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Conservative versus surgical treatment for odontoid fracture: Is the surgical treatment harmful? Systematic review and meta-analysis

Surgery or orthosis for odontoid fracture

Benjamin Pommier MD, PhD^{1,2}; Edouard Ollier MD, PhD³; Jean-Baptiste Pelletier¹; Xavier Castel¹; François Vassal, MD, PhD^{1,2}; Marie-Charlotte Tetard, MD¹

 Service de Neurochirurgie, CHU de Saint Etienne, France ; (2) INSERM U1028, ICD, Université Jean Monnet, Saint Etienne, France ; (3) INSERM U1059, SAINBIOSE, DVH Team, Université Jean Monnet, Saint Etienne, France.

Corresponding author:

Benjamin Pommier, Hôpital Nord, Service de Neurochirurgie, avenue Albert Raimond, F-42055 Saint-Priest en Jarez, France.

Phone : +33 477 7 82 82 52; Fax: +33 477 120 543; E-mail : Benjamin.Pommier@Neurochirurgie.fr

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1 Abstract

2

Background: Odontoid fracture is a common injury especially in elderly people. Despite some
recent studies arguing in favor of surgery, the best treatment is still being debated.

5 **Objective:** Here we systematically review and analyze the comparative literature between 6 surgical and conservative treatments of odontoid fractures.

Method: We systematically searched Medline and Cochrane library for studies published from January 1990 to May 2019 in English language. Comparative studies evaluating the results of surgical and conservative treatments for odontoid fractures were eligible for inclusion. Combined relative risks (RR) for mortality at last follow-up, union or non-union rates, and complications were calculated. Methodological quality was assessed using the Newcastle-Ottawa scale. Influence of age, year of publication on treatment effect was explored using a meta-regression analysis.

Results: A total of 1438 articles were identified, of which 30 articles with 2463 patients were eligible for inclusion. There was a trend toward lower mortality in the surgical group (RR: 0.80; CI: 0.63-1.02). Non-union rates (RR: 0.41; CI: 0.28-0.6) were lower in the surgical group. Union rates were higher in the surgical group (RR: 1.26; CI: 1.11-1.45). No significant influence of age or year of publication on treatment effect was found.

19 **Conclusion**: Based on this meta-analysis of non-randomized comparatives studies, surgical 20 treatment seems not to be inferior to conservative treatments. The conclusions of this study 21 remain limited by the low quality of the evidence currently available. Randomized controlled 22 studies are required.

23 Introduction:

24 The odontoid process is a bony structure projecting from the second cervical vertebra 25 (C2). Because of its bone structure and biomechanical functions, it is the site of one of the most 26 common cervical fracture: odontoid fracture accounts for up to 15% of the cervical spine injuries and its incidence increases with population ageing ^{1,2}. Anderson and D'alonzo proposed a 27 28 classification of odontoid fractures ³: Type I involves the apex of the odontoid peg and is often considered as stable and treated with cervical orthosis^{4,5}; Type II involves the base of the dens; 29 and Type III implicates the odontoid and the lateral mass of C2. These fractures can occur in 30 31 young patients in case of high-kinetic traumatism, but often affect the ageing population, following minor trauma. Of the three types, type II fractures are associated with a high risk of 32 nonunion due to the weaknesses of blood supply and bone density associated to the high amount 33 of biomechanical constraints in the dens. ^{6,7} 34

35 Two major kinds of management have been presented to treat odontoid fractures. On the 36 one hand, the conservative treatment consists in immobilizing the neck with an external orthosis. This treatment can be performed with either a halo-vest, or a kind of cervical collar ^{8,9}. On the 37 38 other hand, the surgical treatment aims to stabilize the fracture using screws and rods through an 39 anterior or a posterior approach 6 . As the condition usually arises among fragile patients, the 40 treatment of choice has long been the conservative treatment, using some external immobilization 41 devices. It constitutes an easy and minimally invasive treatment. Nevertheless, several studies 42 have highlighted a non-negligible rate of delayed complications associated with the conservative 43 treatment, especially respiratory and cutaneous^{8,10}. Immobilizing the neck with an orthosis using 44 a conservative treatment in such cases could be falsely reassuring. Meanwhile, the improvement of surgical procedures in elderly patients and the development of new techniques have resulted in 45

46 a huge increase of surgeries for this indication. Some authors argue in favor of a reduced
47 mortality ^{11,12}.

48 Despite a large interest among spine surgeons and a broad panel of treatments reported, 49 the best management remains under debate, especially because of the variability of described 50 results of each treatment. To date, no systematic study has been conducted to determine the 51 optimal treatment in such cases ^{7,13,14}. Moreover, some recent meta-analyses about this topic are 52 already of low value because of newer published relevant studies, or because of excessively 53 restrictive inclusion criteria. Here we propose to systematically review and analyze the available 54 literature and to summarize the results of the studies comparing surgical and conservative 55 treatments of odontoid fractures for both efficacy and security endpoints. All comparative studies 56 are considered (randomized or non-randomized, prospective or retrospective studies).

57 Material and Methods:

58 Search strategy

59 Literature searches were conducted in MEDLINE and Cochrane Collaboration Library 60 from January 1990 to January 2019. The following search terms were used for the procedure (1) 61 "Fracture OR Injury", (2) "C2 or Axis" and (3) "Odontoid or Dens". Only english-language 62 studies were reviewed. An extensive search among cited bibliographies was also performed.

Two reviewers independently reviewed titles and abstracts of the publications. Subsequently, the full-text of studies that potentially met the inclusion criteria were read to determine the papers to be included. In the event of discrepancies between the reviewers, disagreements were resolved by discussion. No review protocol was registered.

68 Inclusion and exclusion criteria

The following inclusion criteria were applied. Search studies focused on comparison of conservative and surgical treatment of acute odontoid fracture. It included randomized controlled studies, prospective or retrospective comparatives cohort studies. Only adult samples were enrolled and studies should have reported information about mortality, union or pseudarthrosis rates, or complications.

The following exclusion criteria were applied. Studies with less than 10 cases reported.
Review or meta-analysis publications. Studies assessing congenital abnormalities or pathological
fractures.

77

78 Data extraction and quality analysis

Two of the authors independently extracted the relevant data from each selected full-text using a standardized form. In the event of discrepancies between the reviewers, a consensus was reached by discussion. The following information were collected: authors, year of publication, study design, total sample size, sample size for each group, follow-up time, mean age and gender for each group, post-operative procedural and medical complications, pseudarthrosis rate, mortality rate.

Methodological quality of the randomized studies was assessed using the Cochrane tool. Methodological quality of non-randomized studies was assessed using the Newcastle-Ottawa Scale (NOS) ¹⁵. This scale assesses the quality of non-randomized studies for meta-analyses with a maximum of 9 points. It includes 3 categories comprising 4 points for selection of the study groups, 2 points for the comparability and 3 points for ascertainment of the outcome of interest. All these variables are indicated in table 1.

91 Statistical analysis

The summary statistics for the effect size of surgical treatment compared with conservative treatment were generated using a random-effect model and a relative risk (RR) with the corresponding 95% confidence intervals (95% CIs). Weighted incidences were also assessed. We explored the publication bias of the studies included in the final analysis using Begg's funnel plot.

For each meta-analysis, statistical heterogeneity among studies was explored using Occhrane's Q statistic, study consistency being quantified by means of the I^2 statistic. In the event of significant heterogeneity (*P*-value <0.10) with no clear explanation for this, a randomeffect model was used for data analysis.

101 A P-value for the association <0.05 was considered statistically significant. Combined effect estimates were calculated globally, and according to the study design. Interaction was 102 103 systematically tested for retrospective and prospective studies and was considered as significant 104 at p < 0.05. The results of the meta-analysis are presented graphically, including the effect size 105 expressed as RR with the corresponding 95% CI. An RR equal to 1 indicates no difference 106 between the treatments, of <1 indicates that Surgery is better and of >1 indicates that 107 conservative treatment is better except for the fracture healing analysis. Influence of age and year 108 of publication on treatment effect were investigated using a meta-regression analysis.

All statistical analyses were performed using R statistical software (R Foundation for
Statistical Computing, Vienna, Austria), version 3.3.1 with the meta-packages (version 4.7).

111 Results

112 Study selection

The initial search retrieved 1457 publications (Medline = 1438; Cochrane library = 16; Other sources = 3). 1313 duplicates and publications unrelated to the topic were excluded through title and abstract screening. Among the remaining 142 articles, 112 studies were excluded because of their specifications (Fig. 1). 30 papers were finally included in the study as shown in table 1 $^{11,12,16-43}$.

118 Enrolled studies

119 The baseline characteristics of the included studies are shown in table 1. The enrolled 30 120 studies included a total of 2470 patients. There was no randomized controlled study. All included 121 studies were cohort studies. 4 were prospective and 26 retrospective. The individual samples 122 ranged from 19 to 322. On the one hand, a total of 1037 patients were treated surgically: 324 123 underwent an anterior and 334 a posterior surgery. The kind of surgery was unspecified for 379 124 patients. On the other hand, 1426 were treated in a conservative manner: 843 were treated with an 125 orthosis and 368 with a halo-vest. The kind of conservative treatment was unspecified for 215 126 patients.

127 The mean follow-up time was 22.3 months (range = 0.3-60 months). 2 studies ^{19,40} were 128 limited to the in-hospital period with restricted follow-up. The mean age was 72.9 years (+/-129 12.3).

130 The mean NOS score was 4.97 (range 4-7), in favor of moderate quality studies.

132 Mortality

133 26 studies reported mortality at different end-points (Fig. 2). The pooled results showed 134 that last follow-up mortality rates were not significantly different, though there was a tendency 135 toward a lower mortality in the surgical group (RR: 0.80; CI: 0.63-1.02)(Fig. 2). There was 136 significant heterogeneity ($I^2=30\%$, $\tau^2=0.0892$, p=0.07).

137

The mortality rates at 3 and 12 months were reported in 9 studies. At 3 months the weighted mortality incidences were 6% (CI: 6-10) and 12% (CI: 8-17) for surgical and conservative treatment. There was no significant difference, (RR: 1.13; CI: 0.52-2.48). At 12 months, the weighted mortality incidences were 14% (CI: 8-20) and 18% (CI: 12-26). There was still no significant difference (RR: 0.96; CI: 0.62-1.48). A funnel plot to detect publication bias is provided in the appendix. No significant influence of age or year of publication on treatment effect was observed (digital supplementary content).

145

146 Union / Non-union

147 20 studies reported non-union rates (Fig 3.A). The pooled results were in favor of a lower 148 non-union rate in the surgical group (RR: 0.41; CI: 0.28-0.6). There was significant heterogeneity 149 (I²=45%, τ^2 =0.2526, p=0.02)(Fig. 3). Among these studies, the weighted incidences of non-union 150 were 9% (CI: 6-14) and 30% (CI: 23-38) for surgical and conservative treatments.

151 16 studies reported union rates (Fig 3.B). The pooled results were in favor of a higher 152 fracture-healing rate in the surgical group (RR: 1.26; CI: 1.11-1.45). There was significant 153 heterogeneity (I²=65%, τ^2 =0.0324, p<0.01). Among these studies, the weighted incidences of 154 fracture union were 81% (CI: 74-87) and 53% (CI: 43-68) for surgical and conservative 155 treatments. Funnel plots to detect publication bias are provided in the digital supplementary 156 content. Funnel plots for both union and non-union rates were asymmetrical with a lack of law 157 power studies in favor of conservative treatment. Existence of a publication bias cannot be 158 excluded. No significant influence of age or year of publication on treatment effect was observed 159 (digital supplementary content).

160

161 **Complications**

162 9 studies reported systemic complications. The pooled results showed a higher systemic 163 complication rate in the surgical group (RR: 1.43; CI: 1.02-1.99). There was a significant 164 heterogeneity ($I^2=42\%$, $\tau^2=0.0940$, p=0.09).

165 13 studies reported procedural complications (i.e. attributable to treatment). The pooled 166 results showed that patients had less procedural complications in the surgical group (RR: 0.71; 167 CI: 0.53-0.95). There was no significant heterogeneity ($I^2=37\%$, $\tau^2=0.1981$, p=0.08).

15 studies reported the rate of secondary surgery (i.e. because of first treatment failure). The pooled results showed a tendency for patients in the surgical group to be less at risk for secondary surgery (RR: 0.57; CI: 0.24-1.35). There was significant heterogeneity (I²=61%, τ^2 =1.5610, p<0.01).

172

174 **Discussion**

175

176 Odontoid fractures represent up to 15% of all cervical spine fractures ^{1,2} and Type II 177 odontoid fractures are the most common fractures of the cervical spine in people aged 70 years or 178 older. As the population is ageing, the incidence of these fractures is likely to continue increasing 179 ⁴⁴. The best treatment of this condition remains unclear, especially in geriatric patients, because 180 of comorbidities, poor bone quality and impaired physiological reserves. Treatment options for odontoid fractures are either conservative or surgical. Surgical options include mainly anterior 181 182 odontoid screw fixation and posterior atlantoaxial arthrodesis ⁴⁵. Nonsurgical management 183 techniques mostly consist of cervical orthosis and halo-vest ⁴⁶. Although conservative treatment 184 was preferred in the 1990's, surgery has become more prominent in the last two decades. This might reduce mortality and increase rates of fusion ^{11,12}. However, the treatment decision remains 185 highly dependent on patient and institutional factors, leading to heterogeneous treatment 186 187 strategies.

Although geriatric patients generally sustain odontoid fracture without neurological 188 189 damage, several prior studies have documented important morbidity and 1-year mortality, 190 independent of management strategy. Odontoid fracture is indeed associated with in-hospital death of more than 10% ⁴⁷ and reported 1-year mortality rates that can reach more than 20% ^{11,48}. 191 Long-term mortality rates can be even worse with more than 40% related ⁴⁹. 192 Recent and valuables studies suggested that surgical treatment could reduce this mortality ^{7,11,12}. For 193 194 example, Chapman and al¹¹ compared 157 patients treated non operatively and 165 patients 195 treated operatively. The 30-days and maximal follow-up mortality were 14% and 44%, 196 respectively. The surgically treated patients had respective 30-day and 12- month follow-up

197 mortality rates of 7% and 38%, compared to 22% and 57% with conservative treatment. After 198 adjusting for the effects of patient age, sex, and Charlson comorbidity index, the results suggested 199 that surgical treatment of type II odontoid fracture in this elderly population did not negatively 200 impact survival, and, that operative treatment might be associated with a significant better 30-day 201 survival rate compared with non-operatively treated patients. Consistent with this study and some 202 previous meta-analysis using different inclusion criteria ^{7,14}, our meta-analysis shows no 203 increased mortality at last follow-up in the surgical group. There was even a trend toward 204 reduced mortality rate with surgery. Nevertheless, the paucity of data concerning the 205 comparability of surgical and non-surgical groups constitutes one of the major sources of biases 206 of this work. As a matter of fact, the studies offer moderate to poor proof-level with no controlled 207 trial, which makes these conclusions of limited value because of a high risk of bias. Moreover, 208 some studies have pointed out the influence of the old age on these results. It seems that the 209 surgery loses its protector effect for patients 80 years old or older. For example, Schoenfeld et al. 210 ³⁷ compared 112 non operatively treated with 44 operatively treated type II odontoid fractures in 211 elderly patients. This study suggested that surgical treatment was associated with reduced 212 mortality for patients aged from 65 to 74. After 75, this association decreased and the survival 213 curves nearly coincided for patients aged 85 and older. Other studies^{26,40} did not consider the 214 benefits of surgery after 80. In our study, the heterogeneity and the quality of studies prevent us 215 from drawing any conclusions regarding a specific age subclasses.

Data about mortality is closely linked to morbidity. Surgical treatment in frail patients is also associated with major complication rates, especially in octogenarians. Some authors suggest that conservative treatment may be more adequate in elderly people, despite a high rate of nonunion. Others recommend surgical stabilization, because of the risk of residual C1–C2 instability that may cause pain and late myelopathy^{3,27,28,50}. Conservative treatments reported in the 221 literature were not uniform and ranged from soft collars to halo-devices. In elderly patients, halo-222 vest seems to be inappropriate because of significant pain, psychological distress, complications, associated to a limited fusion rate ¹⁰. The morbidity rates associated with halo-vest treatment 223 224 seem comparable or worse than those with surgical treatment ^{19,28}. The major complications 225 reported for the halo-vest include acute respiratory distress syndrome (ARDS) and pneumonia, 226 dysphagia, pins failure and infection. Previous publications also suggested that, from a biomechanical standpoint, immobilization with a Philadelphia cervical collar is equivalent to 227 halo-vest immobilization for stable fractures of the dens ^{29,51}. Because of all these reasons, 228 229 cervical orthosis may be preferred to a halo-vest. .

230 Complications rates are also high in the surgical group, which is consistent with the 231 literature. Medical complications are comparable those found with the halo-vest (i.e., ARDS, 232 Pneumonia, Decubitus ulcer, dysphagia). However, we found significantly fewer procedural 233 complications in the surgical group, and we noted a trend toward less revision surgery. Neurological complications and delayed myelopathy remain rare in both cases^{34,52,53}. Our 234 235 conclusions remain limited by the heterogeneity of the included records, as the complications 236 types and rates are different between anterior and posterior surgery. Mechanical complications 237 are more common after anterior surgery in elderly patients, with more frequent revision surgeries (between 3.6 and 13.6%) compared to posterior fusion ⁵⁴⁻⁵⁶. This is likely due to poor bone 238 239 quality for this group of patients. According to this, the recommended approach could be to favor 240 surgical treatment as much as possible, especially for patients of age 80 or younger. In case of 241 surgery, anterior screwing would be recommenced for young patients, with the aim of preserving 242 motion as this technique can provide good results through a rapid intervention. In elderly people, 243 posterior fusion would be favored to limit the risk of biomechanical failure, dysphagia and 244 pulmonary complications. Moreover, similarly to what has been proposed for hip fractures, these

patients should be managed in a multidisciplinary way, in collaboration with geriatric specialists,
 to decrease perioperative morbidity. ^{57,58}

247 The last parameter studied was fracture union, which has often been considered as the 248 main goal of these treatments. Because of its limited vascular supply, its cortical nature, and the age of occurrence, odontoid fracture pseudarthrosis is a frequent condition ^{59–61}. Bone quality and 249 250 degree of displacement are predisposing factors. The non-union rate in the elderly is high, ranging between 20 and 85%^{27,33,62}. It is found to be especially high in the case of conservative 251 management and more limited for surgical treatment. For example, Di Paolo et al. ²⁰ reported 252 253 91.7% of fusion with surgical treatment, compared to 46.7% with conservative treatment. Once 254 again, our data seems consistent with this information, as we report strongly inferior rates of 255 pseudarthrosis and superior rates of fusion in the surgical group. It is important to note that we 256 separated "union" and "non-union" parameters as the provided data varied among studies, 257 including for deceased or lost-to-follow-up patients. These data are probably heterogeneous 258 because of the variety of techniques used. Concerning conservative treatments, more and more 259 studies are in favor of the use of a collar instead of a halo-vest ^{29,46,51}. However, collars provide 260 the same amount of fusion without comorbidities. That seems different for surgical treatment 261 with no clear evidence, although the data seems to be suggest slightly increased union rates using posterior fusion⁴⁵. 262

As mentioned above, bony union has long been considered as the main goal to achieve. While this aim remains unchanged for young patients, things have changed for elderly patients. The main ambition is now to keep patients mobile and promote respiratory function and mental health. To this aim, achieving fracture stability with only fibrous union can be sufficient ^{59,60}. In fact, non-union does not systematically result in instability, and neurological consequences are very rare ⁵⁹. Some authors underlined the potential risk of delayed myelopathy as an unequivocal

surgical indication. But studies showed that delayed myelopathy rarely occurs^{3,27,28,50}. 269 270 Furthermore, in rare cases delayed myelopathy has been observed after type II odontoid fractures, 271 occurrence could be many years, frequently a decade or more, after the injury. This is far beyond 272 the lifespan of the majority of older patients who sustain such an injury. The persistence of neck 273 pain and instability on dynamic radiographs constitute clues that can indicate a real instability, 274 which can lead to a new treatment. Our results are coherent with that, showing a tendency toward delaying surgery if necessary after initial conservative treatment. This parameter has rarely been 275 276 assessed, leaving our study unconfirmed on this point. The data collected argue in favor of 277 focusing on symptomatic non-union rather than radiological non-union, especially in the elderly. 278 These are not that frequent in the non-surgical group and even rarer in the surgical group, where 279 pseudarthrosis is stabilized by the osteosynthesis

280 Because of a bigger heterogeneity of the data, and to limit the risk of methodological bias, 281 we deliberately chose to exclude non-comparative studies. This parameter can probably dilute the 282 information. Nonetheless our study is, to our knowledge, the biggest to date, summarizing data of 283 30 previous studies comparing surgical and non-surgical treatment of odontoid fractures. None of 284 these studies can be considered as high-level proof and a huge heterogeneity among samples and 285 kind of treatments used should be noted. For instance, mortality data mainly driven by the only 286 few studies that could be included because of their weight in the analysis. We tried to limit this 287 issue by using a random effect model, but these characteristics make the study at high risk of 288 bias. Therefore, these records should be interpreted with caution. Though, it provides data in 289 agreement with previously published records: surgical treatment of odontoid fracture is not 290 riskier than conservative treatment and seems to provide better results in term of fracture union. 291 Some of our results, such as the complications rates, suggest that surgical treatment is slightly 292 harder to tolerate in the initial phase but is probably more efficient on the long-term, as shown by

293	mortality and	fusion	rates.	All	these	results	should	be	confirmed	with a	controlled	randomized

- trial.

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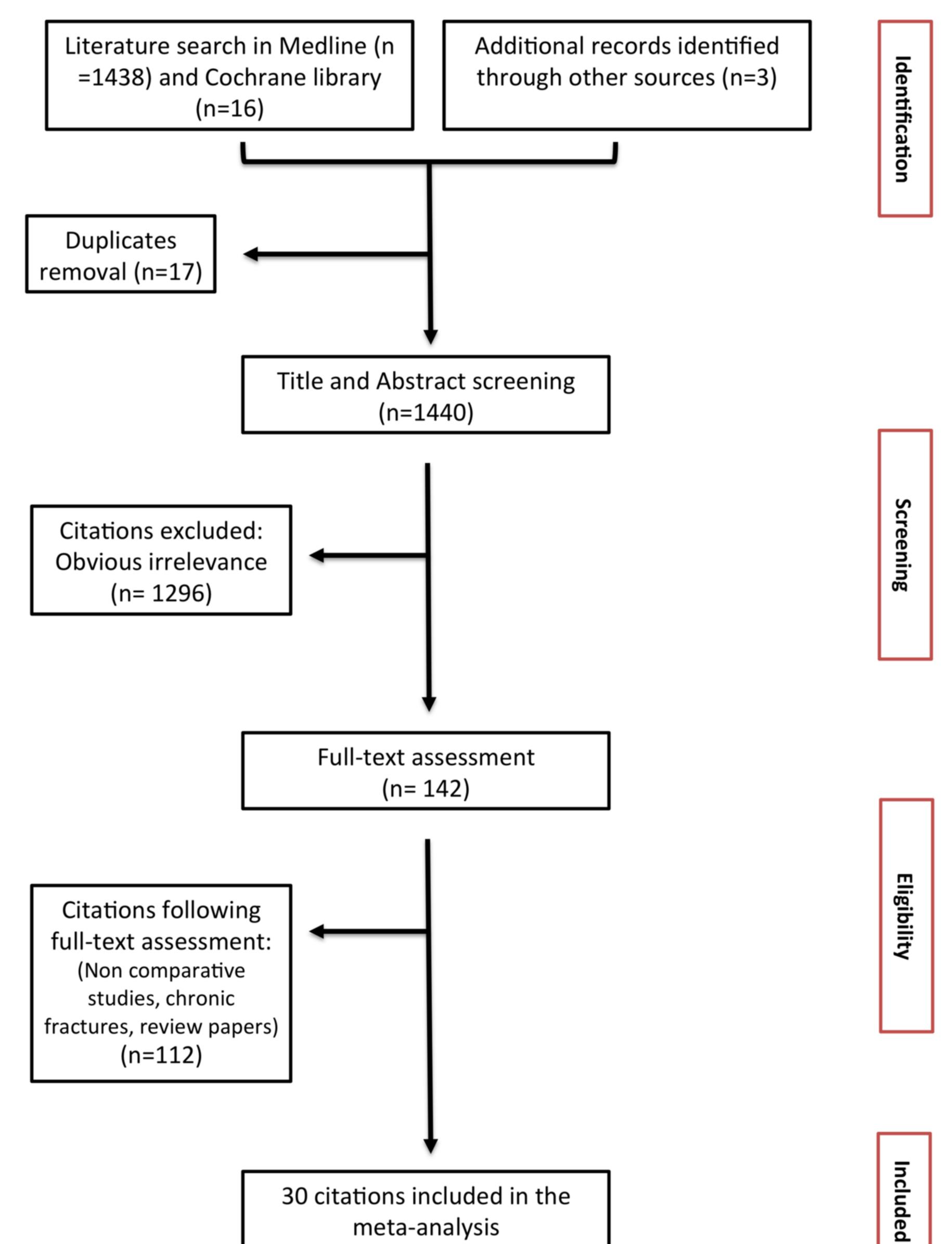
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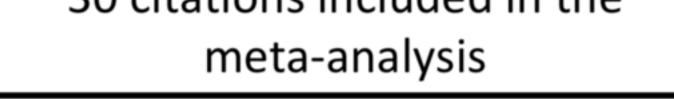
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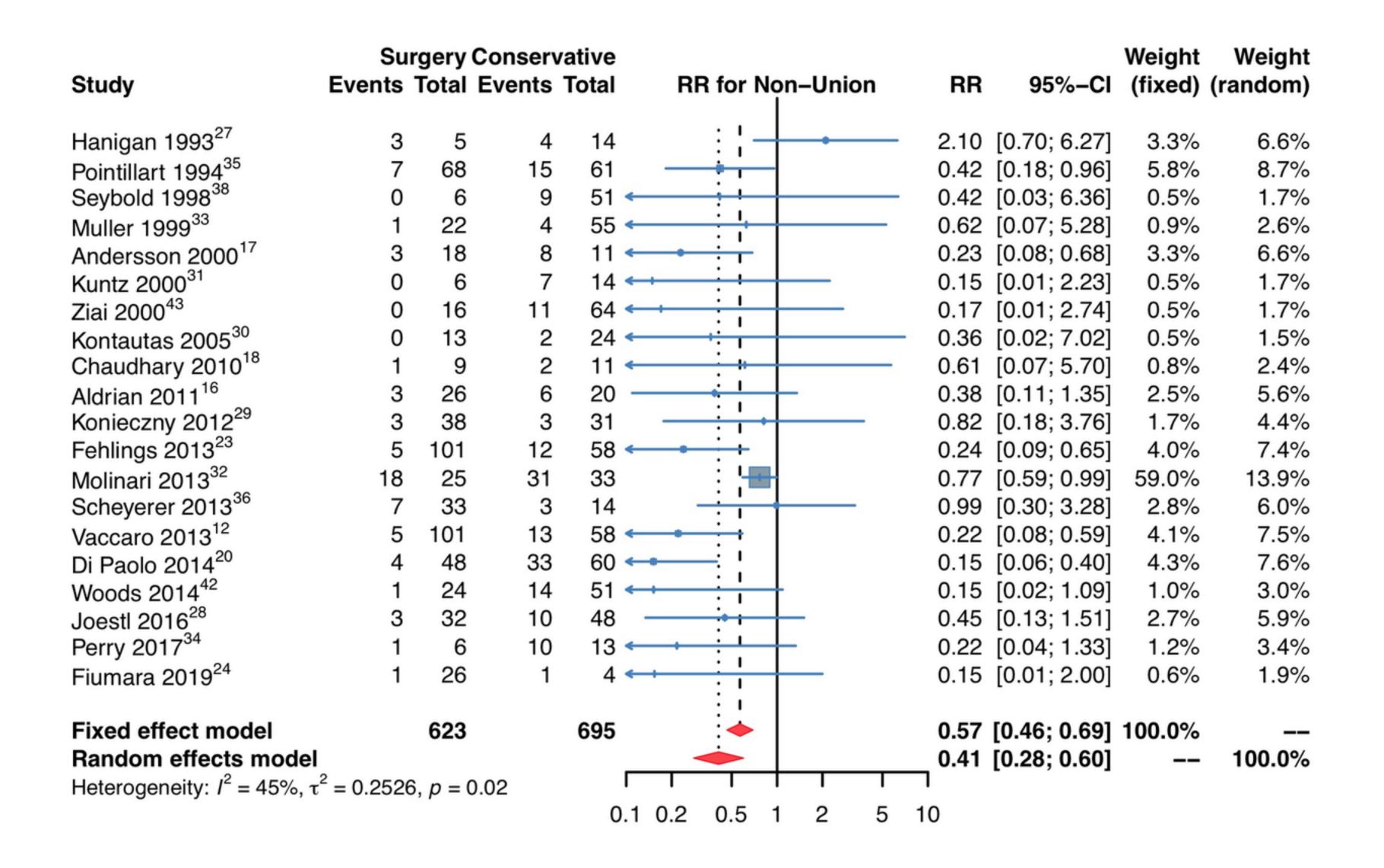
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Study	Su Events		Conser Events		RR for	death	F	R	95%-CI	Weight (fixed)	Weight (random)
DePasse 2016 ¹⁹	0	32	14	94			0	0 01 01	1; 1.63]	0.3%	0.7%
Smith 2008 ⁴⁰	4	32	6						5: 2.701		3.4%
Kontautas 2005 ³⁰	ő	13	1	24					; 13.85]		0.6%
France 2012 ²⁵	2	12	1	25	E				: 41.541		1.0%
Sheikh 2018 ³⁹	1	5	14		<u>t</u>				0: 7.74]		1.6%
Fiumara 2019 ²⁴	i	26	0		i				10.66]		0.6%
Chaudhary 2010 ¹⁸	3		Ĩ	11	E				29.491		1.2%
Ziai 2000 ⁴³	4	16	3		E.				: 21.48]		2.5%
Konieczny 2012 ²⁹	4	38	1	31					27.72		1.2%
Fehlings 2013 ²³	14	101	15		- E				3; 1.03]		7.6%
Graffeo 2016 ²⁸	7	17	39						4: 1.841		8.0%
Vaccaro 201312	14	101	15						3: 1.031		7.6%
Molinari 2013 ³²	5	25	4						9: 5.521	1.7%	3.2%
Kuntz 2000 ³¹	1	6	4	14			0.	58 (0.0	3; 4.19]	0.6%	1.4%
Fagin 2010 ²¹	4	40	12	68			0.		0: 1.641		4.0%
Aldrian 2011 ¹⁶	1	26	1	20	ŧ				: 11.56]		0.8%
Chapman 2013 ¹¹	62	165	80	157			0.	74 [0.5	7; 0.95]	40.5%	14.4%
Venkatesan 201441	1	2	11	30					2: 5.891		2.3%
Seybold 1998 ³⁸	0	6	3	51			→ 1.0	13 10.07	: 19.541	0.3%	0.7%
Scheyerer 2013 ³⁵	8	33	11	14			0.3	31 [0.1	5; 0.60]	5.7%	7.4%
Schoenfeld 201137	11	44	50	112			0.	56 0.3	2; 0.97	8.3%	9.0%
Hanigan 1993 ²⁷	1	5	8	14		_	0.3	35 10.0	5: 2.14	0.8%	1.6%
Muller 1999 ³³	3	22	7	55	- <u>F</u>		1.0	07 0.3	3.77	1.6%	3.0%
Joestl 2016 ²⁸	4	32	3	48			2.	0 [0.4	3; 8.35]	1.2%	2.4%
Perry 2017 ³⁴	4	6	5		÷.		- 10	73 [0.7	1; 4.22]	3.2%	5.1%
Woods 201442	9	24	27	51		-	0.	71 [0.4	D; 1.26]	7.5%	8.6%
					i i i						
Fixed effect model		838		1271						100.0%	
Random effects mode							0.	30 [0.6:	3; 1.02]		100.0%
Heterogeneity: I ² = 30%,	r ² = 0.0892	2, p = 0	0.07				1 7				
				0	.1 0.2 0.5	12	5 10				



Study	Sur Events	gery Co Total E				RR for U	nion		RR	9	5%–CI	Weight (fixed)	Weight (random)
Hanigan 1993 ²⁷	2	5	5	14	-			-	1.12	[0.31;	4.04]	0.2%	1.0%
Seybold 1998 ³⁸	6	6	35	51		<u>i</u>	-		1.45	[1.21;	1.74]	11.3%	11.3%
Andersson 2000 ¹⁷	14	18	2	11				+	4.28	[1.19;	15.35]	0.2%	1.0%
Kuntz 2000 ³¹	4	6	3	14		1	+		3.11	[0.98;	9.84]	0.3%	1.2%
Ziai 2000 ⁴³	9	16	34	64			-		1.06	[0.65;	1.73]	1.6%	4.9%
Kontautas 2005 ³⁰	13	13	21	24		•			1.14	[0.98;	1.32]	17.4%	12.2%
Chaudhary 2010 ¹⁸	7	9	2	11		i i i i i i i i i i i i i i i i i i i		+ + +	4.28	[1.16;	15.72]	0.2%	1.0%
Aldrian 2011 ¹⁶	21	26	14	20		-	-		1.15	[0.82;	1.63]	3.2%	7.3%
Konieczny 2012 ²⁹	35	38	28	31					1.02	[0.88;	1.18]	17.4%	12.1%
Fehlings 2013 ²³	96	101	46	58		+			1.20	[1.04;	1.38]	19.8%	12.4%
Molinari 2013 ³²	7	25	2	33		÷		+	4.62	[1.05;	20.36]	0.2%	0.8%
Scheyerer 2013 ³⁶	17	33	0	14				,	15.15	[0.98; 2	35.27]	0.1%	0.2%
Di Paolo 2014 ²⁰	44	48	27	60			-8-		2.04	[1.52;	2.73]	4.5%	8.5%
Falavigna 2016 ²²	56	65	20	23					0.99	[0.82;	1.19]	11.0%	11.2%
Joestl 2016 ²⁸	29	32	38	48		-			1.14	[0.95;	1.37]	11.4%	11.3%
Fiumara 2019 ²⁴	21	26	3	4					1.08	[0.59;	1.95]	1.1%	3.7%
						i.							
Fixed effect model		467		480		•			1.19	[1.12;	1.26]	100.0%	
Random effects mode				_					1.26	[1.11;	1.45]		100.0%
Heterogeneity: $I^2 = 65\%$,	$\tau^2 = 0.0324$, p < 0.0)1	I	1		I	I	I				
				0.1	0.2	0.5 1	2	51	0				

Β.

Author	Study design	Study design N		6	Inclusion criteria	Exclusion criteria	Surgery			Conservative treatment		
		S	С	0	-		N	Technique	N	Technique	-	
Aldrian 2011 ¹⁶	Retrospective monocentric	3	1	2	Type IIa fractures2 years follow-up	Type IIIIncomplete data sets	25	Odontoid screw	21	Halo-vest	24	
Andersson 2000 ¹⁷	Retrospective monocentric	3	1	1	Type II>65 years		18	Odontoid screw (11) Posterior fusion (7)	11	Cervical orthosis (10) Halo-vest (1)	51	
Chapman 2013 ¹¹	Retrospective multicentric	3	1	1	Type II fractures>65 years		165	NS	157	NS	25	
Chaudhary 2010 ¹⁸	Retrospective multicentric	3	1	0	 Type II fractures >70 years 	 Displacement >4mm Posterior displacement Neurological impairment Halo vest Multiple cervical injuries 	11	Odontoid screw Transarticular screw	9	Cervical orthosis	5.5	
DePasse 2017 19	Retrospective monocentric	3	1	1	Type II>65 years	GCS 3 at presentation48h mortality	32	Odontoid screw Posterior fusion	94	Cervical orthosis (84) Halo-vest (10)	0.3	
<i>Di Paolo 2014</i> ²⁰	Retrospective monocentric	3	1	0	• Type II		48	Odontoid screw (20) Posterior fusion (16) Occipito-cervical fusion (12)	60	Cervical orthosis (20) Halo-vest (40)	4.43	
Fagin 2010 ²¹	Retrospective monocentric	3	1	0	 >60 years 		40	Odontoid screw (23) Posterior fusion (12)	68	Cervical orthosis (64) Halo-vest (4)	20	
Falavigna 2016 ²²	Retrospective multicentric	3	2	1	• Type II	 Incomplete data set 	65	Odontoid screw (42) Posterior fusion (13)	23	Cervical orthosis (15) Halo-vest (8)	23.4	
Fehlings 2013 ²³	Retrospective multicentric	4	1	2	Type II>65 years	 Previous ondontoid fracture Mental incapacity	101	Odontoid screw Anterior transarticular screws Posterior fusion	58	Cervical traction Cervical orthosis Halo-vest	12	
Fiumara 2019 ²⁴	Retrospective multicentric	3	1	0	• Type II		26	Odontoid screw (18) Odontoid and transarticular screws (7) Posterior fusion (1)	4	Cervical orthosis (4)	4	
France 2012 ²⁵	Retrospective monocentric	3	1	0	Type II>65 years	 Pathological fractures 	12	Odontoid screw (7) Posterior fusion (5)	25	Cervical orthosis (9) Halo-vest (16)	7.2	
Graffeo 2017 ²⁶	Retrospective monocentric	3	1	1	 Type II >80 years 	Halo vest	17	Odontoid screw (2) Posterior fusion (15)	94	Cervical orthosis	22	
Hanigan 1993 ²⁷	Retrospective monocentric	3	1	1	Type II>80 years	Pathological fractures	5	Posterior fusion	14	Cervical orthosis (11) Halo-vest (2) Cervical traction (1)	42	
Joestl 2016 ²⁸	Retrospective monocentric	3	1	2	 Type II >65 years ASA>1 5 years F-U 	Type IIIIncomplete data set	32	Odontoid screw	48	Halo-vest	60	

Konieczny 2012 ²⁹	Prospective monocentric	4	1	1			38	Odontoid screw (13)	31	Cervical orthosis	9.7
Kontautas 2005 ³⁰	Prospective monocentric	3	2	1			13	Posterior fusion (25) Posterior fusion	23	Halo-vest	2
Kuntz 2000 ³¹	Retrospective monocentric	3	1	1	 >65 years 		6	Posterior fusion	14	Cervical orthosis (6) Halo-vest (6)	14
Molinari 2013 ³²	Retrospective monocentric	3	1	0	Type II>65 years		25	Posterior fusion	33	Cervical orthosis	14
Müller 1999 33	Retrospective monocentric	3	2	1			22	Odontoid screw (21) Posterior fusion (5)	55	Cervical orthosis (26) Halo-vest (29)	47
Perry 2018 ³⁴	Retrospective monocentric	3	1	0	Type II>80 years		6	Posterior fusion	13	Cervical orthosis	60
Pointillart 1994 ³⁵	Retrospective monocentric	3	1	0	• 1 year follow-up		68	Odontoid screw (19) Posterior fusion (43)	61	Cervical orthosis	6
Scheyerer 2013 ³⁶	Retrospective monocentric	3	1	1	Type II>65 years	Multiple cervical injuries	33	Odontoid screw (17) Posterior fusion (16)	14	Cervical orthosis	31.1
Schoenfeld 2011 ³⁷	Retrospective monocentric	3	1	2	 Type II >65 years 		44	NS	112	Cervical orthosis (84) Halo-vest (28)	36
Seybold 1998 ³⁸	Retrospective monocentric	3	0	1	,		6	Posterior fusion	51	Cervical orthosis (5) Halo-vest (46)	29
Sheikh 2017 ³⁹	Retrospective monocentric	3	0	1	 Type II >65 years 		5	Occipito-cervical fusion	88	Cervical orthosis	3
Smith 2008 ⁴⁰	Retrospective monocentric	3	1	1	Type II>80 years	 Associated spine fractures Neurological impairment 	32	Odontoid screw (10) Posterior fusion (22)	40	Cervical orthosis (24) Halo-vest (16)	0,5
Vaccaro 2013 12	Prospective multicenter	4	1	2	Type II>65 years	 No previous fracture treatment No cognitive impairment 	101	Odontoid screw (12) Posterior fusion (88) Occipito-cervical fusion (1)	58	Cervical orthosis (52) Halo-vest (6)	12
Venkatesan 2014 ⁴¹	Retrospective monocentric	3	1	1	 >65 years 	 Neurological impairment 	2	Posterior fusion	30	Cervical orthosis (26) Halo-vest (4)	29
Woods 2014 42	Retrospective monocentric	3	0	1	 >65 years 	Incomplete data set	24	Odontoid screw (8) Posterior fusion (16)	51	Cervical orthosis (21) Halo-vest (30)	60
Ziai 2000 ⁴³	Retrospective multicentric	3	1	0			16	Odontoid screw (11) Posterior fusion (5)	64	Cervical orthosis (35) Halo-vest (29)	6

Table 1: Main characteristics of the 30 studies enrolled in the meta-analysis. NOS: Newcastle-Ottawa scale with 3 subclasses (S: Selection, C: Comparability, O: Outcome)