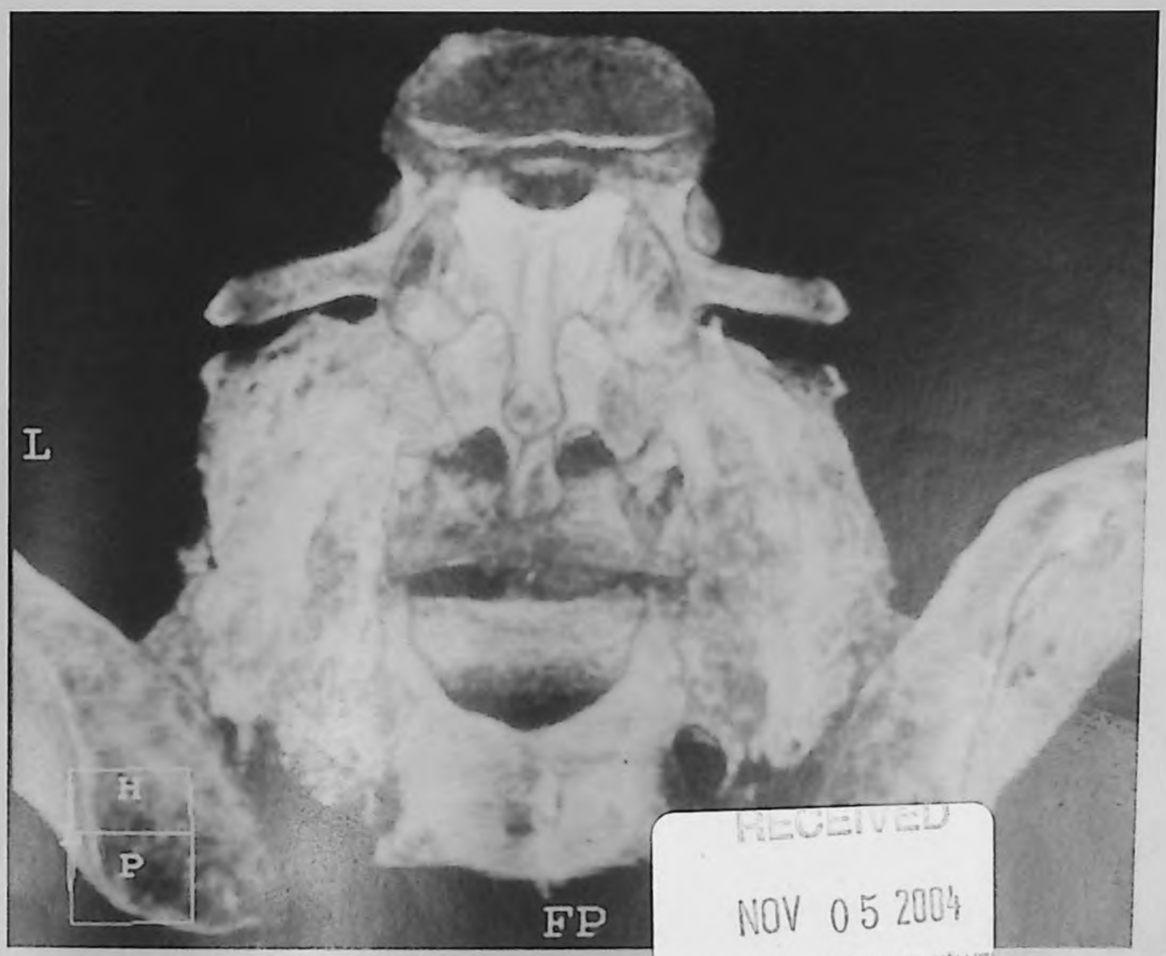
# Lumbar spinal fusion

## Outcome in relation to surgical methods, choice of implant and postoperative rehabilitation

**Finn Bjarke Christensen**



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**Finn Bjarke Christensen**

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# Contents

# List of Papers

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals (I–IX).

I F. B. Christensen, B. Karlsmose, E. S. Hansen, C. E. Bünger. Radiological and functional outcome after anterior lumbar interbody spinal fusion. Eur Spine J (1996) 5: 293–298.

II F. B. Christensen & C. E. Bünger. Retrograde ejaculation after retroperitoneal lower lumbar interbody fusion. Int Orthop (1997) 18: 291-298.

III F. B. Christensen,K. Thomsen, S. P. Eiskjær, J. Gelineck, C. E. Bünger. Functional outcome after posterolateral spinal fusion using pedicle screws: comparison between primary and salvage procedure. Eur Spine J (1998) 7: 321-327.

IV F. B. Christensen, M. Dalstra, F. Sejling, S. Overgaard, C. E. Bünger. Titanium-alloy enhances bone-pedicle screw fixation: mechanical and histomorphometrical results of titanium-alloy versus stainless steel. Euro Spine J (2000) 9: 97-103.

V F. B. Christensen, M. Laursen, J. Gelineck, S. P. Eiskjær, K. Thomsen, C. E. Bünger Interobserver and intraobserver agreement of radiograph interpretation with and without pedicle screw implants. The need for a detailed classification system in posterolateral spinal fusion. Spine (2001) 26: 5; 538-543.

VI F. B. Christensen, M. Laursen, J. Gelineck, E. S. Hansen, C. E. Bünger. Posterolateral spinal fusion at unintended levels due to bone-graft migration. No effect on clinical outcome in 19/130 patients. Acta Orthop Scand (2001) 72: 4; 354-358.

VII F. B. Christensen, E. S. Hansen, M. Laursen, K. Thomsen, C. E. Bünger. The Long-term functional outcome of pedicle screw instrumentation as a support for posterolateral spinal fusion. A randomised clinical study with a 5-year follow-up. Spine (2002) 27: 12; 1269-1277

VIII F. B. Christensen, E. S. Hansen, S. P. Eiskjær, K. Høy, P. Helmig, P. Neumann, B. Niedermann, C. E. Bünger. Circumferential lumbar spinal fusion with a Brantigan cage versus posterolateral fusion with titanium CDI alone: A prospective randomized clinical study. Spine (2002) 27: 23; 2674-2683.

IX F. B. Christensen, I. Laurberg, C. E. Bünger. Importance of the back-café concept to rehabilitation following lumbar spinal fusion. A randomized clinical study with a 2-year follow-up. Spine (2003) 28: 23; 2561-2569.

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Denne afhandling er i forbindelse med ovenfor anførte tidligere publicerede artikler af Det Sundhedsvidenskabelige Fakultet ved Aarhus Universitet, antaget til offentlig forsvar for den medicinske doktorgrad.

Aarhus Universitet 30. juli 2004
Søren Mogensen
Dekan

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# Abstract

Chronic low back pain (CLBP) has become one of the most common causes of disability in adults under 45 years of age and is consequently one of the most common reasons for early retirement in industrialised societies. Accordingly, CLBP represents an expensive drain on society's resources and is a very challenging area for which a consensus for rational therapy is yet to be established. The spinal fusion procedure was introduced as a treatment option for CLBP more than 70 years ago. However, few areas of spinal surgery have caused so much controversy as spinal fusion. The literature reveals divergent opinions about when fusion is indicated and how it should be performed. Furthermore, the significance of the role of postoperative rehabilitation following spinal fusion may be underestimated. There exists no consensus on the design of a program specific for rehabilitation. Ideally, for any given surgical procedure, it should be possible to identify not only possible complications relative to a surgical procedure, but also what symptoms may be expected, and what pain behaviour may be expected of a particular patient.

The overall aims of the current studies were: 1) to introduce patient-based functional outcome evaluation into spinal fusion treatment; 2) to evaluate radiological assessment of different spinal fusion procedures; 3) to investigate the effect of titanium versus stainless steel pedicle screws on mechanical fixation and bone ingrowth in lumbar spinal fusion; 4) to analyse the clinical and radiological outcome of different lumbar spinal fusion techniques; 5) to evaluate complications and re-operation rates following different surgical procedures; and 6) to analyse the effect of different rehabilitation strategies for lumbar spinal fusion patients.

The present thesis comprises 9 studies: 2 clinical retrospective studies, 1 clinical prospective case/reference study, 5 clinical randomised prospective studies and 1 animal study (Mini-pigs). In total, 594 patients were included in the investigation from 1979 to 1999. Each had prior to inclusion at least 2 years of CLBP and had therefore been subjected to most of the conservative treatment modalities. They had all suffered from back and leg pain, due to localized isthmic spondylolisthesis grades I–II or primary or secondary degeneration.

*Patient-based functional outcome:* Patients' self-reported parameters should include the impact of CLBP on daily activity, work and leisure time activities, anxiety/depression, social interests and intensity of back and leg pain. Between 1993 and 2003 approximately 1400 lumbar spinal fusion patients completed the Dallas Pain Questionnaire under prospective design studies. In 1996, the Low Back Pain Rating scale was added to the standard questionnaire packet distributed among spinal fusion patients. In our experience, these tools are valid instruments for clinical assessment of candidates for spinal fusion procedures.

*Radiological assessment:* It is extremely difficult to interpret radiographs of both lumbar posterolateral fusion and anterior interbody fusion. Plain radiographs are clearly not the perfect media for analysis of spinal fusion, but until new and better diagnostic methods are available for clinical use, radiographs will remain the golden standard. Therefore, the development of a detailed reliable radiographic classification system is highly desirable. The classification used in the present thesis for the evaluation of posteroalteral spinal fusion, both with and without instrumentation, demonstrated good interobserver and intraobserver agreement. The classification showed acceptable reliability and may be one way to improve interstudy and intrastudy correlation of radiologic outcomes after posterolateral spinal fusion. Radiology-based evaluation of anterior lumbar interbody fusion is further complicated when cages are employed. The use of different cage designs and materials makes it almost impossible to establish a standard radiological classification system for anterior fusions.

*Bone–screw interface:* Mechanical binding at the bone-screw interface was significantly greater for titanium pedicle screws than it was for stainless steel. This could be explained by the fact that the titanium screws had superior bone on-growth. There was no correlation between screw removal

torques and pull-out strength. Clinically, the use of titanium and titanium-alloy pedicle screws may be preferable for osteoporotic patients and those with decreased osteogenesis.

*Outcome:* The present series of studies observed significant long-term functional improvement for approximately 70% of patients who had undergone lumbar spinal fusion procedure. Solid fusion as determined from radiographs ranged from 52% to 92% depending on the choice of surgical procedure. The choice of surgical procedure should relate to the diagnosis, as patients with isthmic spondylolisthesis (Grades I and II) are best served with posterolateral fusion without instrumentation, and patients with disc degeneration seem to gain most from instrumented posterolateral fusion or circumferential fusion.

*Complications:* The number of perioperative complications increased with the use of pedicle screw systems to support posterolateral fusions and increased further with the use of circumferential fusions. There was no significant association between outcome result and perioperative complications. The risk of reoperation within 2 years after the spinal fusion procedure was, however, significantly lower for those who had received circumferential fusion in comparison to posterolateral fusion with instrumentation. Furthermore, the risk of non-union was found to be significantly lower for patients who had received circumferential fusion as compared to posterolateral fusion with and without instrumentation. The complications of sexual dysfunction and fusion at non-intended levels were found to be significant but without influence on the overall outcome.

*Rehabilitation:* The patients in the Back-café group performed a succession of many daily tasks significantly better and moreover had less pain compared with both the Video and Training groups 2 years after lumbar spinal fusion. The Video group had significantly greater treatment demands outside the hospital system. This study demonstrates the importance of the inclusion of coping schemes and questions the role of intensive exercises in a rehabilitation program for spinal fusion patients.

# Abbreviations

**Ti:** Titanium
**Ss:** Stainless steel
**DPQ:** Dallas Pain Questionnaire
**LBPR:** Low Back Pain Rating scale
**CLBP:** Chronic Low Back Pain
**RCT:** Randomized Controlled Trials
**CT:** Computer Tomography
**MRI:** Magnetic Resonance Imaging
**VAS:** Visual Analog Scale
**ALIF:** Anterior Lumbar Interbody Fusion
**PLIF:** Posterior Lateral Interbody Fusion
**TLIF:** Transforaminal Lateral Interbody Fusion

# Introduction

Chronic low back pain (CLBP) has become one of the most common causes of disability in adults under 45 years of age and is consequently one of the most common reasons for early retirement in industrialised societies. [8] Accordingly, CLBP represents an expensive drain on society's resources and is a very challenging area for which a consensus for rational therapy is yet to be found. The spinal fusion procedure was introduced as a treatment option for CLBP more than 70 years ago. [96] However, few areas of spinal surgery have caused so much controversy as spinal fusion. The literature reveals divergent opinions about when fusion is indicated and how it should be performed. The debate about whether to use an anterior-, posterior- or anterior + posterior fusion approach has persisted since the 1930's. In the mid-70's the posterior-lateral approach was introduced as a method for assessment of the anterior column[17; 130], and recently a transforaminal approach has been newly developed. [132] Epidemiological research has documented extensive variation in the use of spinal fusions from country to country and even between different areas within countries. [33; 51] This suggests differences in opinion about the indications for such surgery and, in turn, perhaps differences in philosophical and cultural orientations as well. It was therefore already clear in the early 1990's that the rationale for spinal fusion and its related surgical procedures needed to be formally clarified. [65; 151; 203] Many technically elegant instrumentation devices have been developed to enhance fusion and correct spinal malalignment. The material chosen for new implants has also changed. Stainless steel was once the material of choice, but titanium, carbon and tantalum are now also employed. These new materials are known to have better bioactivity, flexibility, and in some cases less CT- and MRI signal interference. [113; 184] New instrumentation and materials are often introduced as a result of influence from the industrial market, but they need to be proven equal or superior to their antecedents via well-controlled experimental and clinical tests.

There are many possible determinants underlying CLBP. Pain may derive from nerve-root irritation, diseased disc or other tissues, or segmental instability, but it can also be related to idiosyncratic, psychological factors. In addition to the physio-medical components, social and psychological factors may play contributing roles. As the underlying disease process responsible for the pain is difficult to fully assess, the surgical procedure elected may consequently be inappropriate. The concept of spinal fusion is based on the general assumption that pain arises from segmental motion, and therefore, suppression of intervertebral motion would eliminate the pain. However, pain can also derive from a torn annulus (discogenic pain), e.g., in which case the removal of the annulus would be logically indicated as discogenic pain is believed to be caused by stimulation of nociceptors in the outer annulus. [66] Furthermore, it is well known that substantial axial disc motion is not fully eliminated by posterolateral fusion, and it would therefore be advisable to consider the possibility of the pain being discogenic in origin, before and after a posterolateral fusion. [170]

The role of postoperative rehabilitation might be underestimated for its importance in obtaining optimal outcome. There exists, however, no consensus on the design of a specific program for rehabilitation following lumbar spinal fusion. During the last 15 years several studies have investigated the effect of various exercise and rehabilitation programs in the treatment of acute and chronic low back pain. [15; 71; 101; 109; 114; 115; 131; 136; 145; 155; 197] Overall, the results show that regular back exercise reduces back pain and improves the functional ability of subjects with CLBP on short term bases. There is a growing consensus that a more psychosocial approach to back pain is needed, an approach which acknowledges non-physical factors influencing rehabilitation. Several studies indicate that pain-related fear is one of the most potent predictors of physical performance and is highly correlated with self-reported disability levels. [10; 198]

Ideally, for any given surgical procedure, it should be possible to identify what symptoms may be expected to persist postoperatively, what complications may arise relative to the surgical procedure, and what pain behaviour may be expected of a particular patient. In accordance with the scientific principles, such knowledge can only be achieved through well-controlled experimental and clinical studies.

### *Overall aims of the current studies*

- To introduce patient-based functional outcome evaluation into spinal fusion treatment.
- To evaluate radiological assessment of different spinal fusion procedures.
- To investigate the effect of titanium versus stainless steel pedicle screws on mechanical fixation and bone ingrowth in lumbar spinal fusion.
- To analyse the clinical and radiological outcome of different lumbar spinal fusion techniques.
- To evaluate complications and re-operation rates following different surgical procedures.
- To analyse the effect of different rehabilitation strategies for lumbar spinal fusion patients.

# Methodological considerations

The outcome of a spinal fusion derives from a complex of factors and can therefore be difficult to control in a clinical setting. In some cases it is difficult and impractical to study individual variables clinically. Animal experiments can contribute to the development of methods by which many of these variables can be controlled. However, as data from animal studies are only as relevant as the model from which it is derived, it is clear that animal experiments cannot fully replace human-based studies. The clinical studies performed in the advancement of the present thesis were approved by the Medical Ethics Committee of Aarhus County, Denmark. The Helsinki Declaration II (1975) was followed. The animal study was approved by the Danish Control Board for Animal Research. The pigs were bred for scientific purposes and treated in compliance with Danish laws for the use of experimental animals.

### *Humans*

In total, 594 patients were included in the investigation from 1979 to 1999. Each had at least 2 years of CLBP and had therefore been subjected to most of the conservative treatment modalities. They had all suffered from severe chronic low back and leg pain, static or dynamic, due to localized lumbar or lumbosacral segmental instability caused either by isthmic spondylolisthesis grades I-II, primary degeneration (no previous surgery), secondary degeneration after decompressive/discectomy surgery, or accelerating degeneration after decompressive/discectomy surgery. In practice, if clinically confirmed symptoms or signs suggested instability, and the patient showed no clear sign of spinal stenose or nerve root entrapment but did show signs of vertebral end-plate changes (Modic change)[23], then the mechanical constraints were tested by use of a brace in order to study response to pain under immobilization.

The algorithm used for the selection of spinal fusion candidates is shown in Figure 1.

### *Animals*

Previous studies of bone-implant fixation have used several different animal species. Rabbits and canines have frequently been used for evaluation of posterolateral spinal fusion, whereas goats, sheep and pigs have typically been used for cervical and lumbal interbody fusions with and without implant fixation. For the present investigation the Göttingen mini-pig was chosen as a model because of its vertebral anatomy, with its well-defined pedicles that are well-suited for pedicle screw instrumentation, and because of its potential for early growth plate-closing (<2 years). Furthermore, the mini-pig model allows for the selection of animals from the same litter, which would thereby limit interspecies variation. Our previous mini-pig studies had shown that a solid posterolateral spinal fusion could be achieved within a 3-month observation period.

## Design of studies

All the clinical studies were one-centre studies. Except for Studies I and II, the prospective study design was used. Functional outcome was gauged by means of questionnaires which were filled out by the patients independent of the surgeons and scored by an independent observer. For each patient a basic data sheet was filled out by the surgeon. All outcome and follow-up data were successively stored in the Aarhus spinal fusion database, based on SPSS-software (SPSS Inc. , Chicago, IL).

Study designs, evaluation periods, numbers of patients and the overall radiological and functional follow-ups for the 8 clinical studies included in this thesis are presented in Table 1.

Study IV was an experimental weight/stress-loaded spinal fusion model using randomly selected implant materials. All animals (mini-pigs) were sacrificed 12 weeks after operation.

In Study I [38] each patient filled out forms, which included the Dallas Pain Questionnaire [125], inquir-

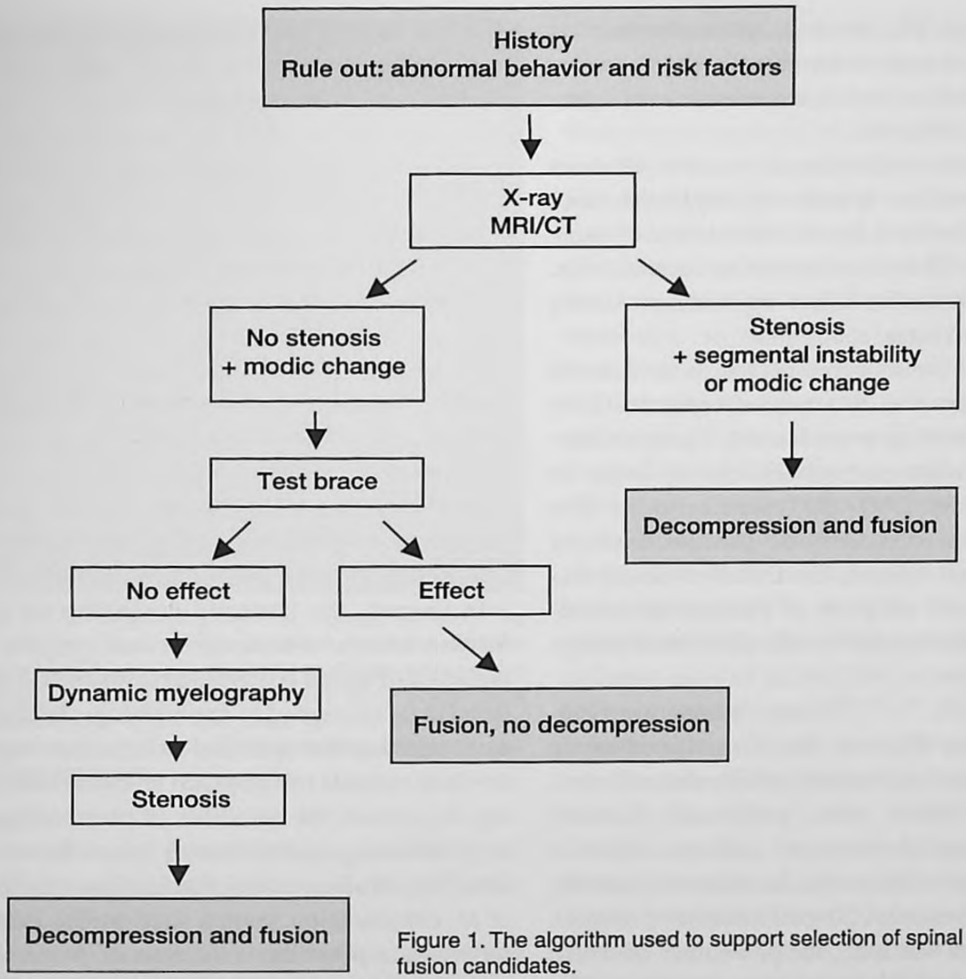


Figure 1. The algorithm used to support selection of spinal fusion candidates.

**Table 1. Clinical study design, evaluation period, number of patients included and follow-up rate**

| Study no. | Study design | Evaluation period (year) | Patients (N) | Follow-up rate (%) Radiologic | Functional |
|---|---|---|---|---|---|
| I | Retrospective follow-up | 5–13 | 120 | 98% | 80% |
| II | Retrospective follow-up | 5–13 | 50 | 98% | 82% |
| III | Prospective case/reference | 2 | 106 | 98% | 88% |
| V | Prospective randomized | 1 | 70 | 99% | |
| VI | Prospective randomized | 5 | 130 | 97% | 93% |
| VII | Prospective randomized | 5 | 130 | 97% | 93% |
| VIII | Prospective randomized | 2 | 148 | 98% | 95% |
| IX | Prospective randomized | 2 | 90 | | 89% |

ing about his/her condition before surgery and at each follow-up. The follow-ups took place between 5–13 years after surgery. The 2-year postoperative X-rays were evaluated by 2 independent observers. Case record registration sheets were filled out by independent observers. Studies I and II were retrospective follow-up studies evaluating both recall data and actual status data. The goal of these nonexperimental studies was to simulate the results of an experiment, had one been possible. The choice of study design was based on the assumption that it provided access to fast and low

cost knowledge. It is, however, undeniable that this type of study design is accompanied by a greater chance for bias and inference mistakes than prospective study designs.

Study II[35], for which each male patient filled out a questionnaire, was specifically designed to analyse the incidence and functional outcome of retrograde ejaculation as a postoperative complication. It was a retrospective follow-up study evaluating both recall and actual status data.

Study III[43] was a prospective case-referent study. The aim was to compare outcomes after primary and salvage procedures. All patients who underwent lumbar posterolateral spinal fusion in the period from 1990–1993 were included. The referent group comprised the patients receiving first time spinal fusions. The inclusion period was determined with the goals of eliminating secondary selection bias and of reaching a relatively large reference series.

Studies V–IX [34; 37; 39-41] were prospective randomized studies. Random allocation offered strong advantages over alternative assignment schemes. Power calculations were performed at study index to ensure inclusion of sufficient numbers of participants to allow the detection of clinically relevant differences. A 20- or 30-number-per-block randomisation was used, the procedures of which had been concealed in separate envelopes. The envelopes were consecutively numbered, thereby assigning a number to each patient in the study. All patients were registered in a log-book. All the studies were one-centre studies, which favoured homogenous patient selection, standardized use of surgical methods, and standardized rehabilitation schemes.

## Radiology

Determining the integrity of a fusion is not without problems. [19; 29; 56; 95; 107; 182] It is generally accepted that solid fusion cannot be confirmed radiographically until 6 to 9 months after surgery. [63; 179] While various imaging techniques have been studied and evaluated, the conventional combination of anterior-posterior and lateral X-rays, accompanied by flexion and extension bending views, is still by far the most commonly used method for evaluating the quality of a spinal fusion. Flexion-extension X-ray views seem irrelevant when instrumentation is used. It is widely understood that the only way to reliably determine the solidity of lumbar fusion is to explore it surgically. Corroborated by surgical inspection, it has been shown that two-dimensional radiographs give a reliable result of presence or absence of posterolateral arthrodesis in approximately 70% of cases. [19; 29; 107] Studies correlating radiographs with second surgical appraisals are generally, however, based on one-observer intraoperative observations. [19; 29; 107] Only one such study has incorporated multiobserver evaluation of the radiographs, and it was based on a routine radiographic assessment with no preindex calibration of the classification used by the observers. [19]

In general, the literature describing the classification criteria to be used for radiographic interpretation of spinal posterolateral fusion has serious deficiencies in regard to methodology. Information as to whether the specified fusion rates represent levels or patients (all intended levels) is often missing. At present, the reliability of plain radiography in determining posterolateral spinal fusion mass integrity remains questionable. The Christensen et al. classification system used in our studies is based on a prestudy evaluation of posterolateral spinal fusions with and without implants. [40] The strategy of this classification was to simplify the "areas of view", thereby enhancing method reliability in the evaluation of the posterolateral spinal fusion masses. Fusion was evaluated at 1- and 2-year follow-ups from plain anteroposterior and lateral radiographs. Each level and each side was judged separately (Figure 2).

Continuity of an intertransverse bony bridge was assumed when a minimum of one of the two sides was adjudged fused at that level. The classification of "fusion" indicated qualitative fusion at all intended levels, "doubtful fusion" indicated suboptimal quality at one or more levels including fusion mass hidden behind the instrumentation, and "non-union" indicated definite lack of fusion at one or more of the intended levels. If the fusion was questionable in any way, the case was not considered "fused". The classification system showed itself to be acceptably reliable and to exhibit good interobserver (mean 88%, kappa 0. 58) and excel-

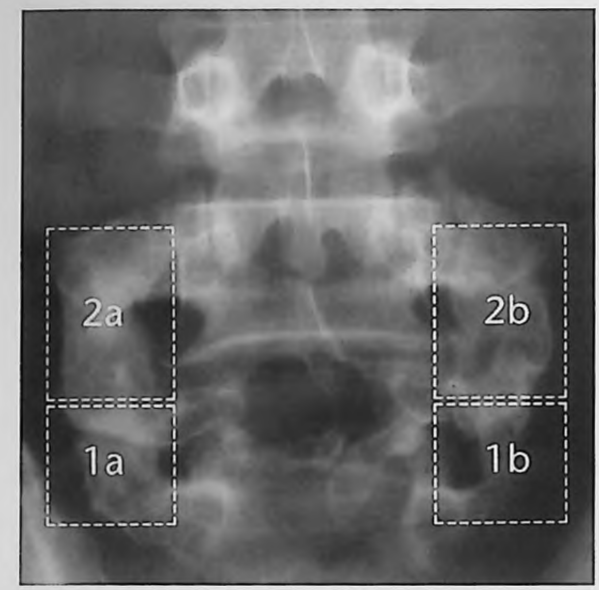


Figure 2. An antero-posterior radiograph showing the evaluation procedure used in assessment of the posterolateral spinal fusion. Each level and each side were judged separately. Continuous intertransverse bony bridge on a minimum of one of the two sides (a. or b. ) indicated a fusion at that level. "Fusion" indicated this quality of fusion at all intended levels.

lent intraobserver (mean 93%, kappa 73) agreement[40]. It accords well with the JL Fleiss[62] classification scheme.

The Christensen et al. classification system was used for evaluation of posterolateral spinal fusion in all the studies. Given the criteria for established fusion, the resultant overall mean fusion rate was 81%. This was based on an agreement of only 68% among all four observers.

Despite the question of reliability, we believe that plain radiographs are of value in daily clinical practices as well as in clinical studies. When using a classification system for fusion, periodic control of the observer's conception of "fusion" is crucial to ensuring radiograph viability.

In Study I anterior fusion was defined as the presence of a continuous trabecular bony structure between the vertebral bodies. The two independent observers who evaluated radiological outcome 2-years after surgery exhibited good interobserver agreement (94%). There were no metallic internal fixation devices to obscure the fusion mass. In Study VIII the ALIF Brantigan cage was used. The cage is made of radiolucent carbon fiber-reinforced polymer which affords improved postoperative assessment of fusion. In this study, anterior fusion was considered solid when there were no radiolucent lines between cage and endplate, and when there was a simultaneous trabecular bony structure between the vertebral bodies within and/or outside the Brantigan cages. It is clearly much more complicated to evaluate an interbody fusion when metal cages have been inserted. [181] The use of different cage designs and materials makes it almost impossible to establish a standard radiological classification system for anterior fusions.

The category "doubtful fusion" is needed to obtain good observer compliance when using a rigorous classification system. According to the classification scheme we used, the mass was occasionally not considered "fused", even when the observers had the impression that fusion could have taken place. In part, the broad fusion rate range found in the literature could be explained by different ways of scoring the cases that were classified as "doubtful fusion".

Bending-view X-rays and CT-scans were carried out in cases of doubtful fusion, but they were of limited value.

All the studies required radiological follow-up after a minimum of 1 year, and evaluation of the X-rays by a minimum of 2 independent observers.

Plain radiographs are clearly not the perfect media for analysis of spinal fusion. Until new and better diagnostic methods emerge that are applicable in daily clinical practice, radiographs will be the golden standard for fusion mass evaluation. CT scans might make more precise estimates of spinal fusion possible, but CT-scanning of a spine containing pedicle screw implants subjects a patient to higher radiation dosage to overcome artefact interference. New CT-scanners which reduce the artefact problem have recently been introduced, but they still operate with a relatively high radiation dose. Furthermore, the CT-scan with 3D reconstruction has to our knowledge never been inter- and intraobserver validated when used to evaluate posterolateral spinal fusion mass or anterior interbody fusion.

## Functional outcome

The large number of assessment techniques

reported in the literature complicates assessment of the clinical results of spinal surgery. [52] Howe and Frymoyer [99] used 14 different, published outcome assessment measures for a group of over 200 patients who had undergone lumbar interverbral disc excision. They found that the proportion of "successes", ranging from 60% to 97%, was significantly influenced by the outcome measurement device used. In Studies I–III and VI–VIII, functional outcome was assessed by means of the Dallas Pain Questionnaire (DPQ) [125] before surgery and either at 1 and 2 year follow-ups or 5–13 year follow-ups. The questionnaire comprises 16 questions analysing the impact of chronic low back pain on the following four functional categories: daily activity, work and leisure time activities, anxiety/depression, and social interest. Each question is answered by marking a VAS scale. The DPQ was chosen because we wanted a validated, self-rated patient questionnaire that included physical, psychological, and social variables. Because psychosocial factors are now widely recognized to have a substantial influence on patient presentation and clinical outcome, it seems incumbent on the researcher that they be taken into consideration. [200] The validity of the DPQ as an instrument for clinical assessment of a group of patients with low back pain has recently been confirmed in a comparison with 6 alternative psychometric tests (Oswestry Disability Scale[60; 71], the Million Visual Analog Scale[144], Waddell disability and Inappropriate Symptoms Scales)[201]. It has also demonstrated its reliability. [86]The Dallas Pain Questionnaire, the Million Visual Analog Scale and Oswestry Disability Scale have been strongly correlated with each other. [187] The DPQ is now widely used to assess the consequences of CLBP. [6; 35; 85; 139; 160; 193]

The Visual Analog Scale is well-established and is the most widely used numerical scale for measuring pain. [143]In contrast to many other pain measurement tools, the VAS makes it possible to compare percentage differences obtained at different points in time. [143] Another advantage of the VAS is that it is easy to administer and score. In measuring back pain the VAS is responsive enough to detect a significant clinical change and the variance of response on the VAS-scale has been found to be 18–19 units. [90] The major disadvantage of the VAS, as with many other rating scales, is that it treats pain as a unidimensional experience. Furthermore, when a patient registers pain relief on a VAS, assessment may not be free of bias (e. g. expectation of change and reliance on memory), which would reduce the validity of its measure. This could be a critical point.

When calculating the Dallas Pain Questionnaire, individual ratings are summed up in 4 categories. If just one question in a category is missing or scored inconclusively, the category will be invalidated for follow-up. Since 1987, our department has routinely used a Danish translation of the Dallas Pain Questionnaire. The Danish version is the result of the process of translation and retranslation. The original version of the Dallas Pain Questionnaire (in English) was first translated into Danish by one individual. This first Danish version was subsequently translated back into English by another translator. The original English version was thereafter compared with the Danish and its translation back to English. Minor modifications were made, and the product was the final Danish version. Study I was used as a pilot study for the final Danish version of the Dallas Pain Questionnaire, and by use of factor analysis it was found that the 16 questions were grouped into the same 4 categories (daily activity, work and leisure activity, anxiety/depression and social interest) as they were in the English version. In some studies social interest scores have indicated poor sensitivity to clinical change. "Poor sensitivity" could suggest either a fixated level of social interest or insignificant clinical change. [85; 139] Our experience is, however, that this tool works well in clinical practice, and it has shown itself to be a valid instrument for clinical assessment of low back pain. The Dallas Pain Questionnaire has been proven capable of detecting changes in the above mentioned 4 areas following treatment for chronic low back pain. [85; 125; 139]

In studies VI–IX back and leg pain were assessed by means of the Low Back Pain Rating Scale (LBPR)[135], by which a patient could grade pain intensity on a box-scale of 0–10, where 10 represents the worst pain. The LBPR has been developed by Manniche for the purpose of monitoring the outcome of clinical treatment of low back pain, and it has been validated. Three catego-

Table 2. The patients received a questionnaire concerning work status and employment and a questionnaire concerning their smoking habits before, around, and after the time of their spinal fusion procedure

**Regarding employment:**
Are you–
- currently working?
- currently studying?
- currently unemployed?
- still on sick leave because of back pain/other illness?
- under revalidation for another job?
- applying for pension due to back pain/other reason?
- a pensioner due to back pain/other reason?
- involved with a work injury case/patient insurance case/indemnity case/complaints case?

**Regarding tobacco consumption:**
What is your present level of tobacco consumption?
What was your tobacco consumption the first 6 months after your operation?
What was your tobacco consumption the 3 months prior to your operation?
Have you smoked earlier in your life?

Table 3. Questions concerning retrograde ejaculation after anterior interbody fusion

- Have you observed any changes in your urination pattern following your anterior lumbar procedure?

  Yes ___
  No ___
  Do not know ___
  If yes, how has it changed? _____
  _____
  How long did it last?
  Weeks ___ Months ___ Years ___

- Have you had any problems with ejaculation related to sexual activity following surgery?

  Yes ___
  No ___
  Do not know ___
  If yes, what was your problem? _____
  _____
  How long did it last?
  Weeks ___ Months ___ Years ___

ries were designed to index pain experience: low back pain at the moment, the worst low back pain within the past two weeks, and the average level of low back pain within the past two weeks. The same questions are asked regarding leg pain[135]. Pain experience as registered on this scale has proven useful. [103]

In Study IX part of the LBPR questionnaire was used to gauge the influence of pain on a patient's daily level of function and his/her psychological state within the 2 weeks preceding examination. [135] This portion was used to assess the following (e. g.): performance of tasks such as watering house-plants, setting the dinner table, putting on socks and shoes, standing bent over a wash basin, use of stairways, walking, running, cycling, driving an automobile, and bearing a bag of market supplies; emotional relationship with one's family; level of sexual activity; and possible influence of the back ailment on future plans. Score alternatives were: 'yes', 'occasionally', 'no', and 'do not know'.

To estimate the nature of a patient's work status/employment [34] and their smoking habits [6] prior to, around and subsequent to the time of their spinal fusion procedure, yet another questionnaire was employed (Table 2).

By use of this questionnaire, the patients in Study IX were also assessed in terms of their need for primary health care by enumerating the consultations sought with a physiotherapist, a general practitioner, a consultant specialist, a chiropractor, and other health-care related persons. This questionnaire was issued to each patient at different points in time. Some form of recall bias could have influenced the registration of the number of contacts made with the primary, back-related health care system. The effect of such recall bias between groups, however, was minimized in the studies where the patients were randomly allocated to different treatment modalities.

To estimate the risk of male genital dysfunction as a complication of anterior interbody fusion, yet another questionnaire was used (Table 3).

The patients were asked whether their urination pattern had changed, and the males were asked if they had any problems with ejaculation following the anterior lumbar procedure. The questionnaire has never been validated and some form of recall bias could have influenced the results. In this study, however, of the 50 male patients who received the questionnaire, 82% returned it, and 3 identified retrograde ejaculation specifically. Notwithstanding the questionnaire's status, our results show that, in general, the questionnaire was understood by the patients and that sexual dysfunction is a complication after ALIF at L5/S1-level.

## Mechanical testing

Both the initial and secondary mechanical fixations of spinal implants are important for both implant survival and spinal fusion support. Even in the case of a good clinical result, screw loosening remains a significant potential problem,[154; 166] which may result in loss of alignment or non-union. In vitro, several factors affect the stability of pedicle screws; these factors include length, outer diameter, design, material, suitability of fit in the pedicle, and bone mineral density (BMD).[27; 118; 174] Most mechanical bone-pedicle screw interface studies have been performed on the spine of human cadaver. These cadaver studies have been important in testing and optimizing new and existing screw designs. Such mechanical test data do not reflect, however, the effect of a biological systemic response (bone remodeling) to variation in mechanical loading, metal implants or to wear debris. For this information a weight/stress-loaded in vivo model is naturally required.

The aim of Study IV was to analyze the effect of Ti-alloy versus Ss-pedicle screws on mechanical fixation and bone ingrowth in a loaded mini-pig model. Mechanical testing was performed using a MTS mini Bionix 858 testing machine (MTS Corp., Minneapolis, USA). The inaccuracy of the measurement devices was less than 1%. As a prestudy, implant stiffness (N/cm) was tested in an established artificial vertebral corpectomy model (two ultrahigh-molecular-weight polyethylene blocks) by use of axial compression load.[48] The stiffness ratio of the Ti-alloy implants was determined to be 68%, as normalized to the mean stiffness of the Ss implants.

We performed a torsion test on the right-side screws and a pull-out test on the left-side screws. The specimens were thawed at room temperature, wrapped in latex to prevent cement from penetrating the bone, embedded in polymethylmethacrylate [164], and fixed into a metal holder. With the tissue block tilted to vertically orient the screw axis, the exposed end of the transpedicular screw was secured in place using two special adapters fixed to the upper load cell (Figure 3).

The torque angle, pull-out force, load cell displacement and moments were recorded directly by a Teststar II acquisition system (790-10 Testware-SX Application, MTS Corp., Minneapolis, USA). For the torsion tests, the screws were rotated 30° counter-clockwise at a speed of 0.5°/s. From the torsion tests, the maximum torque (Nmm) and angle-related stiffness (Nm/°) were calculated. For the pull-out tests, the screws were pulled out 10 mm at a rate of 0.2 mm/s. From the pull-out testing, the stiffness (N/mm), strength (N), and energy (Nmm) precipitating failure of each screw were calculated. Stiffness was determined by calculating the slope of the early, linear portion of the load-displacement curve (Figure 4). To calculate the slope, a least-squares regression was performed on the raw data. Pull-out strength was defined as the maximum load for failure, and energy precipitating failure was obtained by integrating the area under the load-displacement curve to the maximum load.

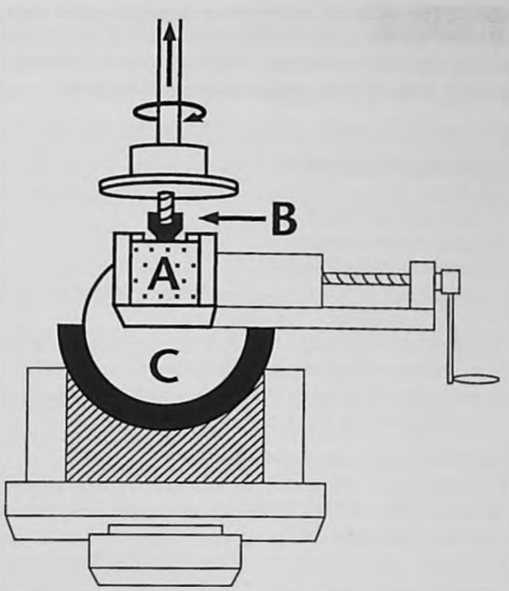


Figure 3. A schematic illustration of the mechanical test frame used for analysing torsion and pull-out strength (MTS model 858 testing machine). A=specimen embedded in polymethylmethacrylate, B=pedicle screw grip, C=universal joint.

One limitation of this study is that the surface roughness was higher for Ti-implants than for Ss-implants. The implants are, however, commercially produced and therefore available to the demands of clinical practice. An unloaded in-vivo study has shown that both polished Ti screws and glass-ball-blasted Ti screws had higher removal torques then stainless steel screws with the same surface roughness[59].


Figure 4. Torque-angulation curve obtained during torsion test. Apparent angular related stiffness was calculated from the slope of the curve (S).

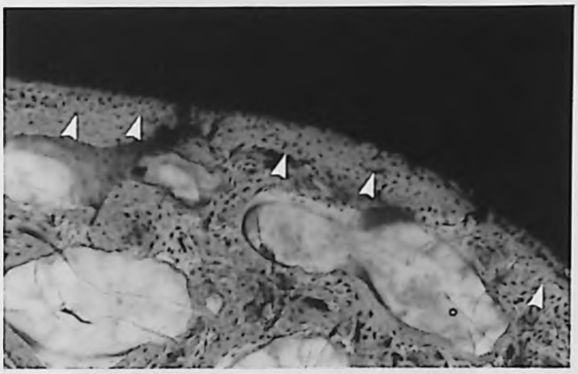

Figure 5. Histomorphometric analysis was performed using linear intercept techniques. The figure shows the direct contact between the implant (black) and bone (arrows) without an intervening fibrous tissue layer at the interface, on the light microscopic level. A typical photograph from the titanium group (original magnification × 25).

Finally, one must be cautious in extrapolating results from this animal study to the human situation due to the fact that the longitudinal load on a pig spine may be significantly different from humans. In vivo screws become loose step-by-step due to repeated loading, which is not simulated with in vitro pull-out and torsional tests, for each of which only a single, nonrecurring pull-out force and torsional load combination is used. For the present study, however, repeated loading on the bone-screw interface was applied for a 3-month observation period.

## Histomorphometric evaluation

In Study IV both the Ti-alloy (TI- 6A1-4V) and Ss-pedicle screw (316L) devices had the same geometric structure and were provided by Compact Cotrel-Dubousset Instrumentation (CCD; pedicle screw dimensions, 4 mm × 25 mm; Sofamor Danek Corp). The surface roughness of both the Ti- and Ss-implants was tested by the Danish Institute of Technology (Taastrup, Denmark). Surface roughness (R) of Ti-alloy screws was 0.90 μm (range 0.82–0.98 μm) and 0.05 μm (range 0.05–0.06 μm) for Ss-screws. Surface roughness was clearly highest for Ti implants. The implants are, however, commercially produced and therefore available to the demands of clinical practice.

Histological evaluation was accomplished by the quantifying means of histomorphometry. Specimens were first dehydrated in graded ethanol (70–99%) containing 0.4% basic Fuchsin, and thereafter embedded in PMMA. A section axis parallel to the long axis of the screw with a random rotation of the section plane around the vertical axis was chosen. Units were serially cut to obtain vertical sections, and the vertical section technique was used to obtain unbiased estimates. [159] Two sections were randomly selected and then cut, ground and polished down to a thickness of 50 μm using a micro-grinding system (EXAKT-Micro Grinding System, Norderstedt, Germany). The section surfaces were counterstained with 2% light green for 15 min and finally subjected to histomorphometry.

Blinded quantitative evaluation of bone ongrowth was performed using the linear intercept technique (magnification, × 25) and a special software program (CAST-Grid, Olympus Denmark A/S, Glostrup, Denmark). The test systems for evaluation of bone ongrowth and ingrowth were calibrated to perform approximately 200 intercepts or points-counts for each parameter per specimen.

Bone ongrowth was defined as bone in direct contact with the screw surface and was recorded as a percentage of the total screw surface (Figure 5). Fibrous tissue and bone marrow with screw contact were also measured as percentage values.

Bone ingrowth was defined as the volume of bone as a percentage of total volume. To do this, a line was drawn between each peak of the threads. Bone ingrowth volume was then determined as

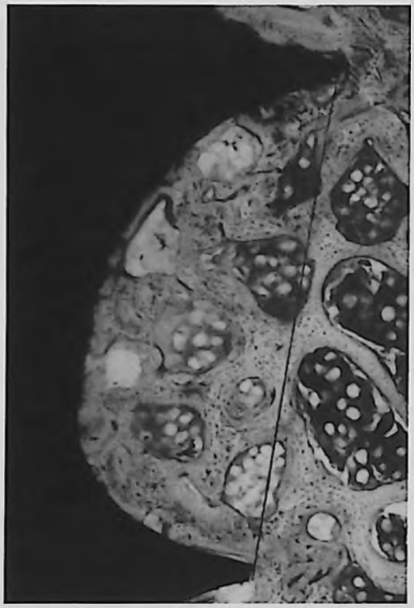

Figure 6. Histomorphometric analysis using linear intercept techniques. A line drawn between each peak of the thread. Bone volume was counted as percentage inside the threads of the screw.

the percentage appearing between screw threads as demarcated by the line (Figure 6). Both bone ingrowth and ongrowth examinations were performed in the body part according to the location of the spinal canal.

Reproducibility (intra-observer variation) calculated from double measurements on bone remodeling parameters have shown coefficient of variation values between 5 and 20%. [44; 93]

## Statistical analysis

In the clinical studies (I–III, VI–IX) statistical analyses were performed by means of standard non-parametric statistical methods. While our variables for the most part comprised ordinal data, we found that the data obtaining from the continuous variables (Visual Analogue Scale) of the DPQ were not quite normally distributed. Standard median, mean and range calculations were carried out on all data. The Mann-Whitney rank sum test and Wilcoxon matched-pairs rank sum test were applied for analysis of the functional categories of both the DPQ and LBPR scales. For calculations with more than one variable per group, either the Chi-squared Test or the Kruskal-Wallis test was used.

The reproducibility of the X-ray classification system was evaluated using Venn diagrams and kappa statistics.

Generally, the magnitudes of any confounding factors, like biases, are not regarded as dependent on the size of the study except in an experiment with randomisation. Rather, they are dependent on the magnitude of the associations from which they derive. *P-values*, on the other hand, depend on both the magnitude of the associations and the size of the study. The principle way to reduce random error and thereby increase precision in a study is, therefore, to enlarge the size of the study. The number of participants sufficient to detect a clinically relevant difference in functional outcome was calculated according to the following equation[177]:

$$N = (n_1 + n_2) = (t_{2\alpha} + t_{\beta})^2 \times 4 \times (SD^2/d^2)$$

N is the total number of participants in the two groups, and $n_1$ and $n_2$ the number of participants in each respective group. The risk of a Type I error, $t_{2\alpha}$, was set to 5% ($t_{2\alpha} = 1.96$), and the risk of a Type II error, $t_{\beta}$, was set to 10% ($t_{\beta} = 0.842$). The standard deviation (SD) of the observation i.e., the SD of the DPQ scores, was calculated from more than 600 patients in our spine database. The symbol *d* indicates the clinically relevant difference. In studies IV, VI and VII a minimum of 65 patients were randomised to each group giving a sample power of around 90%. In relation to other published randomised studies dealing with lumbar spinal fusion, the present studies are clearly among the largest on the basis of sample size. [61; 64; 70; 142; 146; 206]

In Study IX, dealing with rehabilitation after lumbar spinal fusion, the proposed sample size was 29 patients for each of 3 groups and an 80% power. This was calculated from the LBPR scale.

Many statisticians have voiced concern about the interpretation of P-values of "significance" tests when multiple comparisons are made. Is it, however, worthwhile to reduce false positives at the expense of increasing false negatives? The question cannot be answered unambiguously, as an answer would require a deeper understanding of the consequences of false positive and false negative results in the context of the given research setting. In our opinion interpretative results cannot be made more correct by adjusting the P-value or changing the criterion for "significance". Such adjusted values are also impossible to interpret

correctly, since they divulge even less about actual associations. Changing the criterion for "significance" does not actually solve the problem, it merely produces a smaller Type I error at the expense of a greater Type II error. No one has yet recommended making adjustments for multiple comparisons, when the results are reported individually in separate publications, as they have been, for example, by the Swedish Lumbar Spine Study Group [69; 70; 89; 91]. The 5% two-tailed limits of statistical significance were used in all the studies included in this thesis.

Data in Study IV were all normally distributed and analyzed by normality plots. The Student's *t*-test for unpaired observations was used to analyze the difference between titanium and stainless steel, and the Pearson correlation test was used to analyze the correlation between removal torque and pull-out strength. The results are given as mean values (SD).

All data were recorded using the SPSS statistic program (SPSS, Inc., Chicago, IL).

# Results and discussion

## Description and recommendation

Two-thirds of our patients were diagnosed as having primary (no previous surgery), secondary or accelerating degeneration after decompressive surgery. 42% of the patients included in the RCTs had had previous decompressive surgery.

28% of the patients included in our studies were diagnosed as having isthmic spondylolisthesis (Grades 1 or 2). This diagnostic proportion accords well with the related literature. [108]

With the exception of 1 patient in Study I (15 years of age), the patients had an age range of 20–67 years. Mean age was 45 years and 57% were women. They all had had severe chronic low-back pain for a minimum of 1-year, and 80% had had it for more than 2 years. The patients had therefore tried most conservative treatment modalities. Prior to surgery, indication for fusion was determined on the basis of symptomatic history, multiple clinical and neurological examinations, plain radiography, and supplementary CT-myelography and/or MRI. Patients with signs of mechanical pain but without any radiological signs of spinal stenosis underwent test-bracing for 3 weeks. The intended orthotic function of bracing was to simulate fusion stiffness in a preoperative state. In Study I we found a correlation between functional outcome and the effect of test-bracing. The test has been one of the department's routines used in patient selection for 3 decades. Since Study I, however, we have not been able to identify a significant correlation between this test and outcome. This might be explained by the choice of conservative treatment strategies for patients experiencing negative effects from test-bracing. Another study has found that orthosis is not necessarily relevant for the selection of patients for lumbar fusion. [11] Diagnostic external fixation of lumbar vertebral segments was introduced in the mid-1980's, [156] but was later found to have a low prognostic value. [157] Diagnostic external fixation has not been used in any of the present studies.

The techniques basic to a spinal fusion procedure are stabilization, realignment, and the foraminal opening procedure. Spinal fusion might be needed for stabilizing dynamic or unstable forms of spinal stenosis which may accompany "degenerative spondylolisthesis" or "degenerative scoliosis". Using decompression alone in such unstable cases may temporarily relieve a set of neural symptoms, but most often it results in a progressive deformity of the spinal column with an increase in low-back pain and neural symptoms. [92] An account of the algorithm we use and recommend in the selection of candidates for a spinal fusion procedure is seen in Figure 1.

Further improvement in the results might be achieved through better patient selection and identification of patients with predictably poor outcomes. Psychological, social, physical factors and labour-related factors were all assigned predictive values, as they have been in other studies. [30; 54; 55; 75; 82; 88; 105; 173; 186; 193; 202] In accordance with previously published studies [72; 80], we found that patients with ongoing litigation for work injury, patient insurance or other indemnity were at high risk for an inferior functional outcome (Figure 7).

There was also an indication that candidates for revision surgery are likely to have experienced poor social support (Study III). This might be explained by the prolonged duration of symptoms and work disability. [67; 200]

These factors alone do not constitute a satisfactory explanation for all of the operated patients who end up suffering from ongoing back disorders that reduce their quality of life and work ability. Furthermore, it does not explain why 8–21% end up having a radiologically confirmed non-union. [34; 37] It seems therefore crucial to also focus on and identify biological factors of influence on the outcome. An understanding of these factors might facilitate the identification of patients with inferior fusion capacity and ideally improve the selection process of candidates for spinal fusion surgery. These important factors can be classified as either local or systemic (Table 4).

The mechanical stability of the spinal segment to be fused has been shown to affect the success rate

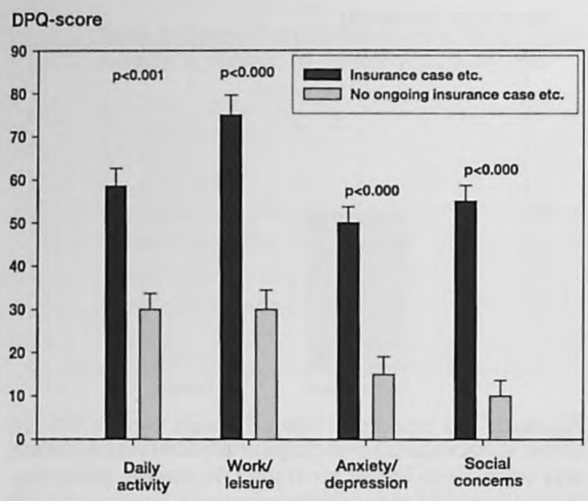


Figure 7. Dallas Pain Questionnaire scores 5 years after posterolateral spinal fusion for patients with and without involvement in a work injury case, patient insurance case, indemnity case or complaints case. Mean values and standard error of the mean for the categories daily activity, work-leisure activities, anxiety-depression and social function. High scores indicate poor condition (NS = not significant).

of fusion. [28; 106; 140] Therefore, the eminent question remains that of how the surgeon is to choose the most appropriate fusion procedure for the individual patient when spinal fusion is indicated. A discussion of this question will be presented in a subsequent section.

The development of new techniques for exploring mechanisms in cellular and molecular biology prompted the development of an improved understanding of the lumbar spinal fusion process. Emphasis has been on the type and quality of bone graft,[5; 24; 31; 45; 205] bone graft substitutes,[13; 20; 45; 138] growth factors and gene-therapies. [20; 46; 47; 94; 124]

Sufficiency of the quantity of bone graft is an essential technical detail for successful spinal fusion. [123] [110] If the amount of autogenous bone available is less than 24 g per fusion segment, we would recommend use of additional bone graft material. [123] The impact of different preoperative handling techniques of the autogenous bone graft has also been studied. It is recommended that cancellous bone graft be either harvested within close range of the reimplantation, or if not, stored in saline. [122] There is evidence that graft-derived cells from fresh bone-graft contribute to all states of the fusion mass remodelling. [79] Again

Table 4. Local and systemic factors affecting bone graft healing

| |
|---|
| **Local factors** |
| Mechanical |
| Stability |
| Loading |
| Biologic |
| Soft tissue bed blood supply |
| Recipient site preparation |
| Bone graft material (quantity and quality) |
| Technique of the grafting procedure |
| **Systemic factors** |
| Smoking |
| Osteoporosis |
| Nutrition |
| Drugs |
| Hormones |

an understanding of these factors might facilitate the identification of patients with inferior fusion capacity and ideally improve the selection process of candidates for spinal fusion surgery. The capacity of the individual patient to sustain biological osteoblast proliferation, which can to be used as a predictor for successful lumbar spinal fusion, has been analyzed. [7; 42; 121] For the present, however, these metabolic activity parameters have not been shown to be of value for patient selection.

Smoking has been widely discussed as a contributing factor in reduced capacity for successful spinal fusion outcome. [1; 6; 127; 176] The cause is thought to be a negative effect of nicotine on early revascularization of bone graft [50], probably exerted by down-regulated gene transcription of fibroblast growth factor, basic vascular endothelial growth factor, some bone morphogenetic proteins, [188] and cytokines known to be important in relation to angiogenesis and osteoblast function. [87; 188] Our own studies have shown smoking to have a negative effect on fusion and overall patient satisfaction, but we have no measurable influence on the functional outcome as assessed by DPQ. [6] We routinely inform the patients of the negative effect of smoking on the fusion process and the benefits of cessation.

## Implant material

The development of posterior spinal fixation devices has focused on intrapedicular systems with

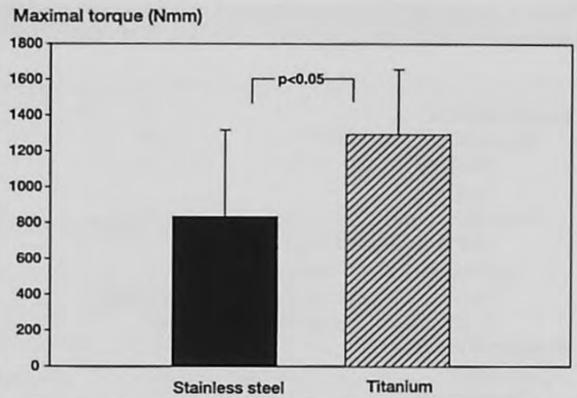


Figure 8. Comparison of maximal torque values shows a higher mean value for Ti screws than for Ss screws. Student's t-test for unpaired observations was used. Values are mean and error bars represent standard deviation.

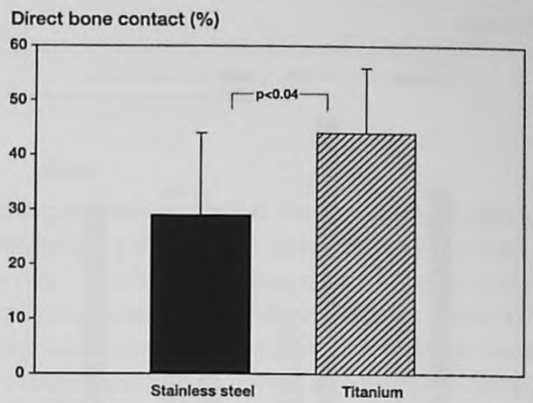


Figure 9. The amount of bone in direct contact with the screw surface, as a percentage of the total screw surface, was significantly higher for Ti than Ss screws. Student's t-test for unpaired observations was used. Values are mean and error bars represent standard deviation.

constrained screw-rod connection. Various systems have been introduced during recent years, but the biomechanical principle is basically the same. The overall stiffness of the implant depends, however, not only on the rod-screw interface but also on the bone-screw interface. [49; 77; 97]

Compared to stainless steel, the advantages of titanium-alloy implants are claimed to include a more "physiological" modulus of elasticity, lower density, and improved biocompatibility and MRI compatibility. [113; 128; 158; 164; 172; 178; 184] The modulus of elasticity is an important physical property of the materials as it indicates the flexibility/rigidity of a component before permanent deformation occurs. The elastic modulus is 16.5 GPa for cortical bone, 105 GPa for Ti-6A1-4V alloy, and 193 GPa for 316 stainless steel. [165] In a weight/stress loaded in-vivo model we analysed the effects of Ti-alloy versus Ss pedicle screws on mechanical fixation and bone ingrowth in a loaded mini-pig model (Study IV)[36]. Through torsional testing we found that although the screws had the same geometrical structure, the maximum removal torque exerted on the screw was significantly higher for Ti than for Ss (Figure 8).

Our study showed that screws from both groups had direct bone contact with the surface, but Ti screws had significantly more bone binding than the Ss (Figure 9). Titanium has become the material of choice for most spinal implants.

Our first clinical studies, including pedicle screw instrumentation were begun in 1992. At that time implants were generally made of Stainless steel. In Studies III and V–VII, we used the Stainless steel Cotrel-Dubousset (CD) instrumentation, but in Study VIII, initiated in 1996, the titanium Cotrel-Dubousset (CDI) instrumentation was employed.

## Surgical methods and complications

An anterior lumbar interbody fusion and its results were first described in 1932, and since then many reports on the outcome and complications associated with the technique have been published. [35; 38; 82; 84; 111; 162; 168; 180; 183; 196; 207] The anterior retroperitoneal approach for anterior interbody fusion was introduced at our institution in the early 70's and remained the treatment of choice for spondylolisthesis and lumbar instability until the late 80's. About the beginning of the 90's, however, this surgical procedure became unpopular. Some surgeons have since avoided using the anterior approach, but recently developed implants such as cages and disc replacements now argue for its utility.

The variability of outcomes of different spinal fusion procedures constitutes a central interest in our studies. In our studies, we used autologous bone graft harvested from the iliac crest, while others have used allograft femoral rings and stuffed them with autologous cancellous bone. [196] The anterior retroperitoneal approach and the iliac graft as described by Thomasen[189] were used in our Study I. In this study the outcome of 120

**Table 5. Dallas Pain Questionnaire (DPQ) score, expressed as median (range), 5–13 years following surgery in relation to radiological outcome**

| | Daily activity | Work / Leisure | Anxiety/ Depression | Social concerns |
|---|---|---|---|---|
| Complete union (n=45) | 26 (0–85) | 30 (0–100) | 10 (0–95) | 10 (0–90) |
| Incomplete union (n=22) | 24 (0–82) | 30 (0–85) | 10 (0–75) | 10 (0–90) |
| Complete + incomplete union (n=67) | 26 (0–85) | 30 (0–100) | 10 (0–95) | 10 (0–90) |
| Missing union (n=24) | 62 (9–100) | 85 (5–100) | 37 (0–100) | 33 (0–100) |
| P-value | <0. 005 | <0. 007 | <0. 002 | <0. 01 |

patients operated on during the period 1979–1987 was evaluated.

Study I showed that solid spinal fusion and good long-term functional outcome could be expected in approximately 66% of cases. This finding accords with the literature accounting for the use of the same techniques [82; 194; 196] The treatment of patients undergoing anterior interbody fusion during the earlier part of the study (n=56) was supplemented with the use of plaster jackets for 3 months postoperatively. Those treated during the latter part of the study underwent fixation of the facet joints with transarticular titanium screws as has been introduced by Magerl. [134] The screws produced immediate stability, which is believed to have rendered rehabilitation more comfortable for the patients while enhancing spinal fusion. [83; 100; 133; 169] No severe neurological complications occurred in connection with the use of translaminar screws on the lumbar spine, which accords with other investigations employing the same technique. [100; 102; 137] In our series of operations the most serious complication was the death of 2 patients as a result of pulmonary embolism. In the 80's neither antibiotic prophylaxes nor thrombotic prophylaxes were used.

At least 6% of the men suffered permanent retrograde ejaculation, [35] a result well-documented in the literature. [18; 141; 191] Study I showed a clear, long-term positive relationship between radiological results and self-reported symptoms (Table 5).

Supplementary pedicle screw fixation in posterolateral lumbar spinal fusion has been claimed to provide several advantages compared to posterolateral spinal fusion alone. One claimed advantage is that instrumentation provides immediate stability, which may improve fusion rate while it readily permits mobilisation without a brace. [78; 195; 206; 208] A secondary advantage has been claimed to be that instrumentation improves the likelihood of a re-establishment of normal lordosis. [120] In our experience, however, restoration of lordosis is not improved by use of posterolateral spinal fusion either with (mean 40° [range 7–74°]) or without instrumentation (mean 40° [range 7–82°]). [37; 116] An issue related to the re-establishment of lordosis is the occurrence of degenerative changes above the level of fusion, which has been reported for many years. [9; 58; 126; 129; 152; 163; 199; 204] The reasons for adjacent segment degeneration are not yet fully understood and various causes have received speculative interest. Factors that have been cited as contributing to adjacent segment degeneration include advanced patient age, female gender, the use of rigid instrumentation and faulty sagittal alignment. [119] Retrolisthesis has also been found to occur frequently at both the adjacent level [119] and the second cephalad segment level above the fused lumbar. [161]

Using controlled study designs, Zdeblick [206] and Fischgrund et al. [61]have been able to detect higher fusion rates by use of pedicle screw instrumentation. The higher fusion rate found by Fischgrund et al. did not, however, influence clinical outcome, which was similar for both the instrumented and the non-instrumented groups. Furthermore, neither the study by Möller and Hedelund [146] nor that by Fritzell et al. (Swedish Lumbar Spine Study) [69] found any significant correlation between radiographically verified fusion and patient overall rating of the results for pain and disability. To date, no randomized study has been able to demonstrate a superior correction of spinal alignment by the use of pedicle screw instrumentation, and no study has

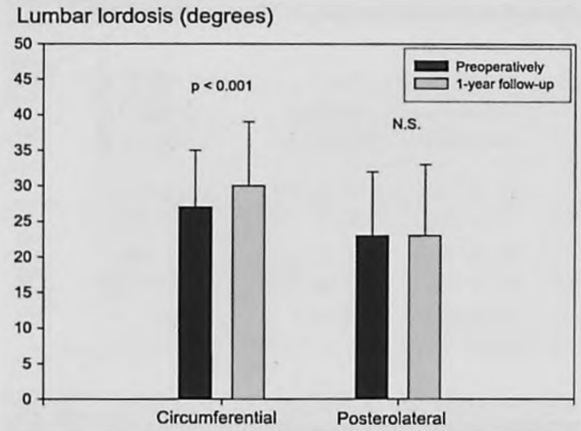


Figure 10. Segmental lordosis analyzed using cobb-angle measurement from upper fusion level to S1, preoperatively and at follow-up.

Table 6. List of perioperative complications accompanying the circumferential and posterolateral procedures

| | |
|---|---|
| Circumferential fusion (2%) | |
| Vascular injuries | 4 |
| Nerve root injuries | 3 |
| Hematoma | 1 |
| Deep infection | 1 |
| 4 urinary tract infections | 4 |
| Posterolateral fusion with instrumentation (1%) | |
| Nerve root injury | 1 |
| Dura lesion | 1 |
| Hematomas | 2 |
| Superficial infection | 1 |
| Urinary tract infections | 3 |
| Posterolateral fusion without instrumentation (1%) | |
| Superficial infection | 1 |
| Urinary tract infections | 3 |
| Deep infection | 1 |

documented the influence of sagittal alignment on functional outcome following lumbar spinal fusion procedures.

In our own studies, fusion rates following primary lumbar spinal fusion and posterolateral lumbar spinal fusion as a salvage procedure were without significant difference (72%–76%) (Study III). [43] Neither did the supplementary pedicle screw fixation have any significant affect on fusion rates in comparison with posterolateral fusion without instrumentation (Study VII). [34] Moreover, the application of pedicle screw instrumentation had unfavourable effects on operation time, peroperative blood loss, and reoperation rate. Nine patients had their implants removed. In 2 cases removal was the consequence of misplaced screws, and in 7 cases due to low back and/or leg pain. (Study VII) However, only 3 of the 7 patients improved after implant removal and then only to moderate extents. All 7 patients were informed before reoperation that major improvement deriving from implant removal was not a certainty.

There is no doubt that pedicle screw fixation of the lumbar spine is a technically challenging procedure. A most serious complication that can arise from an inappropriate placement of the pedicle screws is that of neurological injury. The incidence of malplaced screws varies from 0% to more than 30%, with a general figure of 2–5% for clinically significant malplacement. [12; 25; 26; 57; 98; 195] Our own studies affirm that malplacement of pedicle screws can indeed be a serious complication.

It has also been claimed that circumferential lumbar spinal fusion provides several advantages compared to posterolateral spinal fusion alone. [12; 25; 76; 112; 117; 120; 148] One of the claimed advantages of combined anterior and posterior stabilisation is that it provides a more complete stability, which in turn can improve fusion rates[3]. Our results (Study VIII) support this claim inasmuch as 92% of the patients with circumferential fusion were classified as experiencing union of the posterolateral fusion mass, which was significantly higher than that for the posterolateral group. [37] 82% of the patients had a radiologically verified anterior inter-corporal union. In the remaining 18%, bony growth into the cage from both vertebral endplates could be identified, and as no subsidence or gliding could be seen on plain radiograph, the anterior columns were considered stable. Long-term radiological follow-ups are needed, however, to confirm that there is indeed stability. Importantly, our studies demonstrate that the circumferential surgical procedure is to be recommended in order to restore or maintain lordosis over long term (Figure 10). As could be expected, circumferential fusion involved increased surgical trauma, as it almost doubled the mean operation time. The number of perioperative complications was higher in the circumferential group (Table 6).

There were 4 (5%) vascular injuries, 2 of which were minor and treated within minutes. In 1 case the assistance of a vascular surgeon was required. While such complications are by nature serious,

all 4 patients recovered quickly and ended up with good radiological and functional outcomes. A comparable level of vascular injuries resulted also under the Swedish Lumbar Spine Study: 2 patients (3. 5%). [68] In light of these results we would recommend that spinal surgeons possess the ability to confidently perform basic vascular surgery before performing anterior surgical procedures or to alternatively be assisted by a vascular surgeon. A total of 4 (3%) patients showed postoperative signs of nerve-root compression due to pedicle screw malplacement. Three patients developed permanent sequelae despite removal of instrumentation and decompression of affected nerve roots. Accounting for the significant difference in reoperation rates, 6 patients in the posterolateral group required refusion due to pseudarthrosis, and 7 patients in the same group required implant removal due to low back and/or leg pain (Study VIII).

Generally, the outcome of spinal fusion is largely dependent on many perioperative factors such as type and amount of graft material [4; 16; 21; 123; 153], peroperative bone storage techniques [122], and preparation of the soft tissue bed[22]. Furthermore, performance of the right operation at the wrong level or an inadequate operation at the right level is possible and obviously diminishes the number of successful outcomes. In our studies, surgery was performed on all patients at preoperatively planned levels. In Study VI, a surprisingly high number of patients (15%) showed fusion at unintended fusion levels, and 2/3 of these were patients who underwent posterolateral spinal fusion with instrumentation (Figure 11). [41] This could be explained by neglect in terms of partially dissect the erector spinae muscles of the bony elements of the adjacent segments in order to make room for insertion of supplemental pedicle screw instrumentation. Another possible explanation is that dissection was made at a wrong level. Such eventuality can be detected by fluoroscopy at the time of applying instrumentation, however, graphically marking the desired level prior to skin and fascia incision would be advisable, as it would serve as an aid in accessing the right level. Care must be exercised to minimize trauma to the soft tissue of the neighboring segments, and the technique used in the placement of the bone graft requires correspondingly careful attention.

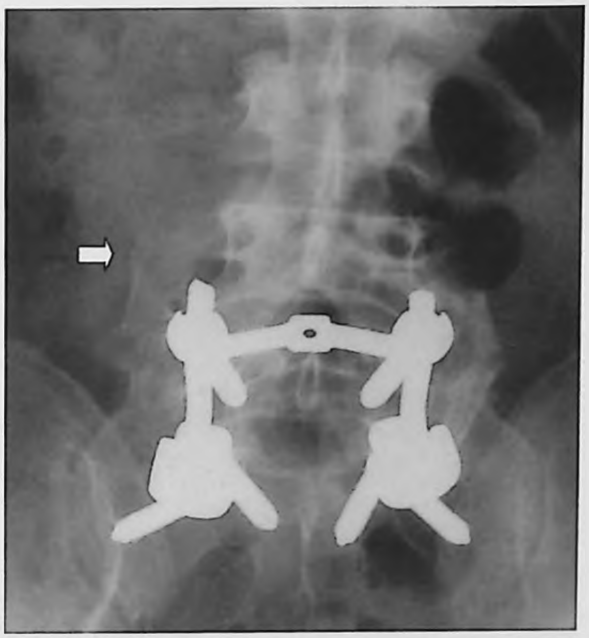

Figure 11. Anterior-posterior radiograph taken at the one-year follow-up showing a non-intended posterolateral fusion (arrows) adjacent to an intended posterolateral fusion with pedicle screw instrumentation.

In Study VI, fusion at an unintended level had no influence on functional outcome as registered at 5-year follow-up by the DPQ. It would seem that a patient whose fusion occurs at an unintended level can also, given that fusion is solid at the intended level, experience reduced pain and good functional outcome. We still believe, however, that fusion at an unintended level should be regarded as a complication, and we maintain that such can be averted by careful attention to preincision marking, careful dissection, and use of fluoroscopy.

## Functional outcome

Our findings are based on recordings of pain, function and disability by 2 validated questionnaires: DPQ and LBPR. Treatment results as evaluated by DPQ under both a retrospective (Studies I–II) and a prospective study design (Studies III, VI–VIII) showed significant overall long-term (2–13 years) improvement for around 70% of patients who had undergone lumbar spinal fusion procedure. Before surgery the patients had significantly higher functional disability scores (daily activities and work/leisure) than psychosocial disability scores

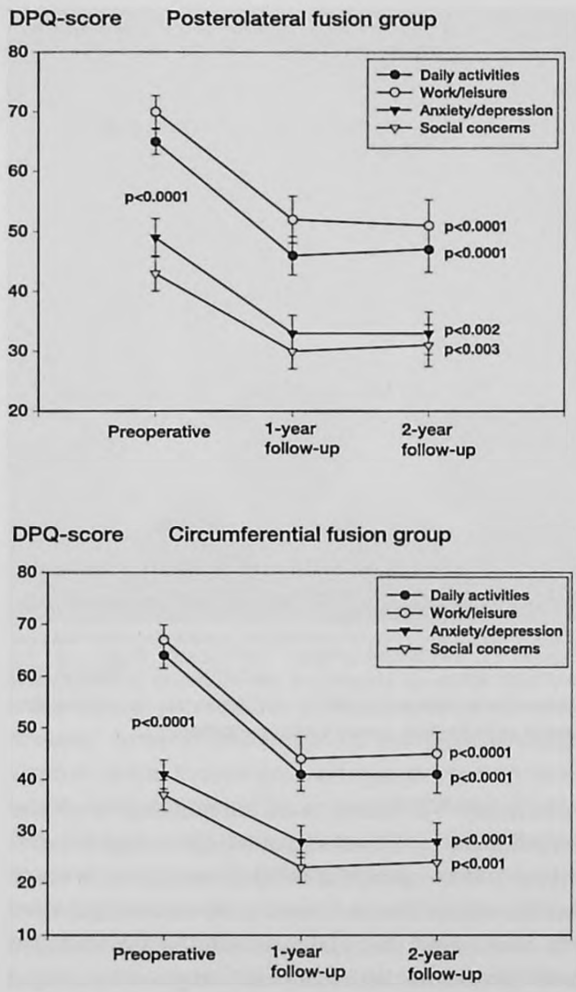


Figure 12. Dallas Pain Questionnaire scores before and 1 and 2 years after posterolateral spinal fusion and circumferential fusion. The lines represent mean values, and bars represent standard error of the means in the DPQ categories daily activity, work-leisure activities, anxiety-depression and social function. High scores indicate poor condition.

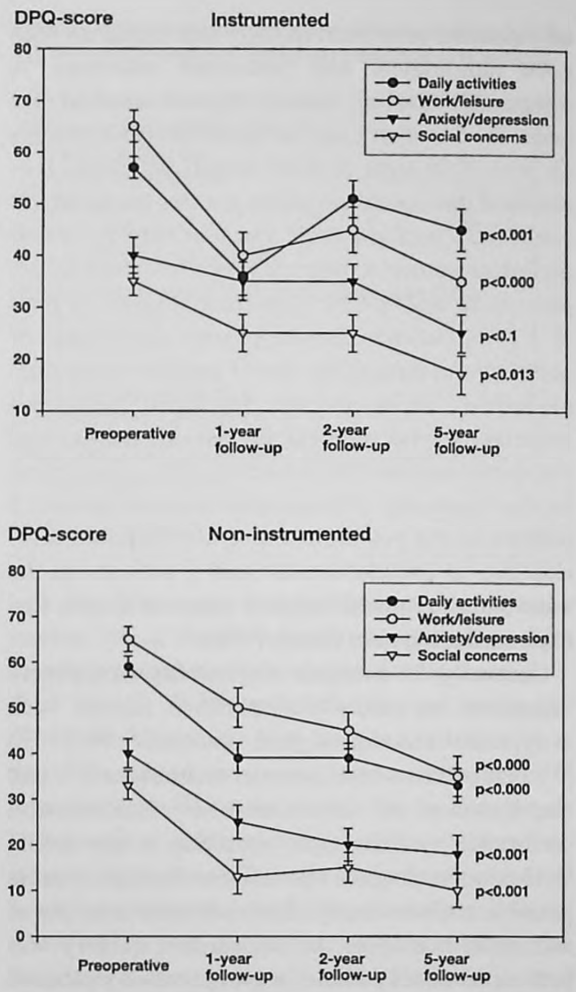


Figure 13. Dallas Pain Questionnaire scores before and 1. , 2. and 5 years after posterolateral spinal fusion with and without instrumentation. The lines represent mean values, and bars represent standard error of the means in the DPQ categories daily activity, work-leisure activities, anxiety-depression and social function. High scores indicate poor condition.

(anxiety and social interest) (Figure 12). A highly significant improvement over preoperative status was found in all the 4 DPQ categories at follow-up (I,III,VI-VIII). Highly significant improvement emerged under both a posterolateral spinal fusion with or without pedicle screw instrumentation (Figure 13) and the combined anterior-posterior approach (Figure 12). These results are supported by 2 recent RCT's dealing with the question of conservative versus operative treatment of patients with low back pain; Moller and Hedlund (isthmic spondylolisthesis) [147], and Fritzell et al (low back pain). [69] Both studies showed significant functional outcome for spinal fusion in situ compared with a more or less organised exercise program.

Factors correlating with poor functional outcome after anterior lumbar interbody fusion (Study I) were previous spinal surgery, poor patient response to preoperative test bracing, age above 45 years, and tobacco smoking. We analysed functional outcome as it followed posterolateral lumbar spinal fusion with CD pedicle screw fixation in order to compare primary and salvage procedures. There were no significant differences between the two study groups in the categories of daily activity, work/leisure activity and anxiety/depression

Table 7. Relative improvement in DPQ-scores from before surgery to the 1- and 2-year follow-ups in the salvage and referent groups. Values are median (range) n

| | Daily activity | Work / Leisure | Anxiety | Social concerns |
|---|---|---|---|---|
| Before – 1-year follow-up: | | | | |
| Salvage group | 23 (-27; 68) 33 | 18 (-30; 95) 32 | 15 (-65; 75) 32 | 15 (-35; 60) 32 |
| Referent group | 18 (-27; 67) 65 | 20 (-55; 75) 61 | 13 (-55; 85) 60 | 10 (-45; 70) 62 |
| Before – 2-year follow-up: | | | | |
| Salvage group | 14 (-18; 68) 34 | 15 (-25; 95) 35 | 13 (-45; 80) 35 | 8 (-60; 55) 34 |
| Referent group | 18 (-63; 62) 57 | 20 (-50; 85) 56 | 10 (-60; 95) 57 | 10 (-30; 70) 57 |
| | | | | $P < 0.05$ |

DPQ score difference in 4 functional categories. The table shows the DPQ scores before surgery minus the scores at the 1- and 2-year follow-ups in the salvage and referent groups. High scores indicate significant improvement. The Mann-Whitney rank sum test and the 5% significance level were used.

(Table 7). Concerning social functioning, however, significantly poorer outcome was found for the salvage group. These results indicate a need for social support following surgical revision.

Within the last 10 years pedicle screw support as a conjunct to posterolateral spinal fusion has been tested in 8 randomized controlled trials (RCT). [28; 61; 64; 70; 142; 146; 190; 206] The follow-ups in all the studies were to be completed in ≤ 2 years. None of the prospective randomized studies by Fischgrund et al. [61], Thomsen et al. [190], Moller et al. [146] and Fritzell[70] were able to show any advantage at 2-year follow-up with respect to functional outcome when supplemental pedicle screw instrumentation was employed. However, it is important to note that for both methods (with and without instrumentation) there was significant improvement in functional outcome at the 2-year follow-up in all 4 of these studies. Our long-term study (Study VII) supports previously published results that show significant improvement in overall functional outcome by the use of a posterolateral spinal fusion procedure without pedicle screw instrumentation while showing no further improvement in functional outcome with pedicle screws (Figure 14). It also showed that results at 2-year follow-up are strongly predictive of long-term results. This agrees with the findings of both Rompe et al. [171] and Greenough et al. [81]

Only one study has compared circumferential fusion with other surgical procedures in a RCT setting,[70] but the circumferential groups had been combined with both ALIF and PLIF groups, which made the real comparison invalid. No difference was found in functional outcome when comparing posterolateral fusion with and without instrumentation. In our Study VIII which compared circumferential (ALIF) with instrumented posterolateral fusion, the overall results showed no significant difference between the two groups as evaluated by the DPQ (Figure 15) and LBPR questionnaires (Table 8). It was notable, however, that the patients with circumferential fusion tended to have better scores in all 4 DPQ categories. At 1-year follow-up, patients with circumferential fusion had significantly less leg pain compared to patients with a posterolateral fusion, but at 2-year follow-up these differences were no longer significant.

## Diagnosis

Our studies found that patients with secondary degeneration had significantly higher pain scores, as registered by the DPQ and LBPR scales, at both index and follow-up assessment in comparison with the patients with isthmic spondylolisthesis and primary degeneration (Figure 16).

We found, however, that patients with spondylolisthesis grades I and II were best served by not applying instrumentation as a support for posterolateral fusion. For these patients the posterolateral fusion without instrumentation seemed to be the best alternative as it resulted in near painlessness (Figure 17 and Table 9).

Moller et al's [146] study supports these findings as their pain index was lower for non-instrumented than it was for instrumented patients with a grade

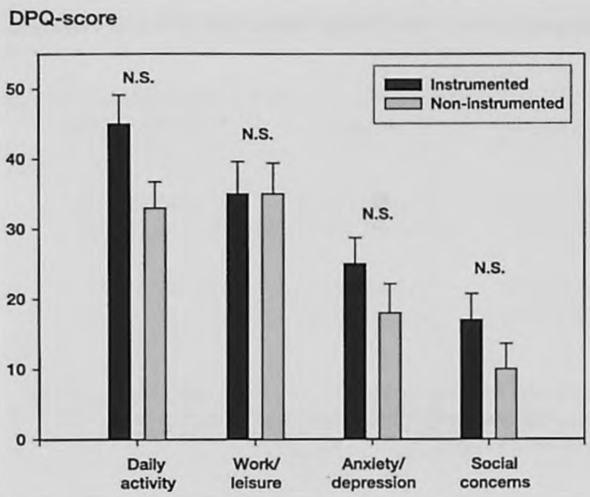


Figure 14. Dallas Pain Questionnaire scores for all patients 5 years after posterolateral spinal fusion with and without instrumentation (mean values, bars represent standard error of the means) for the categories daily activity, work-leisure activities, anxiety-depression and social function. High scores indicate poor condition (NS = not significant).

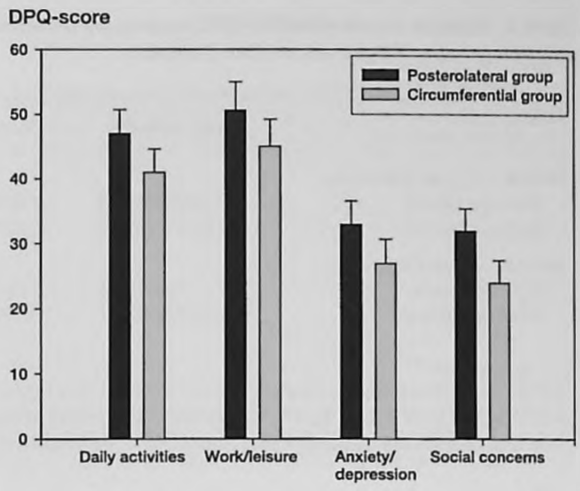


Figure 15. Dallas Pain Questionnaire scores for all patients 2 years after posterolateral spinal fusion and circumferential fusion (mean values, bars represent standard error of the means) for the categories daily activity, work-leisure activities, anxiety-depression and social function. High scores indicate poor condition. There were no significant differences between groups.

**Table 8. Low Back Pain Rating scale preoperatively and at the 1-year and 2-year follow-ups for both the posterolateral fusion group and circumferential fusion group**

| | Preoperatively | 1-year follow-up | 2-year follow-up |
|---|---|---|---|
| Back pain right now | | | |
| Posterolateral | 7 (0–10) | 5 (0–10) | 3 (0–10) |
| Circumferential | 7 (1–10) | 3 (0–10) | 3 (0–9) |
| The worst back pain within the last 14 days | | | |
| Posterolateral | 8 (0–10) | 8 (0–10) | 8 (1–10) |
| Circumferential | 8 (0–10) | 6 (0–10) | 6 (0–10) |
| The mean back pain within the last 14 days | | | |
| Posterolateral | 7 (2–10) | 5 (0–10) | 5 (1–10) |
| Circumferential | 7 (1–10) | 3 (0–10) | 3 (0–10) |
| Leg pain right now | | | |
| Posterolateral | 5 (0–10) | 3 (0–10) | 2 (0–10) |
| Circumferential | 5 (0–10) | 1 (0–10) | 2 (0–10) |
| | | P = 0. 06 | |
| The worst leg pain within the last 14 days | | | |
| Posterolateral | 8 (0–10) | 5. 5 (0–10) | 4 (0–10) |
| Circumferential | 8 (0–10) | 3. 5 (0–10) | 5 (0–10) |
| | | P = 0. 04 | |
| The mean leg pain within the last 14 days | | | |
| Posterolateral | 5 (0–10) | 4 (0–10) | 3 (0–10) |
| Circumferential | 6 (0–10) | 2 (0–10) | 2. 5 (0–10) |
| | | P = 0. 03 | |

Note: Values are median (range). High scores indicate great pain. The Mann-Whitney rank sum test and 5% significance level were used.

II slip. In our study spondylolisthesis patients developed no general leg-pain problems at 5-years postoperatively. By contrast, patients diagnosed as having primary degeneration, who were thereafter randomly allocated to instrumented fusion, showed significant improvement in work and leisure activities on the DPQ and in all 6 questions of the LBPR in comparison with patients allocated to non-instrumented fusion (Study VII).

Furthermore, judging from the DPQ scores of those with primary degeneration, patients who underwent circumferential fusion procedure seemed to indicate greater improvement compared with those undergoing the posterolateral spinal fusion procedure (Figure 18).

The significance of our results might be questioned when viewed from the standpoint of what is generally understood by the concept of "instability". While the term "instability" implies a greater movability, a reduction of movability is also generally accepted to be an effect of disc degeneration. [73; 74] Despite the work of Schultz[175] who demonstrated that pain can be more related to disc pressure and posture than it is to movements, an era in which back pain is thought of as being due to "instability" for which fusion became regarded as a viable solution, was initiated. Our results, however,

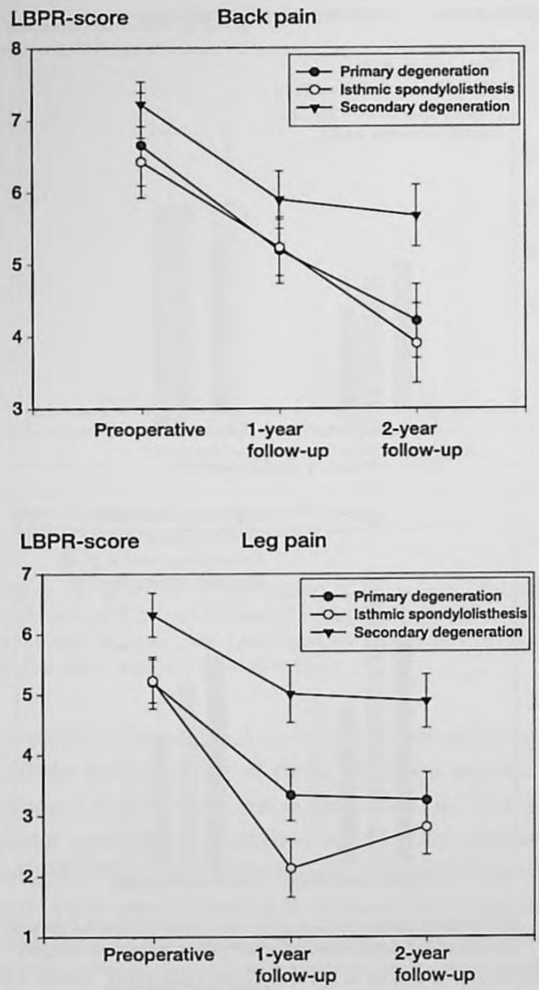


Figure 16. Low Back Pain Rating scale scores preoperatively and at 1- and 2-year follow-ups for mean back pain and mean leg pain in relation to diagnosed isthmic spondylolisthesis, primary degeneration (no previous surgery) and secondary degeneration after decompressive surgery or accelerating degeneration after decompressive surgery. Illustrated by results from Study VIII. There was significant improvement in back and leg pain for all 3 diagnostic categories. High scores indicate poor conditions.

which indicate that patients with degeneration can benefit from some form of major stabilisation, would seem to corroborate the hypothesis of Mulholland and Sengupta[150]: a degenerated disc generates pain at points of abnormal load transmission. Their study underlines the idea that occasions of pain associated with cases of degeneration would be load-related rather than movement-related as suggested by the idea that pain is due to "instability". Both posterior pedicle screw instrumentation and circumferential fusion may to some degree

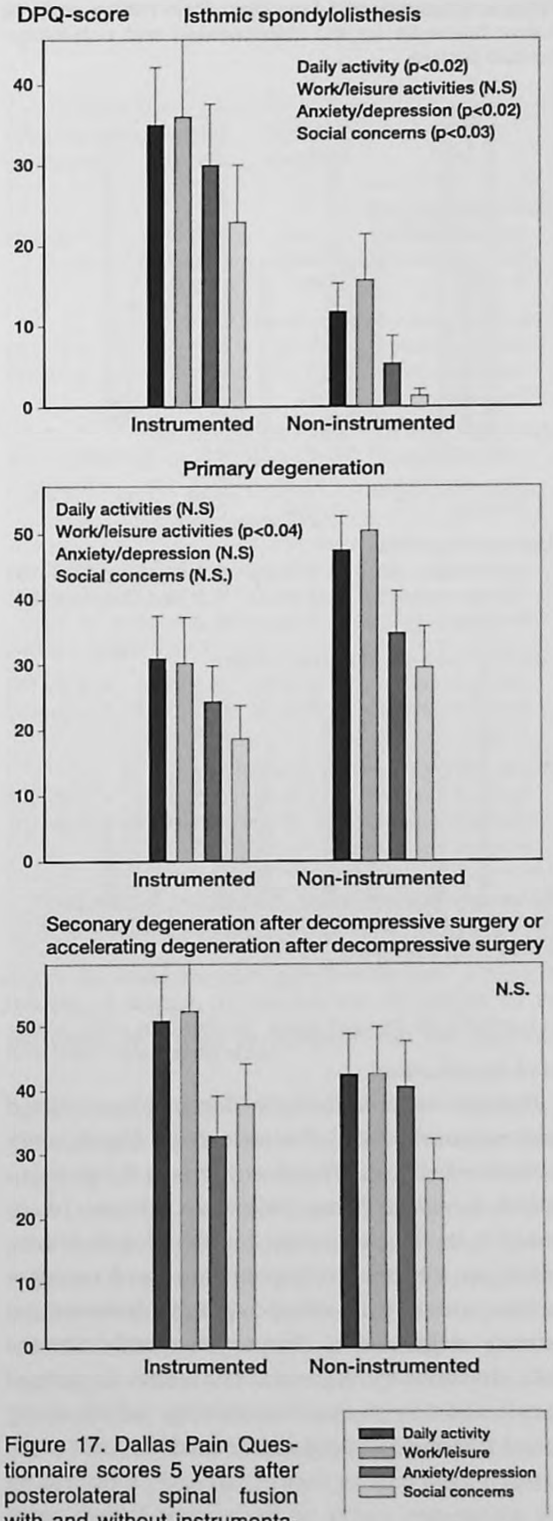


Figure 17. Dallas Pain Questionnaire scores 5 years after posterolateral spinal fusion with and without instrumentation in relation to diagnosed isthmic spondylolisthesis, primary degeneration (no previous surgery) and secondary degeneration after decompressive surgery or accelerating degeneration after decompressive surgery. High scores indicate poor condition.

**Table 9. Diagnosis and Low Back Pain Rating scale at 5-year follow-up for the instrumented and non-instrumented patient**

| | Spondyl-olisthesis | Primary degen. | Secondary degen. |
|---|---|---|---|
| Back pain right now | | | |
| Instrumentation | 3 (0–8) | 3 (0–8) | 5. 5 (0–10) |
| Non-instrument. | 1 (0–6) | 5 (0–10) | 4 (0–9) |
| P-value | 0. 07 | 0. 008 | |
| The worst back within the last 14 days | | | |
| Instrumentation | 5 (0–10) | 4 (0–10) | 6. 5 (1–10) |
| Non-instrument. | 1 (0–6) | 8 (1–10) | 6. 5 (0–10) |
| P-value | 0. 01 | 0. 01 | |
| The mean back pain within the last 14 days | | | |
| Instrumentation | 3. 5 (0–8) | 2. 5 (0–8) | 5. 5 (1–10) |
| Non-instrument. | 1 (0–3) | 6 (1–10) | 4 (0–10) |
| P-value | 0. 004 | 0. 007 | |
| Leg pain right now | | | |
| Instrumentation | 0. 5 (0–9) | 0. 5 (0–9) | 4. 5 (0–10) |
| Non-instrument. | 0. 0 (0–4) | 3. 5 (0–10) | 3. 0 (0–9) |
| P-value | | 0. 09 | |
| The worst leg within the last 14 days | | | |
| Instrumentation | 1. 5 (0–9) | 0. 5 (0–9) | 4. 5 (0–10) |
| Non-instrument. | 1. 0 (0–6) | 5. 0 (0–10) | 5. 0 (0–10) |
| P-value | | 0. 02 | |
| The mean leg pain within the last 14 days | | | |
| Instrumentation | 1. 0 (0–8) | 0. 5 (0–9) | 4. 5 (0–10) |
| Non-instrument. | 1. 0 (0–3) | 4. 5 (0–10) | 4. 0 (0–10) |
| P-value | | 0. 02 | |

Values are median (range). High scores indicate great pain. The Mann-Whitney rank sum test and 5% significance level were used.

preclude the development of points of abnormal load transmission.

Patients with secondary degeneration treated with circumferential fusion scored significantly better on social interest than those in the posterolateral group at 2-year follow-up. Patients diagnosed as having secondary degeneration, however, ended up with relatively poor functional outcome in comparison with isthmic spondylolisthesis and primary degeneration. From functional outcome data of secondary degenerations alone, no general conclusion about the favourability of choosing spinal fusion procedure can be made.

## Rehabilitation

The explicit goal of Study IX was to compare the effects of 3 different, postoperative rehabilitation

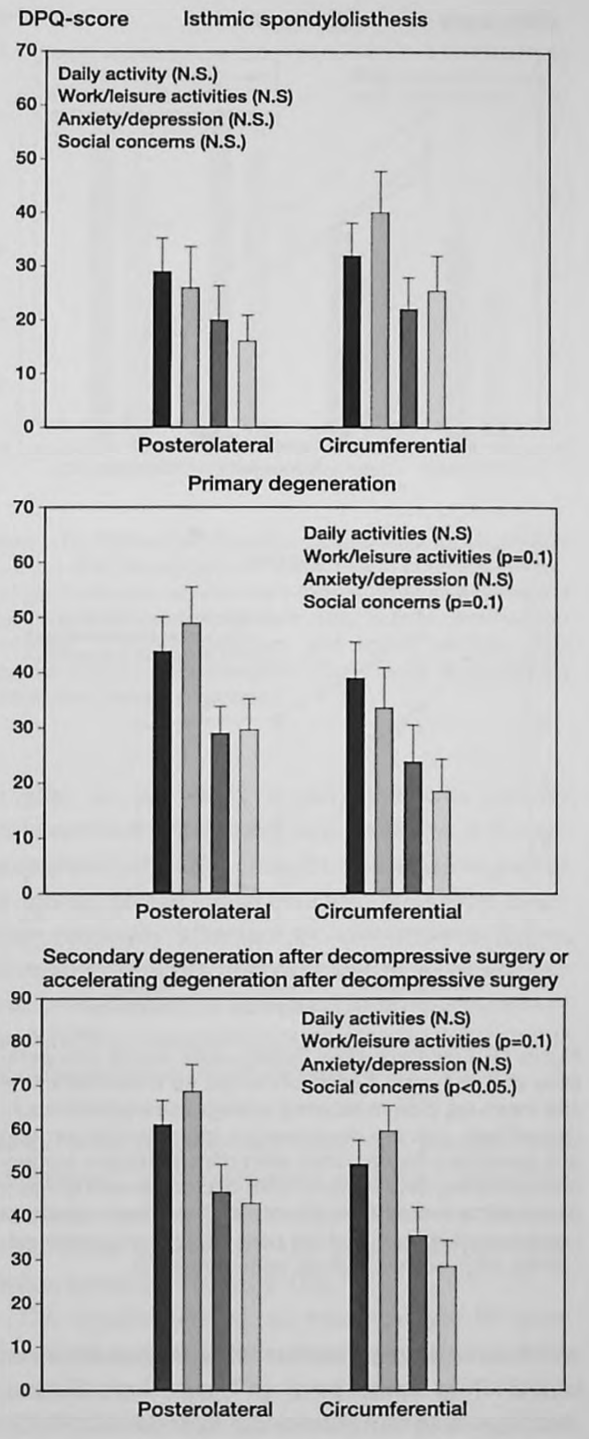


Figure 18. Dallas Pain Questionnaire scores 2 years after posterolateral spinal fusion and circumferential fusion in relation to diagnosed isthmic spondylolisthesis, primary degeneration (no previous surgery) and secondary degeneration after decompressive surgery or accelerating degeneration after decompressive surgery. High scores indicate poor condition.

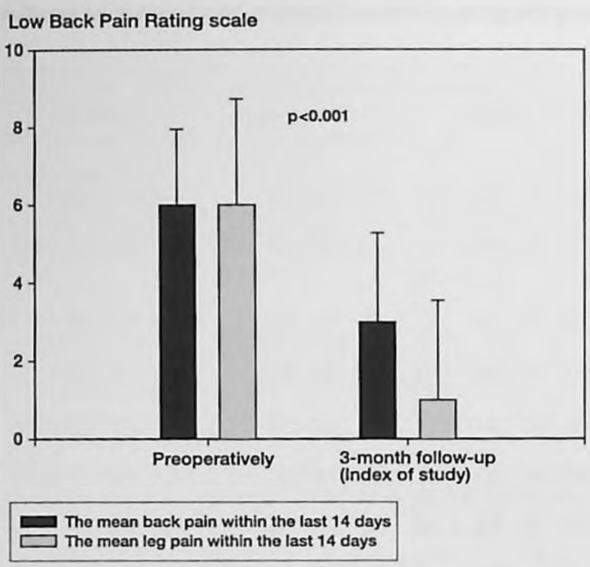


Figure 19. Low Back Pain Rating scale scores preoperatively and at 3-month follow-up (index) for mean back pain and mean leg pain. The bars represent standard deviation. High scores indicate poor condition.

programs (Video, Back-café and Training) on pain and the performance of daily activities and occupational tasks after lumbar spinal fusion. [39] *Video group* participants watched a video of exercises designed for home training and were subsequently and only once provided instruction regarding their use. The *Back-café group* was provided the same program as the Video group, but it was supplemented with arranged meetings with other fusion-operated patients and a physiotherapist (3 meetings over an 8-week period) where coffee and snacks were served. The *Training group* was provided physical therapy training twice weekly for 8 weeks. Both the back and leg pains of all patients in our study improved very significantly within the first 3 months postoperatively as analyzed by the LBPR scale (Figure 19).

While this indicated that the surgery itself resulted in substantial pain relief within the first 3-months, any extenuating factors accounting for pain reduction remained difficult to identify. In this interest it is notable that at 2-year follow-up a tendency towards better back pain scores was observed in the Café group compared to the Video and Training groups. Regarding leg pain, which was a parameter increasing regularly over time, the Training group scored significantly higher pain intensity than the 2 other groups at 2-year follow-

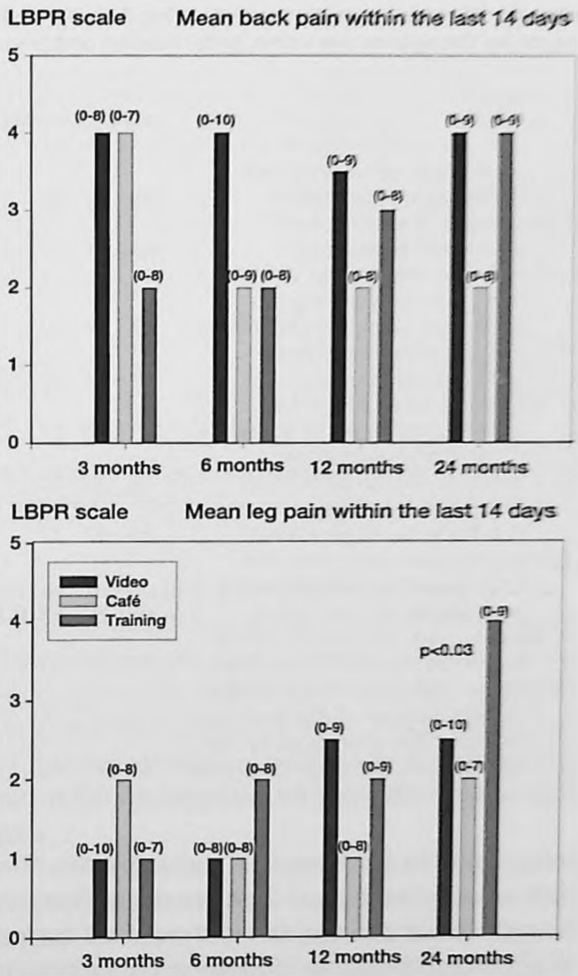


Figure 20. Mean low back pain and leg pain at index (3 months), 6 months, 12 months and 24 months for the video-, café- and training group patients as analyzed by Low Back Pain Rating scale.

up (Figure 20). The Café group was the only group that enjoyed relatively low leg pain scores at both index and 2-year follow-up. This indicates that the social network or inter-patient relationship created during the Café group sessions might have influenced pain copability. Another possibility is, however, that the patients from the different rehabilitation groups had learned or at least employed different home-training strategies. By 2-year follow-up 74% of the patients had adopted some form of home training, and 36% in the Video group and 25% in the 2 other groups were training more than 2 times weekly. When comparing the time used on each training session, it was clear that the Café and Training groups trained significantly longer than the Video group. The Video and Café groups received in principle the same training

**Table 10. Physical capacity for daily living 3, 6, 12, and 24 months postoperative. Numbers represent % of positive response. Categories are video, café, training and p-value**

| | Index (3 months) | | | | 6 months | | | | 12 months | | | | 24 months | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. Can you sleep at night without interfering low back pain? | 69 | 83 | 80 | | 77 | 76 | 84 | | 65 | 78 | 80 | | 59 | 74 | 65 | |
| 2. Can you do your daily work without low back pain? | 24 | 17 | 27 | | 22 | 41 | 36 | | 32 | 59 | 32 | 0.07 | 21 | 58 | 26 | 0.01 |
| 3. Can you do easy doings at home such as watering the flowers or clearing the table? | 97 | 97 | 90 | | 89 | 97 | 88 | | 93 | 96 | 92 | | 93 | 100 | 87 | |
| 4. Can you put on your shoes and socks by your self? | 69 | 77 | 87 | | 89 | 90 | 100 | | 86 | 93 | 92 | | 90 | 93 | 87 | |
| 5. Will you be able to carry two full shopping bags (10 kg. in total)? | 21 | 13 | 27 | | 26 | 45 | 24 | | 43 | 63 | 28 | 0.04 | 35 | 67 | 26 | 0.01 |
| 6. Can you get up from a low armchair without difficulties? | 59 | 60 | 53 | | 52 | 72 | 60 | | 57 | 78 | 60 | | 52 | 82 | 57 | 0.01 |
| 7. Can you bend over the wash basin in order to brush your teeth? | 59 | 67 | 77 | | 59 | 75 | 88 | 0.06 | 64 | 89 | 76 | 0.1 | 66 | 82 | 61 | |
| 8. Can you climb stairs from one floor to another without resting because of low back pain? | 69 | 86 | 93 | 0.04 | 59 | 90 | 88 | 0.01 | 68 | 96 | 76 | 0.05 | 66 | 89 | 52 | 0.01 |
| 9. Can you walk 400 meters without resting because of low back pain? | 72 | 83 | 87 | | 63 | 90 | 80 | 0.05 | 68 | 93 | 80 | 0.07 | 59 | 85 | 70 | 0.09 |
| 10. Can you run 100 meters without resting because of low back pain? | – | – | – | | 15 | 21 | 28 | | 25 | 26 | 32 | | 17 | 33 | 30 | |
| 11. Can you drive a car or go by bus without feeling any low back pain? | 35 | 47 | 40 | | 30 | 48 | 44 | | 32 | 48 | 32 | 0.09 | 28 | 52 | 26 | 0.09 |

information in the form of a training video. The difference between these 2 groups might therefore be regarded as deriving from inter-patient contact or alternatively from an indeterminable variance in the disposition of the physiotherapist attending the Café meetings. It is notable that the patients in the Café group ended up managing daily functions, carrying bags, getting up from a chair and climbing stairs significantly better than the patients in both the Video and Training groups (Table 10). The ability to perform such tasks attests to an acquired superior physical capacity for daily living among the Café patients. Taking the LBPR scores into account, improved physical capacity may result from reduced pain, but it could also, as previously mentioned, be an expression of better pain coping strategy.

It is notable that only 2 patients in the Café group were on sick leave at 2-year follow-up, compared to 10 patients in the Video group and 7 patients in the Training group. Furthermore only 7 patients in the Café group compared to 14 and 15 patients respectively in the other 2 groups had lost their jobs owing to LBP. The patients from the Video group had sought significantly more consultations or treatment modalities with physiotherapists outside the hospital compared to the Café and Training groups. It is clear that the patients in the Training group had the training and support they needed from the hospital's physiotherapist within the first 8 weeks of the rehabilitation program. Within the same period, however, the Café group patients were supported by only 3 Café meetings, which included no training or physical activity. Even so, the Café group patients ended up training significantly more than the Video group.

Another interesting result was that the number of contacts with general practitioners was significantly higher for both the Video and Training groups compared to the Café group. This result probably derives from a difference in pain coping strategies and/or re-socialization of patients in the Café group. Corollary to these findings, the present study clearly indicates furthermore that a rehabilitation program with the lowest primary costs can result in greater secondary expenses, which could together constitute a decline in overall cost-effectiveness. The aim underlying the design of the Café group was low cost and high effect. For all 3 treatment groups a one and the same physiothera-

Table 11. Work and social status at the 1-year and 2-year follow-ups

| | On sick leave | Working | Fired due to LBP | Undergoing revalidation | Applied for pension | Pension assigned |
|---|---|---|---|---|---|---|
| 1-year follow-up | | | | | | |
| Video group | 46% (12/11) | 32% (8) | 54% (14) | 35% (9) | 27% (8/8) | 26% (7/4) |
| Café group | 15% (4/4) | 67% (18) | 27% (7) | 19% (5) | 4% (1/1) | 8% (2/1) |
| Training group | 46% (12/12) | 50% (12) | 50% (11) | 38% (9) | 9% (3/3) | 13% (3/2) |
| P-value | 0. 02 | 0. 04 | 0. 03 | | | |
| 2-years follow-up | | | | | | |
| Video group | 35% (10/6) | 39% (11) | 52% (15) | 25% (7) | 32% (9/9) | 36% (10/8) |
| Café group | 8% (2/2) | 64% (16) | 27% (7) | 12% (3) | 16% (4/4) | 19% (5/4) |
| Training group | 32% (7/6) | 50% (12) | 64% (14) | 23% (5) | 29% (6/6) | 27% (6/6) |
| P-value | 0. 05 | | 0. 01 | | | |

Values are percentage of those answering the questionnaire, and in brackets the actual number. Second number after the / denotes the number of patients assigning LBP as cause. $\chi^2$ – statistics.

pist was the source of information and training and the training/meetings took place in the same department.

## Work status and employability

In general the return-to-work rate was disappointing in the present studies. This could possibly be, however, explained by the fact that the patients included had had back symptoms for more than 2 year prior to surgery. Long-term sick leave is a significant risk factor, as it has been correlated with poor outcome after lumbar spinal fusion and spinal rehabilitation in general. [14; 32; 167] This factor might account for the overall low frequency (37%) of patients returning to work 2 years postoperatively. In comparison, the Swedish Spine Study had also a return-to-work rate of 37% after 2 years. [69] In our studies, working ability showed a mean of 45% at the 2-year follow-up. We believe, however, that it is difficult to use work status as a measure of treatment success due to the fact that both socioeconomic and psychological factors may influence work status. [185]

In the present studies patients who were working had significantly better functional outcome at 2-year follow-up compared to patients who were on sick leave, retired, in rehabilitation programs or unemployed. The studies indicated that choice of surgical procedure had no influence on work status. Study IX showed, however, that the choice of postoperative rehabilitation had a significant influence on patient working status/capacity (Table 11).

At 2-year follow-up only 8% of patients in the Café group were on sick leave compared to the Video group (35%) and the Training group (32%). At 2-year follow-up 52% in the Video group, 22% in the Café group and 64% in the Training group had been discharged from work due to low back pain.

Therefore, when preparing a patient for spinal surgery, it seems imperative that psychosocial aspects be taken into account and a well-planned rehabilitation program be outlined that incorporates the underlying principle of the "Back-café" concept.

## Conclusion

- **Implementation of patient-based evaluation of functional outcome** (Studies I–III, VI–IX). Patient self-reported measures should include not only those analysing the intensity of back and leg pain, but also those gauging the impact of chronic low back pain on daily activity, work and leisure time activities, anxiety/depression, and social interests. Since 1993 approximately 1400 lumbar spinal fusion patients have completed the Dallas Pain Questionnaire under prospective design studies. The Low Back Pain Rating scale was in 1996 added to the standard questionnaire packet given to spinal fusion patients. Our experience is that these tools work well in clinical practice, and they have shown

themselves to be valid instruments for clinical assessment of candidates for spinal fusion procedures.

- **Radiological assessment of different spinal procedures** (Studies I, V and VIII). It is extremely difficult to interpret radiographs of both lumbar posterolateral fusion and anterior interbody fusion. Plain radiographs are clearly not the perfect media for analysis of spinal fusion, but until new and better diagnostic methods are available in the daily clinic, radiographs will remain the golden standard for fusion mass evaluation. Therefore, such an assessment needs to be performed in conjunction with a detailed radiographic classification system. In this thesis, the classification used for the evaluation of the posterolateral spinal fusion revealed good interobserver and intraobserver agreement, both with and without instrumentation. The classification showed acceptable reliability and may be one way to improve interstudy and intrastudy correlation of radiologic outcomes after posterolateral spinal fusion. The evaluation of anterior lumbar interbody fusion is further complicated when cages are employed. The use of different cage designs and materials makes it almost impossible to establish a standard radiological classification system for anterior fusions.

- **Mechanical fixation and bone ingrowth of titanium and stainless steel** (Study IV). Mechanical binding at the bone–screw interface was significantly greater for titanium pedicle screws than it was for stainless steel. This could be explained by the fact that the titanium screws had a superior bone ongrowth. There was no correlation between screw removal torques and pull-out strength. Clinically, the use of titanium and titanium-alloy pedicle screws may be preferable in osteoporotic patients and elderly patients with decreased osteogenesis.

- **Clinical and radiological outcome of different spinal procedures** (Studies I, III, VI–VIII). The present series of studies demonstrates a significant long-term functional improvement for approximately 70% of patients who had undergone lumbar spinal fusion procedure. A solid fusion determined from radiographs ranged from 52% to 92% depending on the choice of surgical procedure. The choice of surgical procedure should be related to the underlying diagnosis, as patients with isthmic spondylolisthesis (grades I and II) are best served with a posterolateral fusion without instrumentation, and patients with disc degeneration seem to gain most from either an instrumented posterolateral fusion or circumferential fusion.

- **Complications and re-operation rates of different spinal procedures** (Studies I–III, VI–VIII). The number of perioperative complications was increased by adding pedicle screw systems to support posterolateral fusions and they were further increased by performing circumferential fusions. There was no significant association between outcome result and perioperative complications (nerve root injury, dura lesions, hematomas, infection, vascular injuries). The risk of reoperation within 2 years after the spinal fusion procedure was, however, significantly lower for those who had received circumferential fusion in comparison to posterolateral fusion with instrumentation. Furthermore, the risk of non-union was found to be significantly lower for patients who had received circumferential fusion compared to posterolateral fusion with and without instrumentation. The occurrence of sexual dysfunction and fusion on non-intended levels as complications to spinal fusion were found to be significant but without influence on the overall outcome.

- **Effect of different rehabilitation strategies** (Study IX). The patients in the Back-café group were significantly better at performing a succession of many daily tasks and had moreover less pain compared with both the Video and Training groups 2 years after lumbar spinal fusion. The Video group had significantly greater treatment demands outside the hospital system. This study demonstrates the importance of the inclusion of coping schemes and questions the role of intensive exercises in a rehabilitation program for spinal fusion patients.

## Suggestions for future studies

The results and discussion of this dissertation point up many questions that remain unanswered; what is indicated is that outcomes associated with different diagnostic categories are affiliated with the choices of surgical procedure. Furtheremore, choice of rehabilitation strategy has been found to be a major outcome factor. Future research should, therefore, focus on new surgical procedures and rehabilitation strategies.

- Controlled clinical trails evaluating new implant types, e. g. Disc Prosthesis[53; 149], the concept of soft stabilization[150], and electrical stimulation of fusion mass[2; 192].
- Controlled clinical studies evaluating new surgical techniques as ex. PLIF or TLIF approach.
- Clinical relevance of growth factors such as Bone Morphogenetic Proteins (BMP) still need to be documented in well-designed clinical studies with a sufficient number of patients included. [104; 124]
- Different bone-graft substitutes need to be evaluated in a clinical setting.
- Further improvement of the results might be achieved by further refinement of the rehabilitation strategy of Back-café meetings.
- Generally, careful cost-effective analysis should be performed prior to the introduction and proposed standardization of new treatment strategies.

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# Dansk resumé

Kroniske ryglidelser er en af de mest dominerende årsager til sygemeldinger for unge under 45 år og er en hyppig årsag til tidlig pensionering i de industrielle lande. Ryglidelser udgør derfor en væsentlig post på de sociale budgetter, og er dermed et udfordrende område for hvilket der endnu ikke er opnået konsensus for behandlingsstrategi.

Den lumbale spondylodesekirurgi til behandling af kroniske lænderyglidelser blev introduceret for mere en 70 år siden. Kun få områder inden for rygkirurgien har skabt så meget uenighed som netop den stivgørende rygkirurgi. Litteraturen præsenterer divergerende forslag til hvornår stivgørende rygkirurgi er indiceret og hvordan dette skal udføres. Rehabilitering efter lumbal spondylodesekirurgi har derimod ikke haft den store opmærksomhed i litteraturen og er måske et undervurderet aspekt for opnåelse af et godt behandlingsresultat. Det ideelle for en hver given kirurgisk procedure ville være at man kunne forudsige ikke blot mulige komplikationer, men også forventede symptomer og smerter for den enkelte patient.

Det overordnede formål med aktuelle studier er: 1) at introducere patientbaseret evaluering af det funktionelle behandlingsresultat efter spondylodesekirurgi; 2) at evaluere radiologiske vurderingsmetoder ved forskellige spondylodeseoperationsmetoder; 3) at analysere effekten af titanium versus kirurgisk stål pedikelskruer på mekanisk fiksering og knogleindvækst ved lumbal spondylodesekirurgi; 4) at analysere det kliniske og radiologiske resultat efter anvendelse af forskellige lumbale spondylodeseteknikker; 5) at evaluere komplikationer og re-operationsrater efter forskellige spondylodese procedurer; 6) at analysere effekten af forskellige rehabiliterings strategier for patienter der har fået foretaget en lumbal spondylodeseoperation.

Aktuelle afhandling består af 9 studier: 2 kliniske retrospektive studier, 1 klinisk prospektivt "case/referent" studie, 5 klinisk randomiserede prospektive studier og 1 dyreeksperimentelt studie (mini-grise). I alt 594 patienter er inkluderet i aktuelle undersøgelser, hvilket er foretaget i perioden 1979 til 1999. Patienterne havde minimum 2 års kronisk ryganamnese og havde derfor gennemgået en række konservative behandlingsregimer. De havde alle ryg og bensmerter på basis af lokaliseret isthmisk spondylolisthese grad I-II eller primær eller sekundær diskus degeneration.

*Patient-baseret funktionelt resultat:* Patient rapporterede resultater bør inkludere indflydelsen af de kroniske smerter på funktioner som daglig aktivitet, arbejds/fritids aktiviteter, ængstelse/depression, social interesse samt en registrering af ryg og bensmerternes intensitet. I perioden 1993 til 2003 har ca. 1400 lumbal spondylodesepatienter udfyldt "Dallas Pain Questionnaire" i et prospektivt studiedesign. I 1996 blev spørgeskemapakken suppleret med "the Low Back Pain Rating scale". Vores erfaring er, at disse spørgeskemaer er valide instrumenter for klinisk vurdering af spondylodesekandidater.

*Radiologisk vurdering:* Der hersker ingen tvivl om at radiologisk vurdering, af både den posterolaterale fusion og den anteriore interkorporale fusion er vanskelig. Konventionel røntgen er ikke det perfekte medie til analyse af spinal fusion, men indtil der foreligger nye og bedre diagnostiske metoder for klinisk anvendelse, må røntgen betragtes som "golden standard". Etablering af et detaljeret reproducerbart radiologisk klassifikationssystem er derfor ønskeligt. Klassifikationen anvendt i denne afhandling til vurdering af den posterolaterale spondylodese viste god interobserver og intraobserver enighed, både med og uden anvendelse af instrumentering. Anvendelsen af denne klassifikation kan være et redskab til optimering af de radiologiske interstudie og intrastudie korrelationer ved posterolateral fusion. Radiologisk vurdering af den anteriore interkorporale fusion er yderligere kompliceret når der anvendes "cages". Anvendelsen af forskellige implantat designs og materialer gør det næsten umuligt, at etablere og anvende standardiserede radiologiske klassifikationssystemer til vurdering af den anteriore dese.

*Knogle-skrue interfasen:* Den mekaniske binding mellem knogle og skrue var signifikant større

for titanium pedikelskruer sammenlignet med kirurgisk stål. Dette kunne forklares ved en større histologisk knoglebinding til titanium skruernes overflade. Der var ingen korrelation mellem skrue "removal torque" og "pull-out" styrke. Anvendelsen af titanium pedikelskruer kan anbefales til osteroporotiske patienter og patienter med nedsat osteogenese.

*Behandlingsresultater:* Aktuelle studier observerede signifikant funktionel langtidsforbedring hos ca. 70% af patienter der havde fået foretaget en lumbal spondylodese. Radiologisk heling varierede fra 52% til 92% afhængig af den valgte kirurgiske procedure. Valg af kirurgisk procedure bør relateres til diagnose, da patienter med isthmisk spondylolisthese (grad I og II) var bedst behandlet med en posterolateral fusion uden instrumentering, mens man fandt en tendens til at patienter med diskus degeneration opnåede bedst resultat ved anvendelse af instrumenteret posterolateral dese eller ved kombineret anterior-posterior dese.

*Komplikationer:* Størrelsen af den perioperative komplikationsrate steg med anvendelse af pedikelskrue systemer til støtte for den posterolaterale dese og yderligere øgning fandt sted ved anvendelse af en anterior-posterior dese. Der var ingen signifikant association mellem det endelige behandlingsresultat og perioperative komplikationer. Re-operations risikoen inden for 2 år efter en spondylodese var imidlertid signifikant lavere for patienter som fik en anterior-posterior dese sammenlignet med patienter med en posterolateral fusion med pedikelskruesystem. Endvidere, var risikoen for manglende heling signifikant lavere ved anterior-posterior dese sammenlignet med posterolateral dese med eller uden pedikelskrue instrumentering. Komplikationer i form af seksuel dysfunktion samt spondylodese på ikke tiltænkte niveauer fandtes signifikante, men uden indflydelse på det endelige behandlingsresultat.

*Rehabilitering:* Patienterne i Ryg café gruppen klarede sig signifikant bedst hvad angår en række daglige funktioner og havde færre smerter sammenlignet med Video og Træningsgruppen 2 år efter en lumbal spondylodese. Video gruppen havde signifikant flere kontakter til primær sektoren uden for hospitalssystemet. Aktuelle studie påpeger vigtigheden at "coping" programmer og stiller spørgsmål ved effekten af intensiv rygtræning til rehabilitering af spondylodese patienter.

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