Optimizing treatment for odontoid fractures in the elderly: a balancing act with the patient at center stage

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CHAPTER

6

GENERAL DISCUSSION AND FUTURE PERSPECTIVES

GENERAL DISCUSSION

The best treatment for odontoid fractures in elderly patients has been a subject of intense debate for decades. In the absence of high-quality evidence, treatment decisions have historically been based on local treatment cultures, as well as the surgeon's training and experience. This has led to considerable national and international practice variation, with some centers advocating for primary surgery, others favoring primary conservative treatment, and still others adopting a fracture- or patient-specific approach.

This thesis aimed to strengthen the quality of the available evidence and support future clinical decision-making by comparing clinical and radiological outcomes of surgical and initial conservative treatments for odontoid fractures in elderly patients. This chapter will provide a general discussion, also addressing the limitations, future perspectives, and direct clinical implications.

Appraisal of historical literature and clinical practice

The existing literature was systematically reviewed and subjected to meta-analysis in the study presented in Chapter 2. The review revealed that historical studies were generally of limited quality and had small sample sizes. Among the 41 studies included, only four studies were prospective, and just one adjusted for confounding variables—qualifying it as a cohort study—while the rest were case series. These designs suffered from inherent limitations such as variability in outcome assessments, missing data, and confounding bias (e.g. surgery for relatively healthy patients and conservative treatment for the most frail).[1] Moreover, outcome parameters varied, with older studies focusing exclusively on fracture healing rather than clinical outcomes. Together, these limitations resulted in substantial heterogeneity in the data. Meta-analyses were feasible only for radiological outcomes, with adjustments limited to baseline differences in mean age and fracture type. Collectively, these factors significantly constrained both the depth of analysis and the strength of the recommendations that could be drawn from historical literature.

In historical literature, patients treated surgically demonstrated higher union rates than those treated conservatively, although this difference may be—at least partly—attributed to the limitations mentioned above.

Furthermore, no clinically relevant differences were observed in Neck Disability Index (NDI), Visual Analogue Scale (VAS) pain, or Smiley-Webster Scale scores, nor fracture stability rates. Other clinical outcome parameters were reported too inconsistently to allow for even univariable analysis. Additionally, the association between clinical outcome and fracture union remained unexplored. It must, therefore, be concluded that historical treatments were not based on robust research.

Despite the limitations discussed, some observations are noteworthy. The treatment approach for odontoid fractures has evolved over recent decades. In the 1990s, case series reported in-hospital mortality rates of over 25% following rigid immobilization and flat bed rest.[2] It is now likely that, at the time, patients died as a result of the treatment rather than from the fracture itself. Since then, the popularity of rigid immobilization methods, such as the halo vest, has gradually declined.[3, 4] Advancements in surgical techniques, including improved implants and intraoperative imaging, have increased the prevalence of surgery among older patients, with surgical treatment rates reaching up to 86% in the United States in 2017.[1, 5-7] These changes were believed to improve union rates, although the clinical benefits for the patient remained unclear. In recent years, the focus has shifted toward prioritizing favorable clinical outcomes.

New insights from the clinical studies in this thesis

The most comprehensive comparison of treatment outcomes to date was presented in Chapter 4. This international prospective comparative study involved 276 patients, with 144 undergoing surgical treatment and 132 receiving conservative treatment. The results provide valuable new insights, particularly regarding clinical outcome, fracture union, fracture stability, and the association between clinical outcome and fracture union.

Clinical outcome

Clinical outcome is now widely considered the most relevant, especially in elderly patients. The primary clinical outcome was assessed using NDI improvement compared to baseline. At the primary assessment at 52 weeks, there was no significant difference in NDI improvement between the surgical and conservative treatment groups. This trend continued throughout the entire 104-week follow-

up, with largely similar NDI improvements observed across both groups. Additionally, NDI improvement was most noticeable between baseline and 26 weeks, with no clear further improvement between 26 and 104 weeks.

Moreover, no relevant differences were found between surgical or conservative treatments in any of the secondary clinical outcome parameters assessed in this thesis. These parameters included VAS neck pain scores, Likert patient-perceived recovery of symptoms, Likert patient-perceived recovery of neck pain, and EuroQol-5D-3L (EQ5D) scores.

Fracture union

Fracture union remains a key objective of treatment and, for some, is still considered the most important outcome parameter. At the primary outcome assessment at 52 weeks, there was no significant difference in fracture union rates between surgical and conservative patients (86% vs. 78%). This similarity in fracture union rates remained consistent throughout the entire 104-week follow-up.

These findings contrast with earlier, lower-quality studies that reported higher union rates following surgery. Those studies had smaller sample sizes, typically relied on univariable analyses, and may have been (more) biased—for instance, by selecting healthier patients for surgery or due to differences in follow-up duration between treatment groups.[1] Illustratively, the univariable analyses in Chapter 5 demonstrated a significant influence of fracture displacement and applied treatment, which was not observed in multivariable analyses.

Fracture stability

Fracture stability, sometimes referred to as fibrous union, has received increasing attention in recent decades. When accompanied by a favorable clinical outcome, it can be considered a successful treatment result in elderly patients. At the primary outcome assessment at 52 weeks, fracture stability was nearly identical between the surgical and conservative groups (99% vs. 98%). This similarity remained consistent throughout the 104-week follow-up.

Association between clinical outcome and fracture union

The association between clinical outcome and fracture union—specifically whether non-union leads to symptoms—has long been uncertain. In the

study presented, there was no relevant difference in NDI improvement between patients with union and those with persistent non-union at the 52-week mark. This lack of difference remained consistent when analyzed separately for each treatment group. In other words, there was no evidence that achieving fracture union resulted in better clinical outcomes for patients compared to persistent non-union.

Complications

Historically, prolonged non-union leading to secondary fracture displacement and potential upper spinal cord injury has been a feared complication, often used as justification for aggressive treatment of odontoid fractures. However, whether this was a likely outcome or merely a theoretical concern has remained unclear, given that reports of secondary deficits are very rare and typically associated with high-impact trauma in previously undiagnosed fractures in non-geriatric patients.[8–10] In the studies included in this thesis, no secondary neurological deficits were identified in any patient—not even in centers with the most liberal collar treatment policies. This suggests that historical concerns about the dangers of undertreatment are unfounded.

As expected, secondary treatment was applied less frequently after surgical treatment than after conservative treatment (6% vs. 19%). This is unsurprising and can be viewed as a logical consequence of the initial conservative approach. Moreover, radiological findings, rather than patient complaints, have primarily driven secondary treatments. In the future, these numbers may decrease as patient complaints become the primary focus, given that only four of the twenty-three patients in the conservative group underwent secondary treatment based on their complaints.

There were no relevant differences between treatment groups in terms of time to secondary treatment, mortality within 52 and 104 weeks, or time to death.

Residual confounding and study design limitations

Despite adjusting for various baseline characteristics in the prospective study in Chapter 4, residual confounding may still have influenced the results. A randomized controlled trial, considered the gold standard, was deemed

infeasible at the time of study design due to variations in local treatment practices and may not even be necessary.[11, 12] An alternative study design—comparing treatment *strategies between centers* in otherwise similar patient populations rather than comparing treatment *modalities within centers*—potentially reduces confounding. This design, also referred to as natural experiment or pseudo-randomization, was applied in the study presented in Chapter 3.[13, 14]

Low-threshold-for-surgery vs. initially-conservative treatment strategy

The retrospective study presented in Chapter 3 compared two distinct treatment strategies between regions in the Netherlands. One region employed a low-threshold-for-surgery approach, performing primary surgery for dislocated fractures in relatively healthy patients, while the other primarily applied a conservative approach for all patients.

Among the 173 patients included (120 in the low-threshold-for-surgery group and 53 in the initially-conservative group), fracture union (53% vs. 43%) and fracture stability (90% vs. 85%) were largely similar between the groups at the last follow-up. These percentages are lower than those in the prospective study, likely due—at least to a large extent—to outcome assessments being conducted at the last available follow-up, which was generally much earlier than the 52-week mark used in the prospective study.

As expected, patients aged 80 and older had worse outcomes in terms of union, stability, and mortality compared to those aged 55-80, regardless of treatment strategy. No cases of secondary neurological deficits were identified, further challenging concerns about the potential consequences of undertreatment.

Interobserver variability in the Anderson and d'Alonzo fracture classification

In the study presented in Chapter 3, all fractures were reassessed using baseline computed tomography (CT) scans, with evaluators blinded to the original scoring. Discrepancies were identified in 26 (15%) fractures, with only substantial agreement (κ=0.69) between the new and original scores. This underscores the limitations of the Anderson and d'Alonzo classification, particularly for fractures that do not clearly classify as type II or III.[15] Therefore, caution should be exercised when using this classification to guide treatment decisions.

Hounsfield unit measurements to predict fracture union

Decreased bone mineral density (BMD) is associated with poorer fracture healing.[16] The role of BMD in odontoid fractures in the elderly had not been previously studied, although it may have influenced study findings. In Chapter 5, Hounsfield units (HU) on baseline CT scans were analyzed as a proxy for BMD in 142 patients from the prospective study in Chapter 4.

There was no relevant difference in baseline HU values between patients who achieved union and those who did not at 52 weeks. Patients in both groups showed decreased HU (cervical HU <300), indicating osteopenia, and HU measurements failed to predict fracture union. These findings suggest that all elderly patients with odontoid fractures should undergo osteoporosis screening and receive appropriate treatment.

Differences in prescribed treatment regimens

There remains considerable variation in how treatment regimens are applied across different centers. For instance, there are no standardized immobilization protocols and practices vary regarding the use of collars—some centers prescribe them only during mobilization, while others mandate continuous use. The duration of collar treatment also varies, with centers prescribing a fixed 6-week period and others continuing until favorable radiological outcomes are achieved, occasionally extending beyond 12 weeks.[17, 18] In some centers, postoperative collar immobilization is routine, while others avoid it altogether.[19, 20]

These variations, although unlikely to affect the overall conclusions, may have influenced the data due to the observational nature of the studies in this thesis. Importantly, there is no evidence that more aggressive treatment regimens improve patient outcomes and, in fact, they may cause unnecessary harm, such as pressure ulcers requiring secondary surgery. Surgeons should therefore remain aware that the prescribed treatment regimen may harm the patient more than the fracture itself.

LIMITATIONS

The studies presented in this thesis have several limitations. None were randomized, and despite adjustments for variables such as age, gender, and

fracture characteristics, residual confounding may still have influenced the results. At the time of the study design, randomization was deemed impracticable due to variations in local treatment practices.

Additionally, no standardized assessments were conducted for baseline health status in the clinical studies. If this influenced the outcome, it most likely favored generally healthier surgical patients.[1] Missing data—largely due to the involvement of older patients, the multicenter nature of the studies, and the relatively frequent follow-up moments—posed challenges for the statistical analyses. In the prospective study, sensitivity analyses using non-imputed data yielded similar overall clinical conclusions, further confirming the robustness of the results.

Unlike the common focus on type II fractures, this thesis examined both type II and III fractures, which was accounted for in the multivariable analyses and type II subgroup analysis. Various surgical (anterior, posterior) and conservative (collar, halo) treatments were analyzed within their respective groups. While these treatment variations may have influenced outcomes, post-hoc analyses in the prospective study found no evidence of differences between treatment subtypes.

The inclusion period spanned over ten years for the retrospective study and over nine years for the prospective study. Although relatively long, this was not expected to introduce methodological issues, as treatment modalities remained largely unchanged throughout the study period.

Lastly, the clinical studies included patients aged 55 and older, a slightly younger cohort than the commonly studied population (≥65 years), which should be considered in future study comparisons.

FUTURE PERSPECTIVES

None of the studies in this thesis found relevant differences between surgical and conservative treatment outcomes. Future research could replicate these findings and address the questions that arise from the presented studies.

Based on the results of this thesis, randomization is now justified in future studies, and preparations for a such study have commenced.[21] Alternatively, future research could evaluate outcomes across centers with varying treatment approaches in similar patient populations, employing a natural experimental

design, as demonstrated in Chapter 3. Ideally, this would involve comparing centers that follow a primary surgical strategy with those that follow a primary conservative approach.

More invasive treatments (surgery, rigid immobilization) did not yield superior outcomes in the studies presented. Given the comparable treatment results, future research should focus on minimizing patient-perceived treatment burden. Future studies may also investigate the long-term (>104 weeks) clinical outcomes of patients with persistent asymptomatic non-union.

Moreover, the natural history of odontoid fractures may be more favorable than previously presumed. Fractures are often diagnosed more than a week after injury, with no clear clinical consequences, and patients can achieve good functional outcomes even if they do not use the prescribed collar.[17, 22] Therefore, further studies should evaluate whether treatment is necessary at all for elderly patients. A current randomized controlled trial is comparing the outcomes of 12-week collar treatment versus no immobilization, which may help answer this important clinical question.[23] Such studies should also take frailty status into account—such as by using the modified 5-Item Frailty Index—to predict complications and mortality.[24] Fracture classifications may be updated to incorporate these factors accordingly to better guide treatment decisions.[25]

From a societal perspective—given the projected increase in the aging population and its associated healthcare burden—future research should also focus on evaluating cost-effectiveness and reducing treatment-related costs without compromising patient care.[26] The findings of this thesis indicate that more aggressive—and presumably more costly—treatment strategies may not be warranted, and future research might even suggest that primary interventions may be unnecessary.

DIRECT CLINICAL IMPLICATIONS

Surgical and initially conservative treatments for odontoid fractures in elderly patients lead to similar clinical and radiological outcomes. Therefore, initial conservative management is justified, with surgery reserved for the relatively rare cases of persistent symptomatic non-union. The primary focus should be on achieving favorable clinical outcomes rather than radiological results.

Historical concerns about undertreatment, such as the risk of secondary fracture displacement leading to upper spinal cord injury, are now considered unwarranted. Asymptomatic non-union can be considered an acceptable treatment outcome and should not automatically prompt secondary surgical intervention. Furthermore, elderly patients with odontoid fractures likely have decreased bone mineral density and should be routinely referred for osteoporosis screening and management.

Primum non nocere—first, do no harm. Although surgeons might interpret these results as a rationale for maintaining their usual treatment practices, they should recognize that similar outcomes can be achieved with treatments that impose a lower burden on the patient and may be less costly. Therefore, surgeons should prioritize minimizing this burden by avoiding overly aggressive treatments that do not improve outcomes and may introduce additional risks. The prescribed treatment regimen could ultimately harm the patient more than the fracture itself.

LIST OF ABBREVIATIONS

BMD — Bone mineral density
CT — Computed tomography
EQ5D — EuroQol-5D-3L
HU — Hounsfield units
K — Kappa
NDI — Neck Disability Index
VAS — Visual Analogue Scale

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