AXA Health

Evidence review #6
November 2020

Cartiva implants

What is the evidence for Cartiva implants for great toe metatarsophalangeal joint pain (MTPJ)?

Patient safety rating: amber

Summary and recommendation

The evidence to date largely comes from one cohort and there is evidence that adverse events and reoperations rates are high. NICE has been notified about this procedure and is currently developing an Interventional Procedure review.

Cartiva implants are currently an approved treatment in the US and EU but there are limited studies available detailing the outcomes of the implant with evidence of potential harms.

Cartiva is currently rated as an unproven treatment (Amber AXA Health Patient Safety Rating) awaiting NICE review.

First review: 26 October 2020
Second review: 10 November 2020

Evidence

The main evidence was generated by Baumhauer et al 2016 study and reviewed for the 2016 FDA PMA approval. Prospective, randomized, multicentered clinical trial assessing safety and efficacy of a synthetic cartilage implant versus first metatarsophalangeal arthrodesis in advanced hallux rigidus.

A prospective, randomised non-inferiority study, with patients from 12 centres in Canada and the UK, randomised (2:1) to a synthetic cartilage implant or first metatarsophalangeal (MTP) joint arthrodesis. 237 patients were enrolled; 197 randomised and 194 competed the study. Subjects were treated between October 2009 and February 2013. The initial two subjects enrolled and treated at each site were not randomised to ensure surgeons were adequately familiar with the procedure.

The majority (80%) of the subjects enrolled in the study were females, consistent with the literature that shows that women have a higher incidence of MTP osteoarthritis compared to men.

The primary endpoint for the study consisted of a single composite endpoint utilising the 3 primary study outcomes (pain, function, and safety). All subjects were evaluated pre-operatively, intra-operatively, post-operatively prior to discharge, and post-operatively at 2 weeks, 6 weeks, and at 3, 6, 12, and 24 months.

At 2 years, the functional improvement was equivalent between the groups. The SF-36 PF were similar at 2-year.

Fourteen (9.2%) implant subjects (14 procedures that were converted to arthrodesis) and 6 (12%) arthrodesis subjects (7 procedures isolated screws or plate and screw removal) had secondary surgeries during the course of the study.

Cartiva Medical funded the PMA submission to the FDA and provided funding to several investigators .

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10 November 2020

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FDA safety analysis

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P150017

The FDA's analysis of safety was based on the Safety Cohort of 202 total subjects treated (22 Cartiva SCI device roll-in subjects, 130 randomised and treated Cartiva SCI device subjects, and 50 arthrodesis control subjects). Adverse events were classified by the Investigator for relationship to the device, severity, and for seriousness of the event. The overall adverse event rate was similar for the Cartiva SCI device group (69.1%) and the arthrodesis control group (72.0%). The majority of the events were mild or moderate in nature as classified by the Investigator for the Cartiva SCI device subjects (86.2%) and arthrodesis control group (78.0%).

A total of 105 Cartiva patients (69.1%) had at least one adverse event within 24 months versus 36 arthrodesis patients (72.0%). A total of 245 events were reported in 105 Cartiva patients and 72 events were reported in 36 arthrodesis patients.

There were three categories of adverse events for Preferred Term in which the Cartiva SCI device group is greater than or equal to approximately 4% points higher for the number of subjects in the study experiencing these adverse events than compared to the arthrodesis group. These PT categories include: Implant site pain (10.5% vs 0%); Arthralgia (9.9% vs 6.0%); and Pain in the Extremity (6.6% vs 2.0%). Specifically, a higher percentage of Cartiva SCI device subjects had adverse events involving pain.

Serious Adverse Events

During the study, there were a total of 37 SAEs in 30 subjects (19.7%) in the Cartiva SCI device arm and 12 serious adverse events in 9 subjects (18.0%) in the arthrodesis arm.

Effectiveness

Cartiva SCI device was shown to be statistically non-inferior compared to arthrodesis when using a 15% non-inferiority margin.

In the per protocol analysis the overall success of the Cartiva SCI device was 101/127 (79.5%) and arthrodesis was 37/47 (78.7%).

Patient Satisfaction and Overall Well Being

The subject global assessment asked the subject to consider his/her overall well-being since the beginning of the study and whether it has improved. Possible responses include: strongly agree, agree, neither agree nor disagree, disagree, and strongly disagree. The percentage of subjects indicating strongly agree or agree in the arthrodesis group was higher at every time point from 6 weeks on.

Panel Meeting Recommendation

At an advisory meeting held on April 20, 2016, the Orthopaedic and Rehabilitation Devices Panel voted 10-2 that there is reasonable assurance the device is safe, 9-3 that there is reasonable assurance that the device is effective, and 8-2 (2 abstentions) that the benefits of the device do outweigh the risks in subjects who meet the criteria specified in the proposed indication. The 24- hour Panel Summary is located at the following link:

Brief Summary of the Orthopaedic and Rehabilitation Devices Panel Meeting – April 20, 2016
https://www.fda.gov/media/97421/download

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We found no NICE guidance on this topic. However, NICE has been notified about this procedure and it is currently developing an Interventional Procedure review Synthetic cartilage implant insertion for first metatarsophalangeal joint osteoarthritis (hallux rigidus). The publication date is still to be confirmed.

A 2020 systematic review The Use of a Synthetic Cartilage Implant for Hallux Rigidus found seven studies. Six of the publications were derived from the same patient group enrolled in the original randomised control trial by Baumhauer et al. (A total of 152 patients underwent placement of a PVA implant). These studies cannot therefore be considered individually as the results are not independent.

The only independent published cohort in the review reports results that are somewhat different. Cassinelli et al conclude in their case series that PVA implantation yielded neutral patient satisfaction, mild pain, and physical dysfunction at early follow-up and a 20% reoperation rate.

The original trial (lead author Baumhauer) Prospective, randomized, multicentered clinical trial assessing safety and efficacy of a synthetic cartilage implant versus first metatarsophalangeal arthrodesis in advanced hallux rigidus was published in 2016.

The systematic review concludes:

"There are limited studies available detailing the outcomes of a PVA implant for hallux rigidus; however, the results that are available demonstrate a high level of evidence."

While the RCT concluded:

"A prospective, randomized (2:1), controlled, noninferiority clinical trial was performed to compare the safety and efficacy of a small synthetic cartilage bone implant to first MTP arthrodesis in patients with advanced-stage hallux rigidus. This study showed equivalent pain relief and functional outcomes. The synthetic implant was an excellent alternative to arthrodesis in patients who wished to maintain first MTP motion. The percentage of secondary surgical procedures was similar between groups. Less than 10% of the implant group required revision to arthrodesis at 2 years."

We found another trial, not randomised, from 2020 Joint sparing management of hallux rigidus: Cartiva SCI vs cheilectomy a comparative review.

In course of the search two papers, published this year, were found exploring adverse events. Both used FDA data but were from different centres. The first, published in May, Adverse events involving hallux metatarsophalangeal joint implants: Analysis of the United States Food and Drug Administration data from 2010 to 2018 reported:

"Results: Among 64 reported hallux MTPJ implant adverse events, the most common modes of adverse events were component loosening (34%), infection (14.1%), component fracture (9.4%), inflammation (9.4%), and allergic reaction (7.8%). Regarding implant type, Cartiva SCI had the highest percentage of adverse events (23.4%), followed by Arthrosurface ToeMotion (20.3%), Ascension MGT (12.5%), Arthrosurface HemiCAP® (10.9%), Futura primus (9.4%), and Osteomed Reflexion (6.3%). There was an increase in reported adverse events after 2016. The MAUDE database does not report the total incidence of implant insertion.

Conclusion: Our study of the MAUDE database demonstrated that component loosening and infection are the most common modes of adverse events for hallux MTPJ implants. Cartiva accounted for one-fourth of the implant-related adverse events during our study period, followed by ToeMotion, and Ascension MGT implants. Continued reporting of adverse events will improve our understanding on short and long-term complications of various hallux MTPJ implants."

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The second paper, published in July, Adverse Events Related to Cartiva Hemiarthroplasty of First Metatarsal: An Analysis of Reports to the United States Food and Drug Administration found:

"Results: A total of 49 events have been reported and implant subsidence was the most common with 16 reports. Others include fragmentation (9), infection (4), bone erosion (3), foreign body reaction (1) and unspecified (16). Thirty-five events mentioned further surgeries at a mean interval of 4.75 months."

Aetna, in 2019, reported:

"Aetna considers modular implants (e.g., the Arthrex metatarsal phalangeal joint implant, the Cartiva Synthetic Cartilage Implant, the METIS prosthesis, the OsteoMed ReFlexion 1st MTP Implant System, and the ToeFit-Plus prosthesis) experimental and investigational for replacement of the first metatarsal phalangeal joint and for other indications because their long-term effectiveness has not been established."

In the wider text Aetna are critical of the 2016 Baumhauer trial, reporting:

"Although the authors claim no conflict of interest in their publication of this study, it is concerning that many of the authors received direct financial support during the study period from the companies that produce this new device. Indeed, it seems that the selective focus on supporting data and disregard for conflicting data is the underlying theme of this article. Imperfect study design and a selective discussion mislead the reader."

The Aetna also covers a wide body of other evidence (much not randomised).

Blue Cross and Blue Shield have also reviewed the topic. In 2020 they published Synthetic Cartilage Implants for Joint Pain which concludes:

"Synthetic cartilage implants are considered investigational for the treatment of articular cartilage damage. BCBSNC does not provide coverage for investigational services or procedures."

They also reported:

"However, the benefit of Cartiva with respect to increased range of motion does not appear to translate to improved activities of daily living, sports activities, or patient report of well-being compared to arthrodesis. In addition, the Cartiva group showed a higher rate of adverse outcomes (Moderate Difficulty, Extreme Difficulty, and Unable to Do) compared to the arthrodesis group for walking for 15 min (16% vs 0%), Up Stairs (6% vs 0%) and Squats (19% vs 8%). Some bias in favor of the novel motion preserving implant was also possible, as suggested by the high dropout rate in the arthrodesis group after randomization."

Evidence: ongoing trials

The Clinical Trials website reports two completed studies for Cartiva and five for synthetic cartilage. None are active randomised trials.