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Early rehabilitation *vs.* conventional immobilization in nonoperative treatment of proximal humeral fracture: a systematic review

R. RANIERI[1], J.D. LACOUTURE-SUAREZ[2], M. FERRERO[1], V. LONGOBARDI[1], F. CACACE[1], A. FERRERO[1], E.M. BERTOLINO[1], E. KON[1,3], M. LIPINA[4], A. LYCHAGIN[4], B. DI MATTEO[1,4], A. CASTAGNA[1,3]

[1]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy
[2]Serena Del Mar Hospital, Cartagena de Indias, Provincia de Cartagena, Bolívar, Colombia
[3]IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy
[4]Department of Traumatology, Orthopedics and Disaster Surgery, Sechenov University, Moscow, Russia

ABSTRACT. – OBJECTIVE: Fractures of the proximal humerus (PHF) are commonly treated conservatively. Evidence suggests that a period of immobilization of one week or less may lead to some advantages compared to a traditional 3-4 weeks of immobilization. The purpose of this systematic review was to assess the clinical and radiological results in the case of early rehabilitation *vs.* delayed rehabilitation after PHF.

MATERIALS AND METHODS: In July 2023, a literature search was carried out on the PubMed, MEDLINE, and Embase databases to identify all the randomized trials comparing early rehabilitation *vs.* delayed rehabilitation after PHF. The following data were extracted from each included study: patients' demographics, study design and level of evidence, follow-up times, treatment groups, evaluation scores adopted, and overall clinical and radiological findings. The quality of the trials was assessed using the Cochrane Risk of Bias Assessment.

RESULTS: A total of 5 studies, including 378 patients and dealing with early *vs.* delayed rehabilitation in case of conservative treatment of PHF, were included in this study. Early rehabilitation was started within 1 week and consisted mainly of pendulum exercise and progressive passive mobilization. Early rehabilitation was associated with better pain and functional scores within the first 3 months in 3 studies. No difference in pain or function was reported at 6 months or longer follow-up, and no differences in complications rate were observed between early vs. delayed rehabilitation groups.

CONCLUSIONS: This systematic review suggests that early mobilization within one week in case of conservative treatment of PHF leads to improved function recovery and reduced pain, especially in the first months of rehabilitation, without differences at longer follow-up and without increasing complications rate. Reducing immobilization time could accelerate function recovery and regaining independence in daily life activities.

Key Words:
Shoulder, Shoulder physiotherapy, Shoulder rehabilitation, Humeral fracture, Conservative treatment, Early mobilization, Proximal humeral fracture.

Introduction

Proximal humeral fractures (PHFs) represent a relatively common clinical condition, accounting for approximately 5% of total fractures[1-4]. Due to an increase in life expectancy, population aging, and consequent rise in osteoporosis prevalence, the incidence of PHFs is steadily increasing, making them the third most common osteoporotic fracture in the elderly[1,5-7]. Other risk factors include female sex, compromised neuromuscular control and fall-related factors[5,6,8,9]. In the population of postmenopausal women older than 50 years PHFs accounted for 17.5% of the total number of osteoporotic fractures[10]. These fractures are characterized by a prolonged and severe disability, and a long and strenuous recovery period is required to regain independence in activities of daily life[11]. Besides a significant impact on the patient's physical function and life independence, recent studies underlined that this condition causes an increased risk of medical complications and mortality[12-15]. Given these considerations, it is evident that PHFs represent an increasingly significant burden on healthcare systems and further social costs.

The treatment of PHFs includes several options and is typically guided by the fracture pattern and the patient's functional demands[16]. The primary treatment goal is to regain optimal range of motion and shoulder functionality. Considering that surgical treatment is associated with high complications and reoperation rate[17-20], and that

Corresponding Author: Ferrero Andrea, MD; e-mail: andrea.ferrero@st.hunimed.eu

comparative studies have questioned the functional benefits of surgical treatment compared to conservative approaches[18,20,21], even in displaced PHFs[18], conservative treatment is often recommended, especially in elderly patients. However, considering the important role of rehabilitation in PHFs, there is a lack of specific evidence regarding non-surgical treatment strategies, which makes recommendations difficult[16,22,23].

Timing is of paramount importance when starting physical therapy. Traditionally, immobilization of 3-4 weeks has been advocated for these fractures. Early mobilization from the fourth day was initially advocated by Brostrom[24]. In 1979, Jull et al[25] underlined that immediate passive mobilization may lead to potential advantages, such as earlier recovery and reduced rehabilitation period. More recently, some evidence suggests that a period of immobilization of one week or less may be preferable following PHF, leading to similar long-term outcomes but faster recovery of physical function and daily life activities[22,23,26-29].

The aim of this paper is, therefore, to make a systematic review of the available evidence to assess the clinical and radiological results following early rehabilitation *vs.* delayed rehabilitation in the conservative treatment of PHF.

Materials and Methods

The present study was conducted following the "PRISMA" protocol guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)[30]. A literature search was carried out on electronic medical databases, such as PubMed, MEDLINE, and Embase, by one independent investigator, using the following keywords that were combined to obtain optimal search strategy: "early-mobilization," "non-surgical treatment," "proximal humerus fracture." The search was limited to studies published between January 1980 and July 2023. Reference lists of all retrieved articles were further analyzed.

All studies included in the analysis were screened by title and abstract based on the following inclusion criteria for article inclusion: (1) studies comparing early *vs.* delayed rehabilitation following proximal humeral fracture; (2) studies providing data on functional outcomes, perceived pain, or quality of life of patients; (3) studies available in the English and published within the above specified time frame.

Exclusion criteria were: (1) studies comparing non-surgical conservative therapeutic approaches with surgical interventions; (2) studies not meeting the above-mentioned inclusion criteria; (3) studies that did not provide sufficient data for analysis; (4) studies written in languages other than English (5) non-comparative studies (case series), systematic reviews, meta-analyses, expert opinions, studies presented at conferences.

Data were independently extracted by 2 investigators (RR, MF) following PRISMA guidelines. Information extracted from individual studies included participant characteristics, treatment details, complications, functional outcomes, pain scores, and quality of life-related outcomes. The conflicts were resolved by the senior investigator.

The quality of the randomized controlled trials (RCTs) included was assessed independently by two reviewers (RR, MF) using the Cochrane Risk of Bias Assessment.

The Cochrane risk-of-bias tool is a standardized approach to evaluate the risk of bias in randomized clinical trials. Researchers can implement the Cochrane tool to assess the methodological quality of studies to ensure their quality and evaluate the inclusion or not when performing a meta-analysis. Each of the seven domains listed below is carefully examined and finally judged as "low", "unclear" or "high"[31]. Random sequence generation is the first criterion. Low bias is considered if the allocations of patients in a study occur randomly therefore taking the human bias out of the equation. Allocation concealments refer to the bias that could arise if group assignment during the process of enrolling participants is known. Blinding of participants and personnel can be a source of bias if any member among the participants or personnel has knowledge of the group assignment. Blinding of outcome assessment prevents assessors from knowing which intervention a participant received. Incomplete outcome data can be identified when there are unaddressed or poorly explained gaps in data reporting. Selective reporting is the sixth criterion. Bias can arise if incomplete or selective reporting of the study outcomes is detected. Other sources of bias are the last criteria of the Cochrane Risk of Bias Assessment; this allows for the reviewer to include any important concerns about bias not addressed in the previous criteria.

Results

Overall, 363 eligible studies were taken into consideration. After careful examination and

full-text analysis, 5 RCTs[27,28,32-34] reporting the comparison between early rehabilitation (ER) and delayed rehabilitation (DR) following proximal humeral fracture were included in this review. A total of 378 participants were included in the studies, and 285 were reviewed at different follow-up times (two studies[32,33] reported the results of the same cohort at different follow-up). A clear overview of the research and evidence selection process is illustrated in the PRISMA flowchart (Figure 1). A synopsis of all the randomized trials included in the present meta-analysis is shown in Table I.

Study Design and Quality

The results of the assessment by the Cochrane Risk of Bias tool for RCTs are detailed in Table II. Randomization was applied in all studies included. Since patient blinding was not possible in these studies, the risk of bias assessed was considered high in all trials. The outcome-assessor's blinding was considered unclear in two out of the five trials.

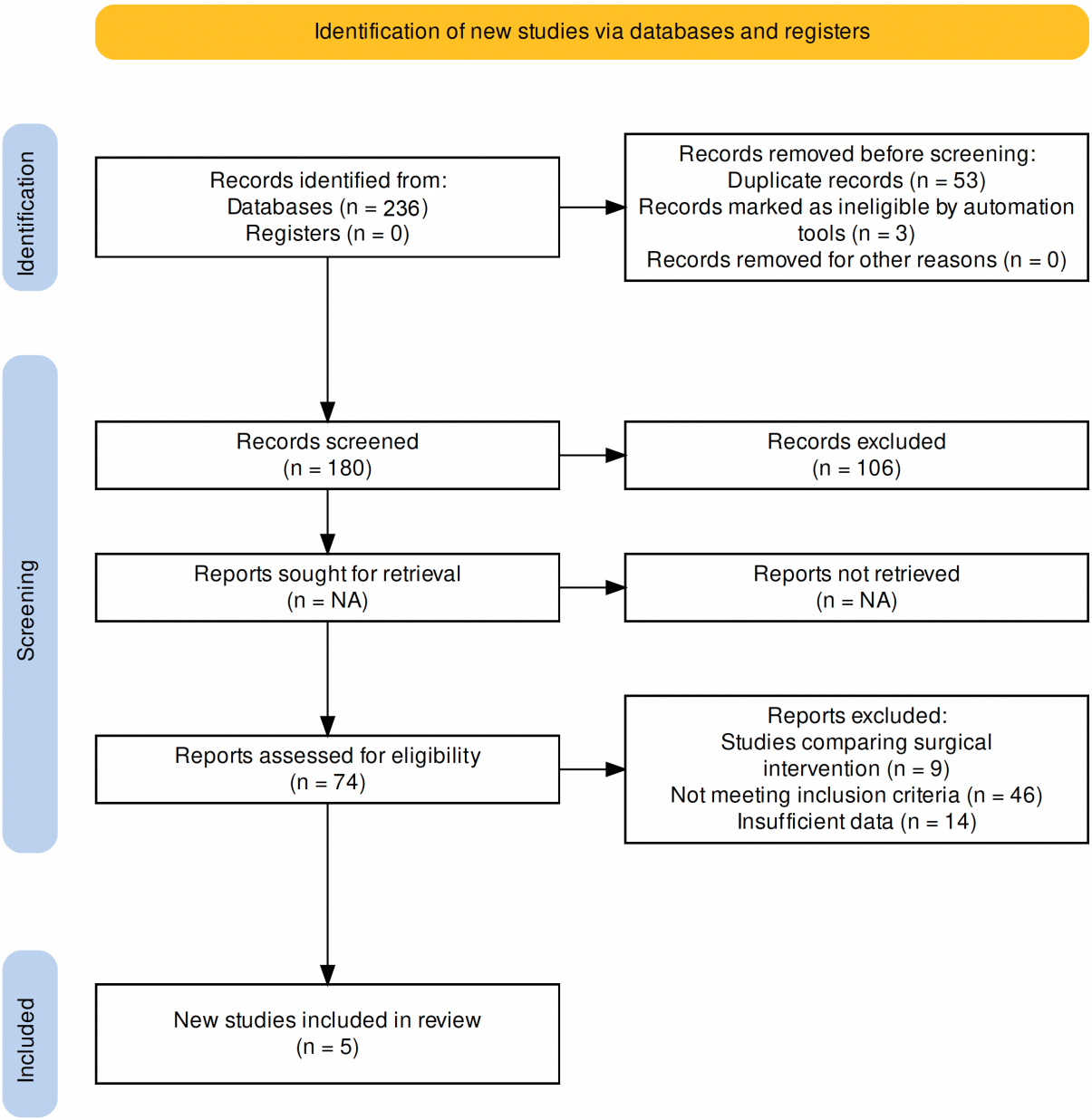

Figure 1. PRISMA flowchart of the included studies.

Table I. Synopsis of all the articles included in the present systematic review.

Study	No. of patients Total (E:D)	No. of evaluated patients at last follow-up Total (E:D)	Age (E:D)	Gender E(M:F)/ D(M:F)	Fracture classification and type	% of displaced fractures	Starting time of treatment in days (E:D)	Follow-up	Outcome measures	X-ray follow-up	Complications	Main clinical results
Kristiansen et al[34]	85 (42:43)	39 (18:21)	72:70	5:13/6:15	Neer: 1-Part (79%), displaced not specified (21%)	21%	7:21	1 month, 3 months, 6 months 1 year, 2 years	Neer score system	No	1 case of reflex dystrophy in each group	Early rehabilitation led to significant better total score due to less pain at 1 month (43 *vs.* 32; $p<0.01$) and 3 months (68 *vs.* 59; $p<0.001$). No differences at other follow-up times.
Hodgson et al[32]	86 (44:42)	81 (41:40)	71:70	11:33/5:37 (considering all the initial cohort)	Neer: 1-Part - surgical neck or isolated greater tuberosity	0%	Within 7:21	8 weeks, 16 weeks, 1 year	Constant score (primary outcome), SF-36	No	1 frozen shoulder after 52 weeks in delayed mobilization group.	Early rehabilitation led to significant better relative Constant score (0.7 *vs.* 0.54; $p=0.001$) and SF-36 pain (72 *vs.* 60; $p=0.01$) and role limitation (62 *vs.* 40; $p=0.02$) at 16 weeks. Not statistically significant better function and lower pain were reported at 1 year.
Hodgson et al[33]	86 (44:42)	74 (37:37)	69:68	8:29/5:32	Neer: 1-Part - surgical neck or isolated greater tuberosity	0%	Within 7:21	1 year, 2 years	Croft shoulder disability questionnaire	No	No	Patients with delayed rehabilitation reported higher rate of disability (72.5% *vs.* 42.8%; $p<0.01$) at 1 year, nearly 3 times more pain on movement and twice as many problems at night at 2 years. At 2 years the rate of disability was not significantly different between the two groups (32.4% *vs.* 35.2%).

Table continued

Table I *(Continued)*. Synopsis of all the articles included in the present systematic review.

Study	No. of patients Total (E:D)	No. of evaluated patients at last follow-up Total (E:D)	Age (E:D)	Gender E(M:F)/ D(M:F)	Fracture classification and type	% of displaced fractures	Starting time of treatment in days (E:D)	Follow-up	Outcome measures	X-ray follow-up	Complications	Main clinical results
Lefevre-Colau et al[27]	64 (37:37)	54 (32:32)	63:63	8:24/2:30 (considering all the initial cohort)	Neer: 1-Part (46%), 2-Part (22%) and 3-Part (32%) **impacted** AO classification: Extra-articular bifocal **impacted** (66%); Extra-articular unifocal **impacted** (30%) Extra-articular unifocal tuberosity (4%)	54%	Within 3:21	Baseline, 6 weeks, 3 months, 6 months	Constant score (primary outcome), VAS, AROM, PROM; Global patient satisfaction	Yes	No	Early rehabilitation led to significant better constant score at 6 weeks (44 *vs.* 34; p=0.01) and 3 months (71 *vs.* 61; p=0.02). Early rehabilitation led to significant better pain at 3 months and higher PROM and AROM at 6 weeks and 3 months. No differences were reported at 6 months. 100% of fracture-healing rate at 3 months and no cases of fracture displacement.
Martínez et al[28]	143 (67:76)	111 (55:56)	70:71	45:10/43:13	Neer: 1-Part (33%) 2-, 3-, 4-Part (67%)	67%	7:21	1 week, 3 weeks, 3 months, 6 months, 1 year, 2 years	VAS (primary outcome); Constant Score; Simple Shoulder test	Yes	11 (9.9%) patients. - *E group*: 2 osteonecrosis, 4 secondary displacement (1 operation for ORIF). - *D group*: 1 osteonecrosis, 2 nonunion, 1 secondary displacement, 1 stiffness. No significant differences in complications rate between the 2 groups (p=0.223)	No significant differences were found between the 2 groups in terms of pain, Constant score or Simple Shoulder test at any time point and complications rate.

E: Early therapy; D: Delayed therapy; ORIF: Open reduction internal fixation; PROM: Passive range of motion; AROM: Active range of motion; VAS: Visual analogue scale for pain; SF-36: Short-Form-36.

Table II. Cochrane risk of bias assessment for the 5 included studies.

Study	Sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel	Blinding of outcome assessors (detection bias)	Incomplete outcome data (attrition bias)	Selective outcome reporting (reporting bias)	Other sources of bias
Kristiansen et al[34]	Unclear	Unclear	High	Unclear	High	Unclear	Unclear
Hodgson et al[32]	Unclear	Low	High	Low	Low	Low	Unclear
Hodgson et al[33]	Unclear	Low	High	Low	Low	Low	Unclear
Lefevre-Colau et al[27]	Low	Low	High	Low	Low	Low	Low
Martinez et al[28]	Low	Low	High	Low	Low	Low	Low

No issues in selective reporting of the results were identified with respect to adherence to the methods described in the studies, and in most cases, the risk of bias was considered to be low.

Qualitative Synthesis of Clinical Results

Patients' characteristics

The mean age was comparable among the different studies ranging from 63 to 72 years. Regarding the fracture type included, most of the studies included minimally displaced (1-part fracture according to Neer score[35])[26,27,31-33]. Kristiansen et al[34] included 21% of displaced, not further specified fractures; Lefevre-Colau et al[27] included 54% of Neer score 2- and 3-part impacted fractures. Differently, Martínez et al[28] mainly included (67%) displaced fractures (Neer score 2, 3, 4). In the early mobilization groups, rehabilitation was started within 7 days in all the trails[27,28,33-34]. Time for follow-up was variable between the different studies, ranging from 1 week to 2 years.

Rehabilitation protocols

Kristiansen et al[34], after 1 or 3 weeks of immobilization in a sling and body bandage, started Codman's pendulum exercises and active movements of the elbow and hand. Hodgson et al[32,33] proposed pendular exercises, passive flexion (within pain tolerance) during the first 2 weeks, followed by progressive full passive flexion and light functional exercises (3^{rd}-4^{th} weeks) and progressive functional exercises at 4 weeks. Lefevre-Colau et al[27] utilized a detailed rehabilitation program supervised by a physiotherapist and characterized by immediate pendulum exercise and progressive passive recovery of abduction, elevation, and external rotation, respectively. Martínez et al[28], after 1 or 3 weeks of immobilization in a sling, suggested a rehabilitation program (including both self-assisted exercises at home and supervised exercises in a rehabilitation center), not further specified.

Pain

Pain scores were reported to be better following ER compared to DR at 1 month[33] and 3 months[27,32,34]. However, no differences in pain were reported at 6 months, 1 year, or 2 years[27,28,32-34]. Martínez et al[28] considered pain as the primary outcome and did not find any significant differences at any time point (1 week, 3 weeks, 3 months, 6 months, 1 year, 2 years).

Shoulder Function

Shoulder function was evaluated using different scores among the different studies, including the Neer score system, Constant score, Simple Shoulder Test, Croft shoulder disability questionnaire, and passive and active range of motion. ER led to better total Neer score system (mainly due to pain) at 1 month and 3 months[34], better Constant score at 6 weeks and 3 months[27,32], better active and passive mobility for abduction and anterior elevation at 6 weeks and 3 months[27]. However, no differences in functional scores were reported at 6 months, 1 year, or 2 years[27,28,32,34]. Martínez et al[28] reported no differences in Constant score or Simple Shoulder Test between the ER group and DR group at any time point (1 week, 3 weeks, 3

months, 6 months, 1 year, 2 years). Only Hodgson et al[33], using the Croft shoulder disability questionnaire, reported a significantly higher rate of shoulder disability at 1 year in the DR group (72.5% *vs.* 42.8%; $p<0.01$) and nearly 3 times more pain on movement, twice as many problems at night with changing position, and disturbances in sleep at 2 years in the DR group.

Health-related quality of life

The Short Form-36 (SF-36) was used in one trial[32]. The trial reported a positive effect in two domains of the SF-36 (role limitation physical, $p<0.02$; pain, $p<0.01$) following ER at 16 weeks, while the differences reduced and did not reach a statistical significance at 1 year.

The patient's global satisfaction (recorded on a 5-point scale) was reported by Lefevre-Colau et al[27], without any differences in the 2 groups at each follow-up time.

Complications

No significant differences in complication rates were reported. Following ER, 1 case of reflex dystrophy[33], 2 osteonecrosis, and 4 secondary displacements (1 underwent operation for osteosynthesis with plate)[28] were reported. In the DR groups 1 case of reflex dystrophy[34], 1 frozen shoulder after 52 weeks[32], 1 osteonecrosis, 2 nonunion, 1 secondary displacement, 1 stiffness[28] were reported. It is relevant to highlight that only 2 studies performed a radiographical analysis[27,28].

Discussion

The main finding of this systematic review is that early rehabilitation within 1 week, compared to delayed rehabilitation with 3 weeks of immobilization, is associated with lower pain, better shoulder range of motion and function during the first 3 months. However, after this period, no relevant differences in terms of function or pain were reported between the two rehabilitation programs and similar recovery was observed between the 6 months and 2 years of follow-up. The rate of complications was similar between the two modalities of treatment. These findings suggest that a short period of immobilization followed by an early rehabilitation program started within one week, may lead to quicker recovery of shoulder function and less time of disability without any consequences at a 2-year follow-up.

The main goal of proximal humeral fracture treatment, especially in the case of elderly patients, should be to recover the shoulder function, shorten the disability period, and regain independence in daily life activities as soon as possible, avoiding possible health-related complications[12,36]. The traditional immobilization for proximal humeral fractures followed the general fracture principles of 3-4 weeks of immobilization, however, this period was questioned by some authors[22,23,25-29,32,33,37]. Complete immobilization is associated with some side effects as joint stiffness and muscle atrophy, which may increase the periods of disability. On the contrary, early passive rehabilitation has the advantage of fast recovery because of possible faster hematoma and swelling drainage, tissue contracture avoidance, and quicker neuromuscular function recovery; moreover, healing of the fracture may be enhanced by the introduction of some micromovements[38-40]. The possible drawback could be an increased risk of complications, such as secondary displacement, non-union, or osteonecrosis. The findings of this systematic review support an early rehabilitation started within 1 week and characterized mainly by a passive movement within the pain limit and pendular exercise.

The main complications associated with non-operative of PHF treatment are non-union, avascular necrosis, secondary displacement, and malunion. A systematic review including 650 patients reported an overall complication rate of 13% following conservative treatment at a mean follow-up of 45.7 months, with a union rate of 98%, 2% avascular necrosis, and malunion reported as the main complication[41]. The rate of complications among the studies included in the present review was comparable with these data, and no higher risk of complications was reported in any studies following early rehabilitation. A relevant rate of complications (9.9%) was reported only by Martínez et al[28], but nearly 70% of the fractures were displaced in this series, and no differences were reported between the two groups. The malunion rate was not reported, but since several studies specifically included displaced fractures, malunion should be considered more acceptable after the decision to adopt a conservative treatment. Two nonunions in the DR group and 3 cases of osteonecrosis were reported by Martínez et al[28]. They reported 5 cases of secondary displacement (4 in the ER group), even if 4 out 5 were already displaced 2-part fractures. Interestingly, in this study, secondary displacement was more common among 2-part surgical neck fractures, suggesting caution to promote early mobilization of this fracture type, considering that a 2-part

(displaced) surgical neck fracture is more unstable and may tolerate less movement in the early healing phase[42]. To date, it is not possible to definitively establish which fracture type should avoid early rehabilitation due to the higher risk of any possible secondary displacement, and the choice is commonly left to the surgeon's preferences[37]. Aguado et al[43], despite good clinical outcomes following an early home-based self-exercise program, reported that fractures involving greater tuberosity presented a risk of cranial tuberosity displacement, a factor associated with potentially detrimental effects on shoulder function[44,45]. Considering the key role of the greater tuberosity and the linked external rotators in shoulder function, when a conservative approach is chosen for fractures involving the tuberosities, caution in early mobilization and serial radiological follow-up is recommended.

Limitations

This systematic review was meticulously conducted, adhering to rigorous methodology, which encompassed establishing inclusion criteria, assessing RCTs using the Cochrane Risk of Bias Assessment tool, and conducting a thorough analysis of references. However, it presents some limitations. First, different fracture patterns were included in the studies involving displaced and non-displaced fractures. However, besides the conservative *vs.* surgical treatment decision, which should be based on other criteria, this finding shows the possibility of widening the early mobilization indication to patients with displaced fractures when conservative treatment is chosen. A second limitation is related to the different rehabilitation protocols utilized by the different authors, introducing a potential bias in extrapolating a definitive conclusion. Nevertheless, the protocols share a common approach of initiating pendulum exercises and progressively mobilizing the joint passively. Another limitation is that some studies lacked sufficient methodological and statistical information, which contributes to some uncertainty in the results. Other authors have already recognized this issue regarding RCT on PHF[46,47]. Finally, only 2 studies[27,28] reported a radiographical analysis, potentially underestimating radiological findings as secondary displacement, non-union, or osteonecrosis. In order to improve the existing evidence, future studies should focus on clearly defined categories of proximal humeral fracture, establishing a standardized rehabilitative protocol and providing more frequent follow-ups at closer intervals with a radiographical analysis to capture both short-term and long-term outcomes accurately. This would enable better comparison of outcomes and facilitate the identification of best practices in fracture rehabilitation.

Conclusions

This systematic review suggests that early mobilization within one week after proximal humeral fracture results in improved recovery of function and reduced pain, especially in the first three months of rehabilitation, while outcomes at subsequent follow-up times show no difference compared to the conventional treatment. Reducing immobilization time in case of conservative treatment of proximal humeral fracture could accelerate function recovery, the ability to perform daily life activity, and regaining patients' independence, without increasing the risk of complications. Future research endeavors should prioritize the adoption of a standardized rehabilitative protocol and the selection of patients with the same fracture pattern to minimize potential study biases.

Conflict of Interest

The authors declare that they have no conflict of interest.

Informed Consent

Not applicable due to the type of study.

Ethics Approval

Not applicable due to the type of study.

Authors' Contributions

Conceptualization, R.R. and D.B.M.; methodology, A.C. and M.F.; validation, E.K., A.C. and D.B.M; formal analysis, V.L. and M.L; investigation, A.F. and E.B.; resources, F.C.; data curation, M.F. and R.R; writing—original draft preparation, M.F. and R.R; writing—review and editing, F.C and L.S.J.D.; visualization, A.L and A.F.; supervision, D.B.M. and E.K.; project administration, A.C. and R.R. All authors have read and agreed to the published version of the manuscript.

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Data Availability

All the data retrieved for the purpose of the present review have been already included in the text.

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