THE LONG TERM CLINICAL OUTCOME OF BRACED AND SURGICALLY TREATED PATIENTS WITH IDIOPATHIC SCOLIOSIS.

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LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

OLVG	Onze Lieve Vrouwe Gasthuis, Amsterdam
PROMs	Patient Reported Outcome Measures
ODI	Oswestry Disability Index
VAS	Visual Analogue Scale
SF-36	36-question Short Form Survey
SRS-22r	Scoliosis Research Society-22 questionnaire
PGWBI	Psychological General Well-Being Index
Sponsor	The sponsor is the party that commissions the organization or performance of the research, for example a pharmaceutical company, academic hospital, scientific organization or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidizing party.
WBP	Personal Data Protection Act (in Dutch: Wet Bescherming Persoonsgevens)
WMO	Medical Research Involving Human Subjects Act (in Dutch: Wet Medisch Wetenschappelijk Onderzoek met Mensen)

1. SUMMARY

Rationale: Idiopathic scoliosis is a complex three-dimensional deformity of the spine affecting approximately 2-3% of the children. In 0.3–0.5% of children require treatment of their scoliosis during adolescence. Despite extensive experience with bracing or surgical treatment of adolescents, the long-term effects of both treatments remain largely unknown. Although most children with scoliosis do not have complaints, up to 45% of the adults suffer from low back pain. Since the long term results after bracing and surgical treatment have never been compared, the aim of this study is to investigate the long term clinical outcome of braced and surgically treated patients with idiopathic scoliosis.

Objective: The main objective of this study is to evaluate the long term (>15 years) clinical outcome of braced and surgically treated patients with idiopathic scoliosis

Study design: Patients will be asked to fill out patient reported outcome measures (ODI, SF-36, SRS-22r, PGWBI) online at home.

Study population: Patients of the OLVG hospital in Amsterdam treated operatively or with a brace between 1981 and 1995.

Main study parameter/endpoint: Long term results (back pain and health related quality of life) of surgically or conservatively treated patients as measured with the ODI and SF-36.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: We do not anticipate treatment related risks related to participation in this study.

2. INTRODUCTION

Idiopathic scoliosis is a complex three-dimensional deformity of the spine and trunk affecting approximately 2-3% of children younger than 16 years of age. In 0.3–0.5% of children, the spinal curve becomes progressive and requires treatment.[1] Severe curves over 45 degrees have a high risk of progression during adulthood and are therefore treated surgically. The only proven non-surgical intervention is rigorous brace treatment during a number of years of the adolescent growth spurt. Bracing aims to maintain the curve below 45 degrees thereby leaving the patient with a deformity with lesser risk of problems in later life. A recent randomized controlled trial confirmed the efficacy of bracing in idiopathic scoliosis by showing a significant reduction of curve progression and subsequent reduction of the need for surgery.[2]

Despite extensive experience with bracing and surgical treatment, the long-term effects of both treatments remain largely unknown. The advantage of brace therapy is the preservation of the mobility of the spine. However, in contrast to the surgical correction, there will remain a considerable deformity in the spine after bracing. Surgical correction of the spine will reduce the deformity better but stiffens the spine and may cause increase stress of the long fused lever arm on the un-instrumented caudal intervertebral discs.

It is well known that many adult scoliosis patients experience back pain.[3] In the past, it has been attempted to correlate the severity of back pain to the scoliosis curve magnitude.[4] However, this correlation was not found. Even those patients with mild curves have twice as much back pain as that experienced by non-deformity controls. So far, few scoliosis studies have focused on the long term outcome of surgical and non-surgical treatments. Whereas the mid-term (10 year follow up) incidences of low back pain varied between 35 to 45% after surgical treatment[5-7], a long term (22 year follow up) incidence of 25% has been reported after brace treatment[8]. Although the clinical outcome after bracing and surgical treatment have never been compared, these numbers may suggest that braced patients perform better compared to surgically treated patients. Therefore, the aim of this study is to investigate the long term clinical outcome of braced and surgically treated patients with idiopathic scoliosis.

3. OBJECTIVES

3.1 Primary objective:

- The purpose of this study is to evaluate the long term (>15 years) clinical outcome of braced and surgically treated patients with idiopathic scoliosis from the Onze Lieve Vrouwe Gasthuis (OLVG)

3.2 Secondary Objectives:

- To investigate the incidence of braced patients requiring surgical as adults and surgically treated adolescent patients requiring second interventions as adults.
- To investigate how patients experienced their treatment period.
- Correlations between heath related quality of life and patient demographics / scoliosis characteristics.

4. STUDY DESIGN

This study concerns a single-center retrospective cross-sectional cohort study with patients diagnosed with idiopathic scoliosis who consulted the outpatient clinic of the Department of Orthopedic Surgery at the OLVG in Amsterdam between 1981 and 1995. All data will be collected by a medical student (J. Heemskerk) as part of a research internship.

5. TREATMENT OF SUBJECTS

5.1 Population

All patients diagnosed with idiopathic scoliosis who consulted the department of Orthopedic Surgery of the OLVG between January 1981 and January 1995 will be included. These subjects will be retrieved from the patient database of the Orthopedic Unit of the OLVG and will be contacted.

5.2 Inclusion criteria

- All patients diagnosed with idiopathic scoliosis
- Consultation in the OLVG between January 1981 and January 1995
- Patients treated with a brace or surgically during adolescence.

5.3 Exclusion criteria

- Inadequate knowledge of Dutch language
- Other forms of scoliosis (e.g. neuromuscular or congenital scoliosis)

6. METHODS

6.1 Study outline

The study will consist of two parts:

Part 1: A retrospective part, which entails collecting clinical and radiologic data from patients records.

Part 2: A cross-sectional part, in which patients are asked to fill out patient reported outcome measures (PROMs) which addresses pain, physical function and heath related quality of life.

6.2 Primary outcome parameters

Oswestry Disability Index and Visual Analogue Scale

Low back pain as determined by the Oswestry Disability Index (ODI) and Visual Analogue Scale(VAS). The ODI is an index is derived from the Oswestry Low Back Pain Questionnaire used by clinicians and researchers to quantify disability for low back pain.[9] The ODI is currently considered by many as the gold standard for measuring degree of disability and estimating quality of life in a person with low back pain.

6.3 Secondary outcome parameters

36-question Short Form Survey
The health related quality of life is determined by the 36-question Short Form Survey (SF-36). The SF-36 is very useful for studying long-term follow-up when pre-treatment clinical data are not available. In this case, the patients' status is compared with the average population values. The SF-36 is commonly used in health economics as a variable in the QALY calculation to determine the effectiveness of treatment. It contains questions about the patients perception on vitality, pain and physical and emotional role of functioning.

Scoliosis Research Society-22 questionnaire
The Scoliosis Research Society-22 questionnaire (SRS-22r) is an a simple disease-specific questionnaire specially developed for scoliosis. The SRS-22 has been translated and validated in Dutch and is a reliable outcome instrument in scoliosis research.[10] It consists of 22 questions and measures five domains: pain, self-image, function, mental health and satisfaction with management.

Psychological General Well-Being Index
The Psychological General Well-Being Index (PGWBI) is a measure of the level of subjective psychological well-being. In detail, it assesses self-representations of intrapersonal affective or emotional states reflecting a sense of subjective well-being or distress and thus captures what we could call a subjective perception of well-being.

Specific questions regarding the previous treatment
Two additional questions are asked regarding the patients perception of the treatment period and its effect on daily life.

6.4 Other study parameters

In the retrospective part, the following data will be collected from the medical records:

Demographic data:	Gender (male / female); present age; body mass index
Brace treatment data:	Pain during adolescence (yes / no); age at the start of the brace treatment; Risser sign at the start of treatment; duration of the treatment; age at the end of the brace treatment; curve size before treatment; curve size at the end of treatment.
Surgical treatment data:	Pain during adolescence (yes / no); age at the time of surgery; pre-surgical brace treatment; curve size before surgery; surgical technique; number of levels fused; curve size after surgery.

7. STUDY PROCEDURES

The study will be performed at the department of Orthopedics of the Onze Lieve Vrouwe Gasthuis in Amsterdam. Patients will be contacted by telephone. First after giving oral information by telephone concerning the study, they will be asked if they are willing to participate, and if so, a patient information letter and an informed consent form will be send to them. Patients will be asked to fill out the patient reported outcomes (ODI, VAS, SF-36, SRS-22r, PGWBI) at home. Proms to be filled in using the Questmanager Software from VitalHealth.

8. ADVERSE EVENTS

There is no anticipation on any adverse events to the patient.

9. STATISTICAL ANALYSIS

All statistical analyses will be performed using SPSS version 18.0 and Microsoft Excel 2003. Data of continuous variables will be summarized using the appropriate measures of central tendency (i.e. mean, median) and dispersion (i.e. standard deviation, range) (depending if the variable is normally distributed). Data of categorical variables will be summarized using the appropriate measures of central tendency (i.e. median) and dispersion (i.e. range).

In order to address the primary and secondary objectives, descriptive statistics will be used (continuous data, normally distributed: means and standard deviations; continuous data, non-normally distributed: median and range; nominal data: frequency and percentages). Data for both surgical and conservative groups will be presented. Differences in patient reported outcomes between the two groups will be tested by the use of a independent student's t-test, in case of normally distributed data, or a Mann-Whitney U test, in case of non-normally distributed data.

10. PATIENT EFFORT AND RISKS

There are no risks to the patient.

11. ETHICAL CONSIDERATIONS

11.1 Regulation statement

The study will be conducted according to the principles of the Declaration of Helsinki (as amended in Tokyo, Venice, Hong Kong and Somerset West) and in accordance with the Medical Research Involving Human Subjects.

11.2 Recruitment and consent

A list of all patients that meet the in- and exclusion criteria will be derived from the central archives in the OLVG by D.H.R. Kempen, MD. Patients will be informed and asked for

participation by phone and a letter. The patient will be given 2 weeks to consider their decision. After 2 weeks the patient will be contacted to inform whether or not he or she wishes to participate. The patient information letter and informed consent form are attached as a separate document to the study protocol.

11.3 Benefits and risks assessment, group relatedness

Subjects participate in this study voluntarily. There will be no direct benefits for the patients participation in this study. This is a non-therapeutic study without minors or incapacitated subjects. Next to the time required for completing the PROMs, there are no risks to be considered and the burden can be considered minimal.

11.4 Compensation for injury

The sponsor/investigator has a liability insurance which is in accordance with article 7, subsection 6 of the WMO. Exemption of insurance for subjects will be requested because the chance of injury in this study is nil.

12. ADMINISTRATIVE ASPECTS AND PUBLICATION

12.1 Handling and storage of data and documents

The patient cooperates voluntarily. All subject data will be anonymized by assigning study numbers to each subject. The key to this study number is only available to the investigators. All the collected data will be digitalized and password protected. Data will only be accessible by the investigators. All data will be stored in a separate database and used only for research purposes. All data will be stored for 10 years.

12.2 Amendments

Amendments are changes made to the research after a favorable opinion by the accredited METC has been given. All amendments will be notified to the METC that gave a favorable opinion.

12.3 Annual progress report

Since the study will not take more then a year, there will be no annual report.

12.4 End of study report

The following text is considered not applicable if no approval is needed by the Medical Ethical Committee according the Dutch law.

The investigator will notify the accredited MEC (or the Scientific Committee of the participating institution in the Netherlands) of the end of the study within a period of 8 weeks. The end of the study is defined as the last patient's completing the PROMs. In case the study is ended prematurely, the investigator will notify the accredited MEC (or the Scientific Committee of the participating institution in the Netherlands) within 15 days, including the reasons for the premature termination. Within one year after the end of the study, the investigator/sponsor will submit a final study report with the results of the

study, including any publications/abstracts of the study, to the accredited MEC (or the Scientific Committee of the participating institution in the Netherlands).

12.5 Public disclosure and publication policy

Results will be presented for publication in a peer reviewed journal.

13. FINANCIAL ASPECTS

There are no financial aspects involved in this study.

14. REFERENCES

1. Altaf F, Gibson A, Dannawi Z, Noordeen H. Adolescent idiopathicscoliosis. BMJ. 2013;346:f2508.
2. Weinstein SL, Dolan LA, Wright JG, Dobbs MB. Effects of bracing in adolescents with idiopathic scoliosis. N Engl J Med. 2013;369:1512-21.
3. Perennou D, Marcelli C, Herisson C, Simon L. Adult lumbar scoliosis: epidemiologic aspects in a low-back pain population. Spine 1994;19(2):123–128.
4. Buttermann GR, Mullin WJ. Pain and disability correlated with disc degeneration via MRI in scoliosis patients. Eur Spine J 2008;17:240-9.
5. Bjerkreim I , Steen H , Brox JI . Idiopathic scoliosis treated with Cotrel-Dubousset instrumentation: evaluation 10 years after surgery. *Spine* 2007;32:2103-10.
6. Benli IT , Ates B , Akalin S , Citak M, Kaya A, Alanay A. Minimum 10 years follow-up surgical results of adolescent idiopathic scoliosis patients treated with TSRH instrumentation . *Eur Spine J* 2007;16:381-91.
7. Takayama K , Nakamura H , Matsuda H. Low back pain in patients treated surgically for scoliosis: longer than sixteen-year follow-up. *Spine* 2009;34:2198-204.
8. Danielsson AJ , Nachemson AL . Back pain and function 22 years after brace treatment for adolescent idiopathic scoliosis: A case control study-part I . *Spine* 2003;28:2078-85.
9. Fairbank JC, Couper J, Davies JB. The Oswestry Low Back Pain Questionnaire. Physiotherapy 1980;66:271-273.
10. Schlösser TP, Stadhouder A, Schimmel JJ, Lehr AM, van der Heijden GJ, **Castelein** RM. Reliability and validity of the adapted Dutch version of the revised Scoliosis Research Society 22-item questionnaire. Spine J 2014;14(8):663-72.