IQWiG Reports – Commission No. N20-05

Independent use of an active controlled motion device in the treatment of ankle fractures[1]

Extract

[1] Translation of Chapters 1 to 6 of the final report N20-05 *Selbstanwendung einer aktiven Bewegungsschiene im Rahmen der Behandlung von Sprunggelenkfrakturen* (Version 1.0; Status: 8 October 2021 [German original], 20 January 2022 [English translation]). Please note: This document was translated by an external translator and is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

Publishing details

Publisher:
Institute for Quality and Efficiency in Health Care

Topic:
Independent use of an active controlled motion device in the treatment of ankle fractures

Commissioning agency:
Federal Joint Committee

Commission awarded on:
15 October 2020

Internal Commission No.:
N20-05

Address of publisher:
Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Im Mediapark 8
50670 Köln
Germany

Phone: +49 221 35685-0
Fax: +49 221 35685-1
E-mail: berichte@iqwig.de
Internet: www.iqwig.de

This report was prepared in collaboration with external experts.

The responsibility for the contents of the report lies solely with IQWiG.

According to §139b (3) No. 2 of Social Code Book (SGB) V, Statutory Health Insurance, external experts who are involved in the Institute's research commissions must disclose "all connections to interest groups and contract organizations, particularly in the pharmaceutical and medical devices industries, including details on the type and amount of any remuneration received". The Institute received the completed *Form for disclosure of potential conflicts of interest* from each external expert. The information provided was reviewed by a Committee of the Institute specifically established to assess conflicts of interests. The information on conflicts of interest provided by the external experts and external reviewers is presented in Chapter A9 of the full report. No conflicts of interest were detected that could endanger professional independence with regard to the work on the present commission.

External expert

- Henning Kunter, Protestant Hospital Kalk, Cologne, Germany

IQWiG thanks the external expert for his collaboration in the project.

IQWiG employees

- Sandra Molnar
- Daniel Fleer
- Corinna Kiefer
- Marco Knelangen
- Fabian Lotz
- Andrea Steinzen

Keywords: Motion Therapy – Continuous Active, Ankle Fractures, Benefit Assessment, Systematic Review

Key statement

Research question

The objective of this investigation is to assess the benefit of independent use of an active motion device, also called controlled active motion (CAM) device, in adult patients with conservatively or surgically treated ankle fracture in comparison with standard care without the independent use of an active motion device with regard to patient-relevant outcomes.

Conclusion

For the independent use of CAM devices following surgical therapy, 1 study was found, comparing postoperative treatment with CAM devices versus postoperative treatment without CAM device. The study population was small, and the study had methodological flaws. However, for the outcomes of foot pain, foot function, other complaints (Visual Analogue Scale Foot and Ankle, VAS FA), full weight-bearing, regaining fitness to work, and health-related quality of life (physical component summary [Short Form (SF)-12]), a hint of benefit of additional mobilization via the independent use of a CAM device in comparison with standard care without CAM device was consistently found.

With regard to the range of motion (ROM) outcomes, health-related quality of life (mental component summary [SF-12]), adverse events, and revision surgery, there was no hint of benefit or harm of the independent use of a CAM device in comparison with standard treatment without CAM device.

No data were available for the outcomes of activities of daily living, dependence on help from others, or participation in professional and social life.

Overall, for independent use by adult patients following a surgically treated ankle fracture, a hint of benefit of additional mobilization via CAM device was found in comparison with standard treatment without CAM device.

No studies were found on additional mobilization through the independent use of a CAM device in patients with conservatively treated ankle fracture. For the subpopulation of conservatively treated adult patients who are allowed partial loading, the results are deemed transferable, and a hint of benefit of a CAM device is found in comparison with standard treatment without CAM device.

Due to the weak evidence on which the benefit assessment is based, conducting a confirmatory randomized controlled trial (RCT) should be considered in the present indication. This RCT should include both adult patients with surgically treated ankle fracture and those with conservatively treated ankle fracture which can be (at least) partially loaded.

For adult patients with conservatively treated ankle fracture who are not allowed partial loading of the joint, the independent use of a CAM device seems inadequately indicated and difficult to implement. Hence, the result cannot be transferred to this subpopulation. For these patients, no hint of benefit nor the potential of a required treatment alternative was found.

Table of contents

List of tables

Page

List of abbreviations

Abbreviation	Meaning
AE	adverse event
AOFAS	American Orthopedic Foot and Ankle Society
CAM	controlled active motion
CI	confidence interval
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
MD	mean difference
RCT	randomized controlled trial
ROM	range of motion
SF-12	Short Form 12
SGB	Sozialgesetzbuch (Social Code Book)
VAS FA	Visual Analogue Scale Foot and Ankle

1 Background

An ankle fracture is an injury of the talocrural joint, which is formed by the tibia, fibula, and talus. The tibia and fibula are elastically connected by the ligamentous structures of the syndesmosis to form the ankle mortise [1-4]. Additional central structures stabilizing the talocrural joint are the lateral and medial ligaments [4,5].

An ankle fracture typically involves at least a fracture of the lateral malleolus [6]. Depending on the fracture location, the Danis-Weber classification distinguishes between type A, type B, and type C injuries [5,7,8]. Fracture of the lateral malleolus distal to the syndesmosis is a type A injury with intact syndesmotic stability [9]. A type B injury involves fracture at the level of the syndesmosis. In this fracture type, the syndesmosis complex is usually injured but not necessarily unstable [5]. Lateral malleolus fractures proximal to the syndesmosis are considered type C injuries with unstable syndesmosis. Fracture of the lateral malleolus can be associated with additional bone and ligament injuries [6], the assessment of which is relevant for estimating the extent of the overall injury [9]. The Working Group for Osteosynthesis Classification [10] has supplemented the Danis-Weber classification by subgroups formed on the basis of the severity of concomitant injuries. These subgroups allow, for instance, breaking down Danis-Weber type B fractures into stable fracture types (B1; isolated lateral malleolar fracture) versus unstable fracture types (B2; including fracture of the medial malleolus) [5]. Another system, developed by Lauge-Hansen [11], classifies fractures based on the mechanism of injury.

In 90 000 patients with ankle fracture who were identified in a Swedish registry analysis of the years 1987 through 2004, the annual incidence rate was 71 per 100 000 person-years [4,12]. A frequently quoted analysis from 1987 reports an incidence of 187 per 100 000 person-years in the city of Rochester, Minnesota [13]. In Germany, about 64 000 inpatient treatments were administered due to ankle fractures in 2018 [14], equalling 77 per 100 000 inhabitants. The mean age of these patients was 56 years. Among young adults, men had a higher incidence than women. The ratio reversed from an age of about 45 years. In the year 2018, women were more commonly affected by ankle fractures, accounting for about 61% of patients.

In more than 8 of 10 cases, ankle fractures result from a dislocation mechanism secondary to a fall or misstep [5,15] – which often occurs during exercise [16]. About every 10^{th} ankle fracture results from deceleration trauma in traffic accidents. Direct force causes less than 5% of ankle fractures [5,15].

The treatment of ankle fractures depends on the fracture type and classification. Conservative treatment is chosen if surgery is contraindicated as well as for closed, non-dislocated fractures without syndesmosis rupture. All other fractures are typically surgically treated, with the goal of achieving anatomically exact reconstruction of osseous and ligamentous structures [6,17,18]. Generally, all types of treatment aim to maximize joint function and minimize the risk of posttraumatic osteoarthritis [19]. The subsequent treatment following conservative or surgical

treatment pursues the same goal. Little evidence is available on optimal subsequent treatment [4,19-23]. In the German context, a surgically treated ankle fracture is typically immobilized for 6 weeks using a cast or orthotic device, but early targeted active and passive mobilization can be started during this period [9]. Goost et al. report that "most patients need early postoperative functional treatment with physiotherapeutic guidance to improve joint function and proprioception and to promote the regression of swelling (lymph drainage)" [4, p. 385]. Following 6 weeks of partial weight bearing, a follow-up X-ray, and removal of any positional screws, weight bearing is incrementally increased so that, as a rule, "full weight bearing and full participation in work and recreational sports are possible 12–16 weeks after the injury" [4, p. 385].

Patients with conservatively treated type A ankle fractures, in contrast, can be treated "in a stabilizing ankle orthosis for early function with pain-adapted full weight-bearing. All fractures that are not of type A should be treated in a so-called walker or vacuum shoe. (...) Over a period of six weeks, the patient should be mobilized in a walker for pain-adapted full weight-bearing" [4, p. 381]. Immobilization might be indicated in the beginning, for instance until soft tissue swelling has regressed [5,18]. In geriatric or multimorbid patients who are treated conservatively due to the high risk posed by surgery, the risk of malunion is accepted, and the joint is generally immobilized using an orthotic device [4].

Controlled active motion (CAM) devices, which are the experimental intervention investigated in this report, are intended for use in the early postoperative treatment phase as additional mobilization which can be carried out independently by patients at their homes. CAM devices are pedalling devices which, depending on the manufacturer, include either both legs or only the surgically treated leg in the mobilization exercise. They allow only guided motion, and the training follows the physiotherapy principle of mobilization and closed kinetic chain exercise since the foot is fixed in place in the CAM device.

2 Research question

The objective of this investigation is to assess the benefit of independent use of an active motion device in adult patients with conservatively or surgically treated ankle fracture in comparison with standard care without the independent use of an active motion device with regard to patient-relevant outcomes.

3 Methods

The target population of the benefit assessment is adult patients with conservatively or surgically treated ankle fracture. The experimental intervention is independent use of an active motion device. The comparator intervention is standard care without independent use of an active motion device.

The investigation examined the following patient-relevant outcomes:

- Morbidity, particularly:
  - physical functioning (e.g. full loading of the ankle joint, range of motion)
  - Activities of daily living and dependence on help from others
- Health-related quality of life, including:
  - participation in professional and social life
- Adverse events

Randomized controlled trials (RCTs) were to be primarily included in the benefit assessment. If the available RCT-based evidence was insufficient for a benefit assessment, quasi-randomized comparative studies and prospective comparative cohort studies were to be included as well. There were no restrictions regarding the study duration.

In parallel to the preparation of the report plan, a search for systematic reviews was conducted in the MEDLINE database (which includes the Cochrane Database of Systematic Reviews) and the Heath Technology Assessment (HTA) database as well as on the websites of the National Institute for Health and Care Excellence (NICE) and the Agency for Healthcare Research and Quality (AHRQ).

It was ascertained whether at least 1 high quality, current systematic review existed whose information retrieval was a suitable basis for the assessment.

When such a high-quality, current, systematic review was available, a supplementary search was performed as a 2nd step for studies covering the time period not covered by the systematic review(s). Otherwise, the search for studies was carried out without restricting the time period.

The systematic search for studies was conducted in the databases MEDLINE, Embase, and Cochrane Central Register of Controlled Trials.

The following sources of information and search techniques were additionally used: trial registries, manufacturer queries, documents sent by the Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA), documents made available from hearing procedures, and author queries.

Relevant studies were selected by 2 persons independently from one another. Any discrepancies were resolved by discussion between them. Data were extracted into standardized tables. To assess the qualitative certainty of results, outcome-specific and study-level criteria for the risk of bias were assessed, and the risk of bias was rated as high or low in each case. The results of the individual studies were organized according to outcomes and described.

In addition to the comparison of the individual studies' results, metaanalyses and sensitivity analyses were to be conducted and effect modifiers investigated, provided that the methodological prerequisites had been met.

For each outcome, a conclusion was drawn on the evidence for (greater) benefit and (greater) harm, with 4 levels of certainty of conclusions: proof (highest certainty of conclusions), indication (moderate certainty of conclusions), hint (lowest certainty of conclusions), or neither of the above 3. The latter is the case if no data are available or the available data do not permit classification into one of the 3 other categories. In that case, the conclusion "There is no hint of (greater) benefit or (greater) harm" was drawn.

Subsequently, an assessment of benefit and harm was carried out across outcomes. If it was not possible to derive any hint of (greater) benefit or (greater) harm, a conclusion was to be drawn on the basis of current knowledge about the potential of the treatment method, and the key points of a possible government co-sponsored study were to be specified.

For the outcome category of morbidity, data were available from 7 different operationalizations, including 4 questionnaires, of which only 1 was taken into account in the assessment, as justified below. The 4 questionnaires substantially overlapped in content; therefore, it was necessary to address the issue of multiplicity. For 2 of the 4 questionnaires, no validation publications were found, resulting in unclear instrument validity. These questionnaires were disregarded in this assessment. From among the 2 questionnaires deemed valid, the Visual Analogue Scale Foot and Ankle (VAS FA) according to Richter was selected. This decision was based on 2 aspects: Firstly, the other questionnaire, i.e., the American Orthopedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Scale, includes range of motion (ROM), which was also reported separately in the study included for the benefit assessment. Hence, presenting both the AOFAS Ankle Hindfoot Scale and ROM would have been associated with multiplicity issues. Secondly, results for both the total score and the subscales of pain, functionality, and other complaints were available for the VAS FA. In addition to its suitability for assessing benefit on the basis of a total score, this questionnaire therefore offered information about the dimensions from which potential effects might come. The data from the AOFAS Ankle Hindfoot Scale were checked for general consistency with those from the VAS FA, and it was determined whether they would generally result in the same evidence. This was the case; in other words, the use of a different or additional questionnaire would not have altered the result of the derivation of evidence.

4 Results

4.1 Results of the information retrieval

No systematic reviews were rated as being current and of high quality and included for the identification of primary studies.

The information retrieval yielded 1 RCT relevant for the research question. This applied to the research question on the independent use of the active motion device following a surgically treated ankle fracture. No studies were found to answer the research question on the independent use of active controlled motion devices in patients with conservatively treated ankle fracture. No planned or ongoing studies were found.

The search strategies for bibliographic databases and trial registries are found in the appendix. The most recent search was conducted on 4 March 2021.

Table 1: Study pool of the benefit assessment

Study		**Available documents**		
	Full publication (in professional journals)	**Registry entry / results report from the study registries**	**Clinical study report from manufacturer documents (not publicly accessible)**	**Other documents**
Ataya 2015	Yes [24]	Yes [25] / no	No	Yes [26]

4.2 Characteristics of the study included in the assessment

The Ataya 2015 study [26] was conducted from September 2011 through July 2013 at 1 study centre in Germany. A total of 50 adult patients with surgically treated type B or type C ankle fracture were randomized to either a postoperative treatment arm with physiotherapy and an additional CAM device or a postoperative treatment arm with physiotherapy alone. In both postoperative treatment arms, physiotherapy started on the first postoperative day, with a daily treatment of 20 minutes during hospitalization. After discharge, both postoperative treatment arms received 20 minutes of physiotherapy 2 to 3 times a week for a period of 6 weeks. In the intervention arm, the CAM device was used additionally, starting on the 2nd to 5th postoperative day. A physiotherapist educated patients in the usage of the CAM device. Afterwards, patients were to independently use the CAM device for training about 30 minutes daily for 6 weeks. Patients in both postoperative treatment arms were allowed to wear an orthotic device postoperatively. The study populations of the two groups were essentially comparable. The follow-up observation duration was 12 weeks.

4.3 Overview of patient-relevant outcomes

Data on patient-relevant outcomes were extracted from 1 study. Table 2 presents an overview of the data on patient-relevant outcomes from the included studies. For the outcome category of morbidity, the benefit assessment used results on the outcome of “foot pain, foot function,

and other complaints" (VAS FA) as well as separately reported results on ROM, full weight bearing, and regaining fitness to work. Further, the study reported data on the outcome of health-related quality of life – surveyed using the Short Form (SF-12) physical and mental component summary – as well as on the outcomes of adverse events (AEs) and reoperation; these data were usable for the benefit assessment. No data were available for the outcomes of activities of daily living, dependence on help from others, and participation in professional and social life.

Table 2: Matrix of patient-relevant outcomes

Study	Outcomes										
	Morbidity						QoL			AEs	
	Foot pain, foot function, other complaints (VAS FA)	ROM	Full weight bearing	Activities of daily living	Dependence on help from others	Regaining fitness to work	Physical component summary (SF-12)	Mental component summary (SF-12)	Participation in professional and social life	AEs	Revision surgery
Ataya 2015	●	●	●[a]	–[b]	–	●	●	●	–	●	●

●: Data were reported and were usable.
–: - Either no data were reported (no further information) or the outcome was not surveyed.
a: For the outcome of full weight bearing of the ankle joint, 2 operationalizations were available: "clinical follow-up after 6 weeks" and "weight-bearing log for surveying time until full weight bearing." The results of the 2nd operationalization were unusable because fewer than 70% of patients filled out the weight-bearing log.
b: This outcome was not separately surveyed and reported. The VAS FA questionnaire also includes activities of daily living; therefore, this outcome was taken into account as part of the outcome of foot pain, foot function, and other complaints (VAS FA).

AE: adverse event; QoL: health-related quality of life; ROM: range of motion; SF-12: Health Survey Short Form 12; VAS FA: Visual Analogue Scale Foot and Ankle according to Richter

4.4 Assessment of the risk of bias of results

The risk of bias of the study was rated as high across outcomes. This was due to the fact that both random sequence generation and group allocation concealment were inadequately described. However, the comparability of both treatment groups' characteristics at baseline (see Section A3.2.1, Table 13 of the full report) gives no reason to question the randomization of study participants. In addition, there was no blinding. It is also unclear whether all outcomes were predefined. Further, study registry entries were surveyed retrospectively.

The high risk of bias on the study level directly affected the risk of bias on the outcome level; therefore, the latter was not assessed any further. However, an additional examination was carried out regarding one relevant aspect: Simply taking analgesics can result in freedom from pain. Hence, taking analgesics would materially affect the reported patient-relevant outcomes.

To rule out this potential cointervention bias, an author query on analgesics use was sent (Section A3.1.2.2.4 of the full report). On the basis of the authors' answers (Chapter A7 of the full report), cointervention bias seems unlikely.

4.5 Results on patient-relevant outcomes

4.5.1 Results on morbidity

4.5.1.1 Results on foot pain, foot function, other complaints (VAS FA)

For the outcome of "foot pain, foot function, other complaints", as surveyed with the VAS FA questionnaire, results on the scale's total score as well as on the subscales of pain, function, and other complaints were reported, with the latter surveying, e.g. limitations in everyday life. Since the subscales are part of the total score, only the results of the total score were used to derive evidence.

A statistically significant difference in favour of the CAM device was found after 6 weeks and after 12 weeks (6 weeks: mean difference (MD) 15.37: 95% confidence interval (CI): [8.28; 22.46]; $p < 0.001$; 12 weeks: MD: 16.32: 95% CI: [7.13; 25.51]; $p < 0.001$),

For both time points, an effect was found in favour of the CAM device (6 weeks: Hedges' g: 1.24, 95% CI [0.62; 1.86]; 12 weeks: Hedges' g 1.06; 95% CI [0.43; 1.70]), whose 95% CI for Hedges' g was completely above the irrelevance threshold (0.2).

These effects resulted from all 3 subscales of pain, function, and other complaints because for each of the 3, a statistically significant difference in favour of the CAM device was found at both time points. Only the pain subscale showed no statistically significant difference after 6 weeks.

For the outcome of "foot pain, foot function, other complaints (VAS FA)", this results in a hint of benefit of the CAM device in comparison with standard care without CAM device.

The data from the AOFAS Ankle Hindfoot Scale were checked for general consistency with those from the VAS FA, and it was determined whether they would generally result in the same evidence. This was the case, i.e., the use of a different or additional questionnaire would not have altered the result of the derivation of evidence.

4.5.1.2 Results on ROM

The included study surveyed the outcome of ROM separately for the ankle (talocrural) joint and subtalar joint using the neutral-zero method. It measured joint ROM in degrees separately for the ankle and subtalar joints. ROM is examined from a defined neutral starting position for motion toward or away from the body. In this case, dorsiflexion and plantarflexion (ankle joint) and pronation and supination, eversion and inversion (subtalar joint) were investigated. However, the publication presents only the total ROM for each ankle; as a result, it is impossible to tell, for instance, by how many degrees dorsiflexion changed after the intervention.

The publication reports the difference in mean between the healthy and the injured side for each treatment group. Since no information is available on the variance in the individual patients' differences between the healthy and injured sides, it is unclear whether and, if so, how, the dependencies between the sides have been taken into account in the authors' calculations. Hence, it was impossible to reproduce the calculations in the study.

Since this is an RCT and the two treatment groups can therefore be assumed to be structurally equivalent, it was possible to disregard the healthy side in this assessment. Consequently, calculations by the Institute for Quality and Efficiency in Health Care (IQWiG) were based exclusively on the ROM of the injured ankles after 6 weeks and after 12 weeks. A positive difference suggests an advantage of the CAM device.

For the subtalar joint ROM, IQWiG calculations showed no statistically significant difference after 6 weeks or after 12 weeks. For 12 weeks, the publication reported a statistically significant difference, but, as described above, this calculation is not reproducible.

For the ankle joint, IQWiG calculations (and the publication) showed a statistically significant difference in favour of the CAM device after 6 weeks (MD: 7.71; 95% CI: [2.05; 13.37]; p = 0.009). Since the publication presented the results for dorsiflexion and plantarflexion jointly, it cannot be ruled out that the difference of 7.71 degrees might have been an irrelevant difference. For normal ambulation, for instance, it is critical for a patient to achieve a dorsiflexion of at least 10° [27,28]. Consequently, it was not possible to assess the patient relevance of this result. After 12 weeks, IQWiG calculations (and the publication) no longer showed any statistically significant difference between the two treatment groups.

For the outcome of ROM, there is consequently no hint of benefit or harm of a CAM device.

4.5.1.3 Results on full weight bearing

The outcome of full weight bearing is defined as the ability to apply the entire body weight to the affected ankle, provided doing so does not cause pain. The study used 2 operationalizations on this outcome: "clinical follow-up after 6 weeks", which determines whether the affected ankle can be loaded with the full body weight, and "weight-bearing log for surveying time until full weight bearing." The results of the 2nd operationalization were unusable because fewer than 70% of patients filled out the weight-bearing log. For the operationalization "clinical follow-up after 6 weeks", there was a statistically significant difference in favour of the CAM device (odds ratio: 9.31; 95% CI: [1.78; 48.72]; p = 0.004).

For the outcome of full weight bearing, this results in a hint of benefit of the CAM device in comparison with standard care without CAM device.

4.5.1.4 Results on activities of daily living

This outcome was not separately surveyed and reported. The VAS FA questionnaire also includes activities of daily living; therefore, this outcome was taken into account as part of the outcome of foot pain, foot function, other complaints (VAS FA) (see Section 4.5.1.1).

4.5.1.5 Results on dependence on help from others

The included study did not report any results on this outcome.

4.5.1.6 Results on regaining fitness to work

The outcome of regaining fitness to work was operationalized by documenting the time in weeks until the patient was able to regaining fitness to work. This was measured for the subpopulation of patients who were in an employment relationship at the time of the study (CAM device group: 16 patients [64%]; comparator group: 14 patients [58%], with analysis data being available for 12 of them [50%]). The outcome was not surveyed in patients who reported their status as retiree, pensioner, student, or unemployed.

Due to the small number of cases in this limited study population, it cannot be ruled out that the occupations and the associated amount of physical activity might have substantially influenced the time to regaining fitness to work in the present indication of ankle fracture. To estimate this potentially biasing effect on the result, the occupational titles for both groups were requested via author query. The authors' response with the occupational titles is found in Chapter A7, Table 24 of the full report. The data made available did not show any major differences regarding the amount of physical activity between the treatment groups; therefore, the results were included in the benefit assessment.

For the outcome of regaining fitness to work, a statistically significant difference in favour of the CAM device was found (MD: -4.14; 95% CI [-7.64; -0.64]; $p = 0.022$).

For the limited population of working patients, this results in a benefit of the CAM device regarding the outcome of regaining fitness to work.

4.5.2 Results on health-related quality of life

4.5.2.1 Results on the physical and mental component summary (SF-12)

For the outcome of health-related quality of life, the physical and mental component summary of the Health Survey Short Form 12 (SF-12) after 6 and 12 weeks was used. For the mental component summary (SF-12), no statistically significant differences were found after 6 weeks or after 12 weeks. For the physical component summary (SF-12), in contrast, statistically significant differences in favour of the CAM device were found after both 6 weeks and 12 weeks (6 weeks: MD: 4.91; 95% CI: [0.86; 8.96]; $p = 0.019$; 12 weeks: MD: 10.38; 95% CI: [4.72; 16.04]; $p < 0.001$). For the 6-week time point, the CI overlapped the 0.2 threshold for the standardized effect (Hedges' g: 0.69; 95% CI: [0.11; 1.28]), so that the effect strength cannot be reliably delimited from the irrelevant range. For the 12-week cutoff

point, an effect in favour of the CAM device was found (Hedges' g: 1.10; 95% CI: [0.43; 1.73]) since the 95% CI for Hedges' g was completely above the irrelevance threshold (0.2).

For the physical component summary (SF-12), this results in a hint of benefit of a CAM device. For the mental component summary (SF-12), in contrast, there is no hint of benefit or harm of the CAM device in comparison with standard care without CAM device.

4.5.2.2 Results on participation in professional and social life

The included study did not report any results on these outcomes.

4.5.3 Results on adverse events

4.5.3.1 Results on adverse events

The Ataya 2015 study reported AEs. It was found that both in the intervention group and in the comparator group, 1 patient experienced failure of the osteosynthesis material in the form of screw loosening. In addition, 1 patient in the intervention group and 2 patients in the comparator group had an infection.

Since AEs were very rare in both treatment groups, the 95% CIs for the relative effect were correspondingly imprecise.

4.5.3.2 Results on revision surgery

One patient in the intervention group and 2 patients in the comparator group had revision surgery.

Since revision surgery rates were very low in both treatment groups, the 95% CIs for relative effect were correspondingly imprecise.

4.6 Overall evaluation of results

Evidence map

Table 3 below shows the evidence map regarding patient-relevant outcomes.

Table 3: Evidence map regarding patient-relevant outcomes

Study	Outcomes										
	Morbidity						QoL			AEs	
	Foot pain, foot function, general foot health (VAS FA)	ROM	Full weight bearing	Activities of daily living	Dependence on help from others	Regaining fitness to work	Physical component summary (SF-12)	Mental component summary (SF-12)	Participation in professional and social life	AEs	Revision surgery
Ataya 2015	⇗	⇔	⇗	–[a]	–	⇗[b]	⇗	⇔	–	(⇔)	(⇔)

⇗: Hint of benefit of CAM device in comparison with standard therapy without CAM device.
⇔: no hint
(⇔): no hint; the 95% confidence interval for relative effect is so imprecise that neither halving nor doubling of effect can be ruled out
-: no data reported
a: This outcome was not separately surveyed and reported. The VAS FA questionnaire also includes activities of daily living; therefore, this outcome was taken into account as part of the outcome of foot pain, foot function, other complaints (VAS FA).
b: For the subpopulation of working patients.

AE: adverse event; CAM: controlled active motion; QoL: health-related quality of life; ROM: range of motion; SF-12: Health Survey Short Form 12; VAS FA: Visual Analogue Scale Foot and Ankle according to Richter

Assessment of the volume of unpublished data

No relevant study without reported results has been found (see Section A3.1.4 of the full report). Therefore, this aspect did not reduce the certainty of results in the present benefit assessment.

Weighing of benefits versus harm

For the independent use of a CAM device following a surgically treated ankle fracture, a hint of benefit was derived for each of the outcomes of foot pain, foot function, other complaints (VAS FA), full weight bearing, regaining fitness to work, and health-related quality of life (physical component summary [SF-12]). Harm events as in AEs were rare. Independent use of additional mobilization using a CAM device did not result in more frequent screw loosening of the osteosynthesis material, infections, or reoperation when compared to the control group. The study population was small, and the study had methodological flaws. However, consistent effects in favour of the intervention to be investigated were found across multiple outcomes. Overall, therefore, a hint of benefit of additional mobilization via the independent use of a CAM device is derived in comparison with standard care without CAM device following the surgical treatment of an ankle fracture.

Transferability of results to the therapy of conservatively treated ankle fractures

Irrespective of the type of treatment – surgical or conservative – the top priority after an ankle fracture is to optimize joint function and minimize the risk of posttraumatic osteoarthritis ([19]; see Chapter 1). Postoperative care likewise pursues this goal through early functional mobilization of the affected joint. Following fractures which are typically not indicated for surgery (e.g. type A fractures), for instance, "pain-adapted full weight bearing" [4] in a stabilizing ankle orthosis is recommended as part of early functional mobilization. Following surgical fracture treatment, immobilization as well as early targeted active and passive mobilization are recommended ([9]; see Chapter 1). Irrespective of the treatment, the fracture morphology requires that during loading, maximum joint motion is prevented. The foot should perform neither maximum dorsiflexion nor maximum plantarflexion. Supination of the subtalar joint should be avoided as well. If at least partial weight bearing is possible after an ankle fracture and hence there is some stability under load, there is no reason not to perform additional mobilization with a CAM device. After all, fixation of the feet in the CAM device prevents any maximum movements of the ankle.

No data were available on patients with conservatively treated ankle fracture. The included study, Ataya 2015, investigated only patients with surgically treated ankle fracture. A key inclusion criterion for all patients of this study was partial weight bearing being possible for at least 6 weeks (see Table 12 of the full report). Some patients with conservatively treated ankle fracture do meet this criterion. As discussed above, there are no reasons precluding these patients from performing additional mobilization using a CAM device. This subpopulation with a (at least) partially loadable, conservatively treated ankle joint can be reasonably deemed sufficiently similar to the included study's surgically treated population. Hence, the results appear transferable in this regard, resulting in a hint of benefit of the CAM device in comparison with standard care without CAM device.

The situation differs for the subpopulation of patients whose ankle joint is conservatively treated but unsuitable for partial weight bearing. In clinical experience, this is the case in a very small percentage of ankle fracture patients. In these patients, surgery is foregone exclusively due to the high surgical risk (e.g. due to multimorbidity); the joint is then immobilized using an orthesis and healing in imperfect position is accepted [4,23]. In such cases, the joint can be expected to tolerate little to no loading. For this population, independent use of a CAM device might not be indicated and would be difficult to implement. Therefore, the results are not transferable to this subpopulation because it substantially differs from the population of the included study. For these patients, there is consequently no hint of benefit. Furthermore, due to the above-described reservations with regard to the independent use of the CAM device, this subpopulation of patients with conservatively treated ankle fractures which cannot be (partially) loaded, the Institute does not recognize any "potential of a required treatment alternative".

5 Classification of the assessment result

Overall, across outcomes, the present benefit assessment derived a hint of benefit of additional mobilization therapy via the independent use of a CAM device in comparison with standard care without CAM device for adult patients with surgically treated ankle fracture. The same applies to the subpopulation of conservatively treated adult patients who can tolerate (at least) partial loading. Function-related effects were found which were clearly above the irrelevance threshold. However, this hint is based on very weak evidence since only 1 small study with methodological flaws was available for inclusion in the benefit assessment. Before inclusion of this method as a statutory health insurance service, therefore, conducting a confirmatory RCT should be considered in the present common and non-life-threatening indication (see Chapter 1). Such a study could be based on the key parameters of the study included in this assessment, but in addition to patients with surgically treated ankle fractures, it should include patients with conservatively treated ankle fractures which can be partially loaded. Unlike the present study, such a study should ensure adequate sample size planning and transparent reporting of the conduct of the RCT.

6 Conclusion

For the independent use of CAM devices following surgical therapy, 1 study was found, comparing postoperative treatment with CAM devices versus postoperative treatment without CAM device. The study population was small, and the study had methodological flaws. However, for the outcomes of foot pain, foot function, other complaints (VAS FA), full weight-bearing, regaining fitness to work, and health-related quality of life (physical component summary [SF-12]), a hint of benefit of additional mobilization via the independent use of a CAM device in comparison with standard care without CAM device was consistently found.

With regard to the outcomes of ROM, health-related quality of life (mental component summary [SF-12]), AEs, and revision surgery, there was no hint of benefit or harm of the independent use of a CAM device in comparison with standard treatment without CAM device.

No data were available for the outcomes of activities of daily living, dependence on help from others, or participation in professional and social life.

Overall, for independent use by adult patients following a surgically treated ankle fracture, a hint of benefit of additional mobilization via CAM device was found in comparison with standard treatment without CAM device.

No studies were found on additional mobilization through the independent use of a CAM device in patients with conservatively treated ankle fracture. For the subpopulation of conservatively treated adult patients who are allowed partial loading, the results are deemed transferable, and a hint of benefit of a CAM device is found in comparison with standard treatment without CAM device.

Due to the weak evidence on which the benefit assessment is based, conducting a confirmatory RCT should be considered in the present indication. This RCT should include both adult patients with surgically treated ankle fracture and those with conservatively treated ankle fracture which can be (at least) partially loaded.

For adult patients with conservatively treated ankle fracture who are not allowed partial loading of the joint, the independent use of a CAM device seems inadequately indicated and difficult to implement. Hence, the result cannot be transferred to this subpopulation. For these patients, no hint of benefit nor the potential of a required treatment alternative was found.

References for English extract

Please see full final report for full reference list.

1. Thormann U, Hentsch S. Knöchelfraktur [online]. 2020 [Accessed: 23.09.2020]. URL: https://www.pschyrembel.de/Kn%C3%B6chelfraktur/K0BTA.

2. Hermans JJ, Beumer A, De Jong TAW et al. Anatomy of the distal tibiofibular syndesmosis in adults: a pictorial essay with a multimodality approach. J Anat 2010; 217(6): 633-645. https://dx.doi.org/10.1111/j.1469-7580.2010.01302.x.

3. Kannus P, Palvanen M, Niemi S et al. Increasing number and incidence of low-trauma ankle fractures in elderly people: Finnish statistics during 1970-2000 and projections for the future. Bone 2002; 31(3): 430-433. https://dx.doi.org/10.1016/s8756-3282(02)00832-3.

4. Goost H, Wimmer MD, Barg A et al. Frakturen des oberen Sprunggelenkes: Diagnostik und Therapieoptionen. Dtsch Arztebl Int 2014; 111(21): 377-388. https://dx.doi.org/10.3238/arztebl.2014.0377.

5. Rammelt S, Grass R, Biewener A et al. Anatomie, Biomechanik und Klassifikation der Sprunggelenkfrakturen. Trauma und Berufskrankh 2004; 6(Suppl 4): S384-S392. https://dx.doi.org/10.1007/s10039-003-0804-2.

6. Deutsche Gesellschaft für Orthopädie und Orthopädische Chirurgie, Berufsverband der Ärzte für Orthopädie. Malleolarfraktur [online]. 2002 [Accessed: 29.09.2020]. URL: https://dgooc.de/images/stories/008_leitlinien/nicht_aktualisierte_ll/malleolarfraktur.pdf.

7. Danis R. Théorie et pratique de l'ostéosynthèse. Paris: Masson & Cie; 1949.

8. Weber BG. Die Verletzungen des oberen Sprunggelenkes. Bern: Huber; 1966.

9. Wichelhaus A, Mittlmeier T. OSG-Frakturen Weber-B/C: was ist Standard? OP-Journal 2014; 30(2): 66-75. https://dx.doi.org/10.1055/s-0034-1383218.

10. Müller ME, Nazarian S, Koch P et al. The comprehensive classification of fractures of long bones. Berlin: Springer; 1990.

11. Lauge-Hansen N. Fractures of the ankle: II. combined experimental-surgical and experimental-roentgenologic investigations. Arch Surg 1950; 60(5): 957-985.

12. Thur CK, Edgren G, Jansson KÅ et al. Epidemiology of adult ankle fractures in Sweden between 1987 and 2004: a population-based study of 91,410 Swedish inpatients. Acta Orthop 2012; 83(3): 276-281. https://dx.doi.org/10.3109/17453674.2012.672091.

13. Daly PJ, Fitzgerald RH, Melton LJ et al. Epidemiology of ankle fractures in Rochester, Minnesota. Acta Orthop Scand 1987; 58(5): 539-544. https://dx.doi.org/10.3109/17453678709146395.

14. Statistisches Bundesamt. Gesundheit: tiefgegliederte Diagnosedaten der Krankenhauspatientinnen und -patienten [online]. 2018 [Accessed: 10.09.2020]. URL: https://www.destatis.de/DE/Themen/Gesellschaft-Umwelt/Gesundheit/Krankenhaeuser/Publikationen/Downloads-Krankenhaeuser/tiefgegliederte-diagnosedaten-5231301187015.xlsx?__blob=publicationFile.

15. Zwipp H. Chirurgie des Fußes. Wien: Springer; 1994.

16. Smeeing DPJ, Houwert RM, Briet JP et al. Weight-bearing and mobilization in the postoperative care of ankle fractures: a systematic review and meta-analysis of randomized controlled trials and cohort studies. PLoS One 2015; 10(2): e0118320. https://dx.doi.org/10.1371/journal.pone.0118320.

17. DynaMed. Ankle fracture [online]. 2020 [Accessed: 16.09.2020]. URL: https://www.dynamed.com/condition/ankle-fracture.

18. Deutsche Gesellschaft für Unfallchirurgie. Sprunggelenkfraktur [online]. 2015 [Accessed: 21.09.2020]. URL: http://www.dgu-online.de/fileadmin/published_content/5.Qualitaet_und_Sicherheit/Leitlinien/LL_DGU_Sprunggelenkfraktur_Novelle_2015_02_01.pdf.

19. Koehler SM, Eiff P. Overview of ankle fractures in adults [online]. 2019 [Accessed: 03.09.2020]. URL: https://www.uptodate.com/contents/overview-of-ankle-fractures-in-adults.

20. Lin CWC, Donkers NAJ, Refshauge KM et al. Rehabilitation for ankle fractures in adults. Cochrane Database Syst Rev 2012; 11: CD005595. https://dx.doi.org/10.1002/14651858.CD005595.pub3.

21. Keene DJ, Williamson E, Bruce J et al. Early ankle movement versus immobilization in the postoperative management of ankle fracture in adults: a systematic review and meta-analysis. The Journal of orthopaedic and sports physical therapy 2014; 44(9): 690-701, C1-7. https://dx.doi.org/10.2519/jospt.2014.5294.

22. National Clinical Guideline Centre. Fractures (non-complex): assessment and management [online]. 2016 [Accessed: 17.09.2020]. URL: https://www.nice.org.uk/guidance/ng38/evidence/full-guideline-pdf-2358460765.

23. DynaMed. Management of ankle fracture [online]. 2020 [Accessed: 16.09.2020]. URL: https://www.dynamed.com/condition/management-of-ankle-fracture.

24. Jansen H, Jordan M, Frey S et al. Active controlled motion in early rehabilitation improves outcome after ankle fractures: a randomized controlled trial. Clin Rehabil 2018; 32(3): 312-318. https://dx.doi.org/10.1177/0269215517724192.

25. Universitätsklinikum Würzburg. Evaluation des Einsatzes von Active controlled motion (ACM) nach operativ versorgten Sprunggelenksbrüchen des Types Danis-Weber-B und C mit Notwendigkeit einer Teilbelastung für 6 Wochen postoperativ [online]. [Accessed: 20.10.2020]. URL: http://www.drks.de/DRKS00009979.

26. Ataya M. „Evaluation des Einsatzes von Active controlled motion (ACM) nach operativ versorgten Sprunggelenksbrüchen des Types Danis-Weber-B und C mit Notwendigkeit einer Teilbelastung für 6 Wochen postoperativ“ [online]. 2015 [Accessed: 03.12.2020]. URL: https://opus.bibliothek.uni-wuerzburg.de/frontdoor/index/index/docId/11459.

27. Castro MD. Ankle biomechanics. Foot Ankle Clin 2002; 7(4): 679-693. https://dx.doi.org/10.1016/s1083-7515(02)00049-9.

28. Brockett CL, Chapman GJ. Biomechanics of the ankle. Orthop Trauma 2016; 30(3): 232-238. https://dx.doi.org/10.1016/j.mporth.2016.04.015.

29. Wong SSL, Wilczynski NL, Haynes RB. Comparison of top-performing search strategies for detecting clinically sound treatment studies and systematic reviews in MEDLINE and EMBASE. J Med Libr Assoc 2006; 94(4): 451-455.

The full report (German version) is published under
https://www.iqwig.de/en/projects/n20-05.html

Appendix A – Search strategies

A.1 – Searches in bibliographic databases

Search for systematic reviews

1. MEDLINE

Search interface: Ovid

- Ovid MEDLINE(R) ALL 1946 to August 31, 2020

The following filters were adopted:

- Systematic review: Wong [29] – High specificity strategy

#	Searches
1	Ankle Fractures/
2	((ankle or malleolar) adj3 fracture*).ti,ab.
3	or/1-2
4	Cochrane database of systematic reviews.jn.
5	(search or MEDLINE or systematic review).tw.
6	meta analysis.pt.
7	or/4-6
8	7 not (exp animals/ not humans.sh.)
9	and/3,8
10	9 and (english or german).lg.
11	..l/ 10 yr=2010-Current

2. Health Technology Assessment Database

Search interface: INAHTA

#	Searches
1	"Ankle Fractures"[mh]
2	(ankle OR malleolar) AND (fracture*)
3	#2 OR #1
4	(#3) FROM 2010 TO 2020

Search for primary studies

1. MEDLINE

Search interface: Ovid

- Ovid MEDLINE(R) 1946 to February Week 4 2021
- Ovid MEDLINE(R) Daily Update March 03, 2021
- Ovid MEDLINE(R) Epub Ahead of Print and In-Process, In-Data-Review & Other Non-Indexed Citations March 03, 2021

#	**Searches**
1	Ankle Injuries/ or Ankle Fractures/
2	((ankle or malleolar or bimalleolar or trimalleolar) adj3 fracture*).ti,ab.
3	or/1-2
4	Motion Therapy, Continuous Passive/
5	Proprioception/ph
6	(active* adj3 motion*).ti,ab.
7	or/4-6
8	and/3,7
9	8 not (exp animals/ not humans.sh.)
10	9 not (comment or editorial).pt.
11	10 and (english or german).lg.

2. Embase

Search interface: Ovid

- Embase 1974 to 2021 March 03

#	**Searches**
1	exp ankle injury/
2	((ankle or malleolar or bimalleolar or trimalleolar) adj3 fracture*).ti,ab.
3	or/1-2
4	Proprioception/
5	(active adj3 motion).ti,ab.
6	or/4-5
7	and/3,6
8	7 not medline.cr.
9	8 not (Conference Abstract or Conference Review or Editorial).pt.
10	9 and (english or german).lg.

3. The Cochrane Library

Search interface: Wiley

- Cochrane Central Register of Controlled Trials Issue 3 of 12, March 2021

#	**Searches**
#1	[mh ^"Ankle Injuries"] or [mh ^"Ankle Fractures"]
#2	((ankle or malleolar or bimalleolar or trimalleolar) NEAR/3 fracture*):ti,ab
#3	#1 or #2
#4	[mh ^"Motion Therapy, Continuous Passive"]
#5	[mh ^"Proprioception"]
#6	(active* NEAR/3 motion*):ti,ab
#7	#4 or #5 or #6
#8	#3 and #7 in Trials
#9	#8 not (*clinicaltrials*gov* OR *who*trialsearch* OR *clinicaltrialsregister*eu* OR *anzctr*org*au* OR *trialregister*nl* OR *irct*ir* OR *isrctn*org* OR *controlled-trials*com* OR *drks*de*):so

A.2 – Searches in study registries

1. ClinicalTrials.gov

Provider: U.S. National Institutes of Health

- URL: http://www.clinicaltrials.gov
- Type of search: Advanced Search

▪ Search strategy
(ankle OR malleolar) AND (fracture OR fractures) AND active AND motion

2. International Clinical Trials Registry Platform Search Portal

Provider: World Health Organization

- URL: http://apps.who.int/trialsearch
- Type of search: Standard Search

▪ Search strategy
ankle AND fracture AND activ* OR malleolar AND fracture AND activ* OR ankle AND fractures AND activ* OR malleolar AND fractures AND activ*