# Supplementary Online Content

Rämö L, Sumrein BO, Lepola V, et al; the FISH Investigators. Effect of surgery vs functional bracing on functional outcome among patients with closed displaced humeral shaft fractures: the FISH randomized clinical trial. *JAMA*. doi:10.1001/jama.2020.3182

**eTable 1.** Inclusion and exclusion criteria used in the FISH trial
**eTable 2.** Rehabilitation protocol
**eTable 3.** Interventions
**eTable 4.** Schedule of enrollment, interventions and assessments
**eTable 5.** Reasons for exclusion in 181 patients
**eTable 6.** Missing data items (no. of patients)
**eTable 7.** Primary and Secondary Outcomes at Different Time Points
**eTable 8.** Sensitivity analysis: as-treated and per protocol with crossover group
**eTable 9.** Sensitivity analysis: Study site as a fixed effect in the statistical mode
**eTable 10.** DASH of the declined cohort
**eTable 11.** Adverse events and crossovers in the declined cohort
**eTable 12.** Proportion of patients with union of the fracture
**eFigure 1.** Trajectories of secondary outcomes
**eFigure 2.** Trajectories of Per Protocol analysis with Crossover group
**eFigure 3.** Parallel line plot of the surgery and bracing groups with crossovers
**eAppendix.** Blinded data interpretation meeting notes

This supplementary material has been provided by the authors to give readers additional information about their work.

Table of Contents:

The FISH Investigators ..... 3
eTable 1 Inclusion and Exclusion Criteria Used in the FISH Trial. ..... 4
eTable 2 Rehabilitation protocol ..... 5
eTable 3 Interventions ..... 6
eTable 4 Schedule of enrollment, interventions and assessments ..... 7
eTable 5 Reasons for exclusion in 181 patients ..... 8
eTable 6 Missing data items ..... 9
eTable 7 Primary and Secondary Outcomes at Different Time Points ..... 10
eTable 8 Sensitivity analysis: As-treated and Per Protocol with Crossover group ..... 13
eTable 9 Sensitivity analysis: Study site as a fixed effect in the statistical model ..... 13
eTable 10 DASH of the declined cohort ..... 13
eTable 11 Adverse events and crossovers in the declined cohort ..... 14
eTable 12 Proportion of patients with union of the fracture ..... 14
eFigure 1 Trajectories of secondary outcomes ..... 15
eFigure 2 Trajectories of Per Protocol analysis with Crossover group ..... 16
eFigure 3 Parallel line plot of the surgery and bracing groups with crossovers ..... 17
Surgeon Experience ..... 18
Data Sharing Statement ..... 19
eAppendix Blinded data interpretation meeting notes ..... 20

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**eTable 1 Inclusion and Exclusion Criteria Used in the FISH Trial.**

Inclusion criteria

1. Age: 18 years or older
2. Unilateral displaced humeral shaft fracture
3. Displacement was at least the amount of the thickness of the cortex or in transverse fractures diastasis of the half of the thickness of the cortex was required
4. The fracture was lying in a zone delimited proximally by the superior border of the pectoralis major tendon attachment and distally by the line lying 5 cm from the upper border of the olecranon fossa as evaluated from the x-ray (see Figure 2 A in the main publication for illustration)
5. The fracture was less than 10 days old
6. The patient was willing to accept both treatment options and willing to participate in all follow-up visits
7. Patient spoke and read fluently either Finnish or Swedish (due to language used in data forms)

Exclusion criteria

1. Bilateral fracture
2. Fracture type where pectoralis major and deltoid muscle tendon insertions were in different fracture fragments causing typically significant fracture gap between the fragments (see Figure 2 B in the main publication for illustration)
3. Other concomitant trauma affecting the same upper extremity (fracture, tendon injury, significant soft tissue injury)
4. Other fracture, thoracic or abdominal injury requiring surgery
5. Open fracture
6. Pathologic fracture
7. Polytraumatized patient
8. Significant vascular injury warranting operative treatment
9. Plexus injury
10. History of trauma of the same upper extremity causing functional deficit
11. Trauma or condition that warranted use of walking aid (crutches, wheelchair etc.)
12. Disease that significantly affected general condition of the patient
13. Significantly impaired ability to co-operate for any reason (substance abuse, mental disorder, dementia)
14. Operative treatment unable to be performed within 14 days of trauma
15. Unwilling to accept both treatment methods

| eTable 2 Rehabilitation protocol | |
|---|---|
| Surgery group | |
| Weeks | Treatment |
| 0-3 | Active non-weight bearing exercises of the upper extremity, guided by physiotherapist before discharge. |
| 3-6 | Visit to physiotherapist at 3 weeks, previous exercises continued. |
| 6-9 | Gradual weight-bearing started. |
| 9-12 | Visit to physiotherapist at 9 weeks. Scapulohumeral rhythm exercises. |
| 12- | Free mobilization if no problems with consolidation. |
| Bracing group | |
| Weeks | Treatment |
| 0-3 | Active non-weight bearing exercises of the elbow and hand. Pendulum exercises of the shoulder. The exercises were taught to the patient at the emergency department if the patient was discharged and illustrated instructions were given. Patients were instructed to tighten the brace daily as the swelling resolved. |
| 3-6 | Visit to physiotherapist at 3 weeks. Passive range of motion (ROM) exercises of the shoulder started. |
| 6-9 | Active exercises of the upper extremity. Gradual weight bearing started. |
| 9-12 | Visit to physiotherapist at 9 weeks. Scapulohumeral rhythm exercises introduced. |
| 12- | Free mobilization if no problems with consolidation. |

| eTable 3 Interventions |
| --- |
| **Surgery group** |
| The operation was done within 14 days after the injury using open reduction and internal fixation with 4.5mm Locking Compression Plate (DePuy Synthes, Raynham, USA). The surgical approach, use of locking or non-locking screws, and use of bridging plate or dynamic compression with anatomic reduction was left at the discretion of the treating surgeon. |
| **Bracing group** |
| The functional brace (see Figure 2 C of the main publication for image) was applied in the emergency department at the time of admission if the patient tolerated the application of the brace. In a few cases the patient first had a U-splint which was changed to a functional brace within 7 days after the admission.<br><br>Braces used in the study:<br>• Helsinki University Hospital: A custom-made functional orthosis at the beginning of the trial, replaced by a ready-made Humerus Comfort brace (NordiCare, Viken, Sweden) in 2014.<br>• Tampere University Hospital: A Humerus Splint (GeniMedical, Houten, Netherlands) throughout the trial. |

| eTable 4 Schedule of enrollment, interventions and assessments | | | | | | | |
|---|---|---|---|---|---|---|---|
| | STUDY PERIOD | | | | | | |
| | Enrolment | Allocation | Post-allocation[b] | | | | |
| TIMEPOINT | Within 10 days after trauma | Within 10 days after trauma | Within 14 days after trauma | 6 weeks | 12 weeks | 6 months | 12 months |
| ENROLMENT: | | | | | | | |
| Eligibility screen | X | | | | | | |
| Informed consent | X | | | | | | |
| Allocation | | X | | | | | |
| INTERVENTIONS: | | | | | | | |
| Surgery | | | X | | | | |
| Bracing | | | ◆ | ——— | ◆ | | |
| ASSESSMENTS: | | | | | | | |
| Baseline data, 15D, DASH | X | X | | | | | |
| Assessment for recovery[a], DASH, Pain-NRS, 15D | | | | X | X | X | X |
| Constant-Murley score, patient questionnaire, x-ray | | | | X | X | X | X |

[a] Recovery is considered achieved when scoring maximum of 10 points more in Disabilities of Arm, Shoulder and Hand (DASH) score compared to preinjury DASH score. Also, the proportion of patients scoring equal or less in DASH score compared to preinjury level is calculated and this score is considered as a definition of a conservative or a 'safe' estimate of recovery to preinjury status.

[b] The measure of time was deployed as nominal time. The median differences between the actual time and nominal time were 2 (IQR -1 to 5), 4.5 (1 to 10), 2 (-1 to 10), and 5.5 (2 to 13.5) days at 6, 12, 26, and 52 weeks post-randomization, respectively.

| eTable 5 Reasons for exclusion in 181 patients[a] | |
|---|---|
| **Reason for exclusion** | **No. of patients having this reason** |
| Too Proximal Fracture | 56 |
| Too Distal Fracture | 35 |
| Compliance problem | 30 |
| Significant health problem | 30 |
| Other trauma affecting the same upper limb | 14 |
| History of older trauma or disease affecting the same upper limb | 13 |
| Polytrauma | 10 |
| Language problem | 8 |
| Pathological fracture | 7 |
| Open fracture | 6 |
| Fracture between deltoid and pectoralis major attachment | 5 |
| Other fracture warranting operation | 4 |
| Periprosthetic fracture | 3 |
| Advancing radial nerve palsy | 3 |
| Needs walking aid | 3 |
| Foreign patient | 2 |
| Fracture not dislocated enough | 2 |
| Plexus injury | 1 |
| Fracture older than 10 days | 1 |
| Bilateral fracture | 0 |
| Floating shoulder | 0 |
| Floating elbow | 0 |
| Vascular injury | 0 |
| **Total** | 233 |

[a] Some of the patients had more than one reason for exclusion.

| eTable 6 Missing data items (no. of patients) | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Baseline | | | 6 weeks | | | 3 months | | | 6 months | | | 12 months | | |
| Outcome | Surgery Group | Bracing Group | Declined Cohort | Surgery Group | Bracing Group | Declined Cohort | Surgery Group | Bracing Group | Declined Cohort | Surgery Group | Bracing Group | Declined Cohort | Surgery Group | Bracing Group | Declined Cohort |
| DASH score[a] | 1[c] | 0 | 0 | 1 | 1 | 6 | 4 | 2 | 8 | 4 | 1 | 9 | 2 | 2 | 7 |
| Pain at rest | N/A | N/A | N/A | 0 | 0 | 6 | 4 | 0 | 8 | 4 | 1 | 9 | 3 | 2 | 6 |
| Pain at activity | N/A | N/A | N/A | 0 | 0 | 6 | 4 | 1 | 8 | 4 | 1 | 9 | 3 | 2 | 6 |
| 15D score[b] | 0 | 0 | 1 | 1 | 1 | 11 | 4 | 3 | 7 | 6 | 2 | 9 | 5 | 2 | 5 |
| Constant-Murley score | N/A | N/A | N/A | 1 | 1 | 8 | 2 | 2 | 7 | 3 | 1 | 9 | 3 | 3 | 6 |
| X-rays not available for assessing union status | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | 1 | 0 | 4 |

[a] DASH score is considered missing data, if more than 3 values are missing making DASH score calculation impossible.

[b] 15D score is considered missing data, if one or more value is missing.

[c] Patient had reported very high values in DASH questionnaire as a baseline data. The values of this patient after 6 weeks were much lower compared to baseline which seems implausible considering the fact that fracture cannot heal that quickly. The Study Group decided to exclude the values this patient gave in baseline data since patient should have reported the situation before the fracture. The patient has died due to reasons not related to the fracture during the trial and it was not possible to obtain corrected values for the baseline data.

| eTable 7 Primary and Secondary Outcomes at Different Time Points[a] | | | | |
|---|---|---|---|---|
| **Outcomes** | **Surgery group (N=38) mean (95% CI)** | **Bracing group (N=44) mean (95% CI)** | **Between-group mean difference (95% CI)** | **P-value** |
| **6 weeks** | | | | |
| *Primary outcome* | | | | |
| DASH score[b] | 39.8 (35.1 to 44.5) | 49.7 (45.4 to 54.0) | -9.9 (-16.3 to -3.5) | 0.002 |
| *Secondary outcome* | | | | |
| Pain at rest[c] | 2.1 (1.5 to 2.7) | 1.9 (1.4 to 2.5) | 0.2 (-0.6 to 0.9) | 0.66 |
| Pain on activities[c] | 4.4 (3.6 to 5.2) | 5.6 (4.8 to 6.3) | -1.2 (-2.3 to -0.1) | 0.04 |
| Constant-Murley score[d] | 53.3 (47.5 to 59.2) | 22.6 (17.2 to 28.0) | 30.7 (22.8 to 38.7) | <0.001 |
| Elbow ROM – degrees[e] | 125 (119 to 131) | 96 (91 to 101) | 29 (21 to 37) | <0.001 |
| 15D score[f] | 0.88 (0.86 to 0.90) | 0.85 (0.83 to 0.87) | 0.03 (-0.01 to 0.07) | 0.13 |
| DASH work module score[g] | 61.9 (51.3 to 72.4) | 83.6 (71.7 to 95.5) | -21.7 (-37.6 to -5.8) | 0.008 |
| DASH sports/performing arts module score[g] | 77.6 (65.4 to 89.9) | 99.6 (85.7 to 100) | -21.9 (-40.5 to -3.4) | 0.02 |
| Patients with acceptable symptomatic state[h] – % | 24 (10 to 38) | 11 (1 to 21) | 12 (-4 to 28) | 0.13 |
| Adequate clinical recovery[i] – % | 6 (0 to 14) | 2 (0 to 6) | 3 (-5 to 11) | 0.45 |
| Satisfaction with shoulder function[j] | 7.1 (6.3 to 7.8) | 5.8 (5.1 to 6.5) | 1.2 (0.2 to 2.3) | 0.02 |
| Satisfaction with elbow function[j] | 7.3 (6.6 to 7.9) | 6.5 (5.8 to 7.1) | 0.8 (-0.1 to 1.7) | 0.08 |
| Satisfaction with upper limb function[j] | 6.5 (5.8 to 7.3) | 4.6 (3.9 to 5.4) | 1.9 (0.8 to 3.0) | <0.001 |
| Patients able to return to previous daily activities – % | 68 (52 to 84) | 66 (52 to 80) | 3 (-17 to 23) | 0.76 |
| Patients able to return to previous hobbies – % | 16 (4 to 28) | 11 (1 to 21) | 5 (-11 to 21) | 0.53 |
| **3 months** | | | | |
| *Primary outcome* | | | | |
| DASH score | 23.8 (18.9 to 28.6) | 33.8 (29.5 to 38.1) | -10.1 (-16.6 to -3.6) | 0.002 |
| *Secondary outcome* | | | | |
| Pain at rest | 1.5 (1.0 to 2.1) | 1.3 (0.7 to 1.8) | 0.3 (-0.5 to 1.1) | 0.48 |
| Pain at activities | 3.5 (2.7 to 4.4) | 4.3 (3.5 to 5.1) | -0.8 (-1.9 to 0.4) | 0.18 |
| Constant-Murley score | 61.9 (56.0 to 67.8) | 46.9 (41.5 to 52.3) | 14.9 (6.9 to 22.9) | <0.001 |
| Elbow ROM – degrees | 134 (129 to 140) | 121 (115 to 126) | 14 (6 to 21) | <0.001 |
| 15D score | 0.91 (0.89 to 0.93) | 0.88 (0.86 to 0.90) | 0.03 (-0.01 to 0.07) | 0.13 |
| DASH work module score | 33.0 (22.5 to 43.6) | 45.2 (33.3 to 57.2) | -12.2 (-28.2 to 3.8) | 0.13 |
| DASH sports/performing arts module score | 55.5 (42.1 to 68.9) | 83.0 (69.5 to 96.6) | -27.5 (-46.6 to -8.4) | 0.005 |
| Patients with acceptable symptomatic state – % | 46 (30 to 62) | 20 (8 to 32) | 26 (6 to 46) | 0.01 |
| Adequate clinical recovery – % | 23 (9 to 37) | 11 (1 to 21) | 12 (-6 to 30) | 0.18 |
| Satisfaction with shoulder function | 6.8 (6.0 to 7.6) | 6.1 (5.4 to 6.8) | 0.6 (-0.4 to 1.7) | 0.24 |
| Satisfaction with elbow function | 7.6 (6.9 to 8.3) | 7.4 (6.8 to 8.1) | 0.2 (-0.8 to 1.1) | 0.74 |
| Satisfaction with upper limb function | 7.1 (6.3 to 7.9) | 5.4 (4.7 to 6.2) | 1.6 (0.6 to 2.7) | 0.003 |
| Patients able to return to previous daily activities – % | 81 (67 to 95) | 78 (66 to 90) | 3 (-15 to 21) | 0.74 |
| Patients able to return to previous hobbies – % | 40 (24 to 56) | 27 (13 to 41) | 12 (-10 to 34) | 0.28 |

| | | | | |
|---|---|---|---|---|
| **6 months** | | | | |
| *Primary outcome* | | | | |
| DASH score | 13.5 (8.7 to 18.3) | 18.4 (14.1 to 22.7) | -4.9 (-11.3 to 1.6) | 0.14 |
| *Secondary outcome* | | | | |
| Pain at rest | 1.0 (0.4 to 1.6) | 0.7 (0.1 to 1.2) | 0.3 (-0.5 to 1.1) | 0.47 |
| Pain at activities | 2.4 (1.6 to 3.2) | 2.5 (1.7 to 3.3) | -0.1 (-1.2 to 1.0) | 0.86 |
| Constant-Murley score | 73.1 (67.1 to 79.0) | 64.3 (58.9 to 69.7) | 8.8 (0.8 to 16.9) | 0.03 |
| Elbow ROM – degrees | 139 (133 to 145) | 133 (127 to 138) | 6 (-2 to 14) | 0.14 |
| 15D score | 0.93 (0.91 to 0.95) | 0.91 (0.89 to 0.93) | 0.02 (-0.02 to 0.06) | 0.32 |
| DASH work module score | 12.3 (1.8 to 22.9) | 25.4 (14.9 to 36.0) | -13.1 (-28.1 to 1.8) | 0.09 |
| DASH sports/performing arts module score | 19.4 (6.8 to 32.1) | 37.4 (24.6 to 50.2) | -18.0 (-36.0 to 0.0) | 0.05 |
| Patients with acceptable symptomatic state – % | 71 (55 to 87) | 51 (35 to 67) | 21 (-1 to 43) | 0.06 |
| Adequate clinical recovery – % | 66 (50 to 82) | 48 (32 to 64) | 17 (-5 to 39) | 0.12 |
| Satisfaction with shoulder function | 8.3 (7.5 to 9.1) | 7.0 (6.3 to 7.7) | 1.3 (0.3 to 2.4) | 0.02 |
| Satisfaction with elbow function | 8.9 (8.2 to 9.6) | 8.0 (7.3 to 8.6) | 0.9 (0 to 1.9) | 0.05 |
| Satisfaction with upper limb function | 8.4 (7.6 to 9.2) | 6.8 (6.1 to 7.6) | 1.5 (0.5 to 2.6) | 0.01 |
| Patients able to return to previous daily activities – % | 95 (87 to 100) | 93 (85 to 100) | 2 (-8 to 12) | 0.69 |
| Patients able to return to previous hobbies – % | 73 (57 to 89) | 60 (46 to 74) | 13 (-9 to 35) | 0.24 |
| **12 months** | | | | |
| *Primary outcome* | | | | |
| DASH score | 8.9 (4.2 to 13.6) | 12.0 (7.7 to 16.4) | -3.1 (-9.6 to 3.3) | 0.34 |
| *Secondary outcome* | | | | |
| Pain at rest | 0.9 (0.4 to 1.5) | 0.7 (0.1 to 1.2) | 0.3 (-0.5 to 1.1) | 0.47 |
| Pain at activities | 2.2 (1.4 to 3.0) | 1.7 (1.0 to 2.5) | 0.5 (-0.7 to 1.6) | 0.40 |
| Constant-Murley score | 78.1 (72.1 to 84.0) | 76.4 (70.9 to 81.8) | 1.7 (-6.4 to 9.8) | 0.68 |
| Elbow ROM – degrees | 143 (138 to 149) | 137 (131 to 142) | 7 (-1 to 15) | 0.10 |
| 15D score | 0.95 (0.93 to 0.97) | 0.92 (0.90 to 0.94) | 0.03 (-0.01 to 0.07) | 0.13 |
| DASH work module score | 5.2 (0 to 15.3) | 8.0 (0 to 18.4) | -2.9 (-17.4 to 11.6) | 0.70 |
| DASH sports/performing arts module score | 6.7 (0 to 19.3) | 27.9 (15.4 to 40.3) | -21.2 (-38.9 to -3.4) | 0.02 |
| Patients with acceptable symptomatic state – % | 82 (70 to 94) | 68 (54 to 82) | 14 (-6 to 34) | 0.16 |
| Adequate clinical recovery – % | 86 (74 to 98) | 73 (59 to 87) | 13 (-5 to 31) | 0.15 |
| Satisfaction with shoulder function | 8.5 (7.7 to 9.3) | 8.0 (7.3 to 8.7) | 0.5 (-0.6 to 1.6) | 0.36 |
| Satisfaction with elbow function | 9.0 (8.3 to 9.7) | 8.8 (8.2 to 9.4) | 0.2 (-0.7 to 1.2) | 0.62 |
| Satisfaction with upper limb function | 8.6 (7.8 to 9.4) | 7.6 (6.9 to 8.4) | 1.0 (-0.1 to 2.1) | 0.08 |
| Patients able to return to previous daily activities – % | 96 (90 to 100) | 91 (83 to 99) | 5 (-5 to 15) | 0.32 |
| Patients able to return to previous hobbies – % | 85 (73 to 97) | 80 (68 to 92) | 5 (-13 to 23) | 0.58 |
| Patients willing to repeat the same treatment[k] – % | 97 (91 to 100) | 71 (58 to 85) | 26 (11 to 40) | 0.003 |

[a] The point estimates are derived from the MMRM ANOVA model using all available data.

[b] Disabilities of Arm, Shoulder and Hand (DASH) score is a widely used and validated tool assessing upper-extremity related deficits and symptoms in daily life reported by the patient. The instrument consists of 30 items. The range of the score is from 0 (no disability) to 100 (extreme disability). Values under 10 points represent a mean value in a randomly selected population aged between 20 and 60 years. 10 points is generally regarded as a minimal important difference in DASH score. A DASH score may not be calculated if there are greater than 3 missing items.

[c] Pain at rest and on activities was reported on 0-10 numerical rating scale where 0 is no pain and 10 is the worst imaginable pain.

[d] The Constant-Murley score is a widely used instrument assessing various conditions affecting shoulder function. It has two subjective (pain, 0-15 points; activities of daily living, 0-20 points) and two objective (shoulder range of motion, 0-40 points; strength, 0-25 points) subscales. The range of the score is from 0 to 100 with higher score

denoting better function. Values around 85 points are considered normal in individuals aged 40 to 60. The measurements were performed by a physiotherapist unaware of the treatment group.

[e] Elbow ROM was measured by the physiotherapist using goniometer and calculated using the difference in degrees between full flexion and full extension.

[f] The 15D instrument is a generic health-related quality-of-life instrument comprising 15 dimensions. The maximum 15D score is 1 (full health), and the minimum score is 0 (death). Values over 0.9 are comparable to randomly selected Finnish population of individuals aged 30 years and over.

[g] DASH work and sports/performing arts modules are optional modules comprising of four questions assessing the effect of upper extremity condition on the work and sports/performing arts. The range of the score is from 0 (no disability) to 100 (extreme disability). Values under 10 points mean the individual can do work or perform sports with minimal limitations, at most. An optional module score may not be calculated if there are any missing items.

[h] Patients with acceptable symptomatic state was determined using patient's global assessment of satisfaction regarding the injured arm and was elicited with the question, "How satisfied are you with the overall condition of your injured upper limb and its effect on your daily life?" Responses were given on a 7-point Likert scale. "Very satisfied" and "Satisfied" were categorized as having acceptable symptomatic state and "Somewhat satisfied", "Neither satisfied nor dissatisfied", "Somewhat dissatisfied", "Dissatisfied," and "Very dissatisfied" as not having acceptable symptomatic state.

[i] Patients reporting a DASH score within a minimal important difference (10 points) of their preinjury score were considered to have adequate clinical recovery.

[j] Satisfaction with shoulder, elbow and upper extremity function was reported on 0-10 numerical rating scale where 0 is the worst and 10 is the best condition.

[k] Patients were asked whether they would like to have the same treatment again if they sustained a similar kind of injury later. Responses were given as "Yes" or "No".

| eTable 8 Sensitivity analysis: As-treated[a] and Per Protocol with Crossover group[b] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | As-treated | | | Per Protocol and Crossover | | | | |
| DASH score | Surgery group mean (95% CI) | Bracing group mean (95% CI) | Between-group mean difference (95% CI) | Surgery group mean (95% CI) | Bracing group mean (95% CI) | Crossover group mean (95% CI) | Between-group mean difference (95% CI) Surgery - Bracing | Between-group mean difference (95% CI) Surgery - Crossover |
| 6 weeks | 42.0 (37.6 to 46.3) | 48.1 (43.9 to 52.3) | -6.2 (-11.9 to -0.4) | 39.8 (35.2 to 44.4) | 49.0 (43.9 to 54.0) | 51.3 (43.6 to 59.0) | -9.2 (-16.0 to -2.3) | -11.5 (-20.4 to -2.5) |
| 3 months | 26.0 (21.6 to 30.4) | 32.6 (28.2 to 37.0) | -6.6 (-12.5 to -0.7) | 23.8 (19.1 to 28.6) | 30.3 (25.2 to 35.4) | 41.7 (34.0 to 49.4) | -6.5 (-13.5 to 0.5) | -17.9 (-26.9 to -8.9) |
| 6 months | 16.1 (12.0 to 20.3) | 16.2 (11.6 to 20.8) | -0.1 (-6.0 to 5.8) | 13.6 (8.8 to 18.3) | 15.0 (10.0 to 20.0) | 26.7 (18.8 to 34.5) | -1.4 (-8.4 to 5.5) | -13.1 (-22.3 to -3.9) |
| 12 months | 11.8 (7.8 to 15.7) | 8.7 (3.8 to 13.6) | 3.1 (-2.9 to 9.0) | 8.9 (4.3 to 13.6) | 8.5 (3.4 to 13.6) | 20.0 (12.3 to 27.7) | 0.4 (-6.5 to 7.4) | -11.1 (-20.1 to -2.1) |

[a] In as-treated analysis groups were analyzed per latest treatment modality (surgery/nonoperative) at the different follow-up time points. The number of patients in surgery group increased in subsequent follow-up points as patients allocated to functional bracing were operated during the 12 months.

[b] In per protocol analyses there were three groups: surgery group, bracing group with no surgery during 12-months follow-up, and a separate crossover group (preplanned subgroup analysis of the patients who were not able to follow the protocol until 12 months. All patients belonging to this group were initially allocated to bracing but had late surgery due to reasons given in Table 3 of the main text).

| eTable 9 Sensitivity analysis: Study site as a fixed effect in the statistical model | | | |
|---|---|---|---|
| | | | |
| DASH score | Surgery group mean (95% CI) | Bracing group mean (95% CI) | Between-group mean difference (95% CI) |
| 6 weeks | 39.8 (35.1 to 44.5) | 49.7 (45.4 to 54.0) | -9.9 (-16.3 to -3.5) |
| 3 months | 23.8 (18.9 to 28.6) | 33.8 (29.5 to 38.1) | -10.0 (-16.5 to -3.5) |
| 6 months | 13.5 (8.7 to 18.4) | 18.4 (14.1 to 22.7) | -4.8 (-11.3 to 1.7) |
| 12 months | 8.9 (4.2 to 13.7) | 12.0 (7.7 to 16.4) | -3.1 (-9.6 to 3.3) |

| eTable 10 DASH of the declined cohort | | | | |
|---|---|---|---|---|
| DASH score | Surgery group mean (95% CI) | Bracing group mean (95% CI) | Between-group mean difference (95% CI) | P-value |
| Baseline | 4.8 (-5.9 to 15.5) | 3.0 ( -2.5 to 8.5) | 1.8 (-10.3 to 13.8) | 0.77 |
| 6 weeks | 36.7 (24.2 to 49.1) | 50.2 (44.5 to 56.0) | -13.6 (-27.3 to 0.2) | 0.05 |
| 3 months | 28.1 (15.6 to 40.5) | 28.0 (22.2 to 33.9) | 0.04 (-13.7 to 13.8) | 1.00 |
| 6 months | 18.3 (5.9 to 30.8) | 13.5 (7.6 to 19.5) | 4.8 (-9.0 to 18.6) | 0.50 |
| 12 months | 13.8 (2.1 to 25.6) | 10.3 (4.4 to 16.1) | 3.6 (-9.5 to 16.7) | 0.59 |

| eTable 11 Adverse events and crossovers in the declined cohort | | |
|---|---|---|
| **Description** | **Surgery group** | **Bracing group** |
| Serious adverse event | | |
| | 0 | 1[a] |
| Minor adverse event | | |
| Fracture non-union[b] | 2 | 6 |
| Implant failure[c] | 1 | |
| Secondary temporary radial nerve palsy[d] | 1 | |
| Sensory disturbance of the hand[e] | | 1 |
| **Reason for crossover** | | |
| Operation due to non-union (time range 5-12 months) | | 6 |

[a] The patient had gastrointestinal bleeding after using nonsteroidal anti-inflammatory drug. The condition stabilized after gastroscopy and transfusion.

[b] 8 patients were operated due to non-union at 12 months. Two of them were in the Surgery group. The other went to union after re-operation and the other patient was operated twice, but the fracture did not heal even after the second re-operation and the patient chose with the treating doctor not to have a third operation. 6 patients in the Bracing group were operated due to nonunion and all united after the operation. The definition for non-union and indication for an operation promoting union was no bridging fracture callus in 3 of the 4 cortices in x-ray (ap- and lateral view) and clinically tested mobility in the fracture site at 12 weeks or later after the fracture.

[c] The patient in Surgery group was re-operated at 3 months due to failure of the too short implant (only 1 bicortical screw at the healthy bone on the proximal side). The patient went to uneventful healing after the reoperation.

[d] The patient was operated promptly after the primary operation due to secondary palsy since there was no mention in the surgical report on the position of radial nerve. The nerve was found intact. The wound could not be closed at this secondary operation and negative wound pressure was applied and the wound was closed at 1 week. The secondary palsy resolved spontaneously.

[e] The patient had a sensory disturbance of the median nerve after the operation for nonunion. The sensory disturbance was permanent.

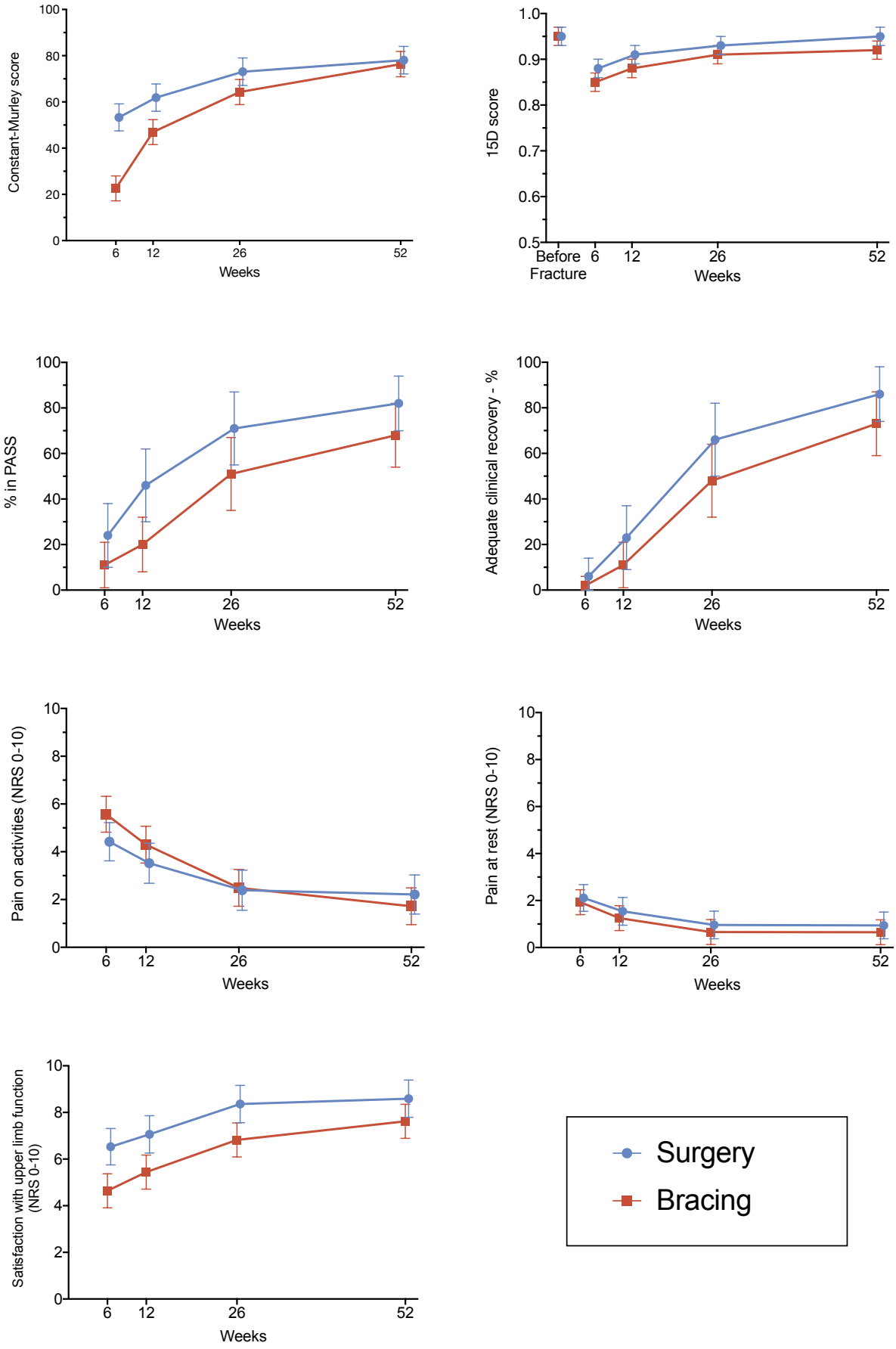
| eTable 12 Proportion of patients with union[a] of the fracture | | |
|---|---|---|
| **Follow-up time point** | **Surgery group n (%)** | **Bracing group n (%)** |
| 6 weeks | 13 (34%) | 10 (23%) |
| 3 months | 26 (68%) | 28 (64%) |
| 6 months | 35 (92%) | 33 (75%) |
| 12 months | 37 (97%)[b] | 40 (91%)[c] |

[a] Union was defined as bridging callus in x-ray on 3 of the 4 cortices or fading of the fracture line in 3 of the 4 cortices in patients operated with absolute stability (no callus formation) and fracture was clinically stable and pain-free in stability testing.

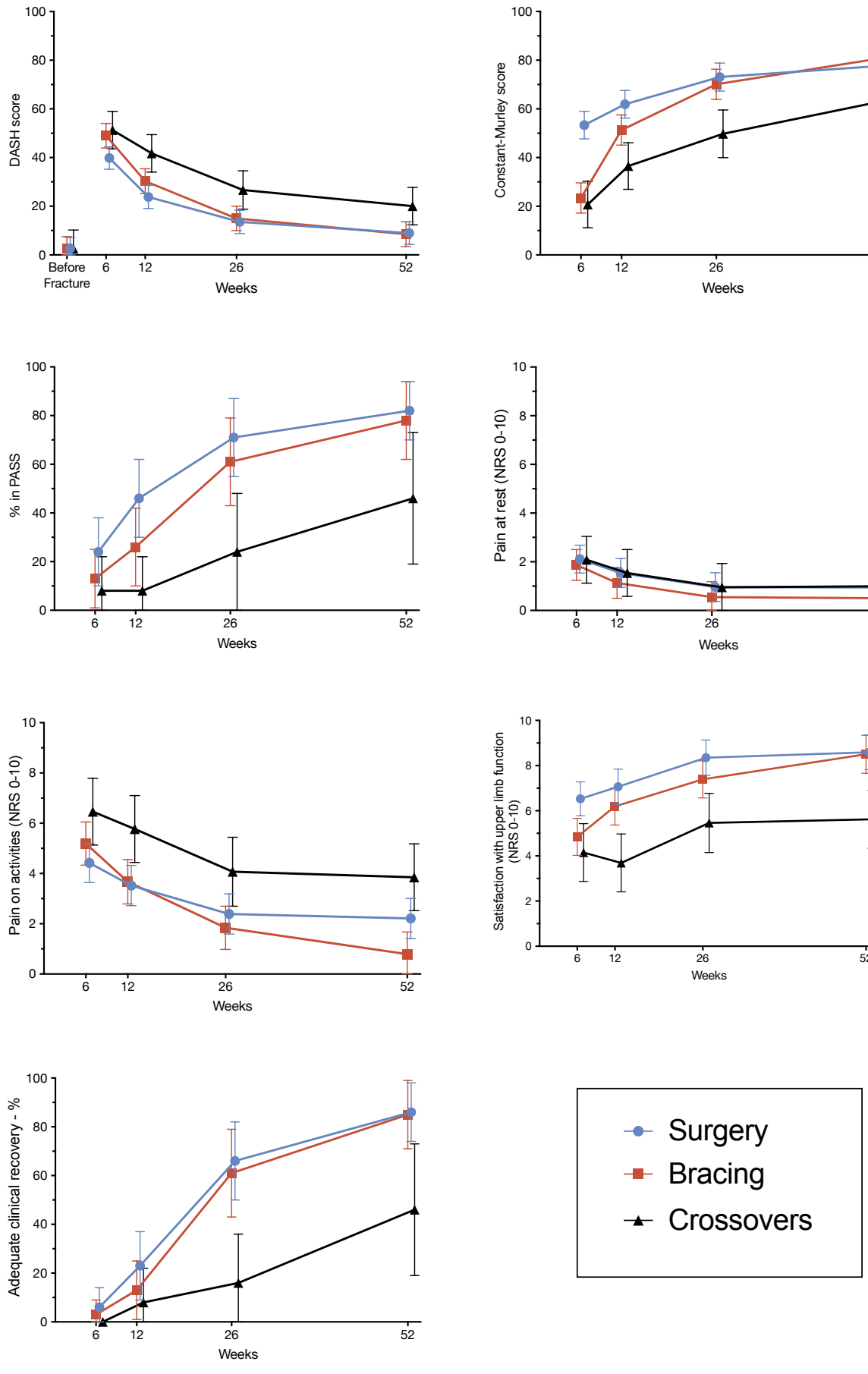
[b] One patient in surgery group did not have follow-up data at 12 months. All other patients in the surgery group had achieved union of the fracture at 12 months.

[c] Three patients in bracing group did not achieve bony union eventually. One of the patients was operated at 15 months (delay due to other health issues) and the fracture united in 3 months.

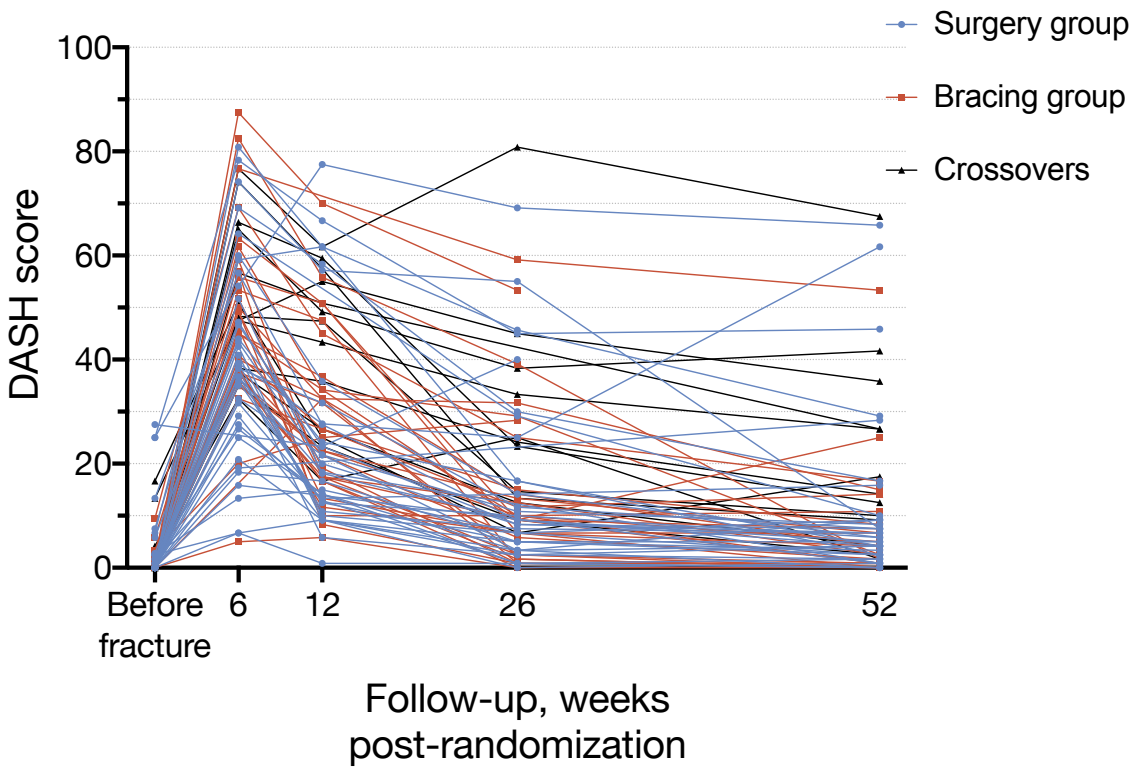
**eFigure 1 Trajectories of secondary outcomes**



**eFigure 2 Trajectories of Per Protocol analysis with Crossover group**



**eFigure 3 Parallel line plot of the surgery and bracing groups with crossovers[a]**




[a] 13 patients originally randomized to bracing underwent surgery during the 12 months and are here categorized as 'crossovers'. See reasons for crossing over in Table 3 of the publication.

**Surgeon Experience**

In Finland, where the FISH trial was carried out, there are 5 university hospitals and the patient recruitment for the trial was performed in 2 of them. Both trial centers are the primary referral centers for major trauma in their respective areas. In the Helsinki University Hospital, the annual number of orthopedic trauma surgeries is about 4200-4450 with about half as many in the Tampere University Hospital.

We did not have any predetermined limit for experience for the FISH surgeons. In essence, the trial was pragmatic in this sense.

Orthopedic attending staff and trainees participating in this trial had at least 3 years of prior surgical experience. The attending surgeons performing the operations or assisting a resident (but responsible of the surgery if present in the OR) had performed a mean of 54 humeral fracture plate osteosynthesis (range 5-155) while working at the study centers prior to participating in the study.

All the operations were carefully planned together with the resident and attending surgeon irrespective of who was designated as the operating surgeon. If the surgery was performed by the resident alone, the attending surgeon was readily available to join the surgery if needed. In 7 cases the primary surgeon was a resident and attending surgeon did not enter the OR. In these cases, the mean prior experience of the residents was 19 (range 5-52) plate osteosynthesis of the humerus fracture. In all the other cases, the surgery was performed either by attending surgeon or by a resident with the attending surgeon present in the operating room.

One of the 7 patients operated by a resident alone developed a wound hematoma/seroma postoperatively, which resolved without additional interventions. All other patients with a postoperative complication (4 temporary radial nerve palsies, 3 superficial infections, 1 adhesive capsulitis) were operated on by an attending surgeon who had prior operative experience of at least 25 humeral fracture plate osteosynthesis surgeries.

**Data Sharing Statement**

Data available: Yes

Data types: Deidentified participant data, Data dictionary

How to access data: Data will be provided on reasonable request to corresponding author Lasse Rämö (lasse.ramo@hus.fi)

When available: With publication

Document types: Templates of informed consent form and other forms used in data collection from participants.

How to access documents: Supporting documents will be provided on reasonable request to corresponding author Lasse Rämö (lasse.ramo@hus.fi)

When available: With publication

Who can access the data: researchers whose proposed use of the data has been approved

Types of analyses: meta-analysis

Mechanisms of data availability: with investigator support after approval of a proposal

December 17, 2019
Helsinki, Finland

Lasse Rämö
Corresponding author of the FISH trial

**eAppendix Blinded data interpretation meeting notes**

## Blinded Data Interpretation Meeting

### Open Reduction and Plate Osteosynthesis versus Functional Bracing for Humeral Shaft Fracture

By

Lasse Rämö, Bakir Sumrein, Tuomas Lähdeoja, Simo Taimela and Mika Paavola
on behalf of Finnish Shaft of Humerus (FISH) Study Group

In Helsinki University Hospital, Helsinki, Finland
On March 13, 2019, at 4:00 p.m.

**Table of contents:**

1. BLINDED DATA ANALYSES STATEMENT OF INTERPRETATION 2
1.1. Background Assumptions of the Primary Comparison 2
1.2. Statistical Commitments 2
1.3. Summary of Key Statistical Analyses 2
1.4. Commitment of Interpretation Based on the Theoretical Commitments 3
2. FORMAT OF REPORTING THE KEY FINDINGS 3
2.1. Figures 3
2.2. Tables 4
3. MINUTES OF THE "BLINDED REVIEW OF THE DATA" 8
3.1. Data Presented by the Statistician 8
3.2. Primary Comparison 8
3.3. Primary Interpretation of the Results 8
3.4. Secondary Analysis of the Data (Hypothesis-Generating) 8
3.5. Brakeage of the Randomization Code 9
4. FINAL INTERPRETATION 9

# 1. BLINDED DATA ANALYSIS STATEMENT OF INTERPRETATION

## 1.1. Background Assumptions of the Primary Comparison

1. Our null hypothesis is that there is no clinically relevant difference in the primary outcome measure between the two treatment groups.
2. We will consider a difference of a minimum of 10 points (used in the sample size calculation) in Disabilities of Arm, Shoulder and Hand (DASH) minimal important difference (MID).
3. To be deemed effective, the other treatment group should have a statistically ($P<0.05$) AND clinically significant ($\geq$10 points) difference over the other treatment group in the primary outcome, DASH score at the primary time point of 12 months.

## 1.2. Statistical Commitments

1. I-T-T is the primary data analysis, but per-protocol (PP) and on-treatment (OT) analysis will also be carried out, if there are treatment conversions of randomized patients in either group.
2. The prespecified time point of primary interest is 12 months after randomization. The mean difference (and 95% confidence interval) between the treatment groups in the DASH score at this timepoint is used in the primary analysis in the blinded data interpretation.
3. All other time points and secondary outcome measures are also included in the blinded data interpretation in the exploratory, hypothesis-generating secondary analysis.
4. After unmasking of the treatment groups, the number of treatment conversions and the frequency of adverse events will be carefully assessed. The adverse events will be categorized into severe and minor as stated in the published protocol paper[1] and the results will be elaborated in the interpretation of the findings in the final publication.
5. In order to maintain blinding, the analysis of treatment conversions (PP, OT) and adverse events will be done after the primary data interpretation.

## 1.3. Summary of Key Statistical Analyses

| **Outcome** | **a) Power analysis performed based on this b) Required sample** | **Statistical method** | **MID** | **Threshold for significance (P value)** |
|---|---|---|---|---|
| Primary outcome | | | | |
| DASH score | a) Yes<br>b) 35 | Anchor/Literature | 10[2] | 0.05 |
| Secondary outcome | | | | |
| Pain at rest (NRS) | a) No | Anchor/Literature | 1.5[3] | 0.05 |
| Pain at activities (NRS) | a) No | Anchor/Literature | 1.5[3] | 0.05 |
| Constant score | a) No | Anchor/Literature | 8,3[3] | 0.05 |
| 15D score | a) No | | | 0.05 |
| Patients with acceptable symptomatic state | a) No | | | 0.05 |
| Patients having DASH score within MID compared to baseline | a) No | | | 0.05 |

| | | | | |
|---|---|---|---|---|
| Patients reporting satisfaction | a) No | | | 0.05 |
| Patients able to return to previous daily activities | a) No | | | 0.05 |
| Patients able to return to previous hobbies | a) No | | | 0.05 |
| Patients willing to repeat the same treatment | a) No | | | 0.05 |

### 1.4. Commitment of Interpretation Based on the Theoretical Commitments

a) If open reduction and internal fixation is found superior to functional bracing, we conclude that patients with a humeral shaft fracture similar to the fractures included in this trial benefit from surgical treatment at 12 months after the fracture when operated in a high-volume university trauma center by or under supervision of experienced trauma surgeon.

b) If there is no clinically meaningful difference in the primary outcome between the groups~~,~~ we conclude that patients with a humeral shaft fracture similar to the fractures included in this trial do not benefit from surgical treatment compared to treatment with functional bracing at 12 months after the fracture. The result is applicable in patients treated in a high-volume university trauma center with usually available care.

c) If bracing group is superior to operative treatment, we conclude that patients with a humeral shaft fracture similar to the fractures included in this trial benefit from treatment with functional brace at 12 months compared to surgical treatment when treated in a high-volume university trauma center with usually available care.

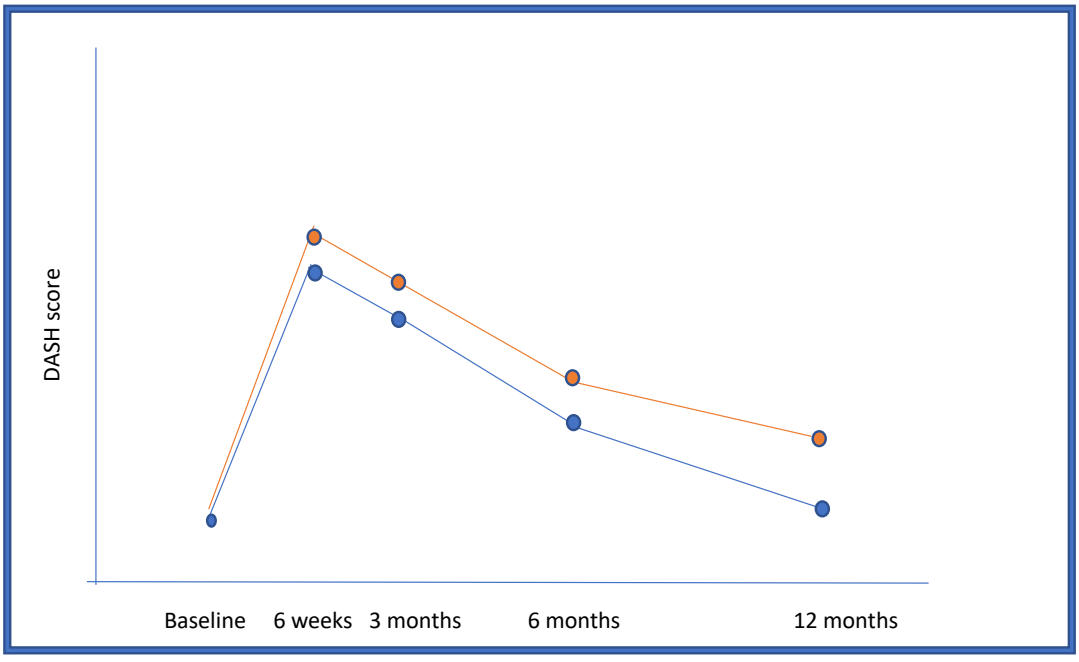
## 2. FORMAT OF REPORTING THE KEY FINDINGS

The Writing Committee decided to represent the key findings of this trial in the following tables and figures.

### 2.1. Figures

**Figure 1.** Flowchart according to Consort Statement.

**Figure 2.** Primary Outcome in Open Reduction Internal Fixation Group versus Bracing Group. (**MOCK-UP**)



### 2.2. Tables

| **Table 1.** Baseline Characteristics of the Patients According to Study Group.* | | |
|---|---|---|
| **Characteristic** | **Group A (N=xx)** | **Group B (N=xx)** |
| Age at allocation – yr | | |
| Male sex – no. (%) | | |
| Weight – kg | | |
| Height – cm | | |
| Body-mass index† | | |
| Smokers – no. (%) | | |
| AO/OTA classification – type‡ | | |
| A – no. (%) | | |
| B – no. (%) | | |
| C – no. (%) | | |
| Fracture location§ | | |
| Proximal – no. (%) | | |
| Middle – no. (%) | | |
| Distal – no. (%) | | |
| Injury mechanism‖ | | |
| Low energy – no. (%) | | |
| High energy – no. (%) | | |
| Dominant limb injured – no. (%) | | |
| DASH score¶ | | |
| DASH optional work module score** (no.) | | |
| DASH optional sports/performing arts module score** (no.) | | |
| 15D score†† | | |

* Plus–minus values are means ±SD.

† The body-mass index is the weight in kilograms divided by the square of the height in meters.

‡ AO/OTA classification of fractures[4]: Type A is a simple fracture, Type B is a fracture containing a wedge fragment and Type C is a segmental fracture.

§ Fracture location is defined by the third of the diaphysis the center of the fracture is located in.

‖ Injury mechanism is classified as high energy if the height of fall was over standing height or if the fracture was sustained in a traffic accident.

¶ Disabilities of Arm, Shoulder and Hand (DASH) score is a widely used and validated tool assessing upper-extremity related deficits and symptoms in daily life reported by the patient. The instrument consists of 30 items. The range of the score is from 0 (no disability) to 100 (extreme disability). At baseline the patient was asked to report the situation just before the fracture. A DASH score may not be calculated if there are greater than 3 missing items.

** DASH work and sports/performing arts modules are optional modules comprising of four questions assessing the effect of upper extremity condition on the work and sports/performing arts. The range of the score is from 0 (no disability) to 100 (extreme disability). An optional module score may not be calculated if there are any missing items.

†† The 15D instrument is a generic health-related quality-of-life instrument comprising 15 dimensions. The maximum 15D score is 1 (full health), and the minimum score is 0 (death). At baseline the patient was asked to report the situation just before the fracture.

| **Table 2.** Primary and Secondary Outcomes at 12 Months.* | | | | |
|---|---|---|---|---|
| **Outcome** | **Group A (N=xx)** | **Group B (N=xx)** | **Between-Group Mean difference (95% CI)** | **P-value** |
| Primary outcome – mean (95% CI) | | | | |
| DASH score | | | | |
| Secondary outcome – mean (95% CI) | | | | |
| Pain at rest† | | | | |
| Pain at activities† | | | | |
| Constant score‡ | | | | |
| Elbow ROM§ – degrees | | | | |
| 15D score | | | | |
| DASH work module score (no.) | | | | |
| DASH sports/performing arts module score (no.) | | | | |
| Patients with acceptable symptomatic state‖ – no. (%) | | | | |
| Patients having DASH score within MID compared to baseline – no. (%) | | | | |
| Patients reporting satisfaction¶ – no. (%) | | | | |
| Patients able to return to previous daily activities – no. (%) | | | | |
| Patients able to return to previous hobbies – no. (%) | | | | |
| Patients willing to repeat the same treatment** – no. (%) | | | | |
| Patients with a serious adverse event – no. (%) | | | | |
| Patients with a minor adverse event – no. (%) | | | | |

* Complete data set of primary and secondary outcomes at different time points is given in supplementary appendix found at NEJM.org.

† Pain at rest and at activities was reported in 0-10 numerical rating scale where 0 is no pain and 10 is the worst imaginable pain.

‡ Constant score was measured by a physiotherapist unaware of the treatment group.

§ Elbow ROM was measured by the physiotherapist using goniometer and calculated using the difference in degrees between full flexion and full extension.

‖ Patients with acceptable symptomatic state was based on our primary outcome DASH and it was determined using patient's global assessment of satisfaction as an anchoring item (patients who are very satisfied or satisfied with the fractured arm are considered having acceptable symptom state).

¶ Patients global satisfaction regarding the injured arm was elicited with the question, "How satisfied are you with the overall condition of your injured upper limb and its effect on your daily life?" Responses were given on a 7-point Likert scale. "Very satisfied" and "Satisfied" were categorized as satisfied and "Somewhat satisfied", "Neither satisfied nor dissatisfied", "Somewhat dissatisfied", "Dissatisfied," and "Very dissatisfied" as dissatisfied.

** Patients were asked whether they would like to have the same treatment again if they sustained a similar kind of injury later. Responses were given as "Yes" or "No".

| Table 3. Primary and Secondary Outcomes at Different Time Points (goes to supplement in publication) | | | | |
|---|---|---|---|---|
| **Outcomes** | **Group A (N=xx)** | **Group B (N=xx)** | **Between-Group Mean Difference (95% CI)** | **P-value** |
| **6 weeks** | | | | |
| Primary outcome – mean (95% CI) | | | | |
| DASH score | | | | |
| Secondary outcome – mean (95% CI) | | | | |
| Pain at rest | | | | |
| Pain at activities | | | | |
| Constant-Murley score | | | | |
| Elbow ROM – degrees | | | | |
| 15D score | | | | |
| DASH work module score (no.) | | | | |
| DASH sports/performing arts module score (no.) | | | | |
| Patients with acceptable symptomatic state – no. (%) | | | | |
| Patients having DASH score within 10 points compared to baseline – no. (%) | | | | |
| Patients reporting satisfaction – no. (%) | | | | |
| Patients able to return to previous daily activities – no. (%) | | | | |
| Patients able to return to previous hobbies – no. (%) | | | | |
| **3 months** | | | | |
| Primary outcome – mean (95% CI) | | | | |
| DASH score | | | | |
| Secondary outcome – mean (95% CI) | | | | |
| Pain at rest | | | | |
| Pain at activities | | | | |
| Constant-Murley score | | | | |
| Elbow ROM – degrees | | | | |
| 15D score | | | | |
| DASH work module score (no.) | | | | |
| DASH sports/performing arts module score (no.) | | | | |
| Patients with acceptable symptomatic state – no. (%) | | | | |
| Patients having DASH score within 10 points compared to baseline – no. (%) | | | | |
| Patients reporting satisfaction – no. (%) | | | | |
| Patients able to return to previous daily activities – no. (%) | | | | |
| Patients able to return to previous hobbies – no. (%) | | | | |
| **6 months** | | | | |
| Primary outcome – mean (95% CI) | | | | |
| DASH score | | | | |
| Secondary outcome – mean (95% CI) | | | | |
| Pain at rest | | | | |
| Pain at activities | | | | |

| | | | | |
|---|---|---|---|---|
| Constant-Murley score | | | | |
| Elbow ROM – degrees | | | | |
| 15D score | | | | |
| DASH work module score (no.) | | | | |
| DASH sports/performing arts module score (no.) | | | | |
| Patients with acceptable symptomatic state – no. (%) | | | | |
| Patients having DASH score within 10 points compared to baseline – no. (%) | | | | |
| Patients reporting satisfaction – no. (%) | | | | |
| Patients able to return to previous daily activities – no. (%) | | | | |
| Patients able to return to previous hobbies – no. (%) | | | | |
| **12 months** | | | | |
| Primary outcome – mean (95% CI) | | | | |
| DASH score | | | | |
| Secondary outcome – mean (95% CI) | | | | |
| Pain at rest | | | | |
| Pain at activities | | | | |
| Constant-Murley score | | | | |
| Elbow ROM§ – degrees | | | | |
| 15D score | | | | |
| DASH work module score (no.) | | | | |
| DASH sports/performing arts module score (no.) | | | | |
| Patients with acceptable symptomatic state – no. (%) | | | | |
| Patients having DASH score within 10 points compared to baseline – no. (%) | | | | |
| Patients reporting satisfaction – no. (%) | | | | |
| Patients able to return to previous daily activities – no. (%) | | | | |
| Patients able to return to previous hobbies – no. (%) | | | | |
| Patients willing to repeat the same treatment – no. (%) | | | | |

This statement was prepared and discussed before the meeting and accepted by the Writing Committee on March 13, 2019, at 4:42 p.m. before seeing any blinded results of the trial.

Lasse Räntö

Bakir Sumrein

Tuomas Lähdeoja

Simo Taimela

Mika Paavola

Leena Caravitis

## 3. MINUTES OF THE "BLINDED REVIEW OF THE DATA"

The Writing committee of the FISH trial (undersigned, below) developed and recorded two interpretations of the results on the basis of a blinded review of the primary outcome data (treatment A compared with treatment B), with one assuming that A was the Open Reduction and Internal Fixation (ORIF) group and another assuming that A was the bracing group. Before the review and analysis of the data, the Writing Committee deliberated and accepted the key analyses (listed above) and presentation format for the primary FISH-publication.

The meeting started on March 13, 2019, at 4:20 p.m. in Helsinki University Hospital, Helsinki, Finland. All Writing Committee members were present as well as research coordinator Leena Caravitis and statistician Pasi Aronen, who started to present the results in a blinded manner at 4:45 p.m.

Research nurse Leena Caravitis had coded the Groups in two groups (Group A and Group B) and at this point, she was the only one aware of the allocation codes of the groups.

### 3.1. Data Presented by the Statistician

The data shown in blinded data interpretation is attached as an appendix of this document.

### 3.2. Primary Comparison

While reviewing the blinded results of the trial, the undersigned noted that the treatment group mean values were virtually identical at the baseline. (Table 1).

Most importantly, we did not note a statistically significant between-group difference in the primary outcome DASH at 12 months (10,70 vs 10,55, p=0,964).

### 3.3. Primary Interpretation of the Results

a) If Group A = Open reduction and internal fixation, ORIF and Group B = Bracing

Our results suggest that patients with a humeral shaft fracture similar to the fractures included in this trial do not benefit from surgical treatment compared to treatment with functional bracing at 12 months after the fracture.

b) If Group A = Bracing and Group B = Open reduction and internal fixation, ORIF

Our results suggest that patients with a humeral shaft fracture similar to the fractures included in this trial do not benefit from surgical treatment compared to treatment with functional bracing at 12 months after the fracture.

### 3.4. Secondary Analysis of the Data (Hypothesis-Generating)

The differences between the groups did not exceed the prespecified MID (10 points) in the primary outcome DASH in any of the time points (6 weeks, 12 weeks, 6 months, 12 months). There was a statistically significant difference (49.0 vs 40.2, p=0.027) between the groups in DASH at 6 weeks in favor of group A.

In secondary outcome measures we noted a statistically significant and clinically meaningful between-group difference in Constant Score favoring group A at 6 weeks (22.6 vs 52.4, p<0.001) and 12 weeks (46.9 vs 58.9, p=0.016).

In 15D there was statistically significant difference of 0.036 points (p=0.041) in favor of group A.

These findings suggest that the patients in group A regain function faster compared to group B, but the difference is not observed at 6 months or 12 months. We will weigh these results against the findings in other secondary outcomes available after unblinding, like adverse events and cross-overs.

### 3.5. Revealing of the Randomization Code

At 6:13 p.m. the randomization code was opened, revealing that the Group A was ORIF group and Group B was bracing group.

## 4. FINAL INTERPRETATION

Blinded data interpretation was conducted as planned.

We conclude that patients with a humeral shaft fracture similar to the fractures included in this trial do not benefit from surgical treatment compared to treatment with functional bracing at 12 months after the fracture. The result is applicable in patients treated in a high-volume university trauma center with usually available care. We will weigh the result against the analysis of secondary outcomes, adverse events and cross-overs in the final manuscript.

We hereby confirm that this document describes the course of events truthfully during the blinded data interpretation meeting of the FISH trial.

Helsinki, March 13, 2019, at 6:30 p.m.

Lasse Rämö

Bakir Sumrein

Tuomas Lähdeoja

Simo Taimela

Mika Paavola

Leena Caravitis

Pasi Aronen

**References**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