

# AOTH

**Acta Orthopaedica et Traumatologica Hellenica**



Official Journal of the  
HELLENIC ASSOCIATION OF ORTHOPAEDIC SURGERY AND TRAUMATOLOGY  
*Athens Academy Award 2004*



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# Instructions for Authors

## 1. Scope

“Acta Orthopaedica et Traumatologica Hellenica (AOTH)” is the official journal of the Hellenic Association of Orthopaedic Surgery and Traumatology, (HAOST) first published in 1948. The current edition of Acta Orthopaedica et Traumatologica Hellenica (AOTH) is published in English, online, without any article processing charges (APCs). It offers a compact forum of communication to orthopaedic surgeons and related science specialists. It publishes only peer reviewed articles. The peer review process is the established method for research validation in science whereby a work is critically assessed by expert referees demonstrating both the right level of knowledge in the field of the work, while being fully independent from it. Acta Orthopaedica et Traumatologica Hellenica (AOTH) follows a blind peer review process mediated and ensured by the Editor-in-Chief and the Editorial Board members. Aiming for clinically pertinent, scientifically correct, ethical, original and review quality research, only scientifically sound articles, deemed of high enough interest and originality that will receive favorable reports from our Editors/Reviewers Board will be accepted for publication.

## 2. Types of papers

The journal accepts and publishes the following types of articles:

**Original articles:** Original articles are encouraged. They should provide novel insights and contribute to continuous medical education and transfer of knowledge. They should include a clear rationale, and the findings/conclusions need to be sound and supported by statistical analysis. When the accuracy of a diagnostic test is assessed, following the Standards for Reporting of Diagnostic Accuracy (STARD) flow diagram (<http://www.stard-statement.org>) is suggested. A structured

abstract of 250 words (divided into Background, Materials and Methods, Results and Conclusions), 3-5 keywords, text up to 4,500 words, figures up to five, tables up to six, and references up to 50 are recommended. (It is at the Editor’s discretion to allow differences in the above numbers).

**Review Articles:** All types are allowed including narrative reviews, systematic reviews, meta-analyses, literature reviews, mini reviews, monographs, and historical reviews on orthopaedic heritage. They should be extensive, educative, informative, adequately illustrated, and appropriately cited with up to date quality citations. An unstructured abstract of 150-250 words, 3-5 keywords, text up to 8,000 words, figures up to eight, tables up to six, references up to 100, and a maximum of six authors are recommended. (It is at the Editor’s discretion to allow differences in the above numbers).

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**Pictorial Essays (Images papers):** The purpose of pictorial essays is to provide a teaching message through high quality images. A brief text (e.g., the history of the patient shown in the illustration) followed by a brief discussion are required to accompany the images. An unstructured abstract of 150-250 words, 3-5 keywords, text up to 4,000 words, figures up to four, tables up to two, references up to 20, and a maximum of four authors are recommended. (It is at the Editor’s discretion to allow differences in the above numbers).

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After submission, the Editorial office and the Editor-in-chief will check the submitted files and if appropriate will assign to section Editors or invite Reviewers. The time allocated for reviewers to assess the manuscript and submit their recommendation is 3 weeks. By that time the Editor-in-chief will make his final decision for publication.

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Submission of a manuscript implies that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute

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Each author needs to disclose any type of financial interest that is related to the study and might create a potential conflict. Funding of the study, if any, needs to be disclosed. If there is no conflict of interest, this should be stated in the manuscript before the Reference section as follows: "The authors declared no conflicts of interest".

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Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) for both the print and online format and to include evidence that such permission has been granted when submitting their papers. Plagiarism, as evidenced by appropriate dedicated software, will not be accepted. If excessive, the manuscripts with plagiarism will be returned to the corresponding author without consideration for peer review.

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A manuscript must contain the following files for submission:

*Cover letter:* Each manuscript should be accompanied by a cover letter signed by the corresponding author on behalf of the rest of the authors stating that the work submitted has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. Any other information such as solicited paper, paper submitted for a special issue, letter to the Editor, etc should be communicated to the Editor in the Cover letter. In case of article resubmission a point-by-point answer to the reviewer’s comments needs to be submitted with the cover letter.

*Title page:* It includes the title of the manuscript (concise, informative and capture of the message), the names of the authors, the affiliations of the authors, and the name, affiliation, address, e-mail address, and telephone number of the corresponding author.

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*Text structure:* the text of the Original Articles needs to be organized as follows: Introduction, Materials and Methods, Results and Discussion. Review Articles should include sections and subsections with appropriate headings depending on the topic; too many headings and subheadings should be avoided because they complicate reading. Case reports should include an Introduction, Case presentation, and Discussion. Pictorial Essays (Images papers) should include an Introduction and Discussion section only.

*Abbreviations:* Abbreviations should be used as minimum as possible, and should include only widely known and accepted abbreviations such as ORIF (open reduction and internal fixation), ICU (intensive care unit), etc. When used, they should be defined the first time they are used, followed by the acronym or abbreviation in parenthesis.

*Acknowledgements, sponsorships and grants:* Acknowledgements should be added at the end of

the manuscript before the References section. It should read as follows: “The authors thank... or acknowledge....”

*Measurement Units:* All measurements should be mentioned in international units (SI). The full stop should be used as a decimal (i.e. 3.5 cm). Spaces should be added around the plus/minus symbol (i.e.  $13.6 \pm 1.2$ ). There should not be any spaces around range indicators (i.e. 15-20) or equality/inequality symbols (i.e.  $r=0.37$ ,  $p<0.005$ ).

*Figure and Tables:* Figures and tables should be cited in the text consecutively in the order in which they appear. They should be cited in parentheses at the end of the respected sentence, and not be referred to in the text. They should be counted in Arabic numbers: i.e. (Figure 1) and (Table 1), and any Figure parts should be identified with lower case letters, i.e. (Figure 1a).

Figures need to be of high quality (minimum resolution of 1,200 dpi) in TIFF or JPEG format.

Patient anonymity should be ensured and patient identifying images such as intraoperative or clinical photographs should be avoided. All identifying data (name, identification numbers, initials) must be removed from text, images and tables.

Figures and Tables legends should be explanatory and appropriate (what the figures and tables show). The legends should be listed at the end of the text, after the References section. The Figures and Tables should not be embedded in the text, but they should be uploaded in separate respective files, named respectively, i.e. (Figure 1a).

Studies cited in the Tables should be cited according to the references list of the manuscript.

## 9. References

References section is not an afterthought but a continuum of the paper. They should be up to date and of acceptable quality. Their accuracy is the responsibility of the authors. They should be cited in the text in the order in which they appear. The numbering needs to be in Arabic numbers and formatted in superscript in the respective areas of the text, after the punctuation (i.e. <sup>1</sup>).

All authors should be listed for all references of a manuscript.

When a book chapter is cited, the authors and title of the chapter, editors, book title, edition, city and country, publisher, year and specific chapter pages should be mentioned.

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#### *References examples:*

Journal article:

Mavrogenis AF, Altsitzioglou P, Tsukamoto S, Errani C. Biopsy Techniques for Musculoskeletal Tumors: Basic Principles and Specialized Techniques. *Curr Oncol.* 2024;31(2):900-917. doi: 10.3390/curroncol31020067.

Sun J, Mavrogenis AF, Scarlat MM. The growth of scientific publications in 2020: a bibliometric analysis based on the number of publications, keywords, and citations in orthopaedic surgery. *Int Orthop.* 2021;45(8):1905-1910. doi: 10.1007/s00264-021-05171-6.

Kolovos S, Sioutis S, Polyzou M, Papakonstantinou ME, Karampikas V, Altsitzioglou P, Serenidis D, Koulalis D, Papagelopoulos PJ, Mavrogenis AF. The risk of DDH between breech and cephalic-delivered neonates using Graf ultrasonography. *Eur J Orthop Surg Traumatol.* 2024;34(2):1103-1109. doi: 10.1007/s00590-023-03770-0.

Book chapters:

Mavrogenis AF, Antoniadou T, Dimopoulos L, Filippidis D, Kelekis A. Metastasis (Chapter 26). In: *Textbook of Musculoskeletal Disorders*. Vincenzo Denaro, Umile Giuseppe Longo (Eds). © Springer Nature. 2023. ISBN 978-3-031-20986-4.

Online document:

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#### **10. Review and Proof reading of manuscripts**

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# AOTH

Acta Orthopaedica et Traumatologica Hellenica

## Call for Papers/Publish in Acta Orthopaedica et Traumatologica Hellenica (AOTH)

Dear Colleagues,

Acta Orthopaedica et Traumatologica Hellenica (AOTH), the Official Journal of the Hellenic Association of Orthopaedic Surgery and Traumatology, is published since 1949 and is devoted to dissemination of news and information on all aspects of orthopaedic surgery.

Beginning from 2025, all papers published in Acta Orthopaedica et Traumatologica Hellenica (AOTH) acquire a DOI (Digital Object Identifier); each published article acquires a specific DOI. Scientific articles that acquire a DOI are identified as first-class articles immediately actionable on the network, therefore reachable to a great community of scientists all over the world.

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**Andreas F. Mavrogenis**

*Editor-in-Chief, Acta Orthopaedica et Traumatologica Hellenica (AOTH)*



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## For Authors

# Writing for Acta Orthopaedica et Traumatologica Hellenica (AOTH)

Andreas F. Mavrogenis

*Editor-in-Chief, Acta Orthopaedica et Traumatologica Hellenica (AOTH)*

This article is addressed to the curious readers who may benefit of some simple rules on how to write a scientific paper. It offers advices and tips on medical writing for the junior authors and the less experienced in medical writing on how to prepare a quality submission. These tips apply to any author and any journal, and it is the Editor's personal view and experience in medical writing. Before starting the paper, search the related literature; choose quality papers that are electronically available; provide appropriate correct citations for any material previously published to avoid plagiarism. Before writing the paper, read the authors' instructions. These instructions will need to be met in any case.

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The number and the order of the authors' names should be fair by reflecting their contribution and the order of their contribution to the manuscript. Those who authored should be listed as authors of the manuscript. Those who have contributed to the work, but not enough to merit their inclusion in the authorship, should be acknowledged in the acknowledgment section. Authorship is not a way to thank a colleague for support, access to resources, or mentorship. Scientific misconduct (fraud) in authorship includes a gift or complimentary authorship, ghost authorship, and coercion authorship.

### Title

It should be short and concise; it should capture the message. Titles raising or answering questions will

far be more appealing than titles merely pointing to the topic. Do not use run-on (long and busy) titles.

### Abstract

It should include all the important information from each section that is the background, questions/purposes, materials/methods, results, and conclusions. The readers should be able to understand the total paper by just reading the Abstract. Some read only the Abstract (e.g., because they do not have the time or access to the full text). Keywords are important for indexing and should be chosen carefully.

### Introduction (approximately 500 words)

It is the most critical section. It should start with focus on the topic. General and irrelevant information should be avoided. The first paragraph should present the background. The second paragraph should present what is important on the topic. Appropriate citations (the related studies) should be added. These studies should be further discussed at the discussion section.

The section should end with a clear rationale. Questions to be asked when formulating the rationale are the following: (1) What is missing from the literature for this study to merit publication? (2) How does this study add to the related literature? (3) Does it confirm or reject previous reports? After the rationale, the purposes of the study (study questions or hypotheses) should be listed. The purposes may be primary (the most important) and secondary (the least important). Writing should be clear and concise.

**Materials and Methods (approximately 1000-1500 words)**

The section should start with the Materials in brevity and clarity. An example could read as follows: *"We present ..... patients admitted and treated at the authors' institution with ..... from 2000 to 2024. There were ... men and ... women with a mean age of ... years (range, ..... years)".* These two sentences provide almost all basic demographic information of the materials of the study. Follow-up is materials and should be provided here; the same for loss to follow-up including the reasons for the loss. Clinical reports must state inclusion and exclusion criteria and whether the series is consecutive or selected; if selected, criteria for selection should be stated. These should inform the readers for any sources of bias.

When reporting clinical studies, the authors must state informed consent (where appropriate) and approval of the institutional review board or ethics committees of their institution. These should be added at the first paragraph of the Materials and Methods sections as follows: *"All patients gave written informed consent for their data to be included in this study. This study was approved by the Institutional Review Board (IRB)-Ethics Committee of the authors' institution".* Alternatively, *"Informed consent was not necessary for review articles"* or *"IRB and Ethics Committee approval was not necessary at the authors' institution for retrospective studies"*.

The Methods should contain adequate detail for another investigator to replicate the study. The authors should clearly present what they did and how they did it in the study and analysis. The Methods should be validated with appropriate citations such as for a used score, method, classification, etc.

If authors use statistical analysis, a paragraph should appear at the end of Materials and Methods stating all statistical tests used. When multiple tests are used, the authors should state which tests are used for which sets of data. The level of statistical significance is 0.05 in most cases.

**Results (approximately 500 words)**

It should be the answers to the study questions in the same order as formulated in the rationale at the

last paragraph of the Introduction section. It is easier and more informative to format the study answers (results) in paragraphs. Each paragraph should start with a key statement of the most important result, and then the description and statistical analysis should follow.

The authors should provide which group/method/analysis is more significant compared to another and parenthetically state the p-value immediately after the comparative terms. Provide the actual p-values instead of p-values greater or lesser than 0.05. Parenthetical reference to all figures and tables enables easier interpretation of the data. Avoid too many numeral data in tables because it complicates and fatigues reading.

**Discussion (approximately 1500-3000 words)**

The Discussion should start with a restatement of the problem or question in brief for emphasis, followed by the study findings and a synthesis of the comparison and the author's new data to arrive at conclusions.

The second paragraph should be the limitations. I prefer the readers should be informed early for the limitations of the study. Failure to explore the limitations suggests the authors either do not know or choose to ignore them, potentially misleading the reader.

In the next paragraphs the authors should discuss their findings in comparison to the literature. They should synthesize their data with that in the literature. The text should be formatted in paragraphs respective to the study questions/answers. Appropriate and quality studies should be used. Generally, many of these reports will include those cited at the Introduction section. A Table that summarizes the results of the most important published related studies would be useful here (refer to papers with similar tables for the format).

The ultimate paragraph of the section should be the conclusions. The conclusions should be based solely on data that come out of the paper. Conclusions irrelevant of the study findings should not be used. General and philosophical statements

should be avoided. Statements such as “need for further research” or “need for future studies” should be avoided because they underpower the study.

### References

Choose quality references, and read the most important papers in full text; approximately 25% of the references used in the references list of a paper are actually read by the authors when writing the paper. References should be accurate and up-to-date. Electronically available citations should be preferred; abstracts and submitted articles (pending publication), newsletters, proceedings, and meetings syllabus should not be used because

many in these categories ultimately do not pass peer review because it is not possible to be traced and cited. Use citations from the journal to submit your paper; this will gain the Editor that you are aware of the journal; it will increase the visibility of the paper and the impact of the journal.

### Figures and Tables

Figures and tables should complement not duplicate material in the text. They present information that would be difficult to describe in text form. Well-written papers contain one or two tables or figures for every study question/purpose posed in the Introduction. The legends should be explanatory and concise; what the figure/table show.

## References

1. Brand RA. Writing for clinical orthopaedics and related research. *Clin Orthop Relat Res.* 2008;466(1):239-47. doi: 10.1007/s11999-007-0038-x.
2. Mavrogenis AF, Auffret Babak I, Caton JH. Writing for SICOT-J. *SICOT J.* 2021;7:E1. doi: 10.1051/sicotj/2021042.
3. Mavrogenis AF, Scarlat MM. Writing for “International Orthopaedics”: authorship, fraud, and ethical concerns. *Int Orthop.* 2021 Oct;45(10):2461-2464. doi: 10.1007/s00264-021-05226-8.

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Acta Orthopaedica et Traumatologica Hellenica

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# Greek fragility hip fracture registry 2025 annual report

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## Abstract

The Greek Fragility Hip Fracture Registry continued its expansion in 2025, its third year of operation, with five additional orthopaedic departments joining the initiative and increasing the number of active centres to thirteen. During the year, data from 2046 patients were recorded, raising the total number of cases in the registry to 4228. The mean patient age was approximately 83 years and the majority were female (71.2%). Most patients lived independently prior to injury and had preserved cognitive function. Intertrochanteric fractures were the most common fracture type (50.7%), followed by displaced intracapsular fractures (34.4%). Operative treatment was performed in most cases, predominantly using intramedullary nailing or hip hemiarthroplasty, although only 35.2% of patients underwent surgery within the recommended 48-hour from admission timeframe. The mean length of hospital stay in 2025 was 9.1 days, slightly reduced compared with the previous year, and in-hospital mortality was 3.2%. Most patients were mobilized on the first postoperative day and were discharged home, while approximately one quarter were transferred to rehabilitation facilities. However, documentation of secondary fracture prevention remained limited, with only 21.2% of patients discharged with recorded anti-osteoporotic treatment. Thirty-day mortality was 11.2%, showing improvement compared with 2024. Overall, the registry continues to provide important national data on fragility hip fracture care and highlights areas requiring further improvement, particularly timely surgery and secondary fracture prevention.

**Keywords:** Hip fracture; fragility fractures; osteoporosis; clinical registry; Greece; geriatric trauma; quality of care; national registry

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## Introduction

Fragility hip fractures constitute a major public health concern in ageing populations, being associated with increased mortality, functional decline, and substantial healthcare utilization.<sup>1</sup> Registries are useful and reliable tools with the view on improving outcomes for these patients, which requires timely surgical management, coordinated multidisciplinary care, and systematic evaluation of clinical practice.<sup>2-4</sup>

The Greek Fragility Hip Fracture Registry was initiated in 2022 by the Greek Fragility Fracture Network (FFN-Gr) to facilitate the systematic nationwide collection of standardized data on the management and outcomes of patients with fragility hip fractures.<sup>5</sup> By providing reliable national data, the registry aims to support quality improvement, identify variations in care, and promote adherence to evidence-based clinical standards.

The present 2025 Annual Report summarizes the registry's activity and development over the past year. Continued participation from collaborating hospitals, together with the inclusion of newly engaged ones, has enhanced the representativeness of the dataset, allowing for a more robust evaluation of Greek patients characteristics and clinical outcomes.

### 2025 Annual Report

#### *Involved Departments*

The Greek Fragility Hip Fracture Registry continued its operation for the third consecutive year in 2025. At the beginning of the year, three new orthopaedic departments joined the registry: the 3<sup>rd</sup> Academic Department of Orthopaedics of the National and Kapodistrian University of Athens at



**Figure 1.** Geographic Map of Greece with the involved departments annotated with a star.

'KAT' General Hospital in Athens, the Orthopaedic Department of the General Hospital of Patras "Agios Andreas" and the Orthopaedic Department of General Hospital of Tripolis. Later in the year, two additional orthopaedic departments from Athens joined the initiative: the 1<sup>st</sup> Department of Trauma and Orthopaedics of the General Hospital of Athens 'G. Gennimatas' and the Orthopaedic Department of the General Prefectural General Hospital of Athens 'Korgialenio - Benakeio' Hellenic Red Cross". With the addition of these four departments, the number of active centres in 2025

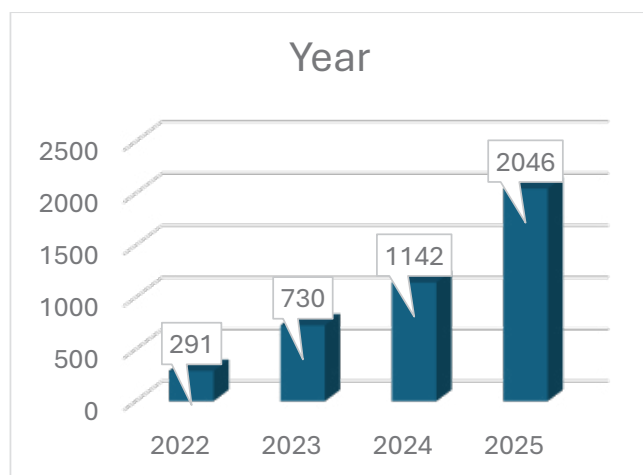


Figure 2. Data entries of the Greek registry per year

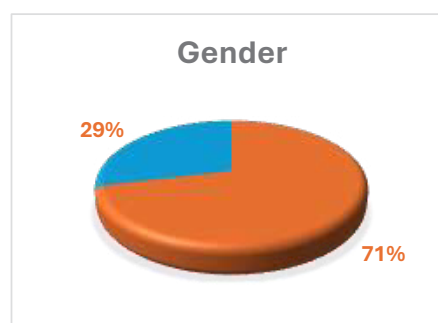


Figure 3. Gender distribution of the 2025 cohort.

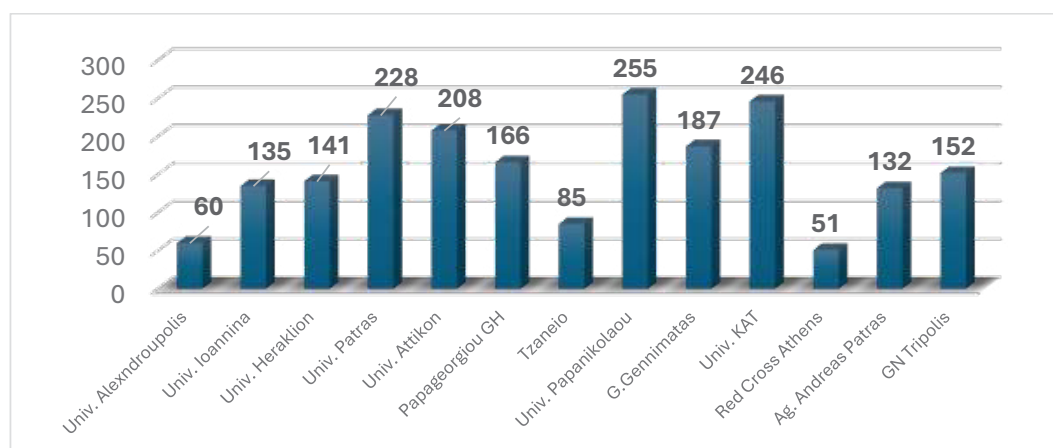


Figure 4. 2025 entries from the different hospitals involved.

increased to thirteen (figure 1). Furthermore, six additional orthopaedic departments from across the country expressed their willingness to participate in the registry and initiated the procedures required for their inclusion.

*Data Collected*

Data from a total of 2046 patients were collected during 2025, increasing the total number of patients included in the Greek registry to 4,228. The year 2025 recorded the highest number of entries to date (Figure 2). The mean age of patients in 2025 was  $83.13 \pm 8$  years, which is slightly higher than the overall registry mean age of  $82.76 \pm 8.3$  years. The

majority of patients were female (71.2%), a proportion similar to the overall registry average of 70.8% (Figure 3).

Most entries this year were made by the Papanikolaou University General hospital of Thessaloniki followed closely by KAT University General Hospital of Athens (figure 4).

The spring of 2025 was the season with least fragility hip fracture admissions, and autumn the with the most admissions. December and August were the busiest months of 2025 (Figures 5&6).

*Patients' pre-injury status*

The mean ASA grade of patients with fragility hip

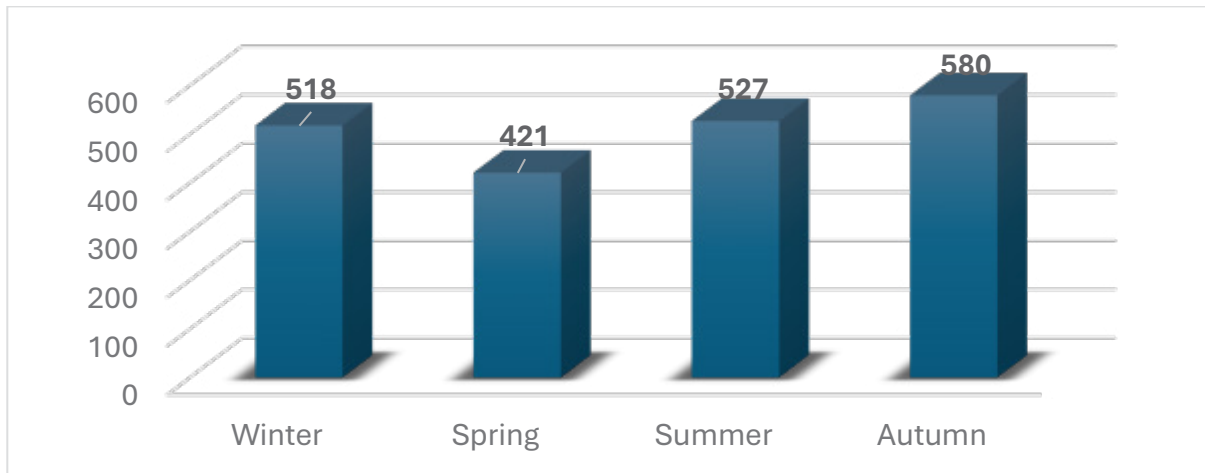


Figure 5. 2024 entries as distributed across the year.

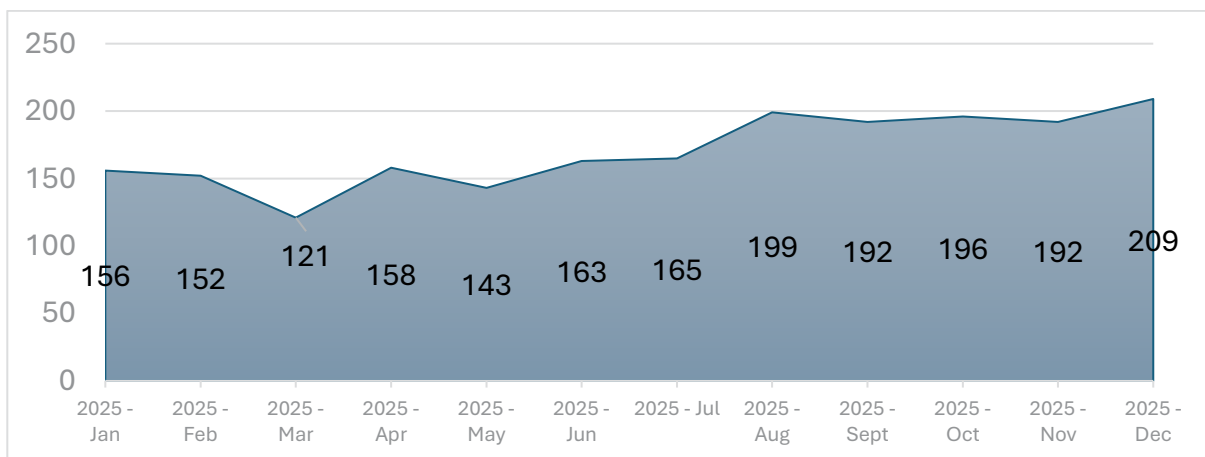


Figure 6. 2025 entries as distributed across the months of the year.

fractures in 2025 was  $2.63 \pm 0.9$ , which is similar to the overall registry average ( $2.68 \pm 0.89$ ). Almost half of the patients (46.3%) were classified as ASA I or II. The cognitive status of the majority of patients was normal (72%); however, 11.4% had positive screening tests for cognitive impairment at admission despite having no previously diagnosed dementia (Figure 7).

Most patients were living in their own homes prior to the injury (92.9%), and a large proportion were functionally independent, with 76.8% able to mobilize outdoors either without aids or using only a single walking stick (Figures 8 and 9).

Fracture type information

Among elderly patients in Greece, intertrochanteric fractures remain the most common type of fragility hip fracture, a pattern that was also observed in 2025. (Table 1 & Figures 10 and 11).

Fracture Type	No	Valid %
Intracapsular Undisplaced	138	6.8
Intracapsular Displaced	703	34.4
Intertrochanteric	1036	50.7
Subtrochanteric	131	6.4

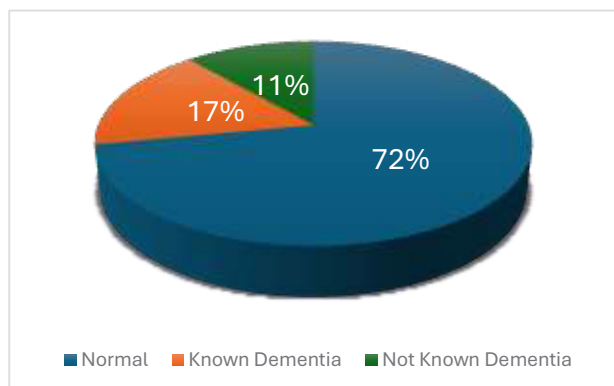


Figure 7. Cognitive status of the cohort.

Other	36	1.8
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*Surgical Procedure Information*

Surgical treatment was considered unsuitable for 6.2% of patients, who were therefore managed conservatively, a slight decrease compared with 6.5% in 2024. The remaining patients underwent operative treatment, which was performed under spinal anaesthesia in the majority of cases (78.5%) (Figure 12). The types of surgical procedures performed are summarized in Table 2. Unfortunately, only 35.2% of patients underwent surgery in a timely manner (within 48 hours of admission), once again highlighting the significant issue of limited operating theatre availability and shortages of anaesthesiology staff in Greek hospitals (Figure 13).

Type of Operation	No	Valid %
Conservative Management	124	6.2
Cannulated Hip Screws	13	0.6
Dynamic Hip Screw	11	0.5
IM nail	1086	54.3
Hip Hemiarthroplasty	699	34.9
Total Hip Arthroplasty	50	2.5
Other	18	0.9

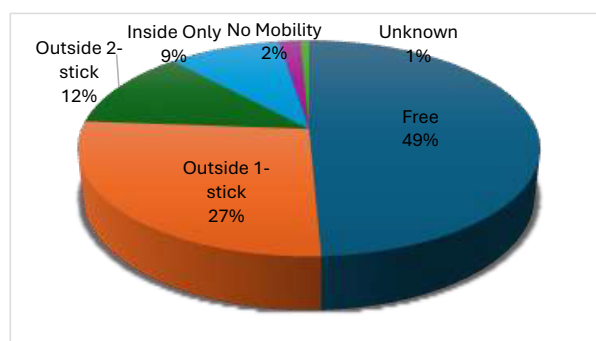
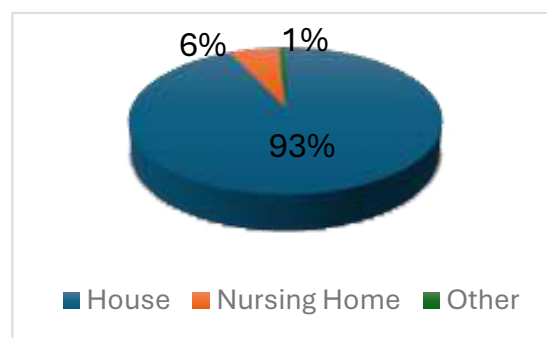


Figure 9. Patients' pre-injury mobility.

*Hospitalization*

The mean length of hospital stay for fragility hip fracture patients in 2025 was  $9.08 \pm 6$  days, lower than the 10.4 days recorded in 2024, reducing the overall average length of stay in the Greek registry to  $9.89 \pm 7.18$  days. In-hospital mortality was 3.2%, representing more than 1% decrease compared with the previous year (4.5%). More than half of the patients (66.7%) were mobilized out of bed on the first postoperative day (Figure 14), while 8.4% developed a new pressure sore during hospitalization (Figure 15). Internal medicine physicians were involved in the management of 47.2% of these patients, highlighting the lack of specialized orthogeriatric services in Greece.

*Discharge Data*

Most patients were discharged home following their admission for fragility hip fracture (65.6%), while discharge to a rehabilitation centre accounted

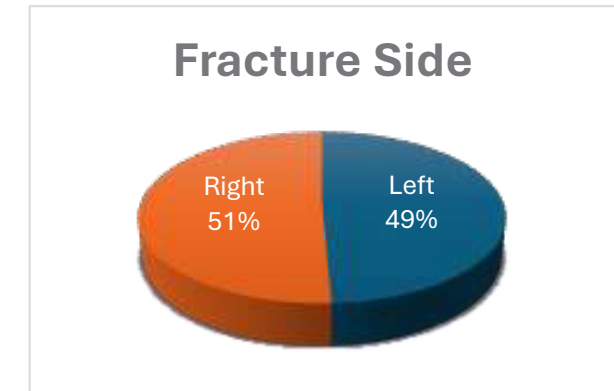
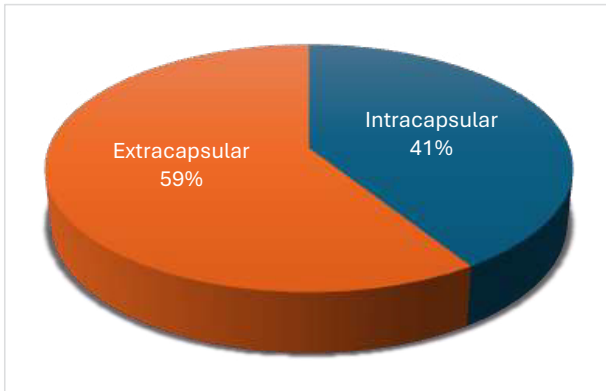


Figure 10. Fragility hip fracture types during 2025

Figure 11. Fracture side percentage during 2025

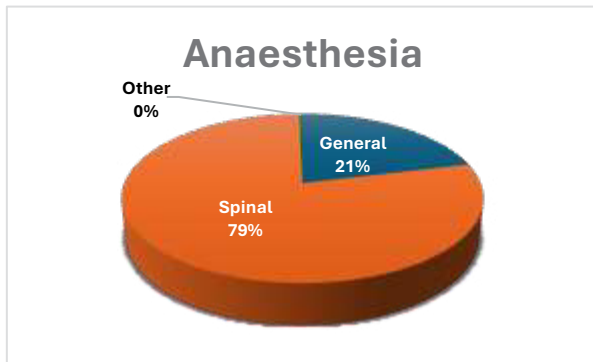


Figure 12. Type of anaesthesia

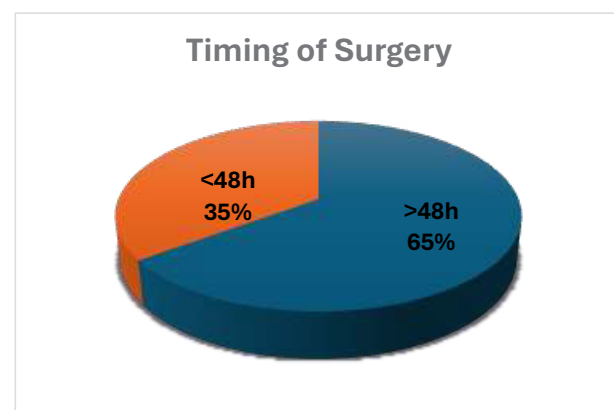


Figure 13. Time to surgery distribution across the cohort.

for 28.1% of cases this year (Figure 16). Only 21.2% of patients were discharged from hospital with documented information regarding the initiation, continuation, or modification of anti-osteoporotic medication, an increase compared with 16.2% in 2024. Nevertheless, the majority of patients still left hospital without a documented attempt at secondary fracture prevention (Figure 17).

*Follow-up Data*

The 30-day mortality for 2025 was 11.2%, similar to the registry total of 11%. This figure was significantly reduced compared to 2024 which was 14.5%.

**Discussion**

The 2025 annual report of the Greek Fragility Hip Fracture Registry represents the third consecutive year of its operation and reflects the continued expansion and maturation of the initiative. Dur-

ing 2025, five additional orthopaedic departments joined the registry, increasing the number of participating centres to thirteen, while six further departments initiated the process of participation. As a result, the registry collected data from 2,046 patients during the year, raising the total number of recorded cases to 4,228. The increasing number of participating centres and recorded cases strengthens the representativeness of the registry and enhances the reliability of the data generated. National registries for fragility hip fractures have proven to be powerful tools for monitoring quality of care and guiding healthcare policy.<sup>6</sup> Established registries such as the National Hip Fracture Database,<sup>7</sup> the Australian and New Zealand Hip Fracture Registry,<sup>8</sup> and the Irish Hip Fracture Database<sup>9</sup> have demonstrated how systematic data collection can drive improvements in patient care and outcomes. The progres-

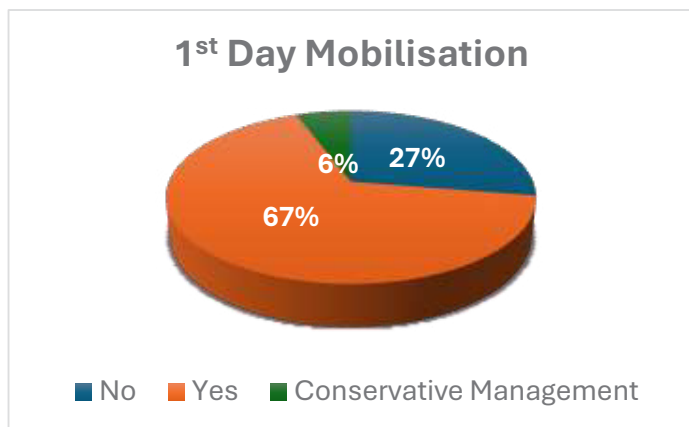


Figure 14. Percentage of patients managed to be mobilised off bed during the 1st post-operative day.

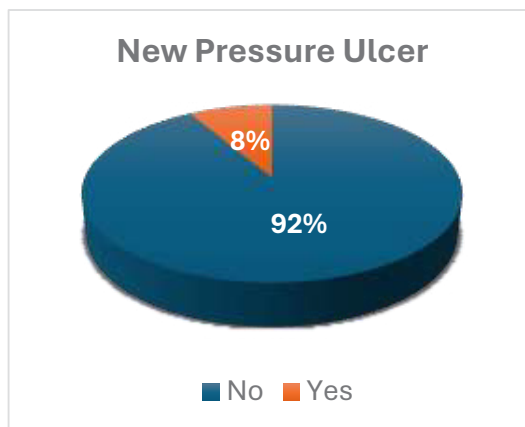


Figure 15. Percentage of patients developed a new pressure ulcer during the acute hospital admission.

sive expansion of the Greek registry represents an important step toward developing a similar national quality improvement framework.

The demographic characteristics of the patients included in the Greek registry remain consistent with those reported internationally. The mean age of approximately 83 years and the predominance of female patients reflect the well-established epidemiology of fragility hip fractures observed across most countries. Similarly, the majority of patients in Greece were living independently at home prior to injury and maintained a relatively high level of pre-fracture mobility. Comparable patterns have been reported by both the National Hip Fracture Database and the Spanish Hip Fracture Registry, highlighting the substantial functional impact that hip fractures have on previously independent older adults.<sup>10,11</sup>

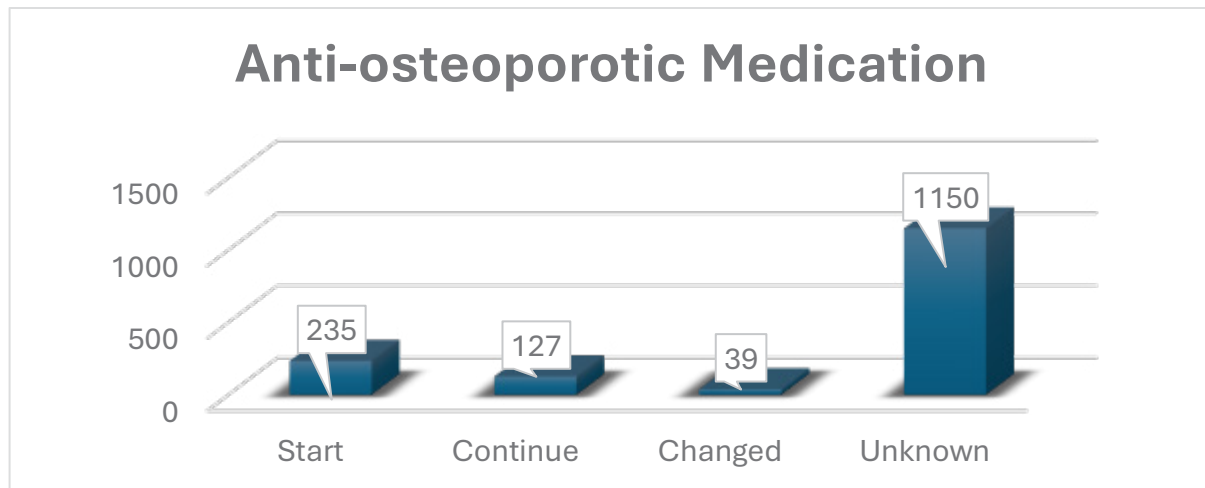
Despite these similarities, several important challenges in the Greek healthcare system remain evident. One of the most significant findings of the present report is the persistent delay in surgical treatment. Only 35.2% of patients underwent surgery within 48 hours of admission. This proportion is considerably lower than the performance indicators reported by well-established registries.<sup>10</sup> In particular, countries such as Germany, Sweden, Finland, and the Netherlands report rates exceeding 90% of surgeries performed within 48 hours. Other



Figure 16. Destination of discharge.

European registries, including those from Ireland, Norway, and Italy, report rates ranging between 65% and 85%. In contrast, among European countries, only Spain and France demonstrate rates comparable to those observed in the Greek registry, with proportions below 50%.<sup>10,12</sup> Similar patterns have also been reported in certain Asian healthcare systems, such as Japan and China.<sup>13,14</sup>

Early surgery is widely recognized as a key quality indicator in hip fracture care, as delays have been associated with increased complications, longer hospital stays, and higher mortality.<sup>15</sup> The relatively low rate of timely surgery observed in



**Figure 17.** Secondary prevention during first admission.

Greece likely reflects a combination of systemic and patient-related factors. Organizational constraints such as limited operating theatre capacity and shortages of anaesthesiology staff in many public hospitals may play an important role. At the same time, as reported in the international literature, patient comorbidities and the need for preoperative optimization are also significant contributors to surgical delay. Further in-depth investigation into the relative impact of these factors in the Greek setting is warranted and will be the focus of future research.

Encouragingly, several clinical outcomes showed modest improvement during 2025 compared with the previous year. The mean length of hospital stay decreased, and both in-hospital mortality and 30-day mortality were reduced compared with 2024.<sup>16</sup> The 30-day mortality rate of 11.2% represents a substantial improvement compared with the 14.5% reported in the previous year and despite being still high, is now closer to the figures reported by some international registries.<sup>10</sup>

Another important finding from the registry concerns the limited implementation of secondary fracture prevention. Only 21.2% of patients were discharged with documented information regarding the initiation, continuation, or modification of anti-osteoporotic medication. Although this represents an improvement compared with the previous year,

the majority of patients still leave hospital without a documented strategy for osteoporosis management. In contrast, countries with established fracture liaison services, including those participating in the Scottish, English and Spanish Hip Fracture Database, report significantly higher rates of secondary prevention interventions.<sup>10</sup>

In Greece, early efforts toward the implementation of structured FLS models have been reported, demonstrating their feasibility and potential impact on improving post-fracture care.<sup>17,18</sup> However, nationwide adoption remains limited. The further development and systematic integration of FLS programs within the Greek healthcare system could represent a key strategy for improving secondary fracture prevention and reducing the risk of subsequent fractures, and the establishment of a nationwide registry can become the first step towards this goal.<sup>19,20</sup>

Overall, the findings of the 2025 report provide valuable insight into the current state of fragility hip fracture care in Greece. The continued growth of the registry represents an important achievement and significantly enhances the ability to monitor clinical practice and outcomes across the country. At the same time, the data clearly identify key areas requiring improvement, particularly the reduction of delays to surgery and the systematic implementation of secondary fracture prevention strategies.

Addressing these issues will be essential for aligning Greek hip fracture care with international standards and improving outcomes for the rapidly growing elderly population.

Further expansion of the registry and increased participation from orthopaedic departments nationwide will strengthen its role as a national quality improvement tool. By providing robust and continuously updated data, the Greek Fragility Hip Fracture Registry has the potential to support evidence-based healthcare planning and guide targeted interventions aimed at improving the care of fragility hip fracture patients in Greece.

### Conclusions

The 2025 annual report of the Greek Fragility Hip Fracture Registry shows continued growth, with more participating centres and recorded cases

strengthening the reliability and national relevance of the data. While the characteristics of Greek hip fracture patients are similar to those reported internationally, the registry highlights ongoing challenges, including delays in surgery and insufficient implementation of secondary fracture prevention. Although some improvements were noted in 2025, such as shorter hospital stays and slightly lower mortality, overall mortality remains higher in comparison to several international registries. These findings underline the need to improve timely access to surgery, strengthen osteoporosis management, and further develop the registry as a national tool for improving fragility hip fracture care in Greece.

### Conflict of Interest

The authors declared no conflicts of interest.

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## Case series

# Metastases of the femur: analysis of 124 patients

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## Abstract

**Background:** There are several studies providing surgical indications for patients treated for femoral metastases. The purpose of this study is to highlight the survival rates of patients with femoral metastases and provide information concerning the treatment of patients suffering from femoral impending fractures and those treated for actual pathological fractures.

**Materials and Methods:** We retrospectively studied 124 patients with femoral metastases from different cancers. The patients were treated with intramedullary nailing, tumor excision and arthroplasty reconstruction, or tumor resection and megaprosthesis reconstruction from 2013 and 2023. The mean follow-up was 18 months. Analysis of patients' survival rates was done based on the cancer type, number and location of metastases, presence of a pathological fracture, and type of surgery.

**Results:** The overall survival of the patients at 60 months was 16%. The presence of an actual pathological fracture, as well as the type of surgery were the only univariate survival predictors, with the first being the only multivariate predictor. Survival was statistically significantly higher in patients treated with tumor excision and arthroplasty reconstruction and patients treated with tumor resection and megaprosthesis reconstruction compared to those treated with nailing ( $p=0.002$ ). The survival of the patients with an impending fracture was statistically significantly higher compared to those with an actual pathological fracture ( $p=0.001$ ). There was no difference in survival among males and females, cancer types or number and location of femoral metastases. The complications rate was 7.2%; the most common complication was infection.

**Conclusions:** Survival rates were higher in patients with femoral metastases treated with tumor excision and arthroplasty reconstruction, or tumor resection and megaprosthesis reconstruction compared to those treated with nailing. Patients with an impending fracture had higher survival rates compared to patients with an actual pathological fracture.

**Keywords:** Metastases; femur; survival; resection; nailing; reconstruction.

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## Introduction

Metastatic bone tumors are the most prevalent skeletal cancers; the skeleton is the third most common site of metastatic disease following the lung and liver.<sup>1</sup> Concerning the incidence of metastatic tumors in the extremities, the femur is the most common long bone to be affected. Patients with primary or metastatic bone tumors usually experience impending fractures or actual pathological fractures leading to significant disability, treatment and prognosis alterations, as well as compromised survival rates.<sup>2-6</sup>

Surgical intervention for bone metastases aims to prevent and adequately manage pathological fractures, along with achieving optimal joint function, bone stability, pain reduction, as well as substantial improvement of quality of life and local control of metastatic lesions.<sup>7,8</sup> In general, impending and pathological fractures require different surgical approaches for stabilization compared to non-pathological fractures. Fixation devices or prosthetic implants used to restore a bone with metastatic disease should be durable and stable for the remaining of patients' lives.<sup>9</sup> Various factors affecting patients' survival and quality of life should be taken into consideration in decision making concerning the time and the surgical technique, including the primary cancer type, the extent of metastatic disease and limb function.<sup>3,10</sup> However, accurate prediction of the postsurgical outcome in these patients remains a challenge, especially due to the paucity of prospective studies analyzing the correlation of the above-mentioned factors with patients' survival.<sup>10,11</sup>

The purpose of this retrospective study is to evaluate the survival and treatment of patients with femoral metastatic disease from various cancers.

## Materials and Methods

We retrospectively studied the files of 124 patients with femoral metastases treated for impending or actual pathological fractures at the authors' institution from January 2013 to January 2023. There were 60 male and 64 female patients with a mean age of 69 years (range, 53-85 years) (Table 1). A pathological fracture was the first symptom to diagnose the primary cancer in 21 patients (34%). All patients or

their relatives gave a written informed consent for their data to be included in the study.

All patients had histological confirmation of their metastatic lesion by a biopsy prior to surgery, and adjuvant therapy administered according to the primary cancer type. All patients underwent surgical treatment within 1 to 45 days (mean, 15 days) after admission to the hospital. Surgical treatment included marginal tumor resection and megaprosthesis reconstruction (16 patients), intralesional excision and cemented hip arthroplasty (28 patients), and closed antegrade intramedullary nailing (80 patients) with reconstruction-type long hip or femoral nails (Tables 1 and 2). Surgical selection of patients with impending pathological fractures was done according to the Mirels' criteria.<sup>14</sup> Indications for intramedullary nailing were: (1) impending or actual pathological intertrochanteric, diaphyseal, or distal femoral fractures without involvement of the distal femoral articular surface, and/or (2) nursing care and pain relief in bedridden patients or patients with deteriorated general health status, deep vein thrombosis, tumor thromboembolism, or short expected survival from widespread cancer. Reconstruction-type nails (interlocking hip or femoral nails) were used in all patients (Fig. 1). Indications for tumor excision and arthroplasty reconstruction were: (1) femoral head and neck metastatic lesions with an impending or actual pathological fracture (Fig. 2), and/or (2) failure of previous hip intramedullary nailing operations. Indications for tumor resection and megaprosthesis reconstruction were: (1) extensive bone loss and bone destruction precluding standard internal fixation or arthroplasty (Fig. 3), (2) prolonged expected survival and solitary metastases of breast, renal cell, or thyroid cancer, and/or (3) impending or actual pathological fracture of the proximal or distal femur involving the articular surface of the hip and knee joint, respectively. A bipolar hip prosthesis was used in all patients.

The mean follow-up was 18 months (range, 2 to 120 months; minimum, 6 months). Eight patients were lost to follow-up; there were one (2/16) patient with tumor resection and megaprosthesis reconstruction, three (4/28) patients with tumor excision

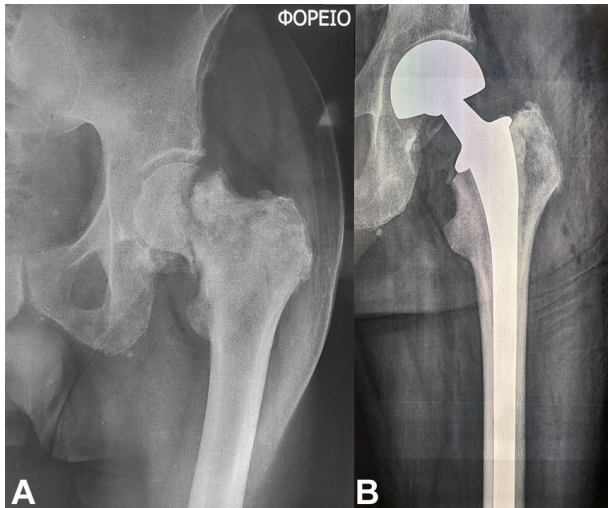
<b>Table 1. Demographic data: presentation and treatment.</b>	
<b>Data</b>	<b>Patients (n = 124)</b>
<i>Age and gender</i>	
Age	Mean 69 years (range, 53–85 years)
Gender (male/female)	60/64
<i>Type of cancer</i>	
Breast	36
Renal	28
Lung	28
Prostate	10
Gastrointestinal (oral, esophagus, stomach, pancreas, colon)	12
Bladder	6
Thyroid	4
<i>Location of metastasis in femur</i>	
Proximal	96
Diaphysis	20
Distal	8
<i>Number of metastases</i>	
Solitary	88
Multiple	36
<i>Pathological fractures</i>	
Impending	72
Actual	52
<i>Surgical treatment</i>	
Intramedullary nailing	80
Excision and arthroplasty reconstruction	28
Resection and megaprosthesis reconstruction	16

and arthroplasty reconstruction, and two (2/80) patients with nailing. Patients' survival was analyzed using the Kaplan–Meier survival analysis with respect to different modes of metastatic presentation

regarding gender, femoral metastases' location, impending and actual pathological fracture, type of surgery type, type of primary cancer, and solitary or multiple metastases.<sup>23</sup> Comparison of the curves



**Figure 1.** (A) A 72-year-old woman with recently diagnosed breast cancer experienced an actual right proximal femoral pathological fracture, and an impending left femoral diaphysis pathological fracture. (B) Long reconstruction type intramedullary nailing was done for both fractures.



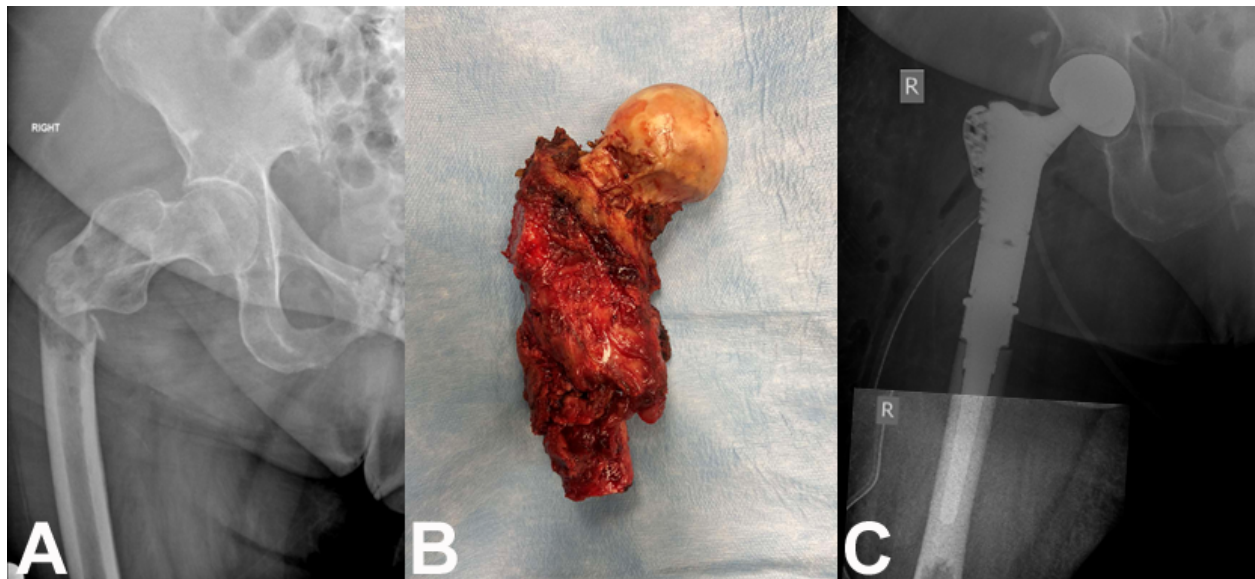
**Figure 2.** (A) A 65-year-old man with urothelial cancer and left proximal femoral pathological fracture (B) treated with a long stem cemented hemiarthroplasty of the hip.

was done with the log-rank test. The differences in survival were evaluated using the chi-square test. Multivariate analysis was performed using the Cox-regression analysis. Complications and death were recorded at routine clinical and imaging follow-up evaluations.

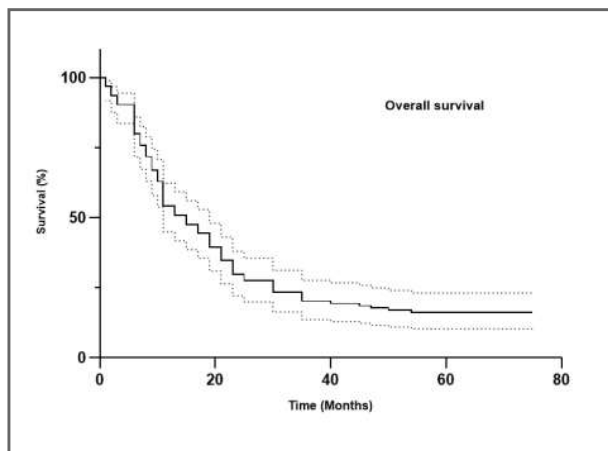
## Results

### Survival

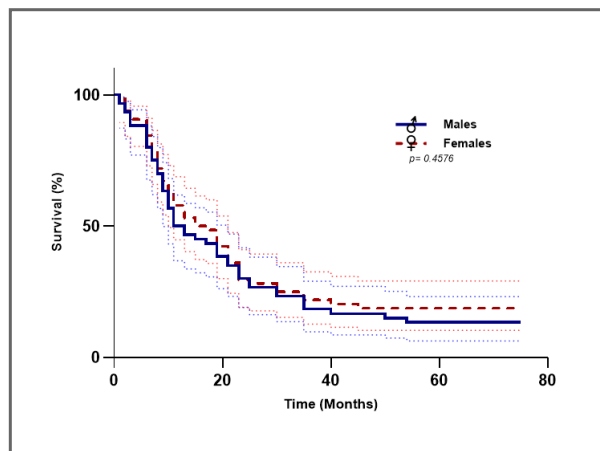
The overall survival of the entire patient population with femoral metastases was 54% at 12 months, 30% at 24 months, 20% at 36 months, 18% at 48 months, and 16% at 60 months (mean survival time, 18 months) (Fig. 4). At the last follow-up, 20 patients were alive with disease and 96 patients were dead with disease. The 60-months survival of male patients was 14% (mean survival time, 12 months) compared to 19% of female patients (mean survival time, 16 months) (Fig. 5). The 60-months survival of patients with breast cancer was 22% compared to 7% of patients with renal cancer, 14% of patients with lung cancer, and 60% of patients with prostate cancer (Fig. 6). The 60-months survival of patients with solitary femoral metastases was 18% compared to 11% of patients with multiple metastases (Fig. 7). The 60-months survival of patients with proximal femoral metastases was 10% compared to 30% of patients with diaphyseal femoral metastases, and 50% of patients with distal femoral metastases (Fig. 8). The 60-months survival of patients with femoral metastases treated with nailing was 16% compared to 24% of patients treated with tumor excision and arthroplasty reconstruction, and 18% of patients treated with tumor resection and megaprosthesis reconstruction.



**Figure 3.** (A) A 78-year-old woman with breast cancer and right proximal femoral pathological fracture treated with (B) resection and (C) proximal femoral megaprosthesis reconstruction.



**Figure 4.** A Kaplan–Meier survival curve shows the overall survival of patients with femoral metastases.



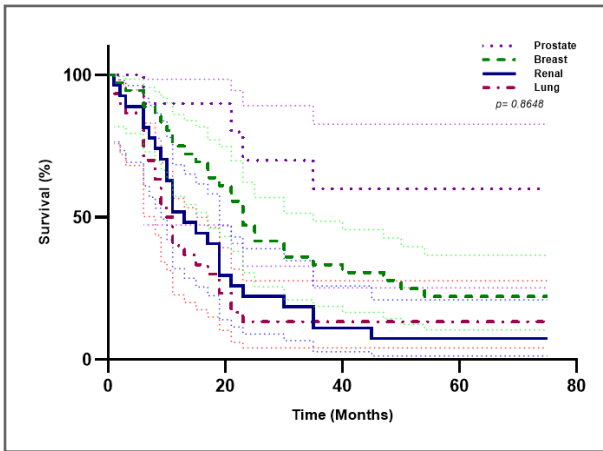
**Figure 5.** A Kaplan–Meier survival curve shows that the survival of male and female patients with femoral metastases was not different among groups

tion (Fig. 9). The 60-months survival of patients with impending pathological fractures was 28% compared to 0% survival of patients with actual fracture (Fig. 10; Table 3).

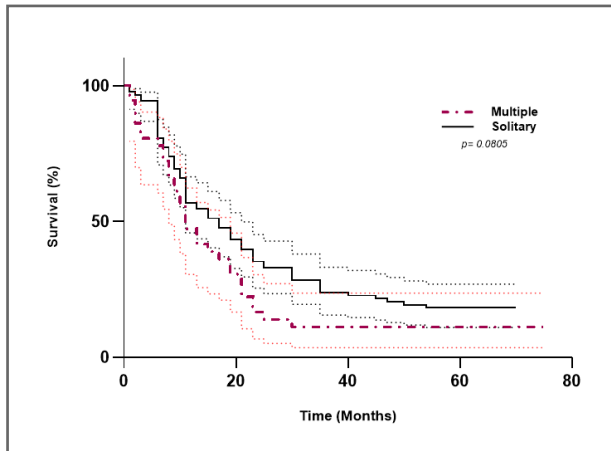
*Univariate and Multivariate Predictors of Survival*

The only factors found to be univariate survival predictors were the presence of a pathological frac-

ture and the type of surgery. Survival was statistically significantly higher only in univariate analysis in patients treated with tumor excision/resection and reconstruction compared to nailing ( $p= 0.002$ ), as well as in patients with impending pathological fractures compared to those with actual pathological fractures ( $p= 0.001$ ). Gender, type of cancer, number and location of metastases were not important



**Figure 6.** A Kaplan–Meier survival curve shows that the survival of patients with breast, renal, lung and prostate cancer femoral metastases was not different among groups.



**Figure 7.** A Kaplan–Meier survival curve shows that the survival of patients with solitary and multiple metastases was not different among groups.

Table 2. Surgical treatment by location of femoral metastases.	
Location of metastasis in femur and type of surgery	Patients (n= 124)
<i>Proximal femur</i>	
Standard and long trochanteric hip nails <sup>a</sup>	54
Proximal femoral excision and arthroplasty reconstruction <sup>c</sup>	28
Proximal femoral resection and megaprosthesis reconstruction <sup>b</sup>	14
<i>Femoral diaphysis</i>	
Long trochanteric hip nails <sup>a</sup>	20
<i>Distal femur</i>	
Long trochanteric hip nails <sup>a</sup>	6
Distal femoral megaprotheses <sup>d</sup>	2

<sup>a</sup>Veronail®, Orthofix, Italy

<sup>b</sup>Mutars® Proximal Femoral Reconstruction, Implantcast, Germany

<sup>c</sup>Quadra®, Medacta International, Switzerland

<sup>d</sup>Mutars® Distal Femoral Reconstruction, Implantcast, Germany

univariate survival predictors (Tables 3 and 4). The only factor found to be multivariate survival predictor was the presence of a pathological fracture (actu-

al pathological fracture) ( $p= 0.001$ ). Gender, type of cancer, number and location of metastases, as well as the type of surgery were not important multivar-

<b>Table 3. Metastatic presentations and their significance for survival.</b>			
<b>Metastatic presentation</b>		<b>Patients (n)</b>	<b>Survival (<i>p</i>-value)</b>
<i>Independent</i>			
Gender	Male vs. female	60/64	No difference (0.457)
Type of cancer	Breast vs. renal, lung, prostate	36/28/28/10	No difference (0.865)
Number of metastases	Solitary vs. multiple	88/36	No difference (0.080)
Location of femoral metastasis	Proximal vs. distal	90/14	No difference (0.626)
Type of surgery	Nailing vs. excision/resection	80/44	Higher in patients treated with excision/resection (0.002)
Pathological fracture	Impending vs. actual	72/52	Higher in patients with impending fracture (0.001)
<i>Associated with pathological fracture, type of surgery, and location of femoral metastasis</i>			
Impending fracture	Nailing vs. excision (arthroplasty)	44/28	No difference (0.155)
Actual fracture	Nailing vs. resection (megaprosthesis)	36/16	Higher in patients with actual fracture treated with resection (0.039)
Solitary metastasis	Impending vs. actual fracture	54/34	Higher in patients with solitary metastasis and impending fracture (0.027)
Multiple metastasis	Impending vs. actual fracture	20/16	No difference (0.194)
Proximal femoral impending fracture	Nailing vs. excision (arthroplasty)	36/28	No difference (0.876)
Proximal femoral actual fracture	Nailing vs. resection (megaprosthesis)	18/14	Higher in patients with proximal femoral actual fracture treated with resection (0.002)

iate predictors of survival (Table 4).

#### *Complications*

The complications rate for the patients with femoral metastases included at the latest follow-up for the purpose of this study was 6.5% (8/124 patients) (Fig. 11). Infection was the most common complication. The mean survival of the patients with complications was 32 months (Table 5).

#### **Discussion**

Among published research, there is an abundance

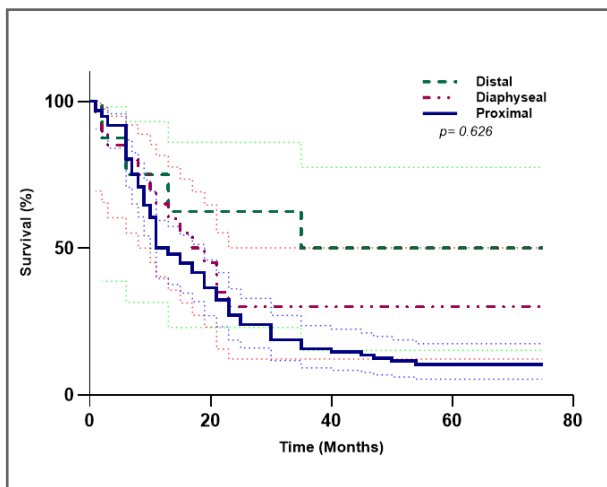
of studies reporting functional and oncological outcomes on surgical modalities for the management of femoral metastases.<sup>6,8,12-18</sup> Capanna and Campanacci et al. attempted to standardize the management of patients with bone metastases by determining which of the patients were suitable candidates for surgical intervention, as well as which of the reconstruction techniques had potentially more favorable outcomes in different clinical situations. Patients were divided into four classes based on several parameters including the metastatic site, life expect-

Table 4. Univariate and multivariate predictors of survival						
Variable	Univariate association	p- value	Multivariate association	p- value	Odds ratio	95% CI
Gender	-	0.457	-	0.224	1.3452	0.5107–1.4021
Type of cancer	-	0.865	-	0.986	1.0197	0.8697–1.1835
Number of metastases	-	0.080	-	0.126	0.7655	0.4267–0.9813
Location of metastasis	-	0.626	-	0.481	1.1212	0.7583–1.6383
Type of surgery	+	0.002 <sup>a</sup>	-	0.072	0.6328	0.4156–1.0229
Actual Pathological fracture	+	0.001 <sup>a</sup>	+	0.002 <sup>b</sup>	2.0794	1.720–3.7110

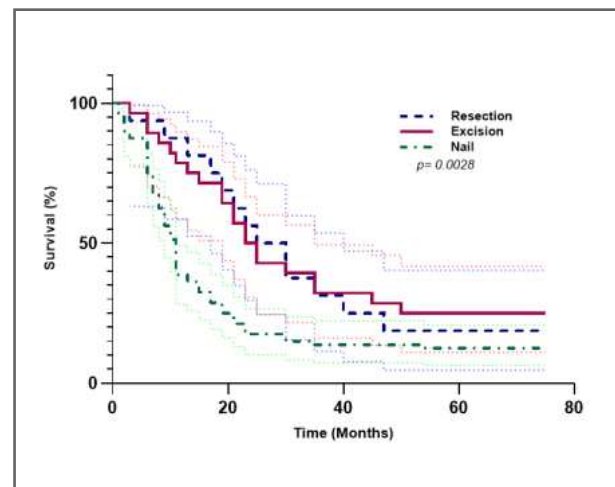
The only significant factor in multivariate association was the occurrence of a pathological fracture (actual pathological fracture).

<sup>a</sup> Statistically significant based on univariate analysis.

<sup>b</sup> Statistically significant based on multiple regression analysis (p= 0.008).



**Figure 8.** A Kaplan–Meier survival curve shows that the survival of patients with proximal, diaphyseal and distal femoral metastases was not different among groups.



**Figure 9.** A Kaplan–Meier survival curve shows the survival of patients treated with nailing or excision/resection; survival was statistically significantly higher in patients treated with tumor excision and arthroplasty reconstruction or tumor resection and megaprosthesis reconstruction.

tancy, tumor type and stage, risk for pathological fractures, presence of visceral metastases, and sensitivity to nonsurgical therapies. According to this protocol, patients are surgically treated with either

prosthetic replacement or osteosynthesis with or without cement.<sup>7,19</sup> Due to extensive disease, a relative contraindication for operative treatment of any metastatic lesion in the extremities is considered to

**Table 5. Complications of surgical treatment.**

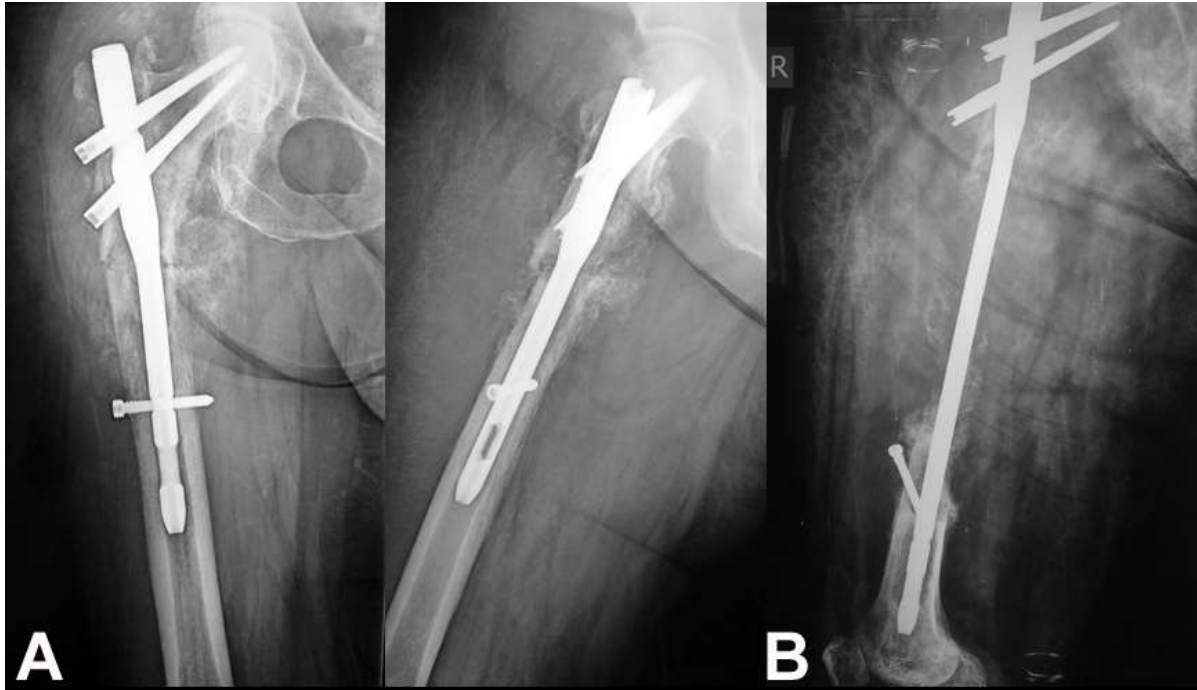
Patient no/ Gender	Metastatic presentation	Type of surgery	Complication	Outcome (months)
1/Female	Proximal femoral actual pathological fracture, gastrointestinal cancer	Intramedullary nailing	Tumor progression	DWD (28 months)
2/Female	Proximal femoral actual pathological fracture, breast cancer	Intramedullary nailing	Nail breakage (revision with a megaprosthesis)	DWD (52 months)
3/Male	Proximal femoral actual pathological fracture, lung cancer	Resection and megaprosthesis reconstruction	Dislocation (open reduction)	DWD (32 months)
4/Male	Proximal femoral actual pathological fracture, prostate cancer	Resection and megaprosthesis reconstruction	Breakage of neck of implant (revision of implant)	AWD (16 months)
5/Female	Proximal femoral actual pathological fracture, gastrointestinal cancer	Excision and arthroplasty reconstruction	Infection (debridement and antibiotics)	DWD (24 months)
6/Male	Proximal femoral actual pathological fracture, lung cancer	Resection and megaprosthesis reconstruction	Disassembly of the megaprosthesis	DWD (9 months)
7/Male	Proximal femoral actual pathological fracture, renal cancer	Excision and arthroplasty reconstruction	Infection (debridement and antibiotics)	AWD (26 months)
8/Female	Proximal femoral actual pathological fracture, breast cancer	Intramedullary nailing	Infection (debridement and antibiotics)	DWD (32 months)

*DWD, dead with disease; AWD, alive with disease.*

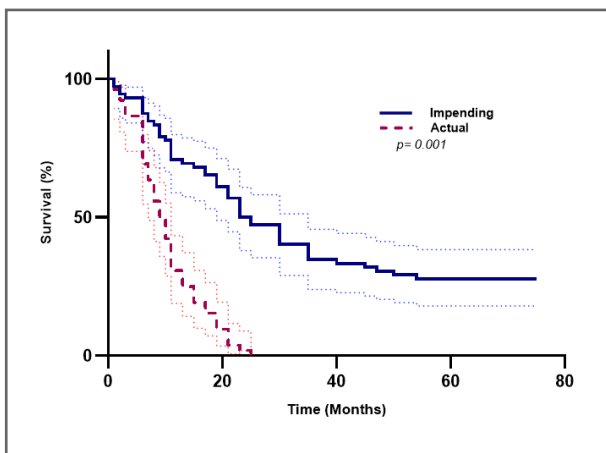
have expected survival of less than 4 - 6 weeks.<sup>20</sup> Less invasive surgery is preferable in patients with a life expectancy of 3 - 12 months, while in those with better prognosis and long-term expected survival (>12months) en bloc resection of the lesion and prosthetic reconstruction, which is more invasive but durable, should be attempted.<sup>3,21,22</sup> During the previous years, several preoperative survival prediction models were utilized with variability of accuracy power. Further development is necessary, so

that these tools become reliably implemented in the daily decision-making of orthopaedic surgeons.<sup>20</sup>

Metastatic bone disease is a common complication of cancer with a wide variety of tumors metastasizing to bones.<sup>23</sup> Higher survival rates at 12 months have been recorded in patients with breast cancer, myeloma, lymphoma and kidney cancer while lung, prostate and unknown cancer as primary tumors are associated with lower patient survival.<sup>24</sup> Breast cancer has proven to be a positive predictor



**Figure 11.** (A) A 75 year-old woman with gastrointestinal cancer and right proximal femoral pathological fracture treated with intramedullary hip nailing and postoperative radiation therapy. (B) Tumor progression and revision operation with a long reconstruction type nail for palliation and nursing.



**Figure 10.** A Kaplan–Meier survival curve shows the survival of patients with impending and actual fractures; survival was statistically significantly higher in patients with impending fractures.

of survival, with 12-months survival rates ranging from 45% to 53% in the literature.<sup>10,25</sup> Ratasvuori et al. reported age under 65 years, Karnofsky score

greater than 70 and solitary skeletal metastases as additional favorable prognostic factors in breast cancer patients.<sup>4</sup> Aggressive treatment of metastatic lesions and reconstruction with modular prostheses are related to prolonged survival, while en bloc resection of a solitary metastasis improves survival rates.<sup>4,5,26,27</sup> Patients affected by lung or gastrointestinal cancer are expected to have worse life expectancy and surgical treatment often plays a palliative role. These patients may benefit from less invasive procedures with durable internal fixation and adjuvant radiation therapy. Among authors, there is an agreement that the presence of visceral metastases is an independent negative prognostic factor for patients' survival.<sup>4,5,28,29</sup>

Concerning the location of the metastatic lesions in the proximal femur, 50% affect the femoral neck, 30% the subtrochanteric area and 20% the intertrochanteric area.<sup>18,30</sup> Overall, 12-months survival in patients with metastatic disease of the proximal femur ranges from 42% to 75%.<sup>15</sup> In a recent study

by Angelini et al. which included 40 patients with proximal femoral metastases, the postoperative survival rate of the patients was 70% at 6 months and 58% at 12 months. Higher survival was recorded in patients treated with resection and reconstruction with endoprostheses (EPR) or proximal femoral replacement (PFR) compared to those treated with intramedullary nailing (mean survival time 8 and 11 months for EPR and PFR respectively, mean survival time 5 months for nailing). However, the presence of pathological fracture and the number of metastases did not significantly affect the outcome in patients' survival.<sup>15</sup> Similarly, Guzik et al. analyzed 122 patients with mean follow-up 27 months and found mean survival of 860 days after modular endoprosthetic replacement and 360 days after bone fixation as surgical treatment for metastatic lesions of proximal femur.<sup>18</sup> On the contrary, metastatic lesions located in the femoral diaphysis are less common. In 25% of patients with diaphyseal femoral metastases and pathological fractures survival is critically affected.<sup>31</sup> Huang et al. conducted a study including 16 patients with diaphyseal pathological femoral fractures who were treated with resection and intercalary prosthetic reconstruction with 18.8% and 12.5% overall survival at 12 and 24 months, respectively.<sup>16</sup>

According to current literature, the presence of pathological fractures is a significant negative factor for patients' survival, as patients who have developed actual pathological fractures are related to worse mortality rates compared to those with impending pathological fractures.<sup>4,13,32</sup> Despite its prognostic value, the occurrence of a pathological fracture in the femur is an indication for surgery, as it may have a devastating effect on patients' quality of life with significant functional impairment and severe pain.<sup>6,28</sup> Internal fixation of pathological fractures in femoral diaphysis and metaphysis managed with intramedullary nailing should be reserved for patients with extensive disease, or those with well-expected response to nonsurgical therapies.<sup>3,7,14,33,34</sup> Survival rates of 40% at 12 months, 25% at 24 months and 15% at 36 months were observed in a study evaluating intramedullary nailing for

treatment of patients with pathological fractures of the femur.<sup>14</sup> Prophylactic stabilization of the femoral bone with metastatic tumor lesions seems to improve patients' survival, as it may enable early postoperative mobilization and avoid treatment delay. Philipp et al. recently studied 950 patients with femoral metastatic lesions, of which 38% (362 patients) underwent prophylactic stabilization. This group of patients recorded lower mortality rates compared to those who were treated after the occurrence of a pathological fracture.<sup>17</sup>

We acknowledge several limitations in this study. First, it is a retrospective study with its inherent limitations. Conducting a research paper on patients with metastatic bone disease is a challenge as this group of patients is usually associated with poor prognosis due to advanced disease. However, useful information concerning prognostic variables and outcomes of surgical procedures can be drawn with well-designed retrospective studies on a topical topic. Yet, as a nonrandomized retrospective study potential selection bias may occur. Second, the standard adjuvant treatments that patients received, such as chemotherapy, hormonal and radiation therapy were not included. Third, the types of cancer varied. We preferred to include all patients with different primary tumors to femoral bone in order to investigate the prognosis and treatment outcome. High grade tumors with multiple metastases in older people appear to have a negative impact on survival. Nevertheless, none of these variables was found important predictor of survival in this study. Fourth, we did not include patients with myeloma even though the principles for pathological fracture management and myeloma have been similar. As a primary hemoproliferative malignancy, we consider myeloma a clinical entity with different prognosis and outcome from metastatic bone lesions.

In conclusion, this study showed variable survival of patients with metastases of the femur from various cancers. The survival was higher in patients with femoral metastases when treated for an impending fracture compared to those experiencing an actual pathological fracture. Additionally, the results of this study showed that patients with prox-

imal and distal femoral pathological fractures have higher survival although having a higher rate of complications when treated with metastatic tumor resection and reconstruction. The later may be biased by the relatively small sample size of the present study. Actual pathological fractures and type of surgery were the univariate predictors of survival;

however, the only multivariate predictor of survival was the presence of a pathological fracture. The rate of complications should be acknowledged and kept to minimum in cancer patients.

#### Conflict of Interest

The authors declared no conflicts of interest.

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## Case report

# Acute middle finger radial collateral ligament rupture in an obstetrician during an obstructed labour: a case report and review of the literature

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## Abstract

**Introduction:** Collateral ligaments (CL) injuries of the finger metacarpophalangeal (MCP) joints, other than the thumb, are not commonly encountered and most of the patients are underrecognized. They require prompt evaluation to ensure proper management and prevent long-term residual laxity, pain, loss of joint motion, stiffness, and finally permanent disability.

**Case presentation:** A 63-year-old male obstetrician was evaluated 3 months after an acute trauma at the radial aspect of the middle finger MCP joint, of his dominant right hand. The mechanism of injury, physical examination, conventional radiographs, and magnetic resonance imaging (MRI) revealed disruption of both (proper and accessory) radial collateral ligaments. A dorsolateral approach was used for surgical intervention and the direct repair of the ligamentous rupture.

**Discussion:** Collateral ligament tears of the MCP joints are more frequent than indicated in the literature and many times are underdiagnosed. If they do not receive the appropriate treatment could cause chronic pain and functional impairment, especially in highly demand patients. The anatomical restoration of the overlying structures significantly determines the postoperative functional results.

**Keywords:** Radial collateral ligaments; metacarpophalangeal joint; middle finger; rupture

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## Introduction

Collateral ligaments (CL) injuries of the finger metacarpophalangeal (MCP) joints other than the thumb are relatively infrequent than in the thumb and most of the patients are underrecognized.<sup>1</sup> As far as there are little data in the literature about fingers' CL ruptures, it is difficult to determine specific diagnostic criteria and treatment guidelines and this commonly leads to untreated cases with long-term residual laxity, pain, swelling, loss of MCP joint equilibrium and finally arthritic lesions and stiffness.

The incidence of CL injuries of the MCP joints is approximately 1 in 1000 hand injuries with up to 39% involving the fingers other than the thumb and among them 33% the long finger.<sup>2</sup> These injuries are most common in the fourth decade of life in non-dominant hands of male patients and radial disruptions are more frequent in the ring and small fingers.<sup>2</sup> Isolate tears of the collateral ligaments are rare and may occur in many different anatomical patterns, within their substance or avulsion from their insertion, with or without fractures, and finally in the form of a Stener-like lesion.<sup>3-6</sup> The surgeon must always investigate for any concomitant lesion that could accompany the major injury such as the rupture of the deep transverse metacarpal ligament (DTML), the proximal interphalangeal joint collateral ligament of the same or an adjacent finger, the dorsal or palmar interosseous tendons and in some rare cases the sagittal bands.<sup>7-9</sup>

The MCP joints of the fingers are complex ginglymus joints.<sup>10</sup> They are stabilized in the frontal plane by the radial and ulnar CLs and the cam shape of the metacarpal head results in a tightening of the CLs, especially the proper portion, and thus in greater stability of the MCP joint during flexion.<sup>11</sup> The radial collateral ligaments are thicker, wider, stronger and more oblique the UCLs and are susceptible to injury from laterally and dorsally directed forces that enforce abduction over 40°. Understanding the basic anatomy of the ligaments of the hand, their functional peculiarities and the high degree of suspicion could replace the lack of a reliable clinical test in the diagnosis of CL ruptures of the MCP joints.

## Case presentation

A 63-year-old male obstetrician was admitted to our

department 3 months after an episode of acute trauma at the radial aspect of the middle finger MCP joint of his dominant, right hand. He described an extreme application of force, in a dorsal to volar and radial to ulnar direction on his long finger during an obstructed labour that led to localized pain, swelling and instability of his 3<sup>rd</sup> MCP joint. The patient reported that his symptoms were worsening while grasping objects or flexing his middle finger. Conventional radiographs (AP, oblique, Brewerton views) were requested without any sign of avulsion fracture, subluxation, or dislocation. Physical examination revealed MCP joint laxity in extension and full flexion without a clear end point and a negative cascade sign test (Figure 1). The patient was unable to hold his middle finger straight in extension and to abduct it towards the index finger. The integrity of the second intermetacarpal space (checking deep transverse metacarpal ligament-DTML- lesion) was detected with palpatory dorso-volar test. MRI imaging showed disruption of both (proper and accessory) without bone erosion or subchondral edema (Figure 2).

The patient was operated under axillary nerve block. Through a dorsolateral approach the extensor apparatus was incised longitudinally through the substance of the radial sagittal band. Once the capsule was exposed a capsulectomy was performed and a complete tear in the substance of the RCLs was revealed (Figure 3a). A careful inspection to diagnose any concomitant lesions of volar plate, deep transverse metacarpal ligament, intrinsic muscles or cartilage damage was ineffectual. Torn RCL were repaired with the use of interrupted 4-0 nylon sutures, with the MCP joint being positioned in about 45° of flexion in order to achieve ideal ligamentous tension during fixation, while the dorsal capsule and the extensor hood were closed in layers. (Figure 3b, c, d). Intraoperative clinical evaluation depicted complete joint stability.

The MCP joint was immobilized in a cast in 45° of flexion with IP joints in extension and a buddy splinting between index and middle finger was used for 3 weeks. Buddy splinting was maintained for 3 additional weeks. Physical therapy with active and passive joint mobilization and lymphatic drainage



**Figure 1.** Physical examination revealed MCP joint laxity of the middle finger without a clear end point in passive ulnar deviation.

started 3 weeks postoperatively to avoid edema, fibrosis, and stiffness. The patient achieved full range of motion without residual pain at the end of 10<sup>th</sup> week of rehabilitation and return to previous manual activities as obstetrician and to sports was allowed the 3<sup>rd</sup> month postop. At 24 months follow-up the patient regained full and painless ROM (Figure 4).

### Discussion

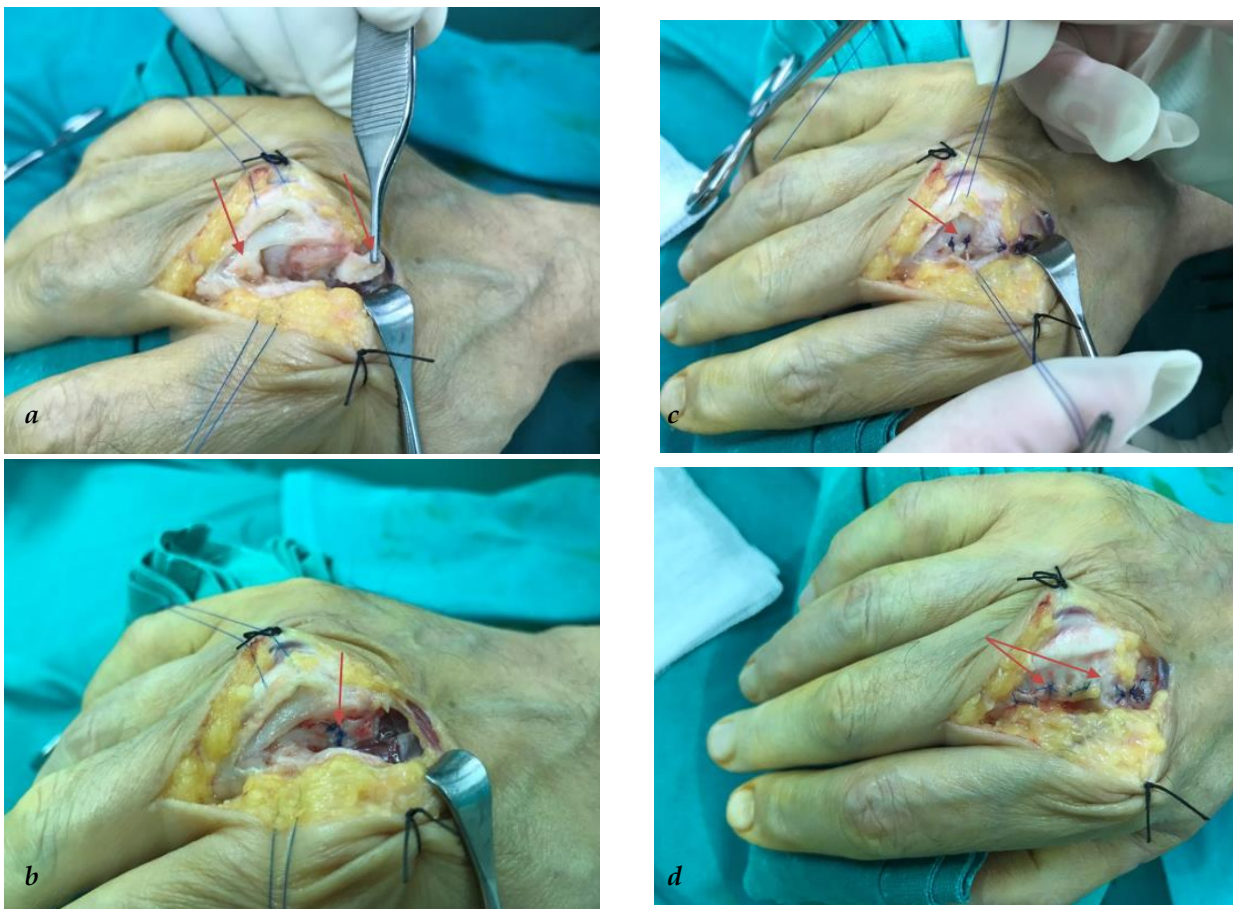
Ruptures of the MCP collateral ligaments of the fingers are considered uncommon compared with thumb lesions and because of this fact, are often underdiagnosed. Although the dynamic support from the interossei muscles, the anatomy and protective action of the adjacent fingers from index to little finger, against the usual forces exerted on the hand justify this point of view, latest studies highlight a greater frequency of these injuries than previous-



**Figure 2.** Preoperative coronal MRI image confirmed rupture of the RCL of the middle finger.

ly believed.<sup>1-2</sup> The collateral ligaments injuries of the MCP joints, other than the thumb, refer to the middle finger in percentage of approximately 33% and may tear most commonly from their insertion, with or without an avulsion fracture.<sup>2,4,12</sup> Sometimes a Stener-like lesion has been described with the interposition of the sagittal band or interosseous tendon and rarely the extension hood between the torn parts of the CLs, that makes conservative treatment inappropriate due to inadequate healing perspective.<sup>2,6,8,13</sup>

Gaston and his colleagues have proposed for these types of injuries a grading system which supports a management algorithm according to the pattern of the MCP collateral ligaments lesion.<sup>14</sup> Grade I is referred to partial CL tear and unaffected joint stability. Grade II characterizes an incomplete tear that



**Figure 3(a, b, c, d).** Once the capsule was exposed and incised a complete tear in the substance of the RCL was revealed, 3b-c-d. Torn RCL was repaired with the use of interrupted 4-0 nylon sutures, with the MCP joint in about 45° of flexion to achieve ideal ligamentous tension during RCL repair, while the dorsal capsule and the extensor hood were closed in layers.

causes laxity problems with a firm end point and Grade III describes a significant joint instability as a result of a complete tear of the MCP collateral ligament. Even though Gaston divided his patients into early stage presenting – acute or late stage – chronic using 4 weeks period as the crucial point, Kang et al. have classified their patients using 6 weeks period as a reference point.<sup>15</sup> Based on the above approximation our patient was obviously classified as a late stage – grade III type of injury. In agreement with most researchers, we categorized the lesion and established a definite surgical indication based mainly in clinical examination.<sup>8,14,16</sup> We believe that appropriate radiological views, MRI or arthrography

could not modify our treatment or surgical indications but only our intraoperative options.

Generally, there is a consensus that surgical intervention is indicated in any Grade III injury which is characterized by a notable laxity with no end point and multiplanar joint instability regardless the cause of these clinical features (avulsion fracture, Stener-like lesion etc). Although, a conservative treatment for Grade I or II acute injuries with interdigital buddy taping, splinting or casting is broadly acceptable, we must have always in mind that an underestimated lower grade injury could lead to sub-optimal results.<sup>8,14,17</sup> We believe that Grade II injuries a) with late presentation and



Figure 4. Patient regained full and painless ROM (24 months follow-up clinical examination).

residual, moderate or severe, symptoms and signs of pain and functional impairment, or b) patients who are not satisfied after any type of conservative treatment especially for the RCL of the index finger must undergo surgery.

In the literature many surgical techniques are well established according to the type of injury like direct repair, pull-out suturing through the bone, capsular shift dorsally, bone suture anchors and ligament reconstruction with a tendon graft like palmaris longus or extensor digiti quinti proprius (figure of eight or trapezoidal configuration).<sup>14-15,17-20</sup> Chronic radial collateral ligament injuries of the metacarpophalangeal joints with arthritic, degenerative pattern may require arthroplasty or MCP fusion.<sup>14-15</sup> Arthroscopic approaches to non-thumb MCP collateral ligament injuries

have been recently studied but there is a need for more extended evaluation in the future for their functional results.<sup>21</sup> In our case, although we had to treat a late stage, grade III type of injury no degenerative lesions were present and a layered reconstruction was possible, leading to an optimal functional result.

In conclusion collateral ligament tears of the MCP joints are often misdiagnosed and if they don't receive the appropriate treatment could cause chronic pain and functional impairment. Clinical suspicion and standardized physical examination are necessary in order to provide the best treatment choice, especially in highly demand patients.

#### Conflict of Interest

The authors declared no conflicts of interest.

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## Review

# Concept of exosome therapy as a treatment for sports injuries to ligaments in the field of orthopaedics: a brief review

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## Abstract

Exosome therapy has emerged as a promising treatment option for sports-related ligament injuries within the field of orthopaedics. Ligament injuries, commonly sustained during physical activities involving rapid or high-impact movements such as running, jumping, or twisting, can lead to pain, swelling, and limited joint mobility. These injuries, if not appropriately managed, can result in long-term functional impairment. Exosomes, small extracellular vesicles rich in proteins, RNA, and growth factors, play a crucial role in cellular communication and tissue regeneration. This study explores the potential of exosome therapy to enhance ligament healing by modulating inflammatory responses, stimulating fibroblast proliferation, and promoting angiogenesis. These mechanisms work synergistically to accelerate tissue repair and improve the biomechanical strength of ligaments, making exosome therapy a more effective treatment option compared to conventional approaches. Unlike traditional stem cell therapy, exosome therapy does not carry the same high immunogenic risks and technical challenges. Preclinical studies have demonstrated the ability of exosomes to reduce inflammation, prevent fibrosis, and improve ligament regeneration. Moreover, exosome therapy can be combined with biomaterials like hydrogels to optimize stability and retention at the injury site, further enhancing its therapeutic potential. Despite promising results in preclinical trials, further research is required to determine optimal dosages, delivery methods, and long-term safety profiles. This review aims to provide insights into the concept of exosome therapy and its potential as a novel, low-risk, and effective treatment for ligament injuries in orthopaedic practice.

**Keywords:** Exosome; ligament; sports injury; orthobiologic therapy

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## Introduction

Ligament injury on sports are common, particularly among athletes and active individuals, as ligaments are crucial for maintaining joint stability and function by connecting bones. Ligament injury on sports, particularly anterior cruciate ligament (ACL) ruptures represent a major burden in active populations worldwide. Recent data from elite European football report an ACL injury incidence of around 0.40 ruptures per 1,000 match hours, while professional Asian leagues show overall injury rates of approximately 5.1 per 1,000 exposure hours with ACL ruptures contributing disproportionately to time-loss.<sup>1,2</sup> Hospital-based and national reports from Indonesia similarly indicate that ligament injuries constitute a substantial proportion of knee pathologies in young, physically active individuals, especially those participating in football, basketball and martial arts.<sup>3</sup> Ligament injuries often result from excessive mechanical trauma, such as sudden acceleration, deceleration, abrupt rotation, or hard impacts. A common example is ACL injuries in the knee, typically caused by pivoting movements involving rotation and excessive valgus stress. The pathophysiology involves collagen fiber rupture, local inflammation, extracellular matrix degradation, and immune cell recruitment, leading to joint instability and a higher risk of complications like osteoarthritis over time.<sup>4</sup> Traditional treatment includes conservative methods like immobilization, physical therapy, and anti-inflammatory medications, with surgical reconstruction for complete ruptures. However, ligament healing is often slow and incomplete due to limited vascularization and the complex tissue structure. Recent advances in regenerative therapies, such as stem cells, growth factors, and biomaterials, aim to accelerate healing by enhancing ligament integrity and reducing excessive inflammation that impedes tissue regeneration.<sup>5,6</sup> Exosome therapy has emerged as a promising innovation in orthobiologic therapy, with exosomes extracellular vesicles containing proteins, RNA, and growth factors—acting as mediators to stimulate tissue regeneration. In ligament injuries, exosomes promote fibroblast proliferation, angiogenesis, and inflammation modulation, improving healing speed

and quality compared to conventional therapies.<sup>5</sup> Recent studies suggest that exosome application improves the biomechanical strength of healed ligaments and enhances tissue integration with bone, offering a safer and more effective treatment. However, further research is necessary to optimize isolation methods, dosage, and long-term safety for broader clinical application.<sup>7</sup>

## Sports Injuries to Ligaments

Ligament injuries are a common issue in orthopaedics, particularly in athletes and active individuals. Ligaments are connective tissues made primarily of type I collagen and elastin, connecting bones and limiting joint movement. These structures are vulnerable to damage from repetitive trauma or direct impact during sports, leading to partial or complete tears, joint dysfunction, pain, and limited movement. Injuries often result from excessive torsional forces that exceed the ligament's elastic capacity. Post-injury inflammation can hinder natural healing, making proper treatment crucial to prevent long-term complications like joint instability and osteoarthritis.<sup>8</sup>

## Pathophysiology of Ligament Injuries

Ligament injuries occur when mechanical forces exceed the elastic capacity of the ligament tissue, causing partial or complete tears in the collagen fibers. These injuries often involve excessive rotation, valgus load, or abnormal bone translation in the joint, leading to micro- to macroscopic disruption of the ligament structure. This damage triggers bleeding, swelling, and an inflammatory response, releasing mediators like histamine and prostaglandins, which cause pain and edema. Infiltrating inflammatory cells, such as neutrophils and macrophages, further damage the ligament by releasing proteolytic enzymes that degrade the extracellular matrix. This inflammatory process exacerbates tissue degradation and alters the ligament's microenvironment, impairing its function. Ligament injuries also result in biomechanical dysfunction, particularly the loss of passive stability, which increases the risk of further damage to supporting structures like the meniscus and articular cartilage, potentially leading

**Table 1. Ligament Injury Grading Classification<sup>11</sup>**

<b>Grade</b>	<b>I</b>	<b>II</b>	<b>III</b>
<b>Description</b>	Strain – stretch  Mild Injury	Partial tear  Moderate injury  • IIa – mild partial tear <50%  • IIb – severe partial tear >50%	Complete tear  Serious injury
<b>Fiber continuity</b>	Intact ligament fibers	Incomplete fiber disruption	Complete fiber disruption
<b>Ligament caliber</b>	Dense ligament fibers are normal or thickened	Ligament thickening or thinning	No ligament fibers at the site of the tear
<b>Tension</b>	Tense	Partial loss	Complete disappearance with retraction
<b>Avulsion fragment</b>	-	Possibly	Possibly
<b>Findings in the early acute stage</b>	-	Ligament edema thickening	Ligament edema thickening

to post-traumatic osteoarthritis. Risk factors such as weak muscles, neuromuscular imbalances, and improper dynamic movements contribute to the high incidence of ligament injuries by increasing mechanical stress on the ligament, highlighting the importance of evaluating biomechanical and neuromuscular risk factors to prevent injuries, especially in athletes or physically active individuals.<sup>9,10,12</sup>

**Clinical Sports Injuries on Ligaments**

Ligament injuries in sports are common, especially in activities involving rapid and sudden movements like football, basketball, tennis, and badminton. These injuries typically present with sudden severe pain, swelling around the injured joint, bruising, and limited range of motion. Patients often feel instability or a “giving way” sensation in the joint and may hear a “pop” at the time of injury. These symptoms indicate damage to the ligament’s collagen fibers and local inflammation, resulting in pain and edema. Swelling may also be accompanied by hemarthrosis (blood accumulation in the joint), increasing discomfort and limiting function.<sup>12,13</sup> Ligament injury grading is based on the severity of the

tear and loss of function, with Grade I (mild) injuries involving small tears without joint instability, Grade II (moderate) injuries causing partial tears and some instability, and Grade III (severe) injuries involving complete tears with total loss of function and stability. Grading is important for determining treatment and prognosis, with Grade III injuries typically requiring more aggressive management, including potential reconstructive surgery.<sup>10</sup> The European Society of Radiology (EPOS) outlines the classification of ligament injuries based on grading, as shown in (Table 1).

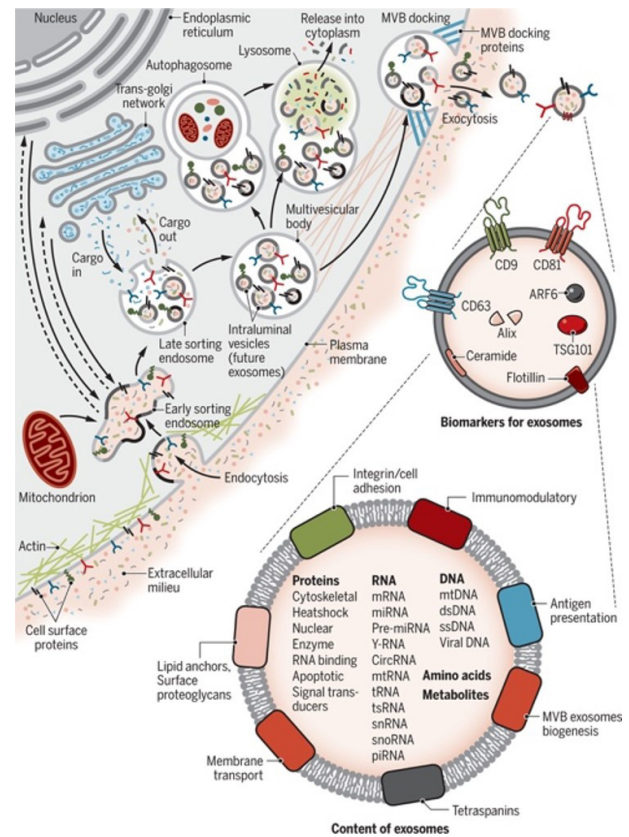
**Ligament Therapy For Sports Injuries**

Conventional therapy for ligament injuries typically involves both conservative and operative approaches tailored to the type and severity of the injury. Non-operative management includes pain modulation, swelling control, physiotherapy modalities, and a gradual rehabilitation exercise program, while operative intervention is reserved for severe injuries that require reconstruction. A multidisciplinary approach and individualized therapy are crucial for optimal outcomes and to minimize long-term complications like joint

instability and osteoarthritis.<sup>14</sup> Physiotherapy rehabilitation plays a key role in restoring joint function and strengthening supporting muscles, with exercises focusing on increasing range of motion (ROM), strengthening the quadriceps and hamstrings, and improving neuromuscular control. These exercises begin with comfortable movement and progress to functional activities such as balance training, proprioception, and closed-chain exercises to enhance joint stability. The goal is to prevent muscle atrophy and reduce re-injury risk by improving knee joint mechanics and stability.<sup>15</sup> In cases of severe ligament injuries, such as total tears of the anterior cruciate ligament (ACL), ligament reconstruction using tendon grafts (e.g., patellar or hamstring tendon) is often necessary to restore mechanical stability and allow patients to resume normal activities. Post-operative rehabilitation is critical for achieving maximum functional recovery, starting with pain reduction, swelling control, and range of motion maintenance, followed by muscle strengthening, balance training, and preparation for return to competitive sports. The success of this therapy depends on accurate diagnosis, patient adherence to rehabilitation, and the selection of appropriate treatment methods for the injury.<sup>10,14</sup>

### Definition and Characteristics of Exosomes

Exosomes are nano-sized extracellular vesicles (ranging from 40 to 160 nm) produced by nearly all eukaryotic cell types through an endosomal biogenesis pathway. They form from the invagination of the plasma membrane and the creation of multivesicular bodies (MVBs), which release intraluminal vesicles into the extracellular space via exocytosis (Figure 1). With a lipid bilayer membrane similar to cells, exosomes contain biomolecules like proteins, lipids, DNA, mRNA, and microRNA, serving as agents of intercellular communication that facilitate the exchange of materials and biological signals, influencing target cell behavior in various physiological and pathological processes such as cancer development, neurodegeneration, and infections. Due to the protection of the lipid bilayer, the proteins and RNA within exosomes remain intact during their journey through biological fluids, making them an effective means of delivering functional molecules to target cells. The composition of exosomes can



**Figure 1. Exosome Biogenesis and Identification.** Exosome surface proteins include tetraspanins, integrins, immunomodulatory proteins, and more. Exosomes can contain various types of cell surface proteins, intracellular proteins, RNA, DNA, amino acids, and metabolites. Fluid and extracellular constituents such as proteins, lipids, metabolites, small molecules, and ions can enter the cell, along with cell surface proteins, through endocytosis and plasma membrane invagination.<sup>16</sup>

be influenced by the microenvironment and metabolic status of the parent cell, making them a key subject in modern therapies and liquid biopsy diagnostics. Exosome products play a crucial role in intercellular communication, reflecting the physiological or pathological state of their parent cells, and are isolated using methods like differential ultracentrifugation, size-exclusion chromatography, immunoprecipitation, and polymer precipitation, each with varying advantages and limitations regarding quality and purity. Standard characterization includes size and morphology analysis using electron microscopy or nanoparticle tracking analysis, along with the identification of protein

markers such as CD9, CD63, and CD81 using Western blotting and flow cytometry, as per the International Society for Extracellular Vesicles (ISEV) guidelines. The development of effective isolation and characterization techniques is crucial for ensuring reproducibility and quality in exosome products for diagnostic and therapeutic applications, including regenerative therapy and orthobiologic therapy.<sup>16,17,18</sup>

### **Exosome Working Mechanism in Ligament Regeneration**

In the context of ligament regeneration, exosomes function as carriers of biological signals that regulate cell proliferation, migration, and differentiation at the site of ligament injury. By delivering messenger RNA (mRNA) and microRNA (miRNA), exosomes stimulate the synthesis of proteins necessary for repairing and replacing damaged ligament tissue, while also regulating immune responses and reducing excessive inflammation to create a favorable healing environment.<sup>19,20</sup> Exosome mechanisms in ligament regeneration include stimulating angiogenesis (formation of new blood vessels), which is essential for supplying nutrients and oxygen to regenerating tissue. Exosomes from mesenchymal stem cells (MSCs) contain growth factors such as VEGF (vascular endothelial growth factor), TGF- $\beta$  (transforming growth factor-beta), and FGF (fibroblast growth factor), which support the growth and maintenance of ligament tissue. Additionally, exosomes inhibit apoptosis (programmed cell death) and fibrosis, which can disrupt regeneration, while enhancing collagen production and extracellular matrix components vital for ligament strength and elasticity.<sup>20,21</sup> Moreover, exosomes regulate local immune modulation by increasing anti-inflammatory cytokines like IL-10 and suppressing pro-inflammatory cytokines, contributing to reduced inflammation and fibrosis that could damage ligament structure. This anti-inflammatory effect is essential for accelerating regeneration and restoring the mechanical function of ligaments. Recent studies suggest that MSC-derived exosomes in ligament regenerative therapy accelerate recovery while reducing inflammatory complications commonly seen after ligament injuries.<sup>20,21</sup>

### **Exosome Therapy in Sports Ligament Injuries**

Exosome therapy for sports ligament injuries is a groundbreaking innovation in regenerative medicine that utilizes small extracellular vesicles produced by cells, particularly mesenchymal stem cells (MSCs). These exosomes serve as carriers of biological signals, delivering molecules like proteins, RNA, and growth factors that regulate tissue repair processes. In ligament injuries, exosomes modulate the inflammatory process, which is crucial in early healing stages, and support fibroblast proliferation and differentiation for extracellular matrix synthesis, essential for reconstructing damaged ligaments.<sup>5,7</sup> Preclinical studies show that exosome administration can enhance biomechanical strength by stimulating angiogenesis (new blood vessel formation) and promoting osteogenesis at the tendon-ligament interface, reducing the risk of graft failure or tissue reconstruction failure.<sup>21</sup> Exosomes also regulate macrophage polarity towards an anti-inflammatory phenotype, helping to suppress excessive inflammation that can impede healing.<sup>7,20</sup> This therapy offers advantages over direct stem cell treatments, such as reduced immunogenicity and technical complications, and can be combined with biomaterials like hydrogels to enhance stability and retention at the injury site, improving clinical effectiveness and recovery time.<sup>20,23</sup> Overall, exosome therapy shows great potential as an alternative and adjunct in treating sports ligament injuries, with mechanisms that modulate inflammation, stimulate tissue regeneration, and repair microstructures of damaged ligaments. Further clinical trials are needed to evaluate dosages, administration methods, and safety profiles, so this therapy can be widely adopted in clinical sports medicine.<sup>24</sup> In orthobiologic therapy, exosome therapy offers a new alternative for repairing musculoskeletal tissues, including bones, ligaments, tendons, and cartilage, and shows promise for treating conditions such as osteoarthritis, ligament injuries, and bone fractures. It can become a standard adjunctive treatment, promoting tissue regeneration, improving biomechanical function, and enhancing patients' quality of life, although challenges remain in developing stable exosome products, optimal dosages, and best delivery methods.<sup>25</sup> Additionally, combining exosomes with scaffolds or

hydrogels could enhance therapy targeting, enabling personalized treatment designs based on injury type and severity.<sup>26</sup> Exosome therapy is expected to revolutionize orthobiologic therapy, especially for acute and chronic injuries, with better regenerative outcomes and minimal side effects.<sup>27</sup> Despite still being in development, its potential as a low-risk, effective regenerative therapy makes it a primary focus for research in the coming decade.<sup>28</sup>

### Conclusion

Sports ligament injuries are common in activities involving sudden movements like running, jumping, or twisting. These injuries can cause pain, swelling, and limited joint function. Exosome therapy, an innovative approach, offers potential for faster and better healing of ligament tissue. Exosomes, small vesicles containing proteins, RNA, and growth factors, promote cell communication, fibroblast proliferation, angiogenesis, and

inflammation regulation, improving ligament regeneration compared to conventional therapies. Exosome therapy has advantages, such as modulating local inflammation and stimulating ligament repair without high immunogenic risks seen in stem cell therapy. Preclinical studies show its effectiveness in improving ligament strength and reducing post-injury complications, but more research is needed to determine optimal dosages, administration, and long-term effects for broader clinical use.

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### Conflict of Interest

The authors declared no conflicts of interest.

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## Review

# Cerebral palsy: elements of current orthopaedic care

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## Abstract

Cerebral palsy is a permanent neurological disorder characterized by static central nervous system injury and progressive musculoskeletal adaptations that impair motor development. The interaction between neurological deficits and evolving orthopaedic changes requires continuous assessment to guide treatment. A structured diagnostic approach, incorporating neurological and orthopaedic examinations, comorbidity evaluation, laboratory testing, and standardized functional scales, is essential for accurate prognosis and individualized care. Deformities in cerebral palsy often worsen with growth, driven not only by spasticity but also by adaptive changes in muscle tissue, highlighting the need for preventive rather than solely reconstructive orthopaedic interventions. Recent insights into muscle pathology support minimally invasive surgical strategies that align with the dynamic nature of the disorder. This review explores the relationship between central nervous system injury, musculoskeletal development, and treatment planning in children with cerebral palsy, emphasizing tailored, timely, and multidisciplinary interventions.

**Keywords:** Cerebral palsy; spasticity; musculoskeletal pathology; muscle contracture; diagnostic matrix; deformity prevention; orthopaedic interventions; minimally invasive operative techniques; goal setting, quality of life

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## Introduction

Cerebral palsy (CP) is a lifelong neurological disorder caused by permanent central nervous system (CNS) injury and progressive musculoskeletal adaptations. The interaction of static neurological damage with growth-related orthopaedic changes profoundly affects motor development in children.<sup>1</sup> Because functional abilities vary widely, comprehensive assessment is essential. A diagnostic framework that integrates neurological and orthopaedic examinations, comorbidity evaluation, laboratory testing, and functional scales enables accurate prognosis and individualized treatment planning.<sup>2</sup> The timing and location of interventions are guided by the recognition that the relationship between deformity and spasticity is multifactorial, with muscle adaptations during growth contributing to progressive contractures and skeletal deformities.<sup>3</sup> Accordingly, pediatric orthopaedic care emphasizes preventive rather than purely reconstructive strategies. Advances in muscle pathology research further support minimally invasive techniques that balance effectiveness with reduced surgical burden. We will investigate the intricate relationships between CNS damage, musculoskeletal changes, and treatment strategies for children with cerebral palsy, highlighting the need for ongoing assessment and tailored interventions.<sup>4,5</sup>

## What is CP; a disease, a description or a diagnosis?

CP is a complex condition that is often misunderstood. It is not classified as a disease; instead, it serves as an umbrella term for a group of permanent disorders affecting movement and posture.<sup>6</sup> According to the International Consensus Definition: "CP describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of CP are often accompanied by comorbidities i.e. disturbances of sensation, perception, cognition, communication and behavior, by epilepsy and by secondary musculoskeletal problems".<sup>7</sup> CP is primarily a clinical diagnosis without a single pathognomonic sign or a definitive test for its identification<sup>8</sup>, resulting from

brain injury at different developmental stages.<sup>9</sup> It presents with musculoskeletal disturbances and often comorbidities.<sup>10</sup> CP is considered part of the Upper Motor Neuron Syndrome (UMNS), which arises from damage to upper motor neurons in conditions such as stroke, spinal cord injury, multiple sclerosis, and degenerative diseases. In CP, UMNS results specifically from a non-progressive brain injury occurring during pregnancy, delivery, or early infancy.<sup>11</sup>

## Forms of CP

CP is categorized by movement disorder, neuromuscular appearance and topographical distribution:<sup>12</sup>

a) The *traditional topographical classification* of CP is based on limb involvement: mono-, hemi-, tri-, and tetra-plegia. The SCPE redefines these as follows: mono/hemiplegia → unilateral CP, di/triple-plegia → bilateral CP, and tetra/quadruplegia → total/whole-body CP.<sup>1</sup>

b) *Movement disorder*: *Pyramidal tract* lesions are associated with spasticity or velocity-dependent hypertonia disorders. *Extra pyramidal tract* lesions with *basal ganglia* involvement are associated with dyskinesias i.e dystonia or choreoathetosis, whereas *cerebellar* involvement is associated with ataxia and hypotonia.<sup>14</sup>

c) The *neuromuscular classification* defines CP by movement disorder. The SCPE recognises spastic, dyskinetic, and ataxic forms; dyskinesia includes dystonia, athetosis, and chorea. Some children show mixed-tone features.<sup>15</sup> Since dystonia and spasticity differ pathophysiologically, they require distinct management.<sup>16</sup>

## What is spasticity?

According to Lance (1980), "spasticity is a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of stretch reflex, as one component of the upper motor neuron syndrome".<sup>17</sup> Thus, spasticity is characterized by excessive resistance during passive muscle stretch, which the examiner feels as a catch which is proportional to the speed at which

■ Spasticity	Velocity-dependent reflex increase. 'Catch' during fast stretch.
■■ Hypertonia	General increase in tone, not velocity-dependent.
■ Synergies	Stereotyped, coupled movement patterns that limit isolated movement.
■■ Co-contraction	Simultaneous activation of opposing muscles, can block or stiffen motion.

Figure 1. Motor abnormalities in UMN syndrome.

stretching is performed.<sup>18</sup> This phenomenon is due to exaggerated stretch reflexes, not merely muscle stiffness.

**Common Misconception:** Spasticity is not just “muscle tightness”- it is a velocity-dependent reflex phenomenon, strictly related to the exaggerated stretch reflex, caused by UMN damage. Spasticity is just ONE component of UMN syndrome. It is often mistakenly used as a broad label for all motor abnormalities seen in UMN lesions<sup>17,11</sup> including (Figure 1):

*Hypertonia* - general increase in muscle tone, not always velocity-dependent

*Abnormal synergies* - stereotyped movement patterns, abnormal muscle coupling

*Co-contractions* - simultaneous activation of opposing muscle groups

Mislabeling it as a catch-all for UMN motor problems can lead to clinical misunderstandings<sup>19</sup> and inappropriate treatment approaches.<sup>20</sup>

**Impact on movement:** Spasticity occurs after motion has begun, indicating that some muscle lengthening has already taken place. This suggests that spasticity is triggered by movement; it is a response to stretch rather than a precursor to movement. The exaggerated stretch reflex associated with spasticity can interfere with muscle function and disrupt normal movement patterns, leading to dysfunction in motor control. This “contamination” of movement execution can lead to a deregulation of motor actions.<sup>21</sup>

#### Clinical picture of CP; is it static?

CP is categorized as a non-progressive static en-

cephalopathy, while the physical manifestations can evolve due to several factors.<sup>1</sup> Progressive musculoskeletal changes are by definition expected<sup>7</sup>; over time, children with CP often experience: increased muscle stiffness, progressive restrictions of joint motion, arising contractures and anatomical changes to normal alignment that can further exacerbate difficulties with movement and posture.<sup>22</sup> In effect, CP is static in terms of brain injury, but progressive in terms of musculoskeletal complications.

#### How might a static encephalopathy result in secondary progressive musculoskeletal deformities?

The “Traditional View” Children may appear normal at birth, but as they grow, muscle hypertonia and spasticity lead to progressive deformities.<sup>23</sup> Mercer Rang (1990) described this process as occurring in three key stages of deformity development.

**Stage 1:** Dynamic Contracture – Range of motion (ROM) limits are experienced during active movements, but passive ROM remains normal

**Stage 2:** Fixed Contracture – Permanent restrictions in joint motion become evident, transitioning to fixed contractures

**Stage 3:** Fixed Contractures with Joint Damage – As contractures become more severe, they lead to joint damage, further complicating movement.

This progressive model, driven mainly by spasticity as the key factor in CP complications, is termed “the traditional view”.<sup>16,24</sup>

#### Consequences of the “traditional view” on CP management

While this view has been influential, it carries several consequences for the management and treatment



Figure 2. Dynamic contractures in CP.



Figure 3. Short muscle disease in CP.

of CP including:

**Linear causation assumption:** The “Traditional View” posits an absolute linear cause-and-effect relation between spasticity and joint contractures in children with CP. This perspective suggests that

exaggerated reflex activity (spasticity) leads to prolonged muscle shortening, resulting in muscle growth failure, joint movement restrictions (contractures), and ultimately, permanent fixed deformities.<sup>25,26</sup>

**Overemphasis on spasticity as the primary cause:** Viewing spasticity as the leading cause of deformities oversimplifies CP, overlooking factors like muscle weakness, abnormal movement, and proprioceptive deficits, and risks neglecting other contributors to functional limitations.<sup>27</sup>

**Anti-spasticity interventions:** The traditional view prioritises anti-spasticity treatments like BTXA and SDR, assuming spasticity reduction will prevent contractures and improve motor skills.<sup>28,29</sup> Orthopaedic surgery is considered a last resort, reflecting a focus on spasticity over structural issues.

#### Does spasticity matter?

The role of spasticity in CP has been a subject of considerable debate among researchers and clinicians.<sup>30-32</sup> Historically, the term *spasticity* was applied broadly to describe a wide range of motor dysfunctions, including abnormal reflexes, impaired motor control, weakness, and even musculoskeletal deformities.<sup>33</sup> Lance defined spasticity as a motor disorder specifically related to *exaggerated stretch reflex activity*<sup>17</sup>, leading to the assumption that reducing it would improve motor function. However, recent research shows that lowering spasticity does not necessarily enhance motor development or outcomes.<sup>34,35</sup>

**Muscle strength vs. spasticity:** Evidence increasingly highlights muscle weakness – not spasticity – as a stronger predictor of function. Ross & Engsborg (2007) found that muscle strength, rather than spasticity, was closely correlated with gait and functional outcomes in children with CP. Spasticity showed little or no significant correlation, suggesting interventions should prioritise strengthening over anti-spasticity alone.<sup>36</sup>

**Limited impact of spasticity on functional development:** Gorter et al. reported only a weak relationship between spasticity and Gross Motor Function Measure (GMFM) development, with environmental and familial influences having greater effects.<sup>37</sup>



*Figure 4. Lever arm disease in CP.*

Similarly, Noble (2019) showed that selective motor control (SMC)-measured via the SCALE tool-was more predictive of GMFM outcomes than muscle volume or joint stiffness, underscoring the limited role of spasticity in functional performance.<sup>38</sup>

**Antispasticity treatments and orthopaedic surgery needs selective dorsal rhizotomy (SDR):** Long-term follow-up studies consistently demonstrate that while selective dorsal rhizotomy (SDR) effectively reduces spasticity, it does not fully prevent musculoskeletal complications. Tendrof et al. (2011), in a 10-year follow-up of 19 children with cerebral palsy, found that despite spasticity reduction, contractures continued to develop, with 16 patients requiring an average of three orthopaedic interventions.<sup>39</sup> In a broader review of 16 studies with  $\geq 10$  years of follow-up, Tendrof et al. (2020) reported that between 28% and 94% of patients required orthopaedic surgery for contracture correction.<sup>40</sup> Similarly, Park et al. (2017), evaluating outcomes of childhood SDR into adulthood, observed that 59% of patients underwent orthopaedic surgery.<sup>41</sup> Tu and Steinbok (2020), in a systematic review of 19 studies involving 1,054 patients, undergoing SDR with 10 years or more of outcome data reported almost identical findings, with 60% of patients requiring

limb surgery.<sup>42</sup> More recent work reinforces these conclusions. MacWilliams, in a follow-up study of over 10 years, compared patients treated with SDR plus antispastic injections to those managed without SDR and limited injections, finding that SDR reduced spasticity and modestly improved gait but did not prevent long-term musculoskeletal complications or improve overall functional outcomes.<sup>43</sup> Likewise, Marron (2023) reported that although SDR may improve gait in the short term, long-term outcomes often mirror those of standard care, underscoring that musculoskeletal complications in CP arise from factors beyond spasticity alone.<sup>44</sup> Collectively, these findings suggest that while SDR addresses spasticity effectively, it does not eliminate the need for orthopaedic interventions, highlighting the multifactorial nature of musculoskeletal deformities in cerebral palsy.

**Botulinum toxin A (BTXA):** Graham et al. and Willoughby et al showed repeated BTX-A injections did not halt hip displacement.<sup>45,46</sup> Fattal-Valevski et al. (2008) found that up to 4 BTX-A injections over 2 years improved long-term gross motor function in children with CP, though tone reduction was short-lived, with optimal benefit after 2-3 treatments.<sup>47</sup> Similarly Tendroff et al. (2009) found only tempo-

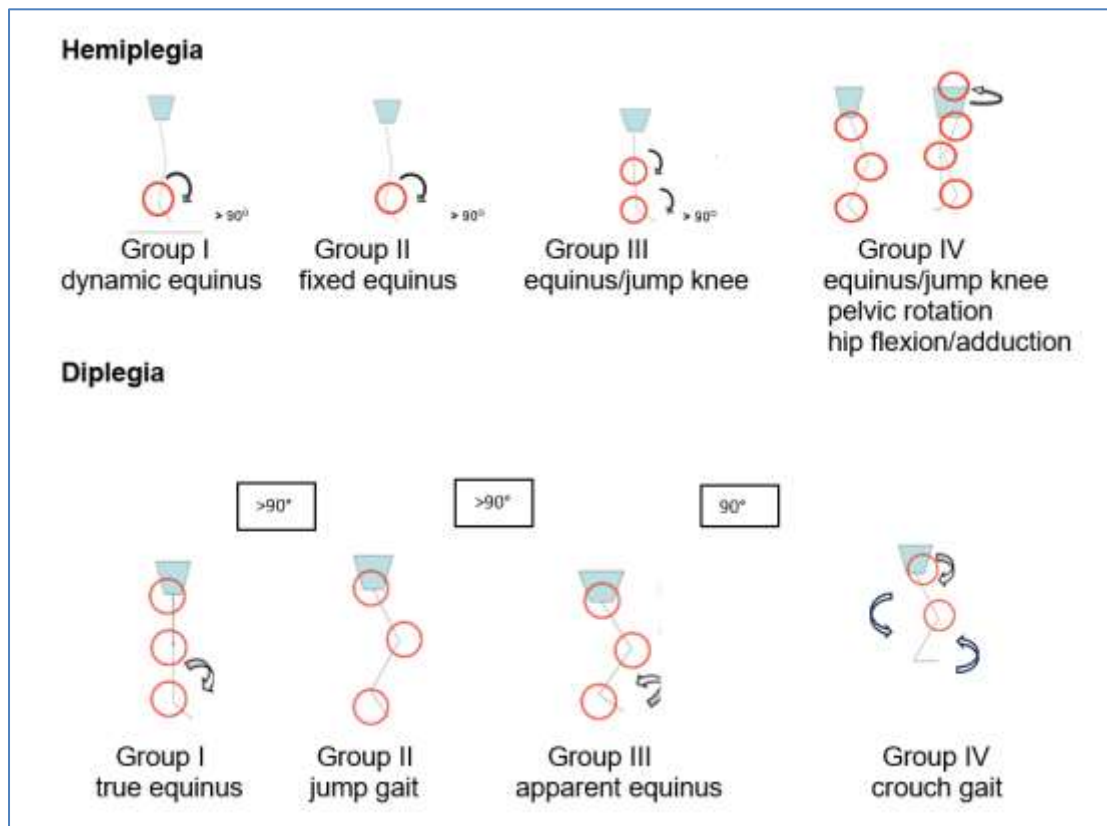


Figure 5. The Winter-Rodda-Gage-Graham Classification in CP.

rary range-of-motion (ROM) improvements, with contractures continuing over time.<sup>48</sup> A systematic review by Sätälä concluded BTXA may “buy time,” but most children older than six still required surgical intervention.<sup>49</sup> Lin et al. also found that among 1,405 CP children (281 BTX-A/1,124 controls) followed for 5 years, outcomes did not differ between groups. BTX-A did not significantly prevent hip dislocation or scoliosis.<sup>50</sup>

**Spasticity and ROM across development:** Spasticity is not static. Lindin et al. found that spasticity increases during early childhood (first 4-5 years) but gradually declines until around age 12-15.<sup>51</sup> Nordmark et al., however, demonstrated a parallel loss of ROM with age, particularly at higher GMFCS levels.<sup>52</sup> The differing trajectories suggest that spasticity and ROM decline are not directly correlated, supporting the view that stiffness arises from mechanisms other than spasticity alone.

**Muscle changes from birth to early childhood:**

Willerslev-Olsen et al. showed that children with CP develop muscle atrophy, reduced growth, and stiffness within the first 1-2 years of life, independent of spasticity.<sup>53</sup> In a complementary population-based study, Clodt et al. found that among 2,693 children examined before age 5, frequent surgeries were required during a 10-year follow-up, with median ages of 4 for hip soft tissue, 7 for foot, and 9 for knee procedures.<sup>54</sup> The early onset of muscle growth reduction and progressive joint contracture implicates impaired muscle development, rather than spasticity alone. Furthermore when comparing the period after 5 years of age, when spasticity typically begins to decline, with the corresponding period of range of motion (ROM) reduction observed beyond 4 years, along with evidence that muscle atrophy and stiffness become established from 3-4 years of age onwards, it is reasonable to infer that progressive

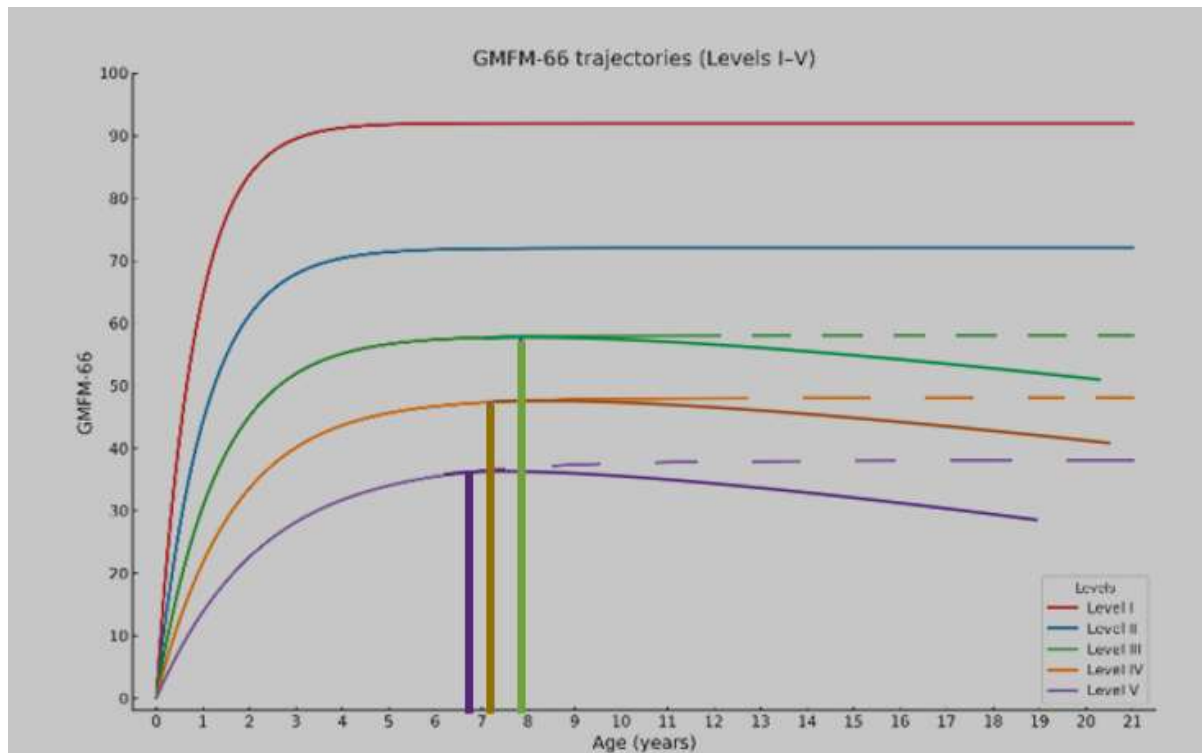


Figure 6. Gross Motor Function (GMF) curves in CP.

ROM restriction is more closely related to ongoing muscle atrophy and shortening rather than to decreasing spasticity. Indeed, muscle relaxation alone does not appear sufficient to prevent the development of contractures in most cases.

### The spastic muscle in CP

The term “*spastic muscle*” reflects a neurological sign of upper motor neuron impairment, not an intrinsic muscle abnormality. Nonetheless, chronic exposure to disordered neural input leads to profound multi-level muscle adaptations.<sup>55,56</sup>

**Muscle as an organ:**<sup>24</sup> Muscle growth lags behind bone growth, leading to shorter, weaker fibers with reduced diameter.<sup>57</sup> This results in decreased strength, increased fatigue, and limited activity. Disuse further compounds weakness and stiffness, reinforcing a cycle of immobility.<sup>58</sup>

**Muscle as a tissue; sarcomere adaptations:** Fewer sarcomeres in series, with remaining sarcomeres overstretched, increase passive resistance and stiffness.<sup>59</sup>

**Extracellular matrix (ECM) alterations:** Hypertrophy of ECM, with excess and abnormally cross-linked collagen, reduces elasticity and heightens stiffness.<sup>60,61</sup>

**Cellular level:** Children with CP have fewer satellite cells, essential for muscle regeneration. Impaired proliferation and maturation further limit hypertrophy and repair capacity.<sup>62</sup>

**Molecular level:** Transcriptomic studies reveal increased expression of ECM-related genes and reduced oxidative metabolism genes in CP muscle, contributing to contracture formation and reduced muscle efficiency.<sup>63,64</sup>

Spasticity and abnormal muscle stiffness reflect distinct, partly dissociating mechanisms. Importantly, contracture is not necessarily linked to spasticity, and reducing spasticity alone does not reliably prevent deformity. Evidence indicates that, although spasticity is clinically relevant, it is not the primary driver of long-term motor impairment in cerebral palsy (CP). Instead, muscle weakness, impaired selective motor control, altered muscle

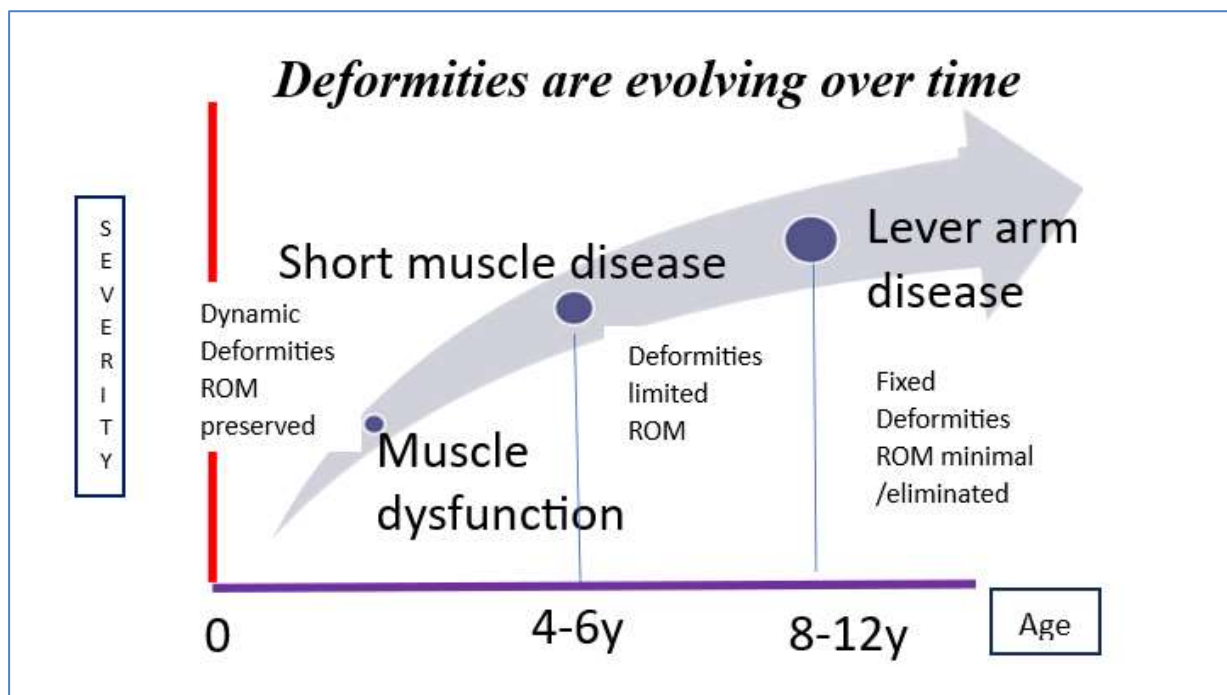


Figure 7. Orthopaedic intervention based on child's age and nature of deformities in CP.

growth, and extracellular matrix (ECM) remodeling appear to play larger roles. Consequently, interventions aimed solely at reducing spasticity (e.g., selective dorsal rhizotomy [SDR], botulinum toxin A [BTXA]) often yield only temporary or partial benefits. More comprehensive approaches that address muscle strength, motor control, and structural adaptations show greater promise for improving functional outcomes and quality of life.

#### Is CP amenable to treatment?

CP constitutes a complex and permanent neurodevelopmental disorder for which no curative therapy is currently available, as CNS damage is irreversible. Given that the CNS represents the locus of permanent impairment, restoration of normal motor function is not feasible, as this would necessitate direct intervention at the level of the central motor drive. Accordingly, therapeutic strategies are directed primarily towards management and functional optimization rather than cure.<sup>2</sup> Moreover, it is essential to acknowledge that the underlying neurological deficits persist despite orthopaedic or other peripheral interventions. The primary aim

of orthopaedic interventions should be to improve the existing biomechanical conditions by creating a more favorable micro-biomechanical environment, enhancing posture, and movement efficiency, ultimately promoting quality of life by correcting or reducing deformities.<sup>65</sup> The “novelle approach” to the pathology of deformities is based on strong evidence that loss of joint ROM is deteriorating over time because of progressive muscle stiffness and diminishing muscle length, while spasticity development is decreasing during the same growth period. Accordingly it becomes crucial the systematic long-term clinical monitoring of both clinical phenotypes aiming to distinguish between these two different pathological entities.

#### Orthopaedic decision-making: luck or science?

In orthopaedic decision-making, successful treatment planning depends on integrating multiple factors through both clinical knowledge and practical experience.<sup>66,67</sup> It is a difficult detection process involving a variety of sources of information from multiple components. A clinician needs to invest significant time and effort into assimilating all the

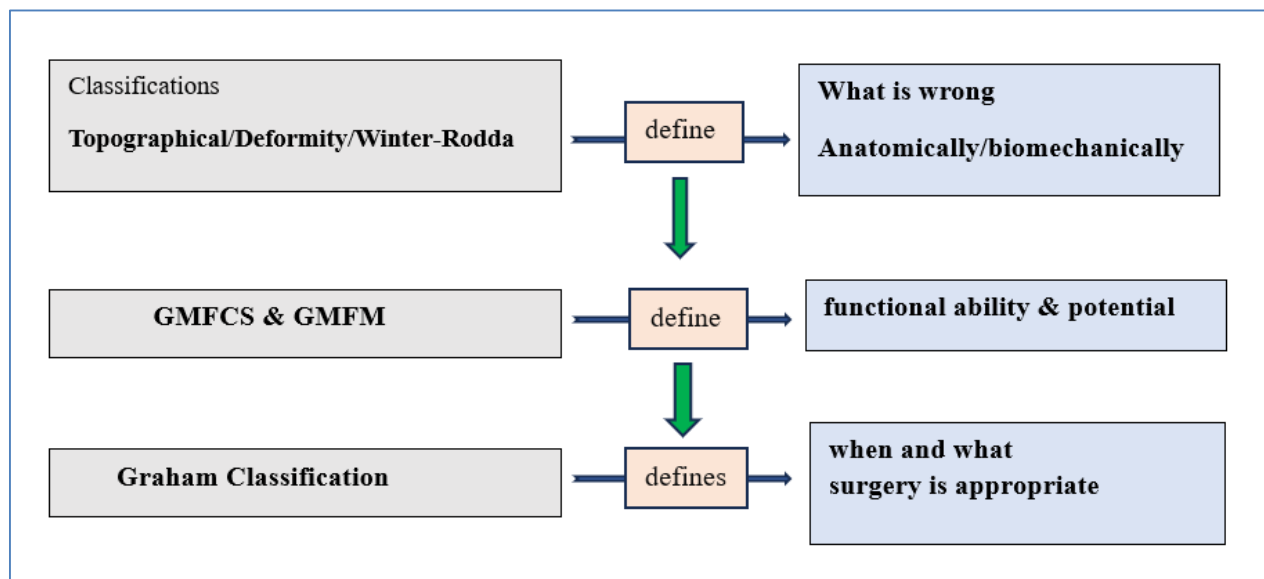


Figure 8. Comprehensive preoperative planning in CP.

available clinical information to determine the impairments that affect a child's capacity to walk.

This complex process requires identifying key elements, which are organized within a diagnostic matrix.<sup>2</sup> The matrix includes several pivotal components:

- 1) **Clinical history**<sup>68</sup>
- 2) **Standardized neurological and orthopaedic clinical examination**
- 3) **Evaluation of spasticity levels**
- 4) **Assessment of soft tissue contractures and deformities:** Joint ROM should be regularly assessed with standardized techniques, documenting changes in muscle length for longitudinal tracking. A key challenge is distinguishing ROM limits caused by spasticity versus structural contractures, since both are tested with passive stretch. To improve accuracy, assessments should be performed at slow and fast stretch velocities in standardized positions, reducing reflex interference [69]. Correctly differentiating spasticity from contracture is crucial, as it determines whether conservative or surgical approaches are most appropriate.
- 5) **Measurement of muscle strength:** Muscle weakness, often more impactful than spasticity, is a key contributor to musculoskeletal deformities. Be-

yond flexor contractures, extensor insufficiency also plays a critical role in limiting range of motion.<sup>70</sup>

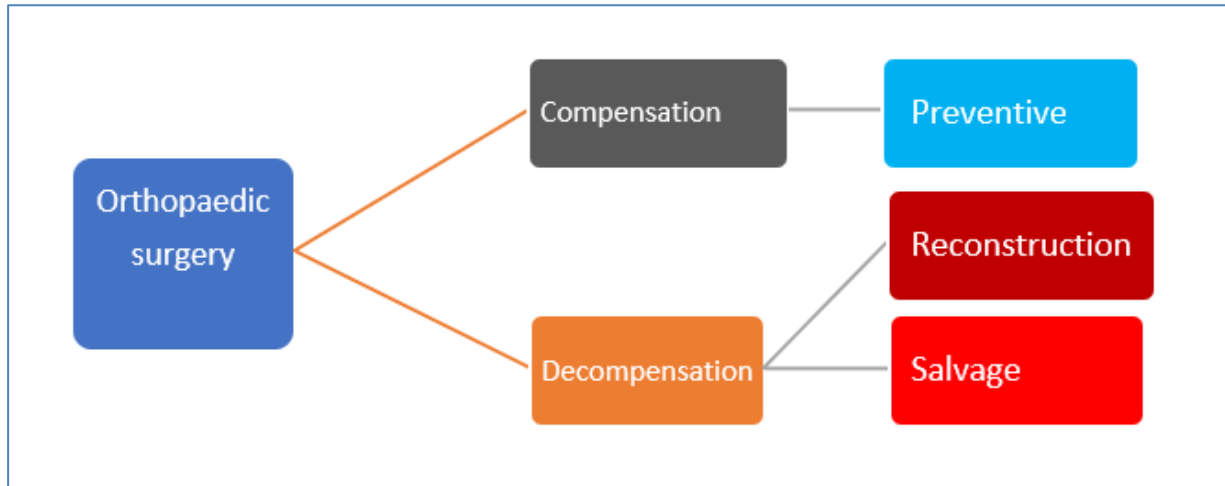
#### 6) Classification of deformities:

a) **Dynamic Contractures** (Figure 2): In this category, movement limitations are transient and occur only during specific motor tasks as a result of exaggerated stretch reflex activity. Importantly, full passive joint ROM is preserved, indicating that muscle length remains within normal limits.<sup>71</sup>

b) **Fixed - short muscle disease** (Figure 3): Over time, muscle tissue may undergo structural changes, becoming increasingly stiff and shortened. This process leads to a progressive loss of joint range of motion. As a result, the initially dynamic nature of contractures diminishes, evolving into a static condition that persistently restricts movement.<sup>71</sup>

c) **Fixed deformities - lever arm disease (LAD)** (Figure 4): Permanent muscle stiffness, shortening, and abnormal movement cause pathological forces on joints and bones, disrupting growth and leading to deformities.<sup>72,73</sup>

7) **Winter-Rodda-Gage-Graham classification** (Figure 5): This four-group system categorizes gait patterns according to the severity of joint involvement and associated deformities. It provides a structured framework for clinical decision-making, help-



*Figure 9. Types of orthopaedic surgery in CP.*

ing to guide the selection of appropriate therapeutic interventions, including orthotic management, botulinum toxin injections, and orthopaedic surgical procedures.<sup>74</sup>

**8) GMFM (Gross Motor Function Measure):** A scoring system that evaluates gross motor function changes based on developmental milestones.<sup>75</sup>

**9) GMFCS (Gross Motor Function Classification System):** A severity grading system that correlates with clinical and musculoskeletal deformity levels. It helps in long-term prognosis and treatment planning.<sup>75</sup>

**10) GMF curves:** These curves represent typical patterns of motor development and are stratified according to the five levels of the GMFCS. Each GMFCS level has a distinct gross motor development curve, reflecting differences in the rate and extent of skill acquisition (Fig. 6). Children in Level I reach higher function and plateau later, while those in Levels IV–V show limited gains and earlier plateaus. Mapping a child's progress on their GMFM curve aids assessment, guides goal setting and intervention, and informs family counseling about likely functional outcomes.<sup>75</sup>

**11) FMS (Functional Mobility Scale):** An outcome measure system used for evaluating changes before and after surgeries.<sup>76</sup>

**12) Diagnostic imaging:** Early identification of

progressive deformities in the spine, lower limbs, feet, and hips.

**13) Instrumented gait analysis (IGA):** This method records and classifies gait deviations, especially complex abnormalities, providing crucial information for treatment planning. These systems and tools are essential for understanding locomotion in CP patients and for tailoring effective treatment strategies.<sup>77</sup>

#### The timing of orthopaedic intervention

The timing of orthopaedic surgery is debated.<sup>78</sup> Traditionally, a staged approach was used starting with anti-spasticity treatments in early childhood and progressing to more invasive orthopaedic surgeries later.<sup>79</sup> More recent recommendations suggest delaying orthopaedic surgery until ages 7–10 (especially for levels GMFCS II & III until ages 10–12) when gait patterns are more mature and the risk of recurrence is lower.<sup>80</sup> At this stage, all fixed muscle contractures and skeletal deformities can be corrected in a single procedure (SEMLS), thereby improving or maintaining walking performance. In the meantime, management often focuses on conservative options such as BTXA, orthoses and physiotherapy.<sup>81</sup>

An alternative interpretation suggests that the optimal window for musculotendinous lengthening procedures of the lower extremities is between

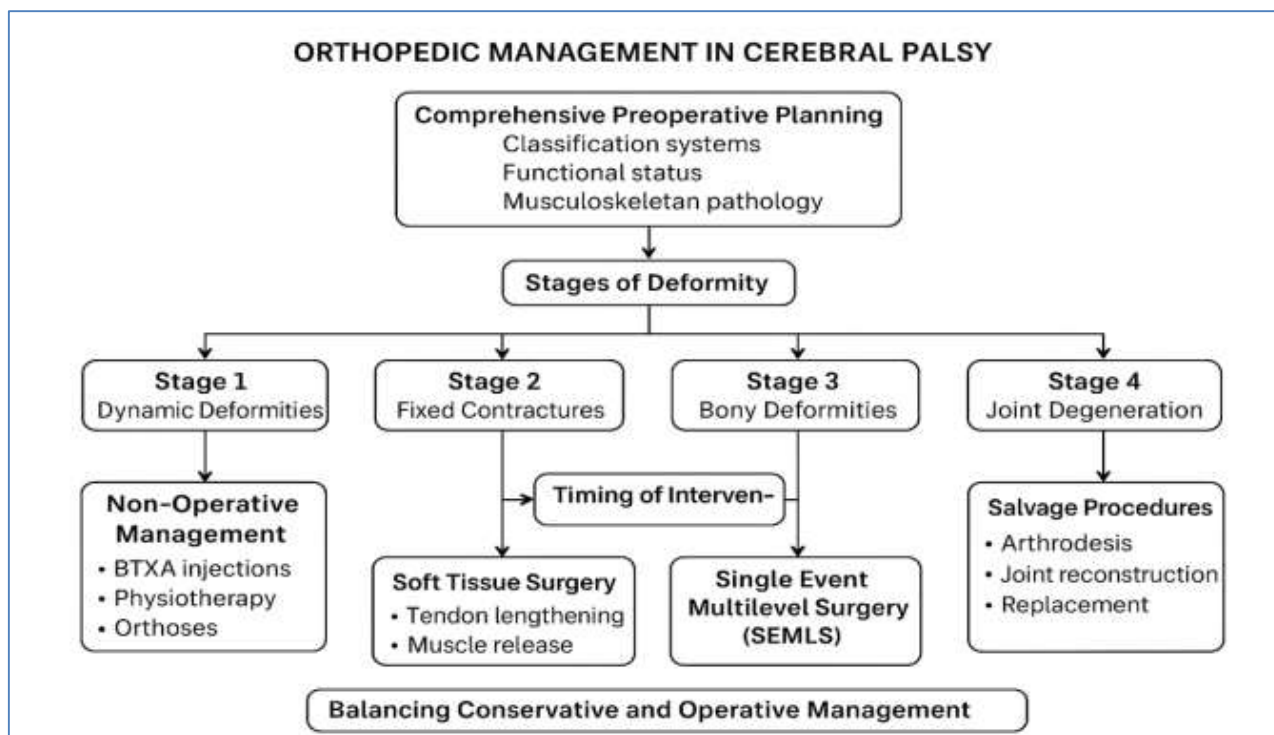


Figure 10. Orthopaedic management in CP.

4 and 7 years of age, given the early onset of lower limb contractures in children with cerebral palsy.<sup>54,82</sup> The rationale is that surgical outcomes are most favorable when performed before the development of severe fixed contractures and skeletal malalignments, which are often responsible for stagnation or regression in gross motor function.<sup>78,83,84</sup> Lennon et al (2024) provide further support for age-sensitive surgical planning, demonstrating that improvements in gait kinematics are strongly influenced by both age and timing of orthopaedic intervention. The most substantial and durable gains were observed in children under 10 years of age, whereas children operated on after this threshold exhibited significantly diminished improvements. Importantly, although surgery was associated with positive outcomes across all age groups, the magnitude of benefit was consistently reduced in older cohorts.<sup>85</sup> Conversely, delaying intervention until after these complications have developed substantially diminishes the effectiveness of surgery due to the presence of complex, decompensated joint and skeletal pathologies.<sup>78</sup>

In 2021, Graham et al. introduced a four-stage classification system that correlates orthopaedic intervention with the child's age and the nature of their deformities<sup>71,86</sup> (Figure 7):

**Stage 1 (dynamic deformities, birth to age 4-6 years):** Characterized by hypertonia with minimal or no contractures. The focus is on tone management, often using BTXA injections to address spasticity.

**Stage 2 (contractures, age 4-12 years):** After the age of 5 years, spasticity tends to diminish, but fixed contractures progressively worsen. Recognizing the transition from dynamic (spasticity-driven) deformities to fixed contractures is crucial. At this stage, orthopaedic soft tissue surgery may be indicated.

**Stage 3 (bony deformity, age 4-12 years):** As contractures develop, secondary bony deformities often arise, further contributing to functional impairment. Management at this stage usually requires a combination of bony realignment procedures (such as osteotomies) and soft tissue releases or lengthenings. These are often performed together during a single

operative session (SEMLS).

**Stage 4 (decompensation, age 10 years to adulthood):** By this stage, severe joint contractures and bony deformities make it difficult to restore optimal function, and interventions are often seen as salvage procedures.

This classification highlights that *orthopaedic intervention is not a last resort*, but rather an integral component of managing fixed deformities at stages 2, 3, and 4. In contrast, BTXA injections or SDR are primarily indicated for, when deformities are still dynamic and spasticity-driven. While non-operative methods are often prioritized initially, it is crucial to recognize that delaying surgical intervention can result in lost functional capacity. Achieving the best outcomes requires balancing conservative management with timely surgery, taking into account the time-sensitive window for optimal functional improvement.<sup>83</sup>

### Comprehensive framework for orthopaedic management in CP

Effective surgical management of orthopaedic problems in patients with CP requires a comprehensive, individualized approach that integrates the patient's functional status, anatomical deformities, underlying muscle pathology, and the patient's developmental trajectory.<sup>2</sup> Central to this process is thorough preoperative planning.

Key components include:

**1. Comprehensive preoperative planning** (Figure 8) Effective planning involves a detailed assessment using multiple classification systems to guide decision-making and prioritize interventions:

#### a. Patient assessment

*Topographical classification*

Identifies distribution of involvement (hemiplegia, diplegia, quadriplegia, etc.)

*Deformity classification*

Structural vs. dynamic deformities

Identifies contractures, torsions, lever-arm dysfunction

*Winter-Rodda classification*

Describes specific gait patterns (e.g., true equinus, jump gait, crouch gait, stiff knee gait)

#### b. Functional capacity

#### GMFCS

Levels I-V (predicts long-term mobility potential)

#### GMFM Curves

Plots developmental trajectory over time

Tracks progress, monitors therapy outcomes, informs goal-setting

#### c. Surgical planning

##### Graham classification

Age-based deformity classification

Incorporates joint restriction and lever-arm dysfunction

Surgery Guides **timing** and **selection** of multilevel procedures (e.g., SEMLS)

## 2. Timing of intervention

**Stage 1 (Dynamic deformities):** Focus on non-operative methods such as BTX-A injections, physiotherapy, and orthoses. Early intervention aims to reduce spasticity and prevent contractures.

**Stages 2–4 (Fixed contractures and bony deformities):** **Soft tissue surgery** (e.g., tendon lengthening, muscle release) addresses persistent contractures.

**Single event multilevel surgery (SEMLS)** may be indicated to correct multiple deformities, by combining multiple orthopaedic procedures (soft tissue and bony procedures) in a single session to reduce recovery time and repeated surgeries.<sup>68</sup> This approach minimizes hospital stays and streamlines rehabilitation processes.<sup>80</sup>

**3. Types of orthopaedic surgery** (Figure 9) Orthopaedic surgeries can be categorized into three main types:<sup>78</sup>

**Preventive surgery:** Aimed at preventing the progression of deformities.

**Reconstructive surgery:** Focused on correcting existing deformities.

**Salvage surgery:** Intended for cases where previous interventions have failed.

**4. Minimally invasive techniques** Minimally invasive surgical techniques are preferred for both bony and soft tissue interventions.<sup>87</sup> Percutaneous muscle lengthening involves making very small incisions to release the appropriate amount of myofascial tissue necessary to lengthen the muscle, re-

ducing spasticity and increasing ease of motion.<sup>88</sup> Regarding osseous procedures, derotation osteotomies of the femur and tibia are optimally performed using closed corticotomy techniques with stabilization provided by titanium elastic nails or Steinmann pins.<sup>89</sup> Additionally, guided growth epiphysiodesis, employing either eight-plates or cannulated screws, represents a minimally invasive approach for correction of angular deformities.<sup>90,91</sup> These procedures reduce recovery time and minimize complications associated with larger interventions.

**5. Muscle selection for interventions** When selecting muscles for surgical intervention, it is crucial to focus on *Multiarticular Muscles* (psoas, rectus femoris, hamstrings, gastrocnemius). These are vital for gait propulsion and coordination but are often more affected by spasticity and weakness, while contributing less to antigravity support compared to single-joint muscles. *Monoarticular muscles* provide joint stability and essential antigravity function, and should generally be preserved to maintain posture and overall function.<sup>92,78</sup>

**6. Consideration of specific muscle pathology:** Soft tissue surgery for neuromuscular disorders should explicitly address intrinsic muscle pathology, particularly the increased passive stiffness resulting from excess extracellular matrix (ECM) hypertrophy and collagen accumulation.<sup>93</sup> In cerebral palsy (CP), maladaptive ECM remodeling—including elevated collagen content, altered cross-linking, and aberrant ECM architecture—contributes significantly to reduced muscle extensibility and functional impairment.<sup>55,56</sup> Surgical techniques like aponeurotic or fractional lengthening are designed to target accessible connective tissue layers (fascia, epimysium, aponeurosis).<sup>94</sup> By releasing these external ECM components, such interventions reduce the mechanical resistance to stretch, permit sarcomere lengthening, improve joint mobility, and restore more favorable force transmission, while preserving overall muscle fiber integrity and the architecture of the muscle-tendon unit.<sup>95,92</sup>

**Aponeurotic lengthening and myofascial release:** The technique involves multiple crosswise incisions

of the fascia/aponeurosis (epimysium), perpendicular to its length, over the adjacent muscle belly. The muscle belly released from a stiffer sheath is allowed to be stretched in a new lengthened position and deformity corrected, while muscle integrity is preserved and muscle belly – tendon ratio improved.<sup>96,92</sup>

**Fractional lengthening:** The target region is the anatomical site where the muscle belly laps into the tendon. The tendon is crosswise transected with multiple perpendicular incisions and the musculotendinous unit continuity is disrupted. The muscle in the region of the cuts is able to stretch in the new lengthened position, which can help reduce spasticity and improve range of motion.<sup>97,95</sup> Both techniques reduce sarcomere tension in sectioned fascia and musculotendinous regions, allowing the muscle to reset at a new resting length. This decreases spasticity and stiffness, improving joint ROM.<sup>98</sup>

**7. Balancing conservative and operative management:** Early stages focus on non-operative care to manage spasticity and maintain mobility. Recognition of time-sensitive surgical windows is essential to preserve or improve functional outcomes. Decisions should consider patient-specific goals, potential functional gains, and risks of delaying surgery (Figure 10).

**8. Goal setting and family counseling:** When setting goals for CP children, it is important to use the GMFCS level and GMFM developmental curves to guide realistic expectations. Families benefit from counseling that explains likely progress, timing of interventions, and long-term planning. Goals should be individualized across key domains—independence, communication, mobility, daily activities, fitness, and social participation—while also preparing for future transitions into adulthood.<sup>4</sup> This holistic approach ensures that therapy focuses not only on motor skills, such as walking, but also on meaningful daily life, inclusion, and long-term quality of life.

## Conclusion

Cerebral palsy presents a multifaceted challenge in terms of definition, clinical manifestations, and therapeutic strategies. It encompasses a range of

disorders with varying etiologies and associated comorbidities. Although the initial central nervous system injury is static, musculoskeletal issues tend to progress during growth. Surgical interventions should be viewed as management strategies rather than definitive treatments aimed at restoring normality. They are designed to enhance mobility, fitness, and independence by addressing movement impairments due to musculoskeletal deformities. Decision-making requires careful consideration of

clinical data collected throughout growth, with an emphasis on age-related factors and specific muscle pathologies. Ultimately, orthopaedic surgery aims to improve biomechanical environments to facilitate better posture and motion while anticipating potential complications from underlying neurological conditions.

#### Conflict of Interest

The authors declared no conflicts of interest.

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Review

# Effectiveness of virtual reality and robotic-assisted therapy for upper limb rehabilitation in spinal cord injury: a narrative review

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## Abstract

Spinal cord injury is a complex neurological condition that impairs upper limb function and independence in activities of daily living. In recent years, robotic-assisted therapy and virtual reality (VR) have appeared as promising approaches in upper limb rehabilitation. This study presents a condensed narrative review of the current literature on the effectiveness of these technologies on the upper limb rehabilitation in individuals with spinal cord injury.

The findings of this review demonstrate that both robotic and VR interventions may improve motor function, strength, and functional independence in upper limbs. However, results remain inconsistent, with several studies reporting no significant differences between the study groups and suggesting that benefits may not be attributable only to technological interventions.

Overall, while these technologies appear safe and promising, further high-quality studies are required to establish their clinical effectiveness.

**Keywords:** Spinal cord injury; virtual reality; robotic rehabilitation; upper limb

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## Introduction

Spinal cord injury (SCI) is considered to be a complex and multifaceted medical condition. Nonetheless, even with a comprehensive understanding of the anatomical and physiological aspects of the human body, the experience of individuals with SCI remains markedly distinct as it is influenced and shaped by a range of environmental factors. Individuals with SCI interact extensively with multiple components of the healthcare system, spanning from emergency medical care and surgical intervention to rehabilitation services. SCI is defined as a critical neurological disorder affecting the central nervous system. However, it subsequently gives rise to complications that affect the respiratory, cardiovascular, musculoskeletal, and genitourinary systems.

Epidemiologically, as of 2024, 15.4 million people have been recorded living with spinal cord injury.<sup>1</sup> In Europe, irrespective of etiology, SCI demonstrates a relatively low annual incidence estimated at 15-25 new cases per million population. The overall prevalence ranges from 300 to 1,000 individuals per million population living with the long-term consequences of SCI. In Greece, a unified national registry for individuals with SCI is currently lacking. Nevertheless, regional epidemiological data indicate an incidence of approximately 33,6 cases per million population.<sup>2</sup>

The International standards for Neurological Classification of spinal cord injury (ISNCSCI) established by the American spinal injury Association (ASIA) constitute the gold standard for the assessment of SCI.<sup>3</sup> This standardized evaluation framework determines both the neurological level of injury and the severity of impairment, thereby providing a structured protocol for clinical management, prognostication, and research applications. Within the ASIA clinical assessment, both motor and sensory functions are systematically evaluated. In the assessment of movement, the muscle strength of key muscle groups is evaluated using a numerical scale from 0 (paralysis) to 5 (normal strength). The motor level of the injury is defined as the lowest spinal level with at least muscle strength that

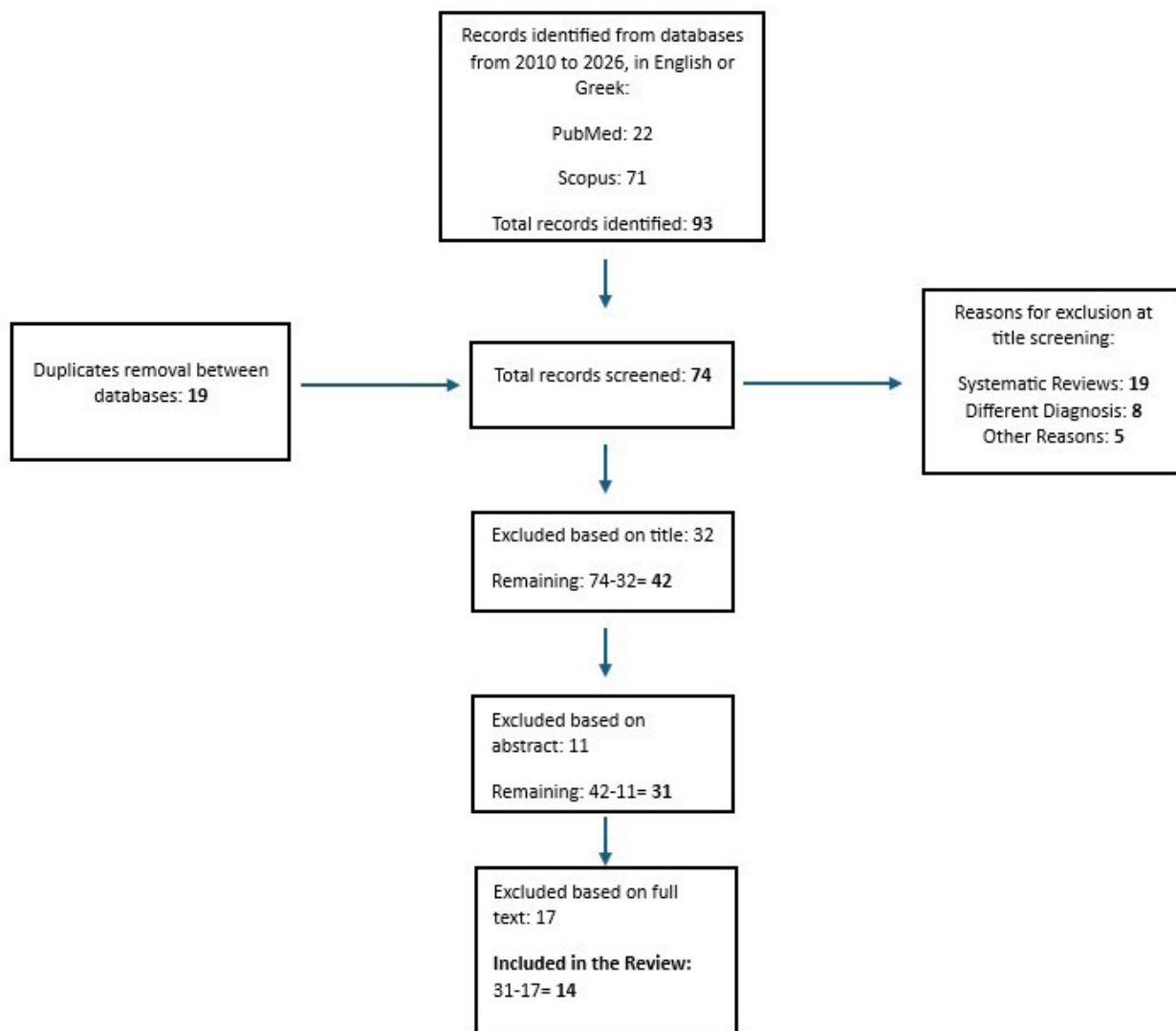
can overcome gravity (grade  $\geq 3$ ), provided that all higher muscle groups are normal (grade 5). Furthermore, in the sensory assessment, 28 dermatomes are examined bilaterally using a numerical scale from 0 (absence of sensation) to 2 (normal sensation), with light touch and pinprick stimuli, using the facial area as a reference point. The lowest dermatome that retains normal sensation bilaterally defines the sensory level of the injury. Of particular importance, the assessment of sacral sparing includes the evaluation of sensory and motor function at the S4-S5 levels, determining the completeness of the injury (incomplete or complete).<sup>4</sup>

The loss of motor and sensory function following spinal cord injury (SCI) does not constitute merely an isolated neurological deficit; rather, it represents a primary etiological factor contributing to a wide range of systemic complications.<sup>3</sup> These encompass both acute and chronic conditions, including autonomic dysreflexia, neurogenic bladder and bowel dysfunction, neuropathic pain, pressure ulcers, spasticity, orthostatic hypotension, impaired thermoregulation, and sexual dysfunction.<sup>4</sup>

Rehabilitation after SCI is not characterized as a linear therapeutic process but as a dynamic, complex, and multifaceted intervention. Its principal objectives include ensuring patient safety, restoring functional capacity, and facilitating social reintegration. Consequently, contemporary international clinical practice advocates for the establishment of a multidisciplinary rehabilitation team, wherein healthcare professionals from diverse specialties collaborate to deliver a holistic, patient-centered approach.<sup>1</sup>

The rehabilitation plan is initiated during the acute phase and extends longitudinally, addressing both the direct sequelae of the injury and the individualized needs of each patient. Within this framework, interdisciplinary collaboration is of paramount importance.<sup>5</sup> The integration of medical management, functional retraining, nursing care, and psychological support constitutes the cornerstone for mitigating secondary complications and promoting patient autonomy and independence.<sup>6</sup>

Occupational therapy extends beyond the mere



*Figure 1. Flow Diagram of Study Selection for Inclusion in the Review*

training of motor skills based on principles of motor learning. It encompasses a comprehensive assessment of the individual’s functional capacity and performance in activities of daily living (ADLs). Therapeutic interventions focus on enhancing dexterity, motor coordination, and upper limb function-key components for independent living, particularly in individuals with cervical spinal cord injuries, where functional demands are significantly increased.

The incorporation of innovative technologies, such as robotic-assisted therapy and virtual reality (VR), has substantially advanced upper limb reha-

bilitation. These modalities enhance patient engagement, motivation, and psychological well-being, factors that are critically important in long-term rehabilitation outcomes. Their application is closely associated with the rapid evolution of neurorehabilitation and biomedical technology since the 1990s. Initially implemented in other neurological conditions, such as stroke,<sup>6</sup> these technologies have subsequently been adapted for use in SCI rehabilitation, to offer motor and sensory retraining, such as that of walking and upper limb function. Dozens of studies in recent years have increasingly utilized ro-

botic and virtual reality systems, aiming to provide intensive and repetitive upper limb training. Most studies have used robotic devices such as: Armeo® Spring (Hocoma AG), Armeo® Power (Hocoma AG), MAHI Exo-II (Rice University). A non-robotic, technology-assisted ReJoyce™ Rehabilitation System and interactive devices AMADEO, DIEGO, PABLO; Tyromotion were also utilized. In addition, numerous virtual reality systems have been utilized, such as: HTC Vive Virtual Reality System (HTC Corporation), Nintendo Wii® Virtual Reality Gaming System (Nintendo Co., Ltd.), Toyra® Virtual Reality System and CyberTouch™ Data Glove (Immersion Corporation), to enhance extrinsic motivation, offering measurable and objective results.

However, despite the considerable technological advancements in the field of neurorehabilitation, there still remains a lack of consensus regarding the relative efficacy of specific robotic and virtual reality systems within occupational therapy intervention protocols.

The aim of present study, as a brief literature review, was to present the current clinical research evidence on the effectiveness of integrating technological systems into occupational therapy interventions, while also considering their limitations.

### Materials and Methods

An extensive literature review was conducted using the following scientific databases: PubMed/NCBI and Scopus. The keywords (mesh terms) used in the search engines of the above data bases were: spinal cord injury OR tetraplegia OR quadriplegia AND upper limb OR upper extremity OR arm function OR hand function AND virtual reality OR VR OR robotic device OR robot-assisted therapy OR exoskeleton OR telerehabilitation OR ReJoyce. The inclusion criteria comprised studies involving female/male participants over the age of sixteen years, with spinal cord injury, assessing upper-limb function, and investigating virtual reality or robotic-assisted interventions. Eligible study designs included randomized controlled trials, clinical trials, and other relevant interventional studies published from 2010 till 2026.

A total of 93 records were identified through database searching, including 71 from Scopus and 22 from PubMed. After removing 19 duplicate records, 74 studies remained for screening. During title screening, 32 studies were excluded based on irrelevance to the topic, including studies with different diagnoses, systematic reviews, and other non-relevant articles. A total of 42 studies were then assessed based on their abstracts, out of which 11 were excluded due to not meeting the inclusion criteria. Then, 31 full-text articles were evaluated for eligibility. After full-text assessment, 17 studies were excluded due to not meeting the inclusion criteria. Finally, 14 studies were included in the present review.

### Discussion

#### *Applications of virtual reality in occupational therapy for upper-limb rehabilitation*

Spinal cord injury is a complex neurological condition that directly disrupts the transmission of motor and sensory signals between the brain and the peripheral nervous system. Anatomically, the spinal cord consists of ascending (sensory) and descending (motor) pathways, including the corticospinal tract, which is responsible for voluntary motor control. Damage to these neural pathways results in muscle weakness, spasticity, and functional impairment, particularly affecting the upper limbs, especially in cases of cervical injury.<sup>4</sup>

Currently, there is no optimal treatment of SCI patients. The foremost treatment is rehabilitation training to enhance the patient's function and quality of life, which necessitates the inclusion of occupational therapy. Conventional therapy approaches used in rehabilitation of SCI patients have demonstrated a degree of effectiveness; however, they may not fully address the complex physical and cognitive challenges associated with the injury.

In fact, VR technologies are immersive, interactive, and constructive. Through this technology, software generates an interface between the user and the computer. The main benefits provided by VR-based interventions can be presented as follows: (a) VR systems enable patients to participate in a

**Table 1. Summary of Virtual Reality-Based Upper Limb Rehabilitation Studies in Spinal Cord Injury**

Author/ country	Type of Study	Participants	Method of VR rehabilitation	Results
Lim DY et al., South Korea (11)	Randomized Controlled Clinical Trial	SCI Incomplete Motor Paralysis, C4-C8	Fully Immersive VR Device HTC VIVE VR RahabWare	IG: Significant increases in grip power, lateral pinch power, and palmar pinch power (ASIA-UEMS) ( $p < 0,05$ ).
Prasad S. et al., India (12)	Pilot randomized, single-blinded, parallel-group trial	SCI complete/ incomplete motor paralysis, C5-C8	Non-immersive Nintendo Wii	IG: Significant improvements in upper limb function, dexterity, and independence (CUE, BBT, and SCIM-SR), ( $p < 0,05$ ).
Dimbwadyo-Terrer I. et al., Spain (13)	Preliminary pilot randomized controlled trial	SCI Complete Thoracic T1-T6	Semi-immersive VR and Data Glove CyberTouch	IG: Clinically meaningful improvements in motor function (MB), functional independence (SCIM, >11-point increase), self-care, dexterity (JHFT), and fine motor skills (NHPT), ( $p > 0,05$ ).
Dimbwadyo-Terrer I. et al., Spain (14)	Pilot Randomized Controlled Trial	SCI motor complete Cervical C5-C8	Semi-immersive VR Toyra	IG: No significant improvements in UL function ( $p > 0,05$ ), high satisfaction and usability scores (QUEST, satisfaction survey).

*Abbreviations: ASIA-UEMS: American Spinal Injury Association – Upper Extremity Motor Score, CUE: Capabilities of Upper Extremity Questionnaire, BBT: Box and Block Test, SCIM: Spinal Cord Independence Measure, SCIM-SR: Spinal Cord Independence Measure – Self Report, MB: Motricity Index / ( Motor Battery), JHFT: Jebsen Hand Function Test, NHPT: Nine Hole Peg Test, QUEST: Quebec User Evaluation of Satisfaction with Assistive Technology.*

*Statistical significance:  $p < 0.05$  was considered statistically significant.*

wide range of task-oriented motor activities within interactive and customizable environments, with adjustable levels of difficulty and repetition (b) they provide continuous, real-time feedback on performance through visual, auditory, and haptic stimuli, facilitating motor learning (c) VR interventions support the adaptability of training, including the

simulation of functional activities of daily living and (d) they offer a safe, motivating, and engaging environment that promotes active participation to therapy.<sup>7</sup> All the above promote motor skills, sensory abilities, cognitive functions, pain management, and psychological well-being by honing their movements.

**Table 2. Summary of Robotic and Technology-Assisted Upper Limb Rehabilitation Studies in Spinal Cord Injury**

Author/country	Type of study	Participants	Method of Robotic Rehabilitation	Results
Vicente Lozano-Berrio et al., Spain (21)	Randomized controlled trial Interventional, Parallel group design	Cervical SCI (>C8), motor incomplete or motor complete with preservation $\geq$ C6	Armeo Spring - passive exoskeleton	IG: Significant improvements in feeding, dressing, grooming (SCIM), and UL strength (UEMS), ( $p < 0,05$ ).
Loreto García-Alén et al., Spain (22)	Randomized controlled clinical trial	SCI Cervical	Armeo Power- active exoskeleton	IG & CG used Armeo Power. Significant improvements in UL function (GRASSP), dexterity (BBT), and motor scores (AIS), ( $p < 0,05$ ). No significant between-group differences ( $p > 0,05$ ).
Vicente Lozano-Berrio et al., Spain (23)	Pilot randomized controlled trial  Parallel group, two-arm design	SCI Cervical C4-C8	Armeo Spring- passive exoskeleton	IG: Significant improvements in UL function (CUE) and functional independence (SCIM), ( $p < 0,05$ ).  No between- group differences ( $p > 0,05$ ), except feeding (SCIM) favoring IG.
Zariffa J. et al., Canada (24)	Pilot interventional study  Single group	SCI Cervical C4-C8	Armeo Spring- passive exoskeleton	Subgroup (patients with residual hand function): Significant improvement in GRASSP Sensibility in the intervention limb ( $p < 0.05$ ). No between-groups statistically significant differences.
Zariffa J. et al., Canada (25)	Multicenter pilot clinical study	SCI Cervical C4-C8	Armeo Spring- passive exoskeleton	Subgroup (patients with residual hand function): Significant improvement in sensory function (GRASSP) in the intervention limb ( $p < 0,05$ ) but not maintained. No between groups statistically significant differences.
Kim J. et al., South Korea (26)	Pilot randomized controlled trial  Parallel group	SCI Cervical	Armeo Power- active exoskeleton	IG: Significant improvements in UL strength (UEMS), ( $p < 0.05$ ), functional independence (SCIM-III total), ( $p < 0.05$ ), and mobility (SCIM mobility subscale), ( $p < 0.05$ ).

Frullo J.M. et al., USA (30)	Controlled Trial Parallel group	SCI Cervical C3- C8	MAHI Exo-II active exoskeleton	AAN & ST used MAHI Exo-II: improvements in UL strength and sensory function over time (GRASSP Strength $p<0.05$ ), (GRASSP Sensibility $p<0.05$ ). No statistically significant differences between groups ( $p>0.05$ ).
Yozbatiran N. et al., USA (31)	Randomized sham-controlled trial Parallel group	SCI In-complete Cervical	MAHI Exo-II active exoskeleton	IG & CG used MAHI Exo-II: Improvements in UL use (MAL-AOU), motor function (UEMS), and muscle tone (MAS). No statistically significant differences between groups ( $p>0.05$ ).
Kowalczewski J. et al., Canada (32)	Randomized controlled crossover trial	SCI Cervical C5-C7	Tele- Rehabilitation ReJoyce Workstation	ReJoyce Tele- Rehab: Significant improvements in hand function (ARAT), dexterity (RAHFT), and strength (Grasp/ pinch force). Significant differences favoring ReJoyce ( $p<0.05$ ).
Mia Maria Kilkki et al., Finland (33)	Pilot randomized controlled crossover trial	SCI In-complete Cervical	Technology-assisted upper rehabilitation using interactive, task-specific devices AMADEO, DIEGO, PABLO; Tyromotion with biofeedback and gamification	IG: Improvements in muscle strength (ASIA-UEMS) and goal attainment (GAS). No statistically significant differences compared to no intervention, except for UEMS ( $p<0.05$ ).

Abbreviations: UEMS: Upper Extremity Motor Score, SCIM: Spinal Cord Independence Measure, GRASSP: Graded Redefined Assessment of Strength, Sensibility and Prehension, BBT: Box and Block Test, AIS: American Spinal Injury Association Impairment Scale, MAS: Modified Ashworth Scale, MAL-AOU: Motor Activity Log – Amount of Use

Statistical significance:  $p<0.05$  was considered statistically significant.

Note: Two studies included technology-assisted, non-robotic systems (Tyromotion and ReJoyce) and were included due to their relevance to UL rehabilitation.

### Applications of robotic devices in occupational therapy for upper-limb rehabilitation

The most prevalent injury is the cervical SCI. It appears to affect the 62% of the SCIs and cause severe functional impairments.<sup>8</sup> Injury to the cervical spinal cord affects arm and hand function to a variable extent depending on the level and severity of inju-

ry. A recent survey documented that currently over 120 devices are being developed to help rehabilitate the upper limbs of patients with neurological disorders.<sup>9</sup>

Robotic-assisted rehabilitation has emerged as a promising approach to upper limb dysfunction in SCI. These technologies are designed to support therapy by providing intensive and task-oriented

training, while delivering consistent and measurable therapeutic input. The main advantages given by robotic-assisted upper limb rehabilitation can be presented as follows: (a) robotic devices enable the performance of repetitive, task-specific upper limb movements at high intensity, facilitating motor re-learning and functional recovery (b) they provide continuous, objective feedback on patient performance, allowing accurate monitoring of progress through measurement systems (c) robotic systems ensure consistent and standardized training, minimizing variability between therapists and (d) they offer a safe and controlled environment for therapy, while reducing the physical burden on clinicians. Collectively, these factors enhance motor recovery, functional improvement, and increase participation in activities of daily living with the aid of neuroplasticity in motor learning.<sup>10</sup>

### ***Recent literature data***

#### **Virtual Reality**

Four interventional studies investigating virtual reality-based systems for upper-limb rehabilitation in individuals with SCI revealed differing results. All studies used different virtual reality systems, which were the HTC Vive, Nintendo Wii, Cyber-Touch™ Data Glove + VR and Toyra. Some studies reported significant improvements in specific motor outcomes, such as grip strength, palmar pinch strength and lateral pinch strength, as well as functional measures (e.g., SCIM, ASIA -UEMS), particularly in the intervention groups.<sup>11</sup> However, most studies did not find statistically significant differences between intervention and control groups in outcome measures, including upper limb function, dexterity, and quality of life.<sup>12-13,14</sup> The outcome may be connected to the limited- duration intervention protocol. Prior research states that short- term interventional programs are often insufficient to reveal the advantages of virtual reality compared to conventional therapy.<sup>15</sup> In several cases, both intervention and control groups showed significant improvements at the post-assessment, suggesting that the observed effects may not be exclusively connected to virtual reality interventions. Due to

the small sample sizes, there is insufficient evidence to support reliable scientific conclusions regarding the method's effectiveness in all four studies. At the opposite end of the spectrum, a smaller sample size, pilot randomized controlled study, reported that conventional therapy combined with VR Toyra tends to indicate improvements in functional and clinical variables.<sup>16</sup>

#### **Robotic Devices**

The Armeo® system (both Spring and Power devices) was the most used robotic device in the included studies. The effectiveness of this series of robotic technologies in upper limb recovery has been extensively researched in individuals with neurological conditions, such as multiple sclerosis,<sup>17</sup> cerebral palsy,<sup>18</sup> and stroke.<sup>12-20</sup> The included studies demonstrated improvements in motor function, muscle strength, and functional independence as reflected in outcome measures such as the Graded Redefined Assessment of Strength, Sensibility and Prehension (GRASSP), Action Research Arm Test (ARAT), Manual Muscle Testing (MMT), and Spinal Cord Independence Measure (SCIM).<sup>21-22,23,24,25,26</sup> Improvements were observed in activities of daily living, including feeding, grooming, toilet mobility, and upper-body dressing, which appear to have a positive outcome on functional performance.<sup>21-23</sup>

Despite within-group improvements, several studies did not report statistically significant differences between the intervention and the control group.<sup>22-23,24,25</sup> In many studies, both groups reported functional improvements over time, but this might not occur exclusively due to the robotic intervention.<sup>21-22</sup> In contrast, a systematic review and meta-analysis demonstrated that the use of robotic-assisted upper limb therapy can compete with the effectiveness of conventional therapy protocols in stroke individuals.<sup>27</sup> Certain studies reported improvements in specific subcategories, such as sensory function or task smoothness (GRASSP), rather than primary outcome measures, presenting variability in treatment effectiveness.<sup>24,25</sup>

In addition, the evidence is characterized by heterogeneity in study design, including differences in

patient populations (e.g., subacute versus chronic spinal cord injury), intervention protocols, and assessment tools.<sup>21-24,25</sup> Also, many of the studies have been conducted with chronic SCI patients, but evidence suggests that the most significant recovery happens in the first six months, attributed to neuroplasticity.<sup>10,28</sup> Some studies suggested greater benefits in patients with milder impairments or preserved residual motor function,<sup>24,26</sup> whereas others indicated limited or non-significant effects of Armeo®-based interventions.<sup>22,24</sup> These findings suggest that while Armeo® systems present an effective technology for enhancing upper limb function and promoting recovery, the evidence remains inconclusive. Similar findings have been reported in previous studies, which suggest that research in cervical SCI shows inconsistent outcomes, possibly due to the differences in therapy intensity.<sup>29</sup> Further high-quality randomized controlled trials are required to determine their effectiveness and to identify the populations most likely to benefit from each intervention.

In addition to Armeo® systems, other robotic-assisted approaches have been explored for upper limb rehabilitation in individuals with spinal cord injury. Including assist-as-needed training, home-based tele-rehabilitation, and combined interventions with transcranial direct current stimulation (tDCS).<sup>30,31,32,33</sup> Some studies demonstrated the feasibility and clinical impact of these interventions. For example, home-based technology-assisted and task-oriented rehabilitation was associated with significant improvements in upper limb function, with higher scores in ARAT and RAHFT observed in the intervention group compared to controls, with the use of ReJoyce Workstation.<sup>32</sup> In addition, patient-centered outcomes were highlighted in another study, where most participants (14 out of 16) reported achieving their rehabilitation goals and perceived improvements in activities of daily living, as measured by the Goal Attainment Scale (GAS).<sup>33</sup> A home-based rehabilitation program using the Soft Extra Muscle Glove further validates the previ-

ous findings.<sup>34</sup> The findings showed significant improvements in hand function, including object manipulation and grip strength, by the TRI-HFT scale. But these findings were less observed at the later follow-up assessment. Similar improvements have been reported with the use of a fabric-based soft robotic glove, demonstrated in hand function and object manipulation assessed by TRI-HFT.<sup>35</sup> This study was the first randomized controlled trial to investigate the effectiveness of technology-assisted device ReJoyce in the cervical SCI population, supporting improvements in upper-limb function (ARAT).<sup>32</sup> Despite these positive findings, such improvements were not always superior across all studies. In some cases, both intervention and control groups showed functional improvements over time, and the addition of techniques, such as tDCS combined with MAHI Exo II robotic system, did not show significant between-group differences, likely due to both groups receiving robotic rehabilitation.<sup>30,31,33</sup> These findings support the potential benefits of robotic-assisted therapy. Overall, the variability in intervention types, treatment protocols, and outcome measures across these studies underscores the lack of standardization in robotic rehabilitation, making it difficult to draw definitive conclusions regarding their effectiveness.

### Conclusion

In conclusion, both virtual reality and robotic-assisted rehabilitation interventions appear to improve the upper limb function in individuals with spinal cord injury. These therapeutic technologies empower intensive, repetitive, and task-oriented training, while reducing the physical burden on therapists. The current evidence remains heterogeneous and inconclusive, highlighting the need for high-quality randomized controlled trials to refine intervention protocols and identify specific patient populations most likely to benefit.

### Conflict of Interest

The authors declared no conflicts of interest.

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