

A Systematic Review of Rehabilitation Protocols Following Matrix-Assisted Autologous Chondrocyte Implantation

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Introduction

- Focal chondral defects (FCDs) of the knee joint can result in pain and swelling
- Current surgical treatments for FCDs of the knee joint include chondroplasty, microfracture (MFx), osteochondral autograft transfer (OAT), osteochondral allograft transplantation (OCA), and autologous chondrocyte implantation (ACI), among others
- Given that third-generation ACI is a relatively novel procedure, postoperative rehabilitation following this procedure is not standardized

Purpose

- To perform a systematic review of postoperative rehabilitation protocols for third-generation autologous chondrocyte implantation (ACI) of the knee joint.

Methods

- Systematic review conducted according to PRISMA guidelines
- Searched PubMed, Embase, Cochrane Library
- Search terms used were: *autologous AND chondrocyte AND randomized*
- Study inclusion criteria:
 - Randomized controlled trials that reported a rehabilitation protocol after third-generation ACI for FCDs of the knee joint
- Study exclusion criteria:
 - Non-randomized studies
 - Studies on first- or second-generation ACI
 - Rehabilitation protocol was not reported

Methods

- Data extracted from each study included the various components of postoperative rehabilitation, such as:
 - Initial weight bearing (WB) status and time to full WB
 - The use of continuous passive motion (CPM)
 - The time to return to play (RTP)
 - Physical therapy modalities used and the timing of their initiation

Results

- Twenty-five studies met inclusion criteria including a total of 905 patients undergoing treatment with ACI
- Mean patient age ranged from 29.1 to 54.8 years
- The mean follow-up time ranged from 3 months to 10.0 years
- The overall percentage of male subjects ranged from 44.4% to 74.2%
- The mean body mass index ranged from 23.3 to 29.0 kg/m²
- The mean lesion size ranged from 1.9 to 5.8 cm²

Results

Study	LOE	N	Male, %	Age at Surgery, y	BMI, kg/m ²	Follow-up, y	Defect size, cm ²	Lesion Location	Type of ACI product
Akgun et al, 2015 ⁴	I	7	57	32.7 ± 10.4	24.3 ± 0.8	2	3.0 ± 0.8	MFC: 5; LFC: 2	Chondro-Gide®
Barié et al, 2020 ⁵	I	9	44.4	30.4 ± 6.8	23.32 ± 1.15	9.6 ± 0.9	4.27 ± 0.2	MFC: 8; LFC: 1	BioSeed®-C
Basad et al, 2010 ⁶	I	40	63.0	33.0	25.3	2	NR	C: 29; PT: 11	ACI-Maix™
Saris et al, 2014 ²⁴ Brittberg et al, 2018 ¹	I	72	62.5	34.8 ± 9.2	26.2 ± 4.3	2	5.8 ± 5.1	MFC: 48; LFC: 13; T: 4	ACI-Maix™
Clavé et al, 2016 ⁷	I	30	66.7	29.2 ± 11.9	23.4 ± 3.1	2	3.1 ± 0.8	NR	Cartipatch®
Crawford et al, 2012 ⁸	I	21	90.0	41 ± 9	29 ± 3	2	2.9 ± 1.4	NR	NeoCart®
Ebert et al, 2008 ¹⁴	I	62	64.5	38.3	NR	3 months	3.3	MFC: 45; LFC: 17	ACI-Maix™
Ebert et al, 2010 ¹³	I	70	64.3	38.2	NR	2	3.3	MFC: 52; LFC: 18	ACI-Maix™
Ebert et al, 2010 ¹²	I	61	63.9	38.5	NR	1	3.3	MFC: 46; LFC: 15	ACI-Maix™
Ebert et al, 2011 ¹⁰	I	69	63.8	38.2	26.6	2	3.3	MFC: 52; LFC: 17	ACI-Maix™
Ebert et al, 2012 ¹¹	I	63	66.7	38.2	26.5	5	3.3	MFC: 47; LFC: 16	ACI-Maix™
Ebert et al, 2020 ⁹	I	60	65.0	37.6	27.5	10	3.27	MFC: 44; LFC: 16	ACI-Maix™
Ebert et al, 2021 ²³ Ebert et al, 2017 ²	I	37	56.8	36.4	25.7	5	3.0	MFC: 27; LFC: 10	ACI-Maix™
Edwards et al, 2013 ¹⁵	I	28	60.7	35.8	25.6	1	2.9	MFC: 20; LFC: 8	ACI-Maix™
Fossum et al, 2019 ¹⁶	II	21	66.7	37.2 ± 10.8	25.7 ± 4.3	2	4.9 ± 4.4	MFC: 7; LFC: 2; T: 7; P: 1; PT: 2; T-MFC: 2	Chondro-Gide®
Hoburg et al, 2021 ¹⁷	I	52	63.5	36 ± 10	25.7 ± 3.3	3	2.2 ± 0.7	C: 52	Spherox
Ibarra et al, 2021 ¹⁸	I	24	70.8	33.7 ± 9.4	25.5 ± 3.1	6.2 ± 0.9	1.9 ± 0.9	MFC: 7; LFC: 9; T: 1; P: 7	Neoveil™
Liu et al, 2021 ¹⁹	I	10	50	54.8 ± 18.0	NR	1.1	2.9 ± 0.8	MFC: 10	Kartigen®
Niemeyer et al, 2019 ²¹	II	52	63.4	36 ± 10	25.7 ± 3.3	2	2.2 ± 0.7	C: 52	Spherox
Niemeyer et al, 2020 ²⁰	I	75	70.7	33.5 ± 9.2	25.2 ± 3.1	4	5.0 ± 1.9	C: 28; P: 47	Spherox
Wondrasch et al 2009 ²⁵ Wondrasch et al. 2015 ³	I	31	74.2	33	24.7	2	4.8	MFC: 22; LFC: 10	HyalograftC
Zeifang et al, 2009 ²²	II	11	54.5	29.1 ± 7.5	NR	2	4.3 ± 1.1	NR	BioSeed®-C

Results

- Twenty-two studies reported on postoperative WB

Study	Initial Weight Bearing Status	Progression to Full Weight Bearing
Akgun et al, 2015 ⁴	Partial WB	12 weeks
Barié et al, 2020 ⁵	Partial WB	6 weeks
Basad et al, 2010 ⁶	Non-WB	8 weeks
Brittberg et al, 2018 ¹	Partial WB	12 weeks
Clavé et al, 2016 ⁷	Non-WB	10 weeks
Crawford et al, 2012 ⁸	Partial WB	6 weeks
Ebert et al, 2020 ⁹	Partial WB	8 weeks/12 weeks*
Ebert et al, 2011 ¹⁰	Partial WB	8 weeks/11 weeks*
Ebert et al, 2021 ¹¹	Partial WB	6 weeks/8 weeks*
Ebert et al, 2012 ²	Partial WB	8 weeks/11 weeks*
Ebert et al, 2010 ¹²	Partial WB	8 weeks/11 weeks*
Ebert et al, 2010 ¹³	Partial WB	8 weeks/11 weeks*
Ebert et al, 2008 ¹⁴	Partial WB	8 weeks/11 weeks*
Edwards et al, 2013 ¹⁵	Partial WB	6 weeks/8 weeks*
Fossum et al, 2019 ¹⁶	Partial WB	6 weeks
Hoburg et al, 2021 ¹⁷	Partial WB	8 weeks
Ibarra et al, 2021 ¹⁸	Partial WB	6 weeks
Liu et al, 2021 ¹⁹	Partial WB	4 weeks
Niemeyer et al, 2020 ²⁰	Partial WB	6 weeks
Niemeyer et al, 2019 ²¹	Partial WB	8 weeks
Wondrasch et al, 2015 ³	Partial WB	6 weeks/10 weeks*
Zeifang et al, 2010 ²²	Partial WB	6 weeks

Results

- Eighteen studies used CPM as part of the rehabilitation process for all patients included
- Nine studies^{1,2,5,11,17,18,20,21,22} allowed RTP at 12 months after ACI and in 1 study,⁸ RTP was allowed after 6 months

Study	Initiation of CPM (postoperatively)	Initial ROM	Duration of CPM
Akgun et al, 2015 ⁴	12-24 hours	0°-30°	1 hour/NR
Barié et al, 2020 ⁵	24 hours	NR	NR/6 weeks
Basad et al, 2010 ⁶	NR	NR	NR
Crawford et al, 2012 ⁸	24 hours	NR	NR
Ebert et al, 2020 ⁹	NR	0°-30°	NR
Ebert et al, 2011 ¹⁰	NR	0°-30°	NR/3 weeks
Ebert et al, 2021 ¹¹	12-24 hours	0°-30°	1 hour/NR
Ebert et al, 2012 ²	12-24 hours	0°-30°	NR
Ebert et al, 2010 ¹³	12-24 hours	0°-30°	NR
Ebert et al, 2008 ¹⁴	12-24 hours	0°-30°	1 hour/NR
Edwards et al, 2013 ¹⁵	12-24 hours	0°-30°	1 hour/NR
Fossum et al, 2019 ¹⁶	NR	NR	4 hours/5 days
Hoburg et al, 2021 ¹⁷	24 hours	0°-60°	NR/6 weeks
Ibarra et al, 2021 ¹⁸	72 hours	0°-40°	4 hours/NR
Niemeyer et al, 2020 ²⁰	24 hours	0°-60°	NR/6 weeks
Niemeyer et al, 2019 ²¹	24 hours	0°-60°	NR/6 weeks
Wondrasch et al, 2015 ²⁵	48 hours	0°-40°	3 hours/NR
Zeifang et al, 2010 ²²	24 hours	NR	NR/6 weeks

Conclusion

- Based on the included studies, most rehabilitation protocols for third-generation ACI initiate CPM within 24 hours postoperatively and allow partial WB immediately following surgery with progression to full WB within 12 weeks
- There is variation of the PT modalities used as well as the timing of their initiation after third-generation ACI

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Systematic Reviews

The Most Common Rehabilitation Protocol After Matrix-Assisted Autologous Chondrocyte Implantation Is Immediate Partial Weight-Bearing and Continuous Passive Motion



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