Moderators, Mediators, and Prognostic Indicators of Treatment With Hip Arthroscopy or Physical Therapy for Femoroacetabular Impingement Syndrome

Secondary Analyses From the Australian FASHIoN Trial

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Background: Although randomized controlled trials comparing hip arthroscopy with physical therapy for the treatment of femoroacetabular impingement (FAI) syndrome have emerged, no studies have investigated potential moderators or mediators of change in hip-related quality of life.

Purpose: To explore potential moderators, mediators, and prognostic indicators of the effect of hip arthroscopy and physical therapy on change in 33-item international Hip Outcome Tool (iHOT-33) score for FAI syndrome.

Study Design: Cohort study; Level of evidence, 2.

Methods: Overall, 99 participants were recruited from the clinics of orthopaedic surgeons and randomly allocated to treatment with hip arthroscopy or physical therapy. Change in iHOT-33 score from baseline to 12 months was the dependent outcome for analyses of moderators, mediators, and prognostic indicators. Variables investigated as potential moderators/prognostic indicators were demographic variables, symptom duration, alpha angle, lateral center-edge angle (LCEA), Hip Osteoarthritis MRI Scoring System (HOAMS) for selected magnetic resonance imaging (MRI) features, and delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) score. Potential mediators investigated were change in chosen bony morphology measures, HOAMS, and dGEMRIC score from baseline to 12 months. For hip arthroscopy, intraoperative procedures performed (femoral ostectomy ± acetabular ostectomy ± labral repair ± ligamentum teres debridement) and quality of surgery graded by a blinded surgical review panel were investigated for potential association with iHOT-33 change. For physical therapy, fidelity to the physical therapy program was investigated for potential association with iHOT-33 change.

Results: A total of 81 participants were included in the final moderator/prognostic indicator analysis and 85 participants in the final mediator analysis after exclusion of those with missing data. No significant moderators or mediators of change in iHOT-33 score from baseline to 12 months were identified. Patients with smaller baseline LCEA ($\beta = -0.82$; $P = .034$), access to private health care ($\beta = 12.91$; $P = .013$), and worse baseline iHOT-33 score ($\beta = -0.48$; $P < .001$) had greater iHOT-33 improvement from baseline to 12 months, irrespective of treatment allocation, and thus were prognostic indicators of treatment response. Unsatisfactory treatment fidelity was associated with worse treatment response ($\beta = -24.27$; $P = .013$) for physical therapy. The quality of surgery and procedures performed were not associated with iHOT-33 change for hip arthroscopy ($P = .460$-$.665$ and $P = .096$-$.824$, respectively).

Conclusion: No moderators or mediators of change in hip-related quality of life were identified for treatment of FAI syndrome with hip arthroscopy or physical therapy in these exploratory analyses. Patients who accessed the Australian private health care system, had smaller LCEAs, and had worse baseline iHOT-33 scores, experienced greater iHOT-33 improvement, irrespective of treatment allocation.

The American Journal of Sports Medicine
1–14
DOI: 10.1177/03635465221136547

Keywords: hip; MRI; dGEMRIC; osteoarthritis; cartilage

Femoroacetabular impingement (FAI) syndrome is a clinical condition caused by abnormal motion between the proximal femur and acetabulum, producing hip pain with accompanying characteristic clinical signs and imaging findings.[17] FAI syndrome is understood to be a leading cause of hip osteoarthritis,[16] which incurs immense morbidity and economic cost[36] for the 25% of people living to age 85 years who develop it.[32] Arthroscopic hip surgery and physical therapy are the mainstays of treatment for FAI syndrome, with clinical trials comparing these treatment modalities emerging in only the past few years. Four recent randomized controlled trials (RCTs)[18,20,30,37] compared hip arthroscopy with physical therapy for the treatment of FAI syndrome, measuring their primary endpoints at different times (8, 12, and 24 months) and arriving at different findings: hip arthroscopy conferred patient-reported benefit as compared with physical therapy in the trials measuring endpoints at 8 and 12 months[18,20,37] but no difference between treatment modalities at the 24-month time point.[30] However, this trial was limited in that it was a single-surgeon, single-center study restricted to military patients and had a high crossover rate. Meta-analyses of the trials have also differed in their conclusions,[1,5,13,15] although most have agreed that hip arthroscopy provides superior patient-reported relief in the short term.

The Australian FASHIoN trial,[20,34] from which the current study draws its data, compared hip arthroscopy with physical therapy by measuring change in delayed gadolinium-enhanced magnetic resonance imaging (MRI) of cartilage (dGEMRIC) from baseline to 12 months as its primary endpoint. It found no significant difference in dGEMRIC change between interventions but replicated other RCTs in finding a statistically and clinically significant difference between treatment groups in hip-related quality of life (QOL) improvement, as measured by the 33-item international Hip Outcome Tool (iHOT-33) at 12-month follow-up. The trial measured other secondary endpoints, including change in radiological measures of bony morphology and structural features associated with hip osteoarthritis using the Hip Osteoarthritis MRI Scoring System (HOAMS).[41]

Hip arthroscopy and physical therapist–led management are understood to act by quite different mechanisms: hip arthroscopy by correcting the abnormal bony morphology and repairing damage to soft tissue structures and physical therapy by addressing the condition's abnormal motion patterns and altered periarticular muscle strength and activation patterns, among others. Given the diversity of patients with FAI syndrome with regard bony morphology,[11] biomechanics,[23] symptoms,[21] and response to treatments,[4] a "one size fits all" approach to treatment may not be best. A targeted approach that aims to match patients with the treatment modality/modalities from which they are most likely to benefit may best take advantage of each treatment's mechanism of action. Analysis of treatment moderators within the context of a randomized trial is a valuable method for exploring which patients are likely to respond to a particular treatment. Moderators constitute patient characteristics measured at baseline that interact with the treatment modality to affect the clinical outcome.[26] No study has yet explored potential moderators of treatment response in FAI syndrome. Determining moderators would constitute a significant advance, enabling patients to move without delay to the treatment from which they are most likely to benefit.

Mediators of change in hip-related QOL are also yet to be studied in FAI syndrome. Mediators are variables through which the independent variable (hip arthroscopy/physical therapy) affects the dependent variable (change in iHOT-33).[26] Determining the variables that mediate patient-reported improvement would aid our understanding of FAI syndrome and enable treatments to focus on the specific variables that mediate improvement. Prognostic indicators are variables that are associated with the clinical outcome without interacting with the intervention.[44]

The purpose of this study was to explore moderators, mediators, and prognostic indicators of the effect of hip arthroscopy and physical therapy on change in hip-related QOL at 12 months for FAI syndrome. In addition to analyzing baseline patient characteristics as potential prognostic indicators, variables unique to each intervention were investigated. This involved analyzing whether the intraoperative procedures performed or the surgical review panel score was associated with the change in hip-related QOL for hip arthroscopy and whether treatment fidelity was associated with the change in hip-related QOL for physical therapy. It was hypothesized that larger bony deformity (ie, higher alpha angle and lateral center-edge angle [LCEA]) would moderate a beneficial response to hip arthroscopy and that patient-reported improvement would be mediated by change in bony morphology as measured by the alpha angle and

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Submitted January 19, 2022; accepted September 9, 2022.

One or more of the authors has declared the following potential conflict of interest or source of funding: This study was funded by a grant from the National Health and Medical Research Council (NHMRC) (APP1069278) and by the Australian Hip Arthroscopy Education and Research Foundation. D.J.H. is a consultant to Pfizer, Lilly, TLCBio, and Merck Serono and is supported by an NHMRC Investigator Fellowship. K.L.B. is supported by an NHMRC Investigator Fellowship (APP1174431). N.E.F. is a National Institute for Health Research (NIHR) senior investigator and was supported through an NIHR Research Professorship (NIHR-RP-011-015). D.R.G. is a consultant to Stryker and Smith & Nephew and received grants from the NIHR. Y.J.K. is a member of the Cytex scientific advisory board. AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.

LCEA. Furthermore, we hypothesized that a worse surgical review panel score and worse treatment fidelity would be associated with worse patient-reported change for hip arthroscopy and physical therapy, respectively.

METHODS

Participants

This study involved exploratory secondary analyses of data collected from all 99 participants in the Australian FASHIoN trial, a pragmatic 2-arm superiority RCT (Australian Clinical Trials: ACTRN12615001177549).[34] The trial was conducted in accordance with the ethics approval granted by St Vincent's Hospital Human Research Ethics Committee (HREC/14/SVH/343). Informed consent was obtained from all study participants before participation in the study.

Participants were recruited between February 2015 and January 2018, through public and private clinics at 10 sites in Australia, after FAI syndrome was diagnosed by 1 of 8 orthopaedic surgeons. Inclusion criteria for participation were age $\geq$16 years, hip pain, cam and/or pincer morphology on imaging (alpha angle $>55°$ and/or LCEA $>40°$ or other radiographic sign of pincer morphology), and the treating surgeon's believing that the patient would benefit from arthroscopic surgery. Exclusion criteria were ipsilateral preexisting osteoarthritis (Tönnis[48] grade >1 or $<$2-mm joint space width on pelvic radiograph), previous significant hip pathology (eg, Perthes disease, avascular necrosis, or slipped upper femoral epiphysis), injury (eg, acetabular fracture, hip dislocation, or femoral neck fracture), or shape-changing surgery. Patients with bilateral FAI nominated the more symptomatic hip satisfying the eligibility criteria for inclusion in the study. On entry to the study and at 12 months, participants recorded demographic data and completed the iHOT-33, a validated measure of hip health–related QOL,[31] in which 0 represents worst possible QOL and 100 best possible QOL.

Interventions

Participants were randomly allocated to treatment with either arthroscopic surgery or physical therapist–led management. Randomization was according to a computer-generated 1:1 ratio, stratified by the study site from which participants were recruited and by the type of FAI (cam, pincer, or mixed) as designated by the orthopaedic surgeon upon study entry. Participants accessed surgery through either the public health care system, with no out-of-pocket cost, or the private health care system, typically associated with additional out-of-pocket costs. Arthroscopic surgery was performed by 1 of 8 participating orthopaedic surgeons experienced in hip arthroscopy. Surgery was performed with the patient in a lateral or supine position, according to the surgeon's usual practice, with central and peripheral portals established under radiographic guidance. Bony resection at the acetabular rim and femoral head-neck junction was performed and assessed intraoperatively by using a radiographic image intensifier and through assessment of impingement-free hip range of motion. The labrum was inspected and labral tears repaired where amenable. Osseointegrative anchors were utilized to minimize the risk of this affecting postoperative MRI or dGEMRIC quality. Management of the hip capsule was according to each surgeon's usual practice: of the 8 surgeons participating in the trial, 3 always repaired the capsule, 3 sometimes repaired it, and 2 never did. Participants were discharged from the hospital when they could walk safely with crutches (generally within 24 hours of surgery). A specific protocol for postoperative rehabilitation was not specified for the trial. Patients were referred to outpatient physical therapy services and offered postoperative rehabilitation per usual practice and protocols without any attempt to standardize these. To prevent contamination between treatment groups, the physical therapists providing postoperative rehabilitation were distinct from those providing the personalized hip therapy (PHT) nonsurgical care intervention.

The physical therapist–led management was named PHT, a program developed for the UK FASHIoN trial to represent a consensus of best nonsurgical care for FAI syndrome.[51] The PHT program was provided by experienced musculoskeletal physical therapists at no cost to participants. It involved a minimum of 6 PHT sessions in the first 12 weeks, with up to an additional 4 sessions available between 12 weeks and 6 months. The core components of the PHT program were (1) an individualized, progressed, supervised exercise program; (2) education regarding FAI syndrome and behavior modification; and (3) advice regarding pain relief, including referral for an ultrasound-guided intra-articular corticosteroid injection if needed.

Imaging Protocol

Imaging acquisition occurred on entry to the trial and at 12 months. The MRI protocol consisted of the following sequences, which are also described in the trial's protocol article[34]:

- Coronal and axial fat-suppressed T1-weighted spin echo sequence: repetition time (TR), 600 ms; echo time (TE), 7.9 ms; slice thickness/slice gap, 3.0 mm/0.3 mm; echo train length, 3; field of view (FOV), 18 $\times$ 18 cm; matrix size, 256 $\times$ 256; number of signal averages, 1; number of slices, 24
- Coronal and sagittal proton density−weighted fat-suppressed fast spin echo sequence: TR, 2230 and 2770 ms; TE, 29 and 36 ms; slice thickness/slice gap, 3.0 mm/0.3 mm; echo train length, 7 and 9; FOV, 18 $\times$ 18 cm; matrix size, 256 $\times$ 256; number of signal averages, 2
- Sagittal 3-dimensional T2-weighted true fast imaging with steady-state precession sequence: TR, 10.2 ms; TE, 4.3 ms; slice thickness, 0.63 mm; FOV, 16 $\times$ 16 cm; matrix size, 256 $\times$ 256; number of signal averages, 1
- Axial fat-suppressed T1-weighted spin echo sequence of the pelvis covering the hip joints: TR, 500 ms; TE, 8.9 ms; slice thickness/slice gap, 3.0 mm/0.9 mm; echo train length, 3; FOV, 36 $\times$ 36 cm; matrix size, 256 $\times$ 256; number of signal averages, 1

- Axial fat-suppressed T1-weighted spin echo sequence of the bilateral knees: TR, 550 ms; TE, 11 ms; slice thickness/slice gap, 5.0 mm/1.5 mm; echo train length, 4; FOV, 32 × 32; number of signal averages, 2
- Axial fat-suppressed T1-weighted spin echo sequence of the bilateral ankles at the Melbourne site only: TR, 470 ms; TE, 12 ms; slice thickness/slice gap, 5.0/1.5 mm; echo train length, 3; FOV, 36 × 36 cm; matrix size, 320 × 320; number of signal averages, 1
- dGEMRIC sequences: spin-echo inversion recovery with fat suppression; sagittal orientation; TR, 2340 ms; TE, 15 ms; slice thickness/slice gap, 3.0 mm/3.0 mm; echo train length, 11; FOV, 16 × 16 cm; matrix size, 256 × 256; number of signal averages, 1; 6 inversion recovery delays at 50, 100, 200, 400, 800, and 1600 ms

Participants also underwent standardized plain radiographs, comprising supine anteroposterior pelvis, 45° modified Dunn views, and false-profile views.

Image Analysis

HOAMS was performed by a musculoskeletal radiologist (E.Davidson) following a consensus scoring exercise and calculation of weighted kappa scores for inter- and intrarater reliability with a second musculoskeletal radiologist (J.M.L.). The labrum, cartilage, bone marrow lesions, subchondral cysts, synovitis, and osteophytes were each scored for severity of damage at several subregions as described in the HOAMS validation article.[41] Labral hypertrophy, greater trochanteric tendinitis, and bursitis were each scored as present or absent.

The inversion recovery dGEMRIC sequences were postprocessed to create T1 maps; after which, regions of interest (ROIs) were defined manually at the chondrolabral transitional zone of the acetabular and femoral head articular cartilages, reaching 3 to 6 mm toward the acetabular fossa, on 3 midsagittal slices for each hip (ie, the 3 slices capturing the most central part of the femoral head).[34] The chondrolabral transitional zone was chosen as the ROI because of its established importance in early osteoarthritic change in FAI syndrome.[2] The mean T1 score, weighted for the size of each ROI across the 3 slices, was calculated and considered the dGEMRIC score for that hip.

Bony morphology measures were made on MRI and plain radiographs. The alpha angle was measured on MRI in 4 reconstructed radial planes at 30° intervals from superior (12 o'clock) to anterior (3 o'clock) using the Orthopaedic Studio OsiriX plug-in (Version 1.3.3b; Carl Siversson, Lund University). Given the large number of potential moderators, only the maximum alpha angle measured across all 4 radial planes for each hip was considered a candidate moderator to reduce the type I error rate. Conversely, the alpha angle in each radial plane was analyzed as a potential mediator given the smaller number of candidate mediators in this study after the removal of those that did not differ between treatment groups (a requirement for a variable to function as a mediator). Radiographic measurements were performed using the Hip2Norm package[46] and for this study included the LCEA and crossover sign.

Treatment Fidelity

Treatment fidelity was analyzed for both interventions using the same methods as the UK FASHIoN trial.[18] A group of experienced hip arthroscopy surgeons not involved in operating on participants in this study formed an independent expert surgical review panel that jointly scored subjective surgical quality for half of the participants. A single member of the review panel (E. Dickenson) scored surgical quality for the remaining half of participants. The blinded pre- and postoperative radiological imaging, intraoperative arthroscopic images, and operation reports for each participant were reviewed, and a subjective rating of *satisfactory*, *borderline*, or *inadequate* was given for each operation based on whether shape abnormalities were treated and whether there was sufficient resection to allow impingement-free range of motion. The fidelity of treatment for the physical therapy group was graded as *satisfactory* or *unsatisfactory* by 2 experienced physical therapists not involved in treating participants for the trial (J.E. and L.S.). They reviewed the blinded case report forms for each participant who underwent the PHT program. Treatment was required to show evidence of individualization, progression, and supervision of exercises. Participants were required to have $\geq$6 PHT sessions within the first 12 weeks of the study and, if needed, a further 4 sessions between 12 weeks and 6 months. Participants were designated as having unsatisfactory treatment fidelity if treatment did not meet the required standard or attendance or if the protocol was breached by inclusion of interventions in addition to those allowed in the protocol. Those who did meet the required standard and attendance without protocol breaches were designated as having satisfactory treatment fidelity.

Intraoperative Procedures Performed

For participants allocated to hip arthroscopy, procedures performed intraoperatively by the treating surgeon (femoral ostectomy ± acetabular ostectomy ± labral repair ± ligamentum teres debridement) were recorded by review of the operation reports and arthroscopic images.

Statistical Analysis

Candidate moderators included selected baseline variables that have been associated with outcomes of hip arthroscopy in longitudinal studies or the presence/severity of symptoms in cross-sectional studies: age,[27,28,42,43] sex,[33,43] body mass index (BMI),[43] health care system accessed,[33] smoking status,[40,52] duration of symptoms,[42] preoperative patient-reported outcomes,[42] alpha angle,[25,29] LCEA,[7,19] cartilage injury,[35] labral abnormalities,[6] trochanteric bursitis,[24,50] and dGEMRIC score.[8] Candidate mediators were variables measured at baseline and 12 months that were expected to plausibly change with treatment and potentially be associated with changes in patient-reported outcomes. These consisted of bony morphology measures (alpha angle and LCEA), features scored on the HOAMS (cartilage lesions,

TABLE 1
Baseline Characteristics for Participants With 12-Month iHOT-33 Follow-up Data Available[a]

Characteristic	Arthroscopy (n = 45)	PHT (n = 46)	Total (N = 91)
Age, y	33.8 ± 11.9	32.7 ± 9.0	33.3 ± 10.5
Sex			
Male	27 (60)	24 (52)	51 (56)
Female	18 (40)	22 (48)	40 (44)
Body mass index	24.2 ± 3.5	24.2 ± 2.5	24.2 ± 3.0
Type of FAI			
Pincer	8 (18)	7 (16)	15 (16)
Mixed	10 (22)	8 (18)	18 (20)
Cam	27 (60)	31 (67)	58 (64)
Health care system accessed			
Public	27 (60)	26 (57)	53 (58)
Private	18 (40)	20 (43)	38 (42)
Smoking status			
Smoker	4 (9)	4 (9)	8 (9)
Nonsmoker	39 (91)	42 (91)	81 (91)
Duration of symptoms, mo	22.7 ± 16.8	34.3 ± 31.1	28.5 ± 25.5
Maximum MRI alpha angle	70.3 ± 11.6	70.7 ± 16.1	70.5 ± 14.0
LCEA, deg	37.0 ± 5.4	34.4 ± 6.7	35.7 ± 6.2
dGEMRIC score	682.7 ± 122.4	681.4 ± 108.7	682.0 ± 114.6
HOAMS: cartilage[b]			
0	27	29	56 (62)
1	4	5	9 (10)
2	12	10	22 (24)
3	0	2	2 (2)
4	1	0	1 (2)
HOAMS: bone marrow lesion[c]			
0	39	40	79 (88)
1	4	3	7 (8)
2	1	3	4 (4)
3	0	0	0
HOAMS: subchondral cyst[c]			
0	30	30	60 (67)
1	14	11	25 (28)
2	0	5	5 (6)
3	0	0	0
HOAMS: osteophyte[b]			
0	36	39	75 (83)
1	4	1	5 (6)
2	4	4	8 (9)
3	0	1	1 (1)
4	0	1	1 (1)
HOAMS: labrum[c]			
0	3	1	4 (4)
1	2	4	6 (7)
2	36	36	72 (80)
3	3	5	8 (9)
HOAMS: synovitis[d]			
0	8	17	25 (28))
1	31	25	56 (62)
2	5	4	9 (10)
HOAMS: trochanteric bursitis			
Present	30	30	60 (69)
Absent	13	14	27 (31)
HOAMS: labral hypertrophy			
Present	17	12	29 (32)
Absent	27	34	61 (68)

[a]Candidate variables that are considered potential moderators are set in bold. Values are presented as mean ± SD or No. (%) or No. dGEMRIC, delayed gadolinium-enhanced MRI of cartilage; HOAMS, Hip Osteoarthritis MRI Scoring System; iHOT-33, 33-item International Hip Outcome Tool; LCEA, lateral center-edge angle; MRI, magnetic resonance imaging.
[b]Grade of maximum severity across: 0-4.
[c]Grade of maximum severity: 0-3.
[d]Grade of maximum severity: 0-2.

TABLE 2
iHOT-33 Score for Participants Undergoing Arthroscopy and Personalized Hip Therapy[a]

	Arthroscopy	Personalized Hip Therapy	Mean Difference[b]	*P* Value
Baseline	43.3 ± 17.9	41.3 ± 19.8		
12 mo	72.9 ± 21.8	56.8 ± 28.8		
Change: 12 mo – baseline	29.6 ± 22.3	15.4 ± 22.3	14.2	<.003

[a]Values are presented as mean ± SD. iHOT-33, 33-item International Hip Outcome Tool.
[b]Arthroscopy minus Personalized Hip Therapy

bone marrow lesions, subchondral cysts, osteophytes, labral damage, and synovitis), and dGEMRIC score.

Table 1 displays the baseline characteristics of participants with 12-month iHOT-33 data available, with variables chosen for analysis as potential moderators in bold. Moderation/prognostic indicator analysis was conducted using multiple linear regression modeling, with change in iHOT-33 score from baseline to 12 months as the dependent variable. Model selection was conducted by exhaustive best subsets screening of all potential models using the R package glmulti,[3] with the final model chosen according to the lowest Bayesian information criterion. This approach was chosen for its suitability for model selection given the number of candidate moderators and relatively modest sample size. Main effects and interactions between treatment allocation (hip arthroscopy or PHT) and the candidate variables were considered in the model. Variables in the final model that interacted with treatment allocation were considered moderators, whereas main effects variables in the final model were considered prognostic indicators (as the main effects variables were associated with iHOT-33 change regardless of treatment allocation). Regression models were adjusted for baseline iHOT-33 score, and the rule of marginality was applied. The dGEMRIC score was analyzed in a separate regression analysis as a potential moderator, given the smaller number of participants with dGEMRIC data available (n = 50).[20]

Mediation analysis was conducted considering the change in iHOT-33 score to be the dependent variable and the change from baseline to 12 months for the variables listed as possible mediators (see Mediator Analysis section). As a preliminary step, potential mediators that were significantly different between treatment groups were identified using simple linear regression models, as this is a prerequisite for mediation. Potential mediators that were significantly different between treatment groups underwent full mediation analysis, which involved using the *mediation* package[47] in R to decompose the total effect of the treatment into the indirect effect (ie, the average causal mediation effect of treatment allocation on change in iHOT-33 score being mediated by the variable being tested) and the average direct effect (ie, the effect of treatment allocation on change in iHOT-33 score that is not passed through the mediator). Significance of the average causal mediation effect was calculated using 1000 bootstrapping replications. Models were adjusted for baseline iHOT-33 score. In addition, a secondary mediation analysis was conducted adjusting for the variables that appeared in the final model for moderation analysis.

Intraoperative procedures performed and surgical review panel score were analyzed for potential association with change in iHOT-33 score for participants undergoing hip arthroscopy. Treatment fidelity was investigated for potential association with change in iHOT-33 score for PHT participants. Multiple linear regression models were constructed for hip arthroscopy and PHT, each adjusted for baseline iHOT-33 score. Secondary analyses were also performed adjusting for variables that appeared in the final model for moderation analysis. Model selection employed the penalized lowest Bayesian information criterion approach with exhaustive best subsets screening using the *glmulti* package in R.[3] Statistical analyses were conducted using RStudio Version 1.3.107 with R Version 3.6.3 and employed intention-to-treat analysis. As this was an exploratory study underpowered for the mediation and moderation analyses undertaken, a post hoc sensitivity analysis was undertaken using G*Power (Version 3.1.9.7)[14] to provide some empirical evidence of the effect size identifiable with the available sample size.

RESULTS

Sample Characteristics

Of the 99 participants recruited, 3 crossed over from PHT to hip arthroscopy during the 12-month follow-up. Eight participants did not complete 12-month iHOT-33 questionnaires owing to withdrawal from the trial (3 participants) or being lost to follow-up (5 participants). There were 91 participants who completed 12-month follow-up iHOT-33 questionnaires and 85 who underwent 12-month follow-up MRI (Figure 1). After exclusion of those with missing data, 81 participants were included in the moderator/prognostic indicator analysis and 85 in the mediator analysis. Demographic characteristics of participants in each treatment group were similar (Table 1). As reported in the primary outcome publication, participants who underwent hip arthroscopy had a significantly greater improvement in iHOT-33 score at 12 months than those who underwent PHT[20] (Table 2).

Moderator and Prognostic Indicator Analysis

There were 81 participants in the final analysis of moderators/prognostic indicators after exclusion of participants with incomplete data available. The dGEMRIC data were analyzed separately from other candidate moderators/

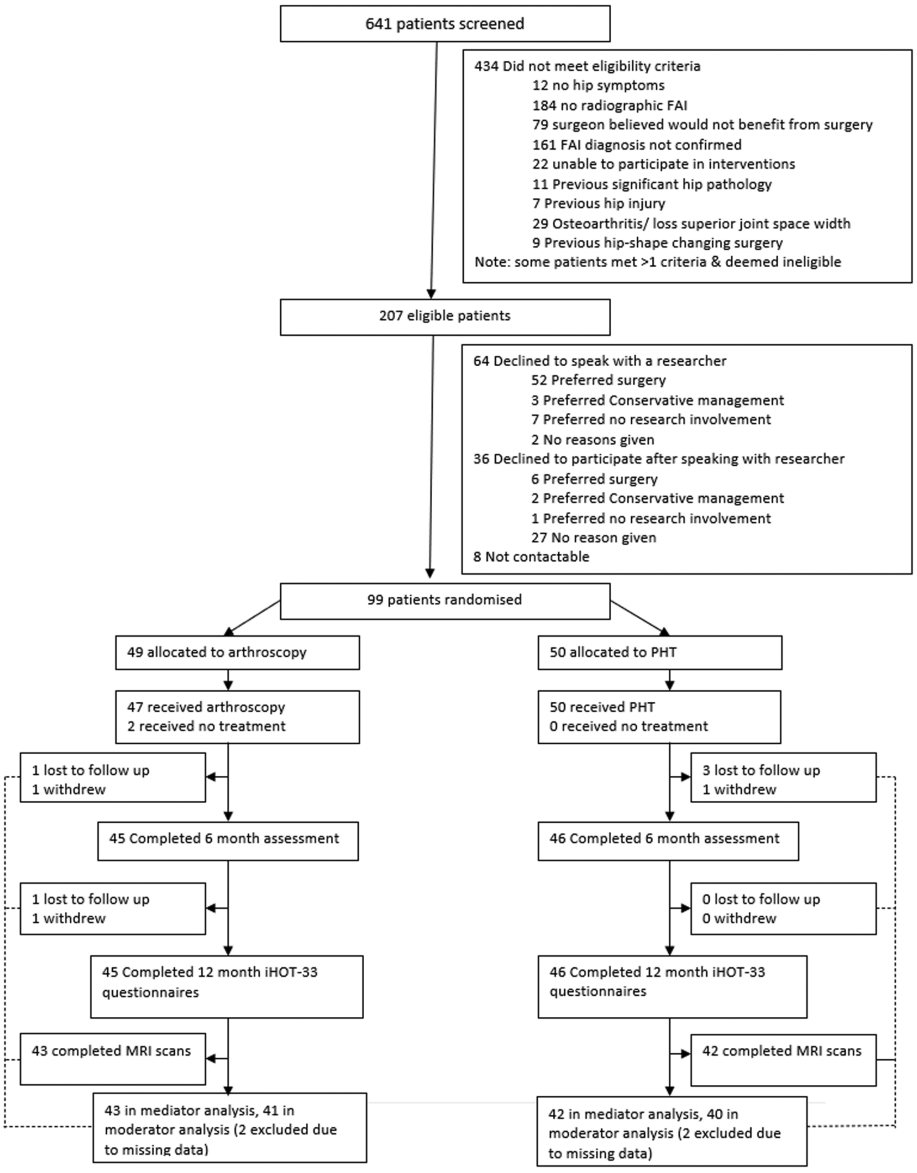

Figure 1. Study flow diagram. FAI, femoroacetabular impingement; iHOT-33, 33-item International Hip Outcome Tool; MRI, magnetic resonance imaging; PHT, personalized hip therapy. Reprinted with permission from Hunter et al.[20]

prognostic indicators because only 50 complete follow-up data sets were available. Table 3 shows, for each candidate moderator, the univariate main effects, the univariate interaction effects with treatment allocation, and the final model selected from multiple variable linear regression modeling. There were no significant moderators of change in iHOT-33 score—that is, no variables interacting with treatment allocation in the final model. Baseline iHOT-33 score, LCEA, and health care system accessed were in the final model but did not interact with treatment allocation, indicating that these variables predicted change in iHOT-33 score regardless of treatment allocation (and thus were prognostic indicators rather than moderators of treatment response). Participants with higher LCEA, those with worse baseline iHOT-33 score, and those accessing the public health care system tended to have less improvement in iHOT-33 score over the 12 months.

To explore cutoffs for LCEA that may be useful in clinical practice, participants were grouped into those with LCEA $<25°$, $25°$ to $35°$, $>35°$ to $45°$, and $>45°$ to denote small, normal, borderline large, and large LCEAs, respectively. Just 2 participants in the trial had LCEA $<25°$: 1 with an LCEA $17.7°$ and 1 with LCEA $22.2°$. A Wald chi-square test of model effects was employed, and the model adjusted for intervention, health care system accessed, and baseline iHOT-33 score. No statistically significant between-group differences were detected ($P = .056$).

TABLE 3
Univariate and Multivariable Regression Models for Moderators of Change in iHOT-33 Score From Baseline to 12 Months[a]

	Univariate Noninteraction		Univariate Interaction With Treatment[b]		Multivariable[c]		
Characteristic	β	*P* Value	β	*P* Value	B	Effect Size, Partial η^2	*P* Value
Age	–0.17 (−0.67 to 0.34)	.516	0.02 (−0.94 to 0.97)	.972			
Sex	–1.31 (−11.77 to 9.15)	.806	–7.72 (−27.00 to 11.56)	.435			
Body mass index	0.54 (−1.19 to 2.27)	.541	1.01 (−2.43 to 4.44)	.568			
Health care system accessed	4.84 (−5.61 to 15.28)	.367	–20.03 (−37.74 to −2.31)	.028	12.91 (2.91 to 22.90)	0.041	.013
Smoking status	–5.17 (−23.63 to 13.30)	.585	19.48 (−13.83 to 52.80)	.255			
Duration of symptoms	–0.16 (−0.36 to 0.03)	.110	0.15 (–0.30 to 0.60)	.507			
Alpha angle: maximum	–0.21 (−0.57 to 0.16)	.275	–0.48 (−1.19 to 0.23)	.186			
LCEA	–0.67 (−1.50 to 0.16)	.119	1.31 (−0.23 to 2.85)	.099	–0.82 (−1.57 to −0.08)	0.216	.034
HOAMS: cartilage[d]							
Grade 1	–17.41 (−35.86 to 1.03)	.068	–2.02 (−36.71 to 32.67)	.909			
Grade 2	–7.02 (−19.30 to 5.27)	.266	–5.55 (−28.59 to 17.50)	.64			
Grade 3	–19.61 (−52.63 to 13.40)	.248	NA	NA			
Grade 4	23.85 (−22.41 to 70.10)	.316	NA	NA			
HOAMS: labrum[d]							
Grade 1	11.13 (−19.16 to 41.43)	.474	–55.36 (−114.69 to 3.95)	.071			
Grade 2	–15.41 (−38.68 to 7.86)	.198	–47.41 (−94.85 to 0.02)	.054			
Grade 3	–17.97 (−46.28 to 10.33)	.217	–29.89 (−86.43 to 26.65)	.304			
HOAMS: trochanteric bursitis	5.77 (−5.54 to 17.09)	.320	2.18 (−18.89 to 23.25)	.840			
HOAMS: labral hypertrophy	–5.55 (−16.51 to 5.41)	.324	–1.914 (−22.06 to 18.23)	.853			
dGEMRIC score	–0.01 (−0.08 to 0.05)	.653	–0.08 (−0.18 to 0.03)	.150			
Baseline iHOT-33 score	–0.32 (−0.59 to −0.06)	.018	NA	NA	–0.48 (−0.75 to −0.22)	0.376	<.001
Treatment allocation	15.99 (6.21 to 25.77)	.002	NA	NA	20.45 (11.36 to 29.55)	0.366	<.001

[a]Values are presented as mean (95% confidence interval); β, beta coefficient of change in iHOT-33 score from baseline to 12 months; dGEMRIC, delayed gadolinium-enhanced MRI of cartilage; HOAMS, Hip Osteoarthritis MRI Scoring System; iHOT-33, 33-item International Hip Outcome Tool; LCEA, lateral center-edge angle; MRI, magnetic resonance imaging; NA, not applicable.
[b]Candidate moderator × treatment allocation. Adjusted for baseline iHOT-33 and treatment allocation.
[c]Including all variables + interaction effects with treatment allocation.
[d]Reference category = grade 0.

Mediator Analysis

There were 85 participants in total for the mediator analysis. The change between baseline and 12 months by treatment group is presented in Table 4 for bony morphology measures and dGEMRIC score and in Table 5 for HOAMS severity. The change in 9 variables from baseline to 12 months differed significantly between treatment groups and so were carried forth to the next stage for full mediation analysis: alpha angle in all radial planes measured, including maximum alpha angle for each hip, LCEA, and HOAMS severity for cartilage and labrum. Table 6 demonstrates the results of the full mediation analysis for these variables, which decomposed the total effect of treatment allocation on change in iHOT-33 score into indirect and direct effects. The indirect effect is the effect of treatment allocation on change in iHOT-33 score acting through the proposed mediator, whereas the direct effect is the treatment effect that is not acting through the proposed mediator. As expected, the total effect was significant ($P < .05$) for all variables considered for full mediation analysis, reflecting that the change in iHOT-33 score differed significantly between treatment groups for these variables. The indirect effect was nonsignificant ($P > .05$) for all variables considered, meaning that the proportion of the total effect acting through each proposed mediator was nonsignificant; thus, no significant mediators were identified. Sensitivity analyses adjusting for the significant prognostic indicators identified (LCEA and health care system accessed) produced no change in the findings.

Variables Associated With Change in iHOT-33 for Hip Arthroscopy and PHT

Table 7 presents the final regression models for variables unique to each treatment that were investigated for potential association with change in iHOT-33 score: femoral ostectomy, acetabular ostectomy, labral repair, and ligamentum teres debridement. Appendix Table A2 (available in the online version of this article) provides a summary of the number of participants who underwent each of these intraoperative procedures, plus other intraoperative procedures (labral debridement, synovectomy, subchondral microfracture). No variables analyzed were significantly associated with change in iHOT-33 score for hip arthroscopy. Quality of surgery, as graded by the surgical review panel, was not associated with change in iHOT-33 score. Satisfactory treatment fidelity in the PHT program was associated with a significant improvement in iHOT-33 score. Sensitivity analyses adjusting for the significant prognostic indictors identified (LCEA and health care system accessed) produced no change in the findings.

TABLE 4
Change From Baseline to 12 Months for Bony Morphology Measurements and dGEMRIC Score Considered Potential Mediators[a]

Outcome	Baseline, Mean ± SD		12 mo, Mean ± SD		Unadjusted Mean Difference (95% CI)	*P* Value
	Arthroscopy	PHT	Arthroscopy	PHT		
Alpha angle						
Maximum[b]	70.2 ± 11.9	70.6 ± 15.6	62.7 ± 16.9	69.2 ± 16.2	–7.4 (−11.5 to −3.4)	<.001[b]
Superior − 12 o'clock[b]	54.4 ± 16.5	53.6 ± 18.1	50.6 ± 15.2	53.9 ± 17.6	–3.3 (−6.4 to −0.2)	.039[b]
Superoanterior − 1 o'clock[b]	64.0 ± 14.0	61.5 ± 15.3	56.7 ± 14.0	62.2 ± 14.5	–7.5 (−11.0 to −4.1)	<.001[b]
Anterosuperior − 2 o'clock[b]	65.0 ± 12.5	61.1 ± 13.8	54.6 ± 16.5	60.5 ± 12.1	–9.8 (−14.1 to −5.4)	<.001[b]
Anterior − 3 o'clock[b]	57.4 ± 11.5	56.8 ± 14.0	49.0 ± 13.0	56.3 ± 15.1	–9.1 (−12.3 to −5.8)	<.001[b]
LCEA	37.1 ± 5.4	34.7 ± 6.6	34.2 ± 6.2	34.0 ± 5.6	–2.5 (−4.3 to −0.8)	.005
dGEMRIC score	679.6 ± 118.6	667.0 ± 127.4	677.0 ± 122.8	722.8 ± 145.7	–56.7 (−140.8 to −27.5)	.181

[a]dGEMRIC, delayed gadolinium-enhanced MRI of cartilage; iHOT-33, 33-item International Hip Outcome Tool; LCEA, lateral center-edge angle; MRI, magnetic resonance imaging; PHT, personalized hip therapy.
[b]Reconstructed radial plane in which alpha angle was measured on MRI.

TABLE 5
Change From Baseline to 12 Months for HOAMS Features Considered as Potential Mediators[a]

MRI Feature/Category	Arthroscopy (n = 42)	PHT (n = 42)	*P* Value[b]
Cartilage			<.001
No change in maximum severity	27 (64)	41 (98)	
Maximum severity better	1 (2)	0	
Maximum severity worse	14 (33)	1 (2)	
Bone marrow lesion			.294
No change in maximum severity	35 (83)	39 (93)	
Maximum severity better	2 (5)	2 (5)	
Maximum severity worse	5 (12)	1 (2)	
Subchondral cyst			.557
No change in maximum severity	32 (76)	33 (79)	
Maximum severity better	6 (14)	3 (7)	
Maximum severity worse	4 (10)	6 (14)	
Osteophyte			.055
No change in maximum severity	37 (88)	42 (100)	
Maximum severity better	5 (12)	0	
Maximum severity worse	0	0	
Labrum			<.001[c]
No change in maximum severity	16 (38)	33 (79)	
Maximum severity better	7 (17)	3 (7)	
Maximum severity worse	19 (45)	6 (14)	
Synovitis			.140
No change in maximum severity	17 (40)	25 (60)	
Maximum severity better	4 (10)	5 (12)	
Maximum severity worse	21 (50)	12 (29)	

[a]Values are presented as No. (%). HOAMS, Hip Osteoarthritis MRI Scoring System; MRI, magnetic resonance imaging; PHT, personalized hip therapy.
[b]Fisher exact test (unless noted otherwise).
[c]Chi-square test.

Post Hoc Sensitivity Analysis

The post hoc sensitivity analysis was conducted for moderation and mediation analyses using G*Power (Version 3.1.9.7).[14] For the moderation analysis, the minimum effect size f^2 that could reliably yield a statistically significant result was calculated as 0.099 (ie, a small to moderate effect size[9]) based on a power of 0.8, an alpha of .05, and a sample size of 85. For the mediation analysis, the minimum effect size f^2 that could reliably yield a statistically significant result was calculated as 0.095 (ie, a small to moderate effect size[9]) based on power of 0.8, an alpha of .05, and a sample size of 81.

TABLE 6
Effect Estimates of the Total, Direct, and Indirect Effects of Treatment Allocation on Change in iHOT-33 Score at 12 Months for Each Potential Mediator Considered for Full Mediation Analysis[a]

	Total Effect		Direct Effect		Indirect Effect[b]	
Potential Mediator	Effect (95% CI)	*P* Value	Effect (95% CI)	*P* Value	Effect (95% CI)	*P* Value
Alpha angle						
Maximum	15.39 (5.78 to 24.85)	.002	15.08 (4.61 to 25.93)	.010	0.32 (−3.73 to 2.90)	.806
Superior − 12 o'clock	15.38 (5.72 to 24.68)	.002	15.49 (5.49 to 25.06)	.004	–0.11 (−1.56 to 1.39)	.906
Superoanterior − 1 o'clock	15.37 (5.52 to 24.34)	.002	16.12 (4.97 to 26.27)	.008	–0.74 (−4.69 to 3.11)	.694
Anterosuperior − 2 o'clock	15.42 (6.38 to 24.26)	<.001	13.87 (2.89 to 24.28)	.014	1.55 (−3.81 to 6.76)	.452
Anterior − 3 o'clock	15.33 (5.01 to 24.21)	.004	17.39 (4.39 to 28.74)	.008	–2.06 (−7.05 to 3.60)	.436
LCEA	14.93 (6.04 to 24.21)	.004	14.27 (5.01 to 23.59)	.006	0.66 (−2.37 to 3.81)	.620
HOAMS						
Labrum	12.95 (3.01 to 23.31)	.024	12.17 (0.37 to 22.40)	.040	0.78 (−1.20 to 5.44)	.426
Cartilage	13.22 (3.04 to 22.47)	.016	12.17 (1.33 to 22.19)	.028	1.05 (−1.38 to 5.12)	.412

[a]HOAMS, Hip Osteoarthritis MRI Scoring System; iHOT-33, 33-item International Hip Outcome Tool; LCEA, lateral center-edge angle; MRI, magnetic resonance imaging.
[b]Mean casual mediation effect.

TABLE 7
Linear Regression Model Examining Potential Variables Associated With Change in iHOT-33 Score From Baseline to 12 Months for Patients Undergoing Hip Arthroscopy and Personalized Hip Therapy[a]

Intervention: Potential Prognostic Indicator	Change in iHOT-33 Score at 12 mo,[b] Mean ± SD	*P* Value
Hip arthroscopy		
Surgical review panel score: satisfactory	0[c]	
Borderline	–5.83 ± −7.82	.460
Inadequate	–4.08 ± 9.36	.665
Ostectomy		
Femoral	16.45 ± 9.66	.096
Acetabular	–1.46 ± 6.53	.824
Labral repair	–4.50 ± 7.07	.528
Ligamentum teres debridement	8.03 ± 6.32	.211
Personalized hip therapy		
Treatment fidelity: satisfactory/unsatisfactory	–24.27 ± 9.36	.013

[a]iHOT-33, 33-item International Hip Outcome Tool.
[b]Adjusted for baseline iHOT-33 score.
[c]Reference category.

DISCUSSION

These exploratory secondary analyses of the Australian FASHIoN trial did not identify any moderators or mediators of change in hip-related QOL for patients with FAI syndrome being treated with hip arthroscopy or PHT. However, prognostic indicators that predicted clinical response regardless of intervention were identified. Access to the private health care system, a smaller baseline LCEA, and a worse baseline iHOT-33 score all predicted improvement in hip-related QOL. In the PHT group, unsatisfactory treatment fidelity was associated with deterioration in iHOT-33 score from baseline to 12 months. In the hip arthroscopy group, neither the intraoperative procedures performed nor the quality of surgery as determined by a surgical review panel was significantly associated with patient-reported changes.

Given the different mechanisms by which each treatment modality is postulated to help FAI syndrome, we hypothesized that participants with more severe bony morphology would obtain greater benefit from arthroscopy than PHT, although this was not borne out by the data. These analyses were exploratory in nature; thus, confirmation on larger data sets is required before negative results can be interpreted with certainty. It is possible that moderators were not detected because their effect size was too small to be detected with the available statistical power. The post hoc sensitivity analyses suggested that mediators or moderators with small effect sizes[9] may not have been reliably detectable with the statistical power available in this study. Although we measured a range of carefully chosen patient demographic factors, bony morphology measures, and structural features in this study, it is possible that unmeasured moderators exist. For instance, patients

who were most likely to benefit from physical therapy may have more substantial abnormalities in hip-related biomechanics; these may warrant investigation as potential moderators in future studies.

Of the prognostic indicators of iHOT-33 change identified in this study (health care system accessed, LCEA, and baseline iHOT-33 score), baseline iHOT-33 score explained the largest proportion of variance of change in iHOT-33 score (partial η^2 effect size = 0.376), even more so than treatment allocation (partial η^2 effect size = 0.366), as shown in the multiple-variable model in Table 2. Our finding that worse baseline iHOT-33 score predicted greater improvement in iHOT-33 score contrasts with previous hip arthroscopy studies, which found that worse patient-reported measures at baseline predicted a poorer clinical response.[38,39] An earlier study using the Australian FASHIoN trial data set[33] noted that baseline iHOT-33 score was most strongly associated with health care system accessed, which is likely associated with various patient demographic variables. Patients with worse baseline symptoms in other studies may have less patient-reported improvement secondary to patient demographic factors unmeasured in those studies. An alternative hypothesis is that this finding relates to a ceiling effect for the iHOT-33 outcome tool, although no such ceiling effect was identified in the tool's development and validation.[31] In the Australian FASHIoN trial cohort, no participants had an iHOT-33 score within the minimal clinically important difference (6.1 points[31]) of the maximum possible iHOT-33 score (100) at baseline, but 12 participants (7 arthroscopy, 5 PHT) did at 12-month follow-up. This raises the possibility that a ceiling effect may have contributed to some extent to this finding.

Health care system accessed explained a smaller proportion of the variance in change in iHOT-33 score (partial η^2 effect size = 0.041). Health care system accessed is likely a surrogate for unmeasured demographic differences, with previous research establishing differences between patients accessing these private and public health care systems in Australia.[12,22,49] Our analysis separately considered several demographic variables, such as BMI, sex, smoking status, and duration of symptoms, with no evidence that they predict change in hip-related QOL. However, additional variables unmeasured in this study likely differ between patients accessing public and private health care and may be the underlying cause of differing patient-reported outcomes—for instance, income, diet, or the presence of comorbidities such as mental health disorders, which have been associated with poorer outcomes for hip arthroscopy in previous studies.[10]

Higher LCEA predicted poorer outcomes in 2 previous cohort studies on hip arthroscopy[7,19]; our study suggested that higher LCEA predicted poorer outcome irrespective of treatment with hip arthroscopy or physical therapy. The partial η^2 effect size (0.216) indicated a medium effect of LCEA on change in iHOT-33 score.[9] A secondary analysis to explore the clinical implications of this finding by breaking LCEA into groups could not detect any statistically significant between-group differences (P = .056). The data revealed a general trend toward patients with large LCEA experiencing less clinical improvement (Figure 2), but this was not due to better/worse outcomes associated with a particular LCEA cutoff. Notably, only 2 participants in the Australian FASHIoN trial cohort had an LCEA <25°, meaning that no conclusions can be drawn about treatment outcomes for those with acetabular undercoverage. Larger data sets are needed to elucidate the implications of LCEA for clinical practice, as this data set was underpowered for LCEA subgroup analysis; thus, the finding must be interpreted cautiously. This could be a target for future studies on prognostic indicators of hip arthroscopy.

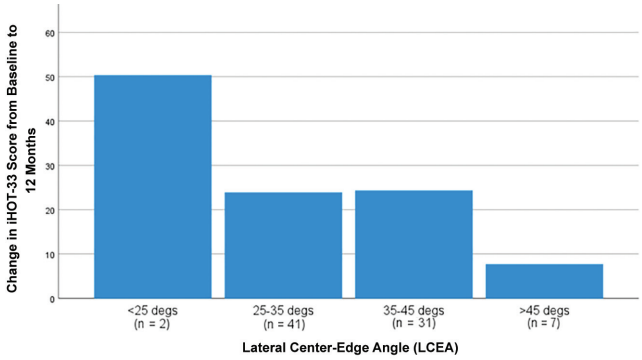

Figure 2. Change in 33-item International Hip Outcome Tool (iHOT-33) score by lateral center-edge angle.

Predictors of symptom change in FAI syndrome have been examined in the context of cohort studies of patients treated with hip arthroscopy. These studies and the meta-analyses combining them commonly revealed a poorer clinical response to be predicted by the presence of hip osteoarthritis, particularly full-thickness chondral damage, and older age.[27,28,35,42] Other variables associated with poorer outcomes less consistently across studies included female sex, higher BMI, and worse preoperative clinical scores.[27,35,45] No previous studies have investigated predictors of patient-reported change in the RCT setting or in patients undergoing physical therapist–led management. Our study did not find that the HOAMS for any osteoarthritis feature predicted poorer outcomes, such as cartilage scores and likewise dGEMRIC scores, likely owing to the strict eligibility criteria and relative homogeneity of trial participants in this regard. Patients with Tönnis grade >1 were excluded from the study, and just 2 participants (1 in each treatment group) had full-thickness chondral damage on baseline MRI analyses. Age, sex, and BMI were not implicated in patient outcomes in our study. Again, relatively small proportions of the Australian FASHIoN trial participants fell into at-risk groups identified in previous studies, with only 4% having BMI >30 and 11% aged >45 years.

Surprisingly, no significant mediators of change in hip-related QOL were identified in this study, despite analyses of MRI-measured change in bony morphology, structural damage, and cartilage health over 12 months. Although there was significant worsening of the maximum severity of cartilage lesions and labral damage in the arthroscopy group as compared with the PHT group—a finding

reported and discussed in the primary outcome publication[20]—this was not significantly associated with change in iHOT-33 score. Equally intriguing was the absence of association between surgical review panel score and effect of hip arthroscopy on change in iHOT-33 score. As with the negative findings for moderation analyses, it is possible that inadequate statistical power underlies these null findings. An alternative explanation is that nonspecific (placebo) effects may differ between hip arthroscopy and physical therapy, potentially obscuring the effects of mediators from being recognized. Sham-controlled trials in the future may aid by removing confounding from nonspecific effects, making mediators of change in hip-related QOL easier to identify.

Unsatisfactory treatment fidelity for the PHT program was associated with worse treatment response. There were 7 PHT participants with unsatisfactory treatment fidelity, all related to participant nonadherence: having fewer than the required 6 sessions (4 participants), receiving treatment extending beyond the maximum of 6 months (2 participants), and seeking additional unapproved treatments (1 participant underwent therapeutic ultrasound). Those participants who did not adhere to the PHT program likely did not feel that they were benefiting from the treatment; hence, it is unsurprising that they reported inferior changes in iHOT-33 scores. In some patients, nonadherence to physical therapy may occur because exercises cause aggravation of symptoms.

This study has strengths that warrant consideration. It utilized data from a well-designed pragmatic multicenter RCT with multiple validated imaging tools collected at baseline and follow-up. These enabled relatively comprehensive measurement of hip joint structural change from baseline to 12 months for moderator and mediator analyses. Furthermore, the statistical methods employed, including a penalized best subsets approach to multiple linear regression model selection, are appropriate in the setting of a relatively large number of candidate variables. This study also has important limitations. The trial was not powered for these secondary analyses, raising the distinct possibility of type II errors. In this context, the findings should be interpreted as hypothesis generating. Relatively short-term follow-up data (12 months) were analyzed in this study. As in any clinical trial, the participants may have characteristics different from those of the wider FAI syndrome population. The trial was thoroughly pragmatic, which inevitably entails some heterogeneity in delivery of the interventions, although this reflects the everyday reality of treatment for FAI syndrome, where different hip arthroscopy surgeons and physical therapists have slightly varying techniques and philosophies. The measurement of the dGEMRIC score at the chondrolabral junction and measurement of alpha angle from the 12- to 3-o'clock regions may not have captured all cartilage lesions and all cam morphology.

No moderators or mediators were identified for treatment of FAI syndrome with hip arthroscopy or physical therapy after 12 months. Patients who accessed the Australian private health care system, had smaller LCEAs, and had worse baseline iHOT-33 scores experienced greater improvement in hip-related QOL, irrespective of treatment allocation. Larger sham-controlled trials would be of benefit in the future, as these would remove potentially confounding nonspecific effects that may differ between hip arthroscopy and physical therapy, facilitating easier detection of mediators and moderators of symptom change.

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ACKNOWLEDGMENT

The protocol for the Australian FASHIoN trial was developed in association with the UK FASHIoN trial. We acknowledge the participants and staff who contributed their time and efforts to data collection.

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REFERENCES

1. Bastos RM, de Carvalho Júnior JG, da Silva SAM, et al. Surgery is no more effective than conservative treatment for femoroacetabular impingement syndrome: systematic review and meta-analysis of randomized controlled trials. *Clin Rehabil*. 2020;35(3):332-341.
2. Beck M, Kalhor M, Leunig M, Ganz R. Hip morphology influences the pattern of damage to the acetabular cartilage: femoroacetabular impingement as a cause of early osteoarthritis of the hip. *J Bone Joint Surg Br*. 2005;87(7):1012-1018.
3. Calcagno V, de Mazancourt C. glmulti: an R package for easy automated model selection with (generalized) linear models. *Journal of Statistical Software*. 2010;34(12):29.
4. Casartelli NC, Bizzini M, Maffiuletti NA, et al. Exercise therapy for the management of femoroacetabular impingement syndrome: preliminary results of clinical responsiveness. *Arthritis Care Res (Hoboken)*. 2019;71(8):1074-1083.
5. Casartelli NC, Valenzuela PL, Maffiuletti NA, Leunig M. Effectiveness of hip arthroscopy on treatment of femoroacetabular impingement syndrome: a meta-analysis of randomized controlled trials. *Arthritis Care Res (Hoboken)*. 2021;73(8):1140-1145.
6. Chahla J, Nwachukwu BU, Beck EC, et al. Influence of acetabular labral tear length on outcomes after hip arthroscopy for femoroacetabular impingement syndrome with capsular plication. *Am J Sports Med*. 2019;47(5):1145-1150.
7. Chandrasekaran S, Darwish N, Chaharbakhshi EO, et al. Minimum 2-year outcomes of hip arthroscopic surgery in patients with acetabular overcoverage and profunda acetabulae compared with matched controls with normal acetabular coverage. *Am J Sports Med*. 2017;45(11):2483-2492.
8. Chandrasekaran S, Vemula SP, Lindner D, et al. Preoperative delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC) for patients undergoing hip arthroscopy: indices are predictive of magnitude of improvement in two-year patient-reported outcomes. *J Bone Joint Surg Am*. 2015;97(16):1305-1315.
9. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. Lawrence Erlbaum Associates; 1988.
10. Dick AG, Smith C, Bankes MJK, George M. The impact of mental health disorders on outcomes following hip arthroscopy for femoro acetabular impingement syndrome: a systematic review. *J Hip Preserv Surg*. 2020;7(2):195-204.
11. Dickenson E, Wall PD, Robinson B, et al. Prevalence of cam hip shape morphology: a systematic review. *Osteoarthritis Cartilage*. 2016;24(6):949-961.
12. Duckett SJ. Private care and public waiting. *Aust Health Rev*. 2005;29(1):87-93.
13. Dwyer T, Whelan D, Shah PS, et al. Operative versus nonoperative treatment of femoroacetabular impingement syndrome: a meta-analysis of short-term outcomes. *Arthroscopy*. 2020;36(1):263-273.
14. Faul F, Erdfelder E, Buchner A, Lang A-G. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods*. 2009;41(4):1149-1160.
15. Ferreira GE, O'Keeffe M, Maher CG, et al. The effectiveness of hip arthroscopic surgery for the treatment of femoroacetabular impingement syndrome: a systematic review and meta-analysis. *J Sci Med Sport*. 2021;24(1):21-29.
16. Ganz R, Parvizi J, Beck M, et al. Femoroacetabular impingement: a cause for osteoarthritis of the hip. *Clin Orthop Relat Res*. 2003;417:112-120.
17. Griffin DR, Dickenson EJ, O'Donnell J, et al. The Warwick Agreement on femoroacetabular impingement syndrome (FAI syndrome): an international consensus statement. *Br J Sports Med*. 2016;50(19):1169-1176.
18. Griffin DR, Dickenson EJ, Wall PDH, et al. Hip arthroscopy versus best conservative care for the treatment of femoroacetabular impingement syndrome (UK FASHIoN): a multicentre randomised controlled trial. *Lancet*. 2018;391(10136):2225-2235.
19. Haefeli PC, Albers CE, Steppacher SD, Tannast M, Büchler L. What are the risk factors for revision surgery after hip arthroscopy for femoroacetabular impingement at 7-year followup? *Clin Orthop Relat Res*. 2017;475(4):1169-1177.
20. Hunter DJ, Eyles J, Murphy NJ, et al. Multi-centre randomised controlled trial comparing arthroscopic hip surgery to physiotherapist-led care for femoroacetabular impingement (FAI) syndrome on hip cartilage metabolism: the Australian FASHIoN trial. *BMC Musculoskelet Disord*. 2021;22(1):697.
21. Jacobs CA, Burnham JM, Jochimsen KN, et al. Preoperative symptoms in femoroacetabular impingement patients are more related to mental health scores than the severity of labral tear or magnitude of bony deformity. *J Arthroplasty*. 2017;32(12):3603-3606.
22. Jessup RL, Osborne RH, Beauchamp A, Bourne A, Buchbinder R. Differences in health literacy profiles of patients admitted to a public and a private hospital in Melbourne, Australia. *BMC Health Serv Res*. 2018;18(1):134.
23. Kapron AL, Aoki SK, Peters CL, Anderson AE. Subject-specific patterns of femur-labrum contact are complex and vary in asymptomatic hips and hips with femoroacetabular impingement. *Clin Orthop Relat Res*. 2014;472(12):3912-3922.
24. Klontzas ME, Karantanas AH. Greater trochanter pain syndrome: a descriptive MR imaging study. *Eur J Radiol*. 2014;83(10):1850-1855.
25. Kopec JA, Qian H, Cibere J, et al. Relationship between hip morphology and hip-related patient-reported outcomes in young and middle-aged individuals: a population-based study. *Arthritis Care Res (Hoboken)*. 2019;71(9):1202-1208.
26. Kraemer HC, Wilson GT, Fairburn CG, Agras WS. Mediators and moderators of treatment effects in randomized clinical trials. *Arch Gen Psychiatry*. 2002;59(10):877-883.

27. Kuroda Y, Saito M, Çınar EN, Norrish A, Khanduja V. Patient-related risk factors associated with less favourable outcomes following hip arthroscopy. *Bone Joint J*. 2020;102(7):822-831.
28. Kyin C, Maldonado DR, Go CC, et al. Mid- to long-term outcomes of hip arthroscopy: a systematic review. *Arthroscopy*. 2021;37(3):1011-1025.
29. Lansdown DA, Kunze K, Ukwuani G, et al. Pre-operative and post-operative alpha angles are significant independent predictors of patient-reported outcome measures at two years after hip arthroscopy. *Orthop J Sports Med*. 2018;6(7)(suppl 4):2325967118S2 325900174.
30. Mansell NS, Rhon DI, Meyer J, Slevin JM, Marchant BG. Arthroscopic surgery or physical therapy for patients with femoroacetabular impingement syndrome: a randomized controlled trial with 2-year follow-up. *Am J Sports Med*. 2018;46(6):1306-1314.
31. Mohtadi NG, Griffin DR, Pedersen ME, et al. The development and validation of a self-administered quality-of-life outcome measure for young, active patients with symptomatic hip disease: the International Hip Outcome Tool (iHOT-33). *Arthroscopy*. 2012;28(5):595-605.
32. Murphy LB, Helmick CG, Schwartz TA, et al. One in four people may develop symptomatic hip osteoarthritis in his or her lifetime. *Osteoarthritis Cartilage*. 2010;18(11):1372-1379.
33. Murphy NJ, Diamond LE, Bennell KL, et al. Which hip morphology measures and patient factors are associated with age of onset and symptom severity in femoroacetabular impingement syndrome? *Hip Int*. Published online August 23, 2021. doi:10.1177/11207000211038550
34. Murphy NJ, Eyles J, Bennell KL, et al. Protocol for a multi-centre randomised controlled trial comparing arthroscopic hip surgery to physiotherapy-led care for femoroacetabular impingement (FAI): the Australian FASHIoN trial. *BMC Musculoskelet Disord*. 2017;18(1):406.
35. Mygind-Klavsen B, Lund B, Nielsen TG, et al. Danish Hip Arthroscopy Registry: predictors of outcome in patients with femoroacetabular impingement (FAI). *Knee Surg Sports Traumatol Arthrosc*. 2019;27(10):3110-3120.
36. Nho SJ, Kymes SM, Callaghan JJ, Felson DT. The burden of hip osteoarthritis in the United States: epidemiologic and economic considerations. *J Am Acad Orthop Surg*. 2013;21(suppl 1):S1-S6.
37. Palmer AJR, Ayyar Gupta V, Fernquest S, et al. Arthroscopic hip surgery compared with physiotherapy and activity modification for the treatment of symptomatic femoroacetabular impingement: multicentre randomised controlled trial. *BMJ*. 2019;364:L185.
38. Philippon MJ, Briggs KK, Yen YM, Kuppersmith DA. Outcomes following hip arthroscopy for femoroacetabular impingement with associated chondrolabral dysfunction: minimum two-year follow-up. *J Bone Joint Surg Br*. 2009;91(1):16-23.
39. Philippon MJ, Schroder ESBG, Briggs KK. Hip arthroscopy for femoroacetabular impingement in patients aged 50 years or older. *Arthroscopy*. 2012;28(1):59-65.
40. Potter MQ, Wylie JD, Sun GS, Beckmann JT, Aoki SK. Psychologic distress reduces preoperative self-assessment scores in femoroacetabular impingement patients. *Clin Orthop Relat Res*. 2014;472(6):1886-1892.
41. Roemer FW, Hunter DJ, Winterstein A, et al. Hip Osteoarthritis MRI Scoring System (HOAMS): reliability and associations with radiographic and clinical findings. *Osteoarthritis Cartilage*. 2011;19(8):946-962.
42. Saadat E, Martin SD, Thornhill TS, et al. Factors associated with the failure of surgical treatment for femoroacetabular impingement: review of the literature. *Am J Sports Med*. 2013;42(6):1487-1495.
43. Serong S, Fickert S, Niemeyer P, et al. Outcome-affecting parameters of hip arthroscopy for femoroacetabular impingement with concomitant cartilage damage-data analysis from the German Cartilage Registry. *J Clin Med*. 2022;11(6):1532.
44. Simms L, Barraclough H, Govindan R. Biostatistics primer: what a clinician ought to know—prognostic and predictive factors. *J Thorac Oncol*. 2013;8(6):808-813.
45. Sogbein OA, Shah A, Kay J, et al. Predictors of outcomes after hip arthroscopic surgery for femoroacetabular impingement: a systematic review. *Orthop J Sports Med*. 2019;7(6):2325967119848982.
46. Tannast M, Mistry S, Steppacher SD, et al. Radiographic analysis of femoroacetabular impingement with Hip2Norm—reliable and validated. *J Orthop Res*. 2008;26(9):1199-1205.
47. Tingley D, Yamamoto T, Hirose K, Keele L, Imai K. Mediation: R package for causal mediation analysis. *J Stat Softw*. 2014;59(5):1-38.
48. Tönnis D, Heinecke A. Acetabular and femoral anteversion: relationship with osteoarthritis of the hip. *J Bone Joint Surg Am*. 1999;81(12):1747-1770.
49. Van Doorslaer E, Clarke P, Savage E, Hall J. Horizontal inequities in Australia's mixed public/private health care system. *Health Policy*. 2008;86(1):97-108.
50. Vap AR, Mitchell JJ, Briggs KK, McNamara SC, Philippon MJ. Outcomes of arthroscopic management of trochanteric bursitis in patients with femoroacetabular impingement: a comparison of two matched patient groups. *Arthroscopy*. 2018;34(5):1455-1460.
51. Wall PD, Dickenson EJ, Robinson D, et al. Personalised hip therapy: development of a non-operative protocol to treat femoroacetabular impingement syndrome in the FASHIoN randomised controlled trial. *Br J Sports Med*. 2016;50(19):1217-1223.
52. Westermann RW, Lynch TS, Jones MH, et al. Predictors of hip pain and function in femoroacetabular impingement: a prospective cohort analysis. *Orthop J Sports Med*. 2017;5(9):2325967117726521.