

1      **Association Between Cervical Spine Degeneration And The Presence Of Dens**

2                   **Fractures.**

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27

28    **Abstract**

29    **Background and purpose**

30    Results of small case series indicate increased risk of dens fractures in patients with  
31    osteoarthritis. Purpose of this retrospective cohort study was to analyze the relative  
32    risk associated with degeneration of the cervical spine in the occurrence of dens  
33    fractures in older patients.

34    **Material and methods**

35    We performed a retrospective CT-study of 1,794 patients > 55 years of age with and  
36    without dens fractures for signs of osteoarthritis (OA).

37    **Results**

38    OA of the atlanto-dens interval (AdI) was present in 75.9% of fracture patients,  
39    whereas 63.5% of non-fracture patients had OA of the AdI ( $p=0.04$ ). In case of  
40    osteoarthritis of the facet joints, we did find a significant increase ( $p<0.001$  –  
41     $p=0.024$ ) in the dens fracture risk in patients with OA ( $p=0.000$  –  $p=.0004$ ).

42    **Interpretation**

43         This study indicates an association between OA of the cervical spine and the  
44    risk of sustaining a dens fracture. OA can lead to a reduction in the range of motion of  
45    the cervical spine. As a consequence, a relative low-energy trauma can induce a  
46    forced sagittal motion, which will produce a torque at the base of the odontoid process  
47    resulting in a fracture.

48

49     **Introduction**

50         Dens fractures have a bimodal age distribution, affecting mainly young and  
51         elderly patients. In young adults, most injuries causing dens fractures involve high-  
52         energy trauma, such as falls from greater than standing height, motor vehicle  
53         accidents, and pedestrians injured by a car or motorcycle (Watanabe et al. 2010).  
54         However, in older patients dens fractures are most often caused by low-energy  
55         trauma, such as a fall from standing or sitting height (Kwerski 1992, Olerud et al.  
56         1999, Lomoschitz et al. 2002). In the elderly, dens fractures are the most common  
57         cervical spine fracture, accounting for 9-18% of all cervical spine fractures, and they  
58         are also associated with a high incidence of mortality (Grauer et al. 2005, Butler et al.  
59         2010, Hsu et al. 2010). Older patients are at greater risk of falling than younger  
60         patients, since older people suffer from reduced visual acuity, decreased reaction  
61         time, and blunted reflexes (Damadi et al. 2008), and because of the biochemical bone  
62         attrition associated with senile osteopenia, the most common cause of primary  
63         osteoporosis (Olerud 1999, Lomoschitz 2002, Malik et al. 2008). In 2005,  
64         Lakshmanan *et al.* reported in a small series of patients that there was a possible  
65         relationship between upper cervical spine degeneration and the incidence of Type II  
66         dens fractures (Lakshmanan et al. 2005). With age, the incidence of cervical spine  
67         osteoarthritis (OA) increases, possibly restricting motion at any one particular cervical  
68         spine joint, which may adversely affect the movement and distribution of force across  
69         that segment after trauma, increasing the likelihood of fracture.

70         Despite the prevalence of dens fractures and their increasing consequence to  
71         overall health of the aging population, there is a paucity of research identifying  
72         anatomic risk factors, such as degenerative disease. We propose that degeneration of  
73         the cervical spine is associated with increased dens fracture risk.

74     **Materials and Methods**

75 We performed a retrospective study of adult trauma patients age 55 and older  
76 who were admitted to our level one trauma center between 01/01/2011 and  
77 12/31/2016. As part of our institution's routine protocol, all trauma patients received a  
78 cervical spine CT scan for cervical spine clearance. Patients who sustained a dens  
79 fracture and obtained a CT scan on the day of injury were included in the study. Of  
80 1,794 patients, 57 had dens fractures. From the remaining group of 1,737, we selected  
81 736 (42.4%) at random, using a random-number generator, for inclusion as non-  
82 fractured controls. Demographic information including age, gender and mechanism of  
83 injuries was obtained from patients' medical records.

84 Degenerative changes of the cervical spine, disc spaces and facet joints, were  
85 determined from CT scans obtained with a CT scanner (Philips Brilliance 64,  
86 Cleveland, OH, USA). A collimation of 0.9-1.5 mm and an increment of 0.2-0.4 mm  
87 were selected, and multiplanar reconstruction (MPR) images were routinely obtained  
88 in arbitrary imaging planes. Degenerative changes were qualitatively assessed by two  
89 fellowship trained orthopedic surgeons using sagittal and coronal views of the upper  
90 cervical spine. Disc space and facet joint degeneration of all joint spaces between C1  
91 and T1 was quantified as previously described (Betsch et al. 2015) (Table 1).

92 Axial, mid-sagittal images, and MPR images were examined by two  
93 orthopedic surgeons for signs of OA (Fig. 1 & 2). For analysis, patients with grades 2  
94 or 3 degeneration were considered to have osteoarthritis and assigned an OA score.  
95 Patients with grade 1 degeneration were considered to have no osteoarthritis of the  
96 respective joint.

#### 97 *Data Analysis*

98 Data were analyzed using SPSS 22.0 (SPSS Inc. Chicago, USA). Normality of  
99 data was evaluated using the Shapiro-Wilk test. For analysis, we divided the  
100 population into two groups comparing patients with and without dens fracture.

101 Differences between groups were assessed using Chi-Square analysis and the level of  
102 significance was set at p<0.05. Additionally, we employed support vector regression  
103 (SVR) (Bartlett et al. 1998) for function estimation within 10-fold cross validation  
104 (Arlot et al. 2010) to build and test whether age and gender was significantly  
105 predictive of dens fracture. The SVR framework has advantages over simple linear  
106 regression; a variety of linear and nonlinear functional forms, or “kernels” can be  
107 tested to obtain the best fit in SVR, as opposed to the single linear function available  
108 for linear regression.

109 *Ethics, funding and potential conflicts of interest*

110 Institutional Review Board approval was obtained and no informed consent was  
111 necessary. No sources of external funding were used for this study and no competing  
112 interest has to be declared.

113 **Results**

114 Patient age ranged from 55 years to 103 years. The study population consisted  
115 of 54.1% men and 45.9% women in the control group, and 39.2% men and 60.8%  
116 women in the fracture group (Table 2). The mean age of patients with a dens fracture  
117 was  $77.2 \pm 10.4$  and  $70.8 \pm 12$  for patients in the control group. Of the 57 patients  
118 with dens fractures, 39 patients (68.4%) sustained a fracture due to a ground level fall,  
119 10 fractures (17.5%) were due to a motor vehicle accident, 2 (3.5%) were due to falls  
120 from greater than standing height, 6 (10.5%) were due to other reasons, and 1 was due  
121 to unknown reasons (Table 3). Nineteen patients (33.0%) sustained a type III dens  
122 fracture, and 38 (67.0%) sustained a type II fracture; categorization of fracture type  
123 was based on Anderson and D’Alonzo classification for dens fractures (Anderson et  
124 al. 1974).

125 Patients with OA of the atlanto-dens interval were two times more likely to  
126 sustain a dens fracture than patients without osteoarthritis (3.9% versus 7.8%; p<0.04)

127 (Figure 3). For all other cervical disc interspaces (C2/3 to C7-T1), we did not find  
128 significant differences between the groups ( $p \geq 0.13$ ). In case of osteoarthritis of the  
129 facet joints C2 to C6, there was a significant increase ( $p \leq 0.024$ ) in the dens fracture  
130 risk between patients with and without osteoarthritis of the respective facet joints. For  
131 the C5/6 facet joints, we found the lowest increase in the relative dens fracture risk of  
132 1.8 (4.8% patients without OA vs. 8.8% with OA), and for the C3/C4 facet joints we  
133 determined the highest increase in the relative dens fracture risk of 4.5 (2.4% without  
134 OA vs. 10.8% with OA) (Fig.4).

135 Unpaired t-tests showed that age and gender differed significantly between  
136 groups ( $p < .01$ ); however, the results of SVR modeling showed that age and gender  
137 were not significantly more predictive for dens fractures than osteoarthritis of the  
138 facet joints. In other words, age and gender do not contribute to dens fracture risk  
139 when osteoarthritis of facet joints is considered.

## 140 Discussion

141 In patients 55 and older, osteoarthritis of the facet joints between C2 and C6  
142 and in the atlanto-dens interval appeared to be associated with an increased risk of  
143 sustaining an odontoid fracture. Despite the increasing incidence and detrimental  
144 health consequences to the aging population, there are only a few studies describing  
145 risk factors for sustaining an odontoid fracture (Amling et al. 1994, Amling et al.  
146 1995, Malik 2008, Watanabe 2010). Most dens fractures occur in the elderly as a  
147 result of a low energy trauma, which was confirmed by a previous study (68.4% after  
148 ground level falls) (Lomoschitz 2002). Therefore, these fractures are thought to be  
149 related to osteoporosis, age, female sex, senility and balance issues all associated with  
150 an aging population (Muller et al. 1999, Lomoschitz 2002, Malik 2008).

151 Spondylotic changes of the cervical spine are associated with ageing, and they  
152 seem to be closely related to wear and tear due to repeated movements and axial

153 loading of the neck during one's lifetime (Badve et al. 2010). It is estimated that over  
154 600 activities occur in the cervical spine region per hour, exposing this region to  
155 significant strain (Badve 2010). The subsequent inability to distribute loads equally in  
156 all directions in osteoarthritic joints causes typical changes at the interface between  
157 the bones and the associated cartilage. Such modifications are joint space narrowing,  
158 cortical thickening, subchondral cyst formation, sclerosis, calcification of ligaments  
159 and vacuum phenomenon (Genez et al. 1990, Zapletal et al. 1995).

160 The relative horizontal orientation of the C1/C2 facet joints allows for  
161 excellent rotation. Therefore, around 40-70% of total neck rotation takes place  
162 between atlas and axis. Head and neck rotation is initiated at the atlanto-axial  
163 articulation, and the facet joints below the level of the axis then contribute to the  
164 extremes of rotation. With age, osteoarthritis leads to decreased mobility of the joints  
165 below the axis, making the atlanto-axial articulation vulnerable to extremes in sagittal  
166 motion, and predisposing it to injury with relatively trivial trauma (Friedenberg et al.  
167 1963, Lestini et al. 1989, Watanabe 2010). This could explain the 1.8 to 4.5 times  
168 increase in dens fracture risk in patients with degeneration of the C2 to C6 facet joints  
169 found in our study compared to the control group.

170 Degeneration of synovial joints may lead to joint space narrowing,  
171 subchondral cyst formation, and synovial hypertrophy. In a previous study by our  
172 group, we found that the atlanto-dens interval narrows linearly with age ( $R^2=0.992$ ,  
173  $p<0.001$ ). We also confirmed that the prevalence of intraosseous dens cyst formation  
174 and the prevalence of calcific synovitis exponentially increase with age (Betsch  
175 2015). Such morphological changes to the atlanto-dens joint can be associated with  
176 the occurrence of dens fractures. In 2014, Shinseki *et al.* found a nearly eightfold  
177 increase in the likelihood of sustaining a dens fracture in patients with intraosseous  
178 dens cysts and a nearly fivefold increase in fracture risk in patients with retro-dens

179 synovitis (Shinseki et al. 2014). The authors state that such degenerative changes may  
180 weaken the dens and therefore predispose elderly patients to a dens fracture after a  
181 trauma. In 2010, Watanabe *et al.* showed that the higher risk of sustaining an odontoid  
182 fracture in the elderly after a minor trauma might be due to the biomechanical bone  
183 properties associated with senile bone osteopenia (Watanabe 2010). However, in our  
184 present study we were not able to evaluate the bone density in patients with a dens  
185 fracture, since we retrospectively examined CT scans in a trauma population. In future  
186 studies, it would be of interest to quantify the bone mineral content with the help of  
187 densitometry to confirm Watanabe's findings.

188 One limitation of our study is that the sample of patients was drawn from a  
189 collective of patients who sustained a trauma that required a cervical spine CT for  
190 clearance. It is unknown if the prevalence of cervical spine degeneration in the control  
191 group is representative of these degenerative elements in a general population of  
192 adults fifty-five years of age and older. Further epidemiological studies with imaging  
193 of the cervical spine would be needed to address this issue. Another limitation is the  
194 low number of patients with a dens fracture in our cohort, which makes it difficult to  
195 perform an analysis between dens fracture types due to lacked statistical power.

196 **Conclusion**

197 Osteoarthritis can lead to a reduction in the range of motion of the cervical  
198 spine. This study indicates an association between osteoarthritis of the facet joints and  
199 the risk of sustaining a dens fracture. Identifying risk factors for dens fractures may  
200 help in the future to better understand, prevent and treat these fractures.

201 **Authors contributions**

202 BM, BS, KB and YJ contributed to the conception and design of the study.  
203 Statistical analysis were run by KB, BM and BS who also drafted the manuscript. All

204 the authors interpreted the results, critically revised the manuscript, and approved the  
205 final version.

206

207    **Tables:**

208    **Table 1: Grading the severity of degenerative changes in the cervical spine.**

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<b>Grade</b>	<b>Definition</b>
<b>1 None-mild</b>	Normal or narrowed joint space with or without minor osteophyte formation.
<b>2 Moderate</b>	Obliterated joint space with or without osteophyte formation.
<b>3 Severe</b>	Ankylosis of the joint with excrescences either in the joint transverse ligament calcification, or both.

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212   **Table 2: Age groups analyzed, including number of patients in each group, mean  
213   age, and sex distribution.**

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	<b>N</b>	<b>Mean Age ± SD</b>	<b>Males</b>	<b>Females</b>
<b>Control</b>	736	$70.7 \pm 12.0$	54.10%	45.90%
<b>Fracture Group</b>	57	$77.7 \pm 9.7$	60.80%	39.20%

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219 **Table 3: The mechanism of injury leading to a dens fracture in the fracture**  
220 **group.**  
221

Mechanism			
Motor Vehicle Accident	Ground Level Fall	Higher Fall	Other
10	39	2	6
17.50%	68.40%	3.50%	10.50%

222  
223

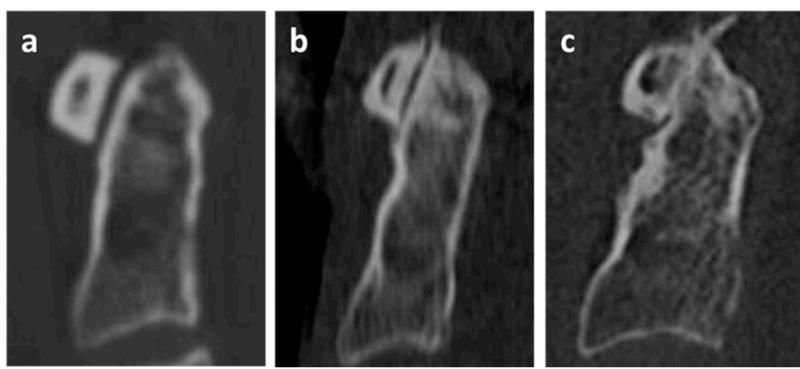
224 **Figures:**

225

226 **Figure 1: Grading of OA disc spaces**

227 Osteoarthritis of the atlanto-axial joint was graded as previously described<sup>11</sup>. For  
228 purposes of our analysis, patients with grade 1 (Fig 1a) degeneration were considered  
229 to have no OA. Patients with grades 2 or 3 (Fig 1b and 1c) degeneration were  
230 considered to have OA of the respective joint.

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235 **Figure 2: Grading OA facet joints**

236 Degeneration of the facet joints: computed tomography representations of all grades  
237 of degenerative changes of the left and right facet joints (C3–C6), shown in the  
238 coronal plane: Grade 1 (Left) shows normal joint space without osteophyte formation.  
239 Grade 2 (Middle) shows obliterated joint space with osteophyte formation. Grade 3  
240 (Right) shows ankylosis of the joint.

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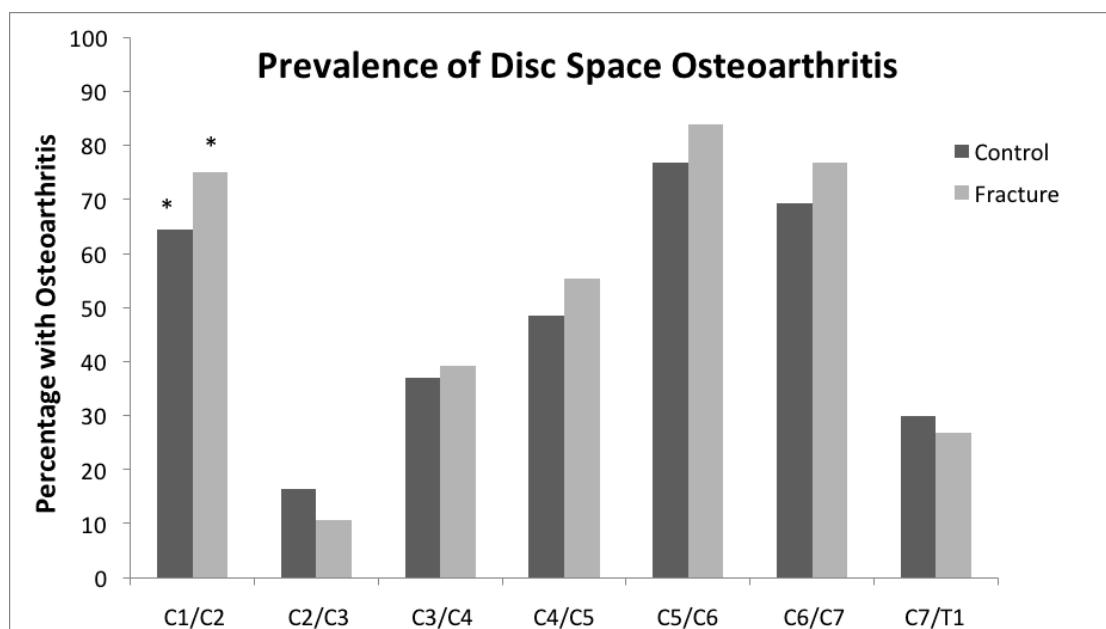
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245 **Figure 3: Prevalence of osteoarthritis of atlanto-axial joint and cervical disc  
246 spaces**

247 We found a significant difference ( $p<0.04$ ) in the prevalence of OA of the C1/C2  
248 interval between the fracture and control group.

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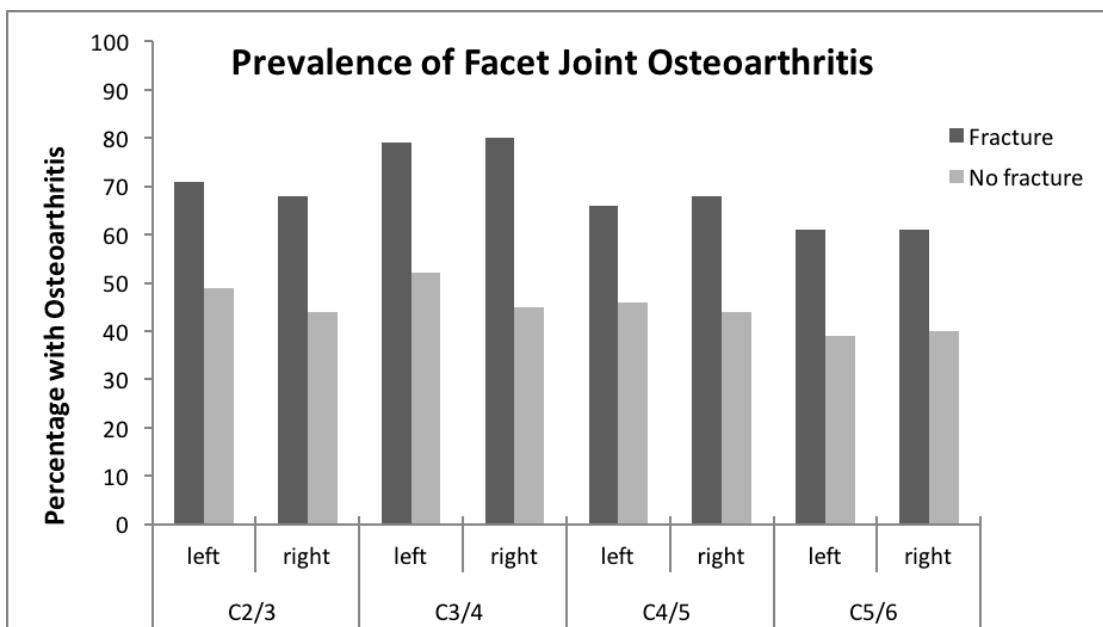


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252 **Figure 4: Prevalence of osteoarthritis in the facet joints of patients with dens  
253 fractures.**

254 We found a significant difference ( $p \leq 0.024$ ) in OA prevalence between fracture and  
255 non-fracture patients at the C2/3 through C5/6 facet joint levels.

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