Supplementary Appendix

What is the incidence of Complex Regional Pain Syndrome (CRPS) Type I within four months of a wrist fracture in the adult population? A systematic review.

Catherine Rolls[1], Candy McCabe[2,3,4], Alison Llewellyn[2,3], Gareth T Jones [5]

[1]Hand Rehabilitation Unit, University Hospitals Bristol

[2]Department of Nursing and Midwifery, University of the West of England, Bristol, UK

[3]CRPS Service, Royal United Hospitals Bath NHS Foundation Trust, Bath, UK

[4]The Florence Nightingale Foundation, London, UK

[5.] Epidemiology Group, Aberdeen Centre for Arthritis and Musculoskeletal Health, University of Aberdeen, UK

Contents

Systematic Review Summary Protocol……3
Systematic search Strategy…… 6
Appendix
A. Modified Newcastle Ottowa Scale (NOS)……17
B. Full scoring for the NOS……18

What Is the incidence Of Complex Regional Pain Syndrome (CRPS) Type I within four months of a wrist fracture in the adult population?, A Systematic Review protocol.

Objectives

The goal of this review is to establish the incidence of CRPS type I within 4 months of a wrist fracture in the adult population. We will document the diagnostic criteria used and, if applicable, discuss any discrepancies in incidence potentially arising from heterogeneity of diagnostic criteria.

Criteria for Inclusion and Exclusion of Studies:

Types of studies

- Observational studies published from 2010 onwards. To include prospective and retrospective cohort, studies as well as published audit or specialist epidemiological survey.

Types of populations

Inclusion Criteria

- Observational studies (as defined above) published after January 2010 with the stated aim of reporting on pain outcome following wrist fracture or injury. If conducted prior to 2010 must have been conducted no earlier than 2005. Studies to have been conducted in the following group of patients;

a) Adults (age 18 and over)who have sustained a wrist fracture. To be defined as a fracture of the distal radius +/- ulna or the carpals, including but not limited to the scaphoid.
b) The fracture can have been conservatively managed or internally fixated. If internally fixed this must have occurred within 3 weeks of the inciting event[1].

- Studies that reported on the incidence of complex regional pain syndrome type I, Sudek's dystrophy, Algodystrophy, or Reflex Sympathetic Dystrophy. Or studies reporting on patient's that fulfil the Atkin's criteria. Must be able to be extract the primary data on specific location of CRPS and inciting incident.

- Retrospective studies or audits documenting the incidence of CRPS Type I in the first 4 months following wrist fracture.

- The authors must state how the diagnosis of CRPS was made in their patient group. Either;

    1. The diagnostic criteria they used or
    2. clinical presentation observed + outcome measures used that lead to a diagnosis of CRPS.

Exclusion Criteria

- Studies not published in full article format, or where the primary diagnostic data cannot be extracted from the paper or retrieved from the authors.

- Studies published in language other than English
- Patients with the occurrence of CRPS following secondary or corrective procedures that occurred later than 3 weeks following the injury or using an external fixation device beyond three weeks of the fracture.
- Patients with CRPS Type II
- Children, to be defined as anyone under 18 at the time of their injury.
- Fractures to the upper limb above the level of the wrist, or with wrist plus an upper arm injury.
- Patients who have a previous history of CRPS, have a pre-existing neurological or chronic pain condition affecting their upper limb, and those with CRPS type II.

1. Current British Orthopaedic Association Standards for Trauma (BOAST) management of distal radius stipulate that a fracture should be fixed within 72 hours of injury, or from detection that the manipulated fracture position has slipped at the 2-week x-ray. We have rounded this up to three weeks. https://www.boa.ac.uk/wp-content/uploads/2017/12/BOAST-Management-of-Distal-Radial-Fractures.pdf

2. The aim of the review is to identify incidence of CRPS occurring acutely after a wrist fracture. For patients wearing an external fixation device for longer than three weeks it is hard to establish whether the fracture of manipulation of the device are the trigger for CRPS. The authors have taken the decision to exclude this data.

Search strategy for Identification of Studies

Electronic Databases to be used

- MEDLINE
- EMBASE
- CINAHL
- BNI
- Psychinfo
- AMED

Search term: See Supplementary information Appendix B

Other Search methods

As well as database searching, the personal libraries of the research team will be manually searched for relevant studies, as will be the reference lists of articles brought up in the primary search.

Method of Review

Selection of studies

In conjunction with a librarian trained in health research searching, we will search for the relevant papers and extract all references into a referencing management software. Each paper will then be allocated an identification number.

All titles and abstracts will be evaluated against the inclusion/exclusion criteria, all those excluded will have a note on why excluded added. If it is unclear if the study is appropriate based on title and abstracts, then the full article will be reviewed.

Assessment of methodological quality

The methodological quality of studies selected will be established using Newcastle Ottowa Scale (NOS) for cohort studies.

Data Extraction

Data to be collected:
Setting/location and study period
Study design (cohort/longitudinal, incidence survey, unclear, other)
Data Source (Clinical data collected for study, Audit, Special survey/interview, Medical records)
Study population (wrist fracture, upper limb fractures, colles fractures.)
Other population characteristics (Age, sex, ethnicity, socioeconomic background)
Number of patients
Place studied (Medical facility, City/Province, National, Other)
Are patients lost to follow-up documented (is there any record of DNA's from the clinic)
What diagnostic criteria was used (Budapest, Veldman, IASP etc)
Number of patients with a wrist fracture (as described in inclusion criteria)?
Number of cases of CRPS type I within 4 months of a wrist fracture? (N.b if incidence is documented at varying time points record these in the comments section)

Data Synthesis

The results are likely to be highly heterogenious so unable to do a quantitative or meta-analytic review. More likely to be tabulated and qualitative review

Systematic Search Strategy

#	Database	Search term	Results
1	Medline	(complex regional pain syndrome).ti,ab	2792
2	Medline	("complex regional pain syndrome").ti,ab	2735
3	Medline	(reflex sympathetic dystrophy).ti,ab	1679
4	Medline	("reflex sympathetic dystrophy").ti,ab	1620
5	Medline	(Algodystrophy).ti,ab	429
6	Medline	(Sudeck*).ti,ab	573
7	Medline	(causalgia).ti,ab	515
8	Medline	(Algoneurodystrophy).ti,ab	60
9	Medline	(Atkin* criteria).ti,ab	31
10	Medline	(1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9)	5549
11	Medline	exp "COMPLEX REGIONAL PAIN SYNDROMES"/ OR exp CAUSALGIA/ OR exp "REFLEX SYMPATHETIC DYSTROPHY"/	5422
12	Medline	(10 OR 11)	7309
13	Medline	(distal radius fracture).ti,ab	4220
14	Medline	("distal radius fracture").ti,ab	1451
15	Medline	(distal radius injur*).ti,ab	1781
16	Medline	(scaphoid fracture*).ti,ab	2246
17	Medline	(carpal fracture*).ti,ab	1889
18	Medline	(scaphoid injur*).ti,ab	948
19	Medline	(carpal injur*).ti,ab	1888

20	Medline	(colles fracture*).ti,ab	930
21	Medline	(wrist fractur*).ti,ab	5394
22	Medline	(wrist injur*).ti,ab	5183
23	Medline	(13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22)	15036
24	Medline	exp "RADIUS FRACTURES"/ OR exp "COLLES' FRACTURE"/	9303
25	Medline	(23 OR 24)	20207
26	Medline	(12 AND 25)	358
27	Medline	12 AND 25 [DT 2010-2019]	131
28	Medline	(inciden*).ti,ab	830080
29	Medline	(outcome*).ti,ab	1574795
30	Medline	(28 OR 29)	2267061
31	Medline	exp INCIDENCE/	247427
32	Medline	(30 OR 31)	2347482
33	Medline	(12 AND 25 AND 32)	123
34	**Medline**	**12 AND 25 AND 32 [DT 2010-2019]**	**68**
35	PubMed	(complex regional pain syndrome).ti,ab	6615
36	PubMed	("complex regional pain syndrome").ti,ab	2800
37	PubMed	(reflex sympathetic dystrophy).ti,ab	4127
38	PubMed	("reflex sympathetic dystrophy").ti,ab	4083
39	PubMed	(Algodystrophy).ti,ab	4219
40	PubMed	(Sudeck*).ti,ab	610

41	PubMed	(causalgia).ti,ab	928
42	PubMed	(Algoneurodystrophy).ti,ab	55
43	PubMed	(Atkin* criteria).ti,ab	1506
44	PubMed	(35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43)	8964
45	PubMed	(distal radius fracture).ti,ab	1730
46	PubMed	("distal radius fracture").ti,ab	1730
47	PubMed	(distal radius injur*).ti,ab	7
48	PubMed	(scaphoid fracture*).ti,ab	1311
49	PubMed	(carpal fracture*).ti,ab	198
50	PubMed	(scaphoid injur*).ti,ab	52
51	PubMed	(carpal injur*).ti,ab	172
52	PubMed	(colles fracture*).ti,ab	1056
53	PubMed	(wrist fractur*).ti,ab	1103
54	PubMed	(wrist injur*).ti,ab	6391
55	PubMed	(45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53)	5242
56	PubMed	(44 AND 55)	143
57	PubMed	(inciden*).ti,ab	937020
58	PubMed	(outcome*).ti,ab	2325028
59	PubMed	(57 OR 58)	3058752
60	**PubMed**	**(44 AND 55 AND 59)**	**67**
61	EMBASE	(complex regional pain syndrome).ti,ab	4051

62	EMBASE	("complex regional pain syndrome").ti,ab	4051
63	EMBASE	(reflex sympathetic dystrophy).ti,ab	2045
64	EMBASE	("reflex sympathetic dystrophy").ti,ab	2045
65	EMBASE	(Algodystrophy).ti,ab	575
66	EMBASE	(Sudeck*).ti,ab	457
67	EMBASE	(causalgia).ti,ab	493
68	EMBASE	(Algoneurodystrophy).ti,ab	64
69	EMBASE	(Atkin* criteria).ti,ab	1
70	EMBASE	(61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69)	6989
71	EMBASE	exp "COMPLEX REGIONAL PAIN SYNDROME TYPE I"/ OR exp "COMPLEX REGIONAL PAIN SYNDROMES"/	8985
72	EMBASE	(70 OR 71)	10273
73	EMBASE	(distal radius fracture).ti,ab	1689
74	EMBASE	("distal radius fracture").ti,ab	1689
75	EMBASE	(distal radius injur*).ti,ab	9
76	EMBASE	(scaphoid fracture*).ti,ab	1442
77	EMBASE	(carpal fracture*).ti,ab	170
78	EMBASE	(scaphoid injur*).ti,ab	57
79	EMBASE	(carpal injur*).ti,ab	161
80	EMBASE	(colles fracture*).ti,ab	860
81	EMBASE	(wrist fractur*).ti,ab	1267

82	EMBASE	(wrist injur*).ti,ab	637
83	EMBASE	(73 OR 74 OR 75 OR 76 OR 77 OR 78 OR 79 OR 80 OR 81 OR 82)	5834
84	EMBASE	exp "RADIUS FRACTURE"/ OR exp "WRIST FRACTURE"/ OR exp "DISTAL RADIUS FRACTURE"/ OR exp "BARTON FRACTURE"/ OR exp "COLLES FRACTURE"/ OR exp "SMITH FRACTURE"/	16266
85	EMBASE	(83 OR 84)	17591
86	EMBASE	(72 AND 85)	581
87	EMBASE	72 AND 85 [DT 2010-2019]	293
88	EMBASE	(inciden*).ti,ab	1178176
89	EMBASE	(outcome*).ti,ab	2367517
90	EMBASE	(88 OR 89)	3316241
91	EMBASE	exp INCIDENCE/	447348
92	EMBASE	(90 OR 91)	3434256
93	EMBASE	(72 AND 85 AND 92)	232
94	**EMBASE**	**72 AND 85 AND 92 [DT 2010-2019]**	**154**
95	PsycINFO	(complex regional pain syndrome).ti,ab	640
96	PsycINFO	("complex regional pain syndrome").ti,ab	636
97	PsycINFO	(reflex sympathetic dystrophy).ti,ab	123
98	PsycINFO	("reflex sympathetic dystrophy").ti,ab	116
99	PsycINFO	(Algodystrophy).ti,ab	0
100	PsycINFO	(Sudeck*).ti,ab	16

101	PsycINFO	(causalgia).ti,ab	56
102	PsycINFO	(Algoneurodystrophy).ti,ab	0
103	PsycINFO	(Atkin* criteria).ti,ab	41
104	PsycINFO	(95 OR 96 OR 97 OR 98 OR 99 OR 100 OR 101 OR 102 OR 103)	804
105	PsycINFO	exp "COMPLEX REGIONAL PAIN SYNDROME (TYPE I)"/	149
106	PsycINFO	(104 OR 105)	807
107	PsycINFO	(distal radius fracture).ti,ab	26
108	PsycINFO	("distal radius fracture").ti,ab	12
109	PsycINFO	(distal radius injur*).ti,ab	8
110	PsycINFO	(scaphoid fracture*).ti,ab	3
111	PsycINFO	(carpal fracture*).ti,ab	6
112	PsycINFO	(scaphoid injur*).ti,ab	1
113	PsycINFO	(carpal injur*).ti,ab	52
114	PsycINFO	(colles fracture*).ti,ab	8
115	PsycINFO	(wrist fractur*).ti,ab	87
116	PsycINFO	(wrist injur*).ti,ab	219
117	PsycINFO	(107 OR 108 OR 109 OR 110 OR 111 OR 112 OR 113 OR 114 OR 115 OR 116)	367
118	PsycINFO	(106 AND 117)	18
119	PsycINFO	106 AND 117 [DT 2010-2019]	8
120	PsycINFO	(inciden*).ti,ab	77242
121	PsycINFO	(outcome*).ti,ab	372822

122	PsycINFO	(120 OR 121)	440500
123	PsycINFO	(106 AND 118 AND 122)	4
124	**PsycINFO**	**106 AND 118 AND 122 [DT 2010-2019]**	**3**
125	CINAHL	(complex regional pain syndrome).ti,ab	1448
126	CINAHL	("complex regional pain syndrome").ti,ab	1412
127	CINAHL	(reflex sympathetic dystrophy).ti,ab	376
128	CINAHL	("reflex sympathetic dystrophy").ti,ab	372
129	CINAHL	(Algodystrophy).ti,ab	19
130	CINAHL	(Sudeck*).ti,ab	14
131	CINAHL	(causalgia).ti,ab	86
132	CINAHL	(Algoneurodystrophy).ti,ab	5
133	CINAHL	(Atkin* criteria).ti,ab	12
134	CINAHL	(125 OR 126 OR 127 OR 128 OR 129 OR 130 OR 131 OR 132 OR 133)	1810
135	CINAHL	exp "COMPLEX REGIONAL PAIN SYNDROMES"/ OR exp "REFLEX SYMPATHETIC DYSTROPHY"/	1958
136	CINAHL	(134 OR 135)	2394
137	CINAHL	(distal radius fracture).ti,ab	0
138	CINAHL	("distal radius fracture").ti,ab	438
139	CINAHL	(distal radius injur*).ti,ab	453
140	CINAHL	(scaphoid fracture*).ti,ab	440
141	CINAHL	(carpal fracture*).ti,ab	298
142	CINAHL	(scaphoid injur*).ti,ab	199

143	CINAHL	(carpal injur*).ti,ab	459
144	CINAHL	(colles fracture*).ti,ab	121
145	CINAHL	(wrist fractur*).ti,ab	1473
146	CINAHL	(wrist injur*).ti,ab	1669
147	CINAHL	(137 OR 138 OR 139 OR 140 OR 141 OR 142 OR 143 OR 144 OR 145 OR 146)	4110
148	CINAHL	exp "RADIUS FRACTURES"/	2153
149	CINAHL	(147 OR 148)	5176
150	CINAHL	(136 AND 149)	82
151	CINAHL	(136 and 149) [DT 2010-2019]	49
152	CINAHL	(inciden*).ti,ab	169243
153	CINAHL	(outcome*).ti,ab	552531
154	CINAHL	(152 OR 153)	681658
155	CINAHL	exp INCIDENCE/	61514
156	CINAHL	(154 OR 155)	704166
157	CINAHL	(136 AND 149 AND 156)	36
158	**CINAHL**	**(136 and 149 and 156) [DT 2010-2019]**	**28**
159	BNI	(complex regional pain syndrome).ti,ab	55
160	BNI	("complex regional pain syndrome").ti,ab	54
161	BNI	(reflex sympathetic dystrophy).ti,ab	35
162	BNI	("reflex sympathetic dystrophy").ti,ab	35
163	BNI	(Algodystrophy).ti,ab	4
164	BNI	(Sudeck*).ti,ab	2

165	BNI	(causalgia).ti,ab	12
166	BNI	(Algoneurodystrophy).ti,ab	0
167	BNI	(Atkin* criteria).ti,ab	1
168	BNI	(159 OR 160 OR 161 OR 162 OR 163 OR 164 OR 165 OR 166 OR 167)	91
169	BNI	(distal radius fracture).ti,ab	30
170	BNI	("distal radius fracture").ti,ab	8
171	BNI	(distal radius injur*).ti,ab	12
172	BNI	(scaphoid fracture*).ti,ab	20
173	BNI	(carpal fracture*).ti,ab	8
174	BNI	(scaphoid injur*).ti,ab	10
175	BNI	(carpal injur*).ti,ab	25
176	BNI	(colles fracture*).ti,ab	29
177	BNI	(wrist fractur*).ti,ab	92
178	BNI	(wrist injur*).ti,ab	65
179	BNI	(169 OR 170 OR 171 OR 172 OR 173 OR 174 OR 175 OR 176 OR 177 OR 178)	207
180	BNI	(168 AND 179)	2
181	BNI	(inciden*).ti,ab	22271
182	BNI	(outcome*).ti,ab	73061
183	BNI	(181 OR 182)	90907
184	BNI	(168 AND 179 AND 183)	0
185	AMED	(complex regional pain syndrome).ti,ab	182

186	AMED	("complex regional pain syndrome").ti,ab	182
187	AMED	(reflex sympathetic dystrophy).ti,ab	143
188	AMED	("reflex sympathetic dystrophy").ti,ab	143
189	AMED	(Algodystrophy).ti,ab	8
190	AMED	(Sudeck*).ti,ab	8
191	AMED	(causalgia).ti,ab	15
192	AMED	(Algoneurodystrophy).ti,ab	0
193	AMED	(Atkin* criteria).ti,ab	0
194	AMED	(185 OR 186 OR 187 OR 188 OR 189 OR 190 OR 191 OR 192 OR 193)	318
195	AMED	(distal radius fracture).ti,ab	27
196	AMED	("distal radius fracture").ti,ab	27
197	AMED	(distal radius injur*).ti,ab	0
198	AMED	(scaphoid fracture*).ti,ab	11
199	AMED	(carpal fracture*).ti,ab	1
200	AMED	(scaphoid injur*).ti,ab	0
201	AMED	(carpal injur*).ti,ab	0
202	AMED	(colles fracture*).ti,ab	33
203	AMED	(wrist fractur*).ti,ab	39
204	AMED	(wrist injur*).ti,ab	30
205	AMED	(195 OR 196 OR 197 OR 198 OR 199 OR 200 OR 201 OR 202 OR 203 OR 204)	134
206	AMED	(inciden*).ti,ab	4656

207	AMED	(outcome*).ti,ab	31091
208	AMED	(206 OR 207)	34744
209	AMED	(194 AND 205 AND 208)	1
210	AMED	(194 and 205 and 208) [DT 2010-2019]	0

Appendix A: Modified NOS

Assessment of quality of a cohort study – Newcastle Ottawa Scale	
Selection (tick one box in each section)	
1. Representativeness of the intervention cohort a) truly representative of the average, wrist fracture population ★ b) somewhat representative of the average, wrist fracture population ★ c) selected group of patients, e.g. only certain wrist fracture groups ie conservative or surgically managed d) no description of the derivation of the cohort	☐ ☐ ☐ ☐
2. Selection of the non intervention cohort : Omitted	
3. Ascertainment of intervention a) secure record (eg health care record) ★ b) structured interview ★ c) written self report d) other / no description	☐ ☐ ☐ ☐
4. Demonstration that outcome of interest (CRPS) was not present at start of study a) yes ★ b) no	☐ ☐
Comparability (Omitted)	
Outcome (tick one box in each section)	
1. Assessment of outcome a) independent blind assessment ★ b) record linkage ★ c) self report d) other / no description	☐ ☐ ☐ ☐
2. Was follow up long enough for outcomes to occur a) yes Over 8 weeks ★ b) no less than 8 weeks	☐ ☐
3. Adequacy of follow up of cohorts a) complete follow up: all subjects accounted for ★ b) subjects lost to follow up unlikely to introduce bias: number lost <= 20%, or description of those lost suggesting no different from those followed ★ c) follow up rate < 80% (select an adequate %) and no description of those lost d) no statement	☐ ☐ ☐ ☐

Appendix B: Full scoring for NOS

	Selection			Outcome			
Paper	**Representativeness**	**Ascertainment**	**Demonstration**	**Assessment**	**Follow-up (f/u)**	**Adequacy**	**Total score**
Farzad[29]	Consecutive wrist fracture patients enrolled, roughly 50:50 male to female ratio (surgical and conservative) who were referred to physio. Considered as a Selected group.	Wrist fractures were enrolled post fracture reduction following referral by an orthopaedic surgeon	previous neurology not clearly documented	Budapest criteria	f/u for 8 weeks consider adequate.	3 patients lost to the 1 year follow-up but all included in the 8 week review which is relevant to this SLR	
stars	0	1	0	1	1	1	**4**
Zyluk[24]	Unclear how the cohort was selected from the wider wrist fracture cohort. All had K-wire fixation for 6 weeks. = A selected group	All patients had a surgical intervention, so ascertained from health record.	No record of exclusion categories at all.	Used IASP and CRPS severity scale with one assessor.	6 and 12 weeks	high number of subjects lost	
stars	0	1	0	1	1	0	**3**
Roh[30]	Surgically treated patients only, and at a major trauma centre. Selective group of patients so bias that more severe fractures may have higher incidence.	All patients had surgical intervention so good ascertainment from medical records.	Exclusion criteria includes previous upper extremity conditions	Budapest criteria	6, 12 and 24 weeks	not stated	
stars	0	1	1	1	1	0	**4**

Dilek[25]	Small sample and from conservative management only. Selected group	Ascertainment of fracture would be by medical records and observation.	No detail of exclusion of prior neurology	Assessed with the IASP	f/u for 8 weeks consider adequate.	Yes all subjects accounted for, 7 of 57 lost = 12%	
stars	0	1	0	1	1	1	**4**
Hall[14]	Small sample but conservative and surgically managed patients so somewhat representative	Health record	exclusion of any condition that precluded bilateral comparison (of which CRPS/neuro would count)	Assessed with the IASP	10-12 weeks	94 % attendance at second review, reasons for withdrawal stated.	
Stars	1	1	1	1	1	1	**6**
Beerthuizen[8]	Large study with conservative and surgical management. Exclude comminuted fractures but otherwise representative.	Health record	Prior CRPS not excluded and is documented in the results. Unable to disentangle these patients from those who developed CRPS in this study.	Three diagnostic criteria used (IASP, Veldman, Harden&Brueh l)	6 weeks 12 weeks and 1 year	Some loss to follow up but minimal and unlikely to introduce bias as demographical ly similar	
Stars	1	1	0	1	1	1	**5**
Moseley[26]	Large study with conservative only, selected group	Health record	Prior CRPS is documented	IASP	4 months	minimal loss to follow up	

Stars	0	1	1	1	1	1	**5**
Jellad[27]	Small sample of conservatively managed extra-articular fractures who attended physio (selective group)	Health record	concomitant injuries of the upper limb to be excluded	Veldman[a]	3 and 6 months	All subjects accounted for	
Stars	0	1	1	0	1	1	**4**
Jesswani[31]	Closed distal radius fractures, but no comment on how fracture was managed. Selective group. More male than female patients with a relatively young mean age. No documentation of how patients were sampled i.e consecutively	Health record	exclusion of pre-existing upper limb disability (can assume that would include CRPS)	IASP and physical examination	16 weeks	No statement	
Stars	0	1	1	1	1	0	**4**
Notes: (a) Referenced Beerthuizen[8] as reason for choosing the Veldman. This paper recommends use of the Budapest criteria. Likely to be institutional bias							