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

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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 patients¹¹), 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 study²⁴), significant (anal or urethral) sphincter dysfunction at presentation,²⁴ complete perianal anesthesia at presentation,^{24,25} bowel dysfunction at presentation¹⁵ and – contradictory enough – male²⁵ or female¹⁵ 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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