mucosa prevents incomplete ductal clearance and guides tailored therapeutic interventions¹⁴. Therefore, PTC is an essential diagnostic and therapeutic adjunct when evaluating persistent mucosal irregularities or strictures in patients with biliary drainage catheters, ensuring diagnostic confidence and optimizing overall procedural success.

The main strength of this case series is real-time, high-resolution cholangioscopy with a histopathologic correlation, providing direct qualitative evidence of device-induced epithelial changes. This study has several limitations that must be acknowledged. First, baseline cholangioscopic evaluations were not available before device placement; thus, preexisting mucosal abnormalities cannot be excluded. Second, all patients had underlying benign biliary conditions, such as hepatolithiasis, recurrent cholangitis, or postoperative strictures, which independently induce chronic mucosal inflammation and ductal remodeling¹⁴. Consequently, these findings should be interpreted as mucosal alterations associated with biliary device exposure rather than as definitive evidence of a causal relationship. Third, the descriptive design, small sample size, and lack of an unexposed control group preclude definitive conclusions about the exact temporal progression and reversibility of these changes after catheter removal.

CONCLUSION

In our case series, prolonged exposure to endobiliary drainage catheters was associated with benign, reactive epithelial changes, including papillary projections and mucosal hyperplasia. PTC enables direct identification, detailed characterization, and targeted biopsy of these device-induced alterations, confirming their benign nature and supporting diagnostic confidence. Integrating PTC and targeted biopsy into the management of benign biliary disease optimizes diagnostic accuracy, prevents unnecessary surgical exploration, and guides tailored therapeutic interventions^{11,14}. Further prospective studies with larger cohorts and longitudinal

follow-up are needed to clarify the natural history of device-associated biliary epithelial changes.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the World Medical Association and the Declaration of Helsinki (1964) and subsequent amendments.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely collected and anonymized clinical data; therefore, individual informed consent was not required.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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Virtual monitors and desktops: a pictorial essay on what radiodiagnosis could become

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ABSTRACT

Radiology has evolved with technological innovation, and virtual reality (VR) is an emerging tool in diagnostic imaging workflows. This pictorial essay explores VR-based workstations and virtual monitors in radiology. It describes how immersive environments may complement conventional reading rooms. VR head-mounted displays (HMDs) enable customizable three-dimensional workspaces where radiologists can view multiple virtual monitors, modify spatial layouts, and collaborate remotely in real time. Current applications, including web-based picture archiving and communication system (PACS) platforms and integrated remote desktop functionality, demonstrate the utility of image visualization and interpretation in immersive environments. Potential advantages include workspace flexibility, portability, reduced physical space requirements, and remote collaboration. However, important limitations include display resolution, luminance performance, field of view, image legibility, visual fatigue, and limited validation for diagnostic interpretation. Although preliminary evidence suggests comparable diagnostic performance between VR and conventional monitors for selected imaging tasks, available studies are limited. As VR technology evolves, immersive workstations may become complementary tools within radiology workflows and teleradiology environments. Further research is needed to assess diagnostic accuracy, ergonomic effects, workflow efficiency, user comfort, and cost-effectiveness before broader clinical implementation, and to establish appropriate technical standards for safe, reliable use in routine clinical practice.

Keywords: Virtual reality. Radiology. Computer peripherals. Teleradiology.

INTRODUCTION

Medicine is an ever-changing field that has undergone many transformational shifts throughout its development¹. One such transformation is the unprecedented advancement of cutting-edge technologies such as nanotechnology, genomics, robotics, three-dimensional (3D) bioprinting, telemedicine, and virtual reality (VR)^{1,2}. The Oxford English Dictionary defines VR as “a computer-generated simulation of a lifelike environment that can

be interacted with in a seemingly real or physical way by a person”³. VR uses computer-simulated environments that receive input from the headset’s own media or from physical desktops, making it possible to experience and interact with 3D workstations. At its most basic level, VR headsets include hardware capable of tracking eye and head movements to position the user within their 3D world⁴. VR headsets include head-mounted displays (HMDs) and motion controllers; within these VR-3D environments, users can move around,

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Figure 1. Meta Quest 2 VR headset showing the HMD and straps on the left and the left and right arm controllers on the right (Creative Commons Attribution 2.0 Generic License)⁸. The same Meta Quest 2 model was used to capture the screenshots for all images in this article.

HMD: head-mounted display; VR: virtual reality.

point at items, move items, resize screens, and create their own desktops for personal use⁵. Although VR use in radiology is limited, research articles have reported its use for preoperative surgical planning,⁶ and it has also been used to teach anatomy to medical students⁷.

A VR radiology workstation replaces or supplements physical monitors with virtual screens projected within an immersive digital environment. This setup relies on an HMD, a specialized VR headset that features dual high-resolution microdisplays positioned directly in front of each eye to generate depth perception and binocular stereopsis. Modern diagnostic HMDs use high-fidelity stereoscopic cameras to capture the surrounding environment in real time and project it back to the user via video passthrough. To ensure visual stability, this process must maintain low passthrough video latency – the microscopic time delay (in milliseconds) between the physical capture of an external event and its rendering on the internal HMD screen – to prevent sensory misalignment and motion-related nausea during prolonged reading sessions.

Furthermore, advanced spatial tracking allows the radiologist to interact with virtual monitors across multiple degrees of freedom, corresponding to the independent

physical axes of movement (translation along and rotation around the X, Y, and Z axes) tracked by hardware sensors. This allows seamless shifts in physical posture and fluid workspace personalization^{6,7}. Figure 1 shows a Meta Quest 2 VR headset with HMD and straps; on the right, both arm controllers are shown (free license, Creative Commons Attribution 2.0 generic license image)⁸. The same Meta Quest 2 model was used to capture the screenshots for all images in this article. Given the novelty and rapidly evolving nature of VR workstation technology in radiology, this pictorial essay provides a conceptual and illustrative overview of currently available technologies and emerging applications. Publications were selected for their relevance to immersive workstations, VR display systems, and radiologic workflow applications.

THE BLUE ROOM: AN OLD BUT RELIABLE STAPLE

Traditional radiology reading rooms required little design consideration. They were often located in basements or dark corners, where radiologists viewed films on banks of light boxes with little concern for an optimal

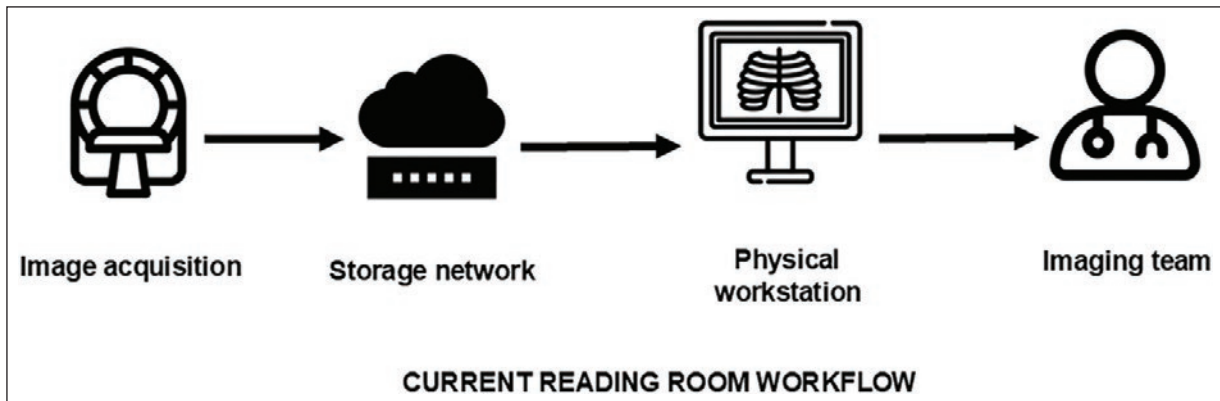


Figure 2. Representation of the radiology blue room. The schematic image shows the sequential flow of diagnostic data from image acquisition to network storage transmission, physical workstation display, and final assessment by the imaging team.

work environment⁹. Figure 2 represents the current radiology blue room. Reading rooms are held to higher standards as fast, precise results are demanded. They should accommodate technology such as high-end, medical-grade monitors and hardware capable of running analysis software and the Picture Archiving and Communication System (PACS). More importantly, they must meet radiologists' physical and visual needs, considering key elements such as acoustics, spatial enclosures, cable management, comfort factors, and suitable lighting⁸. Notably, none of these reading room characteristics have been considered for future-proofing against new technologies like VR. Therefore, some modifications may be required to accommodate the "standing" modalities of virtual desktops, while "sitting" desktops may work from the outset. Figure 3 shows how VR technology intervenes in the radiology reading room.

CURRENT VR APPLICATIONS IN RADIOLOGY

Several VR-based PACS workstation platforms, such as sieVRt, a product of Luxsonic Healthcare (Waterloo, ON, Canada), are under development. sieVRt uses a web-based immersive interface compatible with commercially available VR HMDs and simulates a 3D radiology reading room¹⁰. Although products that simulate virtual reading rooms are scarce, radiologists can use built-in functions such as the Remote Desktop mode on Meta Quest VR headsets to visualize radiologic cases on up to three virtual monitors without installing external applications¹¹. Figure 4 shows a screenshot from a Meta Quest VR headset operating in Remote Desktop mode. The virtual environment displays three virtual

monitors configured to simultaneously visualize radiologic cases within a customizable 3D workspace.

RADIOLOGISTS COLLABORATING BEYOND GEOGRAPHICAL LIMITATIONS

Second opinions in radiology can be crucial when dealing with complex or unique cases. Immediate input from colleagues at different physical workstations, or through a shared simulated virtual workstation, can connect and engage radiologists in real-time discussions of specific cases^{4,12}.

PHYSICAL MONITORS AND VIRTUAL MONITORS: WHY COMPARE THEM?

Physical workstations and the repetitive use of conventional input devices can contribute to work-related musculoskeletal discomfort among radiologists. A 2018 survey found that 32% of radiologists reported neck pain, 32% reported low back pain, and 16% reported additional stress-related injuries. Virtual workstations offer ergonomic flexibility through customizable monitor positioning and immersive spatial arrangements. However, dedicated ergonomic studies evaluating VR-based radiology workflows are limited¹³. HMD use can enhance flexibility and mobility while potentially reducing workstation costs.

Introducing a gain to head rotations when using VR headsets can maintain an acceptable and comfortable range of neck movement when the user is surrounded by multiple horizontally arranged displays¹⁷. This can be achieved with the remote desktop function on Meta Quest headsets and High Tech Computer Corporation

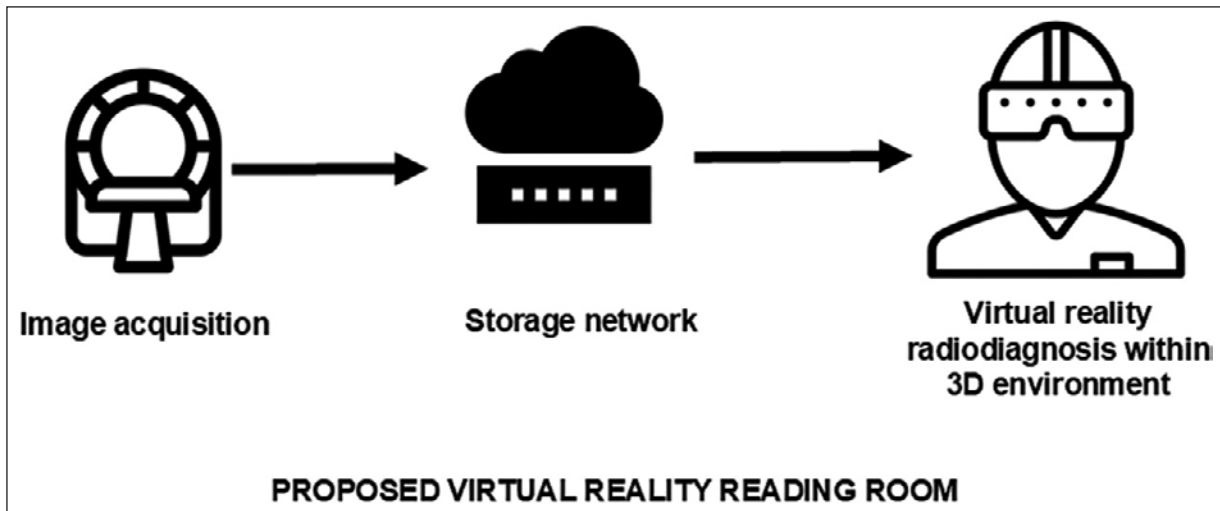


Figure 3. Representation of VR technology intervention in radiology reading rooms, illustrating the proposed virtual reality workflow, where data transition from storage network systems to an immersive 3D VR HMD, bypassing the need for fixed physical workstations.

HMD: head-mounted display; 3D: three-dimensional; VR: virtual reality.

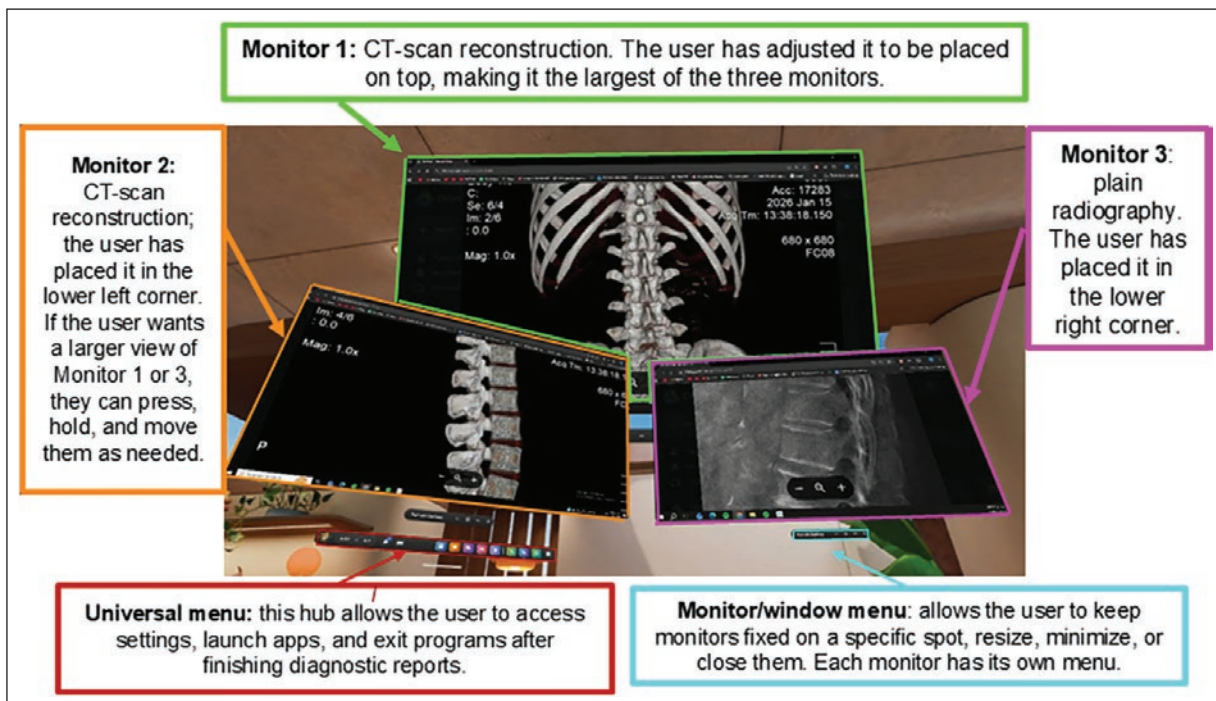


Figure 4. Screenshot from a Meta Quest VR headset operating via the remote desktop function. The VR environment displays three virtual monitors that simultaneously visualize radiologic cases within a customizable 3D workspace.

CT: computed tomography; 3D: three-dimensional; VR: virtual reality.

Vive headsets. Figure 5 shows an example of a customizable VR workstation using a Meta Quest headset with virtual monitors of varying sizes and positions,

demonstrating spatial organization strategies that optimize visualization and reduce excessive head rotation.

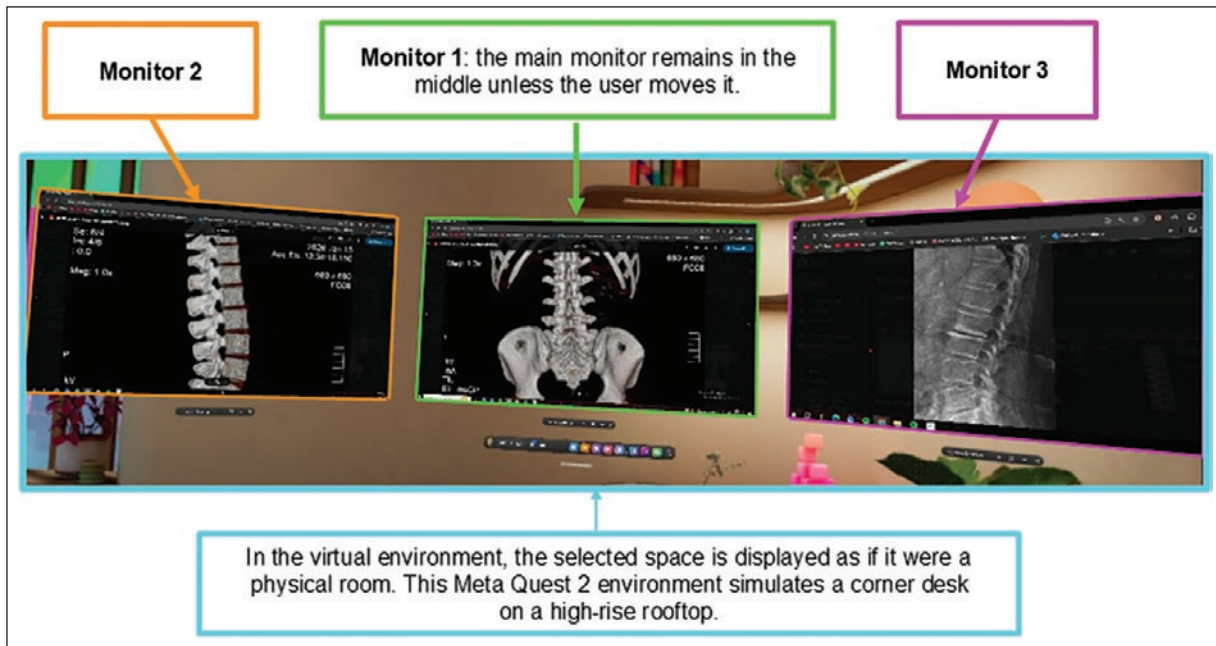


Figure 5. An example of a customizable VR workstation using a Meta Quest headset with virtual monitors of varying sizes and positions. The image illustrates spatial organization strategies designed to optimize visualization and minimize excessive head rotation.

VR: virtual reality.

CAN VIRTUAL MONITORS KEEP UP IN PERFORMANCE?

Table 1 outlines the characteristics of a VR workstation and how immersive environments help address challenges related to limited physical space, ambient noise, and ambient illumination in conventional reading rooms¹⁴⁻¹⁶. Despite promising early applications, several technical limitations currently restrict the widespread implementation of VR workstations for diagnostic radiology. Key considerations include display resolution, luminance uniformity, grayscale contrast perception, refresh rate, and field of view, all of which are critical for visualizing subtle imaging findings. Current VR headsets also depend on high-performance computing hardware and may pose challenges related to prolonged headset use, visual fatigue, and image legibility during extended interpretation sessions. Further validation studies comparing VR systems with medical-grade diagnostic monitors are needed.

Standard diagnostic radiology workstations typically use medical-grade monochrome or specialized color displays with panel resolutions of 3 to 5 megapixels (MP) to accommodate complex imaging data¹⁸. These diagnostic displays operate under strict Digital Imaging and Communications in Medicine (DICOM) Part 14 Grayscale Standard Display Function (GSDF) calibration,

Table 1. VR workstation characteristics

Potential advantages	Current limitations
Reduced physical space requirements	Reduced image legibility compared with diagnostic monitors
Flexible virtual monitor positioning	Limited field of view
Remote collaboration capability	Dependence on headset resolution
Customizable workspace layout	Potential visual fatigue
Potential ergonomic flexibility	Brightness and contrast limitations
Portable workstation environment	Need for high-performance computing hardware

VR: virtual reality.

maintaining maximum luminance between 300-500 cd/m² to ensure precise visibility of subtle, low-contrast findings¹⁹. In contrast, although modern commercial HMDs boast high nominal panel resolutions (e.g., 2064 × 2208 pixels per eye), the critical metric for radiologic interpretation is angular resolution, measured in pixels per degree (PPD)²⁰. Current commercial headsets achieve approximately 22-25 PPD, falling short of the roughly 60 PPD required to match human visual acuity at standard viewing distances and avoid peripheral text or

Table 2. Component and technical footprint of conventional vs. immersive VR workstations

Description	Conventional diagnostic workstation	Immersive VR workstation
Primary display hardware	2-3 physical medical monitors (3 or 5 MP)	1 standalone virtual reality headset with HMD
Secondary display hardware	1-2 standard monitors (RIS/PACS/Dictation)	Infinite, dynamically resizable virtual screens
Spatial footprint required	Dedicated large desk and dark reading room space	Minimal desktop footprint; highly portable
Diagnostic calibration	Native DICOM Part 14 GSDF compliance	Software-level DICOM emulation required
Ambient light tolerance	Strict low-ambient light mandates	High tolerance (isolated via HMD facial interface)
Primary input devices	Dedicated keyboard, ergonomic mouse, dictation microphone	Head display and spatial hand controllers

DICOM: Digital Imaging and Communications in Medicine; HMD: head-mounted display; GSDF: grayscale display function; MP: megapixel; RIS/PACS: Radiology Information System / Picture Archiving and Communication System; VR: virtual reality.



Figure 6. A conceptual illustration of the potential application of VR-based workstations in remote radiology and teleradiology environments (created by IcoGrams Designer; <https://icograms.com/designer>). It depicts a radiologist using an HMD for radiodiagnosis while waiting at a bus stop. The image illustrates how immersive virtual workspaces could enable access to radiologic interpretation platforms from distant locations while maintaining connectivity to digital imaging systems.

HMD: head-mounted display; VR: virtual reality.

edge blurring²⁰. Furthermore, effective luminance and contrast perception are heavily attenuated by the optical lens configurations inherent to commercial headsets, often restricting sustained brightness and limiting native compliance with strict diagnostic display thresholds²¹. Table 2 compares the component and technical footprints of conventional versus immersive VR workstations¹⁸⁻²¹. In a 2018 evaluation of VR detection of thoracic nodules versus standard monitors, no significant differences were found. The investigators measured sensitivity and time to reach a diagnosis; although

no statistical difference was found in time spent, radiologists generally reached a diagnosis faster when using VR²².

POTENTIAL FUTURE APPLICATIONS

Radiology workflows have evolved alongside advances in digital technology, including PACS integration, teleradiology, and remote image interpretation²³. In this context, immersive VR workstations represent a future extension of digital radiology environments. Emerging VR platforms

already enable remote access to customizable 3D workspaces with multiple virtual monitors. Potential applications include collaborative interpretation environments, portable reading stations, and expanded teleradiology capabilities. However, additional studies are needed to evaluate diagnostic accuracy, ergonomic impact, user fatigue, workflow efficiency, and cost-effectiveness before widespread clinical adoption.

Figure 6 presents a conceptual illustration of the potential use of VR-based workstations in remote radiology and teleradiology environments. This illustration depicts a radiologist using an HMD for radiodiagnosis while waiting at a bus stop. The image shows how an immersive virtual workspace could enable access to radiologic interpretation platforms from geographically distant locations while maintaining connectivity with digital imaging systems.

This manuscript is limited by the relatively small number of published studies specifically evaluating VR-based diagnostic radiology workstations and by the rapidly evolving nature of immersive display technologies. Important technical limitations persist, particularly in display performance and image fidelity. Additionally, long-term clinical and diagnostic validation studies are needed before routine implementation can be recommended.

CONCLUSION

VR is an emerging technology with potential applications in radiology workstations and remote imaging interpretation. Although conventional medical-grade monitors remain the standard for diagnostic practice, immersive VR environments may offer advantages in workspace customization, portability, and remote collaboration. At present, VR workstations should be considered complementary and exploratory rather than replacements for conventional radiology reading rooms. Ongoing technological development and further clinical research will determine the future role of immersive workspaces in radiology practice and teleradiology workflows.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of individuals. This study complied with the Declaration of Helsinki (1964) and subsequent amendments.

Confidentiality of data. The authors declare that they followed their center's protocol requirements. Informed consent was not required for this article because it did not include patient data.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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CASE REPORT

Imaging findings and diagnostic challenges in intrahepatic cholangiocarcinoma during pregnancy: a case report

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ABSTRACT

Intrahepatic cholangiocarcinoma (ICC) is exceptionally rare during pregnancy and requires balancing maternal oncologic evaluation with fetal safety. This case report describes non-contrast magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) findings in a woman at 23 weeks' gestation who presented with abdominal pain and jaundice and was diagnosed with moderately differentiated ICC. Abdominal MRI and MRCP showed an intrahepatic lesion measuring 9 × 9.4 × 8.3 cm, predominantly located in the hepatic hilum. The T2-weighted coronal MRI sequence showed a lobulated, heterogeneously hyperintense intrahepatic tumor. Axial diffusion-weighted imaging (DWI) showed predominantly peripheral diffusion restriction (target-like appearance) with an apparent diffusion coefficient (ADC) of 0.7 × 10⁻³ mm²/s. The T1-weighted MRI sequence showed a hypointense lesion. The in-phase and out-of-phase sequences revealed central areas of fatty signal. On axial T2-weighted fat-saturation (FS) MRI, the tumor caused subtle liver capsular retraction and obstruction, with dilatation of the left intrahepatic biliary duct to 15.2 mm, corroborated on MRCP. Percutaneous biopsy and histopathologic examination showed moderately differentiated ICC with positive CK7 immunostaining. After biliary drainage, jaundice improved, and the decision was made to continue the pregnancy. This case report highlights the value of non-contrast MRI and MRCP in evaluating intrahepatic lesions during pregnancy, emphasizing their diagnostic utility in this rare clinical context.

Keywords: Pregnancy. Intrahepatic cholangiocarcinoma. Magnetic resonance imaging. Magnetic resonance cholangiopancreatography.

INTRODUCTION

Neoplasms during pregnancy are rare, with an estimated incidence of 10 cases per 10,000 pregnancies¹. Cholangiocarcinoma is the second most common primary malignant liver neoplasm, and intrahepatic cholangiocarcinoma (ICC) accounts for approximately 5-10% of cases². Its occurrence during pregnancy is extraordinarily rare, with few cases reported globally. Clinical presentation during pregnancy mirrors that in nonpregnant women, with symptoms typically related

to bile duct obstruction, including jaundice, abdominal pain, nausea, vomiting, and weight loss¹.

Early detection of ICC is uncommon. It is usually diagnosed at advanced stages because tumors often remain asymptomatic initially^{1,3}. Intrahepatic lesions are typically identified incidentally on ultrasound (US), the first-line imaging modality. Because gadolinium-based contrast agents cross the placenta, their use is contraindicated during pregnancy, limiting contrast-enhanced imaging⁴⁻⁶. Non-contrast magnetic resonance

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imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) are superior for lesion characterization, offer greater sensitivity for detecting tumor spread along the bile ducts, and are considered safe during pregnancy by the American College of Radiology (ACR)⁴. Additionally, diffusion-weighted imaging MRI (DWI MRI) identifies suspicious malignant lesions without contrast and has high sensitivity and specificity. This case report presents non-contrast MRI and MRCP findings in a 41-year-old woman at 23 weeks' gestation who was diagnosed with ICC, with histopathologic confirmation.

CLINICAL CASE DESCRIPTION

A 41-year-old woman at 23 weeks' gestation presented with a two-month history of nonspecific abdominal symptoms. An initial abdominal US at an external facility identified an intrahepatic lesion. One month later, she developed epigastric pain, bilateral palmoplantar pruritus, and generalized jaundice, prompting referral to our institution. Physical examination revealed a jaundiced woman with a pained expression and a globular abdomen due to a gravid uterus. The uterine fundus measured 20 cm. A single fetus was in a free position, with a fetal heart rate of 150 bpm. No uterine activity was palpable.

Laboratory test results were as follows: total bilirubin, 3.7 mg/dL (reference value, 0.20-1.20 mg/dL); direct bilirubin, 2.7 mg/dL (reference value, 0.00-0.50 mg/dL); indirect bilirubin, 1.0 mg/dL (reference value, 0.00-1.00 mg/dL); aspartate aminotransferase, 134 IU/L (reference value, 11.0-24.0 IU/L); alanine aminotransferase, 197 IU/L (reference value, < 34.0 IU/L); alkaline phosphatase, 749 IU/L (reference value, 46.0-122.0 IU/L); lactate dehydrogenase, 272 IU/L (reference value, 125.0-243.0 IU/L); gamma-glutamyl transpeptidase, 637 IU/L (reference value, < 38.0 IU/L). Tumor markers were as follows: alpha-fetoprotein, 139.7 ng/mL (reference value, < 8.1 ng/mL); carcinoembryonic antigen, 1.73 ng/mL (reference value, < 3.0 ng/mL); CA 19-9, 67.4 IU/mL (reference value, < 37.0 U/mL).

Imaging findings

Abdominal MRI and MRCP were performed on a 1.5T Signa HDxt scanner (GE Healthcare, Chicago, IL, USA), which showed an intrahepatic tumor measuring 9 × 9.4 × 8.3 cm, predominantly located in the hepatic hilum and involving segments IV and V. The T2-weighted coronal MRI sequence showed a

lobulated, heterogeneously hyperintense intrahepatic tumor (Figure 1). Axial DWI ($b = 800 \text{ s/mm}^2$) showed predominantly peripheral diffusion restriction (target-like appearance) with an apparent diffusion coefficient (ADC) of $0.7 \times 10^{-3} \text{ mm}^2/\text{s}$. The T1-weighted MRI sequence showed a hypointense lesion. The in- and out-of-phase sequences revealed central areas of fatty signal, evidenced by signal drop on the out-of-phase images.

In the axial T2-weighted fat-saturation (FS) MRI sequence, the tumor caused subtle liver capsular retraction and obstruction, with dilatation to 15.2 mm of the left intrahepatic biliary duct, corroborated on MRCP (Figure 2). The common bile duct and right intrahepatic biliary duct showed no dilation.

Clinical outcome

The patient developed worsening abdominal pain. Internal-external biliary drainage was performed, followed by a percutaneous tumor biopsy. Histopathology showed moderately differentiated ICC with positive CK7 immunostaining (Figure 3). After biliary drainage, jaundice improved, and the decision was made to continue the pregnancy, with surgical intervention planned for a later date.

DISCUSSION

This case report describes a 41-year-old woman at 23 weeks' gestation, with a two-month history of epigastric pain and generalized jaundice, who was diagnosed with ICC. Non-contrast MRI and MRCP were key in identifying an atypical intrahepatic tumor at the hepatic hilum with distinctive morphologic features, including central fat deposition (target-like appearance), highlighting the critical diagnostic utility of non-contrast MRI in the obstetric population.

Abdominal MRI, MRCP, and multiphasic contrast-enhanced computed tomography (CT) are the gold-standard modalities for ICC diagnosis, characterization, and staging⁷. However, MRI offers superior sensitivity for delineating tumor extension along the bile ducts. Typically, ICC manifests as a heterogeneous hepatic mass with late-enhancing fibrous stroma and early peripheral enhancement. The fibrotic stroma contributes to late-enhancing capsule formation and biliary dilatation^{4,8,9}. In this case report, abdominal MRI and MRCP revealed an intrahepatic tumor at the hepatic hilum with atypical features, including central fat deposition. ICC can present in atypical settings and mimic

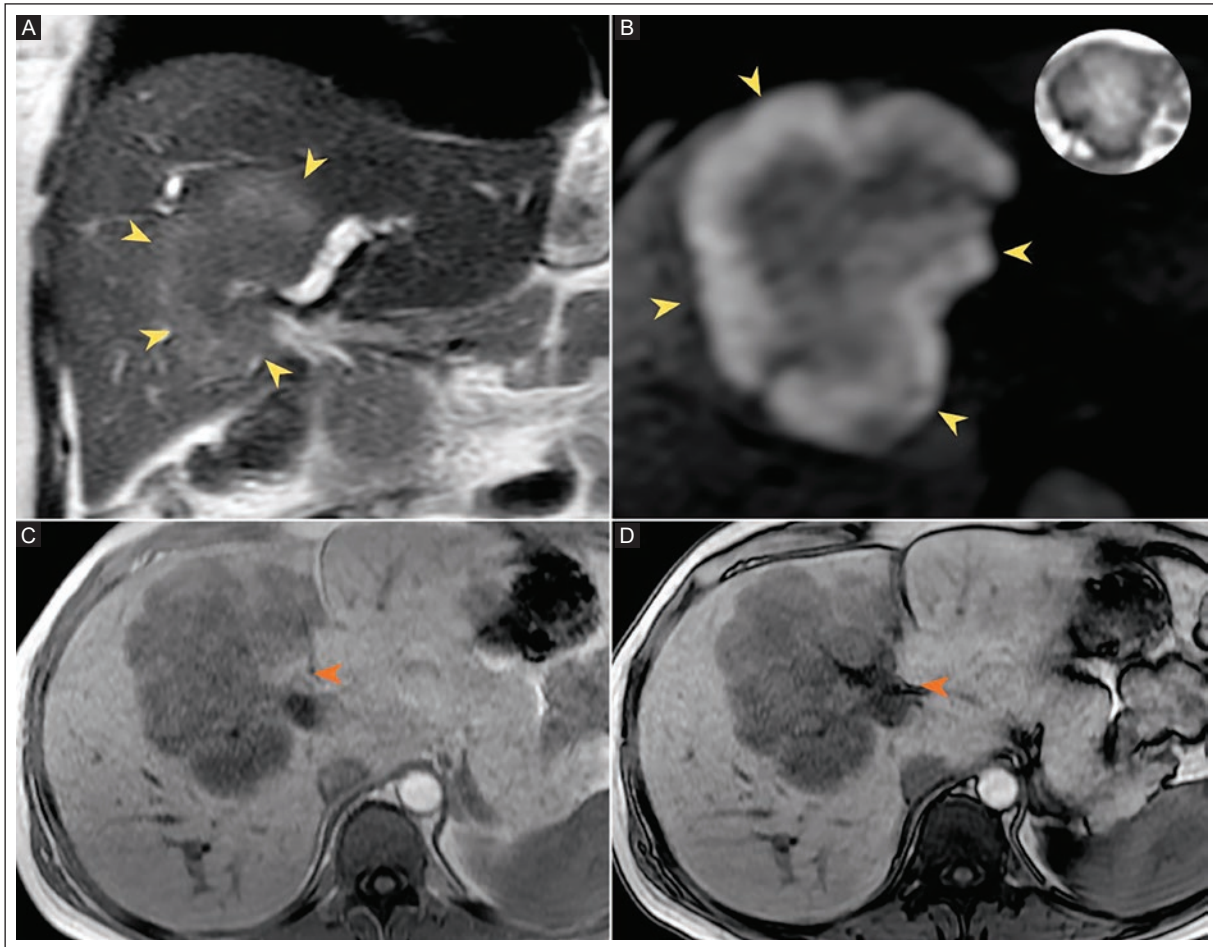


Figure 1. Non-contrast abdominal MRI of a 41-year-old pregnant woman with a two-month history of epigastric pain, bilateral palmoplantar pruritus, and generalized jaundice. **A:** T2-weighted coronal MRI sequence shows a lobulated, heterogeneously hyperintense intrahepatic tumor, predominantly located in the hepatic hilum (yellow arrowheads), measuring $9 \times 9.4 \times 8.3$ cm and involving segments IV and V. **B:** axial DWI ($b = 800$ s/mm²) shows peripheral diffusion restriction with a target-like appearance of the tumor, consisting of a central darker area and a peripheral hyperintense area (yellow arrowheads). The ADC map is shown (circle). The ADC was 0.7×10^{-3} mm²/s (not shown). **C:** axial T1-weighted in-phase, and **D:** out-of-phase sequences, show central areas with fatty signal (orange arrowheads) and a signal drop on the out-of-phase sequence.

ADC: apparent diffusion coefficient; DWI: diffusion-weighted imaging; MRI: magnetic resonance imaging.

common diseases. In pregnant patients with significant biliary dilatation, unexplained hepatic masses, or progressive jaundice, a high index of suspicion is essential to avoid diagnostic delay. Clinicians should be aware that non-contrast MRI is an effective and safe method for characterizing liver lesions in pregnant women. It provides information on lesion location, morphology, and tissue behavior across different sequences.

The DWI MRI sequence is particularly valuable for non-contrast evaluation, with sensitivity and specificity of approximately 84% for detecting malignant lesions⁶. Restricted diffusion correlates well with histopathological malignant findings,⁶ such as the target

sign, characterized by restricted diffusion around the lesion's edges and low signal in the center on high b-value DWI, which may be a distinctive indicator of ICC. This pattern arises because the center contains loose fibrotic stroma with edema, leading to low DWI signal, while the outer area consists of tightly packed viable tumor cells that restrict diffusion, creating dark rings on the ADC map⁷. These imaging features were consistent in our case report, reinforcing MRI's critical diagnostic role during pregnancy and highlighting the importance of non-contrast MRI and MRCP, using sequences that serve as biological markers, such as DWI, to detect malignant neoplasms. In our case report, non-contrast

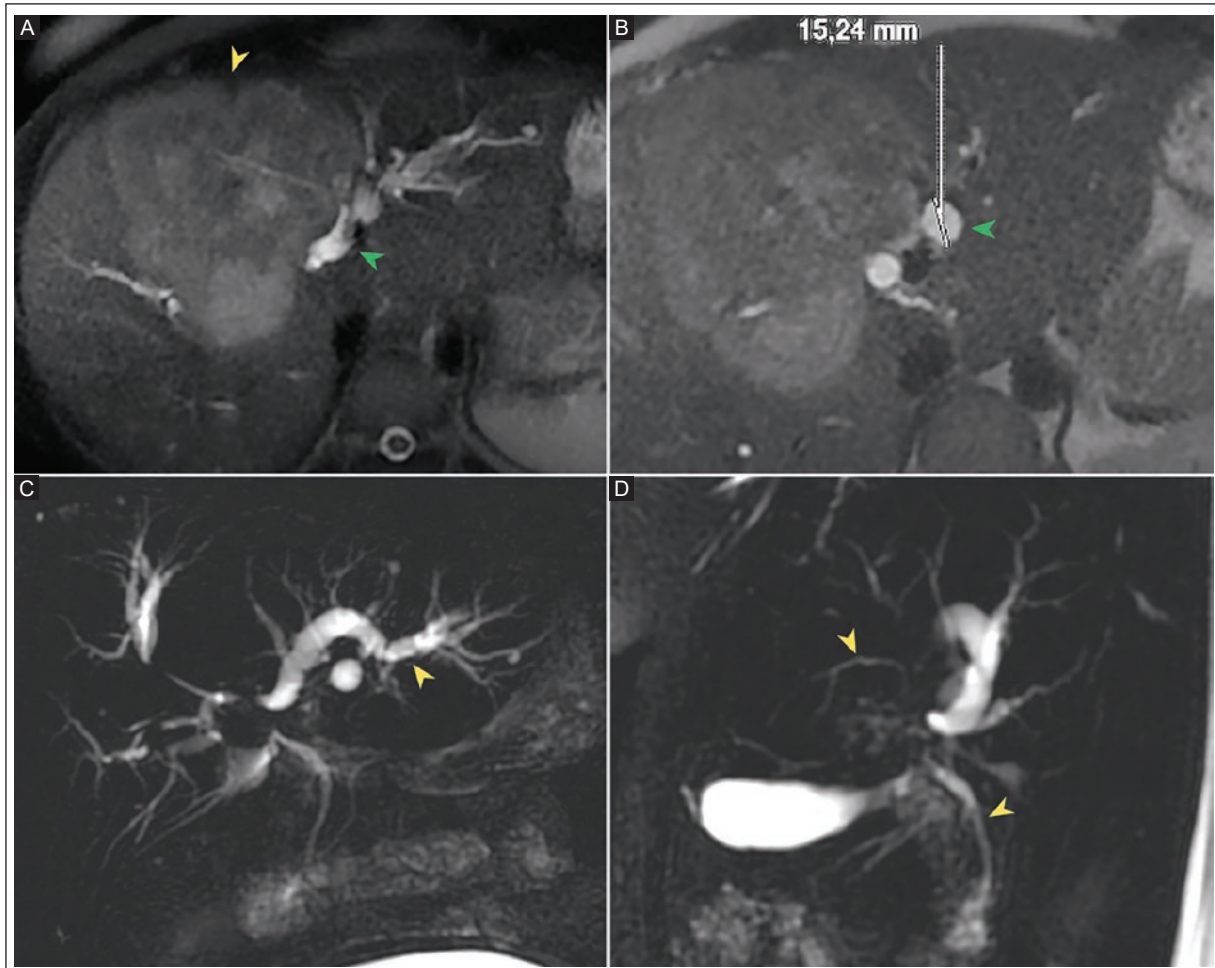


Figure 2. A 41-year-old pregnant woman with a two-month history of epigastric pain, bilateral palmoplantar pruritus, and generalized jaundice. **A:** a non-contrast abdominal T2-weighted FS axial MRI shows a lobulated, heterogeneously hyperintense intrahepatic mass with subtle capsular retraction (yellow arrowhead), causing intrahepatic biliary obstruction and dilation (green arrowhead). **B:** non-contrast axial T2-weighted abdominal FS MRI shows dilation of the left intrahepatic biliary duct measuring 15.24 mm (green arrowhead). **C:** MRCP shows left intrahepatic biliary duct dilation (yellow arrowhead). There is no evidence of dilation of the common bile duct or the right intrahepatic biliary duct. **D:** MRCP shows the common bile duct and the right intrahepatic biliary duct without evidence of dilation (yellow arrowheads).

FS: fat saturation; MRCP: magnetic resonance cholangiopancreatography; MRI: magnetic resonance imaging.

MRI, especially the DWI sequence, was a crucial and safe diagnostic tool during pregnancy for detecting a malignant tumor such as ICC.

Lower quantitative ADC measurements support a diagnosis of malignancy. Onur et al.¹⁰ evaluated 95 hepatic lesions and showed that the mean ADC of benign lesions was significantly higher than that of malignant solid focal lesions across all b-values ($p < 0.001$). Galindo-Félix et al.¹¹ described a 30-year-old Mexican woman at 32 weeks of gestation with upper abdominal pain, weight loss, and jaundice, in whom non-contrast DWI MRI showed a large hepatic mass with marked diffusion restriction. Histopathology confirmed a mass-forming ICC. In our case report, the intrahepatic tumor showed predominantly peripheral

diffusion restriction (target-like appearance) with an ADC of $0.7 \times 10^{-3} \text{ mm}^2/\text{s}$. The high cellularity of malignant lesions such as ICC severely restricts water diffusion, yielding lower ADC values. In our case, restricted diffusion correlated strongly with the histopathologic diagnosis of malignancy.

CONCLUSION

We present non-contrast MRI and MRCP findings of ICC at the hepatic hilum in a 23-week pregnant woman, characterized by peripheral diffusion restriction and an atypical intrahepatic tumor with distinctive morphologic features, including central fat deposition (target-like appearance). Case reports are vital for

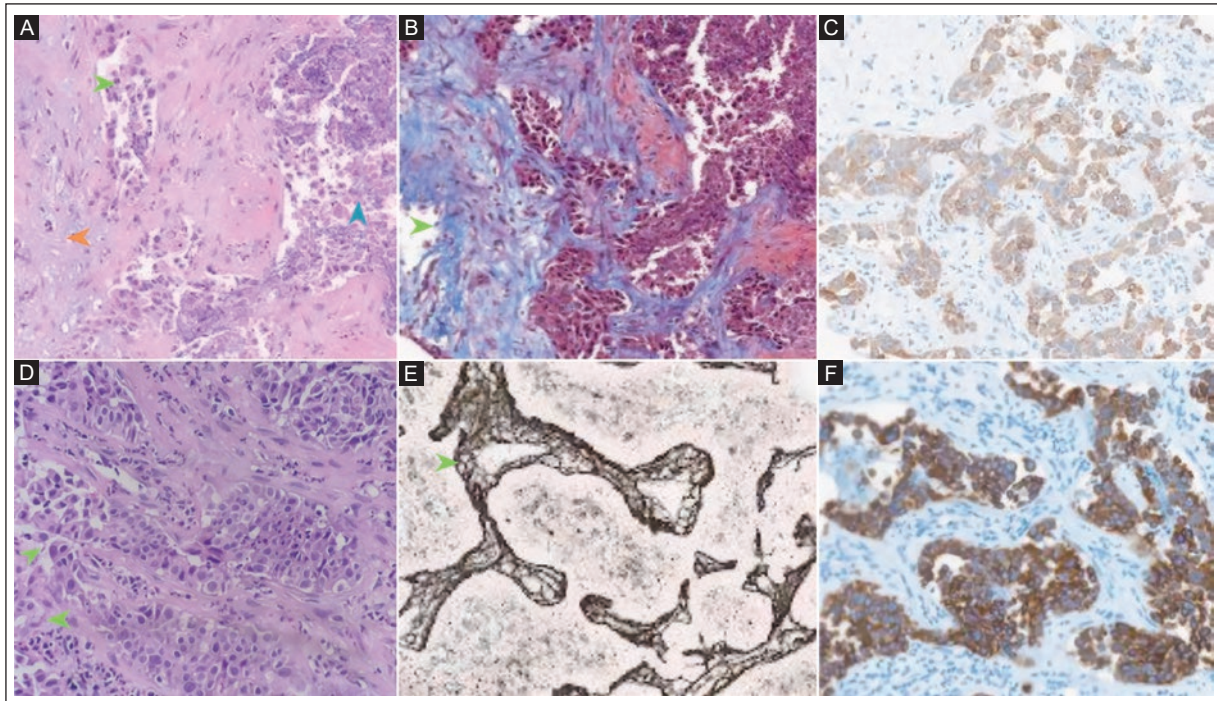


Figure 3. Percutaneous biopsy of the intrahepatic tumor. **A:** infiltrative lesion of discohesive epithelioid cells (green arrowhead) with sparse gland formation in desmoplastic stroma (orange arrowhead) and focal necrosis (blue arrowhead) (H&E stain, 5×). **B:** nests of cells with moderate nuclear atypia and marked pleomorphism, including atypical mitoses (green arrowhead) (H&E stain, 10×). **C:** Masson's stain highlights desmoplastic stromal density and neoplastic infiltration. **D:** reticulin stain for type III collagen fibers shows glandular structures outlined by a reticular network (green arrowheads). **E:** positive staining for CK7, and **F:** positive staining for CK19 on cell membranes. Tissue was negative for Glypican-3 and HepPar1. Therefore, hepatocellular carcinoma and metastases of gynecological, urothelial, colorectal, and pulmonary origin were ruled out. The histopathologic diagnosis was ICC.

H&E: hematoxylin and eosin; ICC: intrahepatic cholangiocarcinoma.

advancing clinical knowledge of rare diseases for which randomized clinical trials are ethically unfeasible. This case report shows that non-contrast MRI and MRCP are safe, noninvasive, and highly accurate diagnostic tools for characterizing complex liver masses in pregnant women.

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MRI in Ledderhose disease: a plantar aponeurosis disorder

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A 66-year-old woman presented with an asymptomatic nodular lesion of unknown duration on the plantar aspect of the right foot. Magnetic resonance imaging (MRI) was performed to characterize the lesion. Axial (Figure 1) and sagittal (Figure 2) sequences revealed three contiguous, solid, expansile lesions within the

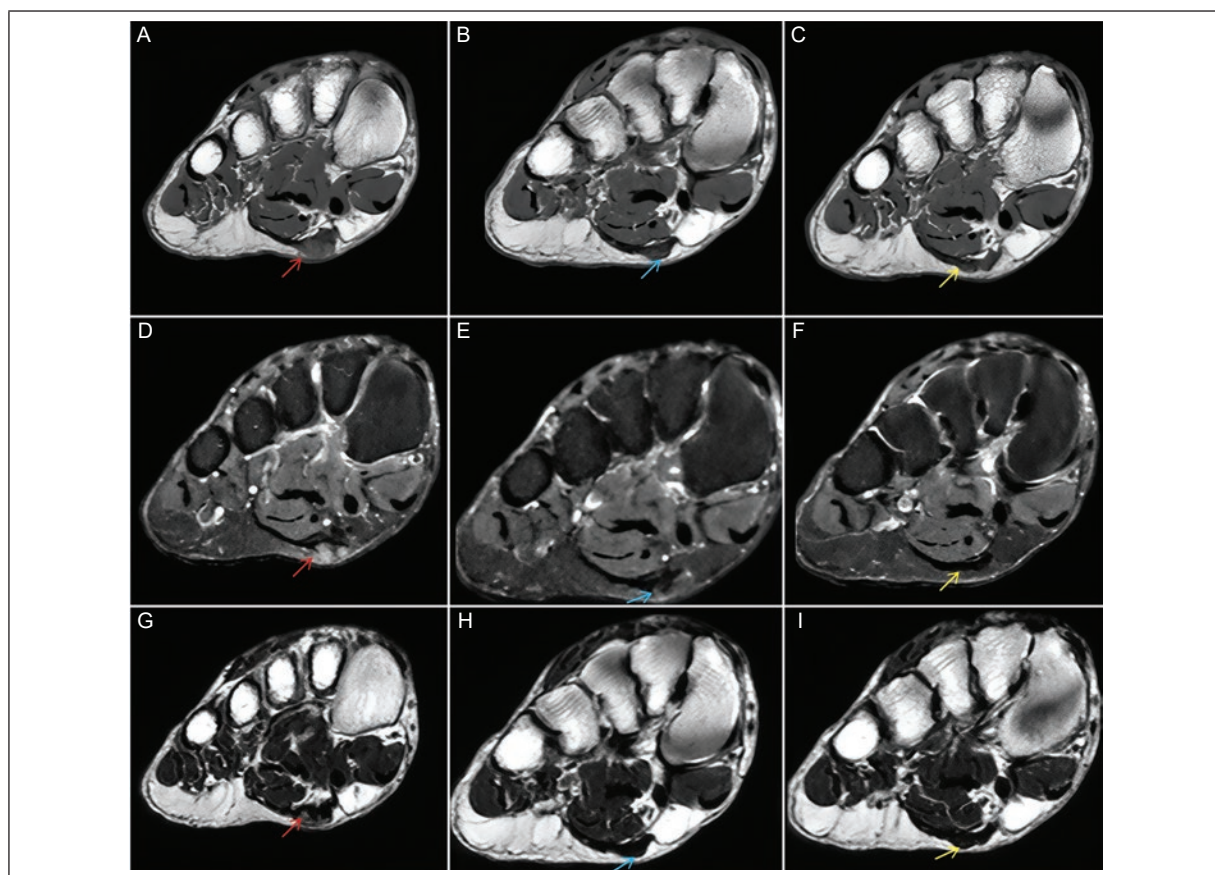


Figure 1. A, B, and C: axial T1-weighted MRI sequences; D, E, and F: PD fat-saturated sequences; G, H, and I: T2-weighted sequences showing three contiguous nodular lesions in the central plantar fascia with intermediate to low signal on all sequences, consistent with plantar fibromatosis (arrows). The larger lesion in D shows high signal on fat-saturated PD, consistent with inflammatory changes.

MRI: magnetic resonance imaging; PD: proton density.

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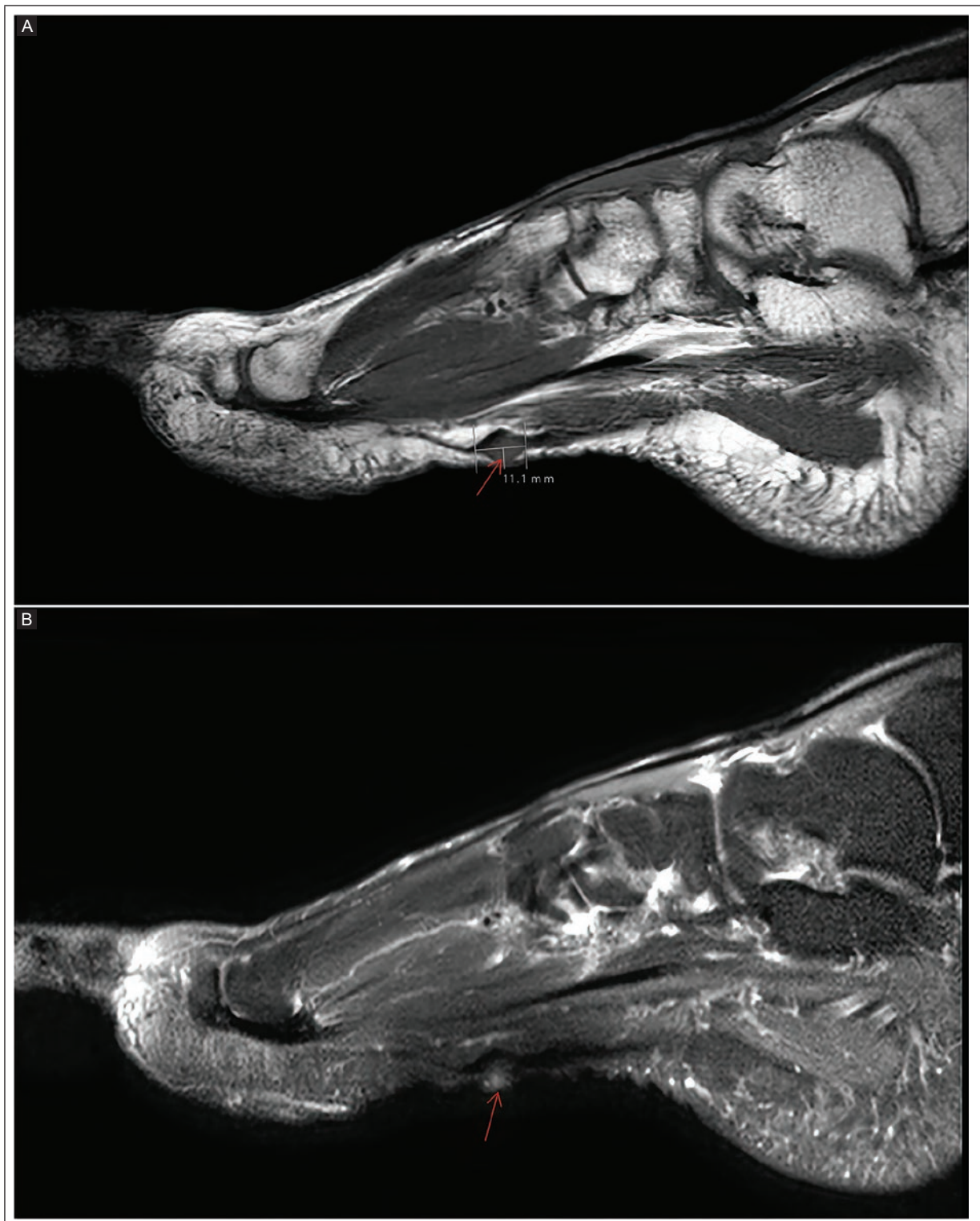


Figure 2 . A: sagittal T1-weighted MRI sequence; **B:** PD fat-saturated sequence showing the larger nodular lesion (11.1 mm) with intermediate signal on T1 and high signal on fat-saturated PD, consistent with plantar fibromatosis and inflammatory changes (arrows).

MRI: magnetic resonance imaging; PD: proton density.

central portion of the plantar aponeurosis. The lesions showed intermediate to low signal intensity on T1- and T2-weighted MRI sequences, consistent with fibrous tissue. The largest lesion measured 11.1 mm and showed intermediate signal on T1 and high signal on fat-saturated proton-density sequences, findings consistent with plantar fibromatosis and associated inflammatory changes. The remaining plantar fascia showed no signs of fasciitis or other abnormalities.

These findings are characteristic of plantar fibromatosis (Ledderhose disease), a benign fibroproliferative disorder of the plantar aponeurosis that is occasionally associated with Dupuytren contracture¹. MRI is particularly useful for diagnosis, allowing detailed assessment of lesion number, size, and local infiltration². Because there was no pain or functional limitation, conservative management was chosen. Recognizing this characteristic MRI appearance ensures a confident diagnosis and guides appropriate treatment.

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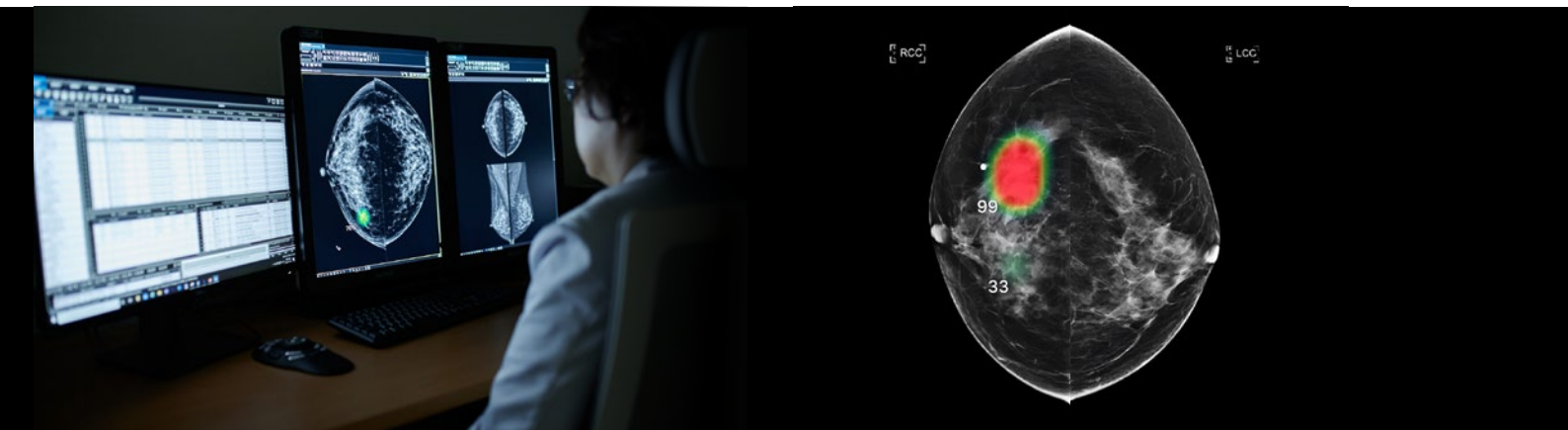
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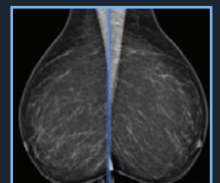
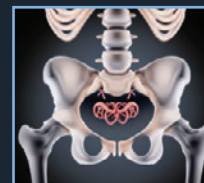
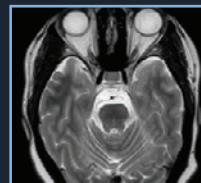
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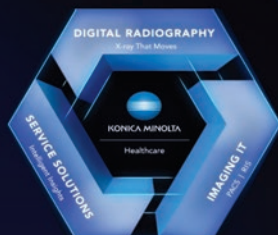
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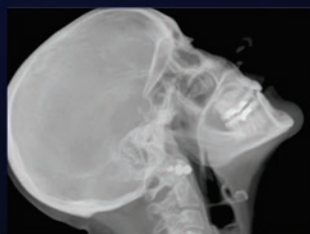


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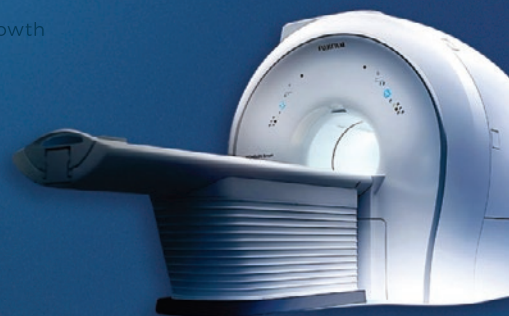
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