Evaluation of treatment for atlantoaxial instability in adult patients with Down Syndrome: Grading the evidence and identifying research gaps

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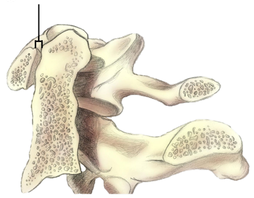
BACKGROUND

Atlantoaxial instability (AAI) is a rare condition in the general population but one that has a notable prevalence in patients with Down Syndrome (DS). The condition is most often asymptomatic but can cause significant cervical spinal cord compression and neurological impairment that warrants effective treatment. Asymptomatic AAI is typically managed nonoperatively, but the mainstay of treatment for symptomatic AAI requires surgical intervention.[1] The diagnostic criteria for AAI are as follows:



Atlantodens interval

Normal
- < 3mm adult
- < 4.5mm child

AAI
- > 3mm adult
- > 5mm child

OBJECTIVES/AIMS

1. Identify original research articles in peer-reviewed medical journals that focus on key questions about treatment options and outcomes for symptomatic AAI amongst adult patients with DS
2. Evaluate the quality of the existing evidence, identify deficiencies in current clinical knowledge, and suggest directions for future research
3. Begin to formulate practical guidelines to support best medical practices for optimizing outcomes in the treatment of symptomatic AAI amongst adult patients with DS

DESIGN/METHODS

We performed a literature search using PubMed with criteria from 1960 to Present with Daily Update Search Strategy in April 2022. The MeSH terms [Down syndrome OR Trisomy 21], [Atlantoaxial Instability], and [Treatment] were used. Case series involving fewer than 5 subjects and review articles were not included.

By consensus, the following key questions were formulated:
- What are the treatment options for adults with DS and symptomatic AAI?
- What are the complications associated with the treatment options?
- What factors influence outcomes of different treatment options?
- What is the pathway to treatment of AAI for patients with DS?
- What is the impact of treatment on morbidity and mortality?
- What are the treatment differences for those with DS versus the general population?

RESULTS/SUMMARY

Search Term: DS OR Trisomy 21 + AAI + Treatment No limits applied	PubMed Limits applied (human, English, age > 18y)
Unfiltered Hits = 10 articles	Filtered Hits = 2 articles
	Excluded articles = 0 Included articles = 2

DATA SUMMARY
- Complication rates range from **75-82.4%** using the studied surgical approaches to treatment
- Complications seen across both studies include wound infection, wound dehiscence, neurologic complications, and loss of reduction
- **Surgical approach** was found to be a predictor of outcomes in both studies
- Cervical decompression and fusion is associated with improved outcomes, decreased rates of complications, and decreased need for reoperation compared to arthrodesis

PubMedID (PBID)	8727197	27448197
Title of article	Complications and long-term outcome of cervical spine arthrodesis in patients with Down syndrome[2]	Complications in Adult Patients with Down Syndrome Undergoing Cervical Spine Surgery Using Current Instrumentation Techniques and rhBMP: A Long-Term Follow-Up[3]
Publication year	1996	2016
Subjects studied (N)	6	17
Age range	19 - 53 y	21 - 49 y
Source of subjects	The University of Pittsburgh Medical Center and the University of Minnesota Medical Center	Single academic medical center
Methods	Retrospective chart review	Retrospective chart review
Key Questions		
What are the treatment options?	Posterior arthrodesis of the upper cervical spine	Cervical spine decompression and fusion with or without recombinant human bone morphogenetic protein (rhBMP-2) Surgical techniques included the **Harm technique** and the **Magerl technique**
What are the complications associated with treatment?	There is a high complication rate associated with this approach to treatment. Complications include nonunion, **loss of reduction**, **neurologic deterioration**, subaxial instability, **wound infection**, and **wound dehiscence**.	Perioperative complications include pneumonia, respiratory distress, reintubation, dysphagia, deep venous thrombosis, sepsis, **wound infection, wound dehiscence, neurologic complications, loss of reduction**, pseudarthrosis, and hardware failure. 70.6% of patients experienced minor complications, 41.2% experienced major complications, and 17.6% experienced no complications.
What factors influence outcomes of treatment?	**Skeletal immaturity** and atlantodens **interval >5mm** were associated with worse outcomes. **C1-C2** fusions yielded worse outcomes than fusions involving the occipital bone	**Surgical approach** was the only variable that demonstrated statistical significance in predicting complications of treatment. **Posterior approach** yields better outcomes than anterior. **rhBMP-2** is associated with increased rates of pseudarthrosis
What is the pathway to treatment?	*Not addressed*	*Not addressed*
What is the impact of treatment on morbidity and mortality?	Posterior arthrodesis is ultimately helpful in treating myelopathies associated with AAI in patients with DS, but often requires multiple surgical attempts.	Cervical spine decompression and fusion is likely to yield stabilization and/or improvement in neurologic status. Compared to arthrodesis, these techniques may also reduce the rates of pseudarthrosis, loss of reduction, instability, and fatality.
What are the treatment differences for DS v general population?	*Not addressed*	*Not addressed*
USPSTF Rating[4]		
Research design	Level III	Level III
Internal Validity	Poor	Poor
External Validity	Poor	Poor

CONCLUSIONS

Gaps in clinical knowledge: Research required to address key questions
- There are currently large gaps in the literature on the topic of treatment options and outcomes of AAI for adult patients with DS.
- The available evidence is only of fair quality (Level III) with poor internal and external validity; it is insufficient to answer all key research questions.

Additional questions include the following:
- What is the compared efficacy of treatment options for AAI in individuals with DS?
- How do treatment options differ for patients with acute onset of symptoms versus patients with chronic development of symptoms?
- As AAI is more likely to become symptomatic in younger individuals with DS, do we have appropriate methods of screening at-risk patients to facilitate timely treatment in adults with DS? Is additional training necessary to help generalist and specialist health care providers recognize signs and symptoms?

Toward practical guidelines: for further consideration by DSMIG-USA
- The current knowledge gaps make it difficult to formulate evidence-based guidelines for treatment of symptomatic AAI in patients with DS.
- Even though current treatment options are proven beneficial in preventing neurologic deficit secondary to AAI, the complication rates are abundant and have shown no improvement with time. These numbers point to a need for further investigation as to how to optimize outcomes, limit the number of adverse events, and minimize the need for reoperation in the DS population.

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