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BMJ Open

Protocol for the ARCR_Pred cohort-study: Swiss-wide multicenter evaluation and prediction of core outcomes in arthroscopic rotator cuff repair

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3 **1 Protocol for the ARCR_Pred cohort-study: Swiss-wide multicenter evaluation and**
4 **2 prediction of core outcomes in arthroscopic rotator cuff repair**
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7 87 prediction of core outcomes in arthroscopic rotator cuff repair
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15 91 **Protocol version** Version 2 (13.12.2019)
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25 96 University Clinic Balgrist, Zurich, Switzerland (UKB) are funding their own participation in the
26
27 97 project.
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32 99 **Roles and responsibilities**
33

34 100 LA and AM are the initiators and project leaders. LA, AM, HB, SA, DS and SH were involved
35
36 101 in the study design, which was reviewed and commented by principal investigators CC, GC,
37
38 102 HD, KE, MF, BJ, AL, BM, PM, CR, MS, MS, CS, TS, KW and MZ.
39

40 103 Preparation of the manuscript was done by LA, AM, SA and TS. HB, DS and SH edited and
41
42 104 critically revised the paper. All authors have read and approved the manuscript. LA is the
43
44 105 guarantor of the manuscript.
45

46 106 This is an investigator initiated project at the University Hospital of Basel. The principal
47
48 107 investigator and project leader (AM) is the official sponsor representative for the project and
49
50 108 was involved in all phases of the project from its conception to the current implementation
51
52 109 steps. The project initiators and project leaders (LA and AM) have ultimate authority over any
53
54 110 of the project activities.
55

56
57 111 A project scientific board (PSB) comprises the project leaders (LA and AM), project
58
59 112 investigators at each site (CC, GC, HD, KE, MF, BJ, AL, BM, PM, CR, MS, MS, CS, TS, KW
60

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2
3 113 and MZ), and project partners (SA, HB, DS and SH). The PSB shall meet at specific time
4
5 114 points during the study: before the study start, after completion of recruitment and the 12-
6
7 115 month follow-up, and at the end of the study. The agenda of these meetings will focus on
8
9 116 (however is not limited to) patient enrollment and the completion of follow-up examinations
10
11 117 and questionnaires, the documentation process in REDCap, data quality issues
12
13 118 (completeness and consistency), monitoring activities, adverse event assessment and
14
15 119 management, baseline patient description, ranking of prognostic factors for prognostic
16
17 120 models, progress of data analysis, publication strategy and decisions regarding data sharing.
18
19 121 Between these meetings, communication will be maintained between the project coordinating
20
21 122 team and investigators via various channels including emails, quarterly newsletters, phone
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23 123 calls and (video) conference calls as required.
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3 126 **Abstract**

4 127 **Introduction** In the field of arthroscopic rotator cuff repair (ARCR), reporting standards of
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6 128 published studies differ dramatically, notably concerning adverse events (AEs). In addition,
7
8 129 prognostic studies are overall methodologically poor, based on small datasets, and explore
9
10 130 only limited numbers of influencing factors. We aim to develop prognostic models for
11
12 131 individual ARCR patients, primarily for the patient-reported assessment of shoulder function
13
14 132 (Oxford Shoulder Score [OSS]) and the occurrence of shoulder stiffness 6 months after
15
16 133 surgery. We also aim to evaluate the use of a consensus Core Event Set (CES) for AEs and
17
18 134 validate a severity classification for these events, considering the patient's perspective.
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23 136 **Methods and analysis** A cohort of 970 primary ARCR patients will be prospectively
24
25 137 documented from several Swiss and German orthopedic clinics up to 24 months
26
27 138 postoperatively. Patient clinical examinations at 6 and 12 months will include shoulder range
28
29 139 of motion and strength (Constant Score). Tendon repair integrity status will be assessed by
30
31 140 ultrasound at 12 months. Patient-reported questionnaires at 6, 12 and 24 months will
32
33 141 determine functional scores (Subjective Shoulder Value, OSS), anxiety and depression
34
35 142 scores, working status, sports activities, quality of life (EuroQol EQ-5D-5L). AEs will be
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37 143 documented according to a CES. Prognostic models will be developed using an
38
39 144 internationally supported regression methodology. Multiple prognostic factors, including
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41 145 patient baseline demographics, psychological, socioeconomic and clinical factors, rotator cuff
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43 146 integrity, concomitant local findings, and (post)operative management factors will be
44
45 147 investigated.
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51 149 **Ethics and dissemination** This project contributes to the development of personalized risk
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53 150 predictions for supporting the surgical decision process in ARCR. The consensus CES may
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55 151 become an international reference for the reporting of complications in clinical studies and
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57 152 registries. Ethical approval was obtained on April 1st, 2020, from the lead ethics committee
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3 153 (EKNZ, Basel Switzerland; ID: 2019-02076). All participants will provide informed, written
4
5 154 consent before enrollment in the study.

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8 9 156 **Strengths and limitations of this study**

- 10
11 157 • Large prospective multicenter observation of routine care
- 12
13 158 • Assessment of patient-reported outcomes (PROMs)
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15 159 • Implementation of an international core outcome set of adverse events (CES)
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17 160 • Internationally supported methodology for prognostic model development
- 18
19 161 • Potential limited response to patient questionnaires at 24 months
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24 163 **Introduction**

25
26 164 Rotator cuff tears are one of the most common injuries of the shoulder joint, which may
27
28 165 cause pain and disability associated with severe restrictions in daily activities. Surgical repair
29
30 166 is indicated when nonoperative treatment fails or follows extended traumatic tears, notably
31
32 167 inactive patients without signs of advanced tendon degeneration or muscle fat infiltration ¹.
33
34 168 Clinical studies have demonstrated clinically-relevant improvement in shoulder function and
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36 169 quality of life after arthroscopic rotator cuff tear repair (ARCR) ²⁻⁵. The number of ARCRs has
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38 170 increased over the last two decades ^{6 7 8 9} due to several contributing factors such as an
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40 171 aging yet active population, improvements in operative repair techniques, and more liberal
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42 172 indications for ARCRs.

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47 174 Not all patients, however, benefit from ARCR ¹⁰. Patients may be affected by complications
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49 175 and/or adverse events (AEs) like persistent pain, shoulder stiffness, infection, neurological
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51 176 problems, and repair failures ^{11 12}. About 20% of patients may show, typically between 6 and
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53 177 12 months following ARCR, a persistent rotator cuff defect ¹³. Patients with healed tendons
54
55 178 may show better functional outcome after repair ^{2 14 15}. Postoperative shoulder stiffness, a
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57 179 major complication reported to occur in 1.5% to 11.1% of ARCRs ¹¹, leads to limitations in
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59 180 everyday activities, prolonged rehabilitation, and, in severe cases, to reoperation (capsular

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3 181 release) ¹⁶⁻¹⁸. Nonetheless, incident data on outcome and AEs are impaired by the
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5 182 heterogeneity in definition and reporting ^{13 19}.
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9 184 Valid and representative data on the safety and effectiveness of ARCR are nonexistent at the
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11 185 Swiss national level. However, such data is paramount for optimizing the indication and
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13 186 outcome of ARCR, and for benchmarking orthopedic clinics. Reporting standards are a
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15 187 prerequisite for outcome and safety data. Recently, a Core Outcome Set (COS) ²⁰ was
16
17 188 defined for shoulder disorders, which includes inner core domains of pain, physical function
18
19 189 and activities, global perceived effect (a person's assessment of their recovery or degree of
20
21 190 improvement), and AEs ^{21 22}. A Core Event Set (CES) was developed by international
22
23 191 consensus in ARCR ^{23 24} and lay the ground for the current project.
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26 192
27
28 193 Appropriate indication of ARCR and judgment on risks for AEs or unsatisfactory patient
29
30 194 outcomes rely on validated clinical prediction tools ^{25 26}, which are still sparse in the field of
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32 195 surgical repair of a rotator cuff tear. Currently existing models focus on early surgical repair
33
34 196 ²⁷, tendon healing ^{28 29} or shoulder functional outcomes ³⁰. A model for shoulder stiffness
35
36 197 included patients with various shoulder pathologies and surgeries ³¹. Furthermore, individual
37
38 198 outcome predictions in ARCR require the identification of relevant patient and management
39
40 199 factors. Several systematic reviews have highlighted the general lack of qualitative studies
41
42 200 focused on prognostic factors for ARCR outcomes ³²⁻³⁶. In addition, we have observed the
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44 201 substantial heterogeneity in terms of applied methodology, core outcomes and studied
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46 202 prognostic factors, where certain factors (e.g., age, tear size, muscle degeneration, smoking)
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48 203 are given greater focus over others (e.g., sex, traumatic onset). The reviews highlight the
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50 204 need for more robust prospective studies to include additional patient-reported outcomes in a
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52 205 multivariable context.
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207 **Objectives**

208 *The overall objective* is to establish a prospective cohort of patients undergoing ARCR with
209 standardized data collection and follow-up for the evaluation and prediction of targeted core
210 safety, and clinical and patient-reported outcome parameters that are to be routinely
211 collected in standard clinical care.

213 *The primary objective* is to develop predictive models for two core outcome parameters: 1)
214 the patient-reported Oxford Shoulder Score (OSS) functional outcome, and 2) the occurrence
215 of shoulder stiffness (primary safety event) as reported by patients and clinicians.

217 *Secondary objectives* are 1) to evaluate the content and applicability of the defined
218 consensus CES (i.e. ARCR CES 1.0)²³ in routine practice considering the patient's
219 perspective, 2) to quantify the incidence of AE up to 24 months after surgery (e.g., persisting
220 or worsening pain, recurrent rotator cuff (RC) defect), 3) to validate an adapted severity
221 classification for postoperative local AEs^{12,37}, and 4) to develop predictive models for other
222 clinically-relevant outcome parameters including patient-reported outcomes (e.g., perception
223 of improvement, return to work, return to sports, quality of life, satisfaction with surgery,
224 acceptability of symptom state), clinical outcomes (e.g., shoulder strength and motion) and
225 specific AEs (e.g. RC defect at 12 months).

227 **Methods and analysis**

228 *Study design and setting*

229 This is a prospective multicenter cohort study in patients undergoing ARCR with 17
230 participating orthopedic centers in Switzerland and one German center.

232 Several sub-projects, associated with the main ARCR cohort study, are planned and include
233 a systematic review of prognostic studies in ARCR, the application of the ARCR CES 1.0 for
234 AE documentation, and the application and validation of an AE severity classification

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3 2354 236 *Eligibility criteria*

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6 237 Adult patients diagnosed with a partial or full-thickness RC tear by magnetic resonance
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8 238 imaging (MRI), planned for a primary arthroscopic surgical repair, and giving their informed
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10 239 consent to participate in the cohort study will be included. Patients undergoing a specific
11
12 240 surgical procedure for irreparable tears (i.e. tendon transfer, subacromial spacer or superior
13
14 241 capsular reconstruction), revision operations, open or mini-open reconstructions will be
15
16 242 excluded. Patients unable to give written informed consent or attend clinics for follow-up
17
18 243 visits, not fluent in German, French, Italian, or English or pregnant females will be excluded.
19
20 244 Patients undergoing bilateral ARCR will only be included for their first intervention.
21
22

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24 24525 246 *Intervention*

26
27 247 Shoulder arthroscopies will be performed according to standardized clinic-specific and
28
29 248 international guidelines³⁸ in the context of routine care with patients in a beach-chair or
30
31 249 lateral decubitus position under general or local anesthesia. The variability in the repair
32
33 250 techniques used between clinics and surgeons will be documented. Typically, after the
34
35 251 diagnostic arthroscopy to assess the type of RC tear (partial or full-thickness tear and
36
37 252 involved tendons, tendon tear delamination, sign of tendon degeneration) and concomitant
38
39 253 injuries or lesions, the ruptured tendons are mobilized until they can be repositioned on the
40
41 254 original footprint with as little tension as possible. Tendon fixation may be performed using
42
43 255 one of multiple anchor and suture configurations according to the surgeon's decision. An
44
45 256 intervention at the biceps tendon is performed if any tendinopathy, or lesions to the superior
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47 257 labrum or biceps pulley system are observed. An anterolateral or lateral acromioplasty is
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49 258 performed at the surgeon's discretion, generally in the presence of a hooked-shaped
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51 259 acromion or a critical shoulder angle larger than 35°, respectively. Operative details,
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53 260 including additional concomitant procedures (acromioplasty, acromioclavicular joint
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55 261 resection, capsulotomy, and biceps tenotomy or tenodesis) and operation duration are
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57 262 recorded immediately after surgery. A standard 3-phase postoperative rehabilitation scheme
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3 263 is usually prescribed and will be documented in detail, including immobilization and passive
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5 264 mobilization in the first phase, active mobilization and coordination training in the second
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7 265 phase, followed by the third phase of specific progressive resistance exercises.
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10 267 *Outcomes*

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13 268 The *first primary outcome* is the patient-reported change in shoulder functional outcome
14
15 269 between baseline and 6 months postoperatively as measured with the Oxford Shoulder
16
17 270 Score (OSS).³⁹ The OSS is a condition-specific questionnaire developed for patients with a
18
19 271 degenerative or inflammatory state of the shoulder. It contains twelve items to be answered
20
21 272 by the patient independently, which deal with pain (degree, time point) and possible
22
23 273 handicaps in private and professional life. There are five categories of response for every
24
25 274 question, corresponding to a score ranging from 0 to 4. Scores are summed to give a single
26
27 275 score with a range from 0 (worst outcome) to 48 (best outcome). Transcultural validations of
28
29 276 this questionnaire for the German and Italian populations have been performed^{40 41} and are
30
31 277 validated for patient-based outcomes after RC repair⁴²⁻⁴⁴. While functional outcome at the
32
33 278 last 24-month follow-up is clinically relevant, the early 6-month primary time point is chosen
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35 279 because of the importance in early surgical recovery and rehabilitation, particularly when
36
37 280 considering the socioeconomic impact on professionally active patients⁴.
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41
42 282 The *second primary outcome* is the occurrence of shoulder stiffness within 6 months after
43
44 283 surgery: this event is poorly defined in the literature¹⁹. We formed a consensus definition of
45
46 284 shoulder stiffness among specialized shoulder surgeons in a Delphi survey, which describes
47
48 285 a postoperative restriction in passive shoulder motion diagnosed within 6 months after ARCR
49
50 286 in at least two of the motion planes of flexion, abduction and external rotation in 0° abduction.
51
52 287 Motion restriction is to be assessed separately for each plane according to specific threshold
53
54 288 criteria (flexion: total motion equal to or below 90° or glenohumeral motion equal to or below
55
56 289 80°; abduction: total motion equal to or below 80° or glenohumeral motion equal to or below
57
58 290 60°; external rotation in 0° abduction: glenohumeral motion equal to or below 20° or no more
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3 291 than 50% of the contralateral side value). In this project, we will identify cases of shoulder
4
5 292 stiffness based on our consensus definition as well as clinical records and reports from
6
7 293 clinicians and their patients.
8

9 294
10
11 295 Secondary outcomes will include: 1) local AEs according to the ARCR CES, in particular the
12
13 296 occurrence of recurrent defect of repaired tendon(s) at 12 months, when at least one
14
15 297 repaired tendon is diagnosed with a recurrent defect by ultrasound examination, persistent or
16
17 298 worsening pain, infection, any local event (composite outcome); 2) functional parameters of
18
19 299 the Constant score (CS)⁴⁵ at 6 and 12 months, shoulder strength (kg) in abduction at 6 and
20
21 300 12 months, patient-reported shoulder pain on the numeric rating scale (NRS) at 6, 12 and 24
22
23 301 months, patient-reported shoulder function: OSS at 6, 12 and 24 months, Subjective
24
25 302 Shoulder Value (SSV)⁴⁶ assessment at 6, 12 and 24 months; 3) general health and
26
27 303 socioeconomic parameters including patient-reported quality of sleep (NRS) at 6, 12 and 24
28
29 304 months⁴⁷, return to work, change of working condition within 6, 12 and 24 months, level of
30
31 305 depression and anxiety at 6, 12 and 24 months based on Patient-Reported Outcomes
32
33 306 Measurement Information System (PROMIS) scores^{48 49}, patient perceived shoulder
34
35 307 improvement, acceptability of own symptom state⁵⁰, quality of life (utilities and general health)
36
37 308 at 6, 12 and 24 months using the European Quality of Life 5 Dimensions 5 Level
38
39 309 questionnaire (EQ-5D-5L), patient satisfaction with the surgical outcome at 12 and 24
40
41 310 months; 4) safety outcome assessment, occurrence of all AEs reported by clinicians and
42
43 311 patients (including non-local AEs within 6 months after surgery), final independent surgeon
44
45 312 and patient-rated assessment of AEs according to perceived severity (rating scale from 0 [no
46
47 313 complication] to 100 [death]⁵¹), comprehensive Complication Index⁵¹ considering all AEs that
48
49 314 occurred within 6 months after surgery.
50
51
52

53 315
54
55 316 Shoulder ultrasound examinations will be performed at 12 months by experienced clinicians
56
57 317 independent of the operating surgeons. The repair integrity will be graded according to the
58
59 318 Sugaya classification (where grade 4 or 5 defines the occurrence of a recurrent effect)^{52 53}.
60

1
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3 319 Other ultrasound parameters include the location of the recurrent defect (at the footprint |
4
5 320 medial cuff failure), long biceps tendon status, signs of anchor displacement, and location
6
7 321 and signs of suture cut-through.
8

9 322

10
11 323 *Participant timeline*

12
13 324 Local investigators will identify patients who meet the eligibility criteria. Patient enrollment
14
15 325 started on June 1st, 2020 and is planned for a maximum period of 12 months. Patients will
16
17 326 complete a preoperative evaluation no more than 2 months before surgery. Follow-up
18
19 327 assessments will be performed at 6 weeks (+/- 1 week), and 6 (+/- 1 month), 12 (+/- 1 month)
20
21 328 and 24 months (+/- 2 months) postoperatively. At the final 24-month time point, only patient
22
23 329 self-reporting assessments will be documented (Figure 1).
24

25 330

26
27 331 *Baseline prognostic factors*

28
29 332 Various baseline parameters, operative details, and postoperative management variables are
30
31 333 known or suspected to influence ARCR outcomes³²⁻³⁶.
32

33 334

34
35
36 335 The following patient-related factors will be recorded: patient demographics [year of birth for
37
38 336 age, sex], socioeconomic parameters [nationality, marital status, the highest level of
39
40 337 education, employment status, last occupational position, daily physical workload], dominant
41
42 338 side, smoking & drinking status, general physical and mental health [Body Mass Index (BMI)
43
44 339 and obesity, American Society of Anesthesiologists (ASA) classification, comorbidities (e.g.
45
46 340 diabetes), concomitant medication, level of depression and anxiety (PROMIS Depression
47
48 341 and Anxiety Short Form 4a)^{48 49}, quality of life (EQ-5D-5L)⁵⁴.
49

50 342

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52
53 343 Disease-related factors are shoulder clinical examinations [pain level on a numeric rating
54
55 344 scale (NRS), range of motion, muscle strength, Constant Score⁴⁵], patient-reported shoulder
56
57 345 function (see outcome measures), radiograph parameters [Critical Shoulder Angle⁵⁵,
58
59 346 acromiohumeral distance⁵⁶], MRI or arthro-Computer Tomography (CT) parameters
60

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2
3 347 [supraspinatus muscle atrophy⁵⁷, tangent sign⁵⁸, grade of fatty infiltration^{59 60}], medical
4
5 348 history [cause of injury (trauma event), symptom duration, previous interventions (operation
6
7 349 and timing of surgery), actual medication, and the extent of physical therapy].
8

9 350
10
11 351 Rotator cuff integrity and concomitant local findings. The RC tear will be determined by MRI
12
13 352 (or arthro-CT) and confirmed intraoperatively: tear size: location (involved tendons) and
14
15 353 grading (partial / complete), tendon retraction grade⁶¹ and tear sagittal size⁶², status of the
16
17 354 biceps tendon, additional intraoperative observation of concomitant local injuries [Superior
18
19 355 Labrum from Anterior to Posterior (SLAP) lesion, Humeral Avulsion Glenohumeral Ligament
20
21 356 (HAGL), Bankart lesion, humeral and glenoid-side chondral lesions].
22

23 357
24
25 358 Operative details and postoperative management: type of ARCR procedure [use of anchors,
26
27 359 suture techniques], augmentation techniques [e.g. platelet concentrates, scaffolds, ...]⁶³,
28
29 360 additional concomitant treatment [acromioplasty, acromioclavicular joint resection,
30
31 361 capsulotomy, biceps tenotomy or tenodesis, treatment of SLAP lesion], operation duration,
32
33 362 duration of hospital stay, postoperative management [immobilization position and duration,
34
35 363 pain medication [e.g. using non-steroidal anti-inflammatory drugs], timing of passive and
36
37 364 active shoulder motion, physiotherapy and muscle training].
38
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40 365
41
42 366 *Adverse event documentation and assessment process*
43
44 367 Operating surgeons will report the occurrence of any intraoperative AE on the operation
45
46 368 form. The occurrence of postoperative local AEs within 24 months will be reported by
47
48 369 investigators at the clinical examination and by patients on the questionnaires. The
49
50 370 occurrence of postoperative non-local AEs that are unrelated to the operation will be
51
52 371 documented in a similar manner, however only within 6 months after surgery. An AE form
53
54 372 was developed according to the ARCR CES 1.0²³. Each AE documentation will be structured
55
56 373 after Audigé et al.⁶⁴ and includes the date/period of occurrence [intra- / postoperative], the
57
58 374 affected body location [local at the operated shoulder / non-local], the event group and
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3 375 specification, applied health-related intervention(s) [operative / nonoperative procedure(s)],
4
5 376 its outcome at the time of reporting (or end of the study), and the assessment of the event
6
7 377 [causal factor(s) / severity grade / seriousness]. Severity grading will be made according to
8
9 378 existing and adapted systems for intraoperative^{65 66} and postoperative^{12 37} complications.
10
11 379 The documentation of AEs will be checked for completeness and consistency remotely as
12
13 380 well as on-site by reviewing selected patient files as part of the monitoring plan. A review
14
15 381 committee (LA, AM, TS, HD and DS) will assess all events reported by surgeons and
16
17 382 patients, and generate queries to the respective sites as required.
18

19 383
20
21 384 Fully documented local events, including their treatment, outcome and possible causative
22
23 385 factors, will be formulated in layman's terms and sent back to the affected patients, so that
24
25 386 they can confirm and validate collected AE data as well as assess their severity on a visual
26
27 387 analogue scale from 0 (not at all severe) to 100 (extremely severe). This subsequent rating
28
29 388 will also be performed by their treating surgeon and four other randomly-selected surgeons
30
31 389 involved in the project, blinded from the original severity grading.
32
33

34 390

35 391 *Sample size determination*

36 392 For sample size calculation, we set up a simulation study and used multiple regression to
37
38 393 predict the change in OSS within 6 months for the most important prognostic factors. The
39
40 394 prognostic factors were derived from an existing ARCR local registry⁶⁷ and include age, sex,
41
42 395 body mass index/obesity status, tendon quality/degeneration, and RC severity³²⁻³⁶. We
43
44 396 accounted for the type I error at 5% for statistical significance and the type II error set at 20%
45
46 397 for 80% statistical power⁶⁸. Two thousand replications were done, and the p-values were
47
48 398 recorded to calculate the mean significance for each of the prognostic factors to reach a
49
50 399 minimum of 80% statistical power. This approach led to a sample of 920 patients.
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52

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55 401 For the second primary outcome of shoulder stiffness, we accounted for a minimum of ten
56
57 402 events per variable to allow for the inclusion of a maximum of ten predictors into the model⁶⁹
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3 403 ⁷⁰. The estimated event rate for shoulder stiffness from our pilot data set was 8.3%, which,
4
5 404 according to our experience, might reflect an underestimation of the true rate ¹⁷. Therefore, a
6
7 405 10% stiffness rate was assumed, which resulted in a sample size calculation of 900 patients.
8
9 406 The higher resulting number determines the final number of patients to be recruited.
10
11 407 Therefore, 920 patients will be included with an additional 50 patients (i.e. 970 patients) due
12
13 408 to the anticipated maximum dropout rate of 5% at 6 months (based on personal experience).
14

15 409

17 410 *Recruitment*

19 411 Study sites and local investigators were selected based on their expertise in ARCR with
20
21 412 support by the shoulder and elbow expert group of Swiss Orthopaedics. Each site was
22
23 413 visited by the project leaders to assess the adequacy of local clinical and research settings
24
25 414 for the project as well as to ensure prior interest and commitment. The number of included
26
27 415 sites was determined based on the reported estimate of the number of ARCR patients that
28
29 416 could be realistically enrolled within one year from each site, and included an allowance for
30
31 417 overestimation (i.e. all sites together estimated that they could recruit up to 40% more than
32
33 418 the expected 970 patients within one year).

36 419 Patients who are enrolled after signing an informed consent form are definitively recruited for
37
38 420 the project after documentation of baseline parameters (clinical examinations and patient
39
40 421 questionnaires) and confirmation of ARCR during surgery. A recruitment curve is prepared
41
42 422 every 2 weeks and sent to the project sites along with a recruitment table presenting the
43
44 423 performance of each site. Sites that are unable to recruit the expected number of patients
45
46 424 within the first 3 months will be considered for exclusion from the project and replaced by
47
48 425 additional sites if the estimated total duration of patient enrollment is delayed for more than 3
49
50 426 months.

52 427

55 428 *Data collection methods*

57 429 Data are collected on electronic or paper-based case report forms or patient questionnaires.
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59 430 Project parameters and used instruments are presented in previous sections of this protocol.
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3 431 A training video was prepared for the collection of CS data ⁴⁵. For the measurement of
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5 432 shoulder muscle strength, several devices were permitted, i.e. IsoForceControl® (MDS
6
7 433 Medical Device Solution, Oberburg, Switzerland), Mark-10 Force Gauge (Mark-10
8
9 434 Corporation, Copiague, USA) as well as hand-held (Lafayette Instrument Co., Lafayette,
10
11 435 USA) or MicroFET 2 (Hoggan Scientific, Salt Lake City, USA) dynamometers; the use of a
12
13 436 spring balance was not allowed.

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15 437
16
17 438 Patient clinical examinations, including baseline imaging assessments, are performed at
18
19 439 each site by experienced clinicians (who may be assisted by locally-trained research staff)
20
21 440 and documented primarily on paper-based case report forms. Baseline MRI and radiographs
22
23 441 are coded and centralized at the University of Basel to ensure data quality control. Operative
24
25 442 data are collected electronically by the respective surgeons shortly after surgery. Patients
26
27 443 complete questionnaires in their preferred language, which is limited to German, French,
28
29 444 Italian or English, either electronically after invitation, by email or on a tablet computer at the
30
31 445 site, or otherwise on paper. AEs are documented electronically by the respective surgeons
32
33 446 with support from their research staff. Data collected on paper forms are entered
34
35 447 electronically at each site or at a central location at the University of Basel based on the
36
37 448 agreement made with each site.

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41 42 450 *Data monitoring*

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44 451 A central project data manager will perform data quality control on all collected data. A
45
46 452 flowchart will be created to describe the number of consecutively recruited patients who had
47
48 453 an RCR by arthroscopic procedure or had a conversion to an open procedure, and who
49
50 454 completed follow-up clinical and imaging examinations as well as self-reported outcome
51
52 455 questionnaires. The reasons for patient dropout and loss to follow-up status will be monitored
53
54 456 and described. All recorded study parameters will be described using standard descriptive
55
56 457 statistics; continuous variables will be presented as means with standard deviations and
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3 458 categorical variables as counts with percentages. The variability of data between clinics will
4
5 459 be explored to support the identification of outlier data.

6
7 460 Weekly site-specific reports, including the patient enrollment list, expected follow-up timing
8
9 461 and identification of missing, erroneous or inconsistent data, are sent to the respective local
10
11 462 project staff. Data-related queries will be resolved remotely or by on-site monitoring visits
12
13 463 before the final analyses are performed.

14
15 464 There is no plan for auditing project conduct other than via reporting at the annual meetings
16
17 465 of the project scientific board.

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20
21 467 *Data management*

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23 468 Study data will be stored using the REDCap web-based electronic data capture system^{71 72}
24
25 469 on a server that is hosted at Schulthess Klinik. REDCap conforms with Good Clinical
26
27 470 Practice guidelines that provide required features for data protection and integrity, e.g.,
28
29 471 password-protected access and change tracking.

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31 472

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34 473 Study data will be coded and exported from the REDCap system into Stata software
35
36 474 (StataCorp LP, College Station, USA) for statistical analyses. Data transformations and
37
38 475 analyses will be primarily implemented using Stata and fully documented within Stata
39
40 476 programming files. Data subsets will be prepared for analyses using alternative software
41
42 477 (e.g. R for prediction models) as appropriate.

43
44 478

45
46 479 All patients with an intraoperatively confirmed RC tear and operated by ARCR will be
47
48 480 included in the analyses. Existing missing data will be imputed if the number of missing data
49
50 481 is non-negligible or could potentially bias the results and conclusions.

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54 483 *Systematic review of prognostic factors*

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56 484 A systematic review of prognostic factors for ARCR outcomes is implemented (PROSPERO
57
58 485 registration ID: CRD42020199257). Briefly, literature from 2014 to 2020 will be checked to

1
2
3 486 identify longitudinal studies including patients diagnosed with a RC tear. These studies
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5 487 should report the effect of at least one factor on one of the following outcomes: shoulder
6
7 488 stiffness, RC tear repair integrity, and shoulder function. Data extraction will follow a pre-
8
9 489 defined template and the collected data will be stored within a separate database using
10
11 490 REDCap. Data from different studies will be described and may be synthesized depending
12
13 491 on the data type and heterogeneity. These data will be used to generate a list of factors most
14
15 492 likely to influence our project outcomes and therefore, should be considered for inclusion in
16
17 493 the predictive model development process.

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19 49420
21 495 *Predictive model development*

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23 496 To develop the predictive model(s), the seven steps proposed by Steyerberg et al.^{73 74} will be
24
25 497 used. The steps comprise: 1) consideration of the research question and initial data
26
27 498 inspection, 2) coding of the predictors, 3) model specification, 4) model estimation, 5)
28
29 499 evaluation of model performance, 6) internal validation, and 7) model presentation.
30
31 500 Depending on the type of outcome, different models will be fitted and evaluated, i.e. multiple
32
33 501 regression models for the change in OSS at 6 months and multivariable logistic regression
34
35 502 models for shoulder stiffness. Model diagnostics will be performed for all models to check the
36
37 503 underlying assumptions.

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40
41 505 The prediction of the model(s) will be based on the baseline, operative, and postoperative
42
43 506 management variables. Firstly, a subset of the potential prognostic factors will be defined
44
45 507 based on whether it is thought to be most predictive. The subset will be selected separately
46
47 508 for each outcome by the Delphi method among the investigators, whereby the factors will be
48
49 509 noted for their known or potential prognostic value on a 5-point Likert scale from 1 (not
50
51 510 important) to 5 (extremely important). These factors, with the highest mean score among
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53 511 investigators, will form the subset.

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3 513 We will then use criterion-based procedures (e.g. Akaike Information Criterion [AIC] or
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5 514 adjusted R^2) to select the best set of predictors for the continuous outcome(s) and for the
6
7 515 binary outcome, we will use the area under receiving operating characteristics curve (AUC).
8
9 516 To assess the predictive performance of the final models as well as the updated version of
10
11 517 the prediction models, the calibration plot and discrimination measures will be used. Thereby,
12
13 518 apparent performance will be evaluated on the respective development data, and internal
14
15 519 validated performance will be determined by bootstrapping. Independent external validation
16
17 520 will be estimated by applying the resulting models from the development data set in the
18
19 521 respective validation data sets. The resulting models will be used to predict the change of
20
21 522 outcome value (i.e. OSS in 6 months) and assess whether a patient will experience the event
22
23 523 (i.e. shoulder stiffness).
24

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28 525 If we observe missing data, then missing data imputation will be performed using a method
29
30 526 that allows for uncertainty in the imputed values (e.g. multiple imputations using chained
31
32 527 equation ⁷⁵). We will account for the clustering of records within clinics as appropriate.
33

34 528

35 36 529 *Adverse events*

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38 530 Occurring AEs other than those listed in the CES as well as events occurring outside the
39
40 531 periods defined by the core set will be analyzed separately for consideration of clinical
41
42 532 relevance. This analysis will be made by the review committee and project scientific board
43
44 533 (PSB) comprising all local project leaders (principal investigators). Recommendations for
45
46 534 change of the ARCR CES 1.0 by the PSB will be formulated.
47

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51 536 The incidence of AEs, specific individual events and groups of events defined within the
52
53 537 ARCR CES 1.0 up to 24 months postoperatively will be displayed as the frequency of
54
55 538 patients with an event relative to the number of patients observed, reported together with its
56
57 539 95% Wilson confidence interval. These results will be presented in a summary table together
58
59 540 with the absolute frequency. Further details on the period of occurrence will be given by

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2
3 541 stratifying for the time point of event occurrence. We will also stratify AEs according to their
4
5 542 severity level and patient relevance. Validation of the postoperative local AE severity
6
7 543 classification system will be implemented using previously used methods ^{76 77}.

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9 544

10 545 *Patient and public involvement*

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12
13 546 No patient or member of the public was involved in the design of this cohort study protocol.
14
15 547 Enrolled patients will contribute to the evaluation and validation of documented AEs and their
16
17 548 severity grading, therefore to a potential revision of the ARCR CES. We are planning to
18
19 549 present initial results to patients and the public, and get feedback for further analyses and
20
21 550 future model development as well as documentation system in ARCR.

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25 552 **Ethics and dissemination**

26 553 *Research ethics approval*

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30 554 Ethical approval was obtained on April 1st 2020 from the lead ethics committee (EKNZ, Basel
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32 555 Switzerland; ID: 2019-02076).

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34 556

35 557 *Protocol amendments*

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38 558 Minor protocol amendments, e.g. database production changes to facilitate monitoring
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40 559 processes or improve outcome assessment by questionnaire, are fully documented. Major
41
42 560 amendments, e.g. changes to the patient information sheet and consent form, change of a
43
44 561 local project leader or the inclusion of a new project site, will be submitted for approval by the
45
46 562 lead ethics committee as required.

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50 564 *Consent or assent*

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53 565 All participants will provide informed written consent prior to being enrolled into the study.
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55 566 The English version of the informed consent form used at the University Hospital of Basel is
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57 567 available as Supplement file 1.

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2 569 *Confidentiality*
3

4 570 Project data will be handled with utmost discretion and can only be accessed by authorized
5
6 571 personnel as outlined by a study delegation list created for each project site. Patient data will
7
8 572 be coded, i.e. identified by a unique participant number. A participant identification list will be
9
10 573 managed and kept in a place (an electronic folder or paper-based form) only accessible to
11
12 574 authorized staff at each site.

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14
15 575 The project leader affirms and upholds the principle of each patient's right to privacy and that
16
17 576 they shall comply with applicable privacy laws. In particular, anonymity of all patients shall be
18
19 577 guaranteed when presenting the data at scientific meetings or publishing them in scientific
20
21 578 journals.

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23 579

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25 580 *Declaration of interests*
26

27 581 None declared.
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32 583 *Access to data*
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34 584 Project data will be shared at the end of the analysis process by the PSB. The Department of
35
36 585 Clinical Research (German Departement Klinische Forschung, DKF) at the University
37
38 586 Hospital of Basel will act as an independent data access committee, and will store the data
39
40 587 at the time of publication on secure servers, maintained and backed-up by the Information
41
42 588 and Communication Technology department at the University Hospital of Basel. Researchers
43
44 589 who wish to reuse data will be able to submit a project synopsis to the DKF at
45
46 590 dkf.unibas.ch/contact. A data-sharing statement referring researchers to the DKF for data
47
48 591 access will be disseminated in the publications. Metadata describing the type, size and
49
50 592 content of the data sets will be shared along with the study protocol on the Harvard
51
52 593 Dataverse repository available online (<https://dataverse.harvard.edu/>). Additionally, the case
53
54 594 report forms will be uploaded on a medical data models portal ([https://medical-data-](https://medical-data-models.org/)
55
56 595 [models.org/](https://medical-data-models.org/)) and all variables will be annotated by their Unified Medical Language System
57
58 596 Concept Unique Identifier to improve accessibility to other clinicians.
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3 5974 598 *Dissemination policy*

599 This project will lead to multiple open-access, peer-reviewed scientific publications, which will
600 be prepared according to international standards (e.g. the STROBE statement⁷⁸ for cohort
601 studies; TRIPOD⁷⁹ statements for prognostic studies; PRISMA⁸⁰ statement for systematic
602 reviews). Publication authorship will regulated according to the guidelines of the Swiss
603 Academies of Arts and Sciences⁸¹. Results will be submitted for presentation at national and
604 international conferences. In addition, lay summary results will be developed and made
605 available for patients and the public.

606

607 *Scientific relevance and broader impact*

608 This project initiates the development of personalized risk predictions to support the surgical
609 decision process in ARCR. The consensus CES may become an international reference for
610 the reporting of complications in clinical studies and registries, and may therefore provide a
611 solid metric for the documentation of surgical safety in ARCR. Methodological insight gained
612 from this project will be easily transferable to similar initiatives and thus, may foster the
613 realization of other cohorts on safety and effectiveness outcome in shoulder surgery (e.g.
614 arthroplasty) and orthopedics in general.

615

616 For patients affected by RC tears and their surgeons, this study will be the first to provide
617 solid data on the incidence of patient-validated AEs and other core outcomes up to two years
618 after surgical repair based on international consensus COS and CES. This study will allow
619 the investigation of a comprehensive list of potential prognostic factors to generate predictive
620 models for these core outcomes and hence, offer personalized health information to support
621 future patients and surgeons in the decision process for surgery. Outcome predictors and
622 risk calculators are increasingly being developed in numerous medical fields including
623 surgery and orthopedics, and they are in development in the field of ARCR.

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2
3 625 This study will assess the structure and content of the ARCR CES and consolidate its validity
4
5 626 in capturing unfavorable events of importance to both patients and surgeons; considering the
6
7 627 patient's perspective is an essential step in the development of a COS. Furthermore, the
8
9 628 validation of an adapted severity classification of AEs in this study will provide an essential
10
11 629 system for assessing surgical morbidity in orthopedics. We expect that the ARCR CES and
12
13 630 the event severity classification will become international standards for the reporting of
14
15 631 ARCR AEs in clinical studies and registries, and therefore provide a solid metric for the
16
17 632 documentation of surgical safety in ARCR.

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19 633
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21 634 This study fosters the enterprise in developing a Swiss-wide registry of ARCR, which will
22
23 635 allow the ongoing evaluation and prediction of targeted core safety, clinical and patient-
24
25 636 reported outcomes. The identification of factors mostly associated with relevant outcomes
26
27 637 will facilitate a lean and straightforward documentation process for ARCR patients in
28
29 638 Switzerland and abroad.

30 639

31 32 640 **Acknowledgments**

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34
35
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37
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39
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43
44 645 proofreading.

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3 916 **Figure legend**

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7 918 **Figure 1:** Flowchart of study procedures

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9 919 w = week; mo = month; FU = follow-up; MRI = Magnetic Resonance Imaging; CT = Arthro-
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11 920 Computer Tomography (*if MRI not possible); Motion = Shoulder range of motion; CS =
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13 921 Constant Score; RC = Rotator Cuff; AE = Adverse Event; Rehab. = recall on postoperative
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15 922 rehabilitation; DE = German; FR = French; IT = Italian; EN = English; NRS = Numeric Rating
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17 923 Scale; OSS = Oxford Shoulder Score; SSV = Subjective Shoulder Value; EQ-5D-5L =
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19 924 European Quality of Life 5 Dimensions 5 Level questionnaire; CES = Core Event Set; AE
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21 925 survey = surgeons and patients survey regarding AE severity (sev)

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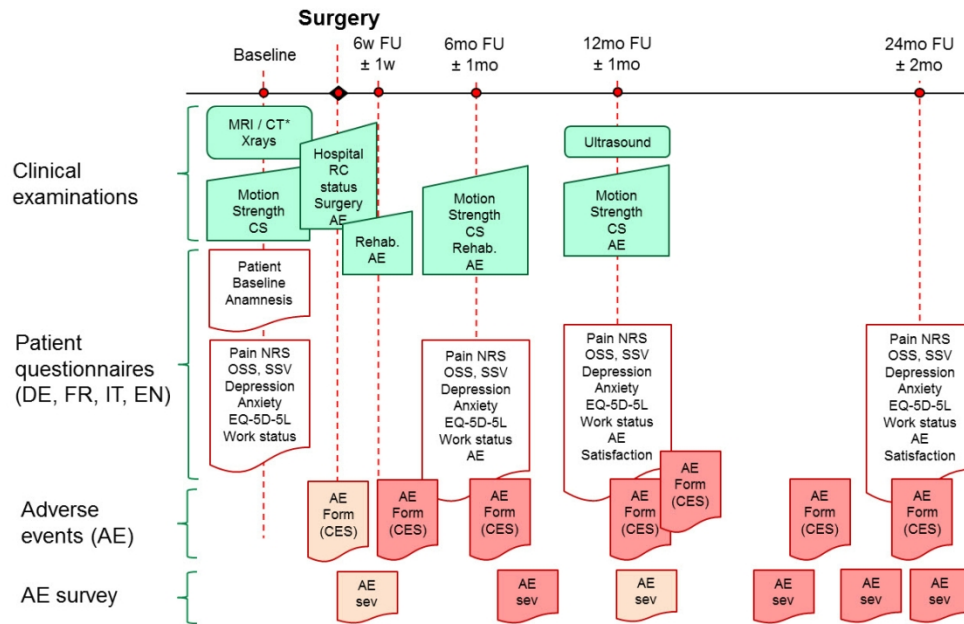


Figure 1: Flowchart of study procedures

w = week; mo = month; FU = follow-up; MRI = Magnetic Resonance Imaging; CT = Arthro-Computer Tomography (*if MRI not possible); Motion = Shoulder range of motion; CS = Constant Score; RC = Rotator Cuff; AE = Adverse Event; Rehab. = recall on postoperative rehabilitation; DE = German; FR = French; IT = Italian; EN = English; NRS = Numeric Rating Scale; OSS = Oxford Shoulder Score; SSV = Subjective Shoulder Value; EQ-5D-5L = European Quality of Life 5 Dimensions 5 Level questionnaire; CES = Core Event Set; AE survey = surgeons and patients survey regarding AE severity (sev)

342x220mm (96 x 96 DPI)

Supplement file 1

Article title Protocol for the ARCR_Pred cohort-study: Swiss-wide multicenter evaluation and prediction of core outcomes in arthroscopic rotator cuff repair

Journal name BMJ Open Access

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* Members of the ARCR_Pred study group are listed in the main publication of this project protocol.

Patient information sheet and informed consent form (English version) for the project site “University Hospital of Basel” (USB)

Engl. Surgical safety and effectiveness in orthopaedics: evaluation of an international consensus core set of adverse events in arthroscopic rotator cuff repair

This project has been organised by: PD Dr. Andreas Müller (project leader; Deputy Consultant of Orthopaedics, Shoulder/Elbow team leader, Orthopaedic and Traumatology Department, University Hospital of Basel) and Prof. Dr. Laurent Audigé (project manager; Research Associate, Orthopaedic and Traumatology Department, University Hospital of Basel and Head of Research Group Upper Extremities, Department of Research and Development, Schulthess Clinic, Zurich)

Sponsor: University Hospital of Basel, PD Dr. Andreas Müller, Deputy Consultant of Orthopaedics and Traumatology

Dear Sir / Madam,

We would like to ask you if you are interested in participating in a research project. The planned project is first presented as a short summary in the table provided below followed by a more detailed description.

Summary of the project

1	<p>Aim of the project The research project will investigate how easily the most important results are predicted following surgical interventions to treat tendinosis (= rotator cuff tears) of the shoulder muscles. In order to do this, we will use and assess a predefined set of adverse events (such as frozen shoulder or persistent pain) in practice.</p>
2	<p>Choice You are an adult suffering from tendinosis of the shoulder muscles, which can be treated with an initial, minimally invasive (i.e. arthroscopic) surgical intervention. That is why we are sending you this information leaflet.</p>
3	<p>General information about the project The collection of clinical data following surgical interventions is very important, and helps to support an established decision-making process within the orthopaedic field. We are carrying out this project so that we can better evaluate and predict the results following the repair of shoulder tendinosis. This evaluation is being carried out on a representative number of male and female patients in Switzerland. Patient safety is essential here. A list of possible adverse events following the arthroscopic intervention was recently defined by a group of more than 80 experts in the field. We would now like to better understand the development of these adverse events from the patient's point of view.</p>
4	<p>Procedure This project will last four years. In total, 970 patients from various clinics in Switzerland and one in Germany will be included in the study within the first year. Various examinations (e.g. measurements of range of motion and strength) will be carried out in the clinic before the operation (= preoperative) and then at the 6- and 12-month postoperative time points. At these times and at 2 years post-surgery, you will receive a questionnaire to complete. We will use ultrasound to check how the tendon is healing twelve months after the operation. Any adverse events will be evaluated independently by the doctor and the patient in question.</p>

5	<p>Usefulness You will gain no personal benefit from participating in the project. However, the results could be important to others who have the same condition.</p>
6	<p>Rights You decide voluntarily whether you want to participate in this project or not. Your decision does not affect your medical treatment/care and you do not have to justify it.</p>
7	<p>Duties If you participate, we ask you to adhere to certain requirements (e.g. attending visits and completing the questionnaires).</p>
8	<p>Risks You are not exposed to any additional risk by participating in the project.</p>
9	<p>Outcomes You will be informed of new results during the project. We will promptly inform you of any additional findings (known as incidental findings) that are detected during the regular study examinations, which may affect your health directly. Any further course of action will then be discussed in detail with you.</p>
10	<p>Confidentiality of data and samples We collect your personal and medical data from you. The Swiss National Science Foundation supports the exchange and reuse of research data. The data will be used for other projects if you give your separate consent. We comply with all legal data protection regulations. All parties involved are bound by confidentiality.</p>
11	<p>Withdrawal You can withdraw from the project at any time and no longer participate. The data collected so far are still being evaluated.</p>
12	<p>Indemnity You will not receive any compensation for participating in the study. Neither your health insurance provider nor you will incur any additional costs from your participation in the study.</p>
13	<p>Liability The liability insurance of the project management is liable for any damages within the scope of the project.</p>
14	<p>Funding The project is paid for by the Swiss National Science Foundation.</p>
15	<p>Contact person: You can receive information on all your questions at any time:</p> <p>PD Dr. Andreas Müller, Senior Consultant, Head Shoulder and Elbow, University Hospital of Basel, Spitalstrasse 21, CH-403 Basel Tel 061 315 25 17 , Email A.Mueller@usb.ch</p>

More detailed information

1. Aim of the project

The aim of this project is to investigate how the most important results (for example, the occurrence of adverse events or shoulder function) are easily predicted following a surgical intervention to treat tendinosis of the shoulder muscles. Furthermore, we want to investigate how well a predefined set of adverse events, which could occur as part of such a surgical intervention, corresponds to what actually occurs in practice.

2. Choice

Participation is open to anyone with a torn tendon in the shoulder muscles, which can be repaired with minimally invasive (i.e. arthroscopic) surgery.

Important: This must be the first intervention on the shoulder in question.

Participation is not open to anyone for whom a detailed medical examination would not be possible or who cannot be called back for check-ups within the follow-up period (e.g. if they live outside Switzerland). Underage persons should also not participate.

3. General information about the project

This project will be carried out in accordance with the laws of Switzerland. The responsible ethics committee has reviewed and approved this project

The collection of clinical data following surgical interventions is very important. You will help:

- to assess the effectiveness and safety of the intervention,
- to make comparisons with other methods,
- to support an established decision-making process within the orthopaedic field.

The study intends to document the most important events following arthroscopic interventions, especially in terms of:

- safety (occurrence of adverse events),
- healing of the tendon repair,
- shoulder pain and function,
- the general state of health and quality of life as well as
- patient satisfaction.

Patients' socio-demographic characteristics, examination parameters and treatment parameters will be investigated to enable a prediction of these events to be made.

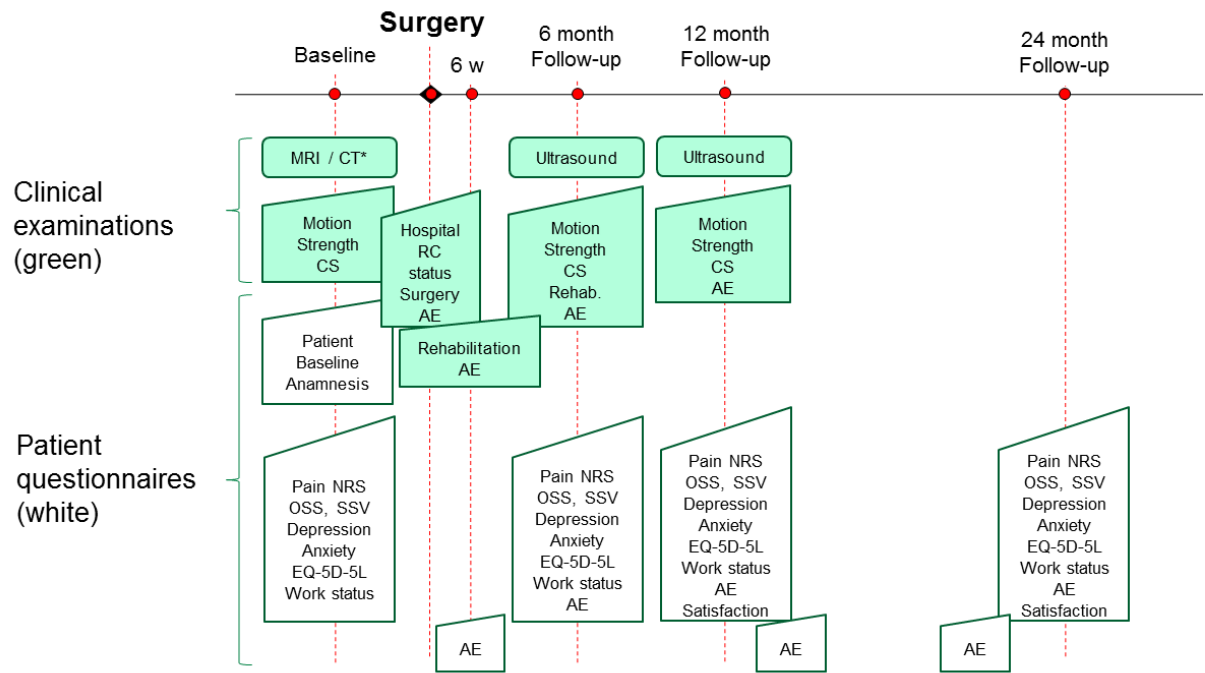
In most areas of orthopaedics, there is currently no international standard for the description of adverse events (often known as complications) resulting from surgical interventions. In shoulder orthopaedics, such a list of events does not exist for arthroscopic interventions used in the treatment of rotator cuff tears (shoulder tendinosis). For this reason, the Shoulder and Elbow Surgery research group at the Schulthess Clinic, Zurich, working together with the Orthopaedic and Traumatology Department of the University Hospital of Basel and over 80 experts working in the field of arthroscopy for rotator cuff tears, have defined a list of possible adverse events.

The aim is to apply and evaluate this predefined list of events. Each event will be evaluated independently by the doctor and the patient in question.

This project is supported by the Swiss National Science Foundation and will last four years. In total, 970 patients will be included in the study within the first year. These patients will be recruited from various clinics in Switzerland and one clinic in Germany. At the University Hospital of Basel about 60 patients are recruited.

4. Procedure

The following diagram shows the course of study events from the time of diagnosis to the follow-up appointment at two years post-surgery.



6 W = 6-week follow-up; AE = adverse events

Figure 1: Schematic representation of the study's progress

For your diagnosis, you will be examined by the doctor using various methods (e.g. functional testing, radiological and magnetic resonance imaging (= MRI)) during the first consultation. If you agree to participate in the project, you will receive a questionnaire, which will ask you to provide your personal details and estimate your current level of functional ability in everyday life. Shortly before the operation, your surgeon will record detailed information about your shoulder injury and the surgical intervention. Six weeks after the operation, your surgeon will ask you about your pain levels, rehabilitation programme and the occurrence of any adverse events.

During further follow-up appointments (at 6 and 12 months post-surgery), various examinations (e.g. measurements of range of motion and strength, see figure 1) are routinely performed in the clinic. An independent examiner will carry out an ultrasound routinely 12 months after the operation to document how the tendon is healing. You will also receive a questionnaire to complete. If you wish, you can complete this questionnaire at home - either on paper or electronically by following an invitation link that will be emailed to you. At the end of this document, you will be asked to provide your email address, if you do prefer to receive the electronic version of the questionnaire. Various questionnaires are already routinely recorded at the University Hospital of Basel.

Two years after the operation, you will be sent the questionnaire again by post or email (no further check-ups will take place at the clinic). This takes place within the framework of the project. If you have experienced one or more adverse events, the questionnaire will ask you to rate each event by severity and by its relationship to your treatment. The study doctors will evaluate all reported events by severity without knowing the patient, to whom these relate or the clinic in which the events occurred.

Each visit to the clinic (before surgery and 6- and 12-months post-surgery) will last 40 to 60 minutes including all the examinations. Completing the patient questionnaire will take an additional 20 to 30 minutes. An adverse event tends to be evaluated in only a few minutes.

We may have to exclude you from this project prematurely. This can occur if no tear of the rotator cuff can be confirmed intraoperatively (i.e. during the operation) (this occurs very rarely) or if a tendon repair is not possible without additional interventions on the shoulder (a so-called irreparable tear). The study doctor will inform you of any such exclusion from the project.

5. Usefulness

You will not personally benefit from participating in the project. The results can be important for others who have the same condition. As described above, the study aims to enable better evaluation and prediction of the risk of adverse events and the effectiveness of a surgical intervention. We want to support the decision-making processes of future interventions of this kind.

6. Rights

You're volunteering. If you do not want to participate or later withdraw your participation, you do not have to justify this. Your medical treatment/care is guaranteed regardless of your decision. You may ask questions about participation and the project at any time. Please contact the person named at the end of this information.

7. Duties

As a participant, it is necessary that you

- adhere to the necessary specifications and requirements of the project management.
- inform your investigator/project management about the course of the disease and report new symptoms, new complaints and changes in well-being.
- inform your investigator/project management about the simultaneous treatment and therapy with another doctor and about taking medication.

8. Risks

You are not exposed to any additional risk by participating in the project.

9. Outcomes

The investigator/project manager will inform you during the project about any new findings that may affect the benefit or your safety and thus your consent to participate. You will be informed of random findings which may contribute to the prevention, detection or treatment of existing or future diseases.

10. Confidentiality of data and samples

Your personal and medical data will be collected for this project. Very few professionals will see your unencrypted data, and only to perform tasks within the scope of the project. Data collection for study purposes is encrypted. Encryption means that all reference data that could identify you (name, date of birth) are deleted and replaced by a key. The key list always remains in the institution/hospital. Those who do not know the key cannot therefore draw any conclusions about you. In the

1
2
3 case of a publication, the summarised data cannot therefore be traced back to you as
4 an individual. Your name will never appear on the Internet or in any publication.
5 Sometimes there is a requirement in a journal for publication that individual data (so-
6 called raw data) must be transmitted. If individual data must be transmitted, then the
7 data is always encrypted and cannot be traced back to you as a person. All persons
8 who have access to your data within the scope of the project are subject to
9 confidentiality. The requirements of data protection are adhered to and you as a
10 participating person have the right to inspect your data at any time.

11
12 If data are stored on site, it is a database for research purposes.

13
14 Each centre will encode and save the data centrally in the project database (server
15 location: Schulthess Clinic, Zurich). The data will be deleted 10 years after the end of
16 the project.

17
18 It is possible that your data may be used for other investigations (projects) at a later
19 date or that they may be sent to another databank in Switzerland for investigations
20 (further use) not yet defined in more detail. This other database must meet the same
21 standards as the database for this project. For this further use we ask you to sign a
22 further declaration of consent at the very end of this document.

23
24 This project may be reviewed by the relevant ethics committee or by the institution that
25 initiated the project. The project manager may need to disclose your personal and
26 medical information for such checks. All persons must maintain absolute confidentiality.
27 We comply with all data protection regulations and will not make your name public
28 either in a publication or on the Internet.

29
30 It is possible that your aftercare physician will be contacted to provide information
31 about your medical condition.

32 33 **11. Withdrawal**

34 You can stop at any time and withdraw from the project if you wish. The data collected
35 so far are still evaluated in encrypted form, otherwise the entire project loses its value.
36 It is not possible to anonymize your data in case of withdrawal, i.e. the data remain
37 encrypted. Please check whether you agree with this before you participate in the
38 project.

39 40 **12. Indemnity**

41 If you participate in this project, you will not receive any compensation. You or your
42 health insurance company will not incur any costs for participation.

43 44 **13. Liability**

45 The prerequisites and procedure relating to liability and safeguarding in the event of a
46 claim are legally regulated. If you suffer a health impairment as a result of the study,
47 please contact the study doctor. The institution that is responsible for carrying out the
48 study is liable for the claim, if you can prove that the injury is due to the project-specific
49 examinations. Liability will not be accepted if the project manager can prove that the
50 injury is only minor and temporary, and does not extend beyond the degree expected by
51 current scientific knowledge.

52 53 **14. Funding**

54 The project is being funded by the Swiss National Science Foundation (SNSF).

55 56 **15. Contact person(s)**

57 If you have any questions, concerns, or emergencies that arise during or after the
58 project, you can always contact one of these contacts.

1
2
3
4 Head at the study location:

5 PD Dr. Andreas Müller, Senior Consultant, Head Shoulder and Elbow

6 University Hospital of Basel, Spitalstrasse 21, CH-403 Basel

7 Tel 061 315 25 17 , Email A.Mueller@usb.ch

8
9 24-hour emergency number: +41 61 265 25 25

10
11 Local project coordination:

12
13 PD Dr. Andreas Müller, Senior Consultant, Head Shoulder and Elbow

14 University Hospital of Basel, Spitalstrasse 21, CH-403 Basel

15 Tel 061 315 25 17 , Email A.Mueller@usb.ch

Declaration of consent

Written declaration of consent for participation in a study project

Please read this form carefully. Please ask if you do not understand or want to know something

BASEC number (after submission):

**Title of the project
(scientific and lay):**

Surgical safety and effectiveness in orthopaedics:
Swiss-wide multicenter evaluation and prediction of
core outcomes in arthroscopic rotator cuff
reconstruction

Surgical safeguarding and effectiveness in
orthopaedics: Swiss-wide multicentre evaluation and
prediction of the most important effects following
arthroscopic repair of shoulder tendons (rotator cuff
reconstruction)

**Responsible institution
(Project management with address):**

University Hospital of Basel
PD Dr. Andreas Müller
Orthopaedics and Traumatology
Spitalstrasse 21, CH-4031 Basel

Place of implementation:

Universitätsspital Basel

**Head of the project at the place of
study:**

PD Dr. Andreas Müller

Participant:

Name, first name: _____

Date of Birth: _____

Female Male

The undersigned investigator informed me verbally and in writing about the purpose, the course of the project, about possible advantages and disadvantages as well as about possible risks.

- I voluntarily participate in this project and accept the content of the written information provided on the above mentioned project. I've had plenty of time to make my decision.
- My questions concerning the participation in this project have been answered. I keep the written information and receive a copy of my written consent.
- I agree that the responsible experts of the project management/client of the project and the ethics committee responsible for this project may inspect my unencrypted data for verification and control purposes, but in strict compliance with confidentiality.
- I will be informed of study results or random findings that directly affect my health. If I don't want that, I'll inform my investigator.
- I know that my health-related and personal data can only be passed on in encrypted form for research purposes **for this project**.

- In the event of further treatment outside the test centre, I authorise my after-treating doctor(s) to forward my after-treatment data relevant to the project to the investigator/project management.
- I can withdraw from participation at any time and without giving reasons, without having any disadvantages in further medical treatment/care. The data collected so far will still be used for the evaluation of the project.
- The liability insurance of the hospital/institution covers any damages.
- I am aware that the obligations stated in the participant information must be complied with.
- If you agree that your email address can be used solely for receiving questionnaires and project-related communications, please enter it here:

_____@_____

Place, Date	Signature of participant

Confirmation from the investigator: I hereby confirm that I have explained the nature, significance and scope of the project to this participant. I assure you that I will fulfil all obligations in connection with this project in accordance with applicable law. If, at any time during the implementation of the project, I become aware of any aspects that might affect the participant's willingness to participate in the project, I will inform the participant immediately.

Place, Date	Name and first name of the informing investigator in block capitals
	Signature of the investigating physician

**Declaration of consent for the further use of data in encrypted form.
(for further use of data of THIS project)**

Participant:

Name, first name: _____

Date of birth: _____

Female

Male

I allow my data from this project to be used in encrypted form for medical research. This means that the data may be stored in a databank and used for future, not yet defined research projects for an indefinite period of time. This consent is unlimited.

I decide voluntarily and can revoke this decision at any time. When I step back, my data is anonymized. I simply inform my investigator/project manager and do not have to justify this decision.

I understand that the data are encrypted and the code is kept safe. The data can be sent to other databanks in Switzerland and abroad for analysis if they comply with the same standards as in Switzerland. All legal requirements regarding data protection are complied with.

Normally, all data are evaluated in their entirety and the results published in summary form. Should a result be relevant for me, it is possible that I will be contacted via my investigator. If I do not wish this, I will inform my investigator/project manager.

If results from the data are handled for commercial purposes, I hereby make no claims on any part of this commercial use.

Place, Date	Signature of participant
-------------	--------------------------

Confirmation from the investigator: I hereby confirm that I have explained to this participant the nature, significance and implications of the further use of data.

Place, Date	Name and first name of the informing investigator in block capitals
	Signature of the investigating physician

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. *BMJ*. 2013;346:e7586

	Reporting Item	Page Number
Administrative information		
Title	#1 Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a Trial identifier and registry name. If not yet registered, name of intended registry	4
Trial registration: data set	#2b All items from the World Health Organization Trial Registration Data Set	n.a.
Protocol version	#3 Date and version identifier	4
Funding	#4 Sources and types of financial, material, and other support	4
Roles and responsibilities: contributorship	#5a Names, affiliations, and roles of protocol contributors	4

1	Roles and	#5b	Name and contact information for the trial sponsor	4
2	responsibilities:			
3	sponsor contact			
4	information			
5				
6				
7	Roles and	#5c	Role of study sponsor and funders, if any, in study	4
8	responsibilities:		design; collection, management, analysis, and	
9	sponsor and funder		interpretation of data; writing of the report; and the	
10			decision to submit the report for publication,	
11			including whether they will have ultimate authority	
12			over any of these activities	
13				
14				
15				
16				
17	Roles and	#5d	Composition, roles, and responsibilities of the	4
18	responsibilities:		coordinating centre, steering committee, endpoint	
19	committees		adjudication committee, data management team,	
20			and other individuals or groups overseeing the trial,	
21			if applicable (see Item 21a for data monitoring	
22			committee)	
23				
24				
25				
26				
27	Introduction			
28				
29	Background and	#6a	Description of research question and justification for	7
30	rationale		undertaking the trial, including summary of relevant	
31			studies (published and unpublished) examining	
32			benefits and harms for each intervention	
33				
34				
35				
36	Background and	#6b	Explanation for choice of comparators	n.a.
37	rationale: choice of			
38	comparators			
39				
40				
41	Objectives	#7	Specific objectives or hypotheses	9
42				
43				
44	Trial design	#8	Description of trial design including type of trial (eg,	9
45			parallel group, crossover, factorial, single group),	
46			allocation ratio, and framework (eg, superiority,	
47			equivalence, non-inferiority, exploratory)	
48				
49				
50				
51	Methods:			
52	Participants,			
53	interventions, and			
54	outcomes			
55				
56				
57	Study setting	#9	Description of study settings (eg, community clinic,	9
58				
59				
60				

1		academic hospital) and list of countries where data	
2		will be collected. Reference to where list of study	
3		sites can be obtained	
4			
5	Eligibility criteria	#10 Inclusion and exclusion criteria for participants. If	10
6		applicable, eligibility criteria for study centres and	
7		individuals who will perform the interventions (eg,	
8		surgeons, psychotherapists)	
9			
10			
11			
12	Interventions:	#11a Interventions for each group with sufficient detail to	10
13	description	allow replication, including how and when they will	
14		be administered	
15			
16			
17	Interventions:	#11b Criteria for discontinuing or modifying allocated	n.a.
18	modifications	interventions for a given trial participant (eg, drug	
19		dose change in response to harms, participant	
20		request, or improving / worsening disease)	
21			
22			
23			
24	Interventions:	#11c Strategies to improve adherence to intervention	n.a.
25	adherence	protocols, and any procedures for monitoring	
26		adherence (eg, drug tablet return; laboratory tests)	
27			
28			
29			
30	Interventions:	#11d Relevant concomitant care and interventions that	10
31	concomitant care	are permitted or prohibited during the trial	
32			
33			
34	Outcomes	#12 Primary, secondary, and other outcomes, including	11
35		the specific measurement variable (eg, systolic	
36		blood pressure), analysis metric (eg, change from	
37		baseline, final value, time to event), method of	
38		aggregation (eg, median, proportion), and time	
39		point for each outcome. Explanation of the clinical	
40		relevance of chosen efficacy and harm outcomes is	
41		strongly recommended	
42			
43			
44			
45			
46	Participant timeline	#13 Time schedule of enrolment, interventions	13
47		(including any run-ins and washouts), assessments,	
48		and visits for participants. A schematic diagram is	
49		highly recommended (see Figure)	
50			
51			
52			
53	Sample size	#14 Estimated number of participants needed to	15
54		achieve study objectives and how it was	
55		determined, including clinical and statistical	
56		assumptions supporting any sample size	
57			
58			
59			
60			

calculations

1
2
3 Recruitment [#15](#) Strategies for achieving adequate participant 16
4 enrolment to reach target sample size
5

6 **Methods:**

7 **Assignment of**
8 **interventions (for**
9 **controlled trials)**
10
11

12
13 Allocation: sequence [#16a](#) Method of generating the allocation sequence (eg, n.a.
14 generation computer-generated random numbers), and list of
15 of any factors for stratification. To reduce predictability
16 of a random sequence, details of any planned
17 restriction (eg, blocking) should be provided in a
18 separate document that is unavailable to those who
19 enrol participants or assign interventions
20
21
22

23
24 Allocation [#16b](#) Mechanism of implementing the allocation n.a.
25 concealment sequence (eg, central telephone; sequentially
26 mechanism numbered, opaque, sealed envelopes), describing
27 any steps to conceal the sequence until
28 interventions are assigned
29
30
31

32
33 Allocation: [#16c](#) Who will generate the allocation sequence, who will n.a.
34 implementation enrol participants, and who will assign participants
35 to interventions
36
37

38 Blinding (masking) [#17a](#) Who will be blinded after assignment to n.a.
39 interventions (eg, trial participants, care providers,
40 outcome assessors, data analysts), and how
41
42

43 Blinding (masking): [#17b](#) If blinded, circumstances under which unblinding is n.a.
44 emergency permissible, and procedure for revealing a
45 unblinding participant's allocated intervention during the trial
46
47

48 **Methods: Data**
49 **collection,**
50 **management, and**
51 **analysis**
52
53

54
55 Data collection plan [#18a](#) Plans for assessment and collection of outcome, 16
56 baseline, and other trial data, including any related
57 processes to promote data quality (eg, duplicate
58
59

measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol

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10	Data collection plan:	#18b	Plans to promote participant retention and complete
11	retention		follow-up, including list of any outcome data to be
12			collected for participants who discontinue or deviate
13			from intervention protocols
14			
15			
16	Data management	#19	Plans for data entry, coding, security, and storage,
17			including any related processes to promote data
18			quality (eg, double data entry; range checks for
19			data values). Reference to where details of data
20			management procedures can be found, if not in the
21			protocol
22			
23			
24			
25			
26	Statistics: outcomes	#20a	Statistical methods for analysing primary and
27			secondary outcomes. Reference to where other
28			details of the statistical analysis plan can be found,
29			if not in the protocol
30			
31			
32			
33	Statistics: additional	#20b	Methods for any additional analyses (eg, subgroup
34	analyses		and adjusted analyses)
35			
36			
37	Statistics: analysis	#20c	Definition of analysis population relating to protocol
38	population and		non-adherence (eg, as randomised analysis), and
39	missing data		any statistical methods to handle missing data (eg,
40			multiple imputation)
41			
42			
43			
44	Methods:		
45	Monitoring		
46			
47			
48	Data monitoring:	#21a	Composition of data monitoring committee (DMC);
49	formal committee		summary of its role and reporting structure;
50			statement of whether it is independent from the
51			sponsor and competing interests; and reference to
52			where further details about its charter can be found,
53			if not in the protocol. Alternatively, an explanation of
54			why a DMC is not needed
55			
56			
57			
58			
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60			

1	Data monitoring:	#21b	Description of any interim analyses and stopping	n.a.
2	interim analysis		guidelines, including who will have access to these	
3			interim results and make the final decision to	
4			terminate the trial	
5				
6				
7				
8	Harms	#22	Plans for collecting, assessing, reporting, and	14
9			managing solicited and spontaneously reported	
10			adverse events and other unintended effects of trial	
11			interventions or trial conduct	
12				
13				
14	Auditing	#23	Frequency and procedures for auditing trial	18
15			conduct, if any, and whether the process will be	
16			independent from investigators and the sponsor	
17				
18				
19				
20	Ethics and			
21	dissemination			
22				
23				
24	Research ethics	#24	Plans for seeking research ethics committee /	21
25	approval		institutional review board (REC / IRB) approval	
26				
27	Protocol	#25	Plans for communicating important protocol	21
28	amendments		modifications (eg, changes to eligibility criteria,	
29			outcomes, analyses) to relevant parties (eg,	
30			investigators, REC / IRBs, trial participants, trial	
31			registries, journals, regulators)	
32				
33				
34				
35				
36	Consent or assent	#26a	Who will obtain informed consent or assent from	21
37			potential trial participants or authorised surrogates,	
38			and how (see Item 32)	
39				
40				
41	Consent or assent:	#26b	Additional consent provisions for collection and use	n.a.
42	ancillary studies		of participant data and biological specimens in	
43			ancillary studies, if applicable	
44				
45				
46	Confidentiality	#27	How personal information about potential and	22
47			enrolled participants will be collected, shared, and	
48			maintained in order to protect confidentiality before,	
49			during, and after the trial	
50				
51				
52				
53	Declaration of	#28	Financial and other competing interests for principal	22
54	interests		investigators for the overall trial and each study site	
55				
56				
57	Data access	#29	Statement of who will have access to the final trial	22
58			dataset, and disclosure of contractual agreements	
59				
60				

that limit such access for investigators

1			
2	Ancillary and post	#30	Provisions, if any, for ancillary and post-trial care, n.a.
3	trial care		
4			and for compensation to those who suffer harm
5			from trial participation
6			
7	Dissemination policy:	#31a	Plans for investigators and sponsor to communicate 23
8	trial results		trial results to participants, healthcare professionals,
9			the public, and other relevant groups (eg, via
10			publication, reporting in results databases, or other
11			data sharing arrangements), including any
12			publication restrictions
13			
14	Dissemination policy:	#31b	Authorship eligibility guidelines and any intended 23
15	authorship		use of professional writers
16			
17	Dissemination policy:	#31c	Plans, if any, for granting public access to the full 22
18	reproducible		protocol, participant-level dataset, and statistical
19	research		code
20			
21			
22			
23			
24			
25			
26			
27	Appendices		
28			
29	Informed consent	#32	Model consent form and other related Supplementary
30	materials		documentation given to participants and authorised file
31			surrogates
32			
33			
34	Biological specimens	#33	Plans for collection, laboratory evaluation, and n.a.
35			storage of biological specimens for genetic or
36			molecular analysis in the current trial and for future
37			use in ancillary studies, if applicable
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40			

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Protocol for the ARCR_Pred cohort-study: Swiss-wide multicenter evaluation and prediction of core outcomes in arthroscopic rotator cuff repair

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3 **1 Protocol for the ARCR_Pred cohort-study: Swiss-wide multicenter evaluation and**
4 **2 prediction of core outcomes in arthroscopic rotator cuff repair**

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3 85 **Administrative information**

4 86 **Title** Protocol for the ARCR_Pred cohort-study: Swiss-wide multicenter evaluation and
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7 87 prediction of core outcomes in arthroscopic rotator cuff repair
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11 89 **Trial registration** ClinicalTrial.gov registration number NCT04321005
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13 90

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15 91 **Protocol version** Version 2 (13.12.2019)
16

17 92

18
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21 94 320030_184959, <http://p3.snf.ch/project-184959>). A complementary grant was provided by
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23 95 Swiss Orthopedics. The sites Charité Medicine University, Berlin, Germany (BER) and
24
25 96 University Clinic Balgrist, Zurich, Switzerland (UKB) are funding their own participation in the
26
27 97 project.
28

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31
32 99 **Roles and responsibilities**
33

34 100 LA and AM are the initiators and project leaders. LA, AM, HB, SA, DS and SH were involved
35
36 101 in the study design, which was reviewed and commented by principal investigators CC, GC,
37
38 102 HD, KE, MF, BJ, AL, BM, PM, CR, MS, MS, CS, T Suter, KW and MZ.
39

40 103 Preparation of the manuscript was done by LA, AM, SA and T Stojanov. HB, DS and SH
41
42 104 edited and critically revised the paper. All authors have read and approved the manuscript.
43
44 105 LA is the guarantor of the manuscript.
45

46 106 This is an investigator initiated project at the University Hospital of Basel. The principal
47
48 107 investigator and project leader (AM) is the official sponsor representative for the project and
49
50 108 was involved in all phases of the project from its conception to the current implementation
51
52 109 steps. The project initiators and project leaders (LA and AM) have ultimate authority over any
53
54 110 of the project activities.
55

56
57 111 A project scientific board (PSB) comprises the project leaders (LA and AM), project
58
59 112 investigators at each site (CC, GC, HD, KE, MF, BJ, AL, BM, PM, CR, MS, MS, CS, T Suter,
60

1
2
3 113 KW and MZ), and project partners (SA, HB, DS and SH). The PSB shall meet at specific time
4
5 114 points during the study: before the study start, after completion of recruitment and the 12-
6
7 115 month follow-up, and at the end of the study. The agenda of these meetings will focus on
8
9 116 (however is not limited to) patient enrollment and the completion of follow-up examinations
10
11 117 and questionnaires, the documentation process in REDCap, data quality issues
12
13 118 (completeness and consistency), monitoring activities, adverse event assessment and
14
15 119 management, baseline patient description, ranking of prognostic factors for prognostic
16
17 120 models, progress of data analysis, publication strategy and decisions regarding data sharing.
18
19 121 Between these meetings, communication will be maintained between the project coordinating
20
21 122 team and investigators via various channels including emails, quarterly newsletters, phone
22
23 123 calls and (video) conference calls as required.
24
25
26 124

27 125 **Competing interests**

28 126 There are no competing interests for any author
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3 128 **Abstract**

4 129 **Introduction** In the field of arthroscopic rotator cuff repair (ARCR), reporting standards of
5
6 130 published studies differ dramatically, notably concerning adverse events (AEs). In addition,
7
8 131 prognostic studies are overall methodologically poor, based on small datasets, and explore
9
10 132 only limited numbers of influencing factors. We aim to develop prognostic models for
11
12 133 individual ARCR patients, primarily for the patient-reported assessment of shoulder function
13
14 134 (Oxford Shoulder Score [OSS]) and the occurrence of shoulder stiffness 6 months after
15
16 135 surgery. We also aim to evaluate the use of a consensus Core Event Set (CES) for AEs and
17
18 136 validate a severity classification for these events, considering the patient's perspective.
19
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21 137

22
23 138 **Methods and analysis** A cohort of 970 primary ARCR patients will be prospectively
24
25 139 documented from several Swiss and German orthopedic clinics up to 24 months
26
27 140 postoperatively. Patient clinical examinations at 6 and 12 months will include shoulder range
28
29 141 of motion and strength (Constant Score). Tendon repair integrity status will be assessed by
30
31 142 ultrasound at 12 months. Patient-reported questionnaires at 6, 12 and 24 months will
32
33 143 determine functional scores (Subjective Shoulder Value, OSS), anxiety and depression
34
35 144 scores, working status, sports activities, quality of life (EuroQol EQ-5D-5L). AEs will be
36
37 145 documented according to a CES. Prognostic models will be developed using an
38
39 146 internationally supported regression methodology. Multiple prognostic factors, including
40
41 147 patient baseline demographics, psychological, socioeconomic and clinical factors, rotator cuff
42
43 148 integrity, concomitant local findings, and (post)operative management factors will be
44
45 149 investigated.
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51 151 **Ethics and dissemination** This project contributes to the development of personalized risk
52
53 152 predictions for supporting the surgical decision process in ARCR. The consensus CES may
54
55 153 become an international reference for the reporting of complications in clinical studies and
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57 154 registries. Ethical approval was obtained on April 1st, 2020, from the lead ethics committee
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59
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3 155 (EKNZ, Basel Switzerland; ID: 2019-02076). All participants will provide informed, written
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5 156 consent before enrollment in the study.

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7 157

8 9 158 **Strengths and limitations of this study**

- 10
11 159 • Large prospective multicenter observation of routine care
- 12
13 160 • Assessment of patient-reported outcomes (PROMs)
- 14
15 161 • Implementation of an international core outcome set of adverse events (CES)
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17 162 • Internationally supported methodology for prognostic model development
- 18
19 163 • Potential limited response to patient questionnaires at 24 months

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23 24 165 **Introduction**

25
26 166 Rotator cuff tears are one of the most common injuries of the shoulder joint, which may
27
28 167 cause pain and disability associated with severe restrictions in daily activities. Surgical repair
29
30 168 is indicated when nonoperative treatment fails or follows extended traumatic tears, notably
31
32 169 inactive patients without signs of advanced tendon degeneration or muscle fat infiltration ¹.
33
34 170 Clinical studies have demonstrated clinically-relevant improvement in shoulder function and
35
36 171 quality of life after arthroscopic rotator cuff tear repair (ARCR) ²⁻⁵. The number of ARCRs has
37
38 172 increased over the last two decades ^{6 7 8 9} due to several contributing factors such as an
39
40 173 aging yet active population, improvements in operative repair techniques, and more liberal
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42 174 indications for ARCRs.

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47 176 Not all patients, however, benefit from ARCR ¹⁰. Patients may be affected by complications
48
49 177 and/or adverse events (AEs) like persistent pain, shoulder stiffness, infection, neurological
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51 178 problems, and repair failures ^{11 12}. About 20% of patients may show, typically between 6 and
52
53 179 12 months following ARCR, a persistent rotator cuff defect ¹³. Patients with healed tendons
54
55 180 may show better functional outcome after repair ^{2 14 15}. Postoperative shoulder stiffness, a
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57 181 major complication reported to occur in 1.5% to 11.1% of ARCRs ¹¹, leads to limitations in
58
59 182 everyday activities, prolonged rehabilitation, and, in severe cases, to reoperation (capsular

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3 183 release) ¹⁶⁻¹⁸. Nonetheless, incident data on outcome and AEs are impaired by the
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5 184 heterogeneity in definition and reporting ^{13 19}.

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9 186 Valid and representative data on the safety and effectiveness of ARCR are nonexistent at the
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11 187 Swiss national level. However, such data is paramount for optimizing the indication and
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13 188 outcome of ARCR, and for benchmarking orthopedic clinics. Reporting standards are a
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15 189 prerequisite for outcome and safety data. Recently, a Core Outcome Set (COS) ²⁰ was
16
17 190 defined for shoulder disorders, which includes inner core domains of pain, physical function
18
19 191 and activities, global perceived effect (a person's assessment of their recovery or degree of
20
21 192 improvement), and AEs ^{21 22}. A Core Event Set (CES) was developed by international
22
23 193 consensus in ARCR ^{23 24} and lay the ground for the current project.

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27
28 195 Appropriate indication of ARCR and judgment on risks for AEs or unsatisfactory patient
29
30 196 outcomes rely on validated clinical prediction tools ^{25 26}, which are still sparse in the field of
31
32 197 surgical repair of a rotator cuff tear. Currently existing models focus on early surgical repair
33
34 198 ²⁷, tendon healing ^{28 29} or shoulder functional outcomes ³⁰. A model for shoulder stiffness
35
36 199 included patients with various shoulder pathologies and surgeries ³¹. Furthermore, individual
37
38 200 outcome predictions in ARCR require the identification of relevant patient and management
39
40 201 factors. Several systematic reviews have highlighted the general lack of qualitative studies
41
42 202 focused on prognostic factors for ARCR outcomes ³²⁻³⁶. In addition, we have observed the
43
44 203 substantial heterogeneity in terms of applied methodology, core outcomes and studied
45
46 204 prognostic factors, where certain factors (e.g., age, tear size, muscle degeneration, smoking)
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48 205 are given greater focus over others (e.g., sex, traumatic onset). The reviews highlight the
49
50 206 need for more robust prospective studies to include additional patient-reported outcomes in a
51
52 207 multivariable context.

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209 **Objectives**

210 *The overall objective* is to establish a prospective cohort of patients undergoing ARCR with
211 standardized data collection and follow-up for the evaluation and prediction of targeted core
212 safety, and clinical and patient-reported outcome parameters that are to be routinely
213 collected in standard clinical care.

214
215 *The primary objective* is to develop predictive models for two core outcome parameters: 1)
216 the patient-reported Oxford Shoulder Score (OSS) functional outcome, and 2) the occurrence
217 of shoulder stiffness (primary safety event) as reported by patients and clinicians.

218
219 *Secondary objectives* are 1) to evaluate the content and applicability of the defined
220 consensus CES (i.e. ARCR CES 1.0)²³ in routine practice considering the patient's
221 perspective, 2) to quantify the incidence of AE up to 24 months after surgery (e.g., persisting
222 or worsening pain, recurrent rotator cuff (RC) defect), 3) to validate an adapted severity
223 classification for postoperative local AEs^{12,37}, and 4) to develop predictive models for other
224 clinically-relevant outcome parameters including patient-reported outcomes (e.g., perception
225 of improvement, return to work, return to sports, quality of life, satisfaction with surgery,
226 acceptability of symptom state), clinical outcomes (e.g., shoulder strength and motion) and
227 specific AEs (e.g. RC defect at 12 months).

229 **Methods and analysis**

230 *Study design and setting*

231 This is a prospective multicenter cohort study in patients undergoing ARCR with 17
232 participating orthopedic centers in Switzerland and one German center.

233
234 Several sub-projects, associated with the main ARCR cohort study, are planned and include
235 a systematic review of prognostic studies in ARCR, the application of the ARCR CES 1.0 for
236 AE documentation, and the application and validation of an AE severity classification

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3 2374 238 *Eligibility criteria*

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6 239 Adult patients diagnosed with a partial or full-thickness RC tear by magnetic resonance
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8 240 imaging (MRI), planned for a primary arthroscopic surgical repair, and giving their informed
9
10 241 consent to participate in the cohort study will be included. Patients undergoing a specific
11
12 242 surgical procedure for irreparable tears (i.e. tendon transfer, subacromial spacer or superior
13
14 243 capsular reconstruction), revision operations, open or mini-open reconstructions will be
15
16 244 excluded. Patients unable to give written informed consent or attend clinics for follow-up
17
18 245 visits, not fluent in German, French, Italian, or English or pregnant females will be excluded.
19
20 246 Patients undergoing bilateral ARCR will only be included for their first intervention.
21
22

23
24 24725 248 *Intervention*

26
27 249 Shoulder arthroscopies will be performed according to standardized clinic-specific and
28
29 250 international guidelines³⁸ in the context of routine care with patients in a beach-chair or
30
31 251 lateral decubitus position under general or local anesthesia. The variability in the repair
32
33 252 techniques used between clinics and surgeons will be documented. Typically, after the
34
35 253 diagnostic arthroscopy to assess the type of RC tear (partial or full-thickness tear and
36
37 254 involved tendons, tendon tear delamination, sign of tendon degeneration) and concomitant
38
39 255 injuries or lesions, the ruptured tendons are mobilized until they can be repositioned on the
40
41 256 original footprint with as little tension as possible. Tendon fixation may be performed using
42
43 257 one of multiple anchor and suture configurations according to the surgeon's decision. An
44
45 258 intervention at the biceps tendon is performed if any tendinopathy, or lesions to the superior
46
47 259 labrum or biceps pulley system are observed. An anterolateral or lateral acromioplasty is
48
49 260 performed at the surgeon's discretion, generally in the presence of a hooked-shaped
50
51 261 acromion or a critical shoulder angle larger than 35°, respectively. Operative details,
52
53 262 including additional concomitant procedures (acromioplasty, acromioclavicular joint
54
55 263 resection, capsulotomy, and biceps tenotomy or tenodesis) and operation duration are
56
57 264 recorded immediately after surgery. A standard 3-phase postoperative rehabilitation scheme
58
59
60

1
2
3 265 is usually prescribed and will be documented in detail, including immobilization and passive
4
5 266 mobilization in the first phase, active mobilization and coordination training in the second
6
7 267 phase, followed by the third phase of specific progressive resistance exercises.
8

9 268

10 11 269 *Outcomes*

12
13 270 The *first primary outcome* is the patient-reported change in shoulder functional outcome
14
15 271 between baseline and 6 months postoperatively as measured with the Oxford Shoulder
16
17 272 Score (OSS).³⁹ The OSS is a condition-specific questionnaire developed for patients with a
18
19 273 degenerative or inflammatory state of the shoulder. It contains twelve items to be answered
20
21 274 by the patient independently, which deal with pain (degree, time point) and possible
22
23 275 handicaps in private and professional life. There are five categories of response for every
24
25 276 question, corresponding to a score ranging from 0 to 4. Scores are summed to give a single
26
27 277 score with a range from 0 (worst outcome) to 48 (best outcome). Transcultural validations of
28
29 278 this questionnaire for the German and Italian populations have been performed^{40 41} and are
30
31 279 validated for patient-based outcomes after RC repair⁴²⁻⁴⁴. While functional outcome at the
32
33 280 last 24-month follow-up is clinically relevant, the early 6-month primary time point is chosen
34
35 281 because of the importance in early surgical recovery and rehabilitation, particularly when
36
37 282 considering the socioeconomic impact on professionally active patients⁴.
38
39

40 283

41
42 284 The *second primary outcome* is the occurrence of shoulder stiffness within 6 months after
43
44 285 surgery: this event is poorly defined in the literature¹⁹. We formed a consensus definition of
45
46 286 shoulder stiffness among specialized shoulder surgeons in a Delphi survey, which describes
47
48 287 a postoperative restriction in passive shoulder motion diagnosed within 6 months after ARCR
49
50 288 in at least two of the motion planes of flexion, abduction and external rotation in 0° abduction.
51
52 289 Motion restriction is to be assessed separately for each plane according to specific threshold
53
54 290 criteria (flexion: total motion equal to or below 90° or glenohumeral motion equal to or below
55
56 291 80°; abduction: total motion equal to or below 80° or glenohumeral motion equal to or below
57
58 292 60°; external rotation in 0° abduction: glenohumeral motion equal to or below 20° or no more
59
60

1
2
3 293 than 50% of the contralateral side value). In this project, we will identify cases of shoulder
4
5 294 stiffness based on our consensus definition as well as clinical records and reports from
6
7 295 clinicians and their patients.
8

9 296
10
11 297 Secondary outcomes will include: 1) local AEs according to the ARCR CES, in particular the
12
13 298 occurrence of recurrent defect of repaired tendon(s) at 12 months, when at least one
14
15 299 repaired tendon is diagnosed with a recurrent defect by ultrasound examination, persistent or
16
17 300 worsening pain, infection, any local event (composite outcome); 2) functional parameters of
18
19 301 the Constant score (CS)⁴⁵ at 6 and 12 months, shoulder strength (kg) in abduction at 6 and
20
21 302 12 months, patient-reported shoulder pain on the numeric rating scale (NRS) at 6, 12 and 24
22
23 303 months, patient-reported shoulder function: OSS at 6, 12 and 24 months, Subjective
24
25 304 Shoulder Value (SSV)⁴⁶ assessment at 6, 12 and 24 months; 3) general health and
26
27 305 socioeconomic parameters including patient-reported quality of sleep (NRS) at 6, 12 and 24
28
29 306 months⁴⁷, return to work, change of working condition within 6, 12 and 24 months, level of
30
31 307 depression and anxiety at 6, 12 and 24 months based on Patient-Reported Outcomes
32
33 308 Measurement Information System (PROMIS) scores^{48 49}, patient perceived shoulder
34
35 309 improvement, acceptability of own symptom state⁵⁰, quality of life (utilities and general health)
36
37 310 at 6, 12 and 24 months using the European Quality of Life 5 Dimensions 5 Level
38
39 311 questionnaire (EQ-5D-5L), patient satisfaction with the surgical outcome at 12 and 24
40
41 312 months; 4) safety outcome assessment, occurrence of all AEs reported by clinicians and
42
43 313 patients (including non-local AEs within 6 months after surgery), final independent surgeon
44
45 314 and patient-rated assessment of AEs according to perceived severity (rating scale from 0 [no
46
47 315 complication] to 100 [death]⁵¹), comprehensive Complication Index⁵¹ considering all AEs that
48
49 316 occurred within 6 months after surgery.
50
51
52

53 317
54
55 318 Shoulder ultrasound examinations will be performed at 12 months by experienced clinicians
56
57 319 independent of the operating surgeons. The repair integrity will be graded according to the
58
59 320 Sugaya classification (where grade 4 or 5 defines the occurrence of a recurrent effect)^{52 53}.
60

1
2
3 321 Other ultrasound parameters include the location of the recurrent defect (at the footprint |
4
5 322 medial cuff failure), long biceps tendon status, signs of anchor displacement, and location
6
7 323 and signs of suture cut-through.
8

9 324

10
11 325 *Participant timeline*

12
13 326 Local investigators will identify patients who meet the eligibility criteria. Patient enrollment
14
15 327 started on June 1st, 2020 and is planned for a maximum period of 15 months. Patients will
16
17 328 complete a preoperative evaluation no more than 2 months before surgery. Follow-up
18
19 329 assessments will be performed at 6 weeks (+/- 1 week), and 6 (+/- 1 month), 12 (+/- 1 month)
20
21 330 and 24 months (+/- 2 months) postoperatively. At the final 24-month time point, only patient
22
23 331 self-reporting assessments, including surveys on adverse events, will be documented (Figure
24
25 332 1). The end date for the study representing the collection of the last patient questionnaire is
26
27 333 expected on November 1st, 2023.
28

29 334

30
31 335 *Baseline prognostic factors*

32
33 336 Various baseline parameters, operative details, and postoperative management variables are
34
35 337 known or suspected to influence ARCR outcomes ³²⁻³⁶.
36
37 338

38 339

39
40 339 The following patient-related factors will be recorded: patient demographics [year of birth for
41
42 340 age, sex], socioeconomic parameters [nationality, marital status, the highest level of
43
44 341 education, employment status, last occupational position, daily physical workload], dominant
45
46 342 side, smoking & drinking status, general physical and mental health [Body Mass Index (BMI)
47
48 343 and obesity, American Society of Anesthesiologists (ASA) classification, comorbidities (e.g.
49
50 344 diabetes), concomitant medication, level of depression and anxiety (PROMIS Depression
51
52 345 and Anxiety Short Form 4a) ^{48 49}, quality of life (EQ-5D-5L) ⁵⁴].
53

54 346

55
56 347 Disease-related factors are shoulder clinical examinations [pain level on a numeric rating
57
58 348 scale (NRS), range of motion, muscle strength, Constant Score ⁴⁵], patient-reported shoulder
59
60

1
2
3 349 function (see outcome measures), radiograph parameters [Critical Shoulder Angle ⁵⁵,
4
5 350 acromiohumeral distance ⁵⁶], MRI or arthro-Computer Tomography (CT) parameters
6
7 351 [supraspinatus muscle atrophy ⁵⁷, tangent sign ⁵⁸, grade of fatty infiltration ^{59 60}], medical
8
9 352 history [cause of injury (trauma event), symptom duration, previous interventions (operation
10
11 353 and timing of surgery), actual medication, and the extent of physical therapy].
12

13 354

15 355 Rotator cuff integrity and concomitant local findings. The RC tear will be determined by MRI
16
17 356 (or arthro-CT) and confirmed intraoperatively: tear size: location (involved tendons) and
18
19 357 grading (partial / complete), tendon retraction grade ⁶¹ and tear sagittal size ⁶² , status of the
20
21 358 biceps tendon, additional intraoperative observation of concomitant local injuries [Superior
22
23 359 Labrum from Anterior to Posterior (SLAP) lesion, Humeral Avulsion Glenohumeral Ligament
24
25 360 (HAGL), Bankart lesion, humeral and glenoid-side chondral lesions].
26
27

28 361

30 362 Operative details and postoperative management: type of ARCR procedure [use of anchors,
31
32 363 suture techniques], augmentation techniques [e.g. platelet concentrates, scaffolds, ...] ⁶³,
33
34 364 additional concomitant treatment [acromioplasty, acromioclavicular joint resection,
35
36 365 capsulotomy, biceps tenotomy or tenodesis, treatment of SLAP lesion], operation duration,
37
38 366 duration of hospital stay, postoperative management [immobilization position and duration,
39
40 367 pain medication [e.g. using non-steroidal anti-inflammatory drugs], timing of passive and
41
42 368 active shoulder motion, physiotherapy and muscle training].
43
44

45 369

47 370 *Adverse event documentation and assessment process*

48
49 371 Operating surgeons will report the occurrence of any intraoperative AE on the operation
50
51 372 form. The occurrence of postoperative local AEs within 24 months will be reported by
52
53 373 investigators at the clinical examination and by patients on the questionnaires. The
54
55 374 occurrence of postoperative non-local AEs that are unrelated to the operation will be
56
57 375 documented in a similar manner, however only within 6 months after surgery. An AE form
58
59 376 was developed according to the ARCR CES 1.0 ²³. Each AE documentation will be structured
60

1
2
3 377 after Audigé et al.⁶⁴ and includes the date/period of occurrence [intra- / postoperative], the
4
5 378 affected body location [local at the operated shoulder / non-local], the event group and
6
7 379 specification, applied health-related intervention(s) [operative / nonoperative procedure(s)],
8
9 380 its outcome at the time of reporting (or end of the study), and the assessment of the event
10
11 381 [causal factor(s) / severity grade / seriousness]. Severity grading will be made according to
12
13 382 existing and adapted systems for intraoperative^{65 66} and postoperative^{12 37} complications.
14
15 383 The documentation of AEs will be checked for completeness and consistency remotely as
16
17 384 well as on-site by reviewing selected patient files as part of the monitoring plan. A review
18
19 385 committee (LA, AM, TS, HD and DS) will assess all events reported by surgeons and
20
21 386 patients, and generate queries to the respective sites as required.
22

23
24 387
25
26 388 Fully documented local events, including their treatment, outcome and possible causative
27
28 389 factors, will be formulated in layman's terms and sent back to the affected patients, so that
29
30 390 they can confirm and validate collected AE data as well as assess their severity on a visual
31
32 391 analogue scale from 0 (not at all severe) to 100 (extremely severe). This subsequent rating
33
34 392 will also be performed by their treating surgeon and four other randomly-selected surgeons
35
36 393 involved in the project, blinded from the original severity grading.
37

38
39 394

40 395 *Sample size determination*

41
42 396 For sample size calculation, we set up a simulation study and used multiple regression to
43
44 397 predict the change in OSS within 6 months for the most important prognostic factors. The
45
46 398 prognostic factors were derived from an existing ARCR local registry⁶⁷ and include age, sex,
47
48 399 body mass index/obesity status, tendon quality/degeneration, and RC severity³²⁻³⁶. We
49
50 400 accounted for the type I error at 5% for statistical significance and the type II error set at 20%
51
52 401 for 80% statistical power⁶⁸. Two thousand replications were done, and the p-values were
53
54 402 recorded to calculate the mean significance for each of the prognostic factors to reach a
55
56 403 minimum of 80% statistical power. This approach led to a sample of 920 patients.
57
58 404

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1
2
3 405 For the second primary outcome of shoulder stiffness, we accounted for a minimum of ten
4
5 406 events per variable to allow for the inclusion of a maximum of ten predictors into the model⁶⁹
6
7 407 ⁷⁰. The estimated event rate for shoulder stiffness from our pilot data set was 8.3%, which,
8
9 408 according to our experience, might reflect an underestimation of the true rate¹⁷. Therefore, a
10
11 409 10% stiffness rate was assumed, which resulted in a sample size calculation of 900 patients.
12
13 410 The higher resulting number determines the final number of patients to be recruited.
14
15 411 Therefore, 920 patients will be included with an additional 50 patients (i.e. 970 patients) due
16
17 412 to the anticipated maximum dropout rate of 5% at 6 months (based on personal experience).
18
19 413

20 413

21 414 *Recruitment*

22
23 415 Study sites and local investigators were selected based on their expertise in ARCR with
24
25 416 support by the shoulder and elbow expert group of Swiss Orthopaedics. Each site was
26
27 417 visited by the project leaders to assess the adequacy of local clinical and research settings
28
29 418 for the project as well as to ensure prior interest and commitment. The number of included
30
31 419 sites was determined based on the reported estimate of the number of ARCR patients that
32
33 420 could be realistically enrolled within one year from each site, and included an allowance for
34
35 421 overestimation (i.e. all sites together estimated that they could recruit up to 40% more than
36
37 422 the expected 970 patients within one year).

38
39 423 Patients who are enrolled after signing an informed consent form are definitively recruited for
40
41 424 the project after documentation of baseline parameters (clinical examinations and patient
42
43 425 questionnaires) and confirmation of ARCR during surgery. A recruitment curve is prepared
44
45 426 every 2 weeks and sent to the project sites along with a recruitment table presenting the
46
47 427 performance of each site. Sites that are unable to recruit the expected number of patients
48
49 428 within the first 3 months will be considered for exclusion from the project and replaced by
50
51 429 additional sites if the estimated total duration of patient enrollment is delayed for more than 3
52
53 430 months.

54 430

55 431 56 432 *Data collection methods*

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2
3 433 Data are collected on electronic or paper-based case report forms or patient questionnaires.
4
5 434 Project parameters and used instruments are presented in previous sections of this protocol.
6
7 435 A training video was prepared for the collection of CS data ⁴⁵. For the measurement of
8
9 436 shoulder muscle strength, several devices were permitted, i.e. IsoForceControl® (MDS
10
11 437 Medical Device Solution, Oberburg, Switzerland), Mark-10 Force Gauge (Mark-10
12
13 438 Corporation, Copiague, USA) as well as hand-held (Lafayette Instrument Co., Lafayette,
14
15 439 USA) or MicroFET 2 (Hoggan Scientific, Salt Lake City, USA) dynamometers; the use of a
16
17 440 spring balance was not allowed.

18
19 441
20
21 442 Patient clinical examinations, including baseline imaging assessments, are performed at
22
23 443 each site by experienced clinicians (who may be assisted by locally-trained research staff)
24
25 444 and documented primarily on paper-based case report forms. Baseline MRI and radiographs
26
27 445 are coded and centralized at the University of Basel to ensure data quality control. Operative
28
29 446 data are collected electronically by the respective surgeons shortly after surgery. Patients
30
31 447 complete questionnaires in their preferred language, which is limited to German, French,
32
33 448 Italian or English, either electronically after invitation, by email or on a tablet computer at the
34
35 449 site, or otherwise on paper. AEs are documented electronically by the respective surgeons
36
37 450 with support from their research staff. Data collected on paper forms are entered
38
39 451 electronically at each site or at a central location at the University of Basel based on the
40
41 452 agreement made with each site.
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46

47 454 *Data monitoring*

48
49 455 A central project data manager will perform data quality control on all collected data. A
50
51 456 flowchart will be created to describe the number of consecutively recruited patients who had
52
53 457 an RCR by arthroscopic procedure or had a conversion to an open procedure, and who
54
55 458 completed follow-up clinical and imaging examinations as well as self-reported outcome
56
57 459 questionnaires. The reasons for patient dropout and loss to follow-up status will be monitored
58
59 460 and described. All recorded study parameters will be described using standard descriptive
60

1
2
3 461 statistics; continuous variables will be presented as means with standard deviations and
4
5 462 categorical variables as counts with percentages. The variability of data between clinics will
6
7 463 be explored to support the identification of outlier data.

8
9 464 Weekly site-specific reports, including the patient enrollment list, expected follow-up timing
10
11 465 and identification of missing, erroneous or inconsistent data, are sent to the respective local
12
13 466 project staff. Data-related queries will be resolved remotely or by on-site monitoring visits
14
15 467 before the final analyses are performed.

16
17 468 There is no plan for auditing project conduct other than via reporting at the annual meetings
18
19 469 of the project scientific board.

20
21
22 470

23 471 *Data management*

24
25 472 Study data will be stored using the REDCap web-based electronic data capture system^{71 72}
26
27
28 473 on a server that is hosted at Schulthess Klinik. REDCap conforms with Good Clinical
29
30 474 Practice guidelines that provide required features for data protection and integrity, e.g.,
31
32 475 password-protected access and change tracking.

33
34 476

35
36 477 Study data will be coded and exported from the REDCap system into Stata software
37
38 478 (StataCorp LP, College Station, USA) for statistical analyses. Data transformations and
39
40 479 analyses will be primarily implemented using Stata and fully documented within Stata
41
42 480 programming files. Data subsets will be prepared for analyses using alternative software
43
44 481 (e.g. R for prediction models) as appropriate.

45
46
47 482

48
49 483 All patients with an intraoperatively confirmed RC tear and operated by ARCR will be
50
51 484 included in the analyses. Existing missing data will be imputed if the number of missing data
52
53 485 is non-negligible or could potentially bias the results and conclusions.

54
55 486

56 57 487 *Systematic review of prognostic factors*

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2
3 488 A systematic review of prognostic factors for ARCR outcomes is implemented (PROSPERO
4
5 489 registration ID: CRD42020199257). Briefly, literature from 2014 to 2020 will be checked to
6
7 490 identify longitudinal studies including patients diagnosed with a RC tear. These studies
8
9 491 should report the effect of at least one factor on one of the following outcomes: shoulder
10
11 492 stiffness, RC tear repair integrity, and shoulder function. Data extraction will follow a pre-
12
13 493 defined template and the collected data will be stored within a separate database using
14
15 494 REDCap. Data from different studies will be described and may be synthesized depending
16
17 495 on the data type and heterogeneity. These data will be used to generate a list of factors most
18
19 496 likely to influence our project outcomes and therefore, should be considered for inclusion in
20
21 497 the predictive model development process.
22

23 498

25 499 *Predictive model development*

27
28 500 To develop the predictive model(s), the seven steps proposed by Steyerberg et al.^{73 74} will be
29
30 501 used. The steps comprise: 1) consideration of the research question and initial data
31
32 502 inspection, 2) coding of the predictors, 3) model specification, 4) model estimation, 5)
33
34 503 evaluation of model performance, 6) internal validation, and 7) model presentation.
35
36 504 Depending on the type of outcome, different models will be fitted and evaluated, i.e. multiple
37
38 505 regression models for the change in OSS at 6 months and multivariable logistic regression
39
40 506 models for shoulder stiffness. Model diagnostics will be performed for all models to check the
41
42 507 underlying assumptions.
43

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46
47 509 The prediction of the model(s) will be based on the baseline, operative, and postoperative
48
49 510 management variables. Firstly, a subset of the potential prognostic factors will be defined
50
51 511 based on whether it is thought to be most predictive. The subset will be selected separately
52
53 512 for each outcome by the Delphi method among the investigators, whereby the factors will be
54
55 513 noted for their known or potential prognostic value on a 5-point Likert scale from 1 (not
56
57 514 important) to 5 (extremely important). These factors, with the highest mean score among
58
59 515 investigators, will form the subset.
60

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3 516
4
5 517 We will then use criterion-based procedures (e.g. Akaike Information Criterion [AIC] or
6
7 518 adjusted R^2) to select the best set of predictors for the continuous outcome(s) and for the
8
9 519 binary outcome, we will use the area under receiving operating characteristics curve (AUC).
10
11 520 To assess the predictive performance of the final models as well as the updated version of
12
13 521 the prediction models, the calibration plot and discrimination measures will be used. Thereby,
14
15 522 apparent performance will be evaluated on the respective development data, and internal
16
17 523 validated performance will be determined by bootstrapping. Independent external validation
18
19 524 will be estimated by applying the resulting models from the development data set in the
20
21 525 respective validation data sets. The resulting models will be used to predict the change of
22
23 526 outcome value (i.e. OSS in 6 months) and assess whether a patient will experience the event
24
25 527 (i.e. shoulder stiffness).
26
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28 528

29
30 529 If we observe missing data, then missing data imputation will be performed using a method
31
32 530 that allows for uncertainty in the imputed values (e.g. multiple imputations using chained
33
34 531 equation ⁷⁵). We will account for the clustering of records within clinics as appropriate.
35

36 532

37 38 533 *Adverse events*

39
40 534 Occurring AEs other than those listed in the CES as well as events occurring outside the
41
42 535 periods defined by the core set will be analyzed separately for consideration of clinical
43
44 536 relevance. This analysis will be made by the review committee and project scientific board
45
46 537 (PSB) comprising all local project leaders (principal investigators). Recommendations for
47
48 538 change of the ARCR CES 1.0 by the PSB will be formulated.
49

50
51 539

52
53 540 The incidence of AEs, specific individual events and groups of events defined within the
54
55 541 ARCR CES 1.0 up to 24 months postoperatively will be displayed as the frequency of
56
57 542 patients with an event relative to the number of patients observed, reported together with its
58
59 543 95% Wilson confidence interval. These results will be presented in a summary table together
60

1
2
3 544 with the absolute frequency. Further details on the period of occurrence will be given by
4
5 545 stratifying for the time point of event occurrence. We will also stratify AEs according to their
6
7 546 severity level and patient relevance. Validation of the postoperative local AE severity
8
9 547 classification system will be implemented using previously used methods ^{76 77}.

10
11 548

12 13 549 *Patient and public involvement*

14
15 550 No patient or member of the public was involved in the design of this cohort study protocol.

16
17 551 Enrolled patients will contribute to the evaluation and validation of documented AEs and their
18
19 552 severity grading, therefore to a potential revision of the ARCR CES. We are planning to
20
21 553 present initial results to patients and the public, and get feedback for further analyses and
22
23 554 future model development as well as documentation system in ARCR.

24
25 555

26 27 28 556 **Ethics and dissemination**

29 30 557 *Research ethics approval*

31
32 558 Ethical approval was obtained on April 1st 2020 from the lead ethics committee (EKNZ, Basel
33
34 559 Switzerland; ID: 2019-02076).

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36 560

37 38 561 *Protocol amendments*

39
40 562 Minor protocol amendments, e.g. database production changes to facilitate monitoring
41
42 563 processes or improve outcome assessment by questionnaire, are fully documented. Major
43
44 564 amendments, e.g. changes to the patient information sheet and consent form, change of a
45
46 565 local project leader or the inclusion of a new project site, will be submitted for approval by the
47
48 566 lead ethics committee as required.

49
50 567

51 52 568 *Consent or assent*

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54 569 All participants will provide informed written consent prior to being enrolled into the study.

55
56 570 The English version of the informed consent form used at the University Hospital of Basel is
57
58 571 available as Supplement file 1.

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3 5724 573 *Confidentiality*

574 Project data will be handled with utmost discretion and can only be accessed by authorized
575 personnel as outlined by a study delegation list created for each project site. Patient data will
576 be coded, i.e. identified by a unique participant number. A participant identification list will be
577 managed and kept in a place (an electronic folder or paper-based form) only accessible to
578 authorized staff at each site.

579 The project leader affirms and upholds the principle of each patient's right to privacy and that
580 they shall comply with applicable privacy laws. In particular, anonymity of all patients shall be
581 guaranteed when presenting the data at scientific meetings or publishing them in scientific
582 journals.

25 583

27 584 *Declaration of interests*

29 585 None declared.

31 586

33 587 *Access to data*

34 588 Project data will be shared at the end of the analysis process by the PSB. The Department of
35 589 Clinical Research (German Departement Klinische Forschung, DKF) at the University
36 590 Hospital of Basel will act as an independent data access committee, and will store the data
37 591 at the time of publication on secure servers, maintained and backed-up by the Information
38 592 and Communication Technology department at the University Hospital of Basel. Researchers
39 593 who wish to reuse data will be able to submit a project synopsis to the DKF at
40 594 dkf.unibas.ch/contact. A data-sharing statement referring researchers to the DKF for data
41 595 access will be disseminated in the publications. Metadata describing the type, size and
42 596 content of the data sets will be shared along with the study protocol on the Harvard
43 597 Dataverse repository available online (<https://dataverse.harvard.edu/>). Additionally, the case
44 598 report forms will be uploaded on a medical data models portal (<https://medical-data->

1
2
3 599 models.org/) and all variables will be annotated by their Unified Medical Language System
4
5 600 Concept Unique Identifier to improve accessibility to other clinicians.

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7 601

8
9 602 *Dissemination policy*

10
11 603 This project will lead to multiple open-access, peer-reviewed scientific publications, which will
12
13 604 be prepared according to international standards (e.g. the STROBE statement⁷⁸ for cohort
14
15 605 studies; TRIPOD⁷⁹ statements for prognostic studies; PRISMA⁸⁰ statement for systematic
16
17 606 reviews). Publication authorship will regulated according to the guidelines of the Swiss
18
19 607 Academies of Arts and Sciences⁸¹. Results will be submitted for presentation at national and
20
21 608 international conferences. In addition, lay summary results will be developed and made
22
23 609 available for patients and the public.

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25 610

26
27 611 *Scientific relevance and broader impact*

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29 612 This project initiates the development of personalized risk predictions to support the surgical
30
31 613 decision process in ARCR. The consensus CES may become an international reference for
32
33 614 the reporting of complications in clinical studies and registries, and may therefore provide a
34
35 615 solid metric for the documentation of surgical safety in ARCR. Methodological insight gained
36
37 616 from this project will be easily transferable to similar initiatives and thus, may foster the
38
39 617 realization of other cohorts on safety and effectiveness outcome in shoulder surgery (e.g.
40
41 618 arthroplasty) and orthopedics in general.

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45
46 620 For patients affected by RC tears and their surgeons, this study will be the first to provide
47
48 621 solid data on the incidence of patient-validated AEs and other core outcomes up to two years
49
50 622 after surgical repair based on international consensus COS and CES. This study will allow
51
52 623 the investigation of a comprehensive list of potential prognostic factors to generate predictive
53
54 624 models for these core outcomes and hence, offer personalized health information to support
55
56 625 future patients and surgeons in the decision process for surgery. Outcome predictors and
57
58 626 risk calculators are increasingly being developed in numerous medical fields including
59
60 627 surgery and orthopedics, and they are in development in the field of ARCR.

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4
5 629 This study will assess the structure and content of the ARCR CES and consolidate its validity
6
7 630 in capturing unfavorable events of importance to both patients and surgeons; considering the
8
9 631 patient's perspective is an essential step in the development of a COS. Furthermore, the
10
11 632 validation of an adapted severity classification of AEs in this study will provide an essential
12
13 633 system for assessing surgical morbidity in orthopedics. We expect that the ARCR CES and
14
15 634 the event severity classification will become international standards for the reporting of
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17 635 ARCR AEs in clinical studies and registries, and therefore provide a solid metric for the
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19 636 documentation of surgical safety in ARCR.
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23 638 This study fosters the enterprise in developing a Swiss-wide registry of ARCR, which will
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25 639 allow the ongoing evaluation and prediction of targeted core safety, clinical and patient-
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27 640 reported outcomes. The identification of factors mostly associated with relevant outcomes
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29 641 will facilitate a lean and straightforward documentation process for ARCR patients in
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31 642 Switzerland and abroad.
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3 911 **Figure legend**

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7 913 **Figure 1:** Flowchart of study procedures

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9 914 w = week; mo = month; FU = follow-up; MRI = Magnetic Resonance Imaging; CT = Arthro-

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11 915 Computer Tomography (*if MRI not possible); Motion = Shoulder range of motion; CS =

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13 916 Constant Score; RC = Rotator Cuff; AE = Adverse Event; Rehab. = recall on postoperative

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15 917 rehabilitation; DE = German; FR = French; IT = Italian; EN = English; NRS = Numeric Rating

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17 918 Scale; OSS = Oxford Shoulder Score; SSV = Subjective Shoulder Value; EQ-5D-5L =

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19 919 European Quality of Life 5 Dimensions 5 Level questionnaire; CES = Core Event Set; AE

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21 920 survey = surgeons and patients survey regarding AE severity (sev)

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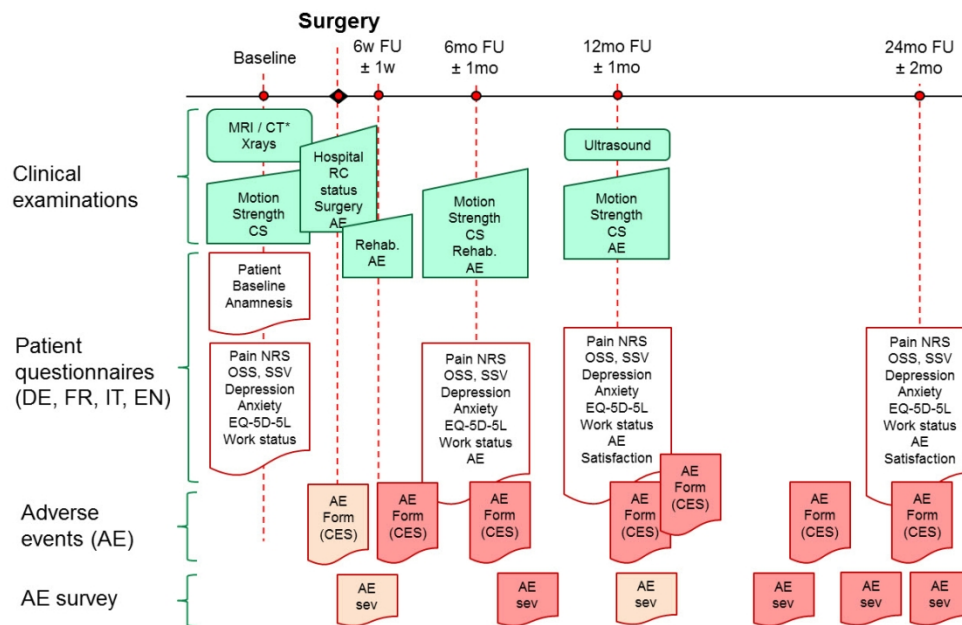


Figure 1: Flowchart of study procedures

28 w = week; mo = month; FU = follow-up; MRI = Magnetic Resonance Imaging; CT = Arthro-Computer
 29 Tomography (*if MRI not possible); Motion = Shoulder range of motion; CS = Constant Score; RC = Rotator
 30 Cuff; AE = Adverse Event; Rehab. = recall on postoperative rehabilitation; DE = German; FR = French; IT =
 31 Italian; EN = English; NRS = Numeric Rating Scale; OSS = Oxford Shoulder Score; SSV = Subjective
 32 Shoulder Value; EQ-5D-5L = European Quality of Life 5 Dimensions 5 Level questionnaire; CES = Core
 33 Event Set; AE survey = surgeons and patients survey regarding AE severity (sev)

342x220mm (96 x 96 DPI)

Supplement file 1

Article title Protocol for the ARCR_Pred cohort-study: Swiss-wide multicenter evaluation and prediction of core outcomes in arthroscopic rotator cuff repair

Journal name BMJ Open Access

Author names Laurent Audigé, Heiner C. Bucher, Soheila Aghlmandi, Thomas Stojanov, David Schwappach, Sabina Hunziker, Christian Candrian, Gregory Cunningham, Holger Durchholz, Karim Eid, Matthias Flury, Bernhard Jost, Alexandre Lädermann, Beat Moor, Philipp Moroder, Claudio Rosso, Michael Schär, Markus Scheibel, Christoph Spormann, Thomas Suter, Karl Wieser, Matthias A. Zumstein, ARCR_Pred Study Group*, Andreas Müller

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e-mail address laurent.audige@kws.ch

* Members of the ARCR_Pred study group are listed in the main publication of this project protocol.

Patient information sheet and informed consent form (English version) for the project site “University Hospital of Basel” (USB)

Engl. Surgical safety and effectiveness in orthopaedics: evaluation of an international consensus core set of adverse events in arthroscopic rotator cuff repair

This project has been organised by: PD Dr. Andreas Müller (project leader; Deputy Consultant of Orthopaedics, Shoulder/Elbow team leader, Orthopaedic and Traumatology Department, University Hospital of Basel) and Prof. Dr. Laurent Audigé (project manager; Research Associate, Orthopaedic and Traumatology Department, University Hospital of Basel and Head of Research Group Upper Extremities, Department of Research and Development, Schulthess Clinic, Zurich)

Sponsor: University Hospital of Basel, PD Dr. Andreas Müller, Deputy Consultant of Orthopaedics and Traumatology

Dear Sir / Madam,

We would like to ask you if you are interested in participating in a research project. The planned project is first presented as a short summary in the table provided below followed by a more detailed description.

Summary of the project

1	<p>Aim of the project</p> <p>The research project will investigate how easily the most important results are predicted following surgical interventions to treat tears of the shoulder muscle (rotator cuff) tendons. In order to do this, we will use and assess a predefined set of adverse events (such as frozen shoulder or persistent pain) in practice.</p>
2	<p>Choice</p> <p>You are an adult suffering from a tear of the shoulder muscle tendons, which can be treated with an initial, minimally invasive (i.e. arthroscopic) surgical intervention. That is why we are sending you this information leaflet.</p>
3	<p>General information about the project</p> <p>The collection of clinical data following surgical interventions is very important, and helps to support an established decision-making process within the orthopaedic field. We are carrying out this project so that we can better evaluate and predict the results following the repair of shoulder muscle tendon tears. This evaluation is being carried out on a representative number of male and female patients in Switzerland.</p> <p>Patient safety is essential here. A list of possible adverse events following the arthroscopic intervention was recently defined by a group of more than 80 experts in the field. We would now like to better understand the development of these adverse events from the patient's point of view.</p>
4	<p>Procedure</p> <p>This project will last four years. In total, 970 patients from various clinics in Switzerland and one in Germany will be included in the study within the first year. Various examinations (e.g. measurements of range of motion and strength) will be carried out in the clinic before the operation (= preoperative) and then at the 6- and 12-month postoperative time points. At these times and at 2 years post-surgery, you will receive a questionnaire to complete. We will use ultrasound to check how the tendon is healing twelve months after the operation. Any adverse events will be evaluated independently by the doctor and the patient in question.</p>

5	<p>Usefulness You will gain no personal benefit from participating in the project. However, the results could be important to others who have the same condition.</p>
6	<p>Rights You decide voluntarily whether you want to participate in this project or not. Your decision does not affect your medical treatment/care and you do not have to justify it.</p>
7	<p>Duties If you participate, we ask you to adhere to certain requirements (e.g. attending visits and completing the questionnaires).</p>
8	<p>Risks You are not exposed to any additional risk by participating in the project.</p>
9	<p>Outcomes You will be informed of new results during the project. We will promptly inform you of any additional findings (known as incidental findings) that are detected during the regular study examinations, which may affect your health directly. Any further course of action will then be discussed in detail with you.</p>
10	<p>Confidentiality of data and samples We collect your personal and medical data from you. The Swiss National Science Foundation supports the exchange and reuse of research data. The data will be used for other projects if you give your separate consent. We comply with all legal data protection regulations. All parties involved are bound by confidentiality.</p>
11	<p>Withdrawal You can withdraw from the project at any time and no longer participate. The data collected so far are still being evaluated.</p>
12	<p>Indemnity You will not receive any compensation for participating in the study. Neither your health insurance provider nor you will incur any additional costs from your participation in the study.</p>
13	<p>Liability The liability insurance of the project management is liable for any damages within the scope of the project.</p>
14	<p>Funding The project is paid for by the Swiss National Science Foundation.</p>
15	<p>Contact person: You can receive information on all your questions at any time:</p> <p>PD Dr. Andreas Müller, Senior Consultant, Head Shoulder and Elbow, University Hospital of Basel, Spitalstrasse 21, CH-403 Basel Tel 061 315 25 17 , Email A.Mueller@usb.ch</p>

More detailed information

1. Aim of the project

The aim of this project is to investigate how the most important results (for example, the occurrence of adverse events or shoulder function) are easily predicted following a surgical intervention to treat **tears of the shoulder muscle tendons**. Furthermore, we want to investigate how well a predefined set of adverse events, which could occur as part of such a surgical intervention, corresponds to what actually occurs in practice.

2. Choice

Participation is open to anyone with a torn tendon in the shoulder muscles, which can be repaired with minimally invasive (i.e. arthroscopic) surgery.

Important: This must be the first intervention on the shoulder in question.

Participation is not open to anyone for whom a detailed medical examination would not be possible or who cannot be called back for check-ups within the follow-up period (e.g. if they live outside Switzerland). Underage persons should also not participate.

3. General information about the project

This project will be carried out in accordance with the laws of Switzerland. The responsible ethics committee has reviewed and approved this project

The collection of clinical data following surgical interventions is very important. You will help:

- to assess the effectiveness and safety of the intervention,
- to make comparisons with other methods,
- to support an established decision-making process within the orthopaedic field.

The study intends to document the most important events following arthroscopic interventions, especially in terms of:

- safety (occurrence of adverse events),
- healing of the tendon repair,
- shoulder pain and function,
- the general state of health and quality of life as well as
- patient satisfaction.

Patients' socio-demographic characteristics, examination parameters and treatment parameters will be investigated to enable a prediction of these events to be made.

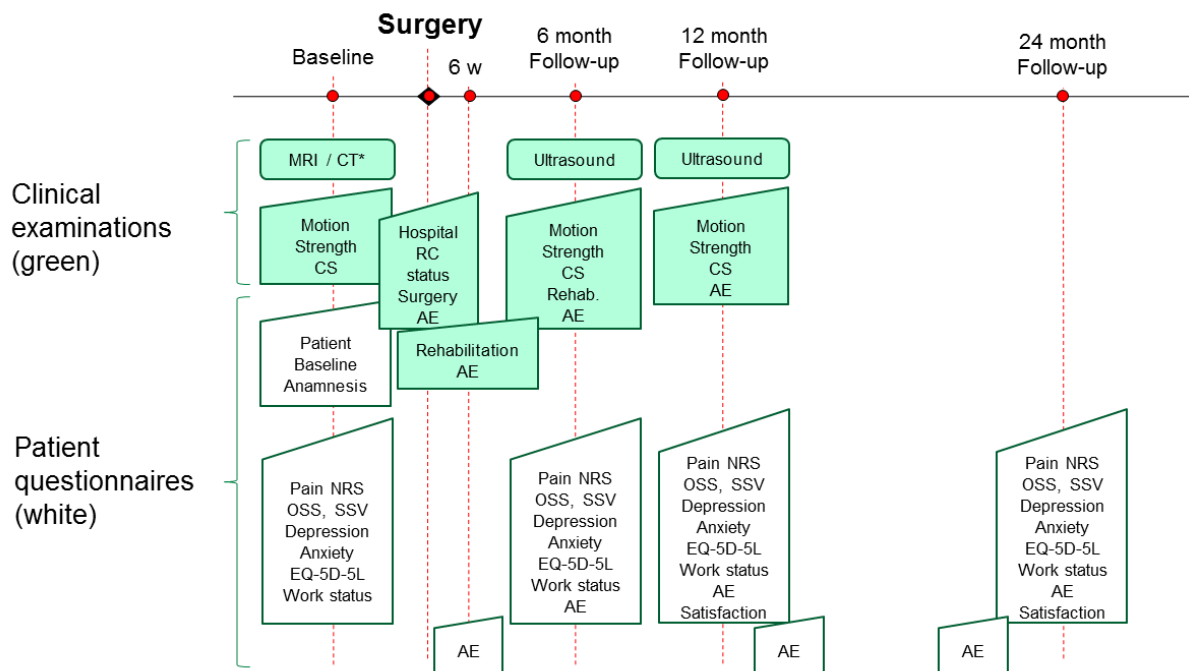
In most areas of orthopaedics, there is currently no international standard for the description of adverse events (often known as complications) resulting from surgical interventions. In shoulder orthopaedics, such a list of events does not exist for arthroscopic interventions used in the treatment of **tears of the shoulder muscle tendons (rotator cuff)**. For this reason, the Shoulder and Elbow Surgery research group at the Schulthess Clinic, Zurich, working together with the Orthopaedic and Traumatology Department of the University Hospital of Basel and over 80 experts working in the field of arthroscopy for rotator cuff tears, have defined a list of possible adverse events.

The aim is to apply and evaluate this predefined list of events. Each event will be evaluated independently by the doctor and the patient in question.

This project is supported by the Swiss National Science Foundation and will last four years. In total, 970 patients will be included in the study within the first year. These patients will be recruited from various clinics in Switzerland and one clinic in Germany. At the University Hospital of Basel about 60 patients are recruited.

4. Procedure

The following diagram shows the course of study events from the time of diagnosis to the follow-up appointment at two years post-surgery.



6 W = 6-week follow-up; AE = adverse events

Figure 1: Schematic representation of the study's progress

For your diagnosis, you will be examined by the doctor using various methods (e.g. functional testing, radiological and magnetic resonance imaging (= MRI)) during the first consultation. If you agree to participate in the project, you will receive a questionnaire, which will ask you to provide your personal details and estimate your current level of functional ability in everyday life. Shortly before the operation, your surgeon will record detailed information about your shoulder injury and the surgical intervention. Six weeks after the operation, your surgeon will ask you about your pain levels, rehabilitation programme and the occurrence of any adverse events.

During further follow-up appointments (at 6 and 12 months post-surgery), various examinations (e.g. measurements of range of motion and strength, see figure 1) are routinely performed in the clinic. An independent examiner will carry out an ultrasound routinely 12 months after the operation to document how the tendon is healing. You will also receive a questionnaire to complete. If you wish, you can complete this questionnaire at home - either on paper or electronically by following an invitation link that will be emailed to you. At the end of this document, you will be asked to provide your email address, if you do prefer to receive the electronic version of the questionnaire. Various questionnaires are already routinely recorded at the University Hospital of Basel.

Two years after the operation, you will be sent the questionnaire again by post or email (no further check-ups will take place at the clinic). This takes place within the framework of the project. If you have experienced one or more adverse events, the questionnaire will ask you to rate each event by severity and by its relationship to your treatment. The study doctors will evaluate all reported events by severity without knowing the patient, to whom these relate or the clinic in which the events occurred.

Each visit to the clinic (before surgery and 6- and 12-months post-surgery) will last 40 to 60 minutes including all the examinations. Completing the patient questionnaire will take an additional 20 to 30 minutes. An adverse event tends to be evaluated in only a few minutes.

We may have to exclude you from this project prematurely. This can occur if no tear of the rotator cuff can be confirmed intraoperatively (i.e. during the operation) (this occurs very rarely) or if a tendon repair is not possible without additional interventions on the shoulder (a so-called irreparable tear). The study doctor will inform you of any such exclusion from the project.

5. Usefulness

You will not personally benefit from participating in the project. The results can be important for others who have the same condition. As described above, the study aims to enable better evaluation and prediction of the risk of adverse events and the effectiveness of a surgical intervention. We want to support the decision-making processes of future interventions of this kind.

6. Rights

You're volunteering. If you do not want to participate or later withdraw your participation, you do not have to justify this. Your medical treatment/care is guaranteed regardless of your decision. You may ask questions about participation and the project at any time. Please contact the person named at the end of this information.

7. Duties

As a participant, it is necessary that you

- adhere to the necessary specifications and requirements of the project management.
- inform your investigator/project management about the course of the disease and report new symptoms, new complaints and changes in well-being.
- inform your investigator/project management about the simultaneous treatment and therapy with another doctor and about taking medication.

8. Risks

You are not exposed to any additional risk by participating in the project.

9. Outcomes

The investigator/project manager will inform you during the project about any new findings that may affect the benefit or your safety and thus your consent to participate. You will be informed of random findings which may contribute to the prevention, detection or treatment of existing or future diseases.

10. Confidentiality of data and samples

Your personal and medical data will be collected for this project. Very few professionals will see your unencrypted data, and only to perform tasks within the scope of the project. Data collection for study purposes is encrypted. Encryption means that all reference data that could identify you (name, date of birth) are deleted and replaced by a key. The key list always remains in the institution/hospital. Those who do not know the key cannot therefore draw any conclusions about you. In the

case of a publication, the summarised data cannot therefore be traced back to you as an individual. Your name will never appear on the Internet or in any publication. Sometimes there is a requirement in a journal for publication that individual data (so-called raw data) must be transmitted. If individual data must be transmitted, then the data is always encrypted and cannot be traced back to you as a person. All persons who have access to your data within the scope of the project are subject to confidentiality. The requirements of data protection are adhered to and you as a participating person have the right to inspect your data at any time.

If data are stored on site, it is a database for research purposes.

Each centre will encode and save the data centrally in the project database (server location: Schulthess Clinic, Zurich). The data will be deleted 10 years after the end of the project.

It is possible that your data may be used for other investigations (projects) at a later date or that they may be sent to another databank in Switzerland for investigations (further use) not yet defined in more detail. This other database must meet the same standards as the database for this project. For this further use we ask you to sign a further declaration of consent at the very end of this document.

This project may be reviewed by the relevant ethics committee or by the institution that initiated the project. The project manager may need to disclose your personal and medical information for such checks. All persons must maintain absolute confidentiality. We comply with all data protection regulations and will not make your name public either in a publication or on the Internet.

It is possible that your aftercare physician will be contacted to provide information about your medical condition.

11. Withdrawal

You can stop at any time and withdraw from the project if you wish. The data collected so far are still evaluated in encrypted form, otherwise the entire project loses its value. It is not possible to anonymize your data in case of withdrawal, i.e. the data remain encrypted. Please check whether you agree with this before you participate in the project.

12. Indemnity

If you participate in this project, you will not receive any compensation. You or your health insurance company will not incur any costs for participation.

13. Liability

The prerequisites and procedure relating to liability and safeguarding in the event of a claim are legally regulated. If you suffer a health impairment as a result of the study, please contact the study doctor. The institution that is responsible for carrying out the study is liable for the claim, if you can prove that the injury is due to the project-specific examinations. Liability will not be accepted if the project manager can prove that the injury is only minor and temporary, and does not extend beyond the degree expected by current scientific knowledge.

14. Funding

The project is being funded by the Swiss National Science Foundation (SNSF).

15. Contact person(s)

If you have any questions, concerns, or emergencies that arise during or after the project, you can always contact one of these contacts.

1
2
3
4 Head at the study location:

5 PD Dr. Andreas Müller, Senior Consultant, Head Shoulder and Elbow

6 University Hospital of Basel, Spitalstrasse 21, CH-403 Basel

7 Tel 061 315 25 17 , Email A.Mueller@usb.ch

8
9 24-hour emergency number: +41 61 265 25 25

10
11 Local project coordination:

12
13 PD Dr. Andreas Müller, Senior Consultant, Head Shoulder and Elbow

14 University Hospital of Basel, Spitalstrasse 21, CH-403 Basel

15 Tel 061 315 25 17 , Email A.Mueller@usb.ch

Declaration of consent

Written declaration of consent for participation in a study project

Please read this form carefully. Please ask if you do not understand or want to know something

BASEC number (after submission):

**Title of the project
(scientific and lay):**

Surgical safety and effectiveness in orthopaedics:
Swiss-wide multicenter evaluation and prediction of
core outcomes in arthroscopic rotator cuff
reconstruction

Surgical safeguarding and effectiveness in
orthopaedics: Swiss-wide multicentre evaluation and
prediction of the most important effects following
arthroscopic repair of shoulder tendons (rotator cuff
reconstruction)

**Responsible institution
(Project management with address):**

University Hospital of Basel
PD Dr. Andreas Müller
Orthopaedics and Traumatology
Spitalstrasse 21, CH-4031 Basel

Place of implementation:

Universitätsspital Basel

**Head of the project at the place of
study:**

PD Dr. Andreas Müller

Participant:

Name, first name: _____

Date of Birth: _____

Female Male

The undersigned investigator informed me verbally and in writing about the purpose, the course of the project, about possible advantages and disadvantages as well as about possible risks.

- I voluntarily participate in this project and accept the content of the written information provided on the above mentioned project. I've had plenty of time to make my decision.
- My questions concerning the participation in this project have been answered. I keep the written information and receive a copy of my written consent.
- I agree that the responsible experts of the project management/client of the project and the ethics committee responsible for this project may inspect my unencrypted data for verification and control purposes, but in strict compliance with confidentiality.
- I will be informed of study results or random findings that directly affect my health. If I don't want that, I'll inform my investigator.
- I know that my health-related and personal data can only be passed on in encrypted form for research purposes **for this project**.

- In the event of further treatment outside the test centre, I authorise my after-treating doctor(s) to forward my after-treatment data relevant to the project to the investigator/project management.
- I can withdraw from participation at any time and without giving reasons, without having any disadvantages in further medical treatment/care. The data collected so far will still be used for the evaluation of the project.
- The liability insurance of the hospital/institution covers any damages.
- I am aware that the obligations stated in the participant information must be complied with.
- If you agree that your email address can be used solely for receiving questionnaires and project-related communications, please enter it here:

_____@_____

Place, Date	Signature of participant

Confirmation from the investigator: I hereby confirm that I have explained the nature, significance and scope of the project to this participant. I assure you that I will fulfil all obligations in connection with this project in accordance with applicable law. If, at any time during the implementation of the project, I become aware of any aspects that might affect the participant's willingness to participate in the project, I will inform the participant immediately.

Place, Date	Name and first name of the informing investigator in block capitals Signature of the investigating physician
-------------	---

**Declaration of consent for the further use of data in encrypted form.
(for further use of data of THIS project)**

Participant:

Name, first name: _____

Date of birth: _____

Female

Male

I allow my data from this project to be used in encrypted form for medical research. This means that the data may be stored in a databank and used for future, not yet defined research projects for an indefinite period of time. This consent is unlimited.

I decide voluntarily and can revoke this decision at any time. When I step back, my data is anonymized. I simply inform my investigator/project manager and do not have to justify this decision.

I understand that the data are encrypted and the code is kept safe. The data can be sent to other databanks in Switzerland and abroad for analysis if they comply with the same standards as in Switzerland. All legal requirements regarding data protection are complied with.

Normally, all data are evaluated in their entirety and the results published in summary form. Should a result be relevant for me, it is possible that I will be contacted via my investigator. If I do not wish this, I will inform my investigator/project manager.

If results from the data are handled for commercial purposes, I hereby make no claims on any part of this commercial use.

Place, Date	Signature of participant
-------------	--------------------------

Confirmation from the investigator: I hereby confirm that I have explained to this participant the nature, significance and implications of the further use of data.

Place, Date	Name and first name of the informing investigator in block capitals
	Signature of the investigating physician

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. *BMJ*. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	4
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	n.a.
Protocol version	#3	Date and version identifier	4
Funding	#4	Sources and types of financial, material, and other support	4
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	4

1	Roles and	#5b	Name and contact information for the trial sponsor	4
2	responsibilities:			
3	sponsor contact			
4	information			
5				
6				
7	Roles and	#5c	Role of study sponsor and funders, if any, in study	4
8	responsibilities:		design; collection, management, analysis, and	
9	sponsor and funder		interpretation of data; writing of the report; and the	
10			decision to submit the report for publication,	
11			including whether they will have ultimate authority	
12			over any of these activities	
13				
14				
15				
16				
17	Roles and	#5d	Composition, roles, and responsibilities of the	4
18	responsibilities:		coordinating centre, steering committee, endpoint	
19	committees		adjudication committee, data management team,	
20			and other individuals or groups overseeing the trial,	
21			if applicable (see Item 21a for data monitoring	
22			committee)	
23				
24				
25				
26				
27	Introduction			
28				
29	Background and	#6a	Description of research question and justification for	7
30	rationale		undertaking the trial, including summary of relevant	
31			studies (published and unpublished) examining	
32			benefits and harms for each intervention	
33				
34				
35				
36	Background and	#6b	Explanation for choice of comparators	n.a.
37	rationale: choice of			
38	comparators			
39				
40				
41	Objectives	#7	Specific objectives or hypotheses	9
42				
43				
44	Trial design	#8	Description of trial design including type of trial (eg,	9
45			parallel group, crossover, factorial, single group),	
46			allocation ratio, and framework (eg, superiority,	
47			equivalence, non-inferiority, exploratory)	
48				
49				
50				
51	Methods:			
52	Participants,			
53	interventions, and			
54	outcomes			
55				
56				
57	Study setting	#9	Description of study settings (eg, community clinic,	9
58				
59				
60				

1		academic hospital) and list of countries where data	
2		will be collected. Reference to where list of study	
3		sites can be obtained	
4			
5	Eligibility criteria	#10 Inclusion and exclusion criteria for participants. If	10
6		applicable, eligibility criteria for study centres and	
7		individuals who will perform the interventions (eg,	
8		surgeons, psychotherapists)	
9			
10			
11			
12	Interventions:	#11a Interventions for each group with sufficient detail to	10
13	description	allow replication, including how and when they will	
14		be administered	
15			
16			
17	Interventions:	#11b Criteria for discontinuing or modifying allocated	n.a.
18	modifications	interventions for a given trial participant (eg, drug	
19		dose change in response to harms, participant	
20		request, or improving / worsening disease)	
21			
22			
23			
24	Interventions:	#11c Strategies to improve adherence to intervention	n.a.
25	adherence	protocols, and any procedures for monitoring	
26		adherence (eg, drug tablet return; laboratory tests)	
27			
28			
29			
30	Interventions:	#11d Relevant concomitant care and interventions that	10
31	concomitant care	are permitted or prohibited during the trial	
32			
33			
34	Outcomes	#12 Primary, secondary, and other outcomes, including	11
35		the specific measurement variable (eg, systolic	
36		blood pressure), analysis metric (eg, change from	
37		baseline, final value, time to event), method of	
38		aggregation (eg, median, proportion), and time	
39		point for each outcome. Explanation of the clinical	
40		relevance of chosen efficacy and harm outcomes is	
41		strongly recommended	
42			
43			
44			
45			
46	Participant timeline	#13 Time schedule of enrolment, interventions	13
47		(including any run-ins and washouts), assessments,	
48		and visits for participants. A schematic diagram is	
49		highly recommended (see Figure)	
50			
51			
52			
53	Sample size	#14 Estimated number of participants needed to	15
54		achieve study objectives and how it was	
55		determined, including clinical and statistical	
56		assumptions supporting any sample size	
57			
58			
59			
60			

calculations

1
2
3 Recruitment [#15](#) Strategies for achieving adequate participant 16
4 enrolment to reach target sample size
5

6 **Methods:**

7 **Assignment of**
8 **interventions (for**
9 **controlled trials)**
10
11

12
13 Allocation: sequence [#16a](#) Method of generating the allocation sequence (eg, n.a.
14 generation computer-generated random numbers), and list of
15 any factors for stratification. To reduce predictability
16 of a random sequence, details of any planned
17 restriction (eg, blocking) should be provided in a
18 separate document that is unavailable to those who
19 enrol participants or assign interventions
20
21
22

23
24 Allocation [#16b](#) Mechanism of implementing the allocation n.a.
25 concealment sequence (eg, central telephone; sequentially
26 mechanism numbered, opaque, sealed envelopes), describing
27 any steps to conceal the sequence until
28 interventions are assigned
29
30
31

32
33 Allocation: [#16c](#) Who will generate the allocation sequence, who will n.a.
34 implementation enrol participants, and who will assign participants
35 to interventions
36
37

38 Blinding (masking) [#17a](#) Who will be blinded after assignment to n.a.
39 interventions (eg, trial participants, care providers,
40 outcome assessors, data analysts), and how
41
42

43 Blinding (masking): [#17b](#) If blinded, circumstances under which unblinding is n.a.
44 emergency permissible, and procedure for revealing a
45 unblinding participant's allocated intervention during the trial
46
47

48 **Methods: Data**
49 **collection,**
50 **management, and**
51 **analysis**
52
53

54
55 Data collection plan [#18a](#) Plans for assessment and collection of outcome, 16
56 baseline, and other trial data, including any related
57 processes to promote data quality (eg, duplicate
58
59

measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol

1			
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4			
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9			
10	Data collection plan:	#18b	Plans to promote participant retention and complete
11	retention		follow-up, including list of any outcome data to be
12			collected for participants who discontinue or deviate
13			from intervention protocols
14			
15			
16			
17	Data management	#19	Plans for data entry, coding, security, and storage,
18			including any related processes to promote data
19			quality (eg, double data entry; range checks for
20			data values). Reference to where details of data
21			management procedures can be found, if not in the
22			protocol
23			
24			
25			
26			
27	Statistics: outcomes	#20a	Statistical methods for analysing primary and
28			secondary outcomes. Reference to where other
29			details of the statistical analysis plan can be found,
30			if not in the protocol
31			
32			
33			
34	Statistics: additional	#20b	Methods for any additional analyses (eg, subgroup
35	analyses		and adjusted analyses)
36			
37	Statistics: analysis	#20c	Definition of analysis population relating to protocol
38	population and		non-adherence (eg, as randomised analysis), and
39	missing data		any statistical methods to handle missing data (eg,
40			multiple imputation)
41			
42			
43			
44	Methods:		
45	Monitoring		
46			
47			
48	Data monitoring:	#21a	Composition of data monitoring committee (DMC);
49	formal committee		summary of its role and reporting structure;
50			statement of whether it is independent from the
51			sponsor and competing interests; and reference to
52			where further details about its charter can be found,
53			if not in the protocol. Alternatively, an explanation of
54			why a DMC is not needed
55			
56			
57			
58			
59			
60			

1	Data monitoring:	#21b	Description of any interim analyses and stopping	n.a.
2	interim analysis		guidelines, including who will have access to these	
3			interim results and make the final decision to	
4			terminate the trial	
5				
6				
7				
8	Harms	#22	Plans for collecting, assessing, reporting, and	14
9			managing solicited and spontaneously reported	
10			adverse events and other unintended effects of trial	
11			interventions or trial conduct	
12				
13				
14	Auditing	#23	Frequency and procedures for auditing trial	18
15			conduct, if any, and whether the process will be	
16			independent from investigators and the sponsor	
17				
18				
19				
20	Ethics and			
21	dissemination			
22				
23				
24	Research ethics	#24	Plans for seeking research ethics committee /	21
25	approval		institutional review board (REC / IRB) approval	
26				
27	Protocol	#25	Plans for communicating important protocol	21
28	amendments		modifications (eg, changes to eligibility criteria,	
29			outcomes, analyses) to relevant parties (eg,	
30			investigators, REC / IRBs, trial participants, trial	
31			registries, journals, regulators)	
32				
33				
34				
35				
36	Consent or assent	#26a	Who will obtain informed consent or assent from	21
37			potential trial participants or authorised surrogates,	
38			and how (see Item 32)	
39				
40				
41	Consent or assent:	#26b	Additional consent provisions for collection and use	n.a.
42	ancillary studies		of participant data and biological specimens in	
43			ancillary studies, if applicable	
44				
45				
46	Confidentiality	#27	How personal information about potential and	22
47			enrolled participants will be collected, shared, and	
48			maintained in order to protect confidentiality before,	
49			during, and after the trial	
50				
51				
52				
53	Declaration of	#28	Financial and other competing interests for principal	22
54	interests		investigators for the overall trial and each study site	
55				
56				
57	Data access	#29	Statement of who will have access to the final trial	22
58			dataset, and disclosure of contractual agreements	
59				
60				

that limit such access for investigators

1				
2	Ancillary and post	#30	Provisions, if any, for ancillary and post-trial care,	n.a.
3	trial care		and for compensation to those who suffer harm	
4			from trial participation	
5				
6				
7	Dissemination policy:	#31a	Plans for investigators and sponsor to communicate	23
8	trial results		trial results to participants, healthcare professionals,	
9			the public, and other relevant groups (eg, via	
10			publication, reporting in results databases, or other	
11			data sharing arrangements), including any	
12			publication restrictions	
13				
14	Dissemination policy:	#31b	Authorship eligibility guidelines and any intended	23
15	authorship		use of professional writers	
16				
17	Dissemination policy:	#31c	Plans, if any, for granting public access to the full	22
18	reproducible		protocol, participant-level dataset, and statistical	
19	research		code	
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26				
27	Appendices			
28				
29	Informed consent	#32	Model consent form and other related	Supplementary
30	materials		documentation given to participants and authorised	file
31			surrogates	
32				
33				
34	Biological specimens	#33	Plans for collection, laboratory evaluation, and	n.a.
35			storage of biological specimens for genetic or	
36			molecular analysis in the current trial and for future	
37			use in ancillary studies, if applicable	
38				
39				
40				

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