

Systematic Review

A comparison of arthrodesis and arthroplasty for hemophilic arthropathy of the ankle: a systematic review

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Abstract

Objective: To conduct a systematic review of the literature on surgical treatment for end-stage hemophilic arthropathy of the ankle joint, describing the results for arthroplasty and arthrodesis.

Methods: We conducted a systematic literature review according to Cochrane (Cochrane Handbook for Systematic Reviews of Interventions version 6.1, 2020) and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) recommendations. The primary outcome was clinical improvement in pain and function of the affected limb. Secondary outcomes included adverse effects and complications from the surgical procedures.

Results: After reviewing 514 studies, 10 were included for data extraction and qualitative analysis (180 patients: 100 arthroplasties and 117 arthrodeses).

Conclusions: Both methods showed low overall complication rates and effectively reduced pain and improved function, allowing a return to work, activities of daily living and, in some cases, sports. One procedure was not clearly better than the other: the choice must be based on the patient's characteristics and clinical judgment.

Level of Evidence III; Therapeutic Studies; Systematic Review of Level III Studies.

Keywords: Ankle; Arthrodesis; Arthropathy; Arthroplasty; Hemophilia.

Introduction

Hemophilic arthropathy (HA) occurs after multiple episodes of hemarthrosis. Its onset is during childhood⁽¹⁾ and its pathophysiology is characterized by progressive proteolytic cartilage degeneration and synovial hypertrophy, in addition to vascular damage to bones in joint regions and reduced joint space⁽²⁾. In advanced stages, it can lead to joint deformity, chronic pain, and range of motion loss in the involved joint, resulting in lower quality of life⁽³⁾.

The ankle is one of the most affected joints in HA⁽¹⁾ and its treatment, especially in advanced cases, has given rise to much discussion⁽⁴⁾. When the ankle joint does not show major signs of degeneration, there are several surgical options

for preserving the joint, including arthroscopic debridement, synovectomy, and supramalleolar osteotomies⁽³⁾. In more advanced cases of ankle arthropathy, non-joint-sparing procedures (arthrodesis and arthroplasty) are performed^(3,5).

In arthrodesis, there is concern about functional limitations and potential overload in other lower limb joints after the procedure, as well as the risk of non-consolidation^(6,7). Total ankle arthroplasty, an alternative to arthrodesis, presents good functional results and pain relief while preserving joint mobility, which improves patient quality of life⁽⁷⁾. However, some studies on hip and knee replacement in patients with hemophilia have reported higher rates of aseptic loosening and deep infection.

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The aim of the present study was to conduct a systematic review of the literature on the surgical treatment of terminal HA of the ankle, comparing the results of arthroplasty and arthrodesis.

Methods

We conducted a systematic review of the literature according to Cochrane (*Cochrane Handbook for Systematic Reviews of Interventions*, version 6.1, 2020) and PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*) recommendations.

The PICO methodology was used to define the review's clinical question and search for evidence, with "P" representing the population included in the studies (hemophilic patients with ankle joint disorders), "I" representing the intervention to be investigated (arthroplasty), "C" representing comparison with standard treatment (arthrodesis), and "O" representing the investigated outcome (conclusions about the intervention and pain, function, and complication outcomes), is arthroplasty better than arthrodesis in patients with hemophilia? Are ankle arthroplasty outcomes comparable to those of ankle arthrodesis in patients with hemophilia? Table 1 shows how the PICO methodology was used in the present review.

Randomized and non-randomized clinical trials were included in this review, in addition to controlled observational studies and case series, without restrictions on year of publication or language. The population of interest included hemophilia patients with joint disorders (hemophilic arthropathy), without age or sex restrictions. Participants could either have been undergoing regular treatment for their underlying disease or not. The included intervention types were arthroplasty or arthrodesis to treat ankle arthropathy. Comparative groups could include no intervention (previous patient status), previous surgical approaches, or arthrodesis in studies assessing arthroplasty and vice versa.

The condition or domain under investigation was the presence of HA and joint disorders in patients with hemophilia. The following article types were excluded: animal and in vitro studies, literature reviews, case reports, duplicate articles, studies that did not assess arthroplasty or arthrodesis to treat hemophilic arthropathy, and articles not published in full.

Primary outcomes included clinical improvement in pain and function of the affected limb. Clinical evaluation included patient satisfaction and results based on specific criteria and questionnaires: the Visual Analog Pain Scale, the American Orthopedic Foot and Ankle Society (AOFAS), Ankle and Hindfoot Score, and the 36-item Short Form Health Survey (SF-36). Secondary outcomes included adverse outcomes and surgical complications.

The studies were identified through systematic searches of electronic databases and search portals, as well as the reference lists of articles. The searches were conducted in the following including eight databases: PubMed (September 1, 2021 to September 9, 2021), PubMed Central (September 9, 2021), VHL/BIREME (September 9, 2021), EBSCOHost (September 9, 2021), Scopus (September 9, 2021), Web of Science (September 9, 2021), EMBASE (September 1, 2021 to September 9, 2021), the Cochrane Library (September 9, 2021), and PROQUEST (until April 2020; conducted on September 9, 2021).

The search strategy involved the following keywords (medical subject headings and free terms): ("Hemophilia A" OR "Hemophilia B") AND ("Joint Diseases" AND Ankle) OR "Ankle Joint" AND ("Arthroplasty, Replacement, Ankle" AND Arthrodesis)).

A total of 514 articles were retrieved, which were exported to the Rayyan reference management program, with titles, abstracts, references and the database of origin. Duplicate studies were automatically removed by the program (280 articles), resulting in a total of 234 articles for analysis and study selection according to the eligibility assessment. In the initial step of the study selection process, the titles and abstracts were independently evaluated by two reviewers (RAFSP and RGP). The full text of each study considered relevant was retrieved and fully reviewed independently by two reviewers (RAFSP and RGP). Each reviewer created a list of studies that met pre-established inclusion and exclusion criteria. The lists were compared, and disagreements were resolved by discussion and consensus.

One author extracted and analyzed the data from the articles, evaluating their eligibility and comparing the results. Information was collected on each study (title, authors, journal name, year of publication, volume, and study type), the participants (total number, age, sex, body mass index, clotting disorder, high titer inhibitor, prophylaxis, hemophilia severity, comorbidities, pain assessment, function, inclusion and exclusion criteria, allocation procedure, blinding, and the number of randomized participants), the interventions (description of the intervention, the methods, other concurrent treatments, and follow-up duration), and outcome measures (description of the measurements, including pain level and quality of life through validated scales).

The risk of bias was assessed by both reviewers, who evaluated adequate randomization (allocation sequence generation), guaranteed allocation concealment, the blinding methods (participants, research team, outcome evaluators), intention-to-treat analysis, follow-up losses, as well as other

Table 1. Structured research construction strategy through the PICO strategy

Acronym	Component	Description
P	Population	Patients with hemophilic arthropathy of the ankle
I	Intervention	Arthroplasty
C	Comparison	Arthrodesis
O	Outcome	Clinical outcomes (pain, function, and complications)

Source: The authors.

sources of bias, such as early discontinuation of the study. Disagreements among the authors were resolved by consensus.

Results

A total of 10 studies were included in this systematic review. Barg et al.⁽⁸⁾ was prospective, while all the others were retrospective. All of the studies evaluated the results of arthroplasty or arthrodesis in the ankle joint of patients with hemophilia; only Ahn et al.⁽⁴⁾ compared the two procedures in the same study.

The 10 articles included a total of 180 patients (100 arthroplasties and 117 arthrodesis), and the same patient may have undergone more than one procedure in a study, since ankle HA can occur bilaterally. The mean patient age at the time of surgery was reported, and in 9 of the 10 studies it was >39 years; the study in which it was lower was aimed at children and adolescents⁽⁹⁾.

The mean follow-up length was reported in all articles (Table 2)^(4,6,8,10-16), being 5.7 and 9.3 years in arthroplasty and arthrodesis studies, respectively.

In all of the studies, the patients underwent replacement and strict regulation of clotting factors throughout the perioperative period, being jointly followed up with the hematology teams of the respective centers.

Although the surgical procedures were indicated according to different criteria, pain was the main symptom. Degenerative changes in the ankle joint were evaluated in different ways: range of motion, functional scores, and radiographic alterations.

The main methods for radiographic evaluation of HA were the Pettersson score⁽¹⁷⁾, which was used in 4 studies, and the Kellgren-Lawrence scale⁽¹⁸⁾, which was used in 2 studies.

Generally speaking, the surgeries were performed using a tourniquet, and antibiotic prophylaxis with first-generation cephalosporins was also performed, in addition to joint follow-up with a hematology team and strict control of clotting factors. The selected articles were then discussed according to surgical procedure: arthroplasty or arthrodesis.

Of the 10 selected studies, 6 involved arthroplasty procedures, the results of which are described in Table 3^(4,8,10-13), and 5 involved arthrodesis, the results of which are described in table 4^(4,6,14-16).

Although the included studies used different methods to evaluate the functional results of the procedures, the main results evaluated were: pain assessment, functional capacity, and quality of life (Table 5)^(4,6,8,10-16).

Seven of the studies assessed pain with the Visual Analogue Scale, and in all studies that used this criterion, improvement was found after the procedures. The mean overall Visual Analogue Scale score was 7.14 before the intervention. Ahn et al.⁽⁴⁾ had the the lowest reported value before the procedure (5.5) and Preis et al.⁽¹²⁾ had the highest (8.5). When comparing the two interventions, the mean score decrease was 7.35 to 1.34 for arthroplasties and 5.75 to 1.28 for arthrodesis.

Six of the 10 studies used the AOFAS score to assess patient functional capacity. Three of these, whose object was arthroplasty^(11,12,14), showed significant improvement in AOFAS scores, with pre-and post-intervention means of 30.9 and 78.4, respectively, which indicates significantly lower ankle pain in these cases. However, among arthrodesis studies, only Wang et al.⁽¹⁶⁾ found significant improvement in AOFAS scores, which increased from 37.9 to 81.4. Among arthrodesis studies, the mean AOFAS score increased from 29.9 to 80.95.

Patient quality of life was assessed with the SF-36 in 4 of the 10 studies. Among arthroplasty studies, statistically important results were found in Barg et al.⁽⁸⁾ and Preis et al.⁽¹²⁾, with mean increases from 34.25 to 80.25 and 54.15 to 80.85 in physical and mental assessment values, respectively. Wang et al.⁽¹⁶⁾, another arthrodesis study, found mean increases from 10 to 82.9 and 59.2 to 72 in physical and mental assessment values, respectively (p<0.05).

The complications observed in the 10 studies are described in Table 6^(4,6,8,10-16).

Table 2. Number of procedures, mean age when they were performed, and mean follow-up period

Authors/data	Technique	Sample	Age	Follow-up
Barg et al. ⁽⁸⁾	Arthroplasty	10 procedures in 8 patients	43.3 years	5.6 years
Strauss et al. ⁽¹⁰⁾	Arthroplasty	11 procedures in 10 patients	49 years	3 years
Asencio et al. ⁽¹¹⁾	Arthroplasty	32 procedures in 21 patients	43.6 years	4.4 years
Preis et al. ⁽¹²⁾	Arthroplasty	14 procedures in 14 patients	51.4 years	5.8 years
Eckers et al. ⁽¹³⁾	Arthroplasty	17 procedures in 14 patients	43 years	9.6 years
Bluth et al. ⁽⁶⁾	Arthrodesis	57 procedures in 45 patients	56.7 years	6.6 years
Eichler et al. ⁽¹⁴⁾	Arthrodesis	11 procedures in 8 patients	39 years	8 years
de l'Escalopier et al. ⁽¹⁵⁾	Arthrodesis	22 procedures in 17 patients	15.5 years	19.7 years
Wang et al. ⁽¹⁶⁾	Arthrodesis	14 patients	40.7 years	3 years
Ahn et al. ⁽⁴⁾	Both	29 patients, (16 arthroplasty and 13 arthrodesis)	44.1 years	6.8 years

Source: Data collected by the authors.

Discussion

We conducted a systematic review on the two main surgical procedures for advanced HA of the ankle. After the selection process, 10 articles were analyzed, totaling 180 patients who underwent 217 procedures (100 arthroplasties and 117 arthrodeses).

Only Ahn et al.⁽⁴⁾ compared the results of arthroplasty and arthrodesis in patients with hemophilia. The included studies

were mostly retrospective or case series without comparison or control groups, which demonstrates the need for studies with higher levels of evidence on the subject.

The mean patient age was 42.6 years at the time of the procedure, although it was >60 years in Kim et al.⁽¹⁹⁾, which could indicate that these patients were operated on earlier, probably due to the clinical course of HA, in which recurrent hemarthrosis attacks the ankle joint beginning in childhood and adolescence^(1,3).

Table 3. Results of articles in the arthroplasty category

Author/data	Sample	Results
Barg et al. ⁽⁹⁾	10 procedures in 8 patients	Non-constrained prostheses were performed, with Achilles tendon stretching necessary in 5 cases. There were no cases of loosening or revision, and arthrofibrosis occurred in only 1 case. The patients reported physical and mental improvements. The procedure was safe and had high success rates, allowing a return to work and sports activities.
Strauss et al. ⁽¹⁰⁾	11 procedures in 10 patients	There were two cases of prosthesis infection. In 8 patients, the mean AOFAS score increased from 21.5 to 68. On the pain scale, the score decreased from 7.6 to 1.9. Among patients without complications, satisfaction was high, making it a reliable option for patients with osteoarthritis due to hemophilia.
Asencio et al. ⁽¹¹⁾	32 procedures in 21 patients	The mean AOFAS score increased from 40.2 to 85.3, functional scores increased from 23.6 to 35.9, and dorsiflexion scores increased from 0.8 to 10.38. Two patients underwent subsequent arthrodesis. The components were stable upon radiographic examination. There were 2 cases each of perioperative and orthopedic complications. Limiting pain was reported by 18 patients before surgery and 0 after surgery.
Preis et al. ⁽¹²⁾	14 procedures in 14 patients	There were 4 complications, pain reduction (8.5 to 1.3), and functional improvement. The patients' physical and mental conditions improved.
Eckers et al. ⁽¹³⁾	17 procedures in 14 patients	Implant survival was 95% at 10 years and 70% at 15 years. Patient satisfaction was 76%, the mean pain scale score was 2, and range of motion increased. The mean AOFAS score was 81 points and there were 10 complications.
Ahn et al. ⁽⁴⁾	16 patients	Pain scores improved for all patients, and the total range of motion increased from 30.8° to 37.3° at the final follow-up. Three cases of osteolysis and 1 case of heterotopic ossification occurred.

Table 4. Results of articles in the arthrodesis category

Author/data	Sample	Results
Bluth et al. ⁽⁶⁾	57 procedures in 45 patients	A total of 33 isolated tibiotalar, 15 tibiotalar and subtalar, and 9 isolated subtalar arthrodeses were performed. Nonunion occurred in 10.4% of tibiotalar procedures and 8.3% of subtalar procedures; new surgical techniques helped reduce these percentages. Pain was eliminated in 75% of the cases; 25% reported moderate pain. The procedure was effective and patient functional capacity improved considerably.
Eichler et al. ⁽¹⁴⁾	11 procedures in 8 patients	All arthrodesis were tibiotalar. Mean AOFAS scores increased from 28 to 69. Fusion was achieved in all 11 ankles after an average of 3.5 months.
de l'Escalopier et al. ⁽¹⁵⁾	22 procedures in 17 patients	Tibiotalar arthrodesis was performed in children and adolescents (mean age 15.5 years). Mean follow-up was 19.7 years, with 86% of the results considered good or excellent.
Wang et al. ⁽¹⁶⁾	14 patients	Bone fusion occurred in all cases after a median of 12.9 weeks. Two cases of superficial infection and 1 case of subtalar arthritis occurred. AOFAS and VAS scores increased, as did physical and mental components. All patients reported satisfaction.
Ahn et al. ⁽⁴⁾	13 patients	Good union and significant pain improvement occurred in all cases. There was 1 case each of synthesis material breakdown and worsening talonavicular degeneration.
Ahn et al. ⁽⁴⁾	16 patients	Pain scores improved for all patients, and the total range of motion increased from 30.8° to 37.3° at the final follow-up. Three cases of osteolysis and 1 case of heterotopic ossification occurred.

In all analyzed articles, follow-up was performed jointly with the hematology team, with careful control of the patients' clotting factors. The articles also mentioned intraoperative procedures to control bleeding (eg, tourniquets were used in all 10 articles). There was also consensus about the use of first-generation cephalosporins for antibiotic prophylaxis, which could be continued for 24 to 48 hours after the procedure.

Regarding functional results, both arthrodesis and arthroplasty had favorable outcomes, especially for pain control. The most common scale used to measure this variable was the Visual Analog Pain Scale, and the mean scores for arthroplasty decreased from 7.35 preoperatively to 1.34 at the end of the follow-up, while for arthrodesis they decreased from 5.75 to 1.28, similar to the results of patients without hemophilia^(19,20).

Table 5. Comparison of study outcomes

Study	Technique	VAS		AOFAS		SF-36			
		Before	After	Before	After	Before		After	
						Physical	Mental	Physical	Mental
Barg et al. ⁽⁸⁾	Arthroplasty	7.1	0.8	38	81	30.4	56.9	83.4	82.8
Strauss et al. ⁽¹⁰⁾	Arthroplasty	7.6	1.9	21.5	68	-	-	-	-
Asencio et al. ⁽¹¹⁾	Arthroplasty	-	-	40.2	85.3	-	-	-	-
Preis et al. ⁽¹²⁾	Arthroplasty	8.5	1.3	23.9	76.6	38.1	51.4	77.7	78.9
Eckers et al. ⁽¹³⁾	Arthroplasty	-	1.9	-	81	-	-	47	57
Bluth et al. ⁽⁶⁾	Arthrodesis	-	0.75	-	90.4	-	-	-	-
Eichler et al. ⁽¹⁴⁾	Arthrodesis	-	-	22	69	-	-	-	-
de l'Escalopier et al. ⁽¹⁵⁾	Arthrodesis	-	-	-	83	-	-	-	-
Wang et al. ⁽¹⁶⁾	Arthrodesis	7.0	1.4	37.9	81.4	10	59.2	82.9	72
Ahn et al. ⁽⁴⁾	Both	5.5	0.9	-	-				
	Arthroplasty	4.5	6.2						
	Arthrodesis	0.7	0.8						

Source: Data collected by the authors.
AOFAS: American Orthopedic Foot and Ankle Society - Ankle and Hindfoot Scale; SF-36: 36-item Short Form Health Survey; VAS: Visual Analog Scale

Table 6. Comparison of complications in the included studies

Authors/data	Technique	Sample	Complications
Barg et al. ⁽⁸⁾	Arthroplasty	10 procedures in 8 patients	1 case of arthrofibrosis
Strauss et al. ⁽¹⁰⁾	Arthroplasty	11 procedures in 10 patients	2 cases of early prosthetic infection
Asencio et al. ⁽¹¹⁾	Arthroplasty	32 procedures in 21 patients	2 cases of progressively worsening pain; 1 case of bleeding associated with anticoagulant use
Preis et al. ⁽¹²⁾	Arthroplasty	14 procedures in 14 patients	1 case of medial malleolus fracture; 2 cases of delayed healing; 2 patients had painful arthrofibrosis
Eckers et al. ⁽¹³⁾	Arthroplasty	17 procedures in 14 patients	1 case of lateral malleolus fracture; 1 case of medial malleolus fracture with medial plantar nerve injury; 1 case of hematoma; 1 case of stress fracture of the calcaneus and 1st metatarsal; 2 cases of lost range of motion; 3 cases of loosening of prosthetic components
Bluth et al. ⁽⁶⁾	Arthrodesis	57 procedures in 45 patients	5 cases of synthesis material removal due to local pain; 3 cases of adjacent joint degeneration; 1 case of transtibial amputation due to osteomyelitis
Eichler et al. ⁽¹⁴⁾	Arthrodesis	11 procedures in 8 patients	2 cases of adjacent joint degeneration
de l'Escalopier et al. ⁽¹⁵⁾	Arthrodesis	22 procedures in 17 patients	2 cases of adjacent joint degeneration; 3 cases of synthesis material removal due to local pain
Wang et al. ⁽¹⁶⁾	Arthrodesis	14 patients	1 case of adjacent joint degeneration; 2 cases of superficial infection of the external fixator pin path
Ahn et al. ⁽⁴⁾	Both	16 arthroplasties	2 cases of intra-articular hematoma; 1 case of heterotopic ossification; 3 cases of osteolysis of the tibial component
		13 arthrodeses	1 case of degenerated adjacent joints; 1 case of breakage of the synthesis material

Other functional indicators also showed positive results, comparable to those reported in the literature. Zaid et al.⁽⁹⁾ performed a systematic review on ankle arthroplasty, finding an increase in AOFAS scores from 40 to 80 points after the procedure, whereas in the present review, the mean AOFAS score increased from 30.9 to 78.4.

Regarding arthrodesis, the results of the present review are also similar to those of the literature for patients with advanced arthrosis of the ankle joint. Van den Heuvel et al.⁽²⁰⁾ performed a systematic review of different access routes for arthrodesis, observing a mean postoperative AOFAS score of 74.9, whereas that of the present review was 80.9.

Finally, low rates of postoperative complications were observed for both procedure types. In this review, a total of 47 complications were reported in 217 procedures (21.6%), and most were resolved with conservative (non-surgical) treatment. Only one case of transtibial amputation after osteomyelitis was reported⁽¹⁷⁾.

The most common complication for arthroplasty was arthrofibrosis or lost range of motion associated or not with local pain (5 cases), the majority being treated with soft tissue repair^(13,15). Three cases of prosthesis component loosening and 2 cases of prosthesis infection were reported, which are the most feared complications of total ankle arthroplasty⁽²⁰⁾.

The most common complication of arthrodesis was the need to remove synthesis material due to local pain (8 cases), followed by adjacent joint degeneration (7 cases). Both complications are described in the literature, and adjacent joint degeneration is one of the main causes of pain in patients undergoing arthrodesis of the ankle joint^(19,21).

Overall, surgery was required more often for arthrodesis complications than arthroplasty complications, which were treated more conservatively. One possible explanation for this would be the shorter mean follow-up time in the arthroplasty studies (5.7 vs 9.3 years). The arthroplasty study reporting the highest number of complications also had the longest mean follow-up time (9.6 years)⁽¹⁵⁾.

One limitation of the included studies was that 9 out of 10 were observational retrospective analyses, which could involve selection and recall bias. However, this reflects the current lack of prospective studies on this subject with high evidence levels.


For advanced HA, total ankle arthroplasty is a viable treatment approach with favorable mid- and long-term clinical outcomes. Ten-year implant survival is similar to that of inflammatory diseases in the general population. Preserving ankle mobility can be an advantage in terms of patient comfort and adjacent joint disease. Although the clinical results are encouraging, follow-up radiographs show component loosening and periprosthetic radiolucency in most cases⁽¹⁶⁾.

In cases of severe HA, more cases and data are available for ankle arthrodesis. The greater technical reproducibility and the consistency of good long-term results make ankle joint fusion surgery a viable treatment choice, especially due to the lack of consistent data about later complications of arthroplasty^(4,7,13).

Conclusions

Total ankle arthroplasty and arthrodesis are currently indicated for HA of the ankle. In the studies included in this review, these procedures had low complication rates, were effective in reducing pain and increasing functional capacity, and allowed a return to daily work activities, resulting in a better quality of life for patients with hemophilia. It cannot be said that one procedure is better than the other; the choice must be based on the patient's characteristics and the professional's technical aptitude.

In addition, studies with larger samples and longer follow-up are needed to adequately assess the possible complications of these surgical procedures in the medium and long term, in addition to further prospective and controlled studies to compare the techniques.

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