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Review Article

Early surgery predicts a better prognosis of urinary function in cauda equina syndrome with retention: a systematic review and meta-analysis

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Abstract: Background: The timing of surgical intervention for cauda equina syndrome with retention remains debated. This systematic review and meta-analysis aimed to investigate the relationship between the timing of surgical intervention and the prognosis of micturition function in cauda equina syndrome with retention.Material and methods: Literatures in PubMed and ELSEVIER between Jan 1, 1990 and Dec 31, 2014 were reviewed. 10 studies were included in our meta-analysis by Generic Inverse Variance method at the 24-, 48-hour time point with Review Manager 5.0 to identify the evidence of urgent surgical decompression in cauda equina syndrome with retention. Events were defined as either the abnormal recovery of urinary function, or the catheterization. Results: There was a significant difference in the abnormal urinary function at 24- hour breakpoint. Operation beyond 24 hours increased the risk of the abnormal urinary function by 54%. Additionally, a significant difference in the catheterization requiring was observed at 48-hour breakpoint. A delayed operation after 48-hours increased the risk of catheterization by 47%. Conclusions: Bladder dysfunction caused by cauda equina syndrome with retention can be effectively attenuated by an early surgery. An operation within 24 hours may prevent the occurrence of abnormal urinary function. Meanwhile, an operation within 48 hours may help to reduce the usage of catheter.

Keywords: Lumbar disc herniation, cauda equina syndrome, urinary retention, surgical outcome, evidence-based medicine

Introduction

Cauda equina syndrome (CES) is a rare but an extremely serious surgery emergency [1-3]. It can be induced by many diseases, such as lumbar disc herniation, lumbar spinal stenosis, trauma, hematoma, tumors and infection [4-7]. This study focuses on the CES originated from lumbar disc herniation with or without lumbar spinal stenosis. The clinical manifestations of CES are very complicated [8, 9]. It has been reported that urinary dysfunction is the most common characteristics of CES [10, 11]. It is well known that voiding dysfunction has a poor prognosis, which seriously affects patients' daily life and emotions. Therefore, the recovery of micturition function is a major concern of CES patients and animportant predictor for the prognosis.

Gleave and Macfarlane classified CES into two stages according to the severity of bladder dysfunction: incomplete cauda equina syndrome (CESI) and cauda equina syndrome with retention (CESR) [12]. CESI was defined as altered urinary sensation, loss of desire to void, poor urinary stream, and the need to strain in order to micturate. CESR was defined as painless urinary retention and/or overflow incontinence. It was indicated that the extents of recovery of bladder function from CESR and CESI were different, with the latter always better [10]. It is inapposite to explore to relationship of surgical timing with clinical outcome in a mixture of the two different patient subpopulations [13]. Unfortunately, most of the studies in the literatures failed to setup a clear classification into-CESR and CESI [10, 14].

The timing of urgent surgical intervention is debated [15-17]. Several investigation sproposed that an early surgical intervention predicted for a better prognosis [13, 18-20]. Others

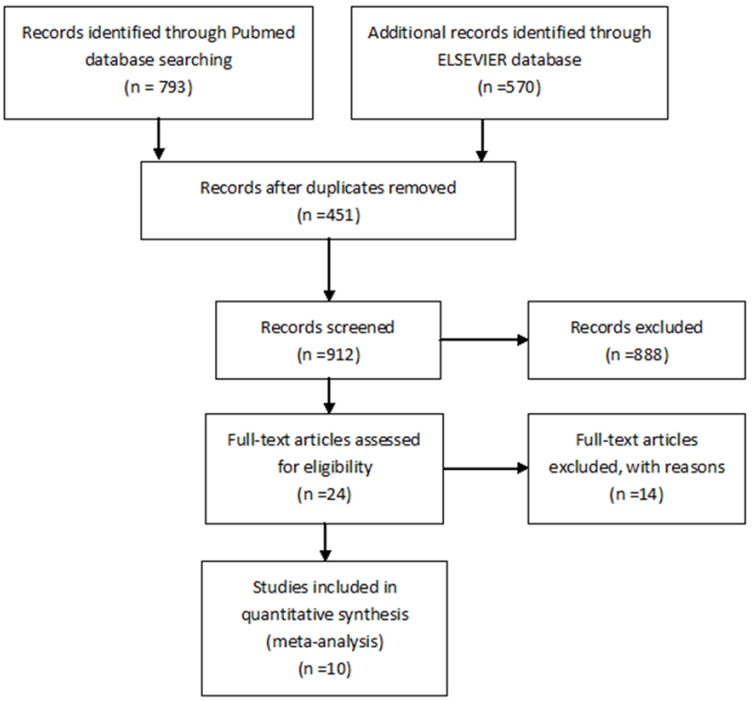

Figure 1. Flow diagram of article searching.

showed no relevance between the prognosis and operation timing [10, 21]. The lack of supporting evidence and the presence of major flaws in statistical methodology lead to the inconsistent results [22-25]. After reviewing a large number of literatures, we suspected that the differences in the research objects and the postoperative evaluation standard of bladder function may introduce the above opposite opinions. So far, previous studies have not stratified the patients and their outcomes according to timing of surgery.

To fill in the gap in knowledge, we investigated the relationship between the timing of urgent surgical intervention and the prognosis of micturition function by meta-analysis. Here, CESR was set as the research object, and the abnormal urinary function and catheterization requiring were set as the outcomes of bladder function at 24- and 48-hours after surgery.

Material and methods

Data resources and searching strategy

Databases: PubMed and ELSEVIER have been chosen for the literature review. PubMed was accessed through NCBI (http://www.ncbi.nlm.nih.gov/pubmed/). ELSEVIER was accessed via Capital Medical University (http://www.sciencedirect.com/science/search). To improve the surgical management, we chose the articles published between Jan. 01 1990 to Dec. 31 2014. The publications focused on the timing effects of surgical treatments on the urinary prognosis among CRES patients were searched using the terms "cauda equina syndrome (ICD-10: J83.4)", "surgery/operation", "human" in various combinations. No language restrictions were applied. The literatures cited in the identified articles were also searched manually. Hongxing Song and Qingkun Song conducted the searches.

Study selection

In the present study, we focused on the timing of the surgical treatment on the urinary recovery from CESR arising from herniated lumbar discs with or without spinal stenosis. We aimed to determine the effects of the operations on clinical outcome in 24 and 48 hours. The inclusion criteria were CESR, cohort design, and original reports. The exclusion criteria were CESI, cross-sectional and case-control study design, reanalysis of previous data, review and comments to the related studies.

Criterion of urinary function outcome

According to Gleave and Macfarlane, postoperative urinary function outcome was defined as: "excellent" for a complete recovery of bladder function in the immediate posterior period; "good" for a complete recovery of bladder function during the follow-up; "fair" for an incomplete recovery of bladder functionnot requiring catheterization; "poor" for permanent urinary incontinence requiring catheterization [12]. In the current studywe used 3 categories of urinary outcome: normal, fair, andpoor. The "normal" group combined the "excellent" and "good" subgroups mentioned above. We conducted two analyses according to the recovery level of bladder function: one analysis is to compare the normal ("excellent" or "good") with the "abnormal" ("fair" or "poor") groups; the

Table 1. Study characteristics of included articles

Reference	Sample size	Timing of surgery	Urinary function outcome			
			Normal (Normal)	Abnormal (Fair+poor)	No cath (Normal+fair)	Cath (Poor)
Dining 1993	14	<24 h	8	1	8	1
		>24 h	1	4	1	4
Sulla 1996	58	<24 h	6	3	6	3
		>24 h	33	16	44	5
		<48 h	12	6	14	4
		>48 h	27	13	36	4
Shapiro 2000	44	<24 h	17	1	18	0
		>24 h	11	15	11	15
		<48 h	19	1	20	0
		>48 h	9	15	9	15
Buchner 2002	22	<24 h	9	2	10	1
		>24 h	8	3	11	0
Mangialardi 2002	5	<24 h	2	2	4	0
		>24 h	1	0	1	0
		<48 h	3	2	5	0
		>48 h	0	0	0	0
Yamanishi 2003	8	<24 h	0	2	1	1
		>24 h	0	6	5	1
		<48 h	0	8	6	2
		>48 h	0	0	0	0
Radulovic 2004	47	<48 h	3	4	6	1
		>48 h	30	10	36	4
McCarthy	24	<24 h	2	0	2	0
		>24 h	15	7	18	4
		<48 h	13	3	14	2
		>48 h	4	4	6	2
Olivero 2009	27	<24 h	4	2	5	1
		>24 h	21	0	21	0
		<48 h	12	2	13	1
		>48 h	13	0	13	0
Todd 2011	34	<24 h	2	5	6	1
		>24 h	0	27	1	26
		<48 h	2	16	7	11
		>48 h	0	16	0	16

second analysis was to compare “no catheterization” (“excellent”, or “good”, or “fair”) group with “catheterization” (“poor”) group.

Data extraction

The data of authorship, publication year, sample size, timing of surgery and urinary function outcome were collected from the eligible studies. The risk ratio and 95% confidence interval were extracted or calculated by the raw data from the included studies. Hongxing Song and Chenli Sun extracted the data. The disagreements were discussed and resolved by Hongxing Song (orthopedics) and Qingkun Song (epidemiology).

Data synthesis

Review Manager (RevMan) is The Cochrane Collaboration’s software for preparing and maintaining Cochrane reviews. We used the

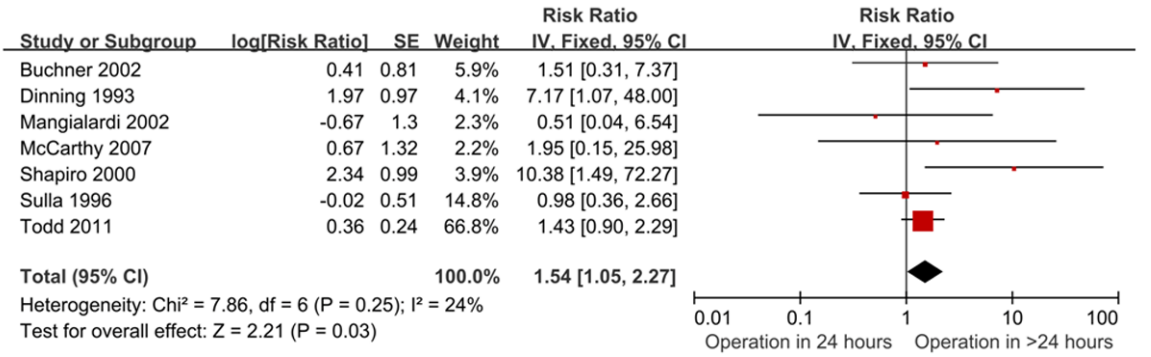

Figure 2. Effect of operation in 24 hours on abnormal urinary function among CESR patients.

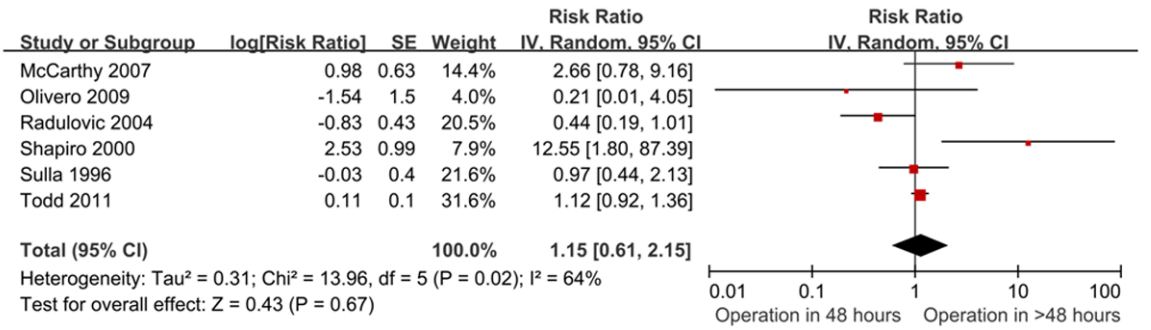

Figure 3. Effect of operation in 48 hours on abnormal urinary function among CESR patients.

version 5.0 to evaluate the pooled effects. "Generic Inverse Variance" method was recommended in RevMan 5.0 to synthesize the data [26]. "Events" were defined as the abnormal recovery of urinary function/catheterization; and the early operation was set as control. Log risk ratio and standard error were input for analyses. In addition, RevMan 5.0 provided not only the summary of estimated effects but also the heterogeneity among the studies. We used Chi^2 tests to assess the heterogeneity where the *P-value* of <0.05 indicated a significant heterogeneity. The random analysis model was used for the significant heterogeneity and the fixed analysis model was used for non-significant heterogeneity. In individual studies that lost follow-up, information biases were assessed. Reporting biases between studies were assessed by Egger's tests.

Results

Over 800 articles were reviewed, however, only 24 studies were considered relevant to our purpose after screening the topics and abstracts. Eventually, 10 studies are included in our meta-analysis at the 24-, 48-hour time point by a careful sorting of the contents [1, 19, 21, 27-38] (**Figure 1** and **Table 1**).

The information on the authorship, publication year, sample size, timing of surgery and urinary function outcome had been extracted from 10 studies between Jan. 1 1990 to Dec. 31 2014, where the sample size was ranged from 6 to 58; timing of surgery was fixed at the 24-, and 48-hour time point. Different groups were classified based on the recovery of bladder function: normal vs. abnormal, no catheterization vs. catheterization. The follow-up was ranged from 1 to 5 years. For limited numbers of case in those studies, the rate of lost follow-up was <1%. The outcomes of abnormal urinary function and catheterization requiring were objectively judged by doctors in hospitals. Risk of biases in individual studies was pretty low.

When we chose the abnormal urinary function as the event, the synthesized RR (relative risk) of the surgical treatment in 24 hours was 1.54 with the 95% CI of (1.05-2.27), compared with that in longer than 24 hours. The heterogeneity

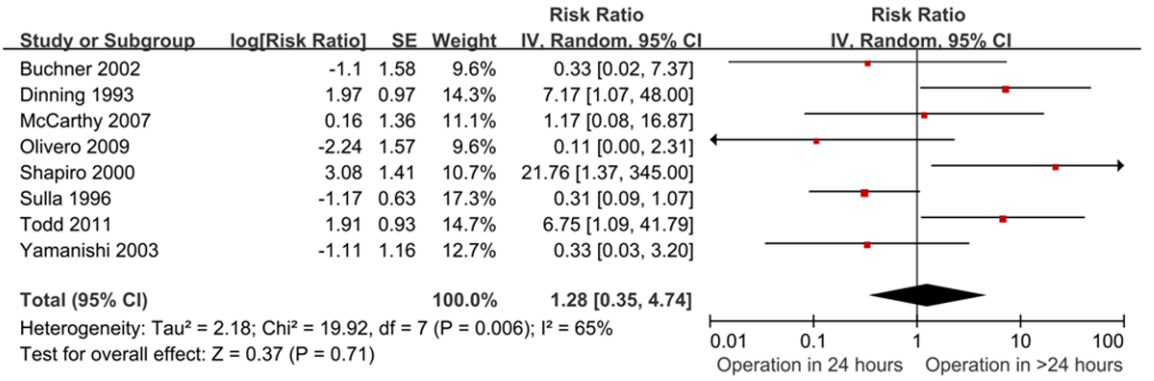

Figure 4. Effect of operation in 24 hours on catheterization requiring among CESR patients.

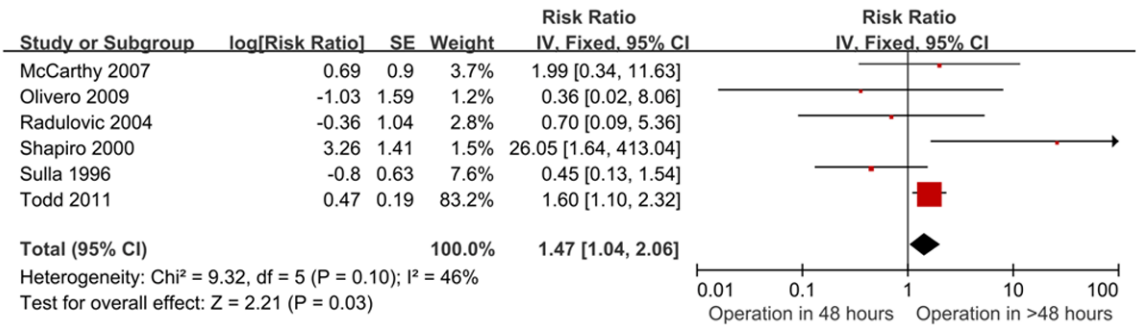

Figure 5. Effect of operation in 48 hours on catheterization requiring among CESR patients.

was non-significant, indicating the operation in more than 24 hours increased the risk of the abnormal urinary function by 54% (**Figure 2**). The operation in more than 48-hours increased the RR to 1.15, the effect was non-significant and the heterogeneity was significant (**Figure 3**).

When we chose catheterization as the event, there was no significant difference in the catheterization requiring for the surgical intervention at ≤24 h vs. >24 h (**Figure 4**). However, the surgical treatment in >48 h was associated with a 47% increased risk of the catheterization requiring (*P*=0.03), in contrast to that ≤48 h. The heterogeneity was non-significant (**Figure 5**).

All the *P*-values in the reporting bias test were >0.05, indicating no significant reporting bias in the analysis (**Table 2**).

Discussion

The relationship between the operation time and the prognosis for CES is unclear. The possible explanation of this uncertainty may be summarized as the following: 1) Complex and various clinical symptoms of CES. There has been no universal standard for the definition and diagnosis of CES in the literatures [39, 40]. Based on 105 published papers, Fraser identified 17 different definitions. Such different definitions reduced the comparability [41]. 2) Different patient population. The study population should be distinguished according to the severity of bladder dysfunction. 3) Lack of well-accepted definition for the degree of the urinary function recovery. Different evaluation systems lead to inconsistent conclusions. 4) Different follow-up time. As the recovery varied from months to years, the results varied accordingly. Further studies are required to be conducted in a large sample size with long-term follow-up, in order to obtain reliable results of the bladder function recovery. 5) CES as a rare disease. Most investigations had very small-sample sizes. The reliability of the results can be undermined by lack of statistical power [33-35]. Therefore, the present study was focused on CESR and set exclusively the abnormal urinary function and the catheterization requiring

Table 2. Test of publication bias in analyses

Events	Treatment time	Egger's test	
		t	P
Abnormal urinary function	≤24 hours	0.40	0.703
	>24 hours		
	≤48 hours	-0.25	0.813
	>48 hours		
Catheterization requiring	≤24 hours	0.90	0.412
	>24 hours		
	≤48 hours	0.15	0.886
	>48 hours		

as the primary endpoints. The included studies were all cohort designs with a mean followed up time for at least 2 years. Limited lost follow-up happened and all of the outcomes were assessed by a standard clinical definition.

It is generally believed that the severity of bladder dysfunction at the time of surgery is the dominant factor for bladder function recovery [10]. An urgent decompression surgery could get a satisfactory recovery of bladder function-for CESI patients, not for CESR patients. Numerous literatures showed that the curative efficiency couldn't be increased even by an early surgery [22]. Nevertheless, Delong et al. reported that the surgical timing was still important for CESR [13]. In the present meta-analysis, the bladder function was improved by the earlier surgery. There was a significant difference in the abnormal urinary function for the surgery at ≤24 h vs. >24 h breakpoint. This result is in accordance with the previous report [13] and may provide a supporting theoretical basis of the early surgery timing for CESR patients. Moreover, a significant difference in catheterization requiring was observed at the ≤48 h vs. >48 h breakpoint, indicating that the patients may discard the urine catheter and recover to void even with various difficulties in urinating, such as straining to void. The 48 h is again a critical time point for the improvement of patients' quality of life and social engagement, and alleviation of depressions. The results are different from a meta-analysis by Delong. It was possibly to be caused by new studies included in our analysis. A 2000 meta-analysis by Ahn et al concluded that a significant improvement in urinary function occurred in patients who underwent decompression within 48 hours versus after 48 hours. But the studies did not classify CESR and CESI definitely. Moreover, criteria of postoperative urinary function outcome did not classified clearly. A 2014 meta-analysis by Chau et al concluded that there was no significant difference in urinary function at the surgery at 48-hours breakpoint. In our study, we further analyzed the urinary function at the 24-hours breakpoint. Moreover, our research analyzed no catheterization with catheterization groups at 24 and 48-hours break point for operation. Simply, our updated meta-analysis set a clear inclusion criterion, classified the outcome definitely and included more studies.

In the present meta-analysis, there was no significant difference in the catheterization remaining at the 24-h breakpoint; nor in the abnormal urinary function at the 48-h breakpoint. This could be a type II error due to the small sample size. CES can cause sphincter dysfunction that may seriously affect the patient's daily life and leads to depression.A recent study including 14 CESR cases reported that a delayed surgical decompression could improve the bladder function obviously, but an early emergency operation would restore the bladder function to the greatest extent [42]. Therefore, we stand for the emergency operation as soon as possible to achieve the maximal benefit.

Tandon and Sankaran classified the CES into 3 subtypes accordingto its onset priorities: suddenly and without a history of back problems (Type I); subacute bladder dysfunction in several days or weeks, with a history of chronic low back pain and/or sciatica (Type II); slowly and insidiously, progressing gradually to severe visceral impairment with urinary retention (Type III).The Onset of symptoms was thought to be critical for decision making [43]. In the present study, the onset priority of the CESR has been not defined yet. The statistical analysis regardless of acute and non-acute patients might introduce inappropriate interpretation. Further study on subtypes of CES should be conducted based on its onset priorities. The prognosis of the surgery intervention must be analyzed separately to draw more convincing and definitive conclusions.

Conclusions

The bladder dysfunction for the CESR patients may be reduced effectively by an early surgery. The operation within 24-hours may decrease

the occurrence of abnormal urinary function. The operation within 48-hours may help to reduce the usage of catheter. We suggest that a universal standard of definition, clinical manifestations, classification, onset priorities, and comprehensive evaluation of CES, and a long-term (extending to several years) follow-up time should be used in the future studies. A multicenter randomized control trial means more to the field.

Disclosure of conflict of interest

None.

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References

[1] Dinning TA and Schaeffer HR. Discogenic compression of the cauda equina: a surgical emergency. Aust N Z J Surg 1993; 63: 927-934.

[2] Khan SN, Hoskins J and Singh K. Cauda equina syndrome: Principles of diagnosis and management. Contemp Spine Surg 2011; 12: 1-5.

[3] Schoenfeld AJ and Bader JO. Cauda equina syndrome: an analysis of incidence rates and risk factors among a closed North American military population. Clin Neurol Neurosurg 2012; 114: 947-950.

[4] Gitelman A, Hishmeh S, Morelli BN, Joseph SA Jr, Casden A, Kuflik P, Neuwirth M and Stephen M. Cauda equina syndrome: a comprehensive review. Am J Orthop (Belle Mead NJ) 2008; 37: 556-562.

[5] Raj D and Coleman N. Cauda equina syndrome secondary to lumbar disc herniation. Acta Orthop Belg 2008; 74: 522-527.

[6] Spector LR, Madigan L, Rhyne A, Darden B 2nd and Kim D. Cauda equina syndrome. J Am Acad Orthop Surg 2008; 16: 471-479.

[7] Siracusa G, Sparacino A and Lentini VL. Neurogenic bladder and disc disease: a brief review. Curr Med Res Opin 2013; 29: 1025-1031.

[8] Balasubramanian K, Kalsi P, Greenough CG and Kuskoor Seetharam MP. Reliability of clinical assessment in diagnosing cauda equina syndrome. Br J Neurosurg 2010; 24: 383-386.

[9] Fairbank J, Hashimoto R, Dailey A, Patel AA and Dettori JR. Does patient history and physical examination predict MRI proven cauda equina syndrome? Evid Based Spine Care J 2011; 2: 27-33.

[10] Qureshi A and Sell P. Cauda equina syndrome treated by surgical decompression: the influence of timing on surgical outcome. Eur Spine J 2007; 16: 2143-2151.

[11] Shi J, Jia L, Yuan W, Shi G, Ma B, Wang B and Wu J. Clinical classification of cauda equina syndrome for proper treatment. Acta Orthop 2010; 81: 391-395.

[12] Gleave JR and Macfarlane R. Cauda equina syndrome: what is the relationship between timing of surgery and outcome? Br J Neurosurg 2002; 16: 325-328.

[13] DeLong WB, Polissar N and Neradilek B. Timing of surgery in cauda equina syndrome with urinary retention: meta-analysis of observational studies. J Neurosurg Spine 2008; 8: 305-320.

[14] Kennedy JG, Soffe KE, McGrath A, Stephens MM, Walsh MG and McManus F. Predictors of outcome in cauda equina syndrome. Eur Spine J 1999; 8: 317-322.

[15] Kohles SS, Kohles DA, Karp AP, Erlich VM and Polissar NL. Time-dependent surgical outcomes following cauda equina syndrome diagnosis: comments on a meta-analysis. Spine (Phila Pa 1976) 2004; 29: 1281-1287.

[16] Daniels EW, Gordon Z, French K, Ahn UM and Ahn NU. Review of medicolegal cases for cauda equina syndrome: what factors lead to an adverse outcome for the provider? Orthopedics 2012; 35: e414-419.

[17] Kumar JR, Krishnan RU and Menon KV. Timing of surgery in cauda equina syndrome. Amrita J Med 2012; 8: 28-30.

[18] Todd NV. Cauda equina syndrome: the timing of surgery probably does influence outcome. Br J Neurosurg 2005; 19: 301-306; discussion 307-308.

[19] Shapiro S. Medical realities of cauda equina syndrome secondary to lumbar disc herniation. Spine (Phila Pa 1976) 2000; 25: 348-351; discussion 352.

[20] Ahn UM, Ahn NU, Buchowski JM, Garrett ES, Sieber AN and Kostuik JP. Cauda equina syndrome secondary to lumbar disc herniation: a meta-analysis of surgical outcomes. Spine (Phila Pa 1976) 2000; 25: 1515-1522.

[21] Olivero WC, Wang H, Hanigan WC, Henderson JP, Tracy PT, Elwood PW, Lister JR and Lyle L. Cauda equina syndrome (CES) from lumbar disc herniations. J Spinal Disord Tech 2009; 22: 202-206.

[22] Chau AM, Xu LL, Pelzer NR and Gragnaniello C. Timing of surgical intervention in cauda equina syndrome: a systematic critical review. World Neurosurg 2014; 81: 640-650.

[23] Bydon M and Gokaslan ZL. Time to treatment of cauda equina syndrome: a time to reevaluate our clinical decision. World Neurosurg 2014; 82: 344-345.

[24] Sonntag VK. Why not decompress early? The cauda equina syndrome. World Neurosurg 2014; 82: 70-71.

[25] Nater A and Fehlings MG. The timing of decompressive spinal surgery in cauda equina syndrome. World Neurosurg 2015; 83: 19-22.
[26] Cohen AJ, Ross Anderson H, Ostro B, Pandey KD, Krzyzanowski M, Kunzli N, Gutschmidt K, Pope A, Romieu I, Samet JM and Smith K. The global burden of disease due to outdoor air pollution. J Toxicol Environ Health A 2005; 68: 1301-1307.
[27] O'Flynn KJ, Murphy R and Thomas DG. Neurogenic bladder dysfunction in lumbar intervertebral disc prolapse. Br J Urol 1992; 69: 38-40.
[28] Busse JW, Bhandari M, Schnittker JB, Reddy K and Dunlop RB. Delayed presentation of cauda equina syndrome secondary to lumbar disc herniation: functional outcomes and health-related quality of life. CJEM 2001; 3: 285-291.
[29] Hussain SA, Gullan RW and Chitnavis BP. Cauda equina syndrome: outcome and implications for management. Br J Neurosurg 2003; 17: 164-167.
[30] Crocker M, Fraser G, Boyd E, Wilson J, Chitnavis BP and Thomas NW. The value of interhospital transfer and emergency MRI for suspected cauda equina syndrome: a 2-year retrospective study. Ann R Coll Surg Engl 2008; 90: 513-516.
[31] Dhatt S, Tahasildar N, Tripathy SK, Bahadur R and Dhillon M. Outcome of spinal decompression in Cauda Equina syndrome presenting late in developing countries: case series of 50 cases. Eur Spine J 2011; 20: 2235-2239.
[32] Sulla I. [The time factor in cauda equina syndrome]. Bratisl Lek Listy 1996; 97: 96-99.
[33] Mangialardi R, Mastorillo G, Minoia L, Garofalo R, Conserva F and Solarino GB. Lumbar disc herniation and cauda equina syndrome. Considerations on a pathology with different clinical manifestations. Chir Organi Mov 2002; 87: 35-42.
[34] Buchner M and Schiltenwolf M. Cauda equina syndrome caused by intervertebral lumbar disk prolapse: mid-term results of 22 patients and literature review. Orthopedics 2002; 25: 727-731.
[35] Yamanishi T, Yasuda K, Yuki T, Sakakibara R, Uchiyama T, Kamai T, Tsujii T and Yoshida K. Urodynamic evaluation of surgical outcome in patients with urinary retention due to central lumbar disc prolapse. Neurourol Urodyn 2003; 22: 670-675.
[36] Radulovic D, Tasic G, Jokovic M and Nikolic I. [The role of surgical decompression of cauda equina in lumbar disc herniation and recovery of bladder function]. Med Pregl 2004; 57: 327-330.
[37] McCarthy MJ, Aylott CE, Grevitt MP and Hegarty J. Cauda equina syndrome: factors affecting long-term functional and sphincteric outcome. Spine (Phila Pa 1976) 2007; 32: 207-216.
[38] Todd NV. Causes and outcomes of cauda equina syndrome in medico-legal practice: a single neurosurgical experience of 40 consecutive cases. Br J Neurosurg 2011; 25: 503-508.
[39] Korse NS, Jacobs WC, Elzevier HW and Vleggeert-Lankamp CL. Complaints of micturition, defecation and sexual function in cauda equina syndrome due to lumbar disk herniation: a systematic review. Eur Spine J 2013; 22: 1019-1029.
[40] Sun JC, Xu T, Chen KF, Qian W, Liu K, Shi JG, Yuan W and Jia LS. Assessment of cauda equina syndrome progression pattern to improve diagnosis. Spine (Phila Pa 1976) 2014; 39: 596-602.
[41] Fraser S, Roberts L and Murphy E. Cauda equina syndrome: a literature review of its definition and clinical presentation. Arch Phys Med Rehabil 2009; 90: 1964-1968.
[42] Aly TA and Aboramadan MO. Efficacy of delayed decompression of lumbar disk herniation causing cauda equina syndrome. Orthopedics 2014; 37: e153-156.
[43] Tandon PN and Sankaran B. Caudaequina syndrome due to lumbar disc prolapse. Indian J Orthop 1967; 1: 112-119.