A multi-perspective approach to cauda equina syndrome dedicated to sex, micturition and defecation

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Citation

Korse, N. S. (2017, June 28). *A multi-perspective approach to cauda equina syndrome dedicated to sex, micturition and defecation*. Retrieved from https://hdl.handle.net/1887/51105

Author: Korse, N.S.
Title: A multi-perspective approach to cauda equina syndrome dedicated to sex, micturition and defecation
Issue Date: 2017-06-28

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ISBN/EAN 978-94-92683-24-3

Cover design M.Q. van Leeuwen & Optima Grafische Communicatie
Lay out & printing Optima Grafische Communicatie
Financial support for printing Dutch Spine Society, ChipSoft

A multi-perspective approach to cauda equina syndrome dedicated to sex, micturition and defecation

PROEFSCHRIFT

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van Rector Magnificus prof. mr. C.J.J.M. Stolker,
volgens besluit van het College voor Promoties

te verdedigen op woensdag 28 juni
klokke 16.15 uur

door

Nina Sophia Korse
geboren te Eindhoven in 1988

Promotor
Prof. dr. W.C. Peul

Co-promotores
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Dr. H.W. Elzevier

Leden promotiecommissie
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CHAPTER 1

Introduction

INTRODUCTION

Cauda equina syndrome (CES) is a rare neurological condition which is caused by compression of several of the nerve roots of the cauda equina. In 1929, Dandy was the first in English literature to publish about CES-like complaints, describing two patients with CES which were surgically decompressed, stating that it was disc material causing CES in those cases, and not, as was suggested before, spinal tumour.[1] Mixter and Barr raised much more attention with their publication five years later in which they demonstrated the effects of surgical decompression in 19 patients with CES due to lumbar herniated disc and thus advocated timely surgical intervention in all such cases.[2]

Although CES can be instigated by any pathological process compressing the cauda equina, e.g. epidural hematoma, tumour, trauma or infection,[3] a herniated lumbar disc is the most common cause of caudal compression in literature (45%).[4] The incidence of CES in operated lumbar herniated disc patients is about 2-6%.[5] Due to the strong indication for (emergency) decompression, CES incidence is believed to be much lower in the total group of sciatica patients.

Clinically, CES is suspected by a combination of complaints, which are not necessarily all manifest at the time of presentation, and which may vary greatly per patient. The most widespread definition of CES is the one proposed by Fraser et al. after reviewing hundreds of CES articles, stating that at least one or more of the following items must be present for diagnosis: 1) bladder and/or bowel dysfunction, 2) reduced sensation in the saddle area, 3) dysfunction of sexuality, with possible neurologic deficit in the lower limb (motor/sensory loss, reflex changes).[4]

Historically, CES is considered to be a strong indication for prompt surgical intervention.[2] Thus, in supporting this conception with scientific evidence, CES research has traditionally concentrated on the effects of time between presentation and surgical decompression (time to decompression). Probably one of the most influential publications in this respect was the meta-analysis of Ahn et al. (2000), concluding a significant worse outcome in case time to decompression exceeded 48 hours.[6] It was however criticized because of methodological flaws and its stringent conclusion about the 48 hour time frame, which was believed to be too strong since figures suggested that early surgery was more beneficial than late surgery, even within the 48 hours group. Critics mentioned that the conclusion of the safety of the 48 hours time frame could lead to devaluation of the benefits of earlier surgery.[7] In any case, Ahn's publication and the reactions it provoked strengthened the indication for emergency surgery in CES more than ever.

This focus on timing has allowed for a gap in current knowledge of CES: even though micturition, defecation and/or sexual function are by definition affected in CES patients, exact data about prevalence of these problems at presentation or at follow up after surgery are seriously lacking. Although most studies about CES evaluate outcome of micturition, only several studies do so for defecation and sexual function. In addition, patient numbers of those studies are small – due to rarity of disease – and follow up rarely exceeds two years, even though outcome is thought to improve up to even several years after surgery.[8] In other medical fields, it has been shown that especially sexual dysfunction is rarely evaluated.[9,10] There are no reasons to believe that this is different for spinal care patients, even though spinal patients, not in the least CES patients – are at high risk of facing sexual dysfunction and reproductive health problems.[11]

Apart from time to decompression, other potential predictors for worse outcome in CES have been studied. However, those results are not unanimous, making it (yet) impossible to identify CES patients with high risk for adverse outcome. A differentiation may lead to more personalized postoperative care. In this light, it is worth mentioning that the predicting value of imaging characteristics in CES patients have never been studied either.

AIMS AND OUTLINE OF THIS THESIS

1) Data about problems of micturition, defecation and sexual function both at presentation and at follow up in patients with cauda equina syndrome (CES) seem to be lacking in literature, even though those functions are by definition affected in CES. The first aim of this thesis is to systematically evaluate literature about prevalence of micturition, defecation and sexual dysfunction in patients with CES due to lumbar herniated disc, both at presentation and at follow up after surgery.
2) Sexual dysfunction and fertility were proven in other medical fields to be not regularly discussed by doctors. This topic has not been studied for spinal patients. The second aim of this thesis is to evaluate the knowledge, attitude and practice of neurosurgeons with regard to discussing sexual function and fertility in spinal care, especially in patients with CES.
3) Existing studies about CES rarely evaluate outcome and predictors of defecation and sexual function next to micturition. The fact that these figures are missing, prevents the clinician from offering CES patients a realistic prognosis and makes it impossible to indicate which selective group of patients are likely to need additional (multidisciplinary) postoperative care. The third aim of this thesis is therefore to evaluate mode of presentation, outcome and predictors focussed on micturition, defecation and sexual function in a cohort of patients with CES due to lumbar herniated disc.
4) Magnetic resonance imaging (MRI) of the spinal canal is done by default in case of (suspected) CES. However, there are no studies evaluating the correlation between clinical and MRI features in CES. In addition, from a pathophysiological perspective, some features deductible from MRI, such as spinal canal size, might indicate

a higher risk for CES; again, however, this association has never been studied. The fourth aim of this thesis is twofold: 1) to evaluate the correlation between clinical and MRI features in a cohort of patients with CES due to lumbar herniated disc and 2) to compare spinal canal diameters of operated herniated disc CES patients with those of herniated disc patients without CES, operated because of sciatica.

5) Follow up of CES patients normally does not exceed two years postoperatively. Existing studies that do evaluate (very) long term outcome, are severely limited by minimal inclusion numbers and incomplete evaluation of defecation and/or sexual function. In addition, it is unknown how CES patients look back at the care they received. The fifth aim of this thesis is twofold: 1) evaluating the long term outcome (e.g. at least five years after decompressive surgery) and predictors of a cohort of patients with CES due to lumbar herniated disc focussed on micturition, defecation and sexual function and 2) evaluating the attitude of CES patients towards delivered hospital care focussed on dysfunction of micturition, defecation and sexual function.

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CHAPTER 2

Complaints of micturition, defecation and sexual function in cauda equina syndrome due to lumbar disk herniation: a systematic review

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Eur Spine J. 2013;22(5):1019-29

ABSTRACT

Purpose. Cauda equina syndrome (CES) is a rare complication of lumbar disc herniation. Although micturition, defecation and/or sexual function are by definition affected, little is known about long term outcome. Aim of this study is to review current literature on outcome of micturition, defecation and sexual function in CES due to lumbar disc herniation.

Methods. A literature search was done in Pubmed, Embase and Web of Science using a sensitive search string combination. Studies were selected by predefined selection criteria and risk of bias was assessed using a Cochrane checklist adjusted for this purpose.

Results. Fifteen studies were included. Risk of bias varied with six studies showing low risk. Mean minimal follow up time was 17.0 months (range 3-25 months). All studies evaluated micturition and reported dysfunction at follow up in 42.5% (range 13.3-90.0%). Defecation and sexual function were evaluated in eight and nine studies, respectively, and were reported to be 49.6% (range 10.5-90.0%) and 44.3% (range 10.0-76.6), respectively. Only two studies assessed sexual function in all patients at follow up.

Conclusion. This review offers an insight into the extent of micturition dysfunction, defecation dysfunction and sexual dysfunction in CES after decompressive surgery. Our findings show that dysfunction is extremely common, even at long term follow up. A condition as invalidating as CES requires proper patient information and the outcomes presented here may help in providing those data. Bias in included studies, lack of universal definitions and incomplete follow up results qualify these data as the best we momentarily have, but still subject to improvement. Since sexual dysfunction (SD) seems to be severely underreported, we recommend further research to explore the extent of this problem, as well as the use of questionnaires in future clinical (prospective) studies to accomplish a more patient-based approach to dysfunction.

INTRODUCTION

Cauda equina syndrome (CES) is an uncommon neurologic condition caused by compression of the cauda equina. The first notion of CES in English literature was taken in 1934 by Mixter and Barr.[1] They described a spectrum of neurological and urological complaints in patients with a lumbar herniated disc and attributed this to a severe compression of the cauda equina, urging for emergency decompression as opposed to a more expectative treatment in uncomplicated hernia nuclei pulposi (HNP). Although CES can be instigated by any pathological process compressing the cauda equina, the lumbar disc is the most prevalent structure: 45% of described CES cases in literature are attributed to the disc.[2] In patients operated on because of HNP, the incidence of CES is 1-10%.[3,4] Because CES is an indication for surgery in HNP, the incidence of CES among general HNP patients is probably lower.[5]

Exact definitions of CES have always been a topic of ambiguity, although most authors agree that micturition dysfunction should be present.[6-9] After reviewing more than a hundred articles, Fraser et al. stated that at least one or more of the following should be present to diagnose CES: (1) micturition and/or defecation dysfunction, (2) reduced sensation in the saddle area, and (3) sexual dysfunction (SD) with possible neurologic deficit in the lower limb (motor/sensory loss, reflex change).[2] Even though the relevance of micturition dysfunction, defecation dysfunction and sexual dysfunction is clear from this definition, little seems to be known about the long term outcome of these functions. This poses a problem for the clinician who needs to provide his or her patient with an accurate prognosis and thereby obtain true informed consent for therapy.

Solid information about long term recovery of micturition, defecation and sexual function in CES is not abundant. One factor is probably the shame that revolves around discussing problems of micturition, defecation and sexual function. Secondly, the extensive focus in literature on the timing of decompression, pushes the actual hard figures on long term outcome more to the background. For the surgeon confronted with a CES patient, however, questions do not arise around the best timing of surgery, since it is generally accepted that decompression should be done as soon as possible. Questions do arise around the long term prognosis. More specifically, the prognoses of micturition, defecation and sexual function, which are so inevitably affected in CES, need to be clarified. Individual studies at best provide the clinician with uncertain estimates based on few patients. The aim of this study is therefore to review current literature on the outcome of micturition, defecation and sexual function in CES due to HNP.

MATERIAL AND METHODS

Data searches and study selection

In January 2012, the electronic databases Pubmed, Embase and Web of Science were searched using the search strategies as shown in Figure 1.

PUBMED (149 results)
(“lumbar disk herniation” OR “lumbar disc herniation” OR “lumbar herniated disk“ OR “lumbar herniated disc“ OR “lumbar diskectomy“ OR “lumbar discectomy“ OR “lumbar disk surgery“ OR “lumbar disc surgery“ OR “lumbar disc“ OR “lumbar disk“ OR “lumbar disk prolapse“ OR “lumbar disc prolapse“ OR “prolapsed intervertebral disk“ OR “prolapsed intervertebral disc“ OR “discogenic compression“) AND (“cauda equina syndrome“ OR “cauda equina compression“ OR “cauda syndrome“ OR "cauda equina"[Majr])

WEB OF SCIENCE (155 results)
Same strategy as used in Pubmed, adjusted for this database.

EMBASE (316 results)
Same strategy as used in Pubmed, adjusted for this database.

Figure 1 Search strategy (performed 22 January 2012)

Two of the authors (NSK, WCHJ) separately screened the articles by title, abstract or by full article, when necessary, to select the studies that met the predefined selection criteria. Selection criteria were stated as followed:

- the article was published in English, Dutch, French, German or Spanish;
- the study included patients diagnosed with cauda equina syndrome due to hernia nuclei pulposi (HNP);
- the study reported the following disease characteristics: HNP diagnosed by means of MRI, CT or X contrast RSG;
- the study reported the following patient characteristics: function of micturition, function of defecation and/or sexual function at base line (e.g. pre-operative) and at follow up (e.g. post operative), with a follow up period of at least two weeks;
- the study included / evaluated a (primary) treatment, excluding reoperations;
- the study was a case study (with a minimum of 10 patients), cohort study or randomized controlled trial. Systematic reviews or meta-analysis were not included;
- the article was published fully in a peer reviewed journal.

Any discrepancy in selection between the two reviewers was resolved in open discussion. Reference screening and citation tracking were performed on the identified articles and as a final check, the meta-analyses found in the first search were studied to make sure no relevant articles were missed.

Quality assessment

The methodological quality of these studies was assessed by two independent reviewers (HWE, CLAVL), using an adjusted version of the checklist for cohort studies of the Dutch Cochrane Centre.[10] When there was no consensus about the assessment, a third reviewer (NSK) was consulted.

The items reviewed in the assessment were: definition of patient group; selection bias; definition of type of surgery (laminectomy/arcectomy); method for assessing outcome (urodynamic/grading/descriptive) and loss to follow up. A point was given for each of the following items: well-defined patient group (information was given about patients age (mean or range), and about presence/absence of saddle anesthesia, radicular complaints and micturition dysfunction at presentation), absence of selection bias and absence of attrition bias (attrition bias: loss to follow up>20%). Studies were divided into different groups by risk of bias, with the maximum of three points indicating the lowest risk of bias.

Statistical analysis

Statistical analyses were done in STATA version 11.0.[11] Mean prevalence and range of micturition, defecation and sexual function were calculated. To evaluate the effect of risk of bias and the time of follow up, as well as preoperative proportion of micturition dysfunction, defecation dysfunction and saddle hypo/anesthesia on the amount of dysfunction of micturition, defecation and sexual function at follow up, a meta-regression was performed. Risk of bias was dichotomized in low risk of bias (three points) and medium to high risk of bias (two points or one point). Follow up was dichotomized in twelve months or less and more than twelve months. Backward elimination was used by repeating the test after removing the least significant factors. A Monte-Carlo permutation test was performed to correct for multiple testing and a probability value of <0.05 was considered statistically significant.[12] Sensitivity analyses were performed for influence of shorter follow up and low risk of bias studies.

For studies that also included patients without preoperative dysfunction, we corrected postoperative prevalence of dysfunction for pre-operative prevalence of dysfunction, in order to make comparison between studies fair.

RESULTS

Characteristics of included studies and risk of bias

Through our search, 620 articles were identified, of which 527 original articles were left after removing duplicates (Figure 2). Selection procedure and subsequent citation tracking resulted in sixteen reports on fifteen different studies that met all criteria.[5,13-27] One study was reported in two publications.[19,20] Reasons to exclude articles were among others small patient numbers,[28,29] inclusion of HNP patients instead of CES patients exclusively,[30-37] inclusion of hemi CES instead of total CES,[38] no imaging done,[3,4,39-41] no evaluation of a primary treatment,[42-44] follow up of at least two weeks not guaranteed[45-49] and no adequate report on post-operative functions.[50]

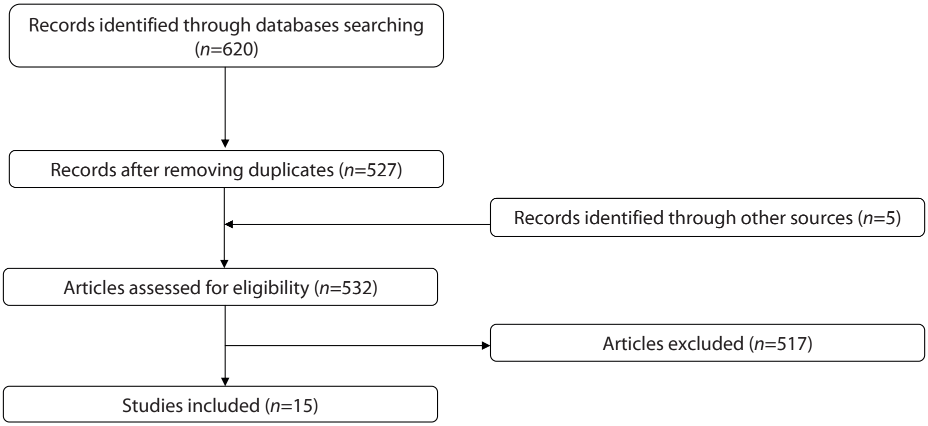

Figure 2 Flow chart of literature search

Fifteen studies, published from 1956 to 2011, were included with 464 patients (Table 1). All were retrospective studies with relatively small sample sizes (range 14 to 54) and a rather young patient population (mean 43.5 years). The mean minimal time of follow up was 17.0 months after surgery. Except for three patients who were treated conservatively,[5,17,24] all patients underwent surgery. Four authors did not give exact information about type of surgery.[5,22-24] Outcome was descriptive in eights studies,[13,14,16,17,21,22,26,27] graded in six studies[5,15,18,20,23,25] and both urodynamic and descriptive in one study.[24]

After consultation of the third reviewer, consensus about risk of bias score was achieved in all cases. Six studies were assessed to have a low risk of bias (Table 2). Two studies showed a high risk with both selection bias and either a poor-defined patient group or attrition bias. The remaining seven studies had an intermediate risk of bias.

Table 1 Characteristics of included studies

Study	n (total 464)	Mean age in years (range)	Male gender (%)	Mode of surgery (number of patients)	Minimal time of follow up in months
Jennett (1956)	25	NR (20-72)	60.0	NR	12
Spännare (1978)	30	NR (20-70)	46.7	Complete laminectomy with discectomy (17), bilateral arcectomy (7), unilateral arcectomy (6)	24
O'Laoire (1981)	29	40.6 (23-69)	58.6	Laminectomy with discectomy (29)	12
Hellström (1986)	17	43 (33-63)	58.8	NR (16), no surgery (1)	24
Kostuik (1986)	31	40 (23-61)	54.8	Wide bilateral laminectomy (30), no surgery (1)	24
Gleave (1990)	33	40.6 (23-67)	NR	Laminectomy (29), fenestration (4)	24
Shapiro (1993)	14	43 (22-67)	64.3	Laminectomy with discectomy (14)	6
Kennedy (1999)	19	55 (31-76)	63.2	Bilateral laminectomy (19)	22
Buchner (2000)	22	42 (22-67)	59.1	Bilateral hemilaminectomy (12), bilateral laminectomy (9)	12
Shapiro (2000)	44	44 (22-67)	61.4	Laminectomy with discectomy (44) of which 1 unilateral microdiscectomy approach	12
Hussain (2003)	20	45 (33-67)	50.0	Bilateral laminectomy with discectomy (20)	10
McCarthy (2007)	54	41 (24-67)	54.8	NR	25
Qureshi (2007)	33	43 (30-79)	57.6	Interlaminar discectomy (15) of which 6 microdiscectomy approach, laminectomy with discectomy (12), hemilaminectomy (6)	3
Crocker (2008)	43	NR	NR	NR	24
Dhatt (2011)	50	48 (25-85)	66.0	Wide laminectomy with discectomy (50)	12
Mean (corrected)	-	43.5	55.7	-	17.0

NR = not reported

Table 2 Risk of bias assessment

Study	Score on risk of bias scale	Well-defined patient group	Absence of selection bias	Absence of attrition bias
Jennett (1956)	***	*	*	*
Spännare (1978)	***	*	*	*
O'Laoire (1981)	***	*	*	*
Hellström (1986)	**	*	-	*
Kostuik (1986)	**	*	-	*
Gleave (1990)	***	*	*	*
Shapiro (1993)	**	-	*	*
Kennedy (1999)	**	*	-	*
Buchner (2000)	***	*	*	*
Shapiro (2000)	*	*	-	#
Hussain (2003)	**	*	*	#
McCarthy (2007)	**	*	*	-
Qureshi (2007)	**	*	*	-
Crocker (2008)	*	-	-	*
Dhatt (2011)	***	*	*	*

 # no information was provided about exact loss to follow up
NB asterisks represent the number of points gained

Clinical presentation of CES

Included studies varied in definition of CES and thus in patient characteristics at presentation (Table 3). Micturition dysfunction was regarded as an important element of CES by most authors and all articles assessed micturition at presentation. Exact definition of micturition dysfunction varied across studies. Mean prevalence of micturition dysfunction at presentation was 88.9%. Eight authors reviewed function of defecation at presentation, resulting in a prevalence of dysfunction in 47.1%. Most authors agreed that saddle anesthesia - or to a lesser extent, saddle hypoesthesia – is one of the hallmarks of the classic presentation of CES. In included studies, saddle anesthesia/hypoesthesia was found in 80.8% of patients at presentation. Pre-operative SD was only assessed in a total of three patients, in three studies.[5,16,22] Sciatica, whether unilateral or bilateral, was present in 95.5% of patients.

Table 3 Characteristics of patients at presentation

Study	Micturition dysfunction in % (*n*)	Defecation dysfunction in % (*n*)	Saddle hypo/ anesthesia in % (*n*)	Sciatica in % (*n*)	Definitions for micturition dysfunction at presentation
Jennett (1956)	92.0 (23/25)	92.0 (23/25)	96.0 (24/25)	100.0 (25/25)	"some degree of paralysis of the anal and vesical sphincters"
Spännare (1978)	100.0 (30/30)	NR	70.0 (21/30)	100.0 (30/30)	"some disorders of micturition"
O'Laoire (1981)	100.0 (29/29)	NR	51.7 (15/29)	82.8 (24/29)	"impaired sphincter function", i.e. "catheterisation required to treat urinary retention or micturition by bladder compression, either by breath-holding or by manually compressing the abdomen"
Hellström (1986)	70.6 (12/17)	NR	94.1 (16/17)	100.0 (17/17)	"retention of urine", urodynamics
Kostuik (1986)	100.0 (31/31)	54.8 (17/31)	54.8 (17/31)	100.0 (31/31)	"urinary retention"
Gleave (1990)	100.0 (33/33)	NR	72.7 (24/33)	90.1 (30/33)	"urinary retention with overflow incontinence", i.e. "inability to void, or bladder enlargement with dribbling incontinence"
Shapiro (1993)	92.9 (13/14)	NR	NR	100.0 (14/14)	"urine incontinence"
Kennedy (1999)	100.0 (19/19)	78.9 (15/19)	100.0 (19/19)	94.7 (18/19)	"symptoms of urinary dysfunction"
Buchner (2000)	100.0 (22/22)	36.4 (8/22)	68.2 (15/22)	100.0 (22/22)	"urinary retention with overflow incontinence requiring catheterization"
Shapiro (2000)	100.0 (44/44)	NR	100.0 (44/44)	100.0 (44/44)	"urologic problems of retention, incontinence or both"
Hussain (2003)	100.0 (20/20)	70.0 (14/20)	100.0 (20/20)	100 (20/20)	"lack of bladder control"
McCarthy (2007)	59.5 (25/42)	50.0 (21/42)	76.2 (32/42)	90.4 (38/42)	"urinary retention"
Qureshi (2007)	90.9 (30/33)	30.3 (10/33)	81.8 (27/33)	84.8 (28/33)	"urological dysfunction"
Crocker (2008)	48.8 (21/43)	NR	81.4 (35/43)	100.0 (43/43)	"sphincter distension"
Dhatt (2011)	100.0 (50/50)	12.0 (6/50)	90.0 (45/50)	NR	"minor or major bladder dysfunction"
Mean	88.9 (402/452)	47.1 (114/242)	80.8 (354/438)	95.5 (384/402)	-

NR = not reported

Outcome

Micturition

Outcome of micturition was evaluated in a total of 409 patients (Table 4). At an average mean minimal follow up time of 17.0 months after surgery, mean prevalence of micturition dysfunction is 42.5% (range 13.3-90.0). The corrected mean prevalence of micturition dysfunction is 45.1% (range 13.3-90.0).

Micturition dysfunction is often defined as incontinence[5,13,14,16,18,19,25] or by the presence of urologic complaints[21,22,24] or disturbances.[15,23,27] Also mentioned are the absence of a 'normal voiding pattern'[17] and 'any residual deficit that was regarded as a physical or psychological impairment'.[26] In one study, in addition to clinical assessment, extensive urodynamics tests were performed to measure micturition outcome, but the author concluded that the complaints patients gave were not always consistent with these functional outcomes.[24]

Variation of prevalence across studies is large. The highest rates of dysfunction were found by Hussain, Dhatt (both 90%) and Jennett (76.9%); these three studies all showed a low to intermediate risk of bias. Lowest prevalences were found by Kostuik and Gleave (13.3% and 21.2%, respectively) which also demonstrated a low to intermediate risk of bias at 24 months post-operative.

Defecation

Outcome of defecation function was evaluated in a total of 238 patients.[5,14-16,18,22,24,26] At an average mean minimal follow up time of 17.0 months after surgery, mean prevalence of defecation dysfunction is 49.6%. Prevalences range from 10.5% to 90.0%.[15,26] Interestingly, the studies that evaluated post-operative function of defecation are not the same studies that evaluated this function pre-operatively.

Different definitions of defecation dysfunction are used: 'a patulous anal sphincter leading usually to faecal incontinence' or 'constipation with defective anal sensation',[5] complaints of 'bowel disturbance',[15,22] 'abnormal sphincter tone',[24] being 'grossly incontinent of stool',[14] no control of flatus and being 'occasional incontinence of faeces',[18] 'poor faecal continence and no control of flatulence'[26] and a state different from 'never or rarely leaked from bowels'.[16]

Sexual function

Outcome of sexual function was reviewed in a total of 201 patients. Only two studies reviewed sexual function in every patient seen at follow up.[15,17] Seven studies recorded sexual function in a selection of included patients, more often in men than in women.[5,13,14,18,22,24,26] At an average mean minimal follow up time of 17.0 months after surgery, mean prevalence of SD is 44.3% (range 10.0-76.6).

Many different varieties of SD are mentioned, even within the same study: impotence,[5,13,14,17,22,24] decreased potency,[14,22,24] more difficult to obtain orgasm,[14] less intense orgasm,[14] anorgasmy,[14,22] decreased[17,22] or absent[14] penile/vaginal sensation, incontinence during intercourse,[14,17] dyspareunia,[22] absent bulbocavernosus reflex,[26] and the very general terms 'SD'[15] and 'abnormal intercourse'.[18]

Table 4 Outcome of micturition, defecation and sexual function at follow up

Study	Micturition dysfunction in % (*n*)	Corrected # micturition dysfunction in % (*n*)	Defecation dysfunction in % (*n*)	Corrected # defecation dysfunction in % (*n*)	Sexual dysfunction in % (*n*)
Jennett (1956)	76.9 (10/13)	idem	84.6 (11/13)	idem	25.0 (1/4)
Spännare (1978)	33.3 (10/30)	idem	NR	NR	NR
O'Laoire (1981)	37.9 (11/29)	idem	37.9 (11/29)	idem	35.3 (6/17)
Hellström (1986)	41.2 (7/17)	58.3 (7/12)	43.8 (7/16)	idem	20.0 (2/10)
Kostuik (1986)	13.3 (4/30)	idem	NR	NR	26.6 (8/30)
Gleave (1990)	21.2 (7/33)	idem	NR	NR	NR
Shapiro (1993)	28.6 (4/14)	30.8 (4/13)	NR	NR	75.0 (6/8)
Kennedy (1999)	26.3 (5/19)	idem	10.5 (2/19)	13.3 (2/15)	10.0 (1/10)
Buchner (2000)	22.7 (5/22)	idem	NR	NR	NR
Shapiro (2000)	36.4 (16/44)	idem	20.5 (9/44)	idem	76.6 (23/30)
Hussain (2003)	90.0 (18/20)	idem	NR	NR	NR
McCarthy (2007)	33.3 (14/42)	56.0 (14/25)	59.5 (25/42)	119.0 (25/21)	57.1 (24/42)
Qureshi (2007)	44.0 (11/25)	idem	32.0 (8/25)	80.0 (8/10)	NR
Crocker (2008)	33.3 (7/21)	idem	NR	NR	NR
Dhatt (2011)	90.0 (45/50)	idem	90.0 (45/50)	750.0 (45/6)	36.0 (18/50)
Mean in % (range)	42.5 (13.3-90.0)	45.1 (13.3-90.0)	49.6 (10.5-90.0)	76.6 (13.3-750.0)	44.3 (10.0-76.6)

#corrected for number of patients with dysfunction at presentation (see Table 3)
NR = not reported

Sensitivity analysis

We looked more closely at the relationship between follow up time and dysfunction (Table 5). Eight studies had a minimal follow up of twelve months or less (average 9.9 months, range 3-12) and seven studies of more than twelve months (average 23.9 months, range 22-25). In the group with follow up time 12 months or less, prevalence of micturition dysfunction was higher than in the group with follow up time more than 12 months (55.3% versus 28.1%). The difference was statistically significant (p=0.043). Regarding post-operative defecation dysfunction, we found the group with follow up time 12 months or less again showing a higher prevalence of dysfunction than the group with follow up time more than twelve months (52.2% versus 44.2%), this difference was not statistically significant. For sexual function, the difference was statistically significant (*p*=0.007), with the group of follow up time with 12 months or less showing a higher prevalence of dysfunction than the group with follow up time with more than 12 months (47.5% versus 38.0%).

Table 5 Effect of follow up time on postoperative dysfunction

	Studies with minimal follow up time ≤12 months	Studies with minimal follow up time >12 months	Adjusted# *p*-value
Postoperative micturition dysfunction in % (*n*)	55.3 (120/217)	28.1 (54/192)	0.043
Postoperative defecation dysfunction in % (*n*)	52.2 (84/161)	44.2 (34/77)	not significant
Postoperative sexual dysfunction (SD) in % (*n*)	47.5 (48/101)	38.0 (35/92)	0.007

 # adjusted for multiple testing

Reviewing the effect of bias on outcome showed that low risk of bias studies reported higher dysfunction of micturition and defecation at follow up (49.7% and 72.8%, respectively) than the intermediate and high risk of bias studies (37.1% and 34.9%, respectively) (Table 6).The difference for defecation was statistically significant (*p*=0.017). Regarding sexual function, less dysfunction was seen in the studies with low risk of bias than in the medium-high risk of bias studies (35.2% versus 49.2%), with the difference being statistically significant (*p*=0.031).

Table 6 Effect of risk of bias on postoperative dysfunction

	Low risk of bias studies (***)	Medium to high risk of bias studies (*/**)	Adjusted# *p*-value
Postoperative micturition dysfunction in % (*n*)	49.7 (88/177)	37.1 (86/232)	not significant
Postoperative defecation dysfunction in % (*n*)	72.8 (67/92)	34.9 (51/146)	0.017
Postoperative sexual dysfunction (SD) in % (*n*)	35.2 (25/71)	49.2 (64/130)	0.031

 # adjusted for multiple testing

Relation of mode of presentation and reported post-operative dysfunction

Since we would like to know if there is any correlation between pre-operative dysfunction and post-operative dysfunction, e.g., whether patients presented with defecation dysfunction show a higher prevalence of post-operative sexual dysfunction, we evaluated the effect of micturition dysfunction, defecation dysfunction and saddle hypo/anesthesia at presentation on postoperative micturition, defecation and sexual function. However, none of these symptoms were found to be statistically prognostic factors for the outcome of micturition, defecation and sexual function.

DISCUSSION

Fifteen studies reviewing outcome of micturition, defecation and sexual function in CES secondary to radiologically confirmed HNP were found, with a minimal mean follow up time of 17.0 months. All reviewed micturition dysfunction (mean prevalence 42.5%), eight studies reviewed defecation dysfunction (49.6%) and nine studies SD (44.3%). Percentages of dysfunction varied largely across studies.

In studies with a shorter follow up time, more dysfunction was reported than in studies with a longer follow up, with a statistically significant difference for micturition and sexual function (p=0.043 and p=0.007, respectively). None of the presenting symptoms analyzed were found to be statistically significant prognostic factors for postoperative micturition, defecation or sexual function.

Lower risk of bias studies reported more dysfunction of micturition and defecation (but less SD; p=0.031), with the difference in defecation dysfunction being statistically significant (p=0.017). We came across several other meta-analyses on various subjects in literature supporting our finding that studies with more risk of bias showed a greater treatment effect.[51-53]

Differences in definition and in reviewing outcome

Reviewing literature on outcome for CES involves combining data from various studies. Differences in definitions of CES pose difficulties in comparing outcome between studies. Different definitions of dysfunction across studies (e.g. Table 3) may cause bias when analyzing results together. The obvious solution to this problem is simply to create a clear and workable term for dysfunction; however, this may be more difficult than it sounds. On the one hand we have the physician, looking at dysfunction as organ failure, based on urodynamics and other physical tests, and on the other hand, there is the patient, experiencing dysfunction by complaints and problems in daily life. These two perspectives do not necessarily agree: e.g. in his study McCarthy measured reduced rectal tone in 21 patients, but found complaints of defecation in 25 patients. When a patient is suffering from defecation complaints due to CES, there is a problem of dysfunction, even without measurable dysfunction of normal rectal tone. In addition, the only study that evaluated micturition objectively by means of urodynamics, concluded that the complaints of patients were not always consistent with those tests.[24] Therefore we would like to mark complaints as dysfunction even in the absence of aberrant test results, since it is quite common to not find any dysfunction by objective tests in these cases. The use of standardized questionnaires to ask for complaints, as was done in the study of Kennedy,[26] therefore seems an elegant way to address dysfunction.

Sexual function

At an average mean minimal follow up time of 17.0 months after surgery, almost half of patients experience SD. Sexual function may not only be directly, but also indirectly affected by CES which is illustrated by the statement of some patients that incontinence of bladder or bowel often causes distress and a great sense of shame during sexual activity.[14,17]

The assessment of sexual function in included studies seems quite arbitrary and is done more often in men than in women. Perhaps inabilities to obtain or maintain erection are perceived as more basic problems than reduced sensation for women, and the participating clinicians, more often men, may find it easier to discuss sexual function with the same sex. In any case, SD seems a topic difficult to discuss for both doctor and patient. Research on this subject, e.g. in the form of questionnaires for clinicians, can provide information about the place sexual problems have in current therapy, and more specifically, ideas to make the treatment of SD more common practice.

Overall, literature evaluating sexual function after CES is scarce.[54] More is written about the effect on sexual function after HNP[31,55,56] and spinal cord injury,[57-59] some with suggestions for treatment.[60]

Overview of literature

This is the first systematic review done on the outcome of micturition, defecation and sexual function in CES. Reviews have been written about these functions separately, but none of these systematically reviewed outcomes combining these three functions. As stated before, this is partly due to traditional focus of literature on timing of decompression. Two large meta-analyses found statistically significant differences in recovery of, among others, micturition and defecation in favour of early decompression.[6,61] Smaller studies reported similar findings.[13,40,41,50] In one study, the differences were statistically significant.[14] The most recent study that was included in this review evaluated outcome after delayed decompression and stated that the high prevalences of post-operative dysfunction that were found, could possibly have been prevented by early decompression.[15] One of the included studies,[16] together with a study from 2009,[49] did not find differences between outcomes. Other authors suggest emergency surgery is more important for some cases of CES than for others.[62-65] However, no doubt arises that CES is an absolute indication for emergency decompression and surgery should be undertaken as soon as possible to obtain better recovery of functions.[34,41]

CLINICAL INTERPRETATION AND CONCLUSION

This review offers an insight into the extent of micturition dysfunction, defecation dysfunction and sexual dysfunction in CES after decompression. Since the discussion about timing of decompression has already been researched extensively in literature, instead we looked at the actual outcomes. Our findings show that dysfunction of micturition, defecation and/or sexual function is extremely common with about half of the patients affected in at least one of these domains at an average mean minimal follow up time of 17 months after surgery. So, even though CES patients get decompression as soon as possible with the aim to restore function, a lot of patients still suffer from dysfunction long after surgery, something for which ideally therapy should be provided. Since micturition, defecation and sexual function are closely related and may affect each other, we believe that already existing individual therapies are best to be combined. A condition as invalidating as CES requires good patient information and the outcomes presented in this review may help in providing those data. Bias in included studies, lack of universal definitions and incomplete follow up qualify these data as the best we momentarily have, but still subject to improvement. Since sexual dysfunction (SD) seems to be severely underreported, we recommend further research to explore the extent of this problem, as well as the use of questionnaires next to urodynamic tests in future clinical (prospective) studies to accomplish a more patient-based approach.

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Letter to the editor
In response to “Cauda equina syndrome: evaluation of clinical outcome” more insights on sexual and defecational recovery in cauda equina syndrome

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Eur Rev Med Pharmacol Sci. 2014;18(23):3547-8

Dear Editor,

With interest we have read the case study of Tamburelli et al.[1] "Cauda equina syndrome (CES): evaluation of clinical outcome". As stated by the author, studies looking at recovery of sexual and bowel function are scarce and they add to our current knowledge revealing that recovery after decompression is limited and can take years.

In 2013, we published a systematic review on the exact same subject: long term recovery of micturition, defecation and sexual function after decompression of CES.[2] Fifteen studies with a total of 464 CES patients were included.

Compared to Tamburelli, we found higher incidences of dysfunction: after 17 months, problems of micturition, defecation and sexual function were present in 43%, 50% and 44% of patients respectively. This might be because our results are based on patients' reported dysfunction instead of on objective measurements, with the exception of one of the included studies. We believe that patients' view on recovery is extremely important next to objective measurements, since, as we found in our review, objective findings do not always correlate with dysfunction in daily life.

Like Tamburelli states, lengthy follow up is essential, since functions might regain slowly, as we demonstrated for micturition and sexual function.

Tamburelli's patients did not report sexual dysfunction at presentation, but it would be interesting to know how many patients were asked *actively* about their sexual function pre-operatively. In our review, we found only 3 out of 463 patients had been asked about sexual function pre-operatively.

Tamburelli states that literature is not strict on timing of decompression, which is supported by a recent review of Chau.[3] Indeed some studies did not find statistically significant differences in outcomes,[4,5] but especially since the meta-analysis of Ahn et al.,[6] CES is regarded as an absolute indication for emergency decompression, and in order to obtain best recovery, decompression should be undertaken as soon as possible.[6-11]

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CHAPTER 3

Discussing sexual health in spinal care

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Eur Spine J. 2016;25(3):766-73

ABSTRACT

Background. The possible detrimental effects of spinal disease on sexual health are widely recognized, however, it is not known to what extent neurosurgeons discuss this topic with their patients. The aim of this study is to identify knowledge, attitude and practice patterns of neurosurgeons counselling their patients about sexual health.
Methods. All members of the Dutch Association of Neurosurgery (neurosurgeons and residents) were sent a questionnaire addressing their attitudes, knowledge and practice patterns regarding discussing sexual health.
Results. Response rate was 62% with 89 questionnaires suitable for analysis. The majority of participants (83%) were male; mean age 42.4 years. The mean experience in neurosurgical practice was 9 years. Respondents assumed that in 34% of their patients, sexual health was affected due to spinal disease. The majority of respondents (64%) stated that responsibility for discussing sexual health lies (partly) with the neurosurgeon, however, 72% indicated to (almost) never do this. The main reasons for not discussing sexual health were patients' old age (42%), lack of knowledge (38%) and lack of patients' initiative to bring up the subject (36%). Twenty-six percent indicated lack of time as a reason. There was no evidence for gender or doctor's age discordance as important barriers. Fifty percent of participants wished to gain more knowledge on discussing sexual health with patients.
Conclusion. This study shows that despite high prevalence of sexual dysfunction (SD) in spinal patients, counselling about sexual health is not often done in neurosurgical care. More training on sexual health counselling early in the residency program seems critical. By initiating the discussion, clinicians who deal with spinal patients have the potential to detect SD and to refer adequately when necessary, thereby improving overall quality of life of their patients.

INTRODUCTION

Since World War II, numerous studies were published concerning the impact of spinal cord injury on sexual health.[1-8] Recently, a study was published about the association between low back pain and sexual dysfunction (SD).[9] Not only physical constraints, but emotional distress as well as other psychological factors have the potential to change the perception of sexuality in the spinal cord injured.[10,11] Alexander et al. reported an incidence of 74% of relationship difficulties concerning sexual health after spinal cord injury in men.[12] In the last few years, new studies have emerged on sexual health in spinal cord injured women, eliciting the pathophysiology and complicated features of SD in women with spinal cord injury, and even more general in neurological disease.[13-16] Despite this emerging body of evidence of the extent of the problem of SD in spinal patients, little is known about the exact prevalence at presentation or about the recovery, even in specific patient groups such as cauda equina patients, though new studies are emerging.[17,18] Despite the problems spinal cord injured patients face to conduct their sexual activities, literature has advocated their need for sexual expression since the 1970s. Recommendations include enhanced counselling to improve quality of life after spinal cord injury.[19] However, sexual health counselling seems completely neglected by the clinician.[20] Cole found that of quadriplegics and paraplegics who he offered a counselling program for sexual health, 60% indicated that (almost) no attention was paid to their sexual condition at first presentation in the hospital, and 80-90% indicated that the hospital staff never or seldom took the initiative to discuss the topic.[21] In Alexander et al.'s study, only 22% of spinal cord injured patients received counseling.[12]

Recent research about counselling for sexual health in neurosurgical care is almost non-existent. This leads to the anomaly that despite the well-documented impact of spinal cord injury on sexual health, no proper study has been conducted among neurosurgeons to explore their counselling practices. Do neurosurgeons incorporate counselling in their clinical care, and if not, for which reasons? To what extent are neurosurgeons actually aware of the problem of sexual dysfunction in their patient population? In order to explore knowledge, attitudes and practice patterns of neurosurgeons concerning discussing sexual health, this questionnaire survey was conducted among Dutch neurosurgeons. This study is unique in its kind and therefore gives us new insights into the extent of the problem. Due to experience in the clinic, we expected both attention and concern for sexual health in neurosurgical care to be quite poor.

MATERIAL AND METHODS

Study design

In March 2013, all members of the Dutch association of Neurosurgery, which comprises of both neurosurgeons and residents in neurosurgery (total 161) were invited to fill in a questionnaire. The questionnaire was developed by the authors of this article, based on the questionnaire used by Nicolai et al.,[22] adapted for this purpose. A pilot study was performed in January 2013 among residents and neurosurgeons of the Neurosurgery department of the Leiden University Medical Centre. According to feedback and comments, the questionnaire was further adjusted which lead to a finalized version which was used for this survey (questionnaire is available upon request). The questionnaire included 34 questions inquiring about several items:

1. Demographic data of respondent;
2. Level of knowledge on sexual dysfunction (SD) and its treatment;
3. Frequency of discussing sexual health with patients;
4. Barriers for discussing sexual health with patients;
5. Responsibility of the neurosurgeon to discuss sexual health;
6. Knowledge about (possibilities for) referring patients with SD.

Various questions were asked repetitively for different groups of patients (male, female, age categories) to facilitate analysis regarding patients' sex and age. Questions were all stated referring to patients with general spine problems, unless specified otherwise. Questionnaires were accompanied by an invitation letter explaining reasons for and content of the study and sent by regular mail. A monetary incentive was used to motivate participants to reply. In case a participant did not reply, reminders were sent one month and two months after initial invitation.

Statistical analyses

Data was analyzed using SPSS Statistics 21.0 (SPSS Inc., Chicago, IL, USA). Internal consistency of the survey was analyzed using Cronbach's coefficient α. Means of numerical demographic values and answers to questions were analyzed with frequencies. Associations between categorical demographic data and numerical variables without Gaussian distribution were tested with the Mann-Whitney-U-test; for paired data (either numerical without Gaussian distribution or ordinal), Wilcoxon signed rank test was used. When paired data was nominal, analyses were done using McNemar's test. Associations between ordinal or categorical independent variables and ordinal data were calculated with Mantel-Haenszel linear-by-linear association chi-squared test (comparable to Armitage's trend); Pearson Chi-square test was used for categorical data. Comparison of paired ordinal data was done using Friedman's test, with Wilcoxon signed rank test and Bonferroni adjustment as post-hoc test. Where associations between ordinal variables and numerical data did not display Gaussian distribution, Kruskal-Wallis H test was performed, with Mann-Whitney-U-test and Bonferroni adjustment as post hoc test; for numerical demographics and numerical data without Gaussian distribution, Spearman correlation was used. Two-sided *p*-values <0.05 were considered statistically significant. Some questions with open, numerical and ordinal answers were grouped together for analyses.

RESULTS

Value of questionnaire

The scores for items regarding the frequency of neurosurgeons asking their patients about sexual health showed a very high internal consistency (α = 0.93). Internal consistency between the items regarding reasons not to inquire about sexual health was good with Cronbach's alpha 0.79.

Participants

Of the 161 eligible participants, 99 returned the survey, either after first invitation (*n*=55) or after first (*n*=26) or second (*n*=18) reminder, resulting in a total response rate of 61.5%. Eight participants used the option of returning the questionnaire empty with specification of a reason; indicated reasons were lack of experience (*n*=3), lack of interest (*n*=2), lack of time (*n*=1) and other reasons such as working with a specific group of patients not suitable for this study (*n*=1) or merely treating patients in emergency settings (*n*=1). One participant returned the questionnaire empty without specifying a reason; another returned it almost empty with too little information available for analysis. This resulted in a total of 89 questionnaires that were suitable for analysis.

Of the participants, 83.3% were male (Table 1). Mean age was 42.4 years (SD 9.6), with 71.6% of respondents being a neurosurgeon versus 28.4% being a resident. Mean experience in neurosurgical care was 9 years. Of the respondents, 42.5% indicated to have spinal surgery as his or her specific field of interest. Male respondents were significantly older than female respondents (mean age 43.6 years [SD 9.43] versus 36.3 years [SD 8.35]; *p*=0.006).

Discussing sexual health

Participants answered the question 'In how many percent of your patients with general spine problems do you think sexual function has changed because of spine problems?' with a mean of 34.4% (SD 29.7). Neurosurgeons working in neurosurgical care for a shorter time evaluated this percentage to be higher (*p*=0.026); so did younger neurosurgeons (*p*=0.025) and residents (*p*=0.023). When asked how often sexual health is

Table 1 Participant characteristics (n=89)

	n (%)
Male gender	74 (83.3)
Mean age	42.4 years (SD 9.6)
Function	
Neurosurgeon	63 (71.6)
Resident	25 (28.4)
Place of practice	
University hospital	40 (45.5)
Teaching hospital	15 (17.0)
District general hospital	3 (3.4)
University + district general hospital	23 (26.1)
University + teaching hospital	6 (6.8)
University + district general + teaching	1 (1.1)
Experience in neurosurgical practice	
< 3 years	3 (3.4)
3-5 years	11 (12.4)
6-10 years	25 (28.1)
11-15 years	15 (16.9)
>15 years	35 (39.3)
Has spinal surgery as field of interest	37 (42.5)

NB n differs because some questions were skipped

discussed with patients, 72.4% said '(almost) never', 20.7% 'in less than half of the cases', 3.4% 'in half of the cases', 2.3% 'in more than half of the cases' and 1.1% '(almost) always'. Sexual health is significantly less frequently discussed with female than with male patients (80.9% '(almost) never' versus 68.5%; p=0.003). This was not statistically significant associated with doctor's gender (p=0.860).

Whether sexual health is discussed, is highly influenced by patients' age. Patients between 20-35 years are most often being asked about sexual health (Table 2); this difference is statistically significant (p<0.0001) except between the groups 20-35 years and

Table 2 When do you discuss sexual health: influence of patients' age

Patients age (years)	Never (%)	Seldom (%)	Regularly (%)	Often (%)
<20	44.8	44.8	8.0	2.3
20-35	36.8	47.1	13.8	2.3
36-50	36.8	49.4	11.5	2.3
51-65	55.2	35.6	6.9	2.3
66-75	69	28.7	2.3	0
>75	73.5	25.3	1.1	0

36-50 years. No significant associations with gender, age or other demographic data of neurosurgeon were found.

Participants consider discussing sexual function more frequently if specific diseases are present; especially in the case of cauda equina syndrome (CES), in which 87.6% of neurosurgeons discusses sexual health (Table 3). In the specific case of CES, sexual health is significantly less often discussed if the field of interest of the respondent is spinal surgery (78.4% versus 94.0%; *p*=0.030) and if the neurosurgeon does not feel responsible to discuss sexual health (75.0% versus 94.7%; *p*=0.007). Asking CES patients about sexual health was associated with significantly more referrals to health care professionals specializing in sexual health (*p*=0.023).

Table 3 Do you discuss sexual health for these specific diseases?

Pathology	Yes (%)
Cauda equina syndrome	87.6
Paraplegia	82.0
Tumour of myelum or spine	70.8
Spinal fracture	36.4
Hernia nuclei pulposi	23.6
Degenerative disease other than HNP	11.2
Never	4.5

HNP = hernia nuclei pulposi
NB total adds up to >100% since more than one answer was possible

Reasons spontaneously mentioned by respondents to discuss sexual health were spinal dysraphias such as tethered cord (*n*=2), a HNP fully obtruding the canal (*n*=1), chronic lumbago (*n*=1), vascular diseases (*n*=1) or 'if the patient brings it up' (*n*=1). One respondent indicated to not discuss SD but to refer to the rehabilitation specialist. Sexual health is never discussed by 4.5% of respondents, regardless of disease.

Responsibility of discussing sexual health

Of respondents, 35.3% believed that the neurosurgeon is responsible for discussing sexual health; 37.5% disagrees and 27.3% don't know. The shorter the time spent in neurosurgical care, the more feelings of responsibility are present, though this association only approached statistical significance (*p*=0.051). Neurosurgeons who deemed themselves responsible discussed sexual health significantly more often (*p*=0.006). When given a list of options with more than one option possible, 64% stated that the neurosurgeon is (partly) responsible for discussing sexual health (Table 4). Almost 63% indicated that it is the patients responsibility, even though the majority of participants (81.6%) also stated that patients '(almost) never' bring up sexual health issues themselves.

Table 4 Who is responsible for discussing SD?	%
Neurosurgeon	64.0
Patient	62.9
General practitioner	57.3
Neurologist	57.3
Partner of patient	25.8
Sexologist	15.7
Nurse	7.9
Psychologist	7.9
Social worker	6.7
Other: Rehabilitation specialist	6.7
Physiotherapist	4.5
Other: Urologist	2.2
Other: Gynaecologist	1.1
Other: Spine centre team	1.1
Other: Doctors in general	1.1
Other: Depends on context/disease	6.7

NB total adds up to >100% since more than one answer was possible

To the question 'Do you mention risks on sexual health when you inform patients about surgery risks (obtaining informed consent)?", 51.7% said '(almost) never', 19.5% 'in less than half of the cases', 3.5% 'in half of the cases', 3.5% 'in more than half of the cases' and 21.8% '(almost) always'. During check up visits, 69.3% do not discuss sexual health; 6.8% does this always.

To the question 'How important is it to screen patients with general spine problems for SD?', 42.7% stated to find this 'somewhat important', 21.3% 'important' and 1.1% 'very important'. It was seen as 'unimportant' by 18% and the remaining 16.9% didn't know whether it is important. Neurosurgeons who thought screening is important, discussed sexual health significantly more often than those who found it unimportant (p=0.005).

Knowledge

The majority of respondents (52.3%) stated they have 'very little knowledge'; 10.2% said to have 'no knowledge at all' about SD and treatment options. One third of respondents said to have 'some knowledge' and 3.3% describes his/her knowledge as 'sufficient'. More knowledge was associated with more experience in neurosurgical care (p=0.046) and higher age of neurosurgeon, though the latter was just not statistically significant (p=0.052). More knowledge was not associated with higher frequency of discussing sexual health (p=0.565). To the question 'Do you wish to enhance your knowledge about discussing sexual health with your patients?' respondents were much divided as 50.6% answered 'yes' and 49.4% 'no'. Neurosurgeons below 36 years of age answered significantly more often affirmative (71.4% versus 41.7%; *p*=0.034) and so did residents (68.0% versus 42.9%; *p*=0.033).

Barriers to discuss sexual health

Respondents were asked to what extent they agreed with given reasons to not discuss sexual health. Reasons most agreed with were old age of patient (41.6%), lack of training/knowledge (37.5%) and lack of patients' initiative to bring up the subject (36%). Characteristics of respondents were analyzed and several factors were statistically significantly associated with reasons not to inquire about sexual health (Table 5). Lack of time was the third most important barrier (26.1%), especially for young and inexperienced doctors.

Table 5 Barriers for inquiring about sexual health

Barriers	Strongly agree %	Agree %	Neutral %	Disagree %	Strongly disagree %	Doctors' characteristics associated with agreeing (*p*-value)
Old age of patient	5.6	36.0	28.1	18.0	12.4	none
Lack of training/knowledge	6.8	30.7	30.7	18.2	13.6	less experience (0.028)
Lack of patients initiative	3.4	32.6	19.1	28.1	16.9	less responsibility (0.002)
Lack of time	6.8	19.3	23.9	31.8	18.2	young age (0.037); less experience (0.020)
Language/ethnicity/religion	2.2	20.2	33.7	27.0	16.9	none
Someone else's responsibility	3.4	14.6	31.5	36.0	14.6	less responsibility (<0.0001)
Patient is too ill	0	12.4	24.7	39.3	23.6	none
Patient is not ready for it	0	3.4	23.6	46.1	27.0	none
Shame to bring up the subject	0	3.4	22.5	44.9	29.2	more responsibility (0.018)
Age discordance	0	1.1	12.4	50.6	36.0	none
Patient is of the opposite sex	1.1	0	7.9	47.2	43.8	none

Referring patients

In the past year, an estimated 1.5% of patients (SD 5.9) was referred to another health care professional because of SD; 69.8% of respondents did not refer any patient in the past year. The majority of respondents (74.2%) stated to have referral options within their own centre, specified in Table 6. Twenty-three percent did not know if there was a health care professional in their centre to refer a patient with SD to; this was not significantly associated with the demographics of the neurosurgeon. A directory of health care professional to whom SD patients can be referred to seemed helpful to 66.3% of respondents; these respondents were significantly younger (*p*=0.026), more often resident (*p*=0.006) and had less experience in neurosurgical care (*p*=0.004).

Table 6 Where to do you refer patients for SD? (*n*=21)

	n
Urologist	10
Sexologist	10
Gynaecologist	5
Rehabilitation specialist	2
Fertility clinic	2
Spine centre team	1
Plastic surgeon for co-aptation of pudendal nerve	1

NB total adds up to >21 since some gave more than one answer

DISCUSSION

Sexual health is not often discussed: 72% of participants (almost) never counsel patients, even though they believe 34% of patients experiences changes in sexual function due to spinal disease. Sixty-four percent of neurosurgeons believed they were (partly) responsible for discussing sexual health. When obtaining informed consent, 53% (almost) never discussed risks of surgery on sexual health. Referring patients to specialized health care workers is not common: 70% had never referred a patient for SD and 23% did not know if there was any availability for referral.

The response rate of this study was above the average response rate for physician surveys (54%).[23] Several strategies were adopted to attain this high rate, including monetary incentive and using mail-based instead of web-based questionnaires, which have both proven to be effective strategies.[24,25] Sending reminders boosted response rate from 35% to 62%.

No response bias regarding demographics of respondents could be identified. However, doctors who are not interested in the topic are naturally more likely to have declined invitations. True rates of discussing sexual health may therefore be even lower in the general neurosurgeon population, although of the eight doctors returning this questionnaire empty with specification of a reason, only 2 stated lack of interest as the reason.

Sexual health was more often discussed with male patients and patients aged between 20-35 years. Doctor demographics were not associated and it remains unclear why doctors find it less important to inquire about sexual health in female patients than in their male counterparts. Maybe societal biases or the assumed passive sexual role of women which was coined by Higgins years ago, still do play a part.[26] Regarding the latter reason, some might even recall Turks blunt statement in 1983: "During sexual intercourse the woman is the more passive partner of the two; is receiving while the man is giving, so it is logical to conclude that the act does not affect women as much as it does men".[27] The respondents predilection of counselling younger patients above older patients is concordant with surveys among other clinicians, showing that sexual health is often neglected in the elderly.[22,28-30] This is underlined by the fact that 42% of participants stated that 'old age of patient' was a reason for not discussing sexual health. Larsen described that sexual activity is most often reduced in elderly people with spinal cord injury, even in the case of complete neurological restitution.[31] Bearing in mind the minimum of counselling done in this older age group, this is not hard to imagine.

Another major reason for not discussing SD found in this study was 'lack of patients initiative to bring up the subject' (36%). It is interesting that 63% of participants stated that patients are responsible to initiate the subject, while 82% indicated that patients do not bring up the subject themselves. A survey among patients showed that patients prefer the physician to initiate the discussion,[32] whereas a different study conducted in primary care stated that patients prefer to initiate the topic themselves, but do not object to doctors who initiate the topic.[33] It seems that by starting the discussion, the doctor simply cannot go wrong.

Naturally, doctors who feel responsible to counsel, discuss sexual health more often. In the specific case of CES, counselling on sexual health is done more frequently by neurosurgeons who feel more confident about their knowledge of sexual health. For the general group of patients however, this was not the case: doctors with more knowledge did not counsel more often. Despite this fact, 37% of participants did indicate 'lack of knowledge' as a barrier to discuss sexual health. This seems reasonable, since merely 3% of respondents rated their knowledge on SD as sufficient. Lack of knowledge is often described in literature as an important barrier to discuss sexual health, with Bachmann reporting in his survey including physicians and gynaecologists, amongst others, that 22% of respondents rated their knowledge and comfort level of discussing sexual female health as poor.[34] This advocates the incorporation of counselling on sexual health in the curriculum, as was proposed by other authors.[35,36] What this study adds to current knowledge, is that the majority of participants is eager to enhance their knowledge, especially young doctors, which offers opportunities to invest in counselling training early in residencies.

The introduction of proper checklists to detect SD could be helpful in this light. Defining female sexual dysfunction can be quite challenging. In order to cater for this problem, Sipski et al. proposed a classification of female sexual dysfunction after spinal cord injury, dividing dysfunction into four categories, including psychogenic and reflex genital arousal.[37] In 2007, due to increased attention for this topic, the American Spinal Injury Association released a standard form to assess sexual function in spinal cord injured patients of both sexes, with items including genital arousal, orgasm and sensation of menses/ejaculation.[38]

Regarding the right time to counsel about sexual health, the critical interval for discussing sexual health with spinal cord injured patients was earlier found to be up to

6 months after inpatient rehabilitation.[39] Bearing this in mind, clinicians can maximize the impact of their counselling. Therapeutic options for SD in spinal cord injured are available and have been evaluated in various studies, though since this is beyond the scope of this article, they will not be discussed here.[40-42] It is sufficient for the counselling doctor to know that there are solutions to this often neglected problem, which makes counselling all the more beneficial.

Lack of time was a barrier for only a reasonably small group of participants (26.1%), in contrast to surveys conducted among other clinicians.[22,34,43,44] The same applied for reasons such as embarrassment, age- and gender discordance and ethnic differences.[29,30,34,43]

CONCLUSION

For the last decades, a body of knowledge has arisen laying down the fundamental concepts of possible sexual health changes in spinal patients. This study shows that counselling is not often done in neurosurgical care, mainly due to lack of knowledge/training, old age of patients and lack of patients initiative. In order to enhance counselling facilities, more training on sexual health counselling early in the residency program seems critical. By initiating the discussion, clinicians who deal with spinal patients have the potential to detect SD and refer adequately when necessary, thereby improving the overall quality of life of their patients.

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CHAPTER 4

Discussing reproductive health in spinal care, part II: fertility issues

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Eur Spine J. 2016;25(9):2945-51

ABSTRACT

Purpose. Due to advancing insights, discussing fertility in spinal care is an emerging topic. Studies among neurosurgeons to evaluate clinical practice about discussing fertility are non-existent. The aim of this study is to review knowledge, attitude and practice patterns regarding discussing fertility in spinal care.

Methods. Dutch neurosurgeons and residents were sent a mail-based questionnaire addressing attitude, knowledge and practice patterns regarding discussing fertility.

Results. Response rate was 62% (compared to mean of 28% in similar surveys) with 89 questionnaires suitable for analysis. Mean age was 42 years with 83% of respondents being male. A quarter of respondents stated neurosurgeons are responsible to discuss fertility, with 12% indicating to actually do this. Fertility is discussed more often with patients with cauda equina syndrome (70%) and with men (p=0.006). Merely 8% stated to have adequate knowledge on fertility preservation (FP); this percentage was higher for doctors with spinal surgery as specialty (p=0.015). In case of cauda equina syndrome, doctors with more knowledge discussed fertility more often (p=0.002). Fifty-three percent of neurosurgeons wished to enhance their knowledge, in order to feel more comfortable to discuss fertility with their patients. Five percent indicated to have ever referred a patient to a fertility specialist.

Conclusion. Fertility is not routinely discussed in spinal care. Fertility is discussed more often with men. Recent guidelines state that initiating the subject fertility is an essential part of good practice in spinal care. Education on fertility and FP needs to be integrated in the neurosurgical training program to create more awareness in neurosurgeons, and enabling them to provide adequate information and care to the patient.

INTRODUCTION

Reproductive health is considered by the WHO to be one of basic human rights, stating 'it is the choice of each individual and couple, (…) to determine if they intend pregnancy, and if so, (…) the timing'.[1] Many diseases jeopardize reproductive health and as a result, fertility issues arise in several medical fields. Oncology care has been among the first to urge the need for discussing fertility, first by running surveys among doctors and patients to expose the lack of discussion about fertility,[2,3] later by developing guidelines regarding the options for fertility preservation (FP) and the initiation of this topic in clinical practice, leading to a new field of "oncofertility".[4-8]

In spinal care, patients are faced with potential hazards to fertility and reproduction as well.[9] For example, among patients with cauda equina syndrome, 44% experiences sexual dysfunction (defined as any problem resulting in abnormal intercourse, ranging from e.g. decreased penile or vaginal sensation to impotence or retrograde ejaculation), therefore, this group is potentially at risk for in- or subfertility.[10] However, discussing reproductive health is far from first priority among spinal surgeons, which was shown in a recent survey among neurosurgeons, displaying only 28% of neurosurgeons discuss sexual health with their patients.[11]

The first article in English literature acknowledging decreased fertility in spinal cord patients was written in 1948 and discussed male patients with spinal cord injury (SCI).[12] Apart from the more obvious reasons for sub- or infertility in men with SCI (e.g. erectile and ejaculatory dysfunction), semen quality was found to be greatly reduced. Three causes were proposed: lifestyle factors (e.g. elevated scrotal temperature, infrequency of ejaculation, recurrent urinary tract infections [UTI]), physiological factors secondary to SCI (e.g. hormonal environment) and alterations in seminal plasma.[13,14] Currently, the latter is considered to be one of the main causes.[15] This is compatible with findings of reduced sperm motility in the ejaculate of SCI men (and adequate number and morphology) versus normal sperm motility in their epididymis.[14] Several treatment options for men were introduced, including in vitro, in utero or even in vagina fertilization after ejaculation through vibratory stimulation or electro ejaculation.[16] Due to several case reports about quickly deteriorating semen quality after SCI, cryopreservation of sperm as soon as possible after injury was proposed by several authors.[17-19]

The focus on the male patient is striking when browsing through literature on SCI and fertility. Data on female fertility and SCI is scarce. Women with SCI however, do experience prolonged amenorrhea after injury, which can take up to 9 months.[20,21] To complicate matters, during this anovulatory phase, unpredictable ovulation might occur, which makes it even more important to properly consult patients on fertility, and contraception.[20] When menses has returned, fertility of SCI women is assumed to be similar to the general population. However, virtually no data on fertility rates in SCI women are available.[22] With regard to pregnancy and labour, several health risks are identified for SCI women.[23,24] In a large study of 472 SCI women of which 14% got pregnant after injury, complications like miscarriage, diabetes of pregnancy, prematurity and low birth weight (corrected for prematurity) were significantly more frequent after injury than before injury (75% versus 50%). In addition, women with SCI displayed higher rates of delivery by caesarean section (18% versus 8%).[25]

Apart from consequences of the disease itself, surgical treatments might impose an additional risk on fertility, in particular for men. Anterior spinal surgery, especially the transperitoneal approach, may cause damage to the hypogastric plexus and therefore cause retrograde ejaculation.[9] In women, damage to the hypogastric plexus has the potential to reduce pain sensations of the uterus and seems not to affect fertility in that sense. One retrospective telephone study in 2007 showed no decreased fertility among women after anterior spinal surgery.[26] However, literature on fertility after spinal surgery in women is extremely scarce and might therefore not be representative. A more important risk of deteriorating medullary cord function, and thereby possibly affecting fertility as stated above, is surgery on the spine for tumor, trauma or degenerative disease. In particular in those interventions in which the surgery is done because the medullary tract is already at risk by the disease, the chance to further damage the cord, is considerable.

In 2010, a guideline was released by the Consortium for Spinal Care Medicine stating that (options of) fertility should be discussed with all SCI patients.[27] In the same period, instruments on how to measure infertility in SCI patients were proposed.[28] Discussing fertility is now adapted as one of the essential elements of primary spinal care.[29] Despite the fact that the attention for reproductive health and fertility issues in spinal care patients is increasing, data about practice patterns for discussing fertility in spinal care is nonexistent. This study was designed to explore knowledge, attitude and practice patterns of neurosurgeons about discussing fertility with spinal care patients.

MATERIAL AND METHODS

Participants

In March 2013, all members of the Dutch association of Neurosurgery, which comprises of both neurosurgeons and residents in neurosurgery (total 161) were invited to fill in a questionnaire. The questionnaire was developed by the authors of this article, based on the questionnaire used by Nicolai et al.,[30] adapted for this purpose. A pilot study was performed in January 2013 among residents and neurosurgeons of the Neurosurgery department of the Leiden University Medical Centre. According to feedback and comments, the questionnaire was further adjusted which leaded to a finalized version which was used for this survey (the questionnaire is available upon request). The questionnaire included 34 questions and was divided into the topics sexual dysfunction and fertility issues. The results of the items on sexual dysfunction are discussed in a previous article.[11] Items that are analyzed in this article:

- Demographic data of respondent;
- Level of knowledge on fertility issues and their treatment;
- Frequency of discussing fertility issues with patients;
- Responsibility of the neurosurgeon to discuss fertility issues;
- Knowledge about (possibilities to) referring patients with fertility problems.

Various questions were asked repetitively for different groups of patients (sex and age categories) to facilitate analysis regarding patients' sex and age. Questions were all stated referring to patients with general spine problems, unless specified otherwise. Questionnaires were accompanied by an invitation letter explaining reasons for and content of the study and sent by regular mail. A monetary incentive (opportunity to win book voucher) was used to motivate participants to reply. In case a participant did not reply, reminders were sent one month and two months after initial invitation.

Statistical analyses

Data were analyzed using SPSS Statistics 23.0 (SPSS Inc., Chicago, IL, USA). Internal consistency of the survey was analyzed using Cronbach's coefficient α. Means of numerical demographic values and answers to questions were analyzed with frequencies. Associations between categorical demographic data and numerical variables without Gaussian distribution were tested with the Mann-Whitney-U-test; for paired data (either numerical without Gaussian distribution or ordinal), Wilcoxon signed rank test was used. Associations between ordinal or categorical independent variables and ordinal data were calculated with Mantel-Haenszel linear-by-linear association chi-squared test (comparable to Armitage's trend); Pearson Chi-square test was used for categorical data. Comparison of paired ordinal data was done using Friedman's test, with Wilcoxon signed rank test and Bonferroni adjustment as post-hoc test. For associations between ordinal variables and numerical data, not displaying Gaussian distribution, Kruskal-Wallis H test was performed, with Mann-Whitney-U-test and Bonferroni adjustment as post hoc test; for numerical demographics and numerical data without Gaussian distribution, Spearman correlation was used. Two-sided p-values <0.05 were considered statistically significant. Some questions with open, numerical and ordinal answers were grouped together for analyses.

RESULTS

Reliability of the questionnaire

Items regarding the frequency participants ask about fertility displayed an acceptable internal consistency (α = 0.70).

Participants

Of the 161 eligible participants, 99 returned the questionnaire, either after first invitation (*n*=55) or after second (*n*=26) or third (*n*=18) invitation, resulting in a total response rate of 61.5%. Nine participants returned the questionnaire empty; reasons not to participate were lack of experience (*n*=3), lack of interest (*n*=2), lack of time (*n*=1), working with a specific patient group not suitable for this study (*n*=2) or no reason indicated (*n*=1). One participant returned an almost empty questionnaire with too little information available for analysis. This resulted in a total of 89 questionnaires that were suitable for analysis.

Of the participants, 83.1% were male, in accordance with the circa 90% male predominance in the Netherlands neurosurgical society. Mean age was 42.4 years (SD 9.6), with 71.6% of respondents being a neurosurgeon versus 28.4% being a resident. Mean experience in neurosurgical care was 9 years. Among the respondents, 42.5% had spinal surgery as his or her specialty. Characteristics of the responders are summarized in Table 1. Male respondents were significantly older than their female counterparts (mean age 43.6 years [SD 9.43] versus 36.3 years [SD 8.35]; *p*=0.006).

Discussing fertility issues and sex of patient

To the question "How often do you discuss the impact of disease on fertility with patients with general spine problems?" 87.5% of respondents answers '(almost) never' and 3.4% '(almost) always'. When asked about cauda equina syndrome, 30.3% states to '(almost) never' discuss fertility issues while 34.8% says to '(almost) always' do that (see Figure 1). Other possible answers were: 'in less than half of the cases' , 'in half of the cases' and 'in more than half of the cases'. Fertility issues are discussed less often with female patients than with male patients: 93.2% of doctors replies to (almost) never discuss this topic with their female patients, versus 84.3% when asked about their male patients (Figure 1). This difference is significant (*p*=0.006).

In addition, doctors discuss fertility issues up to a higher age with their male patients than with their female patients, see Figure 2 and 3 (mean 56.7 years [SD 19.8] versus 47.3 years [SD 13.7], respectively; *p*<0.001). Male doctors discuss fertility issues with their female patients up to a higher age than do their female counterparts (40.4 years versus 35.1 years, respectively). However, this difference is not statistically significant (*p*=0.430). The frequency of asking about fertility issues is not significantly associated with gender, age or any other demographic of the respondents.

Table 1 Characteristics of participants (*n*=89)

	n (%)
Male gender	74 (83.1)
Mean age	42.4 years (SD 9.6)
Function	
Neurosurgeon	63 (71.6)
Resident	25 (28.4)
Place of practice	
University hospital	40 (45.5)
Teaching hospital	15 (17.0)
District general hospital	3 (3.4)
University + district general hospital	23 (26.1)
University + teaching hospital	6 (6.8)
University + district general + teaching	1 (1.1)
Experience in neurosurgical practice	
< 3 years	3 (3.4)
3-5 years	11 (12.4)
6-10 years	25 (28.1)
11-15 years	15 (16.9)
>15 years	35 (39.3)
Spinal surgery as specialty	37 (42.5)

NB n differs because some questions were skipped

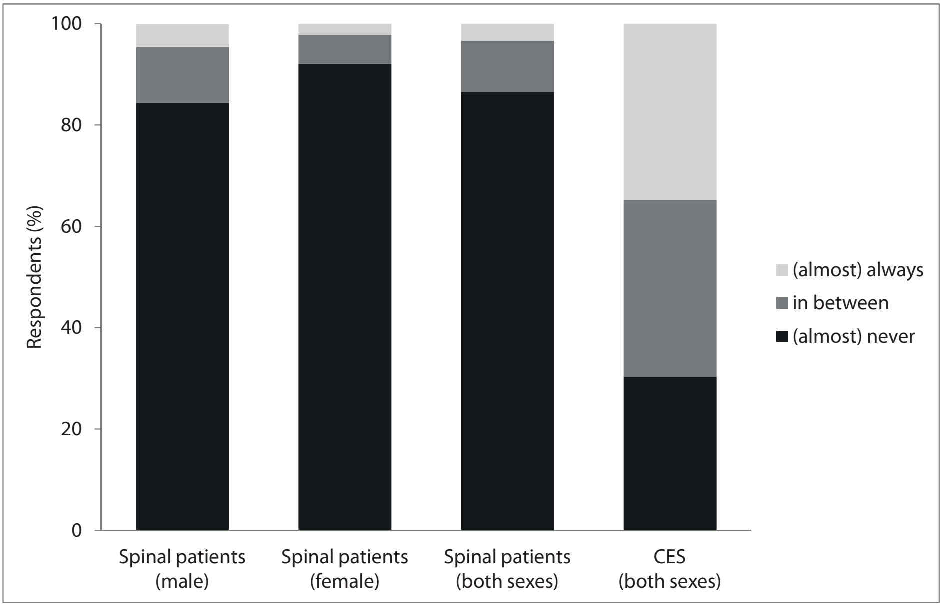

Figure 1 Frequencies of discussing fertility by neurosurgeons per patient category

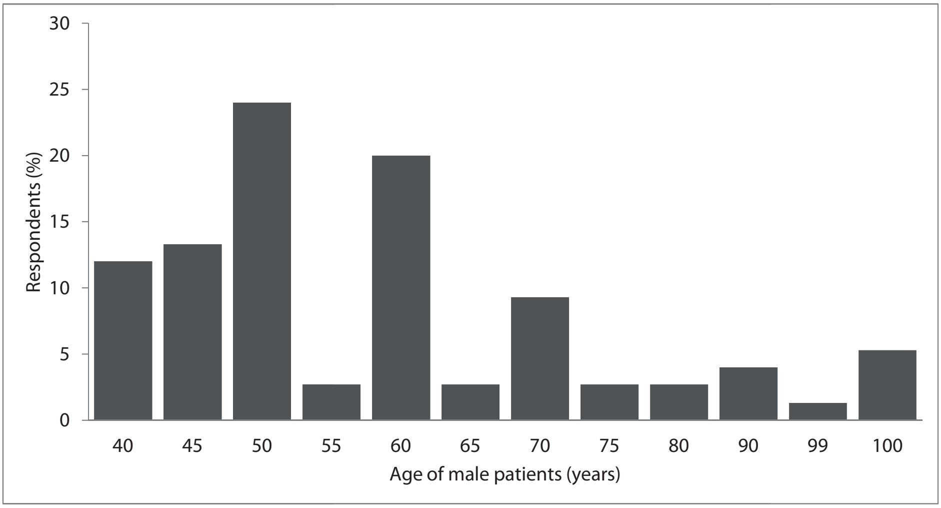

Figure 2 Maximum age of male patients to discuss fertility, according to respondents
NB respondents who replied 'no idea' were omitted (n=14)

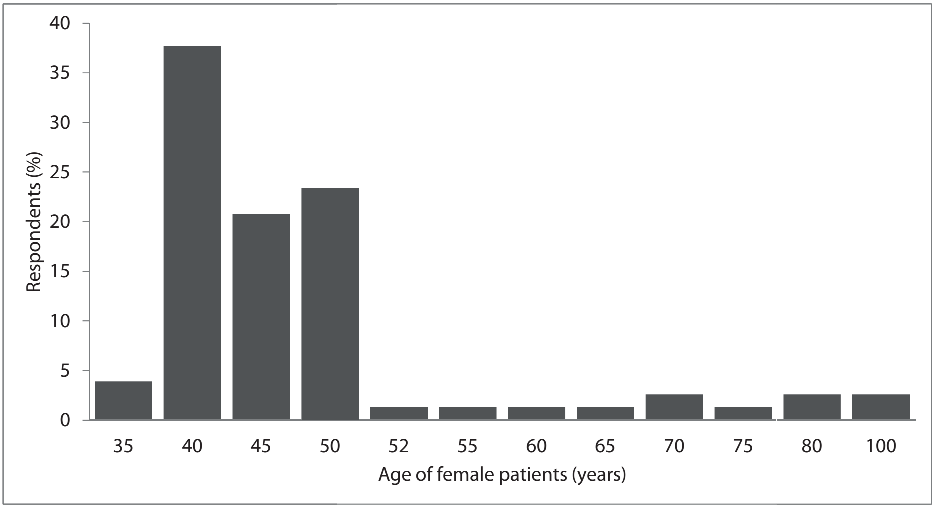

Figure 3 Maximum age of female patients to discuss fertility, according to respondents
NB respondents who replied 'no idea' were omitted (n=12)

Responsibility

According to 21.6% of respondents, the neurosurgeon has the responsibility to discuss fertility issues with patients between 16-44 years with general spine problems; 42.0% doesn't know who is responsible. Respondents who believe that the neurosurgeon is responsible, ask significantly more often about fertility (*p*=0.031). Feelings of responsibility are not statistically significantly associated with demographics of doctor.

Knowledge

Regarding knowledge on FP options in patients with spinal diseases, 69.3% states to have (almost) no knowledge about this topic, 22.7% says to have 'some' knowledge and the remaining 8% indicates to have adequate knowledge. More knowledge is statistically significantly associated with spinal surgery as specialty ($p=0.015$). More knowledge is not statistically significantly associated with more frequent discussion about fertility, apart for patients with cauda equina syndrome, in which neurosurgeons who feel more confident about their knowledge, discuss fertility issues more often ($p=0.002$). No association between present knowledge and feelings of responsibility is found. Doctors who indicate they have more knowledge, discuss fertility up to a higher patients age. This correlation is significant for female patients, but just not for male patients ($p=0.046$ versus $p=0.057$, respectively).

The majority of respondents (52.9%) indicates that they prefer to enhance their knowledge on (discussing) fertility issues; female respondents answer significantly more often affirmative to this question (80.0% versus 47.2%; $p=0.021$), just like doctors below 34 years (84.2% versus 44.8%; $p=0.024$), residents as opposed to specialists (80.0% versus 42.6%; $p=0.002$) and those working in neurosurgical care less than 6 years (78.6% versus 47.9%; $p=0.035$). Doctors who classify their current knowledge as adequate, have statistically significantly less motivation to enhance their knowledge (56.8% versus 0%, respectively; $p=0.026$). Neurosurgeons who feel responsible to discuss fertility issues are significantly more eager to enhance their knowledge ($p<0.0001$).

Referrals

When it comes to referring a patient to a fertility specialist, 95.5% state to '(almost) never' do that; the remaining doctors indicate to do that in less than half of the cases. Neurosurgeons who ask about fertility issues refer their patients significantly more often ($p<0.0001$).

DISCUSSION

Fertility issues are not commonly discussed in spinal care: 88% of respondents (almost) never consults his/her patient on this topic. Cauda equina syndrome is an exception in which 70% of neurosurgeons discuss fertility issues. A quarter of responding neurosurgeons stated that they believe that they have the responsibility to discuss fertility issues with spinal care patients.

Discussion is initiated significantly more often in male than in female patients, regardless of doctors' sex or age. This study confirms that counselling on fertility leads to more referrals to fertility specialists. Merely 4.5% of the responding neurosurgeons has ever referred a patient to a fertility specialist.

This is the first study focussing on the knowledge, attitude and practice patterns of neurosurgeons regarding discussing fertility. Twelve percent of neurosurgeons discusses fertility with their patients; a fairly low percentage when compared to figures from oncology care surveys (60-95%). We hypothesized that a reason for this difference is the fact that oncofertility is a longer standing field and therefore oncologists are more aware of the importance of fertility in their patient population. The earlier introduction of aforementioned oncology guidelines seems to play an essential part in this. Oncology care surveys show a slight increase of discussing fertility from 60% before implementation of guidelines,[2,4,5] to 67-95% afterwards.[31,32] Since this study is performed only after introduction of the Consortium guideline, one can merely guess what the results would have been before implementation.

In order to attain a high response rate, this questionnaire was kept as compact as possible. This, together with other proven effective strategies to increase response rate, such as a monetary incentive and using mail-based questionnaires instead of web-based ones,[33,34] yielded a response rate of 62%. This is extremely high compared to similar surveys with response rates ranging from 15% to 37% (mean 28%).[31,32,35-38] However, it is likely that clinicians who are not interested in the topic of this survey, have declined invitations more often. Therefore, actual rates of discussing fertility may even be lower among the general clinician population. An important remark in this context is that only 2% of neurosurgeons who returned the questionnaire indicated a lack of interest.

More than half of the responding neurosurgeons wishes to enhance their knowledge about FP. This percentage is lower than found among oncologists, of whom 87% wishes to gain more information on FP.[37] Merely 8% of respondents are confident about their knowledge, as opposed to half of oncologists in a similar review.[36]

Referrals to fertility specialists are rarely made (4.5%) and significantly more often by doctors informing their patients about fertility. This contrasts with figures from oncology surveys in which 47% to 82% refers to a fertility specialist. Oncology studies identified the following positive doctor predictors for referring: female sex, favourable attitude, gynaecology or paediatrics as specialty, high frequency of discussing fertility and easy access to fertility specialist.[31,35,38] In the present survey, no positive predictors for referring, apart from high frequency of discussing fertility, were found.

Fertility is discussed more often with men than with women, and as well up to a higher age with male patients. The latter is easily explained by the restricted reproductive age of women compared to men. The fact that neurosurgeons discuss fertility more often with male patients is in concordance with the current focus of spinal literature on male fertility. However, like stated before, the hypothesis that fertility is not affected in SCI women is not supported by constructive research. The need for research on fertility in

SCI women is essential, as was already urged by DeForge in 2005.[22] Unfortunately, no new studies about this topic have emerged since.

Interestingly, doctors discuss fertility up to a higher age with female patients when they feel more confident about their own fertility-knowledge (up to 55 years versus up to 36 years). This could be due to the fact that (1) doctors with more knowledge, have this knowledge because they believe FP options should be easily accessible for everyone and thus also for women with more advanced age, or because (2) doctors with little knowledge, do not know that discussing reproductive health might still be useful for women with more advanced age (e.g. >36 years).

Limitations

Most important limitation of this study is that questions on barriers to discuss fertility were not included in the questionnaire. This was done to obtain a compact questionnaire which greatly helped in attaining a high response rate. In similar oncology surveys, oncologists mentioned barriers such as lack of knowledge, unawareness to whom to refer to, lack of time and too advanced illness of the patient.[37-39] Further studies regarding these barriers for specifically spinal care clinicians are needed.

CONCLUSION

This study shows that fertility is not routinely discussed in spinal care, and that referrals to fertility specialists only rarely take place. There is disagreement about the responsibility the neurosurgeon has in initiating discussion about fertility issues. According to current guidelines and consensus however, part of good practice includes discussing fertility issues in spinal care patients. Results of this study match our expectation that there is still a lot to improve in this area, especially when compared to oncology care. We propose integration of education on fertility in the neurosurgical training program to create more awareness and to enhance knowledge about FP options among neurosurgeons. As displayed in previous studies, creating referring facilities could positively influence the number of referrals. More education will enable neurosurgeons to provide adequate information and care to the patient. In a general light, more research regarding the barriers to initiate discussion about fertility in clinical practice and regarding fertility in women with spinal cord problems is needed.

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CHAPTER 5

Cauda equina syndrome: presentation, outcome and predictors with focus on micturition, defecation and sexual dysfunction

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Eur Spine J. 2017;26(3):894-904

ABSTRACT

Background. Even though micturition, defecation and sexual function are substantially affected in cauda equina syndrome (CES), data on outcome are scarce.

Methods. Medical files of patients operated on lumbar herniated disc were screened for CES and retrospectively analyzed for baseline characteristics, outcome of micturition, defecation and sexual function and possible predictors.

Results. Seventy-five CES patients (52% men) were included with a mean age of 44 years. L5-S1 was the most common affected level. Duration of CES complaints at presentation was on average 84 hours (median 48 hours). Prevalence of symptoms at presentation: sciatica (97%), altered sensation of the saddle area (93%), micturition dysfunction (92%), defecation dysfunction (74%). Only 26 patients were asked about sexual dysfunction of whom 25 patients experienced dysfunction. Female gender was associated with more defecation dysfunction at presentation than male gender (OR 4.11; p=0.039). All patients underwent decompressive surgery. Two postoperative follow up (FU) moments took place after a mean of 75 hours and 63 days. Outcomes at second FU moment: micturition dysfunction 48%, defecation dysfunction 42%, sexual dysfunction 53%, sciatica 48% and altered sensation of the saddle area 57%. A shorter time to decompression was associated with more sciatica at FU 1 (p=0.042) which effect had disappeared at FU 2.

Conclusion. This study is unique in (1) displaying the presenting features in a large cohort of CES patients, (2) demonstrating that recovery after decompression is slow and far from complete in the majority of patients with regard to micturition, defecation and sexual function and (3) evaluating predictors for outcome.

INTRODUCTION

Cauda equina syndrome (CES) is a neurological condition caused by compression of the cauda equina, most commonly described as a combination of sensory loss of the saddle area, motor deficit and/or loss of reflexes of the lower limbs, micturition dysfunction, defecation complaints and/or sexual dysfunction.[1,2] The first article about CES appeared in 1934, in which a combination of neurological and urological complaints in patients with a ruptured intervertebral disc was described.[3] A herniated disc is still the most common cause of cauda equina compression; in literature, 45% of cases of CES are attributed to a lumbar herniated disc.[1]

In the last decades, especially the topic of timing of decompression and its relation to outcome has gained much attention in literature, with several small studies showing better – albeit not always significant – outcomes after early decompression.[4-9] Other studies could not demonstrate a better outcome after early decompression.[10,11] The value of urgent decompression was most convincingly showcased in the meta-analysis of Ahn et al., showing a better prognosis of sensory, motor, urinary and rectal function in patients being decompressed within 48 hours of presentation, compared to the group being decompressed after 48 hours.[12] These results were confirmed by others.[13,14]

In literature, there is little focus on the prognosis of micturition, defecation and sexual function.[2] This is remarkable considering the definition of CES. Recently, clinicians in spinal care were found to barely discuss sexual health and/or defecation at presentation and at follow up, suggested to be due to e.g. lack of knowledge or time.[2,15,16] Clinicians who do want to inform their patients about the prognosis of these functions, are confronted with scarce data. This study was performed in order to (1) evaluate outcome of micturition, defecation and sexual function in CES after decompression and to (2) find possible predictors of outcome. In addition, presenting features of CES were analyzed.

MATERIAL AND METHODS

The medical records of patients operated in the Leiden University Medical Centre (LUMC; university hospital and referral centre for high complex spinal surgery) between January 1995 and September 2010, with the surgery code 'lumbar discectomy' or 'recurrent lumbar discectomy' were screened by two independent researchers (NSK, JAP) to identify patients with CES. Criteria to diagnose a patient with CES were, according to consensus of literature, one or more of the following: 1) dysfunction of micturition, defecation and/or sexual function (not being attributable to use of opiates or previous disease), 2) altered sensation of the saddle area, with possible neurologic deficit in the lower limb (motor or sensory loss or reflex changes).[1,2] Patients filed with a diagnosis of CES but not meeting those criteria were excluded. In case of doubt about the diagnosis of CES, a third assessor (CLAVL) was consulted. In order to check inter observer reliability between the two reviewers, 10% of cases were independently screened by both of them.

The following data were extracted from the medical file:

- Baseline characteristics (at presentation): gender; age; level of herniated disc as stated in the file; relevant medical history; referring centre (if applicable); use of opiates and/or laxatives; duration of complaints of herniated disc (defined by the presence of sciatica); duration of CES complaints; information about micturition, defecation, sexual function, altered sensation of the saddle area and/or sciatica; information about anal sphincter reflex and anal sphincter tension.
- Surgery: time between presentation to first doctor and decompression (time to decompression); type of decompressive surgery.
- Follow up: information about micturition, defecation, sexual function, altered sensation of the saddle area and/or sciatica at three follow up moments: (1) at hospital discharge (FU 1; in case notes were taken several times during the first days post-operative, the last notes before discharge were used); (2) at the first outpatient visit, regularly planned 6 weeks postoperatively (FU 2); (3) at the second outpatient visit, which was not regularly planned (FU 3).

Data were collected in Excel and imported in SPSS.

Statistical analyses

Data were analyzed using SPSS Statistics 23.0 (SPSS Inc., Chicago, IL, USA). Demographic values and other patient characteristics were analyzed with frequencies. Investigating proportions between independent groups of categorical data was done with Pearson's Chi-squared test; Fisher Exact Test was used to compare groups with cell counts less than expected. For paired groups with categorical data, McNemar's test was used. Predictors for outcome and presentation were analyzed using a binary logistic regression model; in case of quasi-complete separation of the data, the concerning model was not run or the concerning predictor was removed from the model in order to maintain reliable models. Two-sided *p*-values<0.05 were considered statistically significant. In case of multiple testing, the Bonferroni method was used to correct *p*-values. Some numerical data were grouped together for analyses, e.g. timing of decompression was stratified into 6 groups: ≤12 hours, 13-24 hours, 25-36 hours, 37-48 hours, 49-72 hours and >72 hours.

Missing data

To run the regression models and for displaying outcome at FU 2, multiple imputation with five imputation sets was used for the following variables: duration of CES complaints; duration of complaints of herniated disc; time to decompression; micturition dysfunction at FU 1, 2 and 3; defecation dysfunction at presentation, FU 1, 2 and 3; altered sensation of the saddle area at FU 1, 2 and 3; sciatica at FU 1, 2 and 3. Multiple imputation was not performed for sexual dysfunction data due to scarcity of these data, to avoid bias. Pooled data (i.e. derived through multiple imputation) are presented as main data. Original data (not derived through multiple imputation) are presented as corrected (corrected for the number of patients for whom documentation is available at the concerning follow up moment) and as raw (not corrected for the number of patients). Due to an anticipated high amount of loss to follow up at FU 3, outcome at FU 2 was defined as main outcome and data at FU 3 were not used for regression analysis. For the patients for whom data at FU 3 are available, this will be mentioned separately.

RESULTS

In the period January 1995-September 2010, a total of 744 surgeries coded as '(recurrent) lumbar discectomy' were performed at LUMC, for a total of 696 patients: 38 patients had surgery twice, 10 patients had triple surgery. Out of 696 patients, 75 patients (10.8%) were found to have CES. One female patient who underwent a lumbar discectomy twice, met CES criteria twice; however, since she had not recovered from her first CES completely, only the first surgery was included for analysis. Inter observer reliability regarding diagnosing CES was analyzed using Cohen's Kappa. There was substantial agreement between the two reviewers' judgement (κ=0.635).

Patient characteristics

For patients characteristics; see Table 1 and Figure 1. Since the LUMC serves as a referral hospital, the majority of included patients presented first at other hospitals (73.7%). Thirty-two patients (42.7%) used opiates at presentation. Use of laxatives was not significantly higher in the group using opiates: 25.0% of opiate positive patients used laxatives versus 19.5% of opiate negative patients (*p*=0.574).

Presenting features of CES

Information about sciatica, altered sensation of the saddle area and micturition dysfunction was available for all patients at presentation and was present in 97.3%, 93.3% and 92.0%, respectively (Figure 2). Majority of sciatica was unilateral (60.3%). Altered sensation of the saddle area was classified as either hypoesthesia (75.7%), anesthesia (17.1%) or dysthesia (7.1%).

Micturition dysfunction was classified as having an indwelling catheter (39.1%), needing clean intermittent catheterization (2.9%), documented residual of bladder (5.3%) or subjective complaints, e.g. reduced feeling of passing urine or mild incontinence (52.2%).

Table 1 Patient characteristics (*n*=75)

	n (%)
Male	39 (52.0)
Mean age	43.6 years (SD 10.4, range 27-78)
Level of disc lesion (as documented in file)*	
L1-L2	1 (1.3)
L2-L3	3 (3.8)
L3-L4	6 (7.6)
L4-L5	29 (36.7)
L5-S1	39 (49.3)
L6-S1	1 (1.3)
Origin of referral	
Neurologist LUMC	15 (20.0)
Emergency Room LUMC	2 (2.7)
Other hospital in the area	55 (73.3)
General practitioner	2 (2.7)
Unknown	1 (1.3)
Use of opiates at presentation	
Yes	32 (42.7)
No	41 (54.6)
Unknown	2 (2.7)
Use of laxatives	
Yes	16 (21.4)
No	58 (77.3)
Unknown	1 (1.3)
Median duration of herniated disc complaints at presentation (*n*=73)	30 days (range: 1 day – 14 years)
Median duration of CES at presentation (*n*=68)	48 hours

**total disc lesions: 79 (4 patients had double lesions: L4-L5+L5-S1 (n=3) and L2-L3+L4-L5)*

Information about the presence of defecation dysfunction was available in 61 patients, of whom 73.8% had dysfunction, classified as any complaint of defecation which did not exist before, which could be e.g. incontinence or changed sensation of passing stool. A patient with faecal incontinence since diagnosis of M. Sjogren several years before CES, was not classified as having complaints of defecation due to CES.

Information about presence of sexual dysfunction was available for 26 patients (19 men), of whom 25 experienced sexual dysfunction. Documented problems were e.g. altered sensation of genitals, inability to reach orgasm, erectile dysfunction and priapism. For two patients, sexual status (active/non active) before onset of CES was documented; for the others, no notes on sexual activity were found.

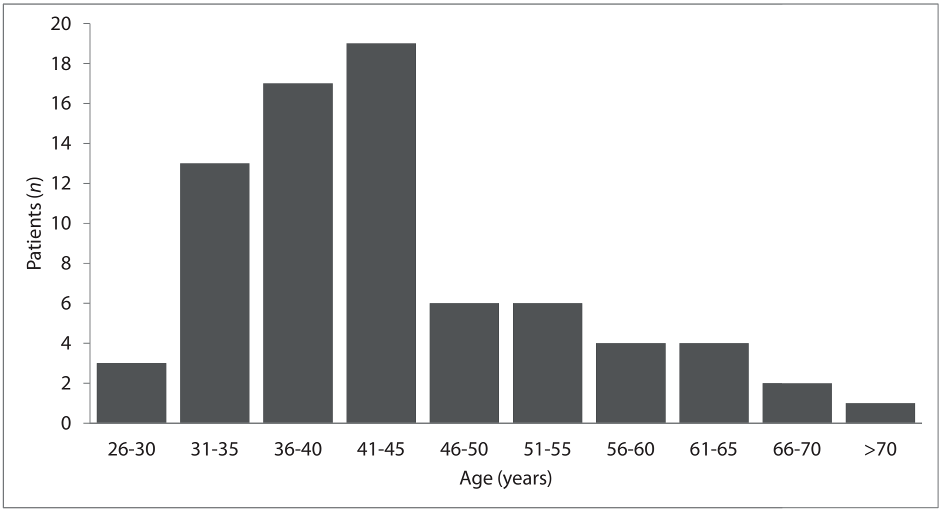

Figure 1 Age distribution of CES patients at time of surgery

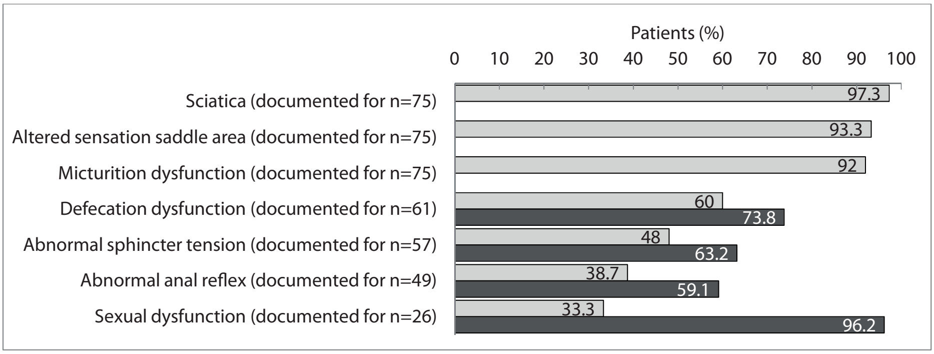

Figure 2 Prevalence of signs and symptoms of CES at presentation. The grey bars indicate the proportion of total patients included in this study (*n*=75); the black bars indicate the proportion of patients for whom documentation was available (*n* specified after each row).

Anal sphincter tension and anal sphincter reflex (anal wink) were tested in 76.0% and 65.3% of patients respectively, and were abnormal in the majority (63.2% and 59.1%, respectively). Abnormal anal sphincter tension was significantly associated with altered sensation of the saddle area (*p*=0.007; Table 2), with a sensitivity for altered sensation of the saddle area of 68%. Abnormal anal sphincter reflex was not significantly associated with defecation dysfunction, although a trend was observed (*p*=0.096; Table 3). Micturition dysfunction was not associated with either abnormal anal sphincter tension nor reflex (Table 4). Since data on sexual dysfunction at presentation were scarce, no analyses were done for sexual dysfunction.

Table 2 Association between altered sensation of the saddle area and sphincter tests. Proportion of patients with abnormal sphincter tests, stratified by sensation of the saddle area (at presentation).

	Altered sensation saddle	Normal sensation saddle	*p*-value
Abnormal anal sphincter reflex	60.9%	33.3%	0.347
Abnormal anal sphincter tension	68%	0%	0.007

Table 3 Association between defecation dysfunction and sphincter tests. Proportion of patients with abnormal sphincter tests, stratified by defecation dysfunction (at presentation).

	Defecation dysfunction	No defecation dysfunction	*p*-value
Abnormal anal sphincter reflex	64.5%	33.3%	0.096
Abnormal anal sphincter tension	63.9%	58.3%	0.731

Table 4 Association between micturition dysfunction and sphincter tests. Proportion of patients with abnormal sphincter tests, stratified by micturition dysfunction (at presentation).

	Micturition dysfunction	No micturition dysfunction	*p*-value
Abnormal anal sphincter reflex	60.9%	33.3%	0.347
Abnormal anal sphincter tension	63.5%	60%	0.878

Association patient characteristics – presenting features

The following factors were evaluated as predictors for presentation: age, gender, duration of complaints of herniated disc, duration of CES complaints, presence of altered sensation of the saddle area (for evaluating defecation and micturition dysfunction at presentation), presence of micturition dysfunction (for evaluating defecation dysfunction and altered sensation of the saddle area at presentation), presence of defecation dysfunction (for evaluating micturition dysfunction and altered sensation of the saddle area at presentation). For sciatica at presentation, the regression model could not be run, nor could sciatica at presentation be added as a predictor to the other models due to quasi-separation of the data. Defecation dysfunction at presentation was significantly associated with female gender (OR 4.11; p=0.039). Micturition dysfunction and altered sensation of the saddle at presentation displayed no predictors.

Surgery

All patients were decompressed by (partial) laminectomy and subsequent discectomy or sequesterectomy. A slight majority of patients (n=36) was decompressed within 24 hours after presentation (Figure 3). Eight patients were decompressed more than 72 hours after presentation to the first doctor, with time to decompression of 96 hours (n=3), 120 hours (n=1), 138 hours (n=1), 168 hours (n=1), 192 hours (n=1) and 216 hours (n=1). In 7 of these cases, majority of the delay was caused by the first doctor (family doctor or neurologist) where the patient presented. Hereafter surgery was performed within 24 hours (*n*=4), 48 hours (*n*=2) and 72 hours (*n*=1) after first presentation to the neurosurgeon. In one case, no discrimination could be made between delay at first and second doctor.

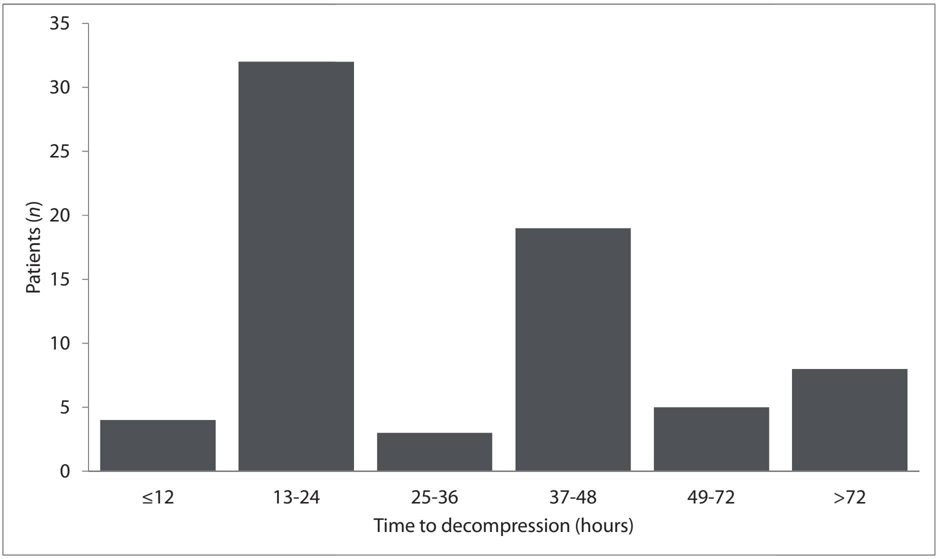

Figure 3 Time to decompression, counted from the first doctor visit until surgery (*n*=71)

Postoperative outcome

The first follow up moment (FU 1) at which micturition, defecation, sexual function and/or altered sensation of the saddle area was documented was on average 75 hours post-operatively (range 4-336 hours; median 48 hours). The latest time of FU 1 was 14 days post-operatively. Documentation on any of the items micturition, defecation, sexual function and/or altered sensation of the saddle area at the second follow up moment (FU 2), was available for 54 patients (72%), with a mean FU time of 63 days (range 4-300 days, median 60 days).

A third follow up moment (FU 3) at any item was documented for 23 patients (31%), with a mean FU time of 265 days (range 56-730 days, median 225 days). FU 3 is reported in the text as corrected, not pooled, and is not used in any regression analysis.

Micturition

Documented micturition dysfunction decreased significantly comparing pre-operative moment with FU 2 (92.0% versus 47.7%, *p*<0.001), Figure 4. In one patient with post-operative dysfunction, requiring intermittent catheterization from the 4th day after surgery for a short period of time with complaints of urinary dysfunction up to the last follow up moment, (6 months later), no complaints of micturition were documented at presentation. This was interpreted as misinformation at baseline. Pooled prevalence of micturition dysfunction was 47.7% at FU 2. Reported dysfunction included: indwelling catheter, on-off catheterisation, suprapubic catheter, reduced feeling of passing urine and (mild) incontinence. At FU 3, 19 patients were evaluated of whom 11 displayed dysfunction (57.9%).

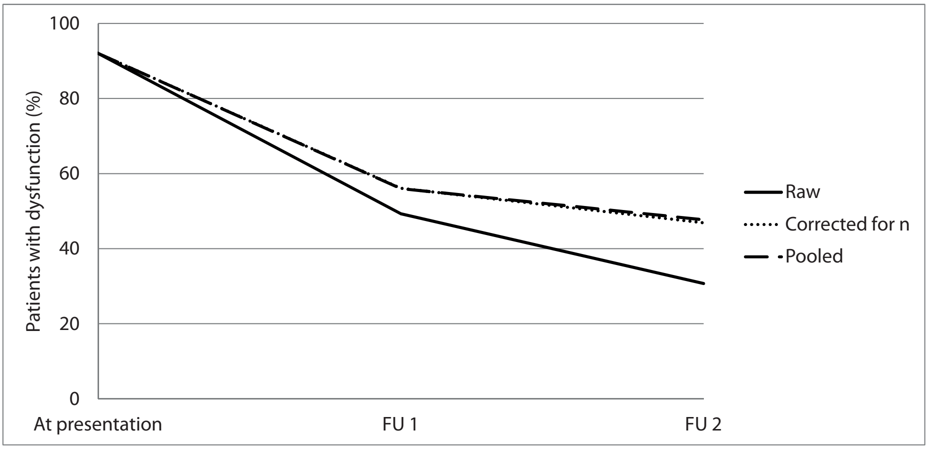

Figure 4 Outcome of micturition dysfunction. Proportion of patients with micturition dysfunction at presentation (documented for *n*=75), FU 1 (documented for *n*=66) and FU 2 (documented for *n*=49).

Defecation

Documented defecation dysfunction had decreased significantly after decompression measured at FU 2 (72.0% versus 41.8%, *p*=0.004), Figure 5. For three patients, defecation dysfunction was documented post-operative but not pre-operative. Pooled prevalence of dysfunction was 41.8% at FU 2. Thirteen patients were evaluated at FU 3, of whom 9 reported dysfunction (69.2%).

Sexual function

Due to scarce data on sexual function, investigating proportions was not done; therefore, no *p*-value for difference between pre- and postoperative dysfunction was derived. Corrected prevalence of sexual dysfunction at FU 2 was 53.3%, Figure 6. Documentation on sexual dysfunction was done for 5 patients at FU 3; four of them displayed dysfunction (80%).

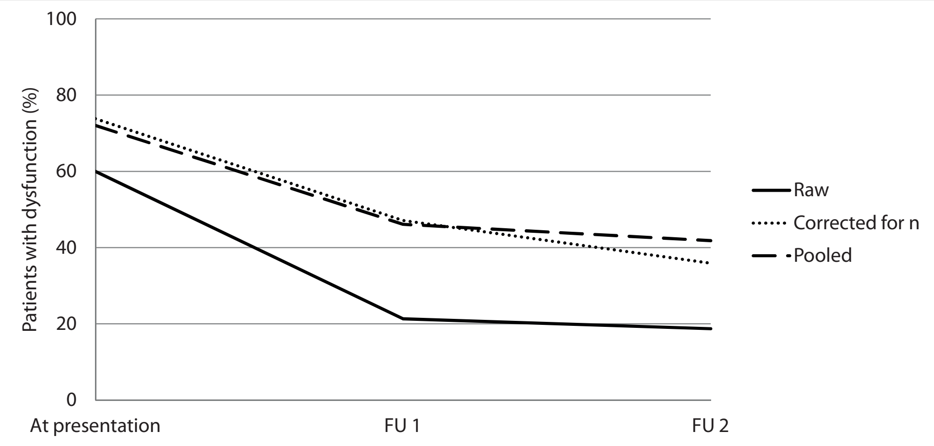

Figure 5 Outcome of defecation dysfunction. Proportion of patients with defecation dysfunction at presentation (documented for *n*=61), FU 1 (documented for *n*=34) and FU 2 (documented for *n*=39).

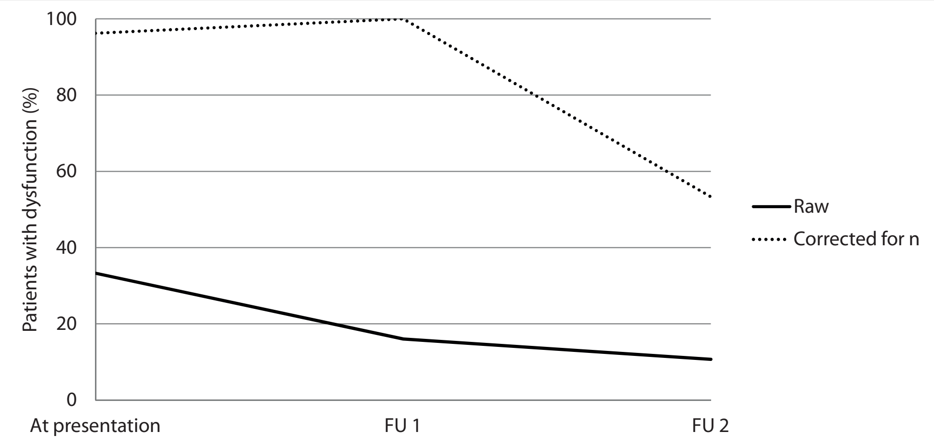

Figure 6 Outcome of sexual dysfunction. Proportion of patients with sexual dysfunction at presentation (documented for *n*=26), FU 1 (documented for *n*=12) and FU 2 (documented for *n*=15). Since multiple imputation was not used for data of sexual dysfunction, pooled data are not available.

Altered sensation of the saddle area and sciatica

Documented altered sensation of the saddle area and sciatica both decreased significantly after decompression measured at FU 2 (93.3% versus 56.5% and 97.3% versus 47.5%, respectively; both $p<0.001$), Figure 7 and 8. At FU 3, 12 out of 18 patient with documentation reported altered sensation of the saddle area (66.7%), and 12 out of 20 reported sciatica (60%).

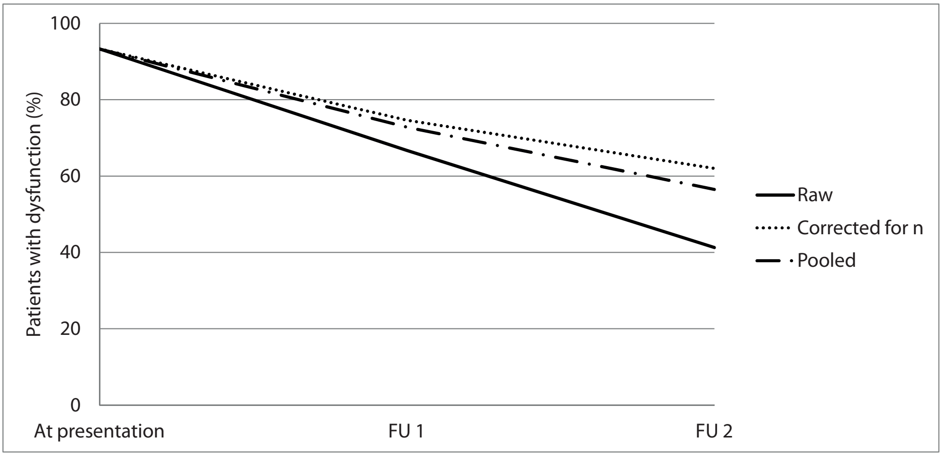

Figure 7 Outcome of altered sensation of the saddle area. Proportion of patients with altered sensation of the saddle area at presentation (documented for *n*=75), FU 1 (documented for *n*=67) and FU 2 (documented for *n*=50).

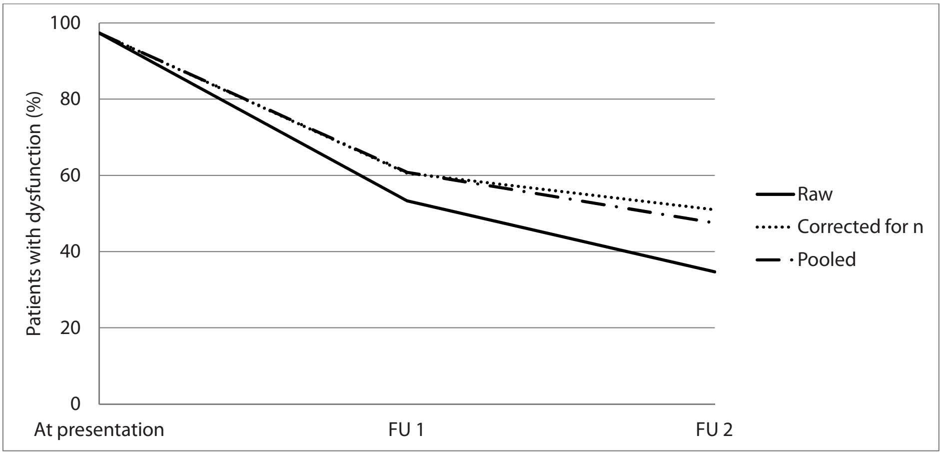

Figure 8 Outcome of sciatica. Proportion of patients with sciatica at presentation (documented for *n*=73), FU 1 (documented for *n*=66) and FU 2 (documented for *n*=51).

Predictors for outcome

The following factors were evaluated as predictors for outcome: age, gender, duration of complaints of herniated disc, duration of CES complaints, time to decompression (stratified groups, see Methods section for details of groups), altered sensation of the saddle area/micturition dysfunction/defecation dysfunction/sciatica at presentation.

Due to quasi-separated data, sciatica at presentation had to be removed from all models except the one for micturition dysfunction at FU 2; altered sensation of the saddle at presentation had to be removed from all models except the one for sciatica at FU 1; micturition dysfunction at presentation had to be removed from the models for sciatica at FU 2 and altered sensation of the saddle area at FU 1 and FU 2.

Timing of decompression was found to be significantly associated with short term outcome (FU 1) of sciatica: less time to decompression was associated with more sciatica at FU 1 (*p*=0.042). After stratifying outcomes for time to decompression using the well known break points from literature of 48 hours[12,14] and 36 hours[13], we found a statistically significant difference for outcome of sciatica at FU 1 comparing decompression before and after 36 hours. Patients decompressed within 36 hours experienced more sciatica than patients decompressed after 36 hours (79.4% versus 37.9%, adjusted *p*=0.032). There was no difference comparing patients being decompressed before and after 48 hours. There was no association between timing to decompression and outcome of sciatica at FU 2 (*p*=0.475). No other statistically significant predictors for micturition, defecation, altered sensation of the saddle area and sciatica at FU 1 and FU 2 were identified.

DISCUSSION

This is the largest single study performed about outcome of micturition, defecation and sexual function in CES (*n*=75). The incidence of CES among patients being operated for herniated disc was relatively high in this study: 10.8% compared to 1-3% in literature.[9,17] This high incidence can be explained by the fact that the LUMC serves as a referral hospital for urgent neurosurgical cases. The CES definition that was used to include patients in this study is widely used in literature, and even though a univocal definition for CES does not exist, the authors believe that using this definition guaranteed a fair representation of CES patients. This study displays unique data on the presenting symptoms of a large group of CES patients, proving that, next to the well acknowledged micturition dysfunction, also defecation and sexual dysfunction are common at presentation.

Anal sphincter tension and anal sphincter reflex are often tested in CES patients, even though several studies found no diagnostic value for these tests.[18-21] In the current study, abnormal anal sphincter reflex was not significantly associated with any of the diagnostic criteria for CES used in this study (closest to an association was defecation dysfunction with *p*=0.096). Abnormal anal sphincter tension is significantly associated with altered sensation of the saddle area (*p*=0.007). Specificity of the test is 100% (all patients without altered sensation of the saddle area displayed normal sphincter tension) and sensitivity is 68% (a substantial proportion of patients with anamnestic altered sensation of the saddle area displayed normal sphincter tension). With a positive predictive value of 100% (all patients with abnormal sphincter tension had anamnestic altered sensation of the saddle area) and a negative predictive value of merely 19%, abnormal anal sphincter tension at physical examination supports the presence of altered sensation of the saddle area, but in no way rules out altered sensation of the saddle area in case it is normal. Considering a specificity of 100%, the question arises whether it is necessary to test sphincter tension in patients without altered sensation of the saddle area since it might cause unnecessary discomfort. Evaluating the anal sphincter reflex data, however, does indicate that sphincter testing might add extra information. Of the five patients with normal sensation of the saddle area at presentation, four were tested for anal sphincter tension (all normal). Two of those four were also tested for the anal sphincter reflex, which in one case was abnormal, demonstrating that with normal sensation of the saddle area and with normal sphincter tension, the anal sphincter reflex can still be abnormal. It could therefore be sensible to do anal sphincter reflex tests even in a patient with normal sensation of the saddle area. The fact that only a small proportion in our study sample demonstrated normal sensation of the saddle are at presentation (*n*=5), limits our data in this aspect and therefore clinical relevance of sphincter tests cannot be secured nor refuted based on those findings.

Prevalence of micturition dysfunction is 47.7% of patients at FU 2. In an older study discussing 13 patients with CES due to herniated disc, the author states that "in all such patients, there was incomplete return of normal micturition".[22] In a more recent study of McCarthy et al., better recovery of micturition has been described: of 42 evaluated patients with CES due to herniated disc, 36% reported urinary incontinence (mean FU time of 60 months).[23] The higher prevalence of micturition dysfunction in the current study might be due to the shorter FU time, assuming that function of micturition will improve gradually over time.

Regarding defecation dysfunction, this study found a prevalence of 41.8% at FU 2; McCarthy et al. found a higher prevalence at follow up (60%): this could be due to attrition bias, the chance of which becomes greater when follow up period of the study is longer – as in McCarthy's study. Sexual dysfunction in the current study was 53.3% at FU 2, which is quite similar to the prevalence of 57% reported by McCarthy et al. The true prevalence of sexual dysfunction might be higher than the ones found in studies; since the threshold to discuss sexual health is very high, it is unlikely that either doctor or patient opens the topic, even if there are complaints.

Two patients in this study displayed a specific feature of sexual dysfunction: priapism. One patient reported spontaneous erections at presentation; unfortunately, no documentation on sexual function was done at follow up for this patient. The second patient presented with a numb feeling of the penis which had changed to priapism at follow up after 7 weeks and after 5.5 months. Priapism as a feature of cauda equina compression is extremely uncommon and only two reports in literature describe such a case: one involves a 61-year old man with a herniated disc at L4-L5,[24] the other a 60-year old man with a degenerative stenosis at L3-L4 and lumbar arachnoiditis.[25] Both patients experienced priapism and a numb respectively a burning sensation at the saddle area when walking, without sphincter disturbances. After decompression of the cauda equina, both patients experienced immediate and complete relieve of their symptoms, suggesting a causal relationship of cauda equina claudicatio and priapism. The parasympathic fibres that are responsible for penile erection arise in S2-S4, and it is thought that their stimulation through (in these two cases: intermittent) compression, had resulted in priapism.[24] To the authors' best knowledge, there are no case reports about priapism in non intermittent cauda equina compression. Even though the course of priapism complaints of the two patients in this study are uncertain, the authors believe that it is not unthinkable that the priapism experienced by the two patients in this study might be attributed to compression of the cauda equina, even though exact mechanisms remain unclear.

This study found that female patients are more likely to present with defecation dysfunction than their male counterparts (OR 4.11; p=0.039). Epidemiologic studies demonstrate that female gender is associated with more constipation, as a baseline fact in the general population as well as in the CES population when focusing on outcome.[26,27]

Sciatica were more often present at FU 1 when time to decompression was shorter (OR 1.86; p=0.042), which association had disappeared at FU 2. This association nowise undermines the importance of emergency decompression. It rather displays a correlation between duration of compression and other (prognostic) factors for which could not be corrected. Those factors are (1) the speed with which the compression has arisen, stating that patients with slowly developing anatomical lesions have a more favourable prognosis,[28,29] and (2) the type of CES lesion, stating that a "complete" CES (with total obstruction) carries a poorer prognosis than an "incomplete" CES, adding that the incomplete type often occurs more gradually (although not exclusively).[22,30] It seems sensible that a patient with sudden onset of heavy symptoms in general presents earlier. This results in a shorter duration of CES complaints (patient delay) as well as a shorter time to decompression (doctor delay), even though outcome is poor (due to the extent of the lesion). Patients that show reasonable outcome when decompression is delayed by weeks,[31] probably had a favourable anatomical lesion and more gradual onset of complaints. Since it is not (yet) possible to distinguish the group with the favourable conditions from the group with the less favourable conditions at the time of presentation (since e.g. the exact correlation of clinical presentation and degree of canal obstruction on imaging is not yet known) it is necessary to decompress every CES patient as soon as possible, to create the best chances for fair recovery.

The authors strongly believe that this study's finding, e.g. that time to decompression is not associated with outcome of micturition, defecation and altered sensation of the saddle area, and does display a correlation of more sciatica at FU 1 when it is shorter, does not implicate that decompression in CES is to be delayed. Firstly, the number of patients with delayed decompression in this study is relatively small (eight patients in the group decompressed after 72 hours, five patients in the group decompressed within 48-72 hours). Previously, meta-analyses have displayed better outcomes with decompression taking place within 48 hours[12,14] or within 36 hours.[13] Some studies with smaller patient numbers display a significant better outcome after earlier decompression as well, with significant better outcomes with decompression within 48 hours[9] and even within 10 days.[4] Studies displaying no difference in outcome are a minority and evaluate relative small patient numbers only.[10,11] The finding in this study that a shorter time to decompression is associated with more sciatica at FU 1, should therefore be weighed by the small patient number of this study and the fact that this finding is not present at FU 2 anymore. Also, in this study, clinical motives – unknown to the authors due to the retrospective study design – could have led to the decision for very early decompression in specific patient groups, which might have caused selection bias. The outcome would then be more influenced by factors on which clinical motives are based (and which have led to a an early time to decompression) than by the actual time to decompression.

Significant predictors such as duration of CES complaints for more than 48 hours as a risk factor for micturition dysfunction[32] and defecation dysfunction at presentation as a risk factor for sexual dysfunction[23] could not be identified in this study.

Missing data in this study are partly attributed to the inclusion of patients that were referred for surgery to LUMC, and were seen for follow up at their original referring hospital (in which case the researchers did not have access to the follow up data). Of the 19 patients that originated from either LUMC or the general practitioner, 100% displayed data at FU 2. Of the 55 patients that originated from a different hospital and were referred to LUMC for surgery, 34 patients (61.8%) displayed data at FU 2. The amount of dysfunction between the group of LUMC patients and the group originating from a different hospital and referred to LUMC, was not significantly different at FU 2: neither for micturition dysfunction (42.1% versus 48.3%; p=0.771) nor for defecation dysfunction (23.5% versus 45.5%; p=0.193), sciatica (57.9% versus 46.9%; p=0.565) or altered sensation of the saddle area (58.8% versus 63.6%; p=0.767). This reason for missing data was therefore not believed to have caused bias.

Apart from loss to follow up of patients belonging to a different original hospital, three other reasons for missing data in this retrospective design are: (1) the topic was not discussed and therefore no notes are available, (2) the topic was discussed, but no notes were taken, (3) the patient did not show up at FU moment. Especially for the latter two reasons, data is more likely to be missing when there are no complaints. To explore the extent of this bias – i.e. the hypothesis that data of patients with no complaints are more prone to be missing –patients with and patients without documented complaints at previous check-up were analyzed for the amount of available data (Figures 9-13). As is displayed, patients without documented complaints at their previous check-up, are more prone to have missing data (apart from the case of defecation dysfunction, which cannot be easily explained). Due to this fact, the authors have chosen to not use FU 3 as main outcome parameter, even more since FU 3 is more likely to be planned for patients with complaints, therefore contributing substantially to attrition bias when it would be used as a main outcome parameter.

Data on sexual function in this study was particularly scarce, as well at presentation as during follow up, which resulted in the inability of performing several analyses regarding sexual dysfunction. Limited data on sexual function is ubiquitous in CES patients in literature,[2] most likely due to barriers on both the patients side as well as on the doctor's side, which could unfortunately not be minimized in this retrospective study design. The nature of the available data on sexual dysfunction at presentation is striking: 25 out of 26 patients experienced sexual dysfunction. The fact that sexual function is more often documented for male patients than for their female counterparts is something that is believed by the authors to be due to both patient factors as well as doctor factors.[15]

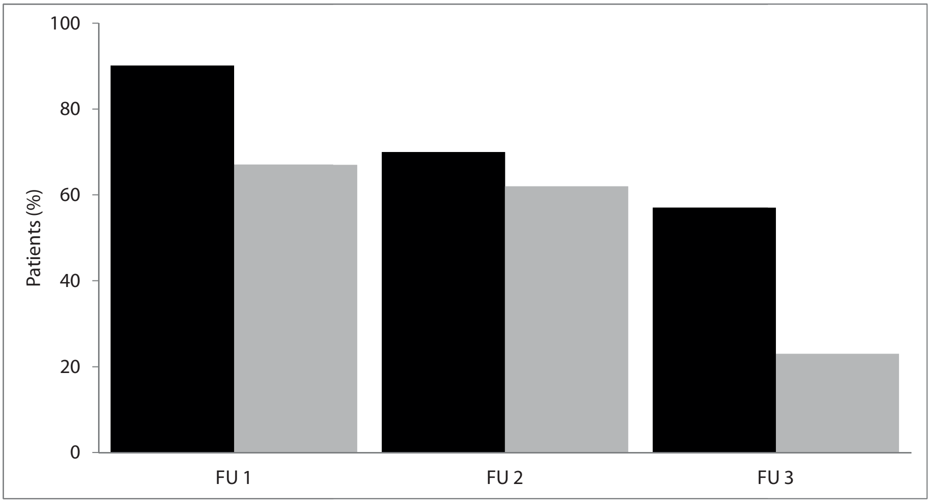

Figure 9 Availability of data on micturition. The proportion of available data per FU moment is stratified by patients for whom complaints were documented at the previous FU moment (black bar) and by patients for whom it was documented that there were no complaints at the previous FU moment (grey bar).

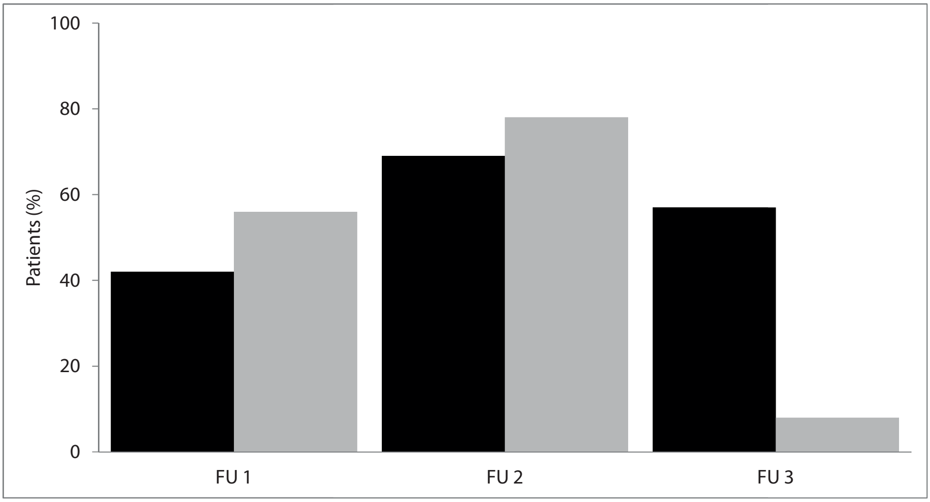

Figure 10 Availability of data on defecation. The proportion of available data per FU moment is stratified by patients for whom complaints were documented at the previous FU moment (black bar) and by patients for whom it was documented that there were no complaints at the previous FU moment (grey bar).

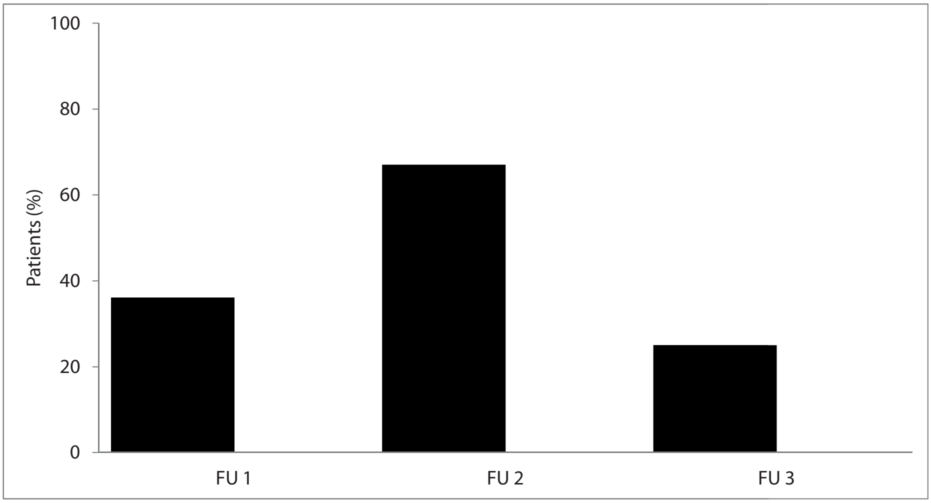

Figure 11 Availability of data on sexual function. The proportion of available data per FU moment is shown for patients for whom complaints were documented at the previous FU moment (black bar). For all patients for whom it was documented that there were no complaints at the previous FU moment, there was no data available at the next FU moment, therefore, there are no grey bars.

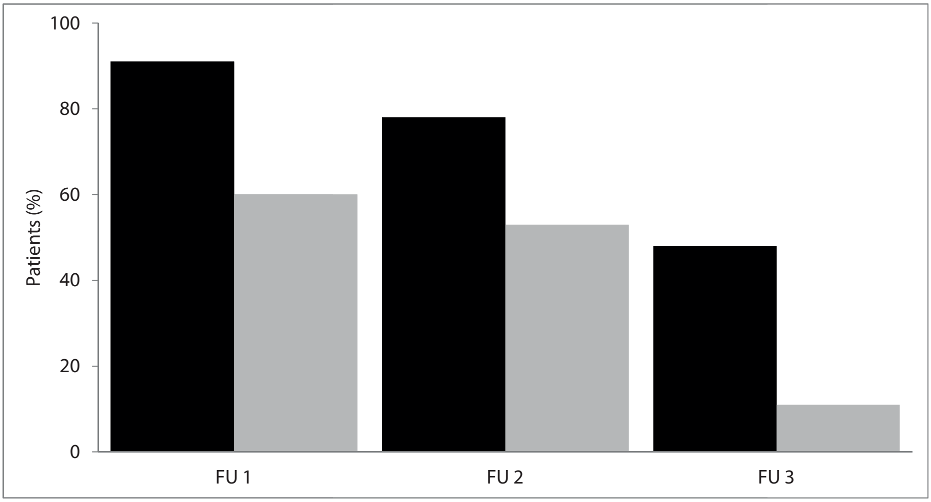

Figure 12 Availability of data on sensation of the saddle area. The proportion of available data per FU moment is stratified by patients for whom complaints were documented at the previous FU moment (black bar) and by patients for whom it was documented that there were no complaints at the previous FU moment (grey bar).

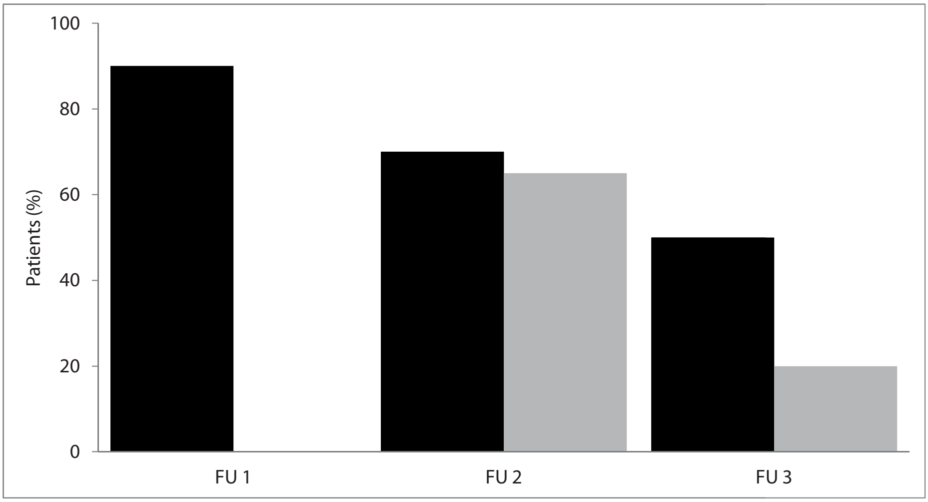

Figure 13 Availability of data on sciatica. The proportion of available data per FU moment is stratified by patients for whom complaints were documented at the previous FU moment (black bar) and by patients for whom it was documented that there were no complaints at the previous FU moment (grey bar). For all patients for whom it was documented that there were no complaints at presentation, there was no data available at FU 1, therefore, there is no grey bar at FU 1.

CONCLUSION

This is the largest single study about outcome in CES after decompression. It displays unique data about the outcome of micturition, defecation, sexual function, sciatica and altered sensation of the saddle area as well as presenting features of a large cohort of CES patients, proving that micturition, defecation and sexual dysfunction are common both at presentation and at follow up. Female patients were found to have significant more defecation dysfunction at presentation than their male counterparts. A shorter time to decompression was a risk factor for sciatica shortly after surgery (at FU 1), but not for long term outcome. Studies on correlation between imaging at presentation and outcome could help identifying the patients being more at risk at presentation. Missing data were handled with multiple imputation with analysis of possible bias. A follow up study is recommended for more long term follow up data. In conclusion, recovery after decompression for CES does take a long time and is not complete in a substantial number of cases; something for which we should adequately prepare our patients when diagnosing CES.

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CHAPTER 6

Lumbar spinal canal MRI diameter is smaller in herniated disc cauda equina syndrome patients

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Submitted to Neuroradiology

ABSTRACT

Introduction. Correlation between magnetic resonance imaging (MRI) and clinical features in cauda equina syndrome (CES) is unknown; nor is known whether there are differences in MRI spinal canal size between lumbar herniated disc patients with CES versus lumbar herniated discs patients without CES, operated for sciatica. The aims of this study are 1) evaluating the association of MRI features with clinical presentation and outcome of CES and 2) comparing lumbar spinal canal diameters of lumbar herniated disc patients with CES versus lumbar herniated disc patients without CES, operated because of sciatica.

Methods. MRIs of CES patients were assessed for the following features: level of disc lesion, type (uni- or bilateral) and severity of caudal compression. Pre- and postoperative clinical features (micturition dysfunction, defecation dysfunction, altered sensation of the saddle area) were retrieved from the medical files. In addition, anteroposterior (AP) lumbar spinal canal diameters of CES patients were measured at MRI. AP diameters of lumbar herniated disc patients without CES, operated for sciatica, were measured for comparison.

Results. 48 CES patients were included. At MRI, bilateral compression was seen in 82%; complete caudal compression in 29%. MRI features were not associated with clinical presentation nor outcome. AP diameter was measured for 26 CES patients and for 31 lumbar herniated disc patients without CES, operated for sciatica. Comparison displayed a significant smaller AP diameter of the lumbar spinal canal in CES patients (largest $p=0.002$). Compared to average diameters in literature, diameters of CES patients were significantly more often below average than that of the sciatica patients (largest $p=0.021$).

Conclusion. This is the first study demonstrating differences in lumbar spinal canal size between lumbar herniated disc patients with CES and lumbar herniated disc patients without CES, operated for sciatica. This finding might imply that lumbar herniated disc patients with a relative small lumbar spinal canal might need to be approached differently in managing complaints of herniated disc. Since the number of studied patients is relatively small, further research should be conducted before clinical consequences are considered.

INTRODUCTION

Cauda equina syndrome (CES) is a rare neurological complication caused by compression of the nerve roots of the cauda equina. CES is – according to literature consensus – defined by presence of one or more of the following symptoms: 1) bladder and/or bowel dysfunction, 2) reduced sensation of the saddle area and/or 3) sexual dysfunction, with possible neurologic deficit in the lower limb.[1] Several systems of sub classification of CES are described, of which the one reported by Gleave and MacFarlane is more commonly used: it distinguishes between CES-R/complete (characterized by painless, urinary retention) and CES-I/incomplete (characterized by urinary difficulties with e.g. sensory loss, but without retention and overflow incontinence), with CES-I believed to have better prognosis.[2] CES can be instigated by a variety of causative agents, such as lumbar herniated disc, tumour, infection, stenosis or hematoma. Lumbar herniated disc is the most common cause described in literature (45%);[1] CES provoked by other pathology is beyond the scope of this article.

The first publication of CES caused by lumbar herniated disc was by Dandy in 1929.[3] Mixter and Barr advocated five years later for prompt surgical decompression in all CES patients, which statement generated much publicity and propelled both research and clinical practice about sciatica and CES forward.[4] Since that time, CES is regarded as an emergency indication for surgery. The value of early surgery has been supported by – among others – the well-known meta-analysis of Ahn et al. (2000), which demonstrated that CES patients surgically decompressed within 48 hours have a significant better outcome of sensory, motor, urinary and rectal function compared to those being operated after 48 hours.[5]

The diagnosis of CES is based on a combination of clinical and imaging features. Interpretation of clinical features alone is difficult due to the great inter patient variation of symptoms. Magnetic resonance imaging (MRI) of the lumbar spine is the current modality of choice in any suspected case of CES to confirm diagnosis and to identify the causative agent and level of caudal compression.[6]

Two aspects about imaging in CES are interesting. Firstly, only 1-10% of patients with a known lumbar herniated disc develop CES.[7-9] It is not possible (yet) to predict which lumbar herniated disc patients will develop CES. By reasoning, a factor such as the (premorbid) size of the lumbar spinal might play a part in the development of clinically evident caudal compression in lumbar herniated disc patients. Exploring imaging characteristics that may herald a higher risk for CES in known lumbar herniated disc patients - such as spinal canal size - might create a unique opportunity for early surgery in lumbar herniated disc patients not yet affected by CES. Prevention is better than cure especially in CES, due to the rather disappointing postoperative outcome in CES patients.[10,11]

Secondly, the rationale behind the inter patient variation of CES complaints at presentation and the differences in posteropative recovery are not well understood. Some possible factors influencing outcome in CES have already been evaluated, of which time to decompression is the most frequently studied parameter.[5,12,13] The association between MRI and clinical CES features however, has never been studied. Associations between imaging and clinical features were evaluated before for other spinal diseases, such as spinal lumbar stenosis[14] and sciatica due to lumbar herniated disc.[15] Identifying MRI characteristics at presentation which are associated with a better or worse outcome of CES after decompressive surgery could substantially improve personalized postoperative care and could lead to a more tailor-made prognosis. Moreover, exploring the relationship between MRI and clinical features at presentation might add to current pathophysiological knowledge, e.g. whether degree of caudal compression at MRI correlates with severity of complaints. The current study is designed to 1) evaluate the association between MRI features and CES complaints at presentation, 2) evaluate the prognostic value of MRI features for outcome of CES complaints and to 3) compare the lumbar spinal canal diameter of operated lumbar herniated disc patients with CES, with the diameter of lumbar herniated disc patients operated because of sciatica without CES and to standardized diameters reported in literature.

MATERIAL AND METHODS

In a recent study, the authors described a cohort of 75 patients with CES due to lumbar herniated disc, identified by screening the medical records of all patients operated in the Leiden University Medical Centre (LUMC; university hospital and referral centre for complex spinal surgery) between 1995 and 2010, with the surgery code 'lumbar discectomy' or 'recurrent lumbar discectomy' (*n*=744 surgeries).[10] CES was defined by presence of one or more of the following symptoms: 1) bladder and/or bowel dysfunction, 2) reduced sensation in the saddle area and 3) sexual dysfunction, with possible neurologic deficit in the lower limb. Baseline characteristics and follow up data of identified CES patients were extracted from the medical records. The following items were extracted: gender; age at surgery; duration of complaints of CES at presentation; duration of complaints of herniated disc (defined by presence of sciatica) at presentation; time to decompression (counted from the moment of presentation with CES to first doctor); presence of micturition dysfunction, defecation dysfunction, altered sensation of the saddle area, sciatica (in case it was specified: bilateral or unilateral) and sexual dysfunction, all both at presentation and at two postoperative follow up moments: at discharge from the hospital (follow up moment 1, FU 1) and at check up at the outpatient department two months after surgery (follow up moment 2, FU 2).

For the current study, MRI scans of the lumbar spine of the identified CES patients were retrieved. MRIs had been performed in the LUMC or referring hospitals (Spaarne Gasthuis; Alrijne Hospital; Westfries Gasthuis; Langeland Hospital; Van Weel-Bethesda Hospital) following standardized imaging protocols (synchronized for sciatica study purposes) and were made at the time of presentation, thus prior to surgery. Retrieved MRIs were assessed by an experienced neurosurgeon specialized in spinal diseases, blinded for clinical information of the patient (CVL). The following MRI characteristics were recorded: 1) level of herniated disc; 2) severity of cauda equina compression (mild, moderate, severe) and 3) type of cauda equina compression (unilateral, bilateral). No patients with spinal degenerative changes other than herniated disc (e.g. stenosis) were included.

Anteroposterior (AP) diameter of the lumbar spinal canal was measured at mid-sagittal level at MRI in millimetres to the nearest tenth, for each disc level (L1-L2, L2-L3, L3-L4, L4-L5, L5-S1) and each mid-vertebral level (L1, L2, L3, L4, L5). The AP diameter at disc level was measured by drawing a line between the posterior border of the discus and the ligamentum flavum at the midline; for each mid-vertebral level, a line was drawn between the posterior border of the mid-vertebra and the ligamentum flavum. Levels with herniated disc were not measured. AP measurements were only done in MRI scans that were digitally available to maintain high levels of accuracy. For comparison of AP diameters, the AP diameters of a group of lumbar herniated disc patients without CES, operated in the same center because of sciatica, were also measured at MRI.

Statistical analysis

Analyses were done in SPSS Statistics 23.0 (SPSS Inc., Chicago, IL, USA). Patient characteristics were analyzed using frequencies. Investigating proportions between unpaired groups of categorical data was done with Chi Square test. Comparison of measurements of the spinal canal between CES patients and lumbar herniated disc patients with sciatica and without CES was done with Mann-Whitney U test. To evaluate the effect of MRI features on clinical presentation and outcome, binary logistic regression models were built, with MRI features as independent variables (severity of cauda equina compression; type of cauda equina compression i.e. unilateral or bilateral; level of disc lesion) and clinical features as dependent variable. Since there were 4 clinical features (presence of micturition dysfunction, defecation dysfunction, altered sensation of the saddle area and sciatica) measured at 3 different moments (at presentation, FU 1 and FU 2), 12 models were created. To correct for possible confounding, the following covariables were added: gender; age at surgery; duration of CES complaints at presentation; duration of complaints of herniated disc at presentation. Two extra covariables were added to the models evaluating clinical features at FU 1 and FU 2: 1) time to decompression and 2) the evaluated clinical feature at presentation (since dysfunction at presentation is correlated with dysfunction at the next follow up moment). Because of anticipated scarce data on sexual dysfunction, sexual dysfunction was not included in nor analyzed by any regression model. In case of quasi-complete separation of data, the concerning variable was not included in the regression model to maintain high quality analysis. Prior to running regression models, missing values of the following parameters were handled by multiple imputation with five imputation sets: duration of CES complaints at presentation; duration of sciatica at presentation; time to decompression; defecation dysfunction at presentation, at FU 1 and at FU 2; micturition dysfunction at FU 1 and at FU 2; altered sensation of the saddle area at FU 1 and at FU 2; sciatica at FU 1 and at FU 2. Some numerical data were grouped for analyses, e.g. time to decompression was stratified into six groups: <12 hours, 13-24 hours, 25-36 hours; 37-48 hours; 49-72 hours; >72 hours. Two-sided *p*-values<0.05 were considered statistically significant.

RESULTS

Due to MRIs that were not available in the archives of LUMC, 27 out of 75 CES patients were excluded. This resulted in a total of 48 included CES patients (Table 1) for whom MRIs were assessed (Table 2).

Table 1 Characteristics of CES patients at presentation (*n*=48)

	n
Male gender	22 (45.8%)
Mean age in years	42.9 (SD 10.5)
Median duration of complaints of herniated disc in days*	29 (range 1-1095)
Median duration of complaints of CES in hours**	48 (range 1-720)
Micturition dysfunction	42 (87.5%)
Altered sensation of the saddle area	44 (91.7%)
Sciatica	48 (100%)
Unilateral	24
Bilateral	22
Not specified	2
Defecation dysfunction***	28 (70.0%)
Sexual dysfunction****	13 (92.9%)

** available for n=46*
*** available for n=44*
**** available for n=40*
***** available for n=14*

Table 2 MRI characteristics at presentation (*n*=48)	*n* (%)
Level of lesion*	
L2-L3	2 (4.1)
L3-L4	4 (8.2)
L4-L5	19 (38.8)
L5-S1	24 (49.0)
Severity of cauda equina compression**	
Mild	10 (22.2)
Moderate	22 (48.9)
Severe	13 (28.9)
Type of cauda equina compression**	
Unilateral	8 (17.8)
Bilateral	37 (82.2)

**total level of lesions adds up to 49, since one patient had two lesions: at L4-L5 and at L5-S1*
***available for n=45*

All 48 patients had been surgically decompressed by open discectomy. Timing to decompression was available for 45 patients and was most commonly within 24 hours (*n*=23) and between 24 to 48 hours (*n*=14). Three patients were decompressed after 48 hours, but within 72 hours. Five patients underwent decompressive surgery more than 72 hours after presentation to the first doctor with time to decompression of 96 hours (*n*=2), 120 hours (*n*=1), 138 hours (*n*=1) and 216 hours (*n*=1). Delay was caused by both patient and doctor. Surgery was performed within 24 hours (*n*=3) and within 48 hours (*n*=2) after first presentation to the neurosurgeon. Follow up moments took place at two intervals: first follow up moment (FU 1) had a median of 48 hours postoperatively (range 8-336 hours), second follow up moment (FU 2, available for *n*=34) demonstrated a median of 56 days (4-300 days).

Association between MRI features and clinical presentation

Thirty-seven patients CES (82%) displayed bilateral compression of the cauda equina at MRI, of whom 19 (51%) indicated that their sciatica was unilateral. There was no correlation between MRI and history of the patient for location of sciatica (*p*=0.631). MRI features (severity of cauda equina compression; type of cauda equina compression i.e. unilateral or bilateral; level of disc lesion) were not associated with absence or presence of any of the clinical features (thus micturition dysfunction, defecation dysfunction, altered sensation of the saddle area or sciatica).

A trend was seen for defecation dysfunction at presentation with the covariable gender, albeit not significant (*p*=0.061): women more often suffered from defecation dysfunction at presentation.

NB the MRI feature 'type of compression' (i.e. uni- or bilateral) was removed from the models evaluating micturition at presentation and at FU 1 and altered sensation of the saddle area at FU 2 due to quasi-complete separation (almost all patients without micturition dysfunction had bilateral compression, and almost all patients with altered sensation of the saddle area had unilateral compression). The model evaluating effects of MRI on sciatica at presentation was not run due to separation of data (all patients suffered from sciatica at presentation).

Association between MRI features and clinical outcome

MRI features were not demonstrated to be associated with outcome of micturition, defecation, sciatica or altered sensation of the saddle area. The covariable time to decompression was correlated with sciatica at FU 1: a shorter FU time correlated with more sciatica at FU 1 (*p*=0.043); this correlation disappeared at FU 2. NB the covariables sciatica and altered sensation of the saddle area at presentation were removed from the models evaluating clinical outcome of those functions due to quasi-complete separation (features were present in (almost) all patients at presentation).

Anteroposterior (AP) diameter of the lumbar spinal canal in CES

For 26 CES patients, MRI scans were digitally available and used to measure the AP diameter of the lumbar spinal canal. For comparison, AP diameters of 31 lumbar herniated disc patients without CES, operated because of sciatica, were also measured. Patient characteristics known to possibly influence spinal canal size (age, gender) were compared between groups (CES patients with AP measurements; CES patients without AP measurements; lumbar herniated disc patients without CES operated because of sciatica) and were non-significant (Table 3). The results of the measurements however, did differ: CES patients displayed a statistically significant smaller lumbar spinal canal diameter at all levels, both disc levels as well as mid-vertebral levels compared to sciatica patients without CES (largest *p*=0.002; Table 4 and Figures 1-10).

Table 3 Baseline characteristics of CES patients versus sciatica patients

	CES patients without measurements *n*=22	CES patients with measurements *n*=26	Sciatica patients *n*=31	*p* -value
Male gender (%)	8 (36.4)	14 (53.8)	12 (38.7)	0.396
Mean age in years (SD)	42.3 years (11.2)	43.4 years (10.1)	41.1 (10.6)	0.836

Table 4 Measurements of the spinal canal. The mean sagittal diameter of the spinal canal, measured in millimetres to the nearest tenth. Compared between CES patients and herniated disc patients without CES, operated because of sciatica.

	CES patients (*n*=26)			**Sciatica patients (*n*=31)**			***p*-value**
	Missing*	Mean ±SD	Min-max	Missing**	Mean ±SD	Min-max	
L1	0	14.06±1.99	10.0-18.0	0	16.10±1.40	14.0-18.0	<0.001
L1-L2	0	12.92±3.19	6.0-20.0	0	15.58±1.52	12.0-18.0	<0.001
L2	0	12.90±2.60	7.0-18.0	0	15.26±1.37	13.0-18.0	<0.001
L2-L3	1	11.88±2.40	6.0-16.0	0	14.55±1.77	11.0-18.0	<0.001
L3	0	11.54±2.16	7.0-16.0	0	14.32±1.72	11.0-17.0	<0.001
L3-L4	3	10.91±2.01	6.0-15.0	1	13.23±1.63	10.0-16.0	<0.001
L4	0	10.58±2.02	7.5-14.0	0	14.13±1.77	11.0-18.0	<0.001
L4-L5	8	10.06±2.30	5.0-14.0	11	12.75±2.51	9.0-20.0	0.002
L5	2	9.94±1.60	7.0-14.0	0	13.87±2.17	10.0-20.0	<0.001
L5-S1	15	9.09±2.35	5.5-14.0	22	15.56±2.40	12.0-20.0	<0.001

**not measured due to herniated disc (n=27, 1 patient had a double lesion); quality too poor at specific level for measurement (n=2, at L5)*

***not measured due to herniated disc (n=33); quality too poor at specific level for measurement (n=1, at L5-S1)*

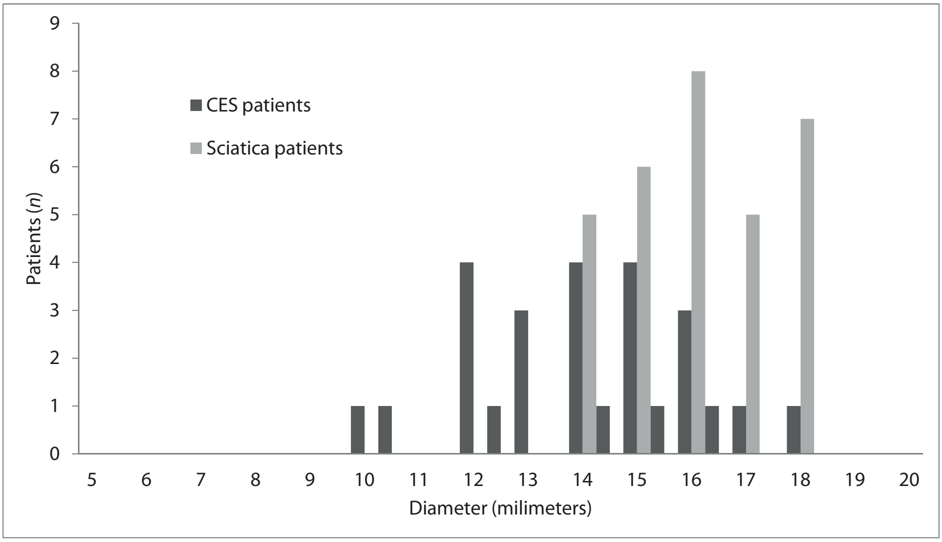

Figure 1 Distribution of the sagittal diameter of the spinal canal at L1

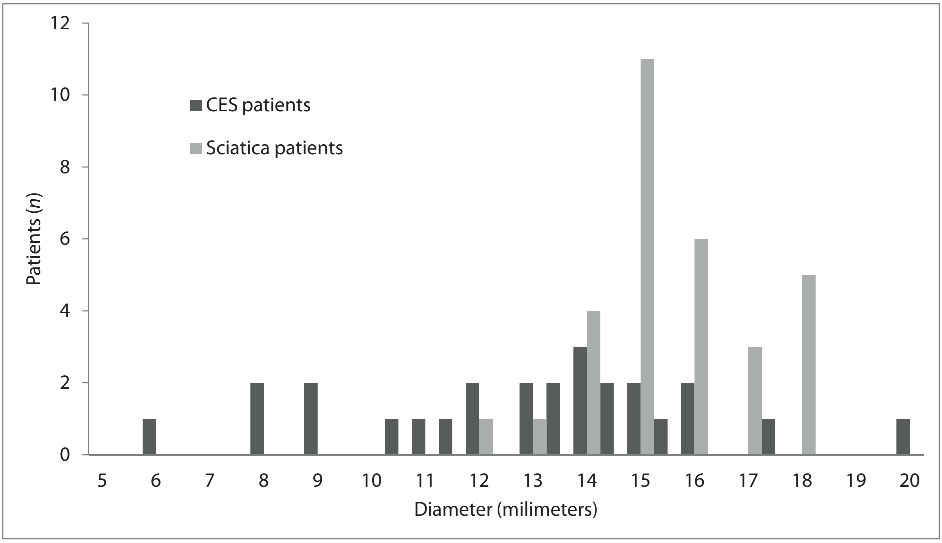

Figure 2 Distribution of the sagittal diameter of the spinal canal at L1-L2

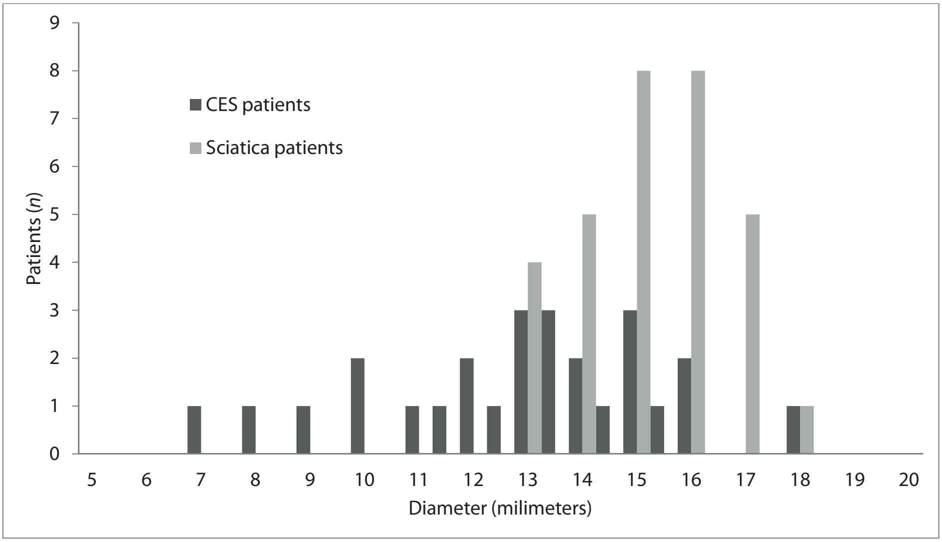

Figure 3 Distribution of the sagittal diameter of the spinal canal at L2

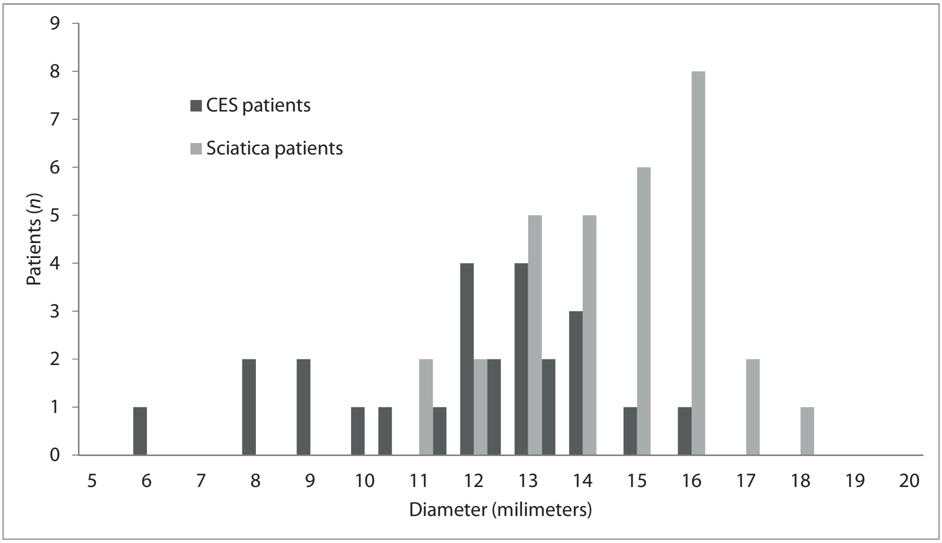

Figure 4 Distribution of the sagittal diameter of the spinal canal at L2-L3

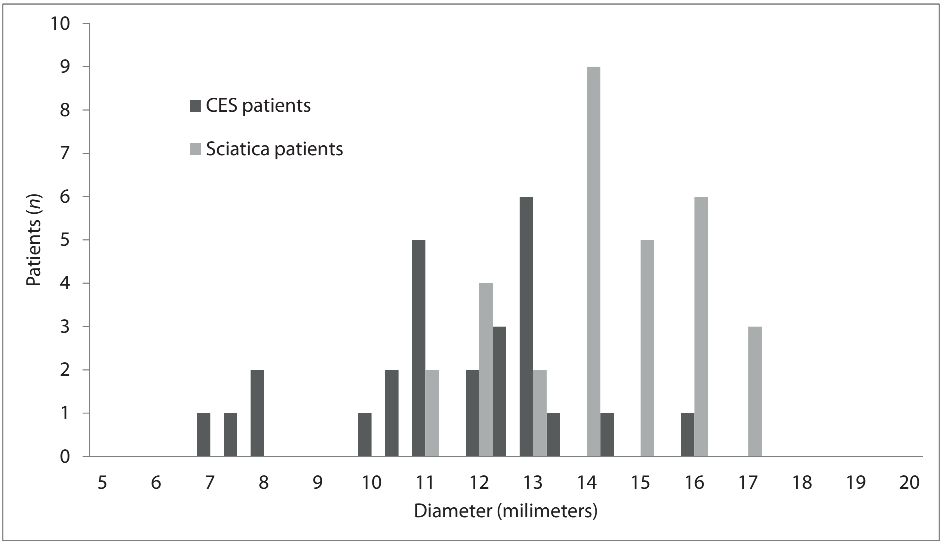

Figure 5 Distribution of the sagittal diameter of the spinal canal at L3

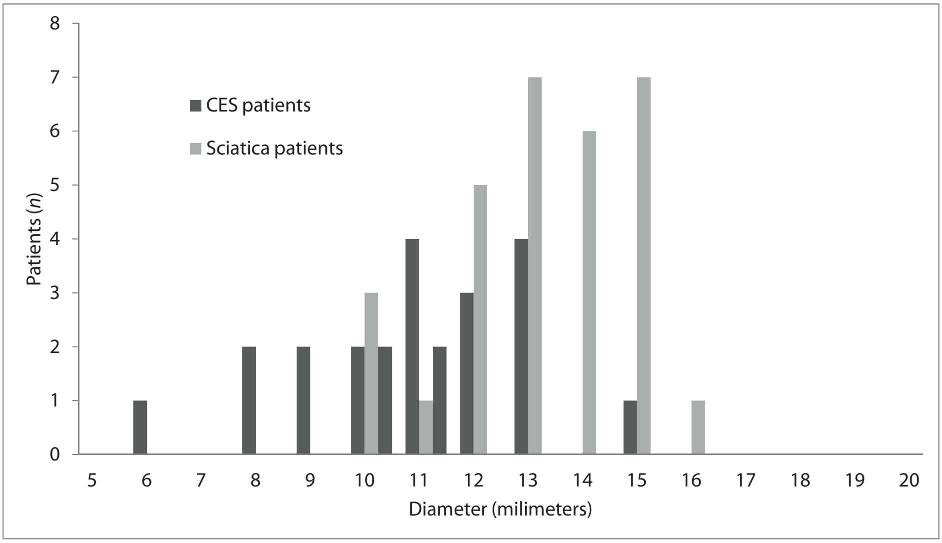

Figure 6 Distribution of the sagittal diameter of the spinal canal at L3-L4

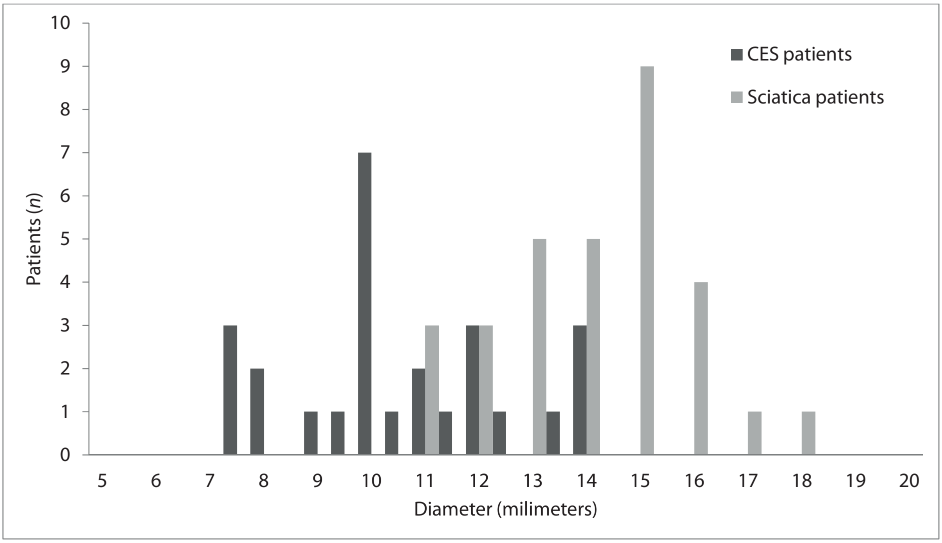

Figure 7 Distribution of the sagittal diameter of the spinal canal at L4

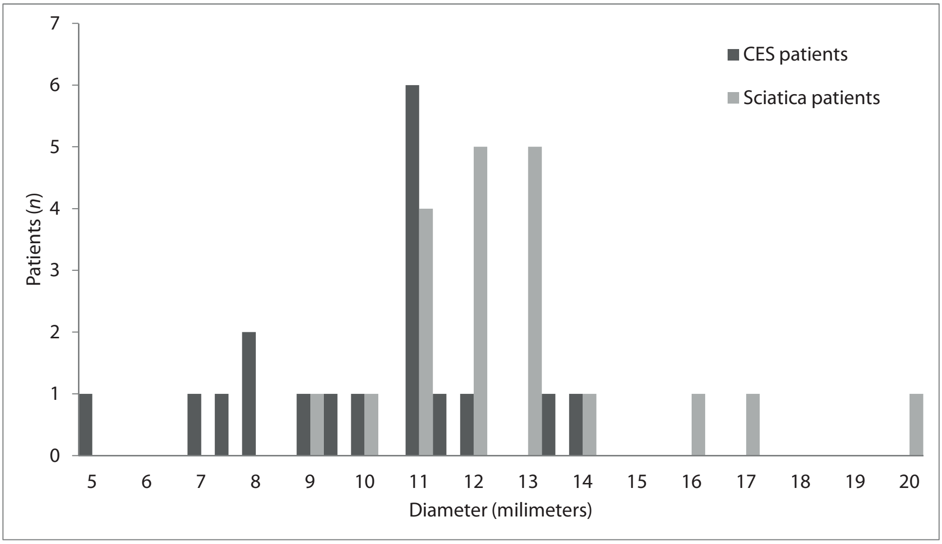

Figure 8 Distribution of the sagittal diameter of the spinal canal at L4-L5

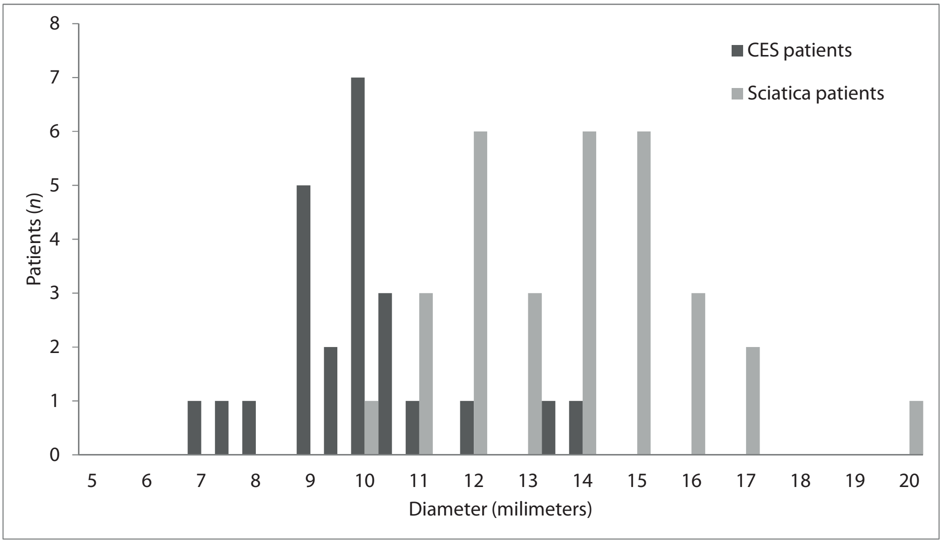

Figure 9 Distribution of the sagittal diameter of the spinal canal at L5

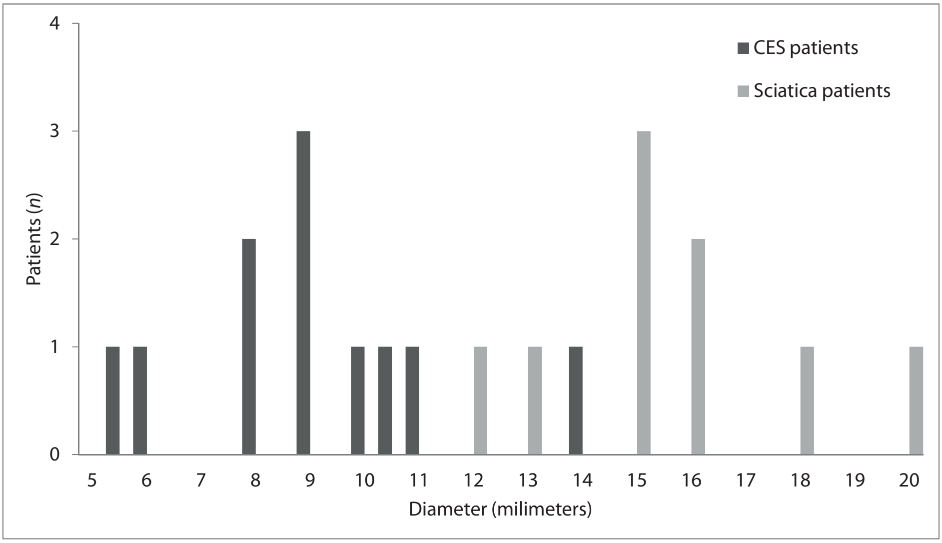

Figure 10 Distribution of the sagittal diameter of the spinal canal at L5-S1

To compare the measured AP diameters of the CES patients and the sciatica patients with standardized spinal canal diameters reported in literature, studies with a normative distribution of the AP diameter of the lumbar spinal canal, measured at MRI, were searched. Some identified studies were not suitable for this comparison since the measured population was biased (e.g. patients referred for low-back pain),[16,17] because the study lacked an exact definition of the subjects for which measurements were taken[18] or because no measurements were available at disc level.[19] The study of Chatha et al. seemed most appropriate for comparison.[20] It describes measurements of the spinal canal in 100 British, symptom-free patients (mean 62 years), who were referred for MRI to screen for presence of metastatic disease without subsequently having evidence of spinal tumours at the concerning MRI. Even though the study of Chatha et al. is subject to selection bias, the sample size is rather large and patients are quite comparable to the patients in the current study with regard to age, and, in addition, probably quite comparable in terms of race (predominantly Caucasian). In addition, it reports spinal canal size both at intervertebral and disc level, in contrast to aforementioned studies.

In order to compare the findings of the current study with the measurements reported by Chatha et al., the average AP spinal canal diameter reported by Chatha et al. was taken as a cut off value. For both the CES patients and the lumbar herniated disc patients without CES, operated because of sciatica, the proportion below the cut off value was indicated (Table 5).

Table 5 Proportion with smaller than average diameter. The average sagittal diameters that are used as cut off values are the ones reported by Chatha et al.[20]*

	% CES patients (*n*=26)	% Sciatica patients (*n*=31)	*p*- value
L1	53.8	16.1	0.003
L1-L2	84.6	54.8	0.016
L2	50.0	12.9	0.002
L2-L3	96.2	64.5	0.004
L3	65.4	16.1	<0.001
L3-L4	84.6	51.6	0.001
L4	80.8	19.4	<0.001
L4-L5	61.5	35.5	0.021
L5	88.5	32.3	<0.001
L5-S1	38.5	29.0	<0.001

**cut off values (in mm): L1<14.1; L1-L2<15.6; L2<13.2; L2-L3<15.1; L3<12.6; L3-L4<13.8; L4<12.4; L4-5<12.9; L5<12.4; L5-S1<11.6*

DISCUSSION

As a major finding, this study clearly demonstrates that patients with CES due to lumbar herniated disc have a significant smaller AP lumbar spinal canal diameter than patients with lumbar herniated disc without CES (operated because of sciatica), applying to all mid-vertebral as well as disc levels. No associations between MRI features and clinical presentation or outcome of CES were identified. Even though the presented cohort is limited, these results may contribute to a beginning of understanding the etiology of CES in herniated disc patients. In addition, the first finding might have potential implications for the selection of lumbar herniated disc patients for decompressive surgery.

Relation to literature

Spinal canal size of CES patients has not been studied before, however, studies about spinal canal size in patients with other spinal diseases are available: Haig et al. for example, compared patients with low back pain, sciatica and lumbar spinal stenosis with controls, concluding that there is no significant difference between patients and healthy subjects with regard to spinal canal measurements.[21]

No associations between MRI and clinical features at presentation or outcome of CES were identified in this study. Since this is the first study to evaluate this correlation, no references are available to state these results. Similar studies have been performed for other spinal diseases such as sciatica[15] or lumbar spinal stenosis,[14,22-24] displaying no correlation between imaging and clinical features, being in line with the current study. The suggestion that other factors than the spinal canal size alone - such as local neurovascular problems, venous obstruction or effect of local inflammatory cytokines – contribute to differences in clinical manifestation of CES, seems sensible.[21]

A non-significant trend was seen between the covariable gender and defecation dysfunction at presentation, namely: female gender was associated with more defecation dysfunction at presentation (non-significant: p=0.061). This finding correlates with current literature stating that e.g. constipation is more common in women than in men, in both CES population as well as in the general population.[25,26]

The covariable time to decompression was correlated with sciatica at FU 1: a shorter time to decompression was associated with more sciatica (p=0.0043), which correlation was not demonstrated for FU 2. This finding does not refute the beneficial effects of early decompression which was demonstrated by others,[5,12,13,27-30] but rather indicates a correlation between factors indicating a worse prognosis and shorter time to decompression (guided by clinical decision making), such as acute compression of the cauda equina, which is believed to have a worse prognosis than a more gradual compression.[27,31]

Implications

If there truly is a difference in lumbar spinal canal size between lumbar herniated disc patients with CES and lumbar herniated disc patients without CES, operated because of sciatica, this might imply that sciatica patients with a small lumbar canal may need to be approached differently in managing complaints. Since this is the only study presently available that evaluated this correlation – and since the setting was retrospective – further prospective research should be conducted before clinical consequences are considered and changes of guidelines are obligatory. A prospective follow up study among sciatica patients would be suitable - measuring the AP diameters at MRI at presentation and ensuring adequate follow up - and permits to correlate the incidence of CES with documented spinal canal size and other MRI features. In case of development of CES, clinical signs and symptoms should be recorded and adequate long term postoperative follow up should take place to evaluate the predictive value of MRI characteristics.

MRI and clinical features were not found to be correlated in the current study. Even though this study has a rather large study population when compared to other CES studies, the limited number of included patients might have caused an inability to detect significant correlations between MRI and clinical features. Aforementioned study proposal with a substantially large cohort and prospective design should be able to give more insights into the predicting value of imaging features in CES patients.

Limitations

The retrospective design of this study introduces information bias, e.g. complaints might be reported in the file differently than they were meant by the patient, notes are interpreted differently by the researcher than the clinician originally meant, or notes are simply missing. It is impossible to eradicate this bias completely in the current study design, however, the authors believe bias was minimized by careful assessment of medical notes. Multiple imputation was used to deal with missing values, which was believed to be non-problematic due to the assumption of missing at random. The alternative to multiple imputation would be a complete case analysis, which was believed to be more prone to bias.[32]

Potential selection bias is introduced with regard to 1) the included CES patients and 2) the samples of CES and sciatica patients for which AP diameter were measured. Firstly, the inclusion criteria of this study correspond to the most used definition of CES. Indeed the broadness of this definition naturally introduces heterogeneity within the studied population. However, this heterogeneity is inherent to CES and is exemplified by the diversity of clinical manifestations. Division into different groups to create more homogeneity per group (by for example using the groups of Tandon and Shankaran[33] or by the groups CES-R and CES-I[2]) could be interesting in case of a larger cohort, preferably with prospective design. Dealing with the current cohort size and retrospective study design however, substantial risk of improper grouping and thus low quality analysis lures when dividing included patients into different groups.

Secondly, as was demonstrated in the Results section, CES patients for whom AP diameters were taken form a representative sample of the complete CES cohort and are also similar to the sampled sciatica patients without CES in terms of age and gender, parameters known to influence measurements.[14,34,35] Height was not available retrospectively and therefore not included; however, this parameter was described previously as a possible influencer of spinal canal measurements.[36] Therefore, height as a confounder cannot be completely eradicated in the current study.

All presented CES and sciatica patients were operated in LUMC. Since LUMC is the appointed centre for CES surgery, some CES patients originated from referring centres (e.g. Alrijne Hospital, Spaarne Hospital). Because the referring centres do not refer uncomplicated sciatica patients to LUMC, the sciatica patients operated in LUMC either originate from LUMC or were referred due to anticipated high-complex surgery. This is a potential source of bias. However, since high-complex surgery in sciatica patients is often due to an anticipated small spinal canal, it is unlikely that inclusion of merely LUMC sciatica patients has led to a larger spinal canal size difference between sciatica and CES patients (e.g., the spinal canal diameters of those LUMC sciatica patients are more likely to be smaller than average than larger).

In this study, no information about degree of decompression is available (i.e. no evaluation of MRI scans was done postoperatively). This could introduce some bias in correlating outcome with the MRI features at presentation: in case decompression was less successful, certainly, more complaints will persist at follow up, which might be not related to the initial MRI features at presentation. However, since all patients were decompressed by similar technique, variations in decompression were expected to be minimal.

This study used mid-sagittal AP diameter as indicator of spinal canal size instead of area measurements. AP diameter is proven to be well correlated with area measurements[37] and is currently the measurement most often used in studies relating to spinal canal size. The authors thus believe AP diameter to be a reliable indicator of spinal canal size. The quite recently introduced "reduced interlaminar angle" was proven to be a relevant measurement in the stenotic population in particular, however, was seen as less relevant in the current study population.[38]

CONCLUSION

There is a difference in lumbar spinal canal size between operated lumbar herniated disc patients with CES and lumbar herniated disc patient without CES, operated because of sciatica. No other MRI characteristics as predictors for presentation or outcome of CES are identified. This finding might imply that sciatica patients with a relative small spinal canal might need to be approached differently in managing complaints of herniated disc, to prevent progression to CES. This hypothesis has to be tested in future studies. Since the current study was retrospective and the number of studied patients relatively small, further prospective research should be conducted before clinical consequences and guideline changes are considered.

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CHAPTER 7

The long term outcome of micturition, defecation and sexual function after spinal surgery for cauda equina syndrome

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PLoS One. 2017;12(4):e0175987

ABSTRACT

Background. Cauda equina syndrome (CES) is a rare neurologic complication of lumbar herniated disc for which emergency surgical decompression should be undertaken. Despite the common belief that the restoration of functions that are affected by CES can take several years postoperatively, follow up seldom exceeds the first year after surgery. Long term outcome of especially micturition, defecation and sexual function - which are by definition affected in CES - are unknown.

The aim of this study is to evaluate 1) postoperative long term outcome of micturition, defecation and sexual function in CES patients 2) attitude of patients towards received hospital care with regard to (recovery of) these functions.

Methods. CES patients were selected by screening the records of all patients operated on lumbar herniated disc in our university hospital between 1995-2010. A questionnaire was sent to the selected CES patients evaluating current complaints of micturition, defecation and sexual function and attitude towards delivered care with focus on micturition, defecation and sexual function.

Results. Thirty-seven of 66 eligible CES patients were included (response rate 71%, inclusion rate 56%). Median time after surgery was 13.8 years (range 5.8 – 21.8 years). Dysfunction at follow up was highly prevalent: 38% micturition dysfunction, 43% defecation dysfunction and 54% sexual dysfunction. Younger age at presentation was associated with sexual dysfunction at follow up: for every year younger at presentation, odds ratio for sexual dysfunction at follow up was 1.11 (p=0.035). Other associations with outcome were not identified. Two-third of the CES patients wished their neurosurgeon had given them more prognostic information about micturition, defecation and sexual function.

Conclusion. The presented data demonstrate that dysfunction of micturition, defecation and sexual function are still highly prevalent in a large number of CES patients even years postoperatively. These alarming follow up data probably have a devastating effect on personal perceived quality of life, which should be studied in more detail. CES patients communicate a clear demand for more prognostic information. The presented figures enable clinicians to inform their CES patients more realistically about long term outcome of micturition, defecation and sexual function after surgical intervention.

INTRODUCTION

Cauda equina syndrome (CES) is a rare condition caused by compression of several nerve roots of the cauda equina, including lower sacral nerves influencing the bladder, rectal and genital function, most often due to a herniated disc.[1] Its classical presentation consists of loss of sensation of the saddle area, sphincter dysfunction (bladder and/or bowel) and/or sexual dysfunction, often in combination with motor deficit with or without reflex changes of the lower limbs.[1,2] Diagnosis is mostly performed on clinical grounds followed by magnetic resonance (MR) or computed tomography (CT) imaging demonstrating the exact location of compression and its causal element. Surgical spinal decompression by bone and herniated disc removal is the only effective measurement that should be taken as soon as possible in case CES is diagnosed. The influence of timing of surgery on outcome has been a topic of hot debate in literature and there is now substantial evidence that decompression within 48 hours yields significantly better outcomes than decompression after 48 hours.[3]

Literature about evidence in timing of surgery for CES is limited in two distinctive ways. Firstly, outcome measurements in published studies are mainly concentrated around bladder function, motor function, general quality of life and sciatic pain. Details about outcome of defecation and/or sexual function are only marginally described, even though those functions are, by definition, often impaired in patients with CES.[2,4,5,6,7] Reasons for this trend are varying, but especially the embarrassment accompanying the conversation about these topics – from the perspective of the patient as well as the doctor – should not be underestimated.

Secondly, follow up of CES patients by neurosurgeons or neurologists rarely passes the first few years after first encounter. Obviously, some studies do include individual patients with follow up of several years, however, those patient numbers are small ($n \leq 8$ patients)[8-9] and evaluation of outcome seldom includes defecation and sexual function.[10-23] Since it is known that both urethral and anal sphincter function can improve even after several years post-surgery,[8,10,24,25] it seems sensible to evaluate long term outcome up to a decade or more after decompressive surgery, next to the evaluation after one or two years.

The lack of information about long term recovery of micturition, defecation and sexual function is bothersome in the case of CES in particular. CES patients pre-eminently face a long period of recovery and the lack of prognostic data prevents the clinician from informing CES patients about recovery prospects of micturition, defecation and sexual dysfunction. This poses the patient in a position of maximum uncertainty. The fact that micturition, defecation and especially sexual function are topics which are difficult to discuss, makes the patient and his or her partner even more prone to discomfort and isolation when experiencing complaints. Aims of this study are therefore to evaluate 1) the outcome of CES after surgical decompression with a minimum follow up of several years, and with a particular interest in micturition, defecation and sexual function; 2) predictors for outcome of these functions; 3) the attitude of CES patients toward delivered hospital care before and after decompressive surgery.

MATERIAL AND METHODS

In a previous publication, the authors described a cohort of 75 patients with cauda equina syndrome (CES), focusing on presentation and outcome up to several months postoperatively.[7] The cohort was selected through screening medical records of patients who had surgery in the Leiden University Medical Centre (LUMC; referral hospital for spinal surgery) with surgery code "lumbar discectomy" or "recurrent lumbar discectomy" between January 1995 and September 2010. According to consensus of literature, definition of CES was set by presence of one or more of the following: 1) dysfunction of micturition and/or defecation, 2) altered sensation of the saddle area, 3) sexual dysfunction, with possible neurologic deficit in the lower limbs (motor or sensory loss or reflex changes).[1,2]

For the current study, contact details of all 75 patients were traced after approval of the local medical ethical committee was granted. In case of death, elusive contact details or otherwise inability to communicate, a patient was considered ineligible for the study. Patients were sent a questionnaire (hard copy) with an accompanying letter explaining the contents of the study and an informed consent form that had to be returned together with the questionnaire.

The questionnaire (not validated) covered the following items: 1) medical history; 2) whether complaints of micturition, defecation, sexual dysfunction, altered sensation of the saddle area and/or sciatica were discussed at first presentation to the neurosurgeon; 3) whether complaints of micturition-, defecation- and sexual dysfunction were present at the time of the postoperative visit at the outpatient department (by default several weeks after surgery); 4) whether the neurosurgeon had paid enough attention to aforementioned complaints during the visit at the outpatient department; 5) whether complaints of micturition, defecation and/or sexual dysfunction are currently present; 6) whether the neurosurgeon – before or after decompressive surgery – had said anything about the prognosis of micturition, defecation and/or sexual function; 7) whether the patient had wished for more information from the neurosurgeon about the prognosis of micturition, defecation and sexual function.

After the initial invitation by hard copy mail, patients which had not sent back the questionnaire were contacted by telephone and asked whether they wanted to participate in the study. If so, a second questionnaire was sent (hard copy). Data of Case Record Forms were collected in Excel and imported in IBM SPSS Statistics version 23.0.

In addition, the following patient characteristics were collected from the medical file: gender; age at surgery; level of herniated disc according to file; duration of complaints of herniated disc at presentation (defined by onset of sciatica); duration of CES complaints at presentation; micturition/defecation/sexual dysfunction at presentation according to file; time between presentation to first doctor and decompressive surgery (in hours). To correlate the patients experiences with the medical file, medical notes about micturition/defecation/sexual function at follow up at the outpatient clinic were collected from the medical file as well.

Statistical analysis

IBM SPSS Statistics version 23.0 was used for analysis. Comparing independent groups with categorical variables was done with Chi Square test; Mann-Whitney U test was used in case of numerical variables. For comparisons between paired groups of categorical variables, McNemar's test was done. Binary logistic regression models were used to evaluate predictors for micturition, defecation and sexual dysfunction at long term follow up, with inclusion of the following variables: gender; age; duration of complaints of herniated disc at presentation; duration of complaints of CES at presentation; time to decompression. Dysfunction of defecation at presentation (according to the file) was added to the models for micturition and sexual dysfunction at follow up; dysfunction of micturition at presentation (according to the file) was added to the models for defecation and sexual dysfunction at follow up. Before running the regression models, missing data was imputed using five imputation sets for the following variables: duration of complaints of herniated disc (n=2 missing); duration of complaints of CES (n=2 missing); defecation dysfunction at presentation (n=7 missing). For the regression model, time to decompression was stratified into six groups: <13 hours; 13-24 hours; 25-36 hours; 37-48 hours; 49-72 hours; >72 hours.

RESULTS

Baseline

Thirty-seven patients were included (Figure 1). Response rate was 71% (10 additional patients responded with a wish to not participate).

Patient characteristics (retrieved from the medical file) are depicted in Table 1. Baseline characteristics of patients who responded (gender; age at surgery; duration of herniated disc complaints at presentation; duration of CES complaints at presentation; prevalence

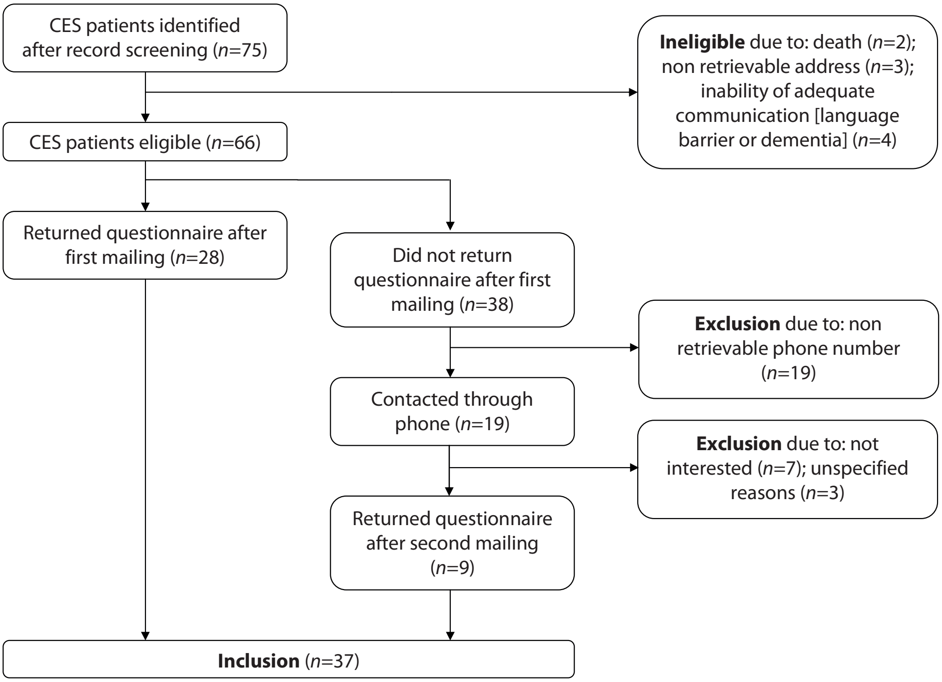

Figure 1 Inclusion of patients

of dysfunction at presentation) were compared with non-responders and revealed no statistically significant differences (smallest *p*=0.174).

The majority of patients was referred to the LUMC by neurologists from referring hospitals (*n*=29). The remaining were referred by neurologists from the LUMC (*n*=6), by doctors in the accidents & emergency department of the LUMC (*n*=1) or by the general practitioner (*n*=1). All patients were surgically decompressed. Time to decompression was 7-12 hours (*n*=2), 13-24 hours (*n*=21), 25-48 hours (*n*=11), 49-72 hours (*n*=1) or >72 hours (*n*=2). Surgical decompression of the latter two patients was delayed primarily by the first doctor to whom they presented: decompressive surgery took place within 24 hours after first presentation to the neurosurgeon (exact start of CES complaints before presentation was not retrievable from the medical file) and within 72 hours after first presentation to the neurosurgeon (start of CES complaints was 21 days before presentation: extreme patient delay).

When asked what they had discussed with the neurosurgeon at presentation, most patients mentioned altered sensation of the saddle area (*n*=24), sciatica (*n*=24) and dysfunction of micturition (*n*=24). Only 9 patients reported to have discussed dysfunction of defecation. One patient did not answer this question with regard to sexual dysfunction, of the remaining 36 patients, 5 indicated to have discussed sexual dysfunction at the moment of presentation (of whom 2 male and 3 female).

Table 1 Patient characteristics at presentation (*n*=37)

	n
Male gender	18 (48.6%)
Mean age in years	44.6 (SD 10.2)
Median duration of complaints of herniated disc in days[I]	30 (range 1-5110)
Level of disc lesion according to file[II]	
L1-L2	1
L2-L3	2
L3-L4	1
L4-L5	12
L5-S1	21
L6-S1	1
Median duration of complaints of CES in hours[III]	48
Micturition dysfunction	34 (91.9%)
Altered sensation of the saddle area	36 (97.3%)
Sciatica	35 (94.6%)
Defecation dysfunction[III]	23 (76.7%)
Sexual dysfunction[IV]	12 (100%)
Decreased anal sphincter tone[V]	18 (64.3%)
Decreased anal sphincter reflex[VI]	13 (56.5%)

[I] *available for n=35*
[II] *total adds up to 38 due to one patient with a double lesion (L2-L3 and L4-L5)*
[III] *available for n=30*
[IV] *available for n=12*
[V] *available for n=28*
[VI] *available for n=23*

Follow up at the outpatient department

The median time between surgery and follow up of CES patients at the outpatient department (FU OPD) was 56 days postoperatively. One respondent did not answer any question about FU OPD, two additional respondents did merely not answer the question about sexual dysfunction at FU OPD. Patient reported data (retrieved from the questionnaires) and doctor reported data (retrieved from the medical files) are mentioned separately and, in addition, are compared to each other.

Micturition

Patient reported data demonstrated 58.3% (21/36) dysfunction of micturition. Doctor reported data displayed dysfunction in 37.0% (27 files with micturition documentation, 10 marked as dysfunction). The differences in reporting dysfunction between patient and doctor data did not reach statistical significance (p=0.289).

Defecation

Patient reported data displayed 47.2% (17/36) dysfunction of defecation. Doctor reported data demonstrated dysfunction in 23.8% (21 files with defecation documentation, 5 marked as dysfunction). The differences in reporting dysfunction between patient and doctor data did not reach statistical significance (*p*=0.219).

Sexual dysfunction

Patient reported data revealed 55.9% (19/34) sexual dysfunction (of whom 9 male and 10 female). Doctor reported data were lacking, since only 7 files contained documentation about sexual function (5 male and 2 female): 4 were indicated to have dysfunction (3 male, 1 female). The differences in reporting dysfunction between patient and doctor data revealed no statistical significant differences (*p*=1.000).

Whether the neurosurgeon had paid enough attention to complaints of micturition, defecation and sexual function at FU OPD was answered by 28/37 patients (no response *n*=4, 'not applicable' *n*=5). One quarter (7/28) judged that the neurosurgeon did not pay enough attention to their complaints at FU OPD; 5 of them were female.

Long term follow up

The median follow up time at the moment of answering the questionnaire was 13.8 years after decompressive surgery (range 5.8 – 21.8 years). Mean age at long term follow up was 57.8 years (SD 11.6). None of the patients reported current medical conditions likely to influence micturition and defecation. Three patients reported to suffer from diabetes mellitus, which was considered by the authors as a disease possibly influencing sexual function.

Micturition

Micturition dysfunction secondary to CES was present in 37.8% (14/37). Complaints that were mentioned: catheterization (*n*=3); incontinence (*n*=1); abnormal sensation of voiding (*n*=3); combination of the latter two (*n*=4); inability to void completely (*n*=1); combination of abnormal sensation of voiding, incontinence and unable to void completely (*n*=1); not specified (*n*=1). Another 5 patients reported 'new' complaints that were not present at FU OPD and thus not designated as caused by CES (designated causes: prostate problems [*n*=3], gynaecological prolapse [*n*=1], surgery [*n*=1]). One additional patient (male, 52 years old) indicated micturition problems at FU OPD but mentioned dripping as his only current complaint, which was regarded as prostate problems.

Defecation

Defecation dysfunction secondary to CES was present in 43.2% (16/37). Complaints that were mentioned: abnormal sensation of passing stool (*n*=4); abnormal sensation of passing stool and incontinence (*n*=1); manual evacuation of stool (*n*=2); constipation (*n*=1); combination of constipation with abnormal sensation of passing stool (*n*=2), incontinence (*n*=1) or uncontrolled flatus (*n*=1); not specified (*n*=4).

Sexual dysfunction

Sexual dysfunction believed to be secondary to CES was present in 54.3% (19/35), of whom 9 male and 10 female. NB one of those patients indicated to suffer from diabetes mellitus. Complaints were: dysaesthesia of the genital region (*n*=8); combination of dysaesthesia of the genital region with problems to reach orgasm (*n*=3) or with erectile dysfunction (*n*=4); delayed erection and orgasm (*n*=1); not specified (*n*=3).

Prevalences of dysfunction were compared between short (FU OPD) and long term follow up; for micturition dysfunction, it had decreased significantly (Table 2). *p*=0.008).

Table 2 Proportion of patients with complaints: comparison between short and long term follow up

	At FU OPD	At long term follow up	*p*-value
Micturition dysfunction	58.3% (21/36)	36.1% (13/36)	0.008
Defecation dysfunction	47.2% (17/36)	41.7% (15/36)	0.500
Sexual dysfunction	55.9 (19/34)	52.9 (18/34)	1.000

NB due to some missing responses, n=36 and n=34 instead of n=37

Information about prognosis

Two-third (22/35) of patients indicated not to have received any information from the neurosurgeon – before or after surgery – about the recovery of micturition, defecation and/or sexual function (Figure 2). More and/or better information from the neurosurgeon about the recovery of functions was demanded by 23 patients (65.7%).

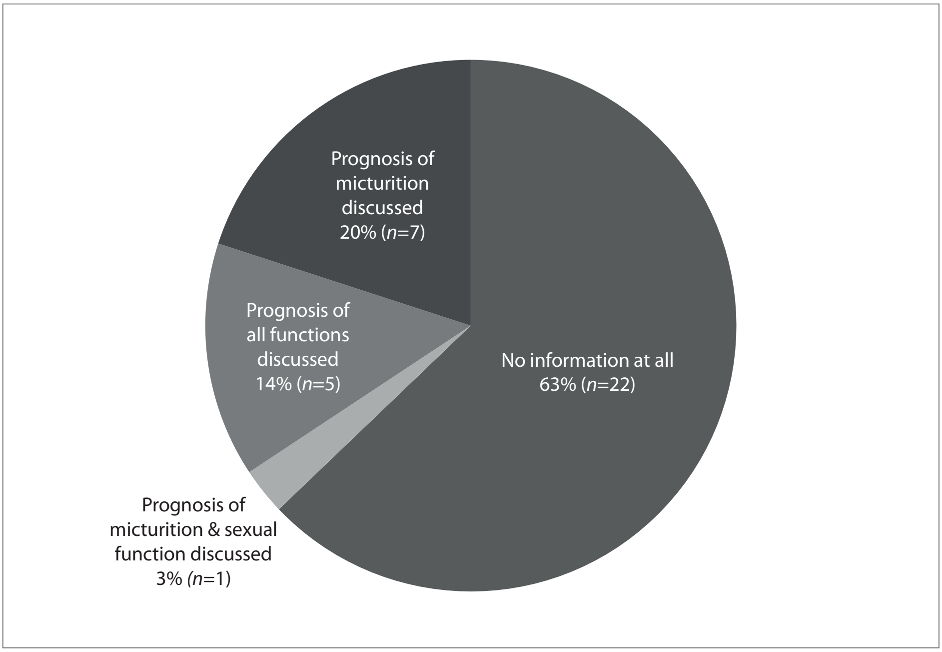

Figure 2 Did you receive information about prognosis of recovery of function(s)?

Predictors for long term outcome

Due to quasi-complete separation of the data of micturition dysfunction at presentation (sign was present in almost all patients), this variable could not be included in the regression models as a potential predictor. None of the tested variables (gender; age; duration of complaints of herniated disc at presentation; duration of complaints of CES at presentation; time to surgery) were identified as a predictor for long term outcome of micturition or defecation. Younger age at presentation was significantly associated with more sexual function dysfunction at follow up: for every year younger at presentation, odds ratio for sexual dysfunction at long term follow up was 1.11 (p=0.035).

Next to the outlined regression analysis, the cohort was evaluated in detail with regard to two presenting characteristics that were described by others to be of predictive value for worse outcome: 1) complete saddle anesthesia[17,19] and 2) significant sphincter dysfunction (defined as either necessary urinary catheterization at presentation for bladder dysfunction and as decreased anal sphincter tension in combination with absent anal sphincter reflex for bowel dysfunction).[17]

With regard to the first characteristic: six patients presented with complete saddle anesthesia. At long term follow up, all 6 patients (100%) reported defecation dysfunction and 4 of them (66.7%) reported micturition dysfunction. Of the 31 patients without complete saddle anesthesia at presentation, 10 (32.3%) reported micturition dysfunction at follow up and 10 (32.3%) reported defecation dysfunction at follow up. NB the total number of patients with micturition or defecation dysfunction was 19, including 11 suffering from both.

Secondly, significant sphincter dysfunction at presentation, thus either 1) necessary bladder catheterization or 2) decreased anal sphincter tone in combination with absent anal sphincter reflex, was evaluated in our cohort. Fifteen patients were given a urinary catheter at presentation; 5 of them (33.3%) reported micturition dysfunction at follow up. Of the 22 patients not being given a urinary catheter at presentation, 9 (40.9%) reported micturition dysfunction at final follow up. Worth mentioning, with regard to evaluating the predicting value of urinary catheterization at presentation, is that reasons for catheterization are varying among patients: e.g., it does not substantiate the amount of dysfunction but might be used as a preventive or diagnostic tool as well. Anal sphincter tone and reflex were not documented for every patient (Table 1); of the patients with documentation, 11 patients were reported to have both reduced tone and absent reflex. Of those 11 patients, 6 (54.5%) reported defecation dysfunction at long term follow up. As a control group, the patients with at least one of the two (either anal sphincter tone or reflex) to be documented as normal at presentation, were evaluated; this were 16 patients. Four (25%) reported defecation dysfunction at follow up. The remaining 10 patients that were not evaluated in this respect were patients without documentation of both anal sphincter tone and reflex at presentation or with one of the two being positive and the other one not documented.

DISCUSSION

Although CES patients undergo acute surgical decompression as a salvage procedure for their deteriorating or absent urinary, defecation and genital function, outcome is usually not evaluated in follow up visits. The presented results of this retrospective survey are alarming as at least one third of patients report micturition problems and about half of all patients complain about defecation- and sexual dysfunction years after surgery. Micturition dysfunction decreases significantly between the follow up moment at the outpatient clinic (median 56 days post-surgery) and the long term follow up moment (median 13.8 years post-surgery), from 58.3% to 36.1% (*p*=0.008).

Findings in relation to literature

Earlier studies suggested that recovery of genito-urinary and rectal functions is possible even several years after decompressive surgery.[8,10,24,25] Up to date, only a few studies have evaluated both micturition, defecation and sexual function after decompressive surgery for CES. The reliability of those results are restricted by small patient cohorts[26] and extremely delayed decompression.[27]

The study of McCarthy et al. evaluated outcome of both micturition, defecation and sexual function in a cohort of 42 CES patients with a shorter follow up time than the current study (mean 5 years, minimum 2.1 years), demonstrating similar rates of dysfunction of micturition (36%), but slightly higher rates of dysfunction of defecation (60%) and sexual function (57%).[28] The higher rates of defecation and sexual dysfunction in the cohort of McCarthy et al. compared to that of the presented cohort, might suggest that improvement is still possible several years post-surgery. Also in the current study, it is displayed that (patient-reported) dysfunction of all three functions is higher at FU OPD than at long term follow up. Since all figures are reported by patients, the possibility of tolerance of complaints over time and therefore, a reported lower rate of dysfunction, should be taken into account.

In our study, younger age at presentation was associated with sexual dysfunction at long term follow up (OR 1.11 for every year younger at presentation; p=0.035). This was not described earlier. This finding is most likely due to higher sexual activity of younger patients, making them more prone to notice and report sexual dysfunction; indeed, decreasing sexual desire in elderly women was reported by Hayes earlier.[29] In our patients, frequency of sexual activity was not evaluated in a structured manner.

Time to decompression is the best described predictor in CES.[3,17,18,30-33] In the presented cohort, time to decompression was included in the regression analysis as a possible confounder, yet was not found to be significantly associated with outcome of evaluated functions. There are multiple reasons for this, such as 1) relatively small patient cohort (several studies reporting an association were meta-analyses);[3,31,33] 2) outcome was separately evaluated for micturition, defecation and sexual function instead of evaluated in a combined matter; 3) relatively few patients were decompressed after 48 hours, which was a break point in several studies.[3,30,33] Interestingly, none of the included patients were decompressed within 6 hours. Reason might be logistics: patients' first presentation was often in a referral hospital.

Literature describes several predictors other than time to decompression. Kennedy et al. evaluated 19 CES patients with a minimum follow up of 1.8 years after decompressive surgery, identifying five patients with poor outcome, with poor outcome defined as any residual deficit regarded as physical or psychological impairment.[17] One of the predictors identified was delayed decompression (>24 hours). Another predictor found was complete perianal anesthesia at presentation: seven out of 19 patients suffered from this, including all five with poor outcome. Third predictor was significant sphincter dysfunction at presentation (bladder or bowel). Significant was defined as urinary catheterization in case of bladder dysfunction (12/19) and as decreased anal sphincter tension and absent anal sphincter reflex in case of bowel dysfunction (15/19): of the five patients with poor outcome, five demonstrated significant bladder sphincter dysfunction and four demonstrated significant bowel sphincter dysfunction at presentation.

We evaluated our cohort in detail with regard to the latter two predictors that were identified by Kennedy et al.; this was outlined in the Results section. Of important note is that in our study, no binary overall outcome measurement was used as Kennedy et al. did (e.g. poor and satisfactory), which makes the results of Kennedy not directly translatable to our results. Since micturition and defecation dysfunction were separate outcome measurements in our study, it seemed sensible to evaluate the patients that were given a urinary catheter at presentation for micturition dysfunction at follow up and the patients with decreased anal sphincter tone in combination with absent anal sphincter reflex for defecation dysfunction at follow up.

Summarizing the evaluations of our cohort it can be concluded that: 1) patients presenting with complete saddle anesthesia do seem more at risk for micturition and defecation dysfunction at follow up (66.7% versus 32.3% and 100% versus 32.3%, respectively); 2) patients being catheterized at presentation do not seem to be more at risk for micturition dysfunction at follow up (33.3% versus 40.0%) – not unlikely due to the fact that catheterization at presentation is not a distinctive characteristic of dysfunction per se; 3) patients with reduced anal sphincter tone and absent anal sphincter reflex do seem more at risk for defecation dysfunction at follow up (54.5% versus 25%). However, no firm conclusions can be drawn from these figures since they were not analyzed through statistics. This was not done because it would create unreliable regression models: adding the parameters complete perianal anesthesia at presentation, catheterization at presentation and reduced anal sphincter tension plus absent reflex at presentation to our regression models for outcome of micturition and defecation dysfunction would lead to overfitting (i.e. when a model consists of more parameters than events). Univariate analysis would be inappropriate due to the high risk of confounding (which risk is significantly reduced by using [multivariate] regression models, as was done in this study). Only in a larger cohort of patients (with thus more events), more parameters can be reliably added to the regression model.

Buchner et al. presented a cohort of 22 CES patients with a mean follow up of 3.8 years postoperatively and mentioned absence of complete perianal anesthesia at presentation and female gender both being predictors of a better postoperative outcome. Postoperative outcome was graded by level of micturition and divided into four groups: excellent, good, fair or poor.[19] In the study of Buchner et al., outcome was regarded as "better" when the outcome shifted in the direction of excellent, regardless where it came from and how much it shifted in that direction. Doubtless, this is a completely different outcome measurement than the one we used in our cohort, and therefore not unlikely, inducing different correlations. In addition, the analysis by Buchner et al. was univariate, which is more prone to confounding than the use of multivariate analysis as was done in the current study.

McCarthy et al. evaluated 42 CES patients with a mean of 5 years after decompressive surgery and demonstrated 1) female gender to be a predictor of urinary incontinence at follow up and 2) bowel dysfunction at presentation to be a predictor of sexual dysfunction at follow up.[28] With regard to the first finding: in our regression analysis, no differentiation was made between urinary incontinence and other micturition problems at follow up. Evaluating the outcome for micturition in our study closer, displays that the 6 patients with urinary incontinence at long term follow up, were all female; of the remaining 8 patients with micturition problems but without incontinence, 3 were female and 5 were male. Thus, indeed, female gender seems to be associated with urinary incontinence at follow up in our cohort as well, however, no association was seen for the total group with micturition dysfunction. McCarthy et al. identified bowel dysfunction at presentation as a predictor of sexual dysfunction at follow up, which was not demonstrated in our study. McCarthy et al. used univariate models and used Bonferroni correction for proper interpretation of *p*-values. The use of univariate models instead of multivariate models could however be an explanation of identifying a predictor which was not found in our study. We believe that the multivariate regression analysis used in our study diminished the risk of confounding.

Differences in reporting between doctor and patient

Micturition and defecation dysfunction at FU OPD were more often reported by the patient than by the doctor (did not reach statistical significance, probably due to small patient numbers). For sexual dysfunction, patient and doctor reported data are much more similar. Reason for this might be that doctors find it easier to discuss micturition and defecation and thus also get to know (and document) about non-symptomatic patients. Sexual dysfunction, however, is more difficult to discuss and therefore, is not often discussed when the patient doesn’t bring up the subject him- or herself. The obvious reason for a patient to bring up this topic is because complaints are present. Consequently, the doctors’ notes about sexual function are relatively more often about dysfunction than the notes about micturition and defecation, suggesting that discussing sexual dysfunction is a barrier, not only for the patient but for the doctor as well.[6]

Implications

Apart from younger age which was associated with sexual dysfunction at follow up, no predictors were identified. This urges the clinician to be attentive to dysfunction during presentation and follow up in all CES patients, bearing in mind the presented results of alarming high rates of dysfunction still years after surgery.

The presented CES patients indicated to be in dire need of recovery prospects. The fact that the majority did not receive any information of this kind, marks the lack of prognostic data in CES literature. With the presented data as best available evidence, it is now possible to start informing CES patients properly. Despite recommendations from the Consortium of Spinal Cord Medicine (2010) to identify threats to sexual wellbeing in high risk spinal patients,[34] discussing sexual dysfunction in CES patients did not get foothold in current practice yet, which is highly regrettable considering the presented prevalence of dysfunction. The authors advocate to identify sexual dysfunction in CES patients at an early stage. Bringing up the subject cannot be left to the patient and is the solemn responsibility of the doctor: too often, the patient is unaware of the link of CES with sexual dysfunction and is too ashamed to ask.

Limitations

This study might seem the largest cohort of CES patients with long term results which was presented up to now, however the total number of patients is still relatively small compared to evaluation studies of other neurological diseases. This restricted cohort size prevents a good intervention-prognostic variable analysis to predict outcome.

Like all surveys, this questionnaire study faced the problem of non-responding. This study achieved a response rate of 71% with inclusion rate of 56%. To accommodate for the best response rate possible, postal surveys were sent instead of web-based surveys and telephone reminders were used as a proven method to improve response rate.[35-37] The average response rate for patient surveys is about 60%, which figure is deducted from studies published in 1991,[36] whereas it is well-known that the response rates have been decreasing ever since, especially for surveys sent by healthcare professionals.[38] More importantly, surveys about sensitive subjects such as sexual dysfunction are proven to be prone to lower response rates and display a decreasing response rate over the years as well.[39] Worth mentioning, the current study has an extremely long follow up time - up to more than 21 years - which makes it more likely that patients are less prone to participate. Baseline characteristics of responders and non responders were not significantly different, making nonresponse bias unlikely.[40]

Of course, long term follow up creates risks for recall bias; i.e., patients report events differently from the true course of events due to loss of memory on the concerning item. This is something that cannot be corrected for in the current study design; any retrospective evaluation of long term outcome will introduce a risk of recall bias.

Obviously, because of the considerable long follow up period, the mean age of included patients has increased substantially during follow up (from 44.6 to 57.8 years). Increasing age changes the prevalence of problems of micturition, defecation and sexual function in the general population, thus might have also influenced the prevalence of dysfunction in the study population. Effort was taken to correct where possible: current medication use and co-morbidity was taken into account wherever dysfunction was reported, and where necessary, correction was used: correction was used for reported complaints that were thought not to be caused by CES but by other diseases such as urological prostate or gynaecological prolapse problems. The authors believe that the risk of bias was therefore minimized in this respect.

CONCLUSION

This study presents data about long term outcome of micturition, defecation and sexual function in CES after decompression and is unique in three aspects 1) markedly large cohort 2) lengthy follow up 3) integral evaluation of defecation and sexual function next to micturition. This report demonstrates dysfunction to be extremely common years after surgery and communicates a clear demand from CES patients for more information about their prognosis on those functions. Without doubt, the presented data adds substantially to the current knowledge about CES. It gives the clinician in spinal care the opportunity to inform CES patients realistically about long term recovery of micturition, defecation and sexual function after decompressive surgery. With regard to the seriousness of genito-urinary and defecation dysfunction and impact on quality of life, a prospective study is necessary, also to evaluate the risk of permanent deficit and to identify predictive variables, which can be influenced by intervention and personal guidance in rehabilitation.

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CHAPTER 8

Discussion and conclusion

DISCUSSION

The systematic review (**chapter 2**) demonstrated that a significant number of patients with CES due to lumbar herniated disc have persistent complaints of micturition (43%), defecation (50%) and sexual function (44%) at postoperative follow up (minimal 1.4 years after surgery). Included studies with a shorter follow up period reported more dysfunction than those with a longer follow up period. This finding supports the idea that, in case recovery of sphincter and sexual function does take place, this may occur very slowly and take several years.[1]

Sexual dysfunction & fertility

Sexual function was indeed demonstrated to be affected in a substantial part of CES patients postoperatively, albeit affected either directly or indirectly (for example by urinary incontinence during intercourse).[2,3] Interestingly, screening for sexual dysfunction was only done in a selection of CES patients, both at presentation and at follow up, more often in male than in female patients. Obviously, at presentation, the presence of other – more acute – complaints such as urinary retention and severe neuropathic pain are likely to interfere with discussing sexual health. Moreover, CES is an acute phenomenon, and it is highly probable that sexual dysfunction is often not even noticed (yet) by the patient at the moment of presentation. However, the fact that also postoperatively, sexual function was rarely documented, is notable: in view of personalized postoperative care, it seems sensible to screen for sexual dysfunction early in the follow up period in high risk populations such as CES patients.

To explore the knowledge, attitude and practice of discussing sexual dysfunction in spinal care, a survey among Dutch neurosurgeons was carried out (**chapter 3**). This survey revealed that 72% of neurosurgeons (almost) never counselled spinal patients of any kind about sexual dysfunction. In case of CES, 13% of neurosurgeons indicated to (almost) never discuss sexual health. This clearly demonstrates that neurosurgeons are aware of the threat CES poses to sexual health, but do not yet screen for sexual dysfunction in all CES patients. Screening CES patients for sexual dysfunction at an early stage (e.g. at the first postoperative visit at the outpatient department) would create the perfect opportunity to start multidisciplinary treatment.

Results of this survey confirmed that sexual function was more often discussed with male than with female patients. Gender of doctor or gender difference between patient and doctor were not identified to influence this. However, there were much less female than male respondents (15 versus 74), which perfectly reflects the male predominance among Dutch neurosurgeons, but makes it difficult to statistically detect a correlation between doctors' gender and the frequency of discussing sex with the patient. It seems sensible that a doctor is more likely to discuss sexual health with a patient of the same gender, which could be one of the reasons that male patients are found to be counselled more often. Another – quite obvious – explanation for the more frequent screening in male patients is the fact that a man requires "technical" support for his sexual act (erection) whereas female sexual dysfunction does not necessarily technically inhibit intercourse. Female dysfunction might therefore be seen as less relevant for the sexual act, obviously a peculiar circumstance.

Several barriers to discuss sexual health were indicated. One of them was advanced age of the patient, which was further supported by the finding that patients in the age category 20-35 were most often counselled, presumably indicated by reproductive motives. Secondly, lack of patients initiative to discuss sexual dysfunction was mentioned by one third of neurosurgeons, which highlights the root of the problem. It is striking that the doctor does not want to raise the topic of sexual dysfunction him or herself, since the patient is often not aware of the link of sexual problems with disease. This makes the presence of sexual dysfunction even more distressing and the barrier to discuss it higher, putting the patient and his or her partner in an isolated position.

Next to the reserve to discuss sexual function when there is a clear indication to do so, another problem arises because a substantial part of the neurosurgeons (23%) are not aware of referral possibilities in case of sexual dysfunction. Imagine the patient who has overcome several barriers to discuss sexual function, but subsequently still does not get proper access to appropriate healthcare professionals because the doctor doesn't know where to refer to.

Finally, an often indicated barrier for neurosurgeons to discuss sexual function was a lack of knowledge and/or training. This is an interesting finding, since the task of the neurosurgeon primarily is to detect concerns of sexual dysfunction in his or her patient, in order to adequately refer. The neurosurgeon is not supposed to (be able to) treat or even diagnose sexual dysfunction. Thus, mere awareness for sexual dysfunction in a group of high risk patients suffices. Integrating the topic of discussing sexual dysfunction in the residency program seems necessary to create this particular awareness.

Because of the inseparability of sexual health with reproductive health, discussion of fertility by neurosurgeons was evaluated as well (**chapter 4**). Discussing fertility was demonstrated to be even more neglected in spinal care, with 88% of neurosurgeons indicating to (almost) never discuss fertility with spinal patients of any kind. In case a patient suffers from CES, 30% of neurosurgeons indicated to (almost) never discuss fertility, displaying again that CES is designated by most neurosurgeons as a high risk profile for reproductive problems, however, fertility is not routinely discussed with those patients. Fertility, like sexual health, is more often discussed with male patients than with female patients. An underlying reason for this finding could be the fact that male sexual dysfunction more directly affects fertility: impotence does certainly not lead to proper conception, whereas a woman not having any sexual pleasure can perfectly become pregnant. Publications about decreased sperm quality in spinal cord injured males[4,5] and warrants to freeze sperm in some cases[6,7] might have added to the awareness of fertility problems in male spinal patients. Even though fertility in female spinal patients is not as much studied,[8] care should be taken to consider women with CES or spinal cord injury to have unaffected reproductive health: pregnancy and labour in those patients have been proven to carry substantial risks for which patients should be adequately counselled by a professional.[9,10]

Retrospective cohort study

A retrospective study among patients with CES due to lumbar herniated disc operated in Leiden University Medical Centre (LUMC; university hospital) was carried out (**chapter 5)**. This study is currently the largest single cohort study published about CES (*n*=75). The incidence of CES among operated herniated disc patients was 11%. This percentage is not representative of the real incidence (literature gives 2-6% among operated herniated disc patients[11]), which is due to the fact that this research was carried out in a referral hospital for urgent neurosurgical cases, with the bulk of regular herniated disc surgeries taking place in the surrounding non university hospitals. Micturition, defecation and sexual dysfunction were commonly affected at presentation. Defecation dysfunction was more often present in female than in male patients at presentation (OR 4.11; *p*=0.039). This finding can be linked to earlier epidemiologic research which demonstrated a higher prevalence of defecation dysfunction (e.g. constipation) in women compared to men in the general American and British population as well.[12]

Postoperative outcome data (median 60 days after surgery) demonstrated that micturition and defecation had improved significantly compared to presentation (micturition dysfunction dropped from 92% to 48%, defecation dysfunction from 74% to 42%). Data about sexual dysfunction was scarce which made statistic comparison between pre- and postoperative prevalence impossible. The lack of data about sexual function once more displayed that sexual health in CES patients is often neglected. Even though the majority of neurosurgeons had indicated in the questionnaire that they discuss sexual function with CES patients, the actual documentation on sexual function in the medical files was missing. Missing figures on sexual function made it impossible to use regression models for identifying predictors for sexual dysfunction. For micturition and defecation dysfunction, no predictors were identified.

Imaging

A study was carried out to evaluate the correlation between MRI and clinical features in CES patients (**chapter 6**): this relationship had not been studied before. MRI features (severity of caudal compression; uni/bilateral caudal compression; level of disc lesion) were not found to be associated with clinical presentation or outcome of CES in the current study. By definition, all patients had clinically significant caudal compression, however, the degree of caudal compression seen at MRI varied. It remains unclear why some people develop CES complaints with a relative mild compression of the herniated disc on the cauda equina. Probably, it is an interplay of several factors instigating clinically relevant compression next to the mechanical compression of the disc alone; factors such as local inflammatory responses and/or vascular changes.[13] Since the studied cohort was restricted in terms of patient number (*n*=48), it seems sensible to evaluate this correlation in a future study in a larger cohort.

As a major finding, the MRI study demonstrated that herniated disc patients with CES have a significant smaller anteroposterior (AP) diameter of the lumbar spinal canal (L1 until L5-S1) than herniated disc patients without CES, which were operated because of sciatica. This was seen at mid-disc as well as at intervertebral levels (largest *p*=0.002). Comparability between the two groups was kept high by selecting only sciatica patients who had surgery (in the same centre). Age and gender – parameters which are believed to influence measurements of the spinal canal – were comparable between groups as well.

In addition, measured AP spinal canal diameters of the CES patients and the sciatica patients were compared to average diameters from literature.[14] Again, AP spinal canal diameters of CES patients were demonstrated to be significantly more often below average than diameters of sciatica patients at all levels of the lumbar spine (largest *p*=0.021). This study is the first to describe the size of the lumbar spinal canal in CES patients, which has potential essential clinical implications. Most importantly, it might suggest that the selection of sciatica patients eligible for surgery, may include evaluation of the size of the lumbar spinal canal, in order to prevent progression to CES. Since this is the first study to present these results, a larger cohort study with a prospective design should be set up before clinical consequences are justified.

Long term outcome after surgery

Long term follow up of CES patients postoperatively rarely exceeds two years in published reports. McCarthy et al. published outcome on micturition, defecation and sexual function with a mean follow up of 5 years, which is the only study currently available evaluating all three functions with a reasonable number of patients (*n*=42) and a fairly long follow up, even though the minimal follow up is 2.1 years only.[15]

A follow up study among CES patients operated in LUMC is presented in **chapter 7**. Questionnaires were used to evaluate postoperative dysfunction. The limited amount of data available about objective outcome measurements in CES – such as urodynamics – displayed that objective tests are often not consistent with the complaints of patients.[16]

Instead of using objective tests to grade dysfunction, it seems therefore more reasonable to take complaints expressed by the patients fully into account as a measurement of dysfunction. Nevertheless, a future prospective study with both patient-reported dysfunction and objective tests such as urodynamics, would be highly interesting to truly determine the (lack of) correlation between the two.

The follow up period of the presented study was median 13.8 years after surgery, with a minimal follow up of 5.8 years. This makes it – to the best of the authors' knowledge – the first single cohort study of CES with such a lengthy follow up in combination with the presented cohort size (*n*=37). Dysfunction was demonstrated to be highly prevalent at long term follow up: patient reported data indicated micturition dysfunction in 38%, defecation dysfunction in 43% and sexual dysfunction in 54% of patients. McCarthy reported slightly higher prevalences for defecation (60%) and sexual dysfunction (57%) at an earlier follow up time (mean 5 years),[15] suggesting that improvement is still possible even several years after surgery. The fact that patients in the current study reported that dysfunction of all three functions had been higher at the earlier follow up moment (median 60 days postoperatively), indeed implies that it is worth following up CES patients postoperatively for a longer period of time than the established several months, to attain to a more correct rate of recovery. Since all data were patient reported, the possibility of tolerance of complaints over time and therefore, a reported lower rate of dysfunction, should be taken into account.

Time to decompression

Evaluating effects of time to decompression on outcome was not a primary aim of this thesis. However, since it is generally regarded as an important predictor for outcome,[17-19] this parameter was included in regression analyses to avoid confounding. Our data were however not able to demonstrate an association between time to decompression and outcome. Probable reasons are: the size of our cohort (even though it is the largest single CES cohort with *n*=75, it still contains relatively few patients), the fact that only few included patients had a delayed compression time beyond 48 hours and the fact that we used separated outcome measures (micturition, defecation and sexual dysfunction) instead of one generalized outcome measure (with outcome primarily based on micturition, as was done in most other studies). In addition, clinical motives that might have influenced decisions about early or late decompression – which is inevitable in any retrospective study design – might have become substantial because of aforementioned reasons such as limited cohort size. Thus, there is no reason to believe that the presented results undermine the indication for emergency decompression in CES.

Interestingly, in the LUMC cohort, a shorter time to decompression (break point 36 hours) was associated with more sciatica shortly after surgery (median 48 hours postoperatively, *p*=0.042). This association was not observed at the next follow up moment (median 60 days postoperatively). This association might seem contradictory with the consensus of the beneficial effects of early decompression, however, most probably merely displays a correlation between short duration of compression and other prognostic factors, which factors are more likely to have caused the higher rate of sciatica than the actual short time to decompression. Those factors are 1) acute caudal compression, since patients with acute lesions have a worse prognosis[20,21] and 2) total caudal obstruction, since patients with a "complete" CES carry a poorer prognosis than those with "incomplete" CES, adding that the incomplete type often occurs more gradually (although not exclusively).[22,23] Those groups of patients are not always easy to distinguish at presentation, subsequently early decompression in every patient presenting with CES is advocated.

The value of predictors

Younger age at presentation was associated with more sexual dysfunction at follow up (OR 1.11 for every year younger at presentation; $p=0.053$). This was not described earlier and the rationale behind this finding is probably simply due to more sexual activity in younger patients, therefore being more prone to notice and report sexual dysfunction. True predictors for outcome were not identified. This is contrary to other single cohort studies about CES reporting delayed decompression (defined as >24 hours in the concerning study[24]), significant (anal or urethral) sphincter dysfunction at presentation,[24] complete perianal anesthesia at presentation,[24,25] bowel dysfunction at presentation[15] and – contradictory enough – male[25] or female[15] gender as predictors for worse outcome.

One of the reasons that those studies identified predictors for poor outcome whereas the current study did not, could be due to different statistics. In the current study, the decision was made to keep several parameters out of the regression models (e.g. urinary catheterization at presentation, anal sphincter tension, anal sphincter reflex) due to the risk of overfitting (an overload of parameters compared to the number of events). Only in a larger cohort, data would be sufficient to statistically adequately rule out or confirm those parameters as a predictor for poor outcome. Bearing this in mind, it is rather interesting that Kennedy et al. reported several predictors: at least 7 parameters are mentioned to have been analyzed as predictors in their cohort of 19 CES patients, of whom 5 patients had a poor outcome.[24] Using multiple parameters in a regression model for a small cohort with few events (in this case: 5 with poor outcome) leads to an unreliable regression model. In addition, it is stated that next to multivariate analysis, univariate analyses for predictors were done, however, significance level or *p*-values are not reported to be adjusted (for example by Bonferroni method). The two other studies used univariate analyses,[15,25] thus correcting less for confounders than a regression models would do. Similar to Kennedy et al., Buchner et al. evaluated a large amount of parameters (13 mentioned) in a rather small cohort with 5 patients having either fair or poor outcome.[25]

Another possible reason why aforementioned studies did find predictors whereas the current study did not, might be differences in outcome measurements. Kennedy et al. used a combined outcome instead of outcome split into micturition, defecation and sexual function, making results less translatable to the current study.[24] Buchner et al. defined outcome simply as "better" when it had shifted in the direction of "excellent", regardless whether it came from (good/fair/poor),[25] which approach was completely different from the one in the presented study.

CES: the next step

Several topics in this thesis were never studied before. Especially the identified difference in spinal canal size between lumbar herniated disc patients with CES and lumbar herniated disc patients without CES, operated because of sciatica, has the potential to leave a mark at the clinic. It is advisable that this association is further evaluated in a larger cohort size, preferably in a multicenter design to guarantee a substantial number of patients. The design should be prospective in order to be able to indicate whether a smaller canal size is a true risk factor of CES. With a prospective design, the predictive value of both clinical and imaging presenting features can be evaluated with more assurance as well. In the ideal case, such a cohort would be large enough to allow stratifying of patients, to create more homogenous subpopulations which might make the translation to the clinic easier. Appropriate subgroups could be for example CES-R (characterized by painless, urinary retention) and CES-I (incomplete: urinary difficulties such as sensory loss without urinary retention and overflow incontinence) as was proposed by Gleave and MacFarlane,[26] or the three groups suggested by Tandon & Sankaran: rapid onset of CES without history of back problems or sciatica; rapid onset of CES with history of back problems and sciatica; slow onset of CES with chronic back problems and sciatica.[27] Those groups are believed to all carry different risks for poor outcome, which hypothesis has never been studied prospectively.

The translation to the clinic is highly necessary. Two-third of CES patients indicated that they had wished their neurosurgeon had given them more and/or better prognostic information about micturition, defecation and sexual function. This finding confirmed the idea at the start of this thesis that there indeed is a dire need from CES patients for a realistic prospect of recovery of those functions that can so seriously impair quality of life. With its multi-perspective approach to CES, strongly dedicated to micturition, defecation and sexual function, this thesis has the potential to become a reference work for the spinal clinician searching for data to adequately inform CES patients about prospects of recovery.

CONCLUSIONS OF THIS THESIS

1) A systematic review of the literature (15 studies, 464 patients) demonstrated that CES complaints are persistent in a large number of CES patients after decompressive surgery (mean 1.4 years postoperatively): 43% micturition dysfunction, 50% defecation dysfunction and 44% sexual dysfunction. A cohort of CES patients operated in Leiden University Medical Centre (*n*=75) displayed similar figures.
2) Sexual dysfunction and fertility problems are not routinely discussed with CES and spinal patients by Dutch neurosurgeons. Most important barriers for neurosurgeons to not discuss sexual dysfunction: advanced age of patient (42%), lack of knowledge (38%) and lack of patients' initiative to bring up the subject (36%).
3) Sexual health and fertility are more often discussed with male than with female patients.
4) MRI features at presentation were not demonstrated to be correlated with clinical presentation nor with outcome of CES.
5) Lumbar herniated disc patients with CES displayed significantly smaller anteroposterior lumbar spinal canal diameters at MRI than lumbar herniated disc patients without CES, operated because of sciatica. This difference was never described before. When replicated in a larger cohort, this finding has the potential to change the selection of sciatica patients due to herniated disc eligible for surgery.
6) Long term follow up of CES patients (median 13.8 years after spinal surgery) demonstrated dramatic outcome of micturition, defecation and sexual function. Patient reported data indicated 38% micturition dysfunction, 43% defecation dysfunction and 54% sexual dysfunction at long term follow up.
7) Dysfunction of micturition, defecation and sexual function were reported by patients to have been higher at earlier follow up moment at median 60 days postoperatively (58%, 47% and 56%, respectively). These figures imply that it is worth following up CES patients postoperatively for a longer period of time than the established several months. Since these data are patient reported, the possibility of tolerance of complaints over time instead of true recovery of function should be taken into account when interpreting these figures.
8) CES patients communicate a clear demand for more and/or better prognostic information about the recovery of micturition, defecation and sexual function after decompressive surgery.
9) The presented studies were not designed to rule out or confirm the effects of time to decompression. Therefore there is no reason to doubt the absolute indication for prompt surgical intervention in all patients presenting with CES.

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CHAPTER 9

Summary

Summary in Dutch (samenvatting)

Curriculum Vitae

Dankwoord

SUMMARY

The cauda equina (Latin: 'horse tail') is the bundle of nerve roots shooting from the conus medullaris, generally starting at the level L1-L2 and running down to the sacral bone. The cauda equina nerve roots innervate the area of the 'saddle' (hips, thighs and buttocks) and the legs, as well as the vesical and anal (internal and external) sphincter, the bladder, the perineum and the genitals. Cauda equina syndrome (CES) is a rare neurologic condition caused by compression of these nerve roots. The complaints of this syndrome differ per patient. For diagnosis, at least one or more of the following should be present: 1) problems with micturition and/or defecation; 2) diminished/altered/absent sensation of the saddle area; 3) sexual dysfunction. In addition, neurologic complaints of the legs are often present, such as motoric or sensoric loss, sciatica and/or reflex changes. Lumbar herniated disc is the most common cause of caudal compression, with 2-6% of lumbar herniated disc patients developing CES. Emergency decompressive surgery is advocated for CES to increase the risks of recovery.

Research about CES traditionally focuses on the effects of time to decompression on outcome. Outcomes are not seldom dichotomous classified and often use dysfunction of micturition as most important indicator of outcome. Defecation and sexual function are only rarely evaluated next to micturition.

In the literature review (15 articles, 464 CES patients), it was demonstrated that dysfunction of micturition, defecation and sexual function are common in CES patients but are not all three regularly evaluated, not pre- nor postoperative (**chapter 2**). Dysfunction of micturition was evaluated in all studies and was present in 89% of patients at presentation. Dysfunction of defecation was evaluated in 8 out of 15 studies and was present in 47% of patients at presentation. Pre-operative documentation of sexual function was only available for three out of 464 patients. Many patients were demonstrated to have persisting complaints after spinal surgery: after a mean follow up period of 1.4 years postoperatively, 43% still had micturition dysfunction, 50% defecation dysfunction and 44% sexual dysfunction. Sexual dysfunction was documented the least: only in two studies, every patient was screened for sexual dysfunction postoperatively.

These findings led to a questionnaire survey among Dutch neurosurgeons about discussing sexual health and fertility with spinal patients (**chapter 3, chapter 4**). Seventy-two percent of the neurosurgeons indicated to (almost) never discuss sexual health and 88% indicated to (almost) never discuss fertility. In case of CES, 13% of neurosurgeons indicated to (almost) never discuss sexual health and 30% indicated to (almost) never discuss fertility. Neurosurgeons are thus aware of the risks for sexual and reproductive health in CES patients, yet do not routinely screen for these problems in CES patients. Barriers indicated to not discuss sexual dysfunction were: more advanced age of the pa-

tient (42%), lack of knowledge of the doctor regarding this topic (38%), lack of patients' initiative to bring up the subject (36%) and lack of time (26%).

Fertility was significantly more often discussed with male patients than with female patients (*p*=0.006), regardless of doctor's gender. In addition, fertility was discussed up to a higher age with male patients than with female patients (mean until 57 years versus mean until 47 years, *p*<0.001), irrespective of the age of the doctor.

To compare the results found in literature with the patient population from Leiden University Medical Centre (LUMC: referral hospital for spinal surgery), patients with CES due to lumbar herniated disc, operated in LUMC, were evaluated (**chapter 5**). CES patients were selected by screening all patients which were operated in LUMC between 1995 and 2010 because of lumbar herniated disc. Out of 744 surgeries for 696 patients, 75 patients had CES (11%). At the first presentation to the neurosurgeon, 92% had urinary complaints and 74% defecation problems. Of the 26 patients that were screened for sexual dysfunction prior to surgery, 25 had sexual dysfunction (96%). At postoperative follow up moment (mean 9 weeks after surgery), 48% had dysfunction of micturition, 42% had dysfunction of defecation and 53% indicated to have sexual dysfunction. Preoperative predictors for worse outcome could not be identified in this cohort.

Even though magnetic resonance imaging (MRI) is done for all patients suspect for CES, the correlation between MRI features and clinical presentation and outcome of CES is not known. To evaluate this correlation, MRI scans of the aforementioned LUMC cohort were assessed (available for *n*=48) and correlated with the pre- and postoperative clinical features (**chapter 6**). Analyses did not find an association between MRI characteristics and clinical characteristics (not at presentation nor at follow up).

To explore the influence of the pre-existing size of the lumbar spinal canal on the development of CES among herniated disc patients, MRI scans of CES patients were used to measure the anteroposterior diameters of the lumbar spinal canal, both at mid-vertebral level and at disc level. For comparison, the anteroposterior diameters of the lumbar spinal canal of lumbar herniated disc patients without CES, operated in LUMC because of sciatica, were measured. Comparing those two groups (*n*=28 and *n*=31) demonstrated that the herniated disc patients with CES had significant smaller spinal canal diameters than the herniated disc patients without CES, which were operated because of sciatica. This was found at all levels (L1 until L5-S1), both at mid-vertebral level as well as at disc level (largest *p*=0.002). Additionally, diameters of both groups were compared with average anteroposterior spinal canal diameters described in literature. This comparison displayed again that diameters of CES patients were significantly smaller than average at all levels (L1 until L5-S1) compared to the diameters of the herniated disc patients without CES, operated because of sciatica (largest *p*=0.021). The size of the lumbar spinal canal of CES patients has not been reported before, neither was it compared to that of herniated disc patients without CES, operated because of sciatica. This finding might lead to important clinical consequences: if herniated disc patient with a smaller spinal canal indeed are more at risk for CES, then spinal canal diameter might become an argument for surgical intervention in case of sciatica, without (yet) evidence of CES. Since the presented number of patients is relatively small, further (prospective) research is needed to validate these results and to justify clinical consequences.

It is known from literature that complaints of micturition, defecation and sexual function due to CES might improve even years after surgery. Therefore, a follow up study of the LUMC cohort was carried out to evaluate dysfunction of micturition, defecation and sexual function several years postoperatively (**chapter 7**). The attitude of patients towards delivered hospital care with regard to these complaints was evaluated as well. Thirty-seven patients participated in this questionnaire survey (response rate 71%, inclusion rate 56%). Median time after surgery at follow up moment was 13.8 years (range 5.8 – 21.8 years). A high proportion of patients was found to still suffer from complaints of CES: 38% micturition dysfunction, 43% defecation dysfunction and 54% sexual dysfunction. Compared to the data of the follow up moment at the outpatient department (mean 8 weeks postoperatively), micturition dysfunction had significantly decreased (p=0.008). Two-third of the patients mentioned that they would have liked to gain more and/or better information from the neurosurgeon about the recovery of micturition, defecation and sexual function. These alarming high prevalences of complaints years after spinal surgery provide an insight into the harsh reality of long term recovery of micturition, defecation and sexual function in CES patients. At the same time, they offer the spinal clinician the opportunity to provide CES patients with a – much wanted – realistic prospect of recovery of functions.

SUMMARY IN DUTCH (SAMENVATTING)

Cauda equina (Latijn: 'paardenstaart') is de groep zenuwwortels die als een uitloper van de conus medullaris vanaf de onderrug (veelal vanaf niveau L1-L2) tot aan het os sacrum loopt. Zenuwwortels van de cauda equina innerveren het gebied van de 'rijbroek' (heupen, dijen en billen) en de benen evenals de vesicale en anale (interne en externe) sfincters, de blaas, het perineum en de genitaliën.

Cauda equina syndroom (CES) is een zeldzame neurologische aandoening veroorzaakt door compressie van de cauda equina. De klachten van CES variëren per persoon, waarbij minstens één van de volgende klachten aanwezig moet zijn voor het stellen van de diagnose: 1) mictie- en of defecatieklachten; 2) verminderd/veranderd/afwezig gevoel van het rijbroekgebied; 3) seksuele dysfunctie. Daarnaast is er bijna altijd sprake van neurologische verschijnselen in de benen zoals parese, dysthesieën, reflexveranderingen en/of sciatica. De belangrijkste oorzaak van cauda equina compressie is een hernia nuclei pulposi (HNP). Lang niet iedereen met een HNP ontwikkelt een CES: onder de patiënten die geopereerd worden in verband met een lumbale hernia heeft slechts 2-6% een CES. Operatieve decompressie bij een verdenking op CES dient zo spoedig mogelijk plaats te vinden om de kans op herstel te vergroten.

Het onderzoek naar CES richt zich van oudsher met name op de effecten die een langere dan wel kortere tijd tot operatieve decompressie heeft op het postoperatieve herstel. De mate van herstel wordt dan vaak gedefinieerd met mictieklachten als belangrijkste determinant en wordt veelal dichotoom geanalyseerd. Zelden vindt naast de evaluatie van mictieklachten een evaluatie plaats van defecatieklachten en seksuele dysfunctie.

In de literatuurreview (15 artikelen, 464 CES patiënten) werd aangetoond dat mictiestoornissen, defecatieproblematiek en seksuele dysfunctie bij CES vaak voorkomen, maar slechts weinig worden geëvalueerd, zowel pre- als postoperatief (**chapter 2**). Mictieklachten werden in alle studies geëvalueerd en waren bij presentatie in 89% aanwezig. Defecatieproblematiek werd in 8 van de 15 studies geëvalueerd bij presentatie en was in 47% aanwezig. Slechts voor 3 van de 464 patiënten was preoperatieve documentatie over seksuele functie aanwezig. Na spinale chirurgie bleken veel patiënten persisterend klachten te hebben: na een gemiddelde follow-up duur van 1.4 jaar postoperatief had nog 43% mictieklachten, 50% defecatieklachten en 44% seksuele dysfunctie. Seksuele gezondheid werd het minst gedocumenteerd: slechts in twee studies werd elke patient postoperatief gescreend voor seksuele dysfunctie.

Deze bevinding leidde tot het opzetten van een vragenlijstonderzoek onder Nederlandse neurochirurgen over het bespreken van seksuele dysfunctie en fertiliteitproblematiek met patiënten met spinale problematiek (**chapter 3, chapter 4**). Tweeënzeventig procent van de ondervraagde neurochirurgen gaf aan (bijna) nooit seksuele gezondheid te bespreken en 88% gaf aan (bijna) nooit fertiliteit te bespreken met spinale patiënten. Voor de specifieke groep patiënten met CES liggen deze getallen anders: indien het een patiënt betreft met CES, gaf 13% van de neurochirurgen aan (bijna) nooit seksuele dysfunctie te bespreken en 30% gaf aan (bijna) nooit vruchtbaarheidproblematiek te bespreken. Neurochirurgen zijn dus op de hoogte van de risico's voor de seksuele gezondheid bij CES patiënten, maar screenen niet elke CES patiënt. Redenen die werden aangegeven om seksuele dysfunctie niet te bespreken waren: hogere leeftijd van patiënt (42%), gebrek aan kennis van de dokter op dit gebied (38%), gebrek aan initiatief van de patiënt om dit onderwerp ter sprake te brengen (36%) en gebrek aan tijd (26%).

Fertiliteit werd significant vaker besproken met mannelijke patiënten (p=0.006), ongeacht het geslacht van de dokter. Eveneens werd fertiliteit tot op hogere leeftijd besproken met mannelijke patiënten dan met vrouwelijke patiënten (gemiddeld tot 57 jaar versus gemiddeld tot 47 jaar, p<0.001), onafhankelijk van de leeftijd van de dokter.

Om de uitkomsten die werden gevonden in de literatuur te staven aan de patiëntenpopulatie in het Leids Universitair Medisch Centrum (LUMC: referentieziekenhuis voor spinale chirurgie), vond een evaluatie plaats van de patiënten met CES secundair aan een HNP die in het LUMC geopereerd waren (**chapter 5**). Selectie vond plaats door screening van alle patiënten die tussen 1995 en 2010 werden geopereerd aan een HNP. Er was sprake van 744 operaties voor 696 patiënten: 75 hiervan hadden CES (11%). Bij het eerste bezoek aan de neurochirurg had 92% mictieklachten en 74% defecatieklachten. Van de 26 patiënten van wie preoperatief documentatie beschikbaar was over seksuele gezondheid, hadden 25 seksuele dysfunctie (96%). Op de poliklinische follow-up (gemiddeld 9 weken postoperatief) had 48% nog mictiestoornissen, 42% defecatieproblematiek en 53% seksuele dysfunctie. Preoperatieve predictoren voor slechte uitkomst konden in dit cohort niet worden aangetoond.

Alhoewel magnetic resonance imaging (MRI) wordt verricht bij alle patienten die worden verdacht van een CES, is er weinig tot niets bekend over de correlatie tussen MRI kenmerken en klinische presentatie en uitkomst van CES. Om deze correlatie te evalueren, werden van voorgaand cohort MRI beelden bij presentatie beoordeeld (beschikbaar voor n=48) en gecorreleerd aan de klinische kenmerken bij presentatie en postoperatief bezoek (**chapter 6**). Analyses toonden geen correlatie aan tussen MRI karakteristieken en klinische karakteristieken (niet pre- noch postoperatief).

Om de invloed van de pre-existente maat van het lumbale spinale kanaal op de ontwikkeling van CES onder HNP patiënten te exploreren, werden op de MRI beelden van de CES patiënten de anteroposterior diameters van het lumbale spinale kanaal gemeten, zowel op mid-vertebraal niveau als op discusniveau. Ter vergelijking werden de anteroposterior diameters van het lumbale spinale kanaal van herniapatiënten zonder CES gemeten, geopereerd in het LUMC vanwege sciatica. Bij vergelijking van deze twee groepen (*n*=28 en *n*=31) bleek dat de patiënten met CES op alle niveaus (L1 t/m L5-S1), zowel op mid-vertebrale als discusniveaus, significant kleinere spinaal kanaal diameters hadden dan de HNP patiënten die geen CES hadden maar werden geopereerd in verband met sciatica (grootste *p*=0.002). Aanvullend werden beide groepen vergeleken met gemiddeldes van de anteroposterior diameter van het lumbale spinale kanaal gerapporteerd in de literatuur. Hieruit volgde opnieuw dat de diameters van de CES patiënten op alle niveaus (L1 t/m L5-S1) significant vaker kleiner dan gemiddeld waren dan die van de HNP patiënten die geen CES hadden, maar geopereerd waren in verband met sciatica (grootste *p*=0.021). Niet eerder werd de grootte van het lumbale spinale kanaal van CES patiënten gerapporteerd en uitgezet tegen dat van HNP patiënten zonder CES, geopereerd in verband met sciatica. In potentie kunnen hieraan belangrijke klinische consequenties worden verbonden: indien HNP patiënten met een nauwer spinaal kanaal inderdaad meer risico lopen op CES, kan de spinaal kanaal diameter een argument worden voor operatief ingrijpen bij een HNP, zonder dat er (al) klachten van een CES bestaan. Vanwege het relatief kleine patiëntenaantal is verder (prospectief) onderzoek noodzakelijk om de gepresenteerde resultaten te bevestigen voordat klinische consequenties worden genomen.

In de literatuur is bekend dat mictie-, defecatie en seksuele stoornissen ten gevolge van een CES nog tot enkele jaren na operatieve decompressie kunnen verbeteren. Er vond daarom evaluatie plaats van mictieklachten, defecatieproblematiek en seksuele stoornissen binnen het cohort CES patiënten, meerdere jaren na de operatie (**chapter 7**). In de evaluatie werden ook de patiëntervaringen meegenomen ten aanzien van de geleverde ziekenhuiszorg omtrent deze klachten. Zevenendertig patiënten namen deel aan deze vragenlijststudie (response rate 71%, inclusion rate 56%). De evaluatie vond plaats met een mediaan van 13.8 jaar postoperatief (range 5.8 – 21.8 jaar). Er bleek veelal sprake te zijn van persisterende klachten van CES: 38% gaf mictieklachten aan, 43% ontlastingsproblematiek en 54% seksuele dysfunctie. Vergeleken met de data van het follow up moment op de polikliniek (gemiddeld 8 weken postoperatief) waren klachten significant afgenomen voor wat betreft mictie (*p*=0.008). Tweederde van de patiënten had graag meer en/of betere informatie over het herstel van mictie- en defecatiestoornissen en seksuele dysfunctie willen krijgen van de neurochirurg. Deze alarmerend hoge prevalenties van klachten jaren na spinale chirurgie geven een inzicht in de harde werkelijkheid van het lange termijn herstel van mictieklachten, ontlastingsproblematiek en seksuele dysfunctie bij CES patiënten. Tegelijkertijd bieden ze clinici in spinale zorg de mogelijkheid om CES patiënten een – hoognodige – realistische prognose te schetsen van het herstel van functies.

CURRICULUM VITAE

Nina Sophia Korse was born in Eindhoven, the Netherlands, on 21 December 1988. In 2007, she graduated summa cum laude for Gymnasium in Eindhoven and she subsequently started with South-East Asian Studies at Leiden University. After obtaining her propaedeutics cum laude, she changed careers and started studying Medicine at Leiden University Medical Centre from 2008 onwards.

The first steps in research were taken at the department of Infectious Diseases. Later on, she started researching cauda equina syndrome at the department of Neurosurgery. During her student years, Nina lost her heart to tropical medicine and acquired experience in the field during prolonged stays in the Sudan, the Gambia, Malawi, Indonesia, Suriname, Curacao and Tanzania.

In 2014 Nina obtained her Master's Degree in Medicine. January 2015 she started specializing in International Health and Tropical Medicine and fulfilled one year residencies at the department of Paediatrics at Rijnstate Hospital in Arnhem and at the department of Obstetrics and Gynaecology at IJsselland Hospital in Capelle aan den IJssel. As part of her training, she attended the Netherlands Course in Tropical Medicine and Hygiene (NTC) at the Royal Tropical Institute (Amsterdam) during Spring 2017.

Nina is currently living in Rotterdam with Wybo. She will soon leave for India to start her final residency programme before formally being certified as Doctor of International Health and Tropical Medicine.