

Abstract**Background and purpose**

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

Material and methods

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

Results

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

Interpretation

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

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Introduction

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

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

Materials and Methods

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

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

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

Data Analysis

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

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

Ethics, funding and potential conflicts of interest

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

Results

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

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

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

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

Discussion

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

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

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

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

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

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

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

Conclusion

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

Authors contributions

BM, BS, KB and YJ contributed to the conception and design of the study. 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.

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207 **Tables:**

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

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

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

	N	Mean Age ± SD	Males	Females
Control	736	70.7 ± 12.0	54.10%	45.90%
Fracture Group	57	77.7 ± 9.7	60.80%	39.20%

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

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

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

Osteoarthritis of the atlanto-axial joint was graded as previously described¹¹. For purposes of our analysis, patients with grade 1 (Fig 1a) degeneration were considered to have no OA. Patients with grades 2 or 3 (Fig 1b and 1c) degeneration were considered to have OA of the respective joint.

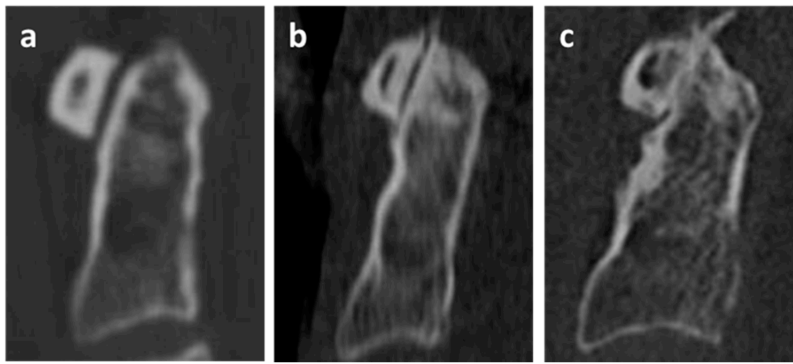


Figure 2: Grading OA facet joints

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



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

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

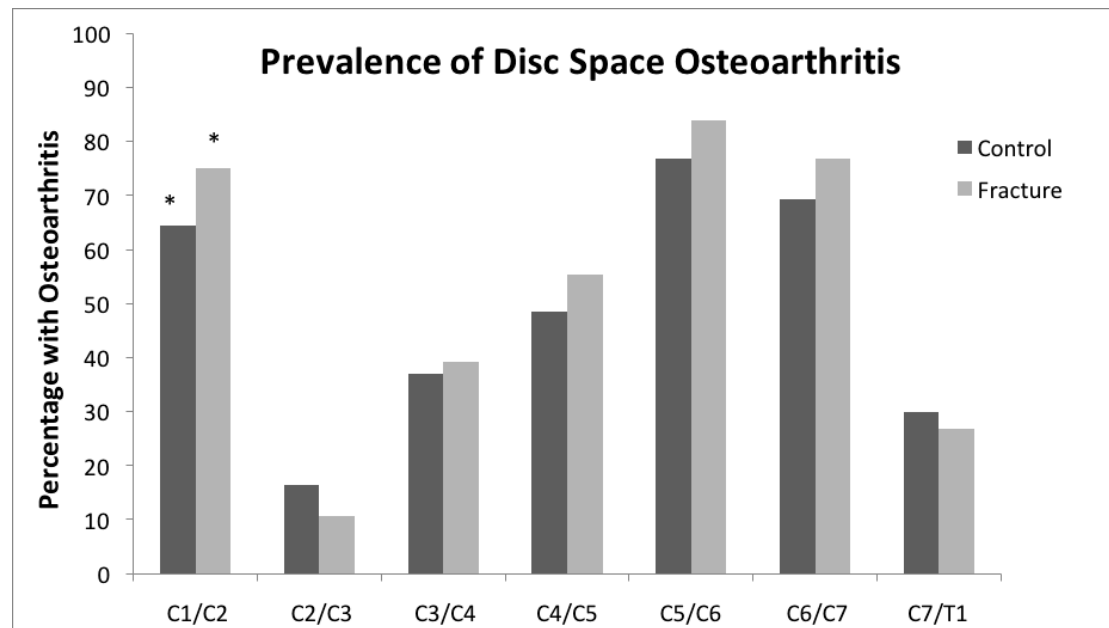
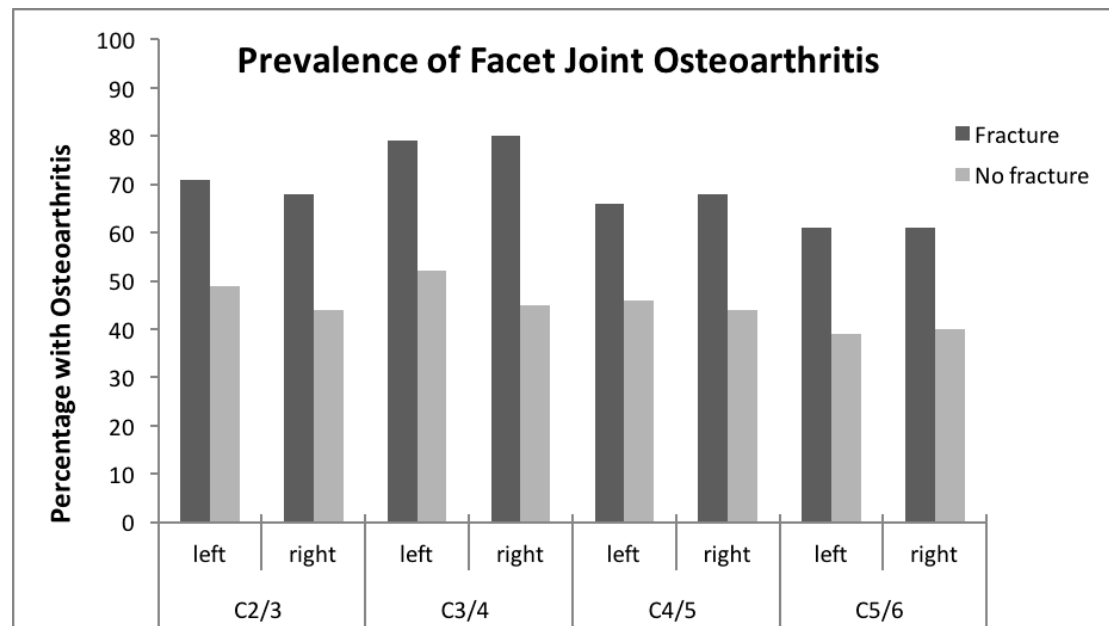


Figure 4: Prevalence of osteoarthritis in the facet joints of patients with dens fractures.

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



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