HTA Austria
Austrian Institute for
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Systematic Review

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Conflict of interest

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Commissioned by the Austrian Ministry of Health, this report systematically assessed the intervention described herein as decision support for the inclusion in the catalogue of benefits.

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Content

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List of abbreviations

APL ..... Abductor pollicis longus
AVN..... Avascular necrosis
bzgl. ..... Bezüglich
CE..... Conformitè Europëenne
CRD ..... Centre for Reviews and Dissemination
CT..... Computed tomography
DMAA..... Distal joint surface angle
EMA ..... European Medicines Agency
EPL ..... Extensor pollicis longus
FDA..... Food and Drug Administration
ggf. ..... Gegebenenfalls
GIZG GmbH..... German Institute for Cell and Tissue Replacement
GRADE..... Grading of Recommendations Assessment, Development and Evaluation
HV ..... Hallux valgus
ICD ..... International Classification of Diseases
IHE..... Institute of Health Economics
IM..... Intermetatarsal
INAHTA..... International Network of Agencies for Health Technology Assessment
MRI..... Magnetic resonance imaging
MTP ..... Metatarsophalangeal
NRCT..... Non-randomised controlled trial
OCD ..... Osteochondritis dissecans
OP ..... Operation
RCT..... Randomised controlled trial
RoB..... Risk of Bias
ROBINS-I..... Risk Of Bias In Non-randomised Studies – of Interventions
SL ..... Scapho-lunate
SNAC ..... Scaphoid nonunion advanced collapse
vs..... Versus

Executive summary

Introduction

Health problem

hallux valgus (HV) most common foot deformity (23-36%)

Hallux valgus (HV) is one of the most common foot deformities globally, afflicting 23 per cent of the 18- to 65-year olds and 36 per cent of adults over 65 years of age. Women are affected around twice as often as men are. Untreated HV deformities can lead to a number of painful complications in or around the first metatarsophalangeal (MTP) joint, but also to further foot deformities affecting the other toes (e.g., hammer or claw toes).

scaphoid fracture the most common carpal fracture (50-80%)

Concerning the hand, a scaphoid fracture is the most common carpal fracture globally, accounting for 50 to 80 per cent of all carpal fractures. Especially young, active men are affected approximately six times more often than women are. Untreated or wrongly treated fractures can cause nonunion or malunion of the fracture (e.g., pseudarthrosis). The main risk factors for developing pseudarthrosis include the shape of the scaphoid, its central role in wrist motion, as well as the position and the degree of severity of the fracture.

often surgery & associated recovery time necessary → societal costs

Both HV deformities and scaphoid fractures/pseudarthroses often involve surgery. In 2014 in Austria, approximately 5,819 hospitalisations were assigned to HV, approximately 413 to scaphoid fractures and approximately 400 to pseudarthroses in scaphoid fractures. After surgery, the patients are unable to continue their daily life routines, including work, for several weeks. In addition, every surgery bears the risk of complications, such as interfering osteosynthesis material that needs to be removed during a second operation. Such re-surgeries require further recovery time. Therefore, the aforementioned diagnoses not only cause a burden to the individual patient, but also have societal implications (e.g., societal costs including productivity losses).

Description of technology

alternative: allogeneic bone screw (Shark Screw®) – expected osteoconductive properties → possible reduced healing time & complication rates?

Currently, metal (e.g., titanium or stainless steel) or bioabsorbable implants (e.g., polymers or magnesium) are frequently used for osteosyntheses. Whereas metal implants are stiff and have high mechanical strength, but sometimes cause pain sensation, soft tissue irritations, allergic reactions or functional inhibition, the bioabsorbable materials are expected to be more compatible but less stable. Hence, another possible alternative is presented by the allogeneic bone screw, Shark Screw®, from Surgebright GmbH Austria, with its expected osteoconductive properties possibly leading to full conversion into autologous bone. It is deemed to combine stabilisation, bone bridge as well as bone replacement in one screw and thus may reduce bone healing time. Moreover, infections or other complications including re-surgeries are expected to be scarce due to its human biological material.

license for the use of human biological material needed

For the manufacturing and distribution of human tissue transplants such as Shark Screw®, no standardised approval process exists; however, a license is needed.

Shark Screw® included in Austrian hospital benefit catalogue

In Austria, the Shark Screw® transplant is already included in the hospital benefit catalogue (code PA040) and thus reimbursed. In 2020, approximately 750 Shark Screw® transplants were distributed to Austrian hospitals. Out of those, around 150 (20%) were distributed for HV surgeries and approximately 60 (8%) for scaphoid surgeries.

Methods

aim: assessment of clinical effectiveness and safety of Shark Screw® concerning economically relevant endpoints

This systematic review aimed to investigate the use of the allogeneic bone screw, Shark Screw®, in patients with HV or scaphoid fractures/pseudarthroses compared to other bone screws. The question was whether Shark Screw® is more effective and equally safe concerning economically relevant endpoints from a health care system perspective. The relevant endpoints were the number and duration of hospitalisations, the duration of the actual surgical procedure, the revision rate, the period of convalescence, implant breakage during surgery, as well as major postoperative complications. The EUnetHTA Core Model® for Rapid Assessment of Relative Effectiveness Version 4.2 was the main source for selecting relevant assessment elements.

systematic literature search in 5 databases & publications submitted from manufacturer → 169 references in total

The systematic literature search was conducted on 18 and 21 December 2020 in five databases and identified 155 citations. In addition, the manufacturer submitted 14 new references, while no further publication could be identified through a separate hand-search. Therefore, the overall number of hits after deduplication was 169. A further search in three clinical trial registries was conducted on January 11, 2021, which yielded 36 potentially relevant ongoing studies.

RoB assessment with different tools & qualitative synthesis according to GRADE scheme planned

For the assessment of the risk of bias (RoB), the use of different tools depending on the study design was planned, e.g., the Cochrane Risk of Bias Tool for randomised controlled trials (RCTs), the ROBINS-I Tool for non-randomised controlled trials (NRCTs) and the Institute of Health Economics (IHE) checklist for single-arm studies. In addition, a qualitative synthesis of identified evidence was planned according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) scheme.

Results

no published evidence identified based on the predefined inclusion criteria

Based on the predefined inclusion criteria, out of the 169 identified references, no RCTs, NRCTs, prospective single-arm studies or health economic evaluations could be identified for the qualitative synthesis of the clinical effectiveness and safety of Shark Screw® in patients with HV or fractures/pseudarthroses of the scaphoid bone. Therefore, the related research questions could not be answered.

Discussion and conclusion

only 1 cost-effectiveness analysis identified, but no full text available

At the time of conducting this review, no published evidence on Shark Screw® could be identified in the systematic literature search or additional hand-search. Only one cost-effectiveness analysis comparing Shark Screw® transplant to other metal devices was identified; however, this could not be included due to the lacking full text.

2 ongoing single-arm studies do not fill the current evidence gap → future controlled studies with special focus on healing & re-surgery rates recommended

Furthermore, two ongoing prospective single-arm studies assessing the clinical effectiveness of Shark Screw® for a one-year follow-up period (n = 32/50) were identified; however, these ongoing studies do not fill the gap of controlled and long-term evidence. Therefore, further, preferably controlled evidence on the clinical effectiveness and safety of Shark Screw®, including a sufficiently large number of patients and a follow-up exceeding one year, is recommended. In particular, evidence on the healing as well as re-surgery rates is needed, as these outcomes are crucial from a patient's but also from a societal and economic perspective.

Zusammenfassung

Einleitung

Indikation und therapeutisches Ziel

Hallux Valgus (HV) häufigste Fußdeformität (23–36 %)

Die Hallux Valgus (HV)-Deformität ist mit zirka 23 Prozent bei den 18- bis 65-Jährigen und mit zirka 36 Prozent bei den über 65-Jährigen eine der häufigsten Fußdeformitäten weltweit. Generell sind Frauen zirka zwei Mal häufiger davon betroffen als Männer. Durch eine abnormale Fußmechanik, eine abnormale Anatomie des ersten Metatarsophalangealgelenks, genetische Einflüsse, aber auch durch unangemessenes Schuhwerk kann das Risiko einer Deformität steigen. Eine unbehandelte HV-Deformität kann zu einer Reihe von schmerzhaften Komplikationen im oder um das erste Metatarsophalangealgelenk, aber auch zu weiteren Vorfußdeformitäten der übrigen Zehen führen, z. B. Hammer- oder Krallenzehen.

Kahnbeinfraktur die häufigste Karpalfraktur (50–80 %)

Die Hand betreffend stellt die Kahnbeinfraktur mit 50 bis 80 Prozent aller Handwurzelfrakturen die häufigste Fraktur der Handwurzel weltweit dar. Insbesondere junge, aktive Männer sind bis zu sechsmal häufiger davon betroffen als Frauen. Ein Sturz auf die ausgestreckte Hand stellt die Hauptursache für eine Kahnbeinfraktur dar. Bleiben diese Frakturen unbehandelt oder werden sie falsch behandelt, kann es zu einer schlechten bzw. fehlenden Heilung kommen (z. B. Pseudarthrose). Demnach stellen eine zu späte Diagnose oder eine unzureichende Behandlung einer Kahnbeinfraktur wesentliche Risikofaktoren für die Entwicklung einer Pseudarthrose dar. Als zusätzliche Risikofaktoren gelten unter anderem die Form und Lage des Kahnbeins, sowie der Schweregrad der Fraktur. Beispielsweise sind instabile Frakturen des proximalen Pols anfälliger für die Entwicklung einer Pseudarthrose.

häufig chirurgische Eingriffe & damit verbundene Erholungszeit erforderlich → gesellschaftliche Kosten

Sowohl HV-Deformitäten als auch Kahnbeinfrakturen/Pseudarthrosen gehen häufig mit einem operativen Eingriff einher. In Österreich (2014) wurden zirka 5.819 Hospitalisierungen dem HV, zirka 413 den Kahnbeinfrakturen und zirka 400 den Pseudarthrosen zugeordnet. Nach einem operativen Eingriff sind die Patient*innen meist für mehrere Wochen in ihrem täglichen Leben beeinträchtigt und teilweise auch vorübergehend arbeitsunfähig. Darüber hinaus birgt jede Operation das Risiko von Komplikationen, wie z. B. störendes Osteosynthesematerial, welches folglich in einer zweiten Operation entfernt werden muss und somit den Heilungsprozess verlängert. Aus diesem Grund stellen HV-Deformitäten bzw. Kahnbeinfrakturen/Pseudarthrosen nicht nur eine Belastung für die Patient*innen dar, sondern haben auch relevante Implikationen aus gesellschaftlicher Sicht (z. B. gesellschaftliche Kosten wie Produktivitätsverlust).

Beschreibung der Technologie

Alternative: allogene Knochenschraube (Shark Screw®): weniger Komplikationen & kürzere Heilungszeit?

Derzeit werden für Osteosynthesen häufig Implantate aus Metall (z. B. Titan oder Edelstahl) oder auch bioresorbierbare Implantate (z. B. aus Polymere oder Magnesium) verwendet. Während Metallimplantate zwar steif sind und somit eine hohe mechanische Festigkeit aufweisen, können sie jedoch Schmerzen, Weichteilirritationen, allergische Reaktionen oder Funktionseinschränkungen hervorrufen. Im Gegensatz dazu gelten die bioabsorbierbaren Materialien zwar als verträglicher jedoch weniger stabil. Eine weitere mögliche Alternative stellt daher die allogene Knochenschraube Shark Screw® von

der Surgebright GmbH aus Österreich dar. Den Angaben des Herstellers zufolge wandelt sich die allogene Knochenschraube aufgrund ihrer erwarteten osteokonduktiven Eigenschaften vollständig in autologen Knochen um. Demnach soll die Schraube Stabilisierung, Knochenbrücke und Knochenersatz in einer Vorrichtung vereinen und dadurch den Heilungsprozess verkürzen. Darüber hinaus gelten aufgrund des humanbiologischen Materials der Shark Screw® Infektionen oder andere Komplikationen und damit einhergehende Re-operationen als selten.

Lizenz für Verwendung von human-biologischem Material erforderlich

Für die Herstellung und den Vertrieb von humanen Gewebetransplantaten, wie der Shark Screw® Knochenschraube, gibt es aktuell kein standardisiertes Zulassungsverfahren. Stattdessen benötigt der Hersteller dafür eine entsprechende Lizenz.

Shark Screw® im österreichischen Krankenhausleistungskatalog gelistet

In Österreich ist das Shark Screw®-Transplantat bereits im Krankenhausleistungskatalog gelistet (Code PA040) und wird somit refundiert. Im Jahr 2020 wurden zirka 750 Shark Screw®-Transplantate an österreichische Krankenhäuser verkauft, davon in etwa 150 Schrauben (20 %) für HV-Operationen und zirka 60 Schrauben (8 %) für Kahnbeinoperationen.

Methoden

Ziel: Bewertung der klinischen Wirksamkeit und Sicherheit von Shark Screw® unter Berücksichtigung ökonomisch relevanter Endpunkte

Ziel dieser systematischen Übersichtsarbeit war es, den Einsatz der allogenen Knochenschraube Shark Screw® bei Patient*innen mit einer HV-Deformität oder einer Kahnbeinfraktur/Pseudarthrose im Vergleich zu anderen Knochenschrauben zu untersuchen. Im Detail wurde die Frage analysiert, ob das Shark Screw®-Transplantat effektiver und gleich sicher ist. Das Augenmerk lag dabei auf Gesundheitssystem-relevanten Endpunkten, wie die Anzahl und Dauer der Krankenhausaufenthalte, die Dauer des chirurgischen Eingriffs, die Revisionsrate, die Rekonvaleszenzzeit, sowie die Rupturrate während der Operation und die Rate an größeren postoperativen Komplikationen. Das EUnetHTA Core Model® for Rapid Assessment of Relative Effectiveness Version 4.2 stellte dabei die Hauptquelle für die Auswahl relevanter Bewertungselemente dar.

systematische Literaturrecherche in 5 Datenbanken & vom Hersteller eingereichte Publikationen → insgesamt 169 Referenzen

Die systematische Literaturrecherche wurde am 18. und 21.12.2020 in fünf Datenbanken durchgeführt und identifizierte 155 Zitate. Zusätzlich wurden vom Hersteller 14 neue Referenzen übermittelt, während durch eine separate Handsuche keine weiteren Publikationen identifiziert werden konnten. Demnach wurden nach Deduplizierung insgesamt 169 Quellen für die Durchsicht identifiziert. Darüber hinaus wurde am 11. Jänner 2021 eine Suche in drei klinischen Studienregistern durchgeführt, die in 36 potenziell relevanten laufenden Studien resultierte.

RoB-Bewertung mit unterschiedlichen Tools sowie qualitative Synthese nach GRADE-Schema geplant

Für die Bewertung des Verzerrungsrisikos war die Verwendung unterschiedlicher Tools in Abhängigkeit des Studiendesigns geplant: z. B. das „Cochrane Risk of Bias Tool“ für randomisierte kontrollierte Studien, das ROBINS-I Tool für nicht-randomisierte kontrollierte Studien und die „Institute of Health Economics“ Checkliste für Fallserien. Darüber hinaus war eine Synthese der vorhandenen Evidenz nach dem „Grading of Recommendations Assessment, Development and Evaluation“ Schema geplant.

Ergebnisse

Basierend auf den vordefinierten Einschlusskriterien konnten aus den 169 identifizierten Quellen keine publizierten Studien oder gesundheitsökonomische Evaluationen für die qualitative Synthese der Wirksamkeit und Sicherheit von Shark Screw® bei Patient*innen mit einer HV-Deformität oder einer Fraktur/Pseudarthrose des Kahnbeins identifiziert werden. Aus diesem Grund konnten die jeweiligen Forschungsfragen nicht beantwortet werden.

keine publizierte Evidenz basierend auf den vordefinierten Einschlusskriterien identifiziert

Diskussion und Fazit

Zum Zeitpunkt der Durchführung dieser Übersichtsarbeit konnte bei der systematischen Literaturrecherche oder der erweiterten Handsuche keine publizierte Evidenz zum Shark Screw®-Transplatat identifiziert werden. Es wurde nur eine Kosten-Effektivitäts-Analyse identifiziert, die Shark Screw®-Transplantate mit anderen Metallschrauben vergleicht. Aufgrund der mangelnden Verfügbarkeit des Volltextes konnte diese Analyse jedoch nicht für die vorliegende Arbeit herangezogen werden.

nur 1 Kosten-Effektivitäts-Analyse identifiziert, jedoch kein Volltext verfügbar

Darüber hinaus wurden zwei laufende einarmige Studien identifiziert, die die Wirksamkeit von Shark Screw®-Transplantaten für eine einjährige Nachbeobachtungszeit (n = 32/50) untersuchen. Diese laufenden Studien füllen jedoch die aktuelle Evidenzlücke nicht. Aus diesem Grund werden für die Zukunft weitere, vorzugsweise kontrollierte Studien zur Wirksamkeit und Sicherheit von Shark Screw® mit einer ausreichend großen Anzahl von Patient*innen und einer Nachbeobachtungszeit von über einem Jahr empfohlen. Darüber hinaus ist insbesondere Evidenz zu den Heilungs- und Re-operationsraten erforderlich. Diese Outcomes sind nicht nur aus Sicht der Patient*innen relevant, sondern haben auch gesellschaftliche und ökonomische Implikationen.

2 laufende einarmige Studien füllen aktuelle Evidenzlücke nicht → zukünftig kontrollierte Studien mit Fokus auf Heilungs- bzw. Re-Operationsraten empfohlen

Empfehlung

Basierend auf dem aktuellen Mangel an publizierter Evidenz zur Wirksamkeit und Sicherheit der bewerteten Technologie, Shark Screw®, wird die Aufnahme der allogenen Knochenschraube in den österreichischen Krankenhausleistungskatalog derzeit nicht empfohlen. Darüber hinaus wird eine Re-evaluierung der Technologie frühestens im Jahr 2025 empfohlen, da zum Zeitpunkt der Berichtverfassung keine laufenden kontrollierten Studien identifiziert werden konnten.

aufgrund mangelnder Evidenz Aufnahme in Leistungskatalog aktuell nicht empfohlen, Re-evaluierung frühestens 2025

1 Background

1.1 Hallux valgus

1.1.1 Overview of the disease, health condition and target population[1]

Hallux valgus (HV) is characterised by a lateral deviation of the hallux (big toe) at the metatarsophalangeal (MTP) joint, often in combination with concurrent rotation of the toe [4, 5]. This rotation often results in a prominent metatarsal head adduced toward the body midline, which can go along with inflammation and overlying bursae on the medial aspect of the MTP joint, also called "bunion" [6]. According to the International Classification of Diseases (ICD-10), the diagnosis of an acquired HV, including inflammation, receives the ICD-10 code M20.1 [7].[2]

Hallux Valgus (HV): seitliche Abweichung des Hallux am Metatarsophalangealgelenk ICD-10: M20.1

The pooled prevalence of HV deformity in the literature has been estimated to be 23 per cent among those 18 to 65 years of age, 36 per cent among adults over 65 years of age, and 30 per cent among adult females [5, 8, 9]. Furthermore, the prevalence of HV is greater among shod compared with barefoot populations; however, it is still found twice as often in women than men in non-shod populations [5].[3]

häufigste Vorfußdeformität (23-36 %) insbesondere bei Frauen

In Austria, approximately 5,819 hospitalisations were assigned to the diagnosis "HV" (ICD-10 M20.1) in 2014 (more recent data not available) (information provided by the manufacturer [3]).[3]

Österreich 2014: ca. 5.819 Krankenhausaufenthalte aufgrund von HV

The reasons for developing HV are most likely of multifactorial origin, including factors such as abnormal foot mechanics affecting the first ray, abnormal first MTP anatomy, joint hypermobility and genetic influences. Moreover, HV is associated with conditions like inflammatory joint diseases [4, 5]. In addition, poor footwear has also frequently been cited as one cause; however, opinions diverge, as some also question whether footwear probably exacerbates underlying bony or mechanical abnormalities rather than acting as a primary factor [5].[4]

Ursachen und Risikofaktoren: abnorme Fußmechanik (z. B. aufgrund von schlechtem Schuhwerk), Genetik, etc.

HV can lead to a number of painful complications in or around the first MTP joint that may result in or occur because of altered weight-bearing forces. This can cause marked discomfort, including inflammation of a medial bursa, degeneration of the crista on the plantar surface of the metatarsal head, entrapment of the medial dorsal cutaneous nerve, central metatarsalgia and degeneration of the cartilage or synovitis. Besides, the valgus position of the big toe regularly results in the small toes no longer having enough space, leading to further foot deformities, such as hammer or claw toes [5, 10].[5]

Symptome, z. B.: Schmerzen, Entzündungen, andere Fußfehlstellungen

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1 This section addresses the EUnetHTA Core Model® domain CUR.

2 A0001 – For which health conditions, and for what purposes is the technology used?; A0002 – What is the disease or health condition in the scope of this assessment?

3 A0007 – What is the target population in this assessment?; A0023 – How many people belong to the target population?

4 A0003 – What are the known risk factors for HV?

5 A0004 – What is the natural course of HV?; A0005 – What is the burden of disease for patients with HV?

1.1.2 Current clinical practice[1]

Diagnose umfasst klinische Untersuchung & Röntgen zur Winkelbestimmung

The diagnosis of HV primarily includes a clinical examination of the foot by the naked eye (e.g., examination of trophic skin lesions, bursa, foot position, range of motion in the first MTP joint, and the position of the smaller toes). In addition, radiographs may be used to examine the exact HV angle and the intermetatarsal (IM I/II) angle (see Figure 1-1), as well as to determine the presence of damage to the articular surfaces of the first MTP joint [5, 10-12].[6]

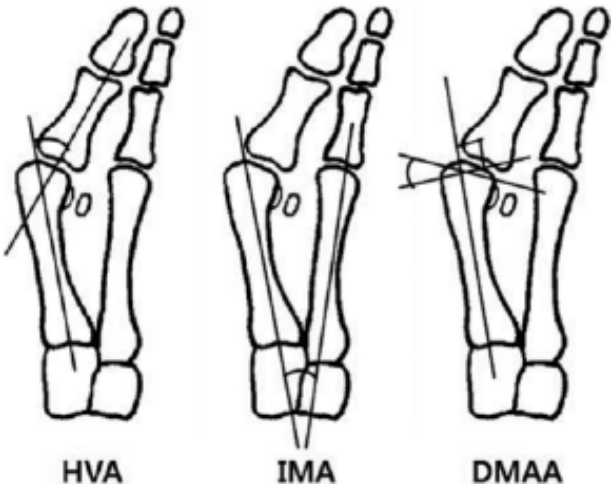

Figure 1-1: Radiographic parameter of the hallux valgus
Abbreviations: DMAA – Distal joint surface angle, HVA – Hallux valgus angle, IMA – Intermetatarsal angle; Adapted figure from: [2]

Klassifizierung in milde bis schwerwiegende Deformitäten

According to guidelines, a classification into mild to severe HV cases is recommended when it comes to the choice of the treatments. An overview is presented in Table 1-1:

Table 1-1: Classification of the hallux valgus severity according to radiological aspects

	Mild deformity	Moderate deformity	Severe deformity
Severity	I	II	III
HV angle	21-30°	31-40°	>40°
IM I/II angle	11-15°	16-20°	>20°
Symptoms	Occasional pain in daily life, redness and thickened skin possible	Frequent pain in daily life, redness, pressure marks on the ball of the foot, pain when wearing shoes	Pain also at rest, as well as when walking and running
Conservative treatment	Physiotherapy, foot gymnastics, splints, insoles	Optimised footwear, foot gymnastics	Foot gymnastics
Surgical treatment	Chevron osteotomy	Scarf osteotomy	Scarf osteotomy or Lapidus arthrodesis

Abbreviations: HV – Hallux Valgus, IM I/II – First and second intermetatarsal angle; own presentation based on [3, 11-13]

[6] A0024 – How is HV currently diagnosed according to published guidelines and in practice?

zahlreiche konservative vs. operative Therapieoptionen

There are numerous different conservative and surgical treatment options for HV deformities. According to several guidelines, conservative therapies are recommended before a surgical referral is made [5, 12]. However, for patients with severe pain or dysfunction and for those whose symptoms do not improve under a conservative treatment regimen, there are approximately 150 different surgical procedures to correct the HV deformity [5, 10]. In general, a distinction can be made between joint-preserving and joint-resecting surgical techniques, where the latter is primarily used for more severe cases [11]. The most frequently performed open surgical techniques are briefly presented as follows:[7]

gelenkserhaltende Operation vs. Gelenksresektion:

- **Chevron-Osteotomie: gelenkserhaltend für milde Deformitäten**

  The **Chevron osteotomy** is one of the joint-preserving, load-stabilising distal osteotomy techniques. It is used for mild deformities (severity I) mostly affecting younger patients. The deformity should still be flexibly correctable and without radiological signs of arthrosis in the first MTP joint. The procedure includes the fixation of the displaced bone fragments with a screw of 2.5-3.5 mm [10, 11].

- **Scarf-Osteotomie: gelenkserhaltend für moderate Deformitäten**

  The **Scarf osteotomy** is also a joint-preserving and early load-stabilising procedure. The osteotomy plane runs in a Z-shape along the shaft, which corrects larger deformities (severity II) compared to the Chevron osteotomy. Two screws with a diameter of 2.5-3.5 mm are inserted at the end of the operation to fix the displaced bone fragments [10, 11].

- **Lapidus-Arthrodese: Gelenksresektion für schwerwiegende Deformitäten**

  Lapidus arthrodesis is indicated in cases of severe deformity with a clear deformity of the splayfoot and incongruence of the first MTP joint due to subluxation of the proximal phalanx, as well as clinical instability at the first MTP joint (severity III). It presents a joint stiffening procedure that is also used for arthrosis in the first MTP joint. Mostly women in middle to older age undergo this procedure. With this technique, the bone is exposed in its entire depth and length. Two crossed screws with a diameter of 3.5 mm or a plate (as an angular stable implant) can be used for osteosynthesis [10, 11].

keine Empfehlungen zum bevorzugten Schraubenmaterial

With respect to the preferred material of the used bone screws, no recommendation could be identified in several guidelines [4-6, 12].

zusätzliche Eingriffe möglich

The aforementioned surgical procedures that primarily correct HV and IM angles often include additional interventions, such as the correction of the distal joint surface angle (DMAA) (see Figure 1-1), a resection of the pseudoexostosis or accompanying procedures on the neighbouring toes (e.g., in the case of claw or hammer toe deformities) [11].[7]

Operationsdauer abhängig vom Verfahren

The average cutting/suture time depends on the performed technique and whether an accompanying procedure was performed or not. In general, the duration of joint-preserving techniques, such as the Chevron osteotomy, is shorter (approximately 65 minutes) compared to joint-stiffening procedures, such as the Lapidus arthrodesis (approximately 80 minutes) [11].[7]

minimal-invasive bzw. perkutane Verfahren weitere Option

Apart from the open surgical techniques, minimally invasive or percutaneous surgery for correcting HV deformities is used with increasing frequency; however, the evidence remains scarce [5].[7]

[7] A0025 – How is HV currently managed according to published guidelines and in practice?

Kontraindikationen, z. B.: arterielle Verschlusskrankheit, ggf. beginnende Polyneuropathie (Diabetes)

A major contraindication to HV corrective surgery is arterial occlusive disease. Since the foot is the farthermost from the heart, reduced blood flow is the first thing to manifest itself in the hallux. Accordingly, surgery can only be performed if there is sufficient perfusion of the foot. Furthermore, in the case of diabetes with incipient polyneuropathy or the case of existing chronic polyarthritis or other rheumatic diseases, the choice of surgical procedure must be made accordingly [10].[7]

Heilungszeit zwischen 6-8 Wochen → gesellschaftliche Kosten

If an osteotomy is performed, healing corresponds to complete bony union, which occurs at around six to eight weeks postoperatively. As the time needed to return to work also generally coincides with the bone healing time, the average time to return to work is approximately six weeks, whereas the return to hard physical work or sports may take around eight weeks [5]. Therefore, HV and the according therapies go along with societal costs, e.g., due to temporary productivity losses.[8]

Risiken: Rezidiv, anhaltender Schmerz, Infektionen

→ Re-Operationen möglich → zusätzliche gesellschaftliche Kosten

Besides, like any operation, the surgical correction of an HV deformity involves certain risks. The most commonly reported unintended outcomes from surgical corrections include recurrence of HV deformity, persistent pain, secondary metatarsalgia, nerve injury, infection, delayed union or nonunion that often cause secondary procedures, e.g., for osteosynthesis material removal [9]. In clinical series, material removal was frequently noted with general rates of up to 25 per cent (independent of the used material) [9]. Hence, resurgeries cause further burden to the individual patient and have further societal implications (e.g., prolonged recovery time causing extended inability to work). For this reason, the material is also left in place if it does not cause any discomfort [10].[8]

1.2 Fractures of the scaphoid bone

1.2.1 Overview of the disease, health condition and target population[9]

Kahnbeinfraktur: Bruch des Kahnbeins, ICD-10: S62.0

The scaphoid bone is required for stability and coordination. A fracture of the scaphoid bone involves a break in one of the eight small carpal bones located at the wrist (see Figure 1-2) [1, 14]. According to the ICD-10, the diagnosis of a fracture of the scaphoid bone receives the ICD-10 code S62.0 [15].[10]

häufigste Fraktur der Handwurzelknochen (50-80 %),

Globally, fracture of the scaphoid bone is the most common carpal fracture, accounting for 50 to 80 per cent of all carpal fractures and two to seven per cent of all fractures. In particular, men suffer scaphoid fractures six times as frequently as women, with a peak in the age group 20 to 30 years [16].[11]

[8] A0006 – What are the consequences of HV for the society?

[9] This section addresses the EUnetHTA Core Model® domain CUR.

[10] A0001 – For which health conditions, and for what purposes is the technology used?; A0002 – What is the disease or health condition in the scope of this assessment?

[11] A0007 – What is the target population in this assessment?; A0023 – How many people belong to the target population?

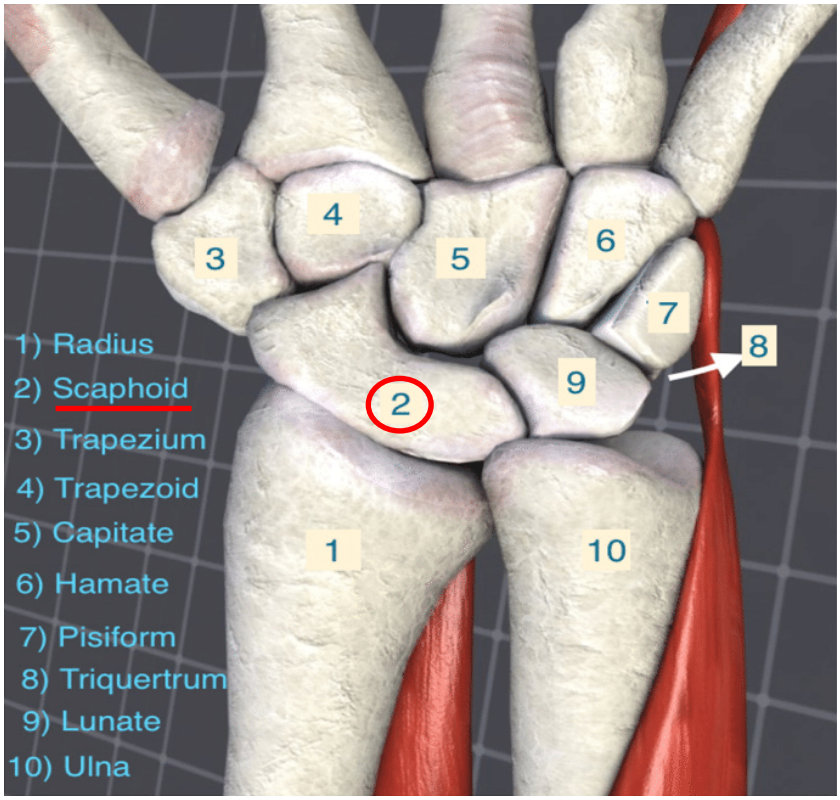

Figure 1-2: Illustration of the eight carpal bones and two long bones of the wrist. Reference: [1]

Österreich 2014: ca. 412 Krankenhausaufenthalte wegen Kahnbeinfrakturen

In Austria, approximately 412 hospitalisations were assigned to the diagnosis "fracture of the scaphoid bone" (ICD-10 S62.0) in 2014 (more recent data not available) (information provided by the manufacturer [3]).[11]

Hauptursache: Fall auf ausgestreckte Hand

The main cause of a scaphoid fracture is the fall onto an outstretched hand [1, 14]. In particular, active young adults have an increased risk. However, also individuals suffering from osteoporosis, having low muscle mass, poor muscle strength or lacking agility are at risk of having these fractures [1].[12]

Symptome, z. B.: Schmerzen, Schwellung, reduzierte Bewegungsfreiheit

Patients with scaphoid fractures suffer from pain localised to the radial aspect of the wrist, often in the area just proximal to the metacarpal bone of the thumb, while swelling may or may not be noticeable, but if present, usually on the dorsoradial aspect of the wrist. Moreover, the range of motion of the wrist may be slightly reduced unless there is a concomitant fracture-dislocation [14, 16].[13]

bei fehlender oder falscher Behandlung auch gesellschaftliche Konsequenzen

If untreated or wrongly treated, the burden to the patients but also to the society increases, as nonunion or malunion ultimately lengthen symptom duration and inability to work (see Chapter 1.3 about scaphoid pseudarthrosis) [17].[13]

[12] A0003 – What are the known risk factors for scaphoid fractures?

[13] A0005 – What is the burden of disease for patients with scaphoid fractures?; A0004 – What is the natural course of scaphoid fractures?; A0006 – What are the consequences of scaphoid fractures for the society?

1.2.2 Current clinical practice[9]

Diagnose umfasst klinische Untersuchung, 3 standardisierte Röntgenaufnahmen & CT bzw. MRI

The diagnosis of a scaphoid fracture includes a clinical examination involving palpation of the anatomical snuffbox[14] with the wrist ulnar deviated so that the whole central portion of the scaphoid can be palpated between different thumb muscles, like the extensor pollicis longus (EPL) and the abductor pollicis longus (APL) [17]. In addition, the diagnosis of scaphoid fractures includes three standard x-ray projections (dorsopalmar, lateral, and Stecher projections). However, up to 30 per cent of fresh, non-displaced scaphoid fractures appear unremarkable on conventional radiography [16, 18]. Therefore, computed tomography (CT) and/or magnetic resonance imaging (MRI) are additionally recommended to correctly identify the degree of displacement [14, 16, 18].[15]

Klassifizierung nach Frakturlokalisation oder nach Krimmer et al. in stabile vs. instabile Frakturen

The most common classification of scaphoid fractures categorises them by location into the distal third (distal pole, around 10% of the patients), the central third (waist, around 65%) and proximal third (proximal pole, around 15%) [14]. Furthermore, Krimmer et al. classified scaphoid fractures based on the combination of the Herbert and Fischer classification and CT findings. Accordingly, scaphoid fractures are subdivided into stable and unstable fractures. There are different treatment options available, which aim to avoid long immobilisation or bone healing disorders, such as pseudoarthrosis, and to subsequently gain normal wrist function (see Table 1-2) [18, 19].

Table 1-2: Krimmer scaphoid fracture classification and associated treatment recommendations

Classification	Description	Recommended treatment
Type A	Fresh stable fractures	
A1	Non-dislocated scaphoid tubercle fracture	Conservative therapy with a plaster cast for 4 weeks
A2	Non-dislocated crack fractures with a transverse course in the middle or distal third	Conservative therapy with a plaster cast for 6-8 weeks OR minimally invasive surgery for patients with the wish for timely resilience
Type B	Fresh unstable fractures	Surgical therapies, e.g. screw osteosynthesis ■ Minimally invasive surgery for non-displaced fractures ■ Open reposition and internal fixation for displaced fractures
B1	Oblique fractures	
B2	Dislocated or gaping fractures	
B3	Fractures of the proximal third	
B4	Trans-scaphoid fracture (de Quervain) with lunate dislocation	

Own presentation based on [16, 18]

[14] An anatomical snuffbox is a triangular deepening on the radial, dorsal aspect of the hand at the level of the carpal bones, specifically, the scaphoid and trapezium bones forming the floor.

[15] A0024 – How is a scaphoid fracture currently diagnosed according to published guidelines and in practice?

konservative, minimalinvasive und operative Therapieoptionen:

The treatment options for scaphoid fractures are divided into conservative, minimally invasive and surgical options. Non-operative (conservative) management, casting, is recommended for non-displaced, stable fractures. The duration of immobilisation ranges between four to eight weeks depending on the position of the fracture [14, 18]. In case a definitive diagnosis cannot be determined at presentation and a scaphoid fracture is suspected on clinical grounds (even if radiographs are negative), immobilisation should still be guaranteed until a definitive imaging examination can be performed [14, 18].[16]

nicht-dislozierte, stabile Frakturen: konservative Behandlung (Gips)

For patients who wish timely resilience, minimally invasive surgeries such as minimally invasive screw osteosynthesis also present a treatment option [16].[16]

dislozierte, instabile Frakturen: offene operative Verfahren:

In contrast, surgical treatment is generally recommended for unstable fractures, including fractures with a displacement of ≥1 mm or ≥2 mm, oblique or comminuted fractures, perilunate fracture-dislocation or all fractures in the proximal third because of the higher risk for pseudarthrosis [14, 16, 18]. In the following, three different open surgical procedures are described [1, 16]:[16]

- While an **open reposition,** the surgeon manipulates the bone back into the proper position. Therefore, the patient receives an anaesthetic.

  offene Reposition

- **Internal fixation** involves surgeons using implants to correct and stabilise the scaphoid in the correct position until it is completely healed. Most frequently, non-biodegradable metallic implants are used, specifically titanium or steel alloys [20]. Risks with this technique include stiffness, infections, nerve injury and the potential for nonunion, resulting in the possibility of a re-operation.

  interne Fixierung: Verwendung von Implantaten (meist Titan- oder Stahlschrauben)

- In some situations, a **bone graft** (autogenous, allogenic, biological, synthetical) might be used with or without internal fixation, especially in the case of comminuted fractures to promote proper bone healing.

  Verwendung eines Knochentransplantats ggf. mit interner Fixierung

Dauer des Heilungsprozesses Einfluss auf gesellschaftliche Kosten

In general, the chances of recovery from a scaphoid fracture depend on the location of the fracture, its size, as well as prompt treatment. If surgery was performed, reintegration in daily life, including work, can be expected seven to ten weeks after the procedure, while full exposure of the wrist takes at least eleven weeks. Therefore, scaphoid fractures also go along with societal costs [19, 20].[17]

Risiken: verzögerte Heilung, Pseudarthrose, Re-Operationen → zusätzliche gesellschaftliche Kosten

Moreover, surgical treatment options particularly involve certain risks, such as delayed fracture healing, scaphoid necrosis, instability in the carpal joint, secondary arthrosis or pseudarthrosis (see Chapter 1.3) [16]. In some cases, implants may also be interfering for the patient, leading to the removal of the inserted osteosynthesis material after osseous buildup of the fracture. However, material removal is avoided wherever possible to prevent further burden to the patient and societal implications [16, 17].

[16] A0025 – How are scaphoid fractures currently managed according to published guidelines and in practice?

[17] A0006 – What are the consequences of scaphoid fractures for the society?

1.3 Pseudoarthrosis of the scaphoid bone

1.3.1 Overview of the disease, health condition and target population[18]

mögliche Komplikation einer Kahnbeinfraktur = Pseudarthrose ICD-10: M84.14

A typical and serious complication of a scaphoid fracture is pseudarthrosis. It is distinguished from acute fractures through the history of the injury (e.g., no evidence of bony healing six months after the fracture) and radiological findings (e.g., resorption in fracture crack, sclerotic fracture ends, cysts and increasing displacement) [17, 21]. According to the ICD-10, the diagnosis of pseudarthrosis in the scaphoid fracture receives the code M84.14 [22].[19]

in ca. 10 % bei konservativ behandelten Frakturen, Österreich 2014: ca. 400 Krankenhaus-aufenthalte aufgrund von Pseudarthrosen

Generally, the probability of suffering pseudarthrosis in recognised and conservatively treated scaphoid fractures is deemed very low, at approximately ten per cent of the patients. As with scaphoid fractures, mostly young men develop pseudarthrosis in the fracture [21].[20]

In Austria, approximately 400 estimated hospital stays per year can be assigned to the diagnosis "pseudoarthrosis of the scaphoid bone" in 2014 (more recent data not available) (information provided by the manufacturer [3]).[20]

Risikofaktoren: unzureichende Behandlung bzw. zu späte Diagnose

Overall, the shape of the scaphoid and its central role in wrist motion, which makes secure immobilisation very difficult, favour the development of pseudoarthrosis. Therefore, the main risk factors include insufficiently treated fractures or those that have been diagnosed too late. In particular, dislocated and unstable fractures of the proximal pole are associated with an increased risk, because of the poorer blood supply to the bone, which causes delayed bone healing [21, 23].[21]

unbehandelte Pseudarthrose → degenerative Veränderungen des Handgelenks möglich

Patients with a delayed union or nonunion of the fractured scaphoid indicate persistent pain, recurrent swelling, loss of strength in the area of restricted wrist motion and significant tenderness in the anatomical snuffbox[14] and palmar over the scaphoid tubercle [21]. Moreover, untreated scaphoid pseudarthroses trigger degenerative changes in the wrist. Therefore, no treatment or incorrect treatment of pseudarthrosis can lead to irreparable damage and permanent functional limitations in the wrist and hand area [21].[22]

1.3.2 Current clinical practice[18]

Diagnose umfasst eine klinische Untersuchung, Röntgen, CT & MRI

In the clinical examination, especially pressure pain in the anatomical snuffbox[14] and a positive Watson test[23] are indicative. In addition to the clinical examination, x-rays and CTs are essential for planning treatments and allow

[18] This section addresses the EUnetHTA Core Model® domain CUR.

[19] A0001 – For which health conditions, and for what purposes is the technology used?; A0002 – What is the disease or health condition in the scope of this assessment?

[20] A0007 – What is the target population in this assessment?; A0023 – How many people belong to the target population?

[21] A0003 – What are the known risk factors for scaphoid fractures?

[22] A0005 – What is the burden of disease for patients with scaphoid fractures?; A0004 – What is the natural course of scaphoid fractures?

[23] The Watson test is used to check the instability of the scapho-lunate (SL) ligament. The thumb is pressed on the distal-palmar tubercle of the scaphoid and at the same time the wrist is passively guided from radial to ulna. Reference: [16].

calculations of a potentially necessary bone chip size and shape. In addition, on the one hand, MRI is important for assessing the extent to which a proximal pole fragment is supplied with blood. On the other hand, MRI is indicated in rare cases of hidden pseudarthrosis [21, 23].[24]

Klassifizierung nach Herbert und Filan: 4 Stadien von stabil zu AVN and SNAC

In clinical practice, the modified classification according to Herbert and Filan, which divides pseudarthrosis into four groups, is used (see Table 1-3). Firstly, type D1 pseudarthrosis describes stable and tight pseudarthrosis. The length and shape of the scaphoid are preserved and fibrous bridging of the defect has occurred. Secondly, a pseudarthrosis of type D2 forms an unstable, mobile pseudarthrosis without arthrosis, while type D3 presents a pseudarthrosis with arthrosis. Finally, type D4 pseudarthrosis is characterised by avascular necrosis (AVN) of the proximal scaphoid pole and a carpal collapse of the type "scaphoid nonunion advanced collapse" (SNAC) [21, 24].[24]

Table 1-3: Classification of pseudoarthrosis in scaphoid fractures according to Herbert and Filan

Type	Characteristic
D1	Tight/fibrous pseudarthrosis
D2	Mobile pseudarthrosis
D3	Mobile pseudarthrosis, arthrosis
D4	Mobile pseudarthrosis with AVN und SNAC

Abbreviations: AVN – Avascular necrosis, SNAC – Scaphoid nonunion advanced collapse
Referenz: [24]

Operation = Therapie der Wahl, konservative Verfahren nur in Ausnahmefällen

Pseudarthroses in scaphoid fractures are generally treated surgically with the aim of bone healing, reconstruction of the anatomical shape and restoration of the axial alignment of the scaphoid, thereby reducing symptoms such as chronic pain or limited mobility. In contrast, conservative treatment should only be attempted in exceptional cases (e.g., concomitant diseases, high risk of surgery, lack of operability) [17, 21].[25]

verschiedene operative Verfahren:

In the following, different surgical treatment options are presented [21, 25, 26]:[25]

reine Schrauben-Osteosynthese

- **Pure screw osteosynthesis without bone grafting** is a safe treatment procedure for late-detected or delayed healing and stable pseudarthroses. The prerequisite for isolated screw osteosynthesis is a scaphoid preserved in shape and length. Headless, cannulated double-threaded screws are currently the preferred implants for fixation in scaphoid pseudarthroses.

Schrauben-Osteosynthese mit Knochentransplantat

- **Screw osteosynthesis with bone grafting** is recommended for unstable scaphoid pseudarthroses including a bony defect, as the use of allogenic bone, for example, is deemed to increase fusion rates. The prerequisites for this procedure include the absence of signs of arthrosis and SNAC or AVN.

Kirschnerdraht-Osteosynthese mit Knochentransplantat

- As an alternative to screw osteosyntheses, **the Kirschner wire osteosynthesis with a bone graft** can be performed, which is mainly indicated in small and unstable fragments.

[24] A0024 – How is a scaphoid fracture currently diagnosed according to published guidelines and in practice?

[25] A0025 – How are scaphoid fractures currently managed according to published guidelines and in practice?

Osteosynthesen mit kortikospongiösem Knochenspan

- For unstable pseudarthroses with an already pronounced bony defect zone, there is the option of a **screw or Kirschner wire osteosynthesis with an (often autologous) corticocancellous bone chip**. This bone chip offers the possibility of safely bridging even larger defects and stabilising the shape-reconstructed scaphoid and its alignment.

zusätzliche gesellschaftliche Kosten durch Komplikationen, wie Pseudarthrosen

Overall, the age of the patient and the duration of pseudarthrosis are not expected to have any influence on the healing result, given that no degenerative changes have occurred at the time of the procedure [21]. If an osteosynthesis is performed with bone grafting, patients can expect immobilisation of approximately four weeks for pseudarthrosis in the distal and middle thirds, and approximately six weeks for pseudarthrosis in the proximal third [23]. Because of the healing process over several weeks, pseudarthroses – as a complication of acute scaphoid fractures – is accompanied by additional societal costs (e.g., prolonged productivity losses) [20, 23].[26]

1.4 Features of the intervention[27]

kortikales Knochenallotransplantat von postmortalen Spendern

The Shark Screw® transplant is a human cortical bone allograft of post-mortem donors in the form of a cortical screw, which is used for osteosynthesis [3, 27].[28] The allograft is manufactured by the Austrian tissue bank Surgebright GmbH [3] in collaboration with the German Institute for Cell and Tissue Replacement (DIZG GmbH). Since Shark Screw® is human tissue, the approval procedure does not include approval by the European Medicines Agency (EMA) or a "Conformité Européenne" (CE) mark. Instead, a license for manufacturing and distributing human tissue is required [3, 28].[29]

Lizenz für Herstellung und Vertrieb notwendig

Indikationen, z. B.: OCD, Kahnbeinfrakturen, Arthrosen, Mittelfußfrakturen

The main indications for which Shark Screw® can be used include osteosyntheses in the foot, knee, elbow and hand, as well as procedures on the pediatric musculoskeletal system. In detail, the bone graft can be used for screw fixation of, for example, small bone fragments in osteochondritis dissecans (OCD) or scaphoid fractures, partial wrist arthrodesis, fixation of fractures of the long tubular bones of the upper extremity or for fixations of grafts for partial condylar replacement. On the foot, the bone screw is particularly used in Chevron osteotomy and metatarsal fractures (information provided by the manufacturer [3]).[29]

OP-Raum & wiederverwendbare OP-Instrumente, OP unter lokaler oder Vollnarkose

As with other surgeries, an operation room including all necessary surgical instruments is required for the procedure with Shark Screw®. Thereby, only reusable surgical instruments are used. Furthermore, the implantation of the screw requires a specialist in orthopaedics or trauma surgery. Depending on the patient's preference, the operation can be performed under local or general anaesthesia.[30]

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[26] A0006 – What are the consequences of HV for the society?

[27] This section addresses the EUnetHTA Core Model® domain TEC.

[28] B0001 – What are the technology and the comparators?

[29] A0020 – For which indications has Shark Screw® received marketing authorisation or CE marking?

[30] B0004 – Who administers Shark Screw® and the comparators and in what context and level of care are they provided?; B0008 – What kind of special premises are needed to use Shark Screw® and the comparators?;
B0009 – What supplies are needed to use the Shark Screw® and the comparators?

spezielle Shark Screw®-Workshops

For the surgeons who are going to use Shark Screw®, workshops on donor specimens are organised together with the Medical University of Vienna, the Medical Training Academy of Upper Austria and experienced Shark Screw® surgeons to allow them to practice various surgical techniques with the screw (information provided by the manufacturer [3]).[30]

aktuell meist Metall- oder bioabsorbierbare Knochenschrauben in Verwendung:

Currently, often metal (e.g., titanium or stainless steel) or bioabsorbable implants (e.g., polymers or magnesium) are used for osteosyntheses.[28]

Metallschrauben stabil, aber schlechter verträglich

Metal implants are stiff and have high mechanical strength in comparison to their biodegradable counterparts. In particular, titanium alloys are used due to their good integration with bone tissue [29]. However, metals, including titanium, often remain within the body as a foreign matter, which can cause pain sensation, soft tissue irritations, allergic reactions or functional inhibition. Consequently, the removal of the screw may be necessary, involving an additional surgery [29-33]. For example, for patients with HV, the frequency of metal removals ranged from 8.9 per cent for Chevron osteotomy to 32.3 per cent for Lapidus arthrodesis within the first 21 months after surgery [11].[28]

bioabsorbierbare Schrauben weniger stabil als Metallschrauben

Bioabsorbable osteosynthesis devices can be used alternatively to metal devices. However, bioabsorbable materials and their degeneration products may interfere with bone healing and hence trigger an inflammatory response during degradation [29, 34]. In addition, long-term stability also remains an unsolved challenge with these materials [29, 33].[28]

weitere Alternative: allogene Knochenschraube mit erwarteten ostokonduktiven Eigenschaften (Shark Screw®) → reduzierte Heilungszeit & Komplikationsraten?

Given the disadvantages of metal as well as bioabsorbable bone screws, another possible alternative is cortical bone screws, which had already been invented in 1918 [33]. Today, the only commercially available allogeneic bone screw, Shark Screw®, presents such an alternative in orthopaedics and trauma surgery. In contrast to its metal or biodegradable counterparts, Shark Screw® is expected to exhibit osteoconductive properties promoting the ingrowth of blood vessels and bone cells and leading to full conversion into autologous bone [3, 35]. Therefore, Shark Screw® is deemed to combine stabilisation, bone bridge and bone replacement in one screw and may reduce the bone healing time (example presented in Box 1). Furthermore, there may be a low risk of infections or other complications as well as re-surgeries since Shark Screw® consists of human biological material (information provided by the manufacturer [3]). Table 1-4 presents an overview of the characteristics of Shark Screw® and its counterparts.[31]

Box 1: Screw osteosynthesis with bone graft versus pure screw osteosynthesis with Shark Screw® in patients with pseudarthrosis in a scaphoid fracture

In patients with pseudarthosis in a scaphoid fracture, the patient's own bone is often harvested from the iliac crest or the radius. Subsequently, the autologous graft is fixed in the scaphoid with a metal screw and/or metal plate (see Chapter 1.3.2).
This procedure is accompanied by immobilisation for approximately twelve weeks. When using Shark Screw® (allogenic bone graft), bone plasty is not necessary, as Shark Screw® is expected to combine stabilisation, bone bridge as well as bone replacement. Accordingly, the immobilisation period is expected to reduce to two to four weeks (information provided by the manufacturer [3]).

[31] B0002 – What is the claimed benefit of Shark Screw® in relation to the comparators?

Shark Screw® im österreichischen Leistungskatalog gelistet

Regarding the reimbursement of Shark Screw® in Austria, it is already included in the hospital benefit catalogue and therefore reimbursed with a certain lump sum. Currently, the procedure with Shark Screw® is coded with PA040. This code includes the use of a bone from a bone bank or bone substitute material for defect filling [3, 36].[32]

Österreich 2020: ca. 750 Shark Screw® Schrauben an Krankenhäuser verkauft

In 2020, around 750 Shark Screw® units were sold to Austrian hospitals. With regard to the indications covered in this report, approximately 150 out of the 750 Shark Screw® transplants (20%) were distributed for HV surgeries and approximately 60 Shark Screw® transplants (8%) were distributed for surgeries of the scaphoid bone (information provided by the manufacturer [3]).[32]

[32] B0003 – What is the phase of development and implementation of Shark Screw®?;
A0021 – What is the reimbursement status of Shark Screw®?;
A0011 – How much are Shark Screws® utilised?

Table 1-4: Features of the intervention and comparators

	Intervention	Comparartors				
Material	**Allogeneic bone**	**Titanium & titanium alloys***	**Stainless steel***	**Magnesium & magnesium alloys**	**Bioceramics (from calcium phosphate)**	**Plastics (polymers: polylactide or polylactide-polyglycolic acid copolymers)***
Proprietary name (manufacturer, location)	Shark Screw® (Surgebright GmbH, Austria)	■ TiMAX® Surface Treatment (Biomet Orthopedics, USA) ■ RapidFire® Titanium Technology (Biomet Microfixation, USA) ■ HCS 2.4/3.0. (DePuy Synthes a Johnson & Johnson company, USA) ■ Acutrak Headless Compression Screw System & Acutrak 2 Headless Compression Screw System (Acumed, USA) ■ Compression screw (Integra LifeSciences, USA) ■ SpeedTip® Cannulated Compression Screws (Medartis AG, Switzerland) ■ ExtremiFix cannulated screw system (Osteomed, USA) ■ Headless 1.7, 2.3, 3.0, 3.5 Screws (TriMed, USA)	■ HCS 2.4/3.0. (DePuy Synthes a Johnson & Johnson company, USA) ■ AutoFIX (Small Bone Innovations a Stryker Corporation company, USA)	MAGNEZIX® CS or CBS (Syntellix AG, Germany)	NI**	■ iFix® Interference Screw (Cayenne Medical, a Zimmer Biomet Company, USA) ■ TwistCut™ EndoSorb™ (Merete Medical, Inc. One, USA) ■ Biotrak Headless Resorbable Compression System (Acumed, USA) ■ BioScrew® (ConMed, France)
Characteristics:						
Expected mechanism	■ Oestoconductive properties leading to full conversion into autologous bone → screw combines stabilisation, bone bridge and bone replacement ■ Made of human biological material, thus recognised as endogenous → low risk of infections or complications	Stable, corrosion-resistant, allergically harmless, but risk of postoperative infection	■ Low tissue adherence → formation of a connective tissue capsule possible ■ Cheaper than titanium screws, but not completely free of corrosion → metallosis possible	■ Resorbable screw without allergenic effect ■ Extended resorption time by the admixture of other substances such as aluminium, zinc or rare earth metals	■ Completely absorbable by the body ■ Well tolerated and allergological harmless	■ Resorbable by the organism → duration depends on size: complete dissolution after 1-5 years ■ Soft tissue irritation rare but possible
Removal of material	No removal/no second surgery necessary	Removal of screw/second surgery can be necessary	Removal of the screw/ second surgery necessary	No removal/no second surgery necessary	No removal/no second surgery necessary	No removal/no second surgery necessary

Abbreviations: NI – No information, USA – United States of America

Own representation based on [3, 28, 37]

* *Due to a large number of different manufacturers of bone screws, only examples were presented.*

** *No manufacturer producing screws from calcium phosphate could be identified.*

2 Objectives and scope

2.1 PICO question

PIKO-Frage

Is Shark Screw®, a human cortical bone allograft, in comparison to metal or biodegradable bone screws in patients with hallux valgus or fractures/pseudarthroses of the scaphoid bone more effective and equally safe from a health care system perspective concerning economically relevant outcomes, such as the number and duration of hospitalisations, the duration of the actual surgical procedure, the revision rate, the period of convalescence, implant breakage during surgery, as well as major postoperative complications?

2.2 Inclusion criteria

Einschlusskriterien für relevante Studien

Inclusion criteria for relevant studies are summarised in Table 2-1.

Table 2-1: Inclusion criteria

Population	Patients with ■ Hallux valgus (**MeSH Term:** Bunion) ■ Fracture of the scaphoid bone ■ Pseudoarthrosis in a scaphoid fracture
Intervention	Surgery with allogenic bone screws **Product name:** Shark Screw® from Surgebright GmbH, Austria **MeSH Term:** biodegradable, bioabsorbable, allograft, human tissue, osteoconductive
Control	Surgery with alternative bone screws: ■ Screws out of titanium and titanium alloy ■ Screws out of stainless high-grade steel ■ Screws out of magnesium and magnesium alloy ■ Screws out of medical ceramics (calcium phosphate) ■ Screws out of polymers (e.g., polylactides or polylactide-polyglycolic acid copolymers)
Outcomes	
Efficacy	■ **Number of hospitalisations** ■ **Duration of hospitalisation** ■ **Duration of the intervention/surgery** ■ **Revision rate** ■ **Period of convalescence**
Safety	**Implant breakage during surgery** **Major postoperative complications (implant failure):** ■ Graft rupture ■ Symptomatic foreign body reactions or other adverse tissue reaction (e.g., inflammation) ■ Effusion and treated arthrofibrosis and related conditions ■ Etc.

Study design for efficacy and safety	**Clinical studies:** ■ Randomised controlled trials ■ Non-randomised controlled trials ■ Prospective single-arm studies **Health economic studies:** ■ Health economic evaluations (CEA, CUA, CMA) ■ Budget impact analyses
Language(s)	German, English
Publication period	Until 12/2020

***Abbreviations**: CEA – Cost-effectiveness analysis, CMA – Cost-minimisation analysis, CUA – Cost-utility analysis*

3 Methods

3.1 Research questions

Assessment elements regarding clinical effectiveness (Element ID D) from the EUnetHTA Core Model® for screening technologies Version 4.2 were customised so that they could be used for the purposes of this assessment [46].

angepasste Forschungsfragen zur Effektivität

Table 3-1: Health problem and current use

Element ID	Research question
A0001	For which health conditions, and for what purposes is Shark Screw® used?
A0002	What is the disease or health condition in the scope of this assessment?
A0007	What is the target population in this assessment?
A0023	How many people belong to the target population?
A0003	What are the known risk factors for HV or fracture/pseudarthrosis of the scaphoid bone?
A0004	What is the natural course of HV or fracture/pseudarthrosis of the scaphoid bone?
A0005	What is the burden of disease for the patients with HV or fracture/pseudarthrosis of the scaphoid bone?
A0006	What are the consequences of HV or fracture/pseudarthrosis of the scaphoid bone for the society?
A0024	How is HV or fracture/pseudarthrosis of the scaphoid bone currently diagnosed according to published guidelines and in practice?
A0025	How is HV or fracture/pseudarthrosis of the scaphoid bone currently managed according to published guidelines and in practice?

Table 3-2: Description of the technology

Description of the technology	
Element ID	**Research question**
B0001	What are the technology and the comparators?
A0020	For which indications has Shark Screw® received marketing authorisation or CE marking?
B0002	What is the claimed benefit of Shark Screw® in relation to the comparators?
B0004	Who administers Shark Screw® and the comparators and in what context and level of care are they provided?
B0008	What kind of special premises are needed to use Shark Screw® and the comparators?
B0009	What supplies are needed to use Shark Screw® and the comparators?
B0003	What is the phase of development and implementation of Shark Screw®?
A0021	What is the reimbursement status of Shark Screw®?
A0011	How much are Shark Screws® utilised?

Table 3-3: Clinical effectiveness (with a focus on economic relevance)

Element ID	Research question
D0001	What is the expected beneficial effect of Shark Screw® on the number and duration of hospitalisations?
D0003	What is the effect of Shark Screw® on the duration of the actual surgical procedure?
D0006	How does Shark Screw® affect progression (or recurrence) of HV or fracture/pseudarthrosis of the scaphoid bone?
D0005	How does Shark Screw® affect the rate of re-operations?
D0011	What is the effect of Shark Screw® on patients' body functions?
D0016	How does the use of Shark Screw® affect activities of daily living?
D0014	What is the effect of Shark Screw® on the period of convalescence?

Table 3-4: Safety

Element ID	Research question
C0008	How safe is Shark Screw® in comparison to the comparators?
C0002	Are the harms related to the frequency of applying Shark Screw®?
C0004	How does the frequency or severity of harms change over time or in different settings?
C0005	What are the susceptible patient groups that are more likely to be harmed through the use of Shark Screw®?
C0007	Are Shark Screw® and comparators associated with user-dependent harms?

3.2 Clinical effectiveness and safety (with a focus on economic relevance)

3.2.1 Systematic literature search

systematische Literatursuche in 5 Datenbanken

The systematic literature search was conducted on 18 and 21 December 2020 in the following databases:

- Medline via Ovid
- Embase
- The Cochrane Library
- Centre for Reviews and Dissemination (CRD: DARE, NHS-EED, HTA)
- International Network of Agencies for Health Technology Assessment (INAHTA)

nach Deduplizierung insgesamt 155 Hits

The systematic search included publications until December 2020, prospective randomised or non-randomised controlled trials (RCTs, NRCTs), prospective single-arm studies, as well as health economic evaluations published in English or German. After deduplication, a total of 155 citations were identified. The specific search strategy employed can be found in the Appendix (see Literature search strategies).

14 zusätzliche Zitate von Hersteller darunter vor allem Hintergrund und vertrauliche Daten

In addition, the manufacturer (Surgebright GmbH) of the product under review (Shark Screw®) submitted 17 potentially relevant references in total, of which 14 were not identified in the systematic literature search. These 14 references mainly involved background information and abstracts as well as confidential data, but no clinical studies as defined by the inclusion criteria (see Table 2-1).

insgesamt 169 Referenzen identifiziert

No additional citations could be identified by hand-search, resulting in 169 hits overall.

Suche nach laufenden Studien: 36 Treffer

Furthermore, to identify ongoing and unpublished studies, a search in three clinical trials registries (ClinicalTrials.gov; WHO-ICTRP; EU Clinical Trials) was conducted on 11 January 2021, resulting in 36 potentially relevant hits.

3.2.2 Flow chart of study selection

Two independent researchers (SW and CS) screened the 169 identified references. In case of disagreement, a third researcher was involved to solve the differences. In the end, based on the predefined inclusion criteria, no published study could be identified for the qualitative synthesis. Figure 3-1 displays the selection process.

Literaturauswahl: keine Studien für qualitative Synthese eingeschlossen

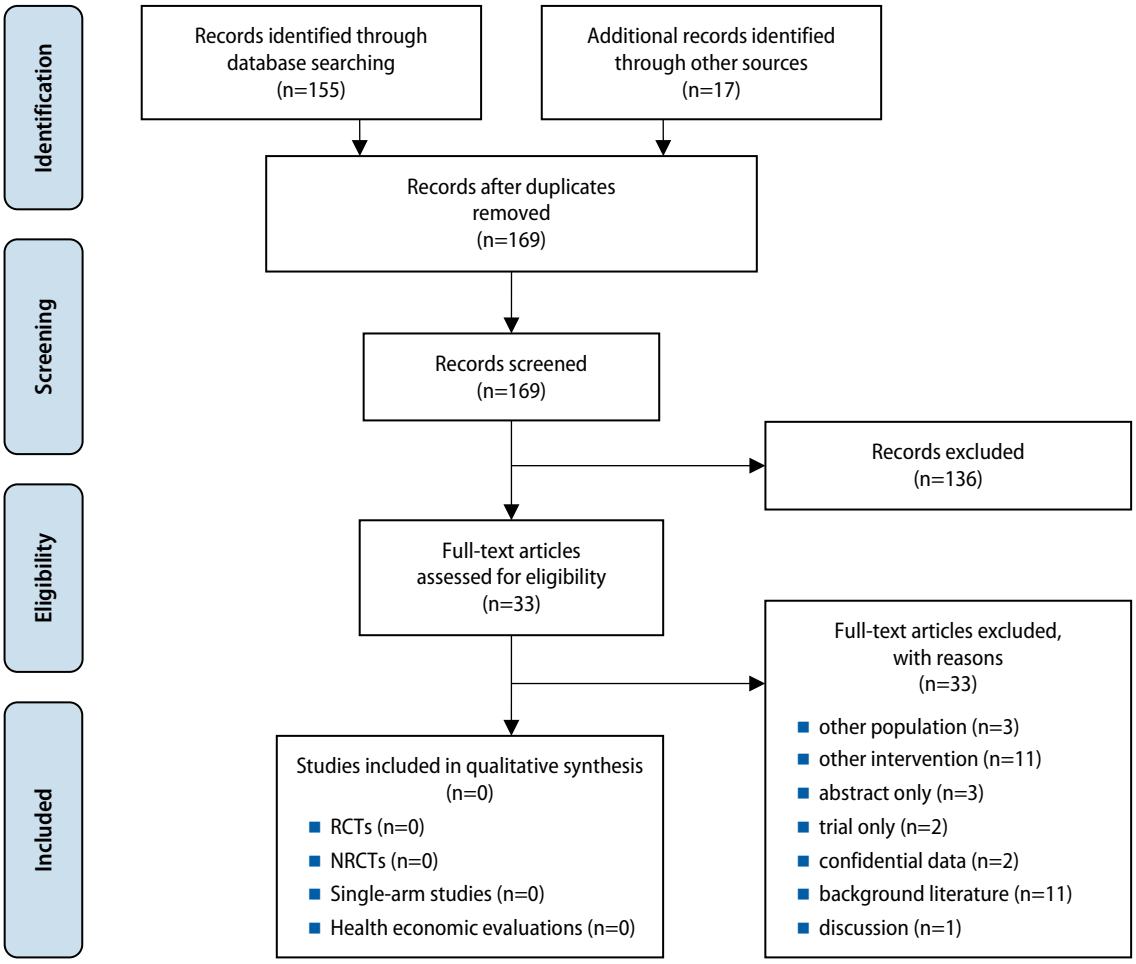

Figure 3-1: Flow chart of study selection (PRISMA Flow Diagram)

3.2.3 Analysis

keine Datenextraktion & kein RoB-Assessment

As no published studies were included for the qualitative analysis, the planned risk of bias (RoB) assessment by using different tools depending on the study design was not applied:

- Cochrane RoB tool for RCTs [38]
- Risk Of Bias In Non-randomised Studies – of Interventions (ROBINS-I) tool for NRCTs [39]
- Institute of Health Economics (IHE) Checklist for case series studies [40]

3.2.4 Synthesis

keine Evidenzsynthese mittels GRADE

In addition, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) scheme [41] could not be applied and the associated research questions could not be answered.

4 Results: Clinical effectiveness and safety (with a focus on economic relevance)

4.1 Outcomes

4.1.1 Clinical effectiveness outcomes (with economic relevance)

The following outcomes on the clinical effectiveness of Shark Screw® in patients with HV or a fracture/pseudarthrosis of the scaphoid bone were defined as *crucial* to derive a recommendation:

- **Number of hospitalisations:** How many hospital stays were needed for the surgical treatment of HV or a fracture/pseudarthrosis of the scaphoid bone with Shark Screw®?
- **Duration of hospitalisation:** How long did the patients on average stay in the hospital after surgery with Shark Screw®?
- **Duration of the intervention**: What was the mean duration of the surgical procedure with Shark Screw®?
- **Revision rate:** In how many per cent of the patients with HV or a fracture/pseudarthrosis of the scaphoid bone, who underwent surgery with Shark Screw®, was a re-operation needed?
- **Period of convalescence:** What was the mean duration for the patients coming back to their daily life, including work and sports?

entscheidende, ökonomisch relevante Wirksamkeitsendpunkte:

z. B.
Anzahl & Dauer der Krankenhausaufenthalte, Operationsdauer, Revisionsrate

4.1.2 Safety outcomes

The following safety outcomes were defined as *crucial* to derive a recommendation:

- **Implant breakage during surgery:** In what percentage of patients with HV or a fracture/pseudarthrosis of the scaphoid bone, who underwent surgery with Shark Screw®, did the material break during the procedure?
- **Major postoperative complications considered as implant failure:**
  - In what percentage of patients with HV or a fracture/pseudarthrosis of the scaphoid bone, who underwent surgery with Shark Screw®, did the graft rupture postoperatively?
  - How many per cent of patients with HV or a fracture/pseudarthrosis of the scaphoid bone, who underwent surgery with Shark Screw®, had postoperative symptomatic foreign body reactions or other adverse tissue reactions, e.g., inflammation?
  - How many per cent of the patients with HV or a fracture/pseudarthrosis of the scaphoid bone, who underwent surgery with Shark Screw®, developed effusion, treated arthrofibrosis or related conditions after the procedure?

entscheidende Sicherheitsendpunkte:

z. B.
Bruch des Implantats während/nach der OP, symptomatische Fremdkörperreaktionen

4.2 Included studies

4.2.1 Included studies for clinical effectiveness

keine publizierte Evidenz zur Wirksamkeit von Shark Screw®

Based on the predefined inclusion criteria (see Table 2-1), no RCTs, NRCTs, prospective single-arm studies or health economic evaluations could be included for the qualitative synthesis of the clinical effectiveness of Shark Screw® in patients with HV or fractures/pseudarthroses of the scaphoid bone (see Table A-1).

4.2.2 Additional included studies for safety

keine publizierte Evidenz zur Sicherheit von Shark Screw®

Furthermore, also no RCTs, NRCTs, prospective single-arm studies or health economic evaluations could be identified for the qualitative synthesis of the safety of Shark Screw® in patients with HV or fractures/pseudarthroses of the scaphoid bone (see Table A-1).

4.3 Results

4.3.1 Clinical effectiveness

keine publizierte Evidenz zur Wirksamkeit von Shark Screw®

No published evidence was available to assess the clinical effectiveness of Shark Screw® in patients with HV or fractures/pseudarthroses of the scaphoid bone. Therefore, the related research questions could not be answered.[33]

4.3.2 Patient safety

keine publizierte Evidenz zur Sicherheit von Shark Screw®

Moreover, no published evidence was available to answer the research questions regarding the safety of Shark Screw® in patients with HV or fractures/pseudarthroses of the scaphoid bone.[34]

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[33] D0001 – What is the expected beneficial effect of Shark Screw® on the number and duration of hospitalisations?;
D0003 – What is the effect of Shark Screw® on the duration of the surgical procedure?;
D0006 – How does Shark Screw® affect progression (or recurrence) of HV or fracture/pseudarthrosis of the scaphoid bone?; D0005 – How does Shark Screw® affect the rate of re-operations?;
D0011 – What is the effect of Shark Screw® on patients' body functions?;
D0016 – How does the use of Shark Screw® affect activities of daily living?;
D0014 – What is the effect of Shark Screw® on the period of convalescence?

[34] C0008 – How safe is Shark Screw® in comparison to the comparators?;
C0002 – Are the harms related to the frequency of Shark Screw®?;
C0004 – How does the frequency or severity of harms change over time or in different settings?;
C0005 – What are the susceptible patient groups that are more likely to be harmed through the use of Shark Screw®?;
C0007 – Are Shark Screw® and comparators associated with user-dependent harms?

5 Discussion

Today, various bone screws, including metal and bioabsorbable screws, are available on the market. Thus, one of the main challenges in bone fixation is the identification of the ideal osteosynthetic material. Several factors influence the selection of a particular material, including the biomechanical properties, the biocompatibility (e.g., non-toxicity to the host tissue, osteoconductive properties), the clinical practicability (e.g., size and shape of the screw) and economically relevant aspects (e.g., the number and duration of hospitalisations, the duration of the surgical procedure, revision rates, the period of convalescence, implant breakage during surgery, as well as major postoperative complications) [29, 33]. Hence, each screw type has its advantages and disadvantages that need to be scrutinised. For example, metal screws including titanium and stainless-steel screws are stiff and have higher mechanical strength in comparison to their biodegradable counterparts. However, metallic material can lead to postoperative complications, such as inflammatory or other foreign body reactions, that result in material removal [29-33]. For that reason, biodegradable screws including polymers, medical ceramics or magnesium screws have been developed. These kinds of screws are expected to assist as scaffolds or to support the bone healing process due to their progressive degradation over time. Thus, the removal of biodegradable screws is not necessary in most cases. However, the main disadvantage of these materials is their decreased mechanical strength compared to their metallic counterparts [29, 33, 34].

unterschiedliche Knochenschrauben verfügbar:

Metallschrauben: hohe mechanische Belastbarkeit, jedoch höheres Risiko für Fremdkörperreaktionen

biologisch abbaubare Schrauben: meist verträglicher, aber geringere mechanische Belastbarkeit

Given the disadvantages of metallic or biodegradable bone screws, allogeneic bone screws such as the currently commercially available Shark Screw® transplant may present a further alternative in orthopaedics and trauma surgery. In contrast to its metal or biodegradable counterparts, Shark Screw® is expected to exhibit osteoconductive properties possibly leading to full conversion into autologous bone [3, 35]. Therefore, Shark Screw® is deemed to combine stabilisation, bone bridge and bone replacement in one screw and consequently may reduce bone healing time. Furthermore, there may be a low risk of infections or other complications and subsequently of re-surgeries since Shark Screw® consists of human biological material. Given the possible advantages of Shark Screw®, it might also have economic advantages (e.g., lower re-surgery rates, shorter sick leaves) compared to other bone screws [3].

Alternative: allogene Knochenschraube,

Shark Screw®: kürzere Heilungszeit & geringeres Risiko für Komplikationen bzw. Re-operationen?

→ ökonomische Vorteile?

However, the use of allogeneic bone material is also accompanied by several issues, including ethical aspects such as the risk of disease transmissions [29]. Moreover, there is no standardised and transparent approval process through the EMA and no CE marking for human tissue. Rather, responsible manufacturers need a specific license to produce and market devices out of human tissue. For example, the Austrian manufacturer and tissue bank Surgebright GmbH that works in collaboration with the German Institute for Cell and Tissue Replacement (DIZG GmbH) is licensed for the production and distribution of Shark Screw® allografts [3, 28].

kein transparenter Zulassungsprozess für Produkte aus humanbiologischem Material

Against this background, the present systematic review aimed to investigate whether the allogeneic bone screw, Shark Screw®, is more effective and equally safe in comparison to other bone screws in patients with hallux valgus or scaphoid fractures/pseudarthroses. Thereby, the focus lied on economically relevant outcomes from a health care system point of view, including the number and duration of hospitalisations, the duration of the actual surgical procedure, the revision rates, the period of convalescence, the implant breakage during surgery, as well as other major postoperative complications.

Projektziel: Analyse der Effektivität & Sicherheit von Shark Screw® mit Fokus auf ökonomisch relevanten Endpunkten

Summary of evidence

keine publizierte Evidenz zu Shark Screw® identifiziert

Based on the predefined inclusion criteria (see Table 2-1), no evidence including RCTs, NRCTs, prospective single-arm studies or economic evaluations on Shark Screw® in patients with HV or scaphoid fractures/pseudarthroses could be identified in the systematic literature search or additional hand-search and by the manufacturer.

1 Kosteneffektivitätsstudie zu Shark Screw® identifiziert, jedoch kein Volltext verfügbar

Only one cost-effectiveness analysis comparing Shark Screw® to other metal devices could be identified in the systematic literature search [42]. This economic study was based on assumptions, but not on empirical data regarding the effectiveness and safety of Shark Screw®. The main results of the cost-effectiveness analysis suggest that the Shark Screw® transplants dominate metal screws by indicating fewer complications and re-operations at lower costs. However, due to the lacking full text, the analysis could not be included for qualitative synthesis in the present report.

2 laufende einarmige Studien:

Furthermore, the clinical trial search resulted in two ongoing prospective single-arm studies sponsored by the manufacturer Surgebright GmbH, Austria [3]:

NCT03884907 (n=50): Patient*innen mit HV, Status: Rekrutierung, ökonomisch relevante Endpunkte erhoben

One ongoing prospective single-arm study (NCT03884907) assesses human bone graft correction with Shark Screw® according to the Austin procedure in approximately 50 HV patients for a one-year follow-up period. Recruiting of patients is still ongoing. Next to clinically relevant outcomes, such as HV angle, IM angle, postoperative pain and incidence of postoperative pseudoarthrosis, the study also assesses economically relevant outcomes like the incidence of surgical revisions and the duration of postoperative job-related incapacity.

NCT04109469 (n=32): Shark Screw® bei Hand- oder Fuß-OPs, Rekrutierung abgeschlossen, keine Daten publiziert

The second ongoing prospective single-arm study (NCT04109469) assesses the application of Shark Screw® in 32 patients who undergo hand-or foot surgery due to arthrodesis or osteotomy. Thereby, clinical outcomes, such as the osseous consolidation of the transplant, as well as pre-and postoperative pain, are assessed. Patients are followed-up for one year. According to clinicaltrials.gov, the recruitment of the patients is already completed, but no study results have been published yet.

Table A-2 of the Appendix gives detailed information about the currently ongoing studies.

Further evidence needed

kontrollierte Langzeitevidenz mit ausreichend vielen Patient*innen & Berücksichtigung ökonomisch relevanter Endpunkte empfohlen

The identified ongoing prospective single-arm studies assessing the Shark Screw® transplant do not fill the current gap of controlled and long-term evidence. Therefore, controlled evidence on the clinical effectiveness and safety of Shark Screw®, including a sufficiently large number of patients and a follow-up exceeding one year, is recommended.

In addition, due to the possible economic impact of the application of Shark Screw®, future studies should also assess economically relevant outcomes from a health care system perspective, including the duration until full recovery and re-surgery rates.

standardisierte Dokumentation der Shark Screw® Patient*innen wichtig

Furthermore, the generation of real-world evidence of patients who receive Shark Screw® in Austrian hospitals is crucial, as Shark Screw® is already part of the Austrian hospital catalogue (code PA040) and therefore reimbursed [3, 36].

Limitations to this report

Schwachstellen des Berichts:

Although the present report followed a transparent and systematic methodology, including a systematic literature search according to the PICO scheme, it also has a few weaknesses.

Fokus auf lediglich 3 Indikationen

Firstly, even if Shark Screw® is applied for several indications in practice, including the hand, hip, knees and foot, the present report only focused on three indications, namely HV, scaphoid fractures and pseudarthroses in scaphoid fractures [3].

keine graue Literatur berücksichtigt

Secondly, no additional hand-search for grey and unpublished literature was conducted, because only published controlled, single-arm and health economic studies were considered for inclusion. Therefore, unpublished literature regarding the Shark Screw® transplant might be missing.

allogenes Knochenimplantat Allofix® nicht berücksichtigt

Thirdly, the systematic literature search identified a preliminary report on the fixation with the allogeneic bone-implant Allofix® [43, 44]. However, the Allofix® device was not considered for this report, as, on the one hand, the focus of this report solely lay on the allogeneic bone screw Shark Srew®. On the other hand, there was a Food and Drug Administration (FDA) recall of one specific Allofix® device in 2015 and the device was no longer marketed thereafter [45].

Conclusions

aktuell keine publizierte Evidenz zu Shark Screw® vorhanden → keine Aussage bzgl. Wirksamkeit & Sicherheit möglich

At the time of conducting this review, no published evidence was available to assess the clinical effectiveness and safety of the allogeneic bone screw, Shark Screw®, in patients with HV or fractures/pseudarthroses of the scaphoid bone. Therefore, no statement whether Shark Screw® is more effective and equally safe compared to alternative bone screws is currently possible. Moreover, no conclusions from an economic point of view regarding the number and duration of hospitalisations, the duration of the surgical procedure, the revision rates, the period of convalescence, implant breakages during surgery and/or other major postoperative complications can be made.

in Zukunft kontrollierte Evidenz notwendig, insbesondere zur Heilungs- & Re-operationsrate

Nevertheless, the allogeneic bone transplant, Shark Screw®, probably reduces complications, including re-operations and healing rates, due to its human tissue material and possibly osteoconductive properties [3]. For this reason, further evidence on Shark Screw®, preferably controlled long-term studies with a sufficiently large number of patients, is recommended. In addition, a special focus should lie on healing and re-operation rates, as these outcomes are crucial from a patient's but also from a societal and economic point of view.

6 Recommendation

In Table 6-1 the scheme for recommendations is displayed and the according choice is highlighted.

Aufnahme in Leistungskatalog aktuell nicht empfohlen

Table 6-1: Evidence-based recommendations

	The **inclusion** in the catalogue of benefits is **recommended**.
	The **inclusion** in the catalogue of benefits is **recommended with restrictions**.
X	The inclusion in the catalogue of benefits is **currently not recommended**.
	The **inclusion in** the catalogue of benefits is **not recommended**.

Reasoning:

Currently, there is no published evidence to prove that the assessed technology, allogeneic Shark Screw® transplant, is more effective than or as safe as metal or biodegradable bone screws in patients with HV or fractures/pseudarthroses of the scaphoid bone concerning the number and duration of hospitalisations, the duration of the surgical procedure, the revision rates, the period of convalescence, implant breakage during surgery, as well as major postoperative complications. New study results, preferably controlled long-term studies with a sufficiently large number of patients, will influence the effect estimate considerably.

aktuell unzureichende Evidenzlage für eine Aussage bzgl. der Wirksamkeit und Sicherheit von Shark Screw®

A re-evaluation is recommended in 2025 at the earliest, as the clinical trial search did not identify any ongoing controlled studies.

Re-evaluierung frühestens 2025

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Appendix

Evidence tables of individual studies including clinical effectiveness and safety

Table A-1: Shark Screw® Extraction table

Author, year	NA
Country	–
Sponsor	–
Intervention/Product	–
Comparator	–
Study design	–
Number of pts	–
Inclusion criteria	–
Age of patients (yrs)	–
Follow-up (months)	–
Loss to follow-up, n (%)	–
Outcomes	
Clinical efficacy (with economic relevance)	
Number of hospitalisations	–
Duration of hospitalisation	–
Duration of the intervention/surgery	–
Revision rate	–
Period of convalescence	–
Safety	
Implant breakage during surgery	–
Major postoperative complications (implant failure):	–
■ Graft rupture	–
■ Symptomatic foreign body reactions or other adverse tissue reaction	–
■ Effusion and treated arthrofibrosis and related conditions	–

Abbreviations: NA – Not available

List of ongoing randomised controlled trials

Table A-2: List of ongoing randomised controlled trials of Shark Screw®

Identifier/ Trial name	Patient population	Intervention	Comparison	Primary Outcome	Primary completion date	Sponsor
NCT03884907	Patients with hallux valgus (estimated enrollment: n=50)	Human bone graft (Shark Screw®) correction according to the Austin procedure	NA	Follow-up: 1 year: ■ Incidence of surgical revisions ■ Incidence of loosening of the screw ■ Incidence of cracking of the screw ■ Hallux valgus angle ■ Intermetatarsal angle ■ Incidence of postoperative pseudoarthrosis ■ Evaluation of postoperative pain ■ Duration of postoperative job-related incapacity	21 August 2019 Recruitment status: Recruiting	Surgebright GmbH
NCT04109469	Patients who underwent hand- or foot surgery due to arthrodesis or osteotomy (n=32)	Application of human bone graft (Shark Screw®)	NA	Follow-up: 1 year ■ Osseous consolidation of the transplant ■ Evaluation pre-and postoperative pain	7 February 2019 Recruitment status: Completed, but no results published	Surgebright GmbH

Literature search strategies

Search strategy for Cochrane

Search Name: Allogenic bone screws	
Last saved: 18.12.2020	
Comment: MEL 2021 SW/CS	
ID	Search
#1	MeSH DESCRIPTOR Hallux Valgus EXPLODE ALL TREES
#2	(hallux*)
#3	MeSH DESCRIPTOR Bunion EXPLODE ALL TREES
#4	(bunion*)
#5	(navicular*)
#6	MeSH DESCRIPTOR Tarsal Bones EXPLODE ALL TREES
#7	MeSH DESCRIPTOR Scaphoid Bone EXPLODE ALL TREES
#8	(scaphoid*)
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
#10	MeSH DESCRIPTOR Bone Screws EXPLODE ALL TREES
#11	(bone NEAR (screw* OR pin* OR nail* OR rod*))
#12	(bonescrew*)
#13	(bonepin*)
#14	(bonenail*)
#15	(bonerod*)
#16	(spongiosa*)
#17	(shark screw*)
#18	(sharkscrew*)
#19	(surgebright*)
#20	((allog* OR biodegrad* OR bio-degrad* OR bioabsor* OR bio-absor* OR bioadsor* OR bio-adsor* OR biocompatib* OR bio-compatib*) NEAR (screw* OR bone* OR pin* OR nail* OR rod*))
#21	#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20
#22	#9 AND #21
Total: 2 Hits	

Search strategy for CDR

Search Name: Allogenic bone screws	
Comment: MEL2021 SW/CS 18.12.2020	
ID	Search
1	MeSH DESCRIPTOR Hallux Valgus EXPLODE ALL TREES
2	(hallux*)
3	MeSH DESCRIPTOR Bunion EXPLODE ALL TREES
4	(bunion*)
5	(navicular*)
6	MeSH DESCRIPTOR Tarsal Bones EXPLODE ALL TREES
7	MeSH DESCRIPTOR Scaphoid Bone EXPLODE ALL TREES
8	(scaphoid*)
9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
10	MeSH DESCRIPTOR Bone Screws EXPLODE ALL TREES
11	(bone NEAR (screw* OR pin* OR nail* OR rod*))
12	(bonescrew*)
13	(bonepin*)
14	(bonenail*)
15	(bonerod*)
16	(spongiosa*)
17	(shark screw*)
18	(sharkscrew*)
19	(surgebright*)
20	((allog* OR biodegrad* OR bio-degrad* OR bioabsor* OR bio-absor* OR bioadsor* OR bio-adsor* OR biocompatib* OR bio-compatib*) NEAR (screw* OR bone* OR pin* OR nail* OR rod*))
21	#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20
22	#9 AND #21
Total: 2 Hit	

Search strategy for Embase

Search Name: Allogenic bone screws		
Comment: MEL2021 SW/CG 18.12.2020		
No.	Query Results	Results
#41	#40 AND ([english]/lim OR [german]/lim)	68
#40	#36 OR #37 OR #38 OR #39	71
#39	surgebright*:ti,ab,kw,lnk,de,df	
#38	'sharkscrew*':ti,ab,kw,lnk,de,dn	
#37	'shark screw*':ti,ab,kw,lnk,de,dn	1
#36	#10 AND #35	70
#35	#33 OR #34	3,037
#34	((allog* OR biodegrad* OR 'bio degrad*' OR bioabsor* OR 'bio absor*' OR bioadsor* OR 'bio adsor*' OR biocompatib* OR 'bio compatib*') NEAR/5 (screw* OR bone* OR pin* OR nail* OR rod*) NEAR/3 fixation*):ti,ab,kw,lnk,de	476
#33	#19 AND #32	2,813
#32	#20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31	343,249
#31	allograft*:ti,ab,kw,lnk,de	115,660
#30	allogen*:ti,ab,kw,lnk,de	124,006
#29	'allograft'/exp	42,486
#28	'allotransplantation'/exp	36,677
#27	'bio-adsor*':ti,ab,kw,lnk,de	160
#26	bioadsor*:ti,ab,kw,lnk,de	472
#25	'bioadsorption'/exp	11
#24	'bio-absor*':ti,ab,kw,lnk,de	303
#23	'bioabsor*':ti,ab,kw,lnk,de	4,526
#22	'bio-degrad*':ti,ab,kw,lnk,de	534
#21	biodegrad*:ti,ab,kw,lnk,de	89,985
#20	'biodegradable implant'/exp	7,013
#19	#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18	48,028
#18	spongiosa*:ti,ab,kw,lnk,de	1,950
#17	bonerod*:ti,ab,kw,lnk,de	3
#16	bonenail*:ti,ab,kw,lnk,de	15
#15	bonepin*:ti,ab,kw,lnk,de	47
#14	bonescrew*:ti,ab,kw,lnk,de	207
#13	(bone NEAR/3 (screw* OR pin* OR nail* OR rod*)):ti,ab,kw,lnk,de	33,662
#12	'pedicle screw fixation device'/exp	770
#11	'bone screw'/exp	37,734
#10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9	20,764
#9	scaphoid*:ti,ab,kw,lnk,de	6,842
#8	'scaphoid fracture'/exp	2,137
#7	'scaphoid bone'/exp	3,023
#6	navicular*:ti,ab,kw,lnk,de	3,193
#5	'navicular bone fracture'/exp	19
#4	'navicular bone'/exp	338
#3	bunion*:ti,ab,kw,lnk,de	1,312
#2	hallux*:ti,ab,kw,lnk,de	10,730
#1	'hallux valgus'/exp	4,935

Search strategy for Medline

Search Name: Allogenic bone screws		
Comment: MEL2021 SW/CS 17.12.2020		
ID	Search	Results
1	exp Hallux Valgus	4,019
2	hallux*.mp.	9,083
3	exp Bunion/	138
4	bunion*.mp.	1,191
5	navicular*.mp.	3,095
6	exp Tarsal Bones/	15,539
7	exp Scaphoid Bone/	2,773
8	scaphoid*.mp.	6,771
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	33,345
10	exp Bone Screws/	30,825
11	(bone adj3 (screw* or pin* or nail* or rod*)).mp.	42,578
12	bonescrew*.mp.	0
13	bonepin*.mp.	1
14	bonenail*.mp.	0
15	bonerod*.mp.	0
16	spongiosa*.mp.	1,796
17	shark screw*.mp.	0
18	sharkscrew*.mp.	0
19	surgebright*.mp.	0
20	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19	47,232
21	exp Absorbable Implants/	11,617
22	exp Biocompatible Materials/	143,462
23	biodegrad*.mp.	112,321
24	bio-degrad*.mp.	577
25	bioabsor*.mp.	3,608
26	bio-absor*.mp.	253
27	bioadsor*.mp.	412
28	bio-adsor*.mp.	223
29	allogen*.mp.	87,765
30	exp Allogeneic Cells/	78
31	exp Allografts/	14,314
32	allograft*.mp.	90,889
33	exp Transplantation, Homologous/	93,770
34	21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33	460,035
35	20 and 34	3,385
36	((allog* or biodegrad* or bio-degrad* or bioabsor* or bio-absor* or bioadsor* or bio-adsor* or biocompatib* or bio-compatib*) adj5 ((screw* or bone* or pin* or nail* or rod*) adj3 fixation*)).mp.	537
37	35 or 36	3,609
38	9 and 37	139
39	remove duplicates from 38	112
40	limit 39 to (english or german)	104

Search strategy for INAHTA

Search Name: Allogenic bone screws	
Comment: MEL2021 SW/CS 18.12.2020	
ID	Search
#8	(scaphoid*) OR ("Scaphoid Bone"[mhe]) OR ("Tarsal Bones"[mhe]) OR (navicular*) OR (bunion*) OR ("Bunion"[mhe]) OR ((hallux*)),"9","2020-12-21T11:24:41.000000Z"
#7	scaphoid*,"1","2020-12-21T11:23:24.000000Z"
#6	"Scaphoid Bone"[mhe],"0","2020-12-21T11:23:01.000000Z"
#5	"Tarsal Bones"[mhe],"3","2020-12-21T11:22:32.000000Z"
#4	navicular*,"0","2020-12-21T11:22:05.000000Z"
#3	bunion*,"1","2020-12-21T11:21:27.000000Z"
#2	"Bunion"[mhe],"0","2020-12-21T11:21:14.000000Z"
#1	(hallux*),"5","2020-12-21T11:20:52.000000Z"
Hits	7 (#8 limited to English/German)

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