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ORIGINAL ARTICLE

Impact of the associated anorectal malformation on the outcome of spinal dysraphism after untethering surgery

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Abstract

Purpose To analyze the outcome after untethering surgery in patients with spinal dysraphism (SD), with or without associated anorectal malformation (ARM).

Methods Patients operated on for SD, with (Group A) or without (Group B) associated ARM (1999–2015), were included. The post-operative outcome was analyzed in the two groups in terms of improving of clinical symptoms (neuro-motor deficits, bladder dysfunction, bowel dysfunction) and of instrumental examinations (urodynamics, bladder ultrasound, neurophysiology). Fisher's exact test and χ^2 test were used as appropriate; $p < 0.05$ was considered statistically significant.

Main results Ten patients in Group A and 24 in Group B were consecutively treated. One patient was lost at follow up. Six patients (25%) in Group B underwent prophylactic surgery. The analysis of the pre-operative symptoms in the two groups showed that a significantly higher number of patients in group A needed bowel management and presented with neuro-motor deficits, compared to group B ($p = 0.0035$ and $p = 0.04$, respectively). Group A showed a significant post-operative neuro-motor improvement as compared to group B ($p = 0.002$).

Conclusions Based on our results, untethering seems to be effective in neuro-motor symptoms in selected patients with ARM. In ARM patients, untethering surgery does not seem to benefit intestinal and urinary symptoms. The presence of the associated ARM does not seem to impact the medium-term outcome of patients operated for SD.

Keywords Anorectal malformations · Spinal dysraphism · Tethered cord syndrome · Untethering surgery · Bowel function · Neurogenic bladder

Introduction

Patients with anorectal malformations (ARM) often present with associated anomalies of the spectrum of the VACTERL association, which includes spinal and/or vertebral defects (V), anorectal malformations (A), congenital cardiac anomalies (C), esophageal atresia/tracheoesophageal fistula (TE), renal and urinary abnormalities (R), and limb lesions (L) [1]. In particular, spinal dysraphism (SD) has been reported in up to 46% of the patients with ARMs [2, 3]. Therefore, neonates with ARM are screened at birth for the possible association with the above anomalies, and a spinal ultrasound (US) is performed in the neonatal period to detect spinal anomalies, confirmed or not by magnetic resonance imaging (MRI). When symptomatic, the presence of SD (both isolated or associated with ARM) may lead to the tethered cord syndrome (TCS), with symptoms mainly related to neuro-motor disorders, but also to urologic abnormalities

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and bowel dysfunction. In patients with SD associated with ARM, early symptoms of TCS may sometimes overlap with clinical manifestations proper of the ARM or its surgical correction (i.e. urinary and fecal incontinence), this still leading to disputed indications to surgical management of TCS, with some suggesting neurosurgery while others proposing a ''wait and see'' approach [4, 5].

Our previous studies on ARM and SD were focused on the definition of their association, their embryogenetic implications and the impact of SD on the outcome of patients with ARM [6, 7]. In the present study, we aimed to analyze the outcome after untethering surgery in patients with SD, with or without associated ARM.

Materials and methods

All patients with SD with/without associated ARM treated between January 1999 and December 2015 were considered and retrospectively evaluated. All patients with ARM were screened for SD on a regular basis with spinal ultrasounds in the neonatal period (< 3 months of age) and spinal MRI offered at 1 year of age [8]. Of those, only patients who were diagnosed with SD at MRI and operated on were included in this study (Group A). Patients diagnosed with isolated SD, referred to the Neurosurgery Unit and operated on for SD in the same period were included in Group B. Tethered spinal cord was defined as MRI images of a conus medullaris below the L2–L3 vertebra level, associated or not with SD. Tethered spinal cord can develop in symptomatic TCS, with patient presenting with neuro-motor disorders of the back and legs, urinary, and/or bowel dysfunction. Asymptomatic patients with syrinx at MRI underwent a neuroimaging follow-up in order to control the progression of the syringomyelia. Indication to neurosurgery was given in patients with symptomatic and/or clinical worsening of TCS, when the MRI showed progression of the syringomyelia, or in SDs at high risk of developing TCS. We considered as "SDs at high risk of TCS" those defects of the neural tube closure, showing a large lipoma at the MRI, tightly attached to the spinal cord and to the roots of the cauda equina.

The two groups were compared for: age at neurosurgery, post-operative complications, mean post-operative follow-up, pre- and post-operative functional outcome, and presence of cutaneous stigmata (i.e. dermal sinus, localized hypertrichosis, hyperpigmented lesion).

Functional outcome

Bowel evaluation was performed by neonatal/pediatric surgeons in terms of fecal incontinence and constipation. Bowel management (BM) was indicated in patients with soiling grade 2 or 3 and/or constipation grade 2 or 3, according to Krickenbeck score [9], who did not respond to conventional dietary and medical therapy.

Urological evaluation was performed by pediatric neurourologists in terms of bladder US (calyceal ectasia, bladder wall thickening, post-void residual) pad test and diary, and urodynamic evaluation in selected cases after 2 years of age. Urinary incontinence was considered when the child (toilet-trained) was unable to hold the urine at day time. Pathological urodynamic pattern in patients with SD was considered as a sign of neurogenic voiding dysfunction.

Neuro-motor function was assessed by neurosurgeons with physical examinations. Intraoperative neurophysiological monitoring (IONM) was performed using somatosensory evoked potentials (SEP), motor evoked potentials (MEP), and bulbocavernosus reflex (BCR). Neuro-motor deficits include back pain worsened by activity and relieved with rest, leg pain, leg numbness or tingling, changes in leg strength, leg and/or foot deformities, gait disorders, and scoliosis.

In patients with tests both before and after neurosurgery, the evolution of bowel function, urinary function and neuromotor function was also studied.

Statistical analysis

Data were analyzed using GraphPad Prism 5.0 Macintosh Version (GraphPad Software, San Diego CA USA, http://www.graphpad.com). Groups were compared using the Fisher's exact test and χ^2 test for trend as appropriate. Results are reported as median and range; $p \leq 0.05$ (two- sided) was considered statistically significant.

Results

During the study period, 83 patients were diagnosed at MRI with ARM-associated SD and 38 patients with isolated SD. Of those, 10 patients with ARM-associated SD had neuro-motor deficits and bladder dysfunction and underwent untethering surgery for symptomatic TCS (group A). Twenty-four patients with isolated SD (group B) underwent untethering surgery, 6 (25%) of which had prophylactic surgery in order to prevent the development of a TCS, strictly related to the complexity of their spinal dysraphism. One patient in group B was a myelomeningocele and was excluded from the study. The severity of this type of SD, compared to the others, would have determined a bias in the outcome.

Table 1 shows the distribution of different types of SD in both groups. In particular, group A was associated with a less severe type of lipoma, the filum lipoma ($p = 0.057$), with spinal lipoma only presenting in group B. Interestingly, in our series, most of the patients with isolated SD (87%)

Table 1 Patients characteristics

	Group A $n=10$	Group B $n=23$	p
Sex			0.01
Male	10	12	
Female	0	11	
Age at untethering (months)	90.1	56.9	ns
Mean follow-up time (months)	33.6	25.9	ns
Type of SD			
Filum lipoma	8	9	ns
Spinal lipoma	0	3	ns
Lipomyelocele	1	4	ns
Lipomyelomeningocele	1	6	ns
Epidermoid cyst	0	1	ns
Cutaneous stigmata	2	20	0.0004

SD spinal dysraphism

presented with cutaneous stigmata, compared to a minority (20%) in ARM-associated SD group ($p=0.0004$). Also, all patients in group A were male, compared to 52% in group B ($p=0.01$).

Table 2 reports data obtained from the pre- and post-operative clinical and instrumental examination of the two groups, in terms of intestinal, urologic and neuro-motor function. Neurophysiological pre-operative data were collected for the two groups from standard pre-operative exams and baseline IONM recordings. They were considered "altered" if at least one of the included techniques showed abnormalities. A significantly higher number of patients in group A needed bowel management and presented with neuro-motor deficits, compared to group B ($p=0.0035$ and $p=0.04$ respectively). Group A showed a significant post-operative neuro-motor improvement as compared to group B ($p=0.002$).

Three patients in group B (2 lipomyelocele, 1 lipomyelomeningocele) and no patient in group A underwent redo-detethering surgery for residual lipoma ($p=$ns). Also, three patients in group A developed post-operative minor complications: one localized epidural subcutaneous infection treated with wound toilet and local disinfection, and two intermittent leg pain and leg tiredness resolved spontaneously within 12 months from the untethering surgery ($p=$ns).

Discussion

The association between ARM and SD has been widely documented in the literature [2, 5, 10]. The high variability over the years in the reported incidence and in the surgical approach to this spinal anomaly is mainly due to the evolution of the diagnostic and therapeutic techniques. Thus, the widespread of the MRI as a method of early screening, has led to an increased recognition of this association. Also, the surgical approach results extremely variable between authors, with some advising prophylactic surgery, the majority agreeing on the benefits of the neurosurgery only in symptomatic patients [4, 5, 11]. However, to our knowledge, no previous studies have analyzed if the associated

Table 2 Pre- and post-operative functional outcome in both groups

	Group A $n=10$	Group B $n=23$	p
BM pre-op	4/9	0/23	0.0035
BM post-op	5/9	2/23	0.01
Improvement	0/9	0/23	ns
Worsening	1/9	2/23	ns
Bladder US anomalies pre-op	4/8	10/23	ns
Bladder US anomalies post-op	6/8	13/23	ns
Improvement	0/7	2/23	ns
Worsening	2/7	9/23	ns
Urodynamic anomalies pre-op	7/9	12/13	ns
Urodynamics anomalies post-op	2/7	11/19	ns
Improvement	4/7	3/11	ns
Worsening	0/7	0/11	ns
Neuro-motor deficit pre-op	7/9	8/23	0.04
Neuro-motor deficit post-op	1/9	5/23	ns
Improvement	6/9	3/23	0.002
Worsening	0/9	0/23	ns
Neurophysiological abnormalities pre-op	3/10	5/18	ns

BM bowel management, *US* ultrasound

ARM may influence the functional outcome of patients with SD who underwent untethering surgery.

In the present study, we evaluated the medium-term functional outcome in terms of anorectal, urological, and neuro-motor function of patients with ARM associated SD, compared to patients with isolated SD, after untethering surgery. To assess the anorectal function, we retrospectively evaluated only patients aged 3 years and older, hence toilet trained. The results obtained in terms of bowel function showed that a significantly higher number of patients with ARM-associated SD needs bowel management, not improving after untethering surgery (Table 2). As discussed above, the neurosurgical treatment of patients with ARM-associated SD remains controversial. In fact, SD can present with a wide spectrum of clinical manifestations, some of which may mimic the sequelae of ARM or its surgical correction (i.e., lower urinary tract dysfunctions and fecal incontinence). Our results showed that patients with pre-operative bowel dysfunction, did not experienced a functional improvement after detethering. Despite the relatively small number of patients in this series, these data support the idea that the anorectal symptoms only, in both patient groups, are not sufficient to justify the neurosurgical indication [10, 12].

Urodynamics (UDS) has been commonly suggested in children with ARM-associated SD, either in the preoperative evaluation or in the postoperative course, after untethering surgery [13]. The role of UDS is crucial for the early and correct diagnosis of neurogenic bladder dysfunction (NBD) that may lead to incontinence, urinary tract infections (UTIs), vesico-ureteral reflux (VUR), and renal scarring [14]. If not managed properly, NBD is cause of renal failure, requiring dialysis or transplantation. According to our protocol, invasive UDS is performed when MRI detects a SD or when NBD is suspected, on the basis of non-invasive urodynamic evaluation [15]. Also, in children with ARM and SD the role of lower urinary tract dysfunction (LUTD) has been largely debated in the past, especially in male patients. LUTD have been related to the ARM itself or to the presence of post-operative urethral stricture or fistula remnants. For this reason, untethering surgery on the base of LUTD has been criticized by some authors and considered unnecessary. Patients in group A, did not experience urodynamic worsening after surgery, suggesting that LUTD cannot be related to the urethral stricture or to the presence of the fistula remnants. These data are important as all patients of group A are males, at higher risk of urethral lesions during ARM surgery. Furthermore, the improvement seen in UDS, although not reaching significance, suggests that detethering can be useful in selected cases, even if the UDS improvement is more evident than the clinical one.

The analysis of the type of SD in both groups showed that the ARMs seem to be associated with a less complex type of spinal lipoma, possibly based on the stages of neural tube formation during embryogenesis [16]. In our series, the highest number of patients with isolated SD (group B) suffered from SD developing as a result of a failure in the primary neurulation phase, as demonstrated in our previous study [7]. The more complex type of SD in group B may explain the need for redo-untethering surgery in three patients in group B, and the lack of post-operative complications in group A as compared to the isolated SD group. The difference in the histological type of spinal dysraphism in the two groups, more severe in group B, could also explain why patients with isolated SD were treated earlier for neurosurgery and, some of them, even before becoming symptomatic. Similarly, it may explain why a higher proportion of patients with ARM, symptomatic for TCS and treated for untethering, improved after surgery as compared to those with isolated SD ($p=0.002$). We can speculate that the type of spinal dysraphism, therefore the relationship of the lipoma with the spinal cord and the roots of the cauda equina, could be associated with sensory-motor deficits more or less reversible after surgery. Despite these considerations, the preservation of the neurological status and the absence of a clinical worsening after surgery, as evident in our series, could be considered a good post-operative outcome and should be taken into account among the criteria for the neurosurgical treatment.

Conclusions

This study has some limitations, mainly due to its retrospective nature. Most of the data on the functional outcome were obtained by clinical notes where symptoms and physical examination were often reported with a non-systematic method. Also, the lack of complete pre- and/or post-operative functional tests, such as UDS and neurophysiological studies, further limits the number of patients to compare in the final analysis. Finally, we had data from a relatively small cohort of patients with ARM-associated and isolated SD.

Despite these limitations, our results show the importance of defining a pre-operative clinical and instrumental diagnostic pathway before planning the neurosurgical treatment of patients with ARM associated SD. In fact, the rough definition of the pre-operative functional status for each patient could lead to the incorrect indication to surgery.

Further prospective, randomized clinical studies are needed to assess the efficacy of pre- and post-operative functional tests in patients with ARM associated SD, requiring neurosurgical treatment. Well-collected neurophysiological data both in the pre-surgical and in the follow up assessment, could be compared to establish if they can be predictive for a sensory-motor functional improvement.

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