Pediatr Surg Int (2015) 31:805–808
DOI 10.1007/s00383-015-3745-5

ORIGINAL ARTICLE

VACTERL association in anorectal malformation: effect on the outcome

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Accepted: 23 June 2015 / Published online: 5 July 2015

Abstract
Purpose Anorectal malformations (ARM) can commonly occur in association with other congenital anomalies or as part of the combined anomaly. The present study aims to assess the outcome of patients with ARM and patients with ARM in VACTERL association.
Methods A 12-year retrospective analysis of all patients treated at a single tertiary children's institution with a diagnosis of ARM. We identified and compared patients with ARM to those with ARM in VACTERL association (3 or more anomalies). Data were collected for both groups to assess type of ARM, urinary incontinence (UI), constipation, soiling, dietary/laxative treatment, bowel management (BM) and surgical complications. Type of lesion and clinical outcomes were classified according to Krickenbeck International classification. Patients lost to follow-up, dead or not yet toilet-trained (or <4 years old) were excluded.
Results One hundred ninety-eight patients were identified, 174 enrolled in the study. Lesions were classified for each study group (VACTERL− vs VACTERL+) as perineal fistulas (36.4 vs 9.7 %, $p = 0.0028$), rectourethral fistulas (prostatic and bulbar) (23.1 vs 38.7 %, $p =$ ns), rectovesical fistulas (3.5 vs 9.7 %, $p =$ ns), rectovestibular fistulas (19.6 vs 22.6 %, $p =$ ns), cloacal malformations (4.9 vs 9.7 %, $p =$ ns), no fistula (4.9 vs 3.2 %, p=), others (7.7 vs 6.4 %, $p =$ ns). The frequency of both dietary/laxative treatment and BM, as well as surgical complications were significantly higher in patients with VACTERL.
Conclusions The coexistence of VACTERL anomalies negatively affects not only the surgical outcome but also the bowel functioning. Therefore, a dedicated follow-up is strongly recommended. Further studies are needed to assess if this has an impact on the quality of life of these patients.

Keywords Anorectal malformations · Bowel management · Surgical complications · Spinal dysraphism · VACTERL

Introduction

Anorectal malformations (ARMs) are among the more common congenital anomalies in the newborn, with an estimated incidence ranging between 1 and 3 in 5000 live births [1–3]. Their association with other congenital defects has been widely described in the literature, varying among different studies, between 20 and 70 % [2]. The non-random coexistence of anomalies of the spine or vertebrae (V), anorectal malformations (A), congenital cardiac anomalies (C), esophageal atresia/tracheoesophageal fistula (TE), renal and urinary abnormalities (R), and limb lesions (L) is referred to as VACTERL association [4]. Originally described by Quan and Smith in 1973 as VATER, and in 1974 as VACTERL when Temtamy and Miller included the cardiac (C) and limb (L) components as part of the spectrum, VACTERL association is frequently encountered by the pediatric surgeon in patients operated on for esophageal atresia/tracheoesophageal fistula (EA/TEF) or ARM.

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The surgical and medical management of patients with ARMs is extremely variable and not only depending on the type of anorectal defect. In fact, the co-occurrence of other congenital abnormalities can result in an extreme complex care of these patients, affecting both their short and long-term surgical and medical outcome. The aim of the present study was to evaluate the impact of VACTERL association on the outcome of patients with ARM.

Materials and methods

A retrospective analysis was performed of all infants diagnosed with ARM and treated at our single tertiary children's hospital between January 1999 and December 2011 ARMs were described based on the Krickenbeck anatomical classification [5]. Patients with rectobulbar and rectoprostatic fistulas were considered in the same group of rectourethral fistulas. Patients were divided in two groups based on whether ARM was in the context of VACTERL association (3 or more among vertebral, anal, cardiac, tracheoesophageal, renal and limb anomalies) or not. Data were collected from a dedicated database and patients' clinical notes. The two groups were compared for type of ARM, associated congenital anomalies, type of surgical repair, additional surgical procedures, presence of colostomy, clinical outcome, and surgical complications. Associated anomalies were classified as chromosomal, spinal, limb, central nervous system, cardiovascular, gastrointestinal (including esophageal atresia/tracheoesophageal fistula), urogenital, and others. Clinical outcomes, including constipation, soiling and bowel management were classified according to the Krickenbeck International classification [5]. A telephone interview was also administered to all families by a single surgeon to collect data about urinary incontinence (UI), constipation, soiling, dietary/laxative treatment and need for bowel management (BM). BM was performed in patients with Grade 3 soiling/constipation, when the laxative therapy failed. BM was intended as enema or transanal irrigation system (Peristeen® Anal Irrigation System; Coloplast A/S, Kokkedal, Denmark or Mallinckrodt, St Louis, MO) every 24/48 h. Patients lost to follow-up, dead or not yet toilet-trained (or <4 years old) were excluded from the study. Patients were considered "lost at follow-up" when the essential data from the clinical notes were not entirely available.

Statistical analysis

Data were analyzed using GraphPad Prism 5.0 Macintosh Version (GraphPad Software, San Diego, California, USA, http://www.graphpad.com). Groups were compared using the unpaired *t* test or the Fisher's exact test. Results are mean ± standard error (SE) or prevalence; $p < 0.05$ (two-sided) was considered statistically significant.

Results

Data from one hundred ninety-eight patients operated on for ARM during the study period were reviewed; 174 fulfilled the criteria for inclusion in the study. Overall, there were 102 (58.6 %) male patients. One hundred fifteen (66.1 %) patients had at least one associated anomaly or syndrome, leaving only 59 patients (33.9 %) with isolated ARM (Table 1). Spinal disorders were the most common single abnormality encountered (33.3 %). Taken together genitourinary abnormalities were more frequent than spinal anomalies, but when separated (urogenital or renal) they were less frequent. VACTERL association was found in 31 (17.8%) children. Table 2 summarizes the

Table 1 Type of anomalies and syndromes associated with ARM

Type	VACTERL− ($n = 143$)	VACTERL+ ($n = 31$)	*p*
Chromosomal	5 (3.5 %)	4 (12.9 %)	ns
Spinal	42 (29.4 %)	16 (51.6 %)	0.0215
Limb	1 (0.7 %)	8 (25.8 %)	<0.0001
Central nervous system	20 (14.0 %)	8 (25.8 %)	ns
Cardiovascular	9 (6.3 %)	19 (61.3 %)	<0.0001
Gastrointestinal	0 (0 %)	17 (54.8 %)	<0.0001
Genitourinary	45 (31.5 %)	24 (77.4 %)	<0.0001
Other syndromes and malformations	17[a] (11.9 %)	3[a] (9.7 %)	ns

[a] Including Williams Syndrome, Cat Eye Syndrome, Di George Syndrome, Kabuki Syndrome, Klinefelter Syndrome, Down Syndrome, tracheomalacia, labioschisis and hypothyroidism

Table 2 Type of ARM according to the Krickenbeck anatomic classification

Type of ARM	VACTERL− ($n = 143$)	VACTERL+ ($n = 31$)	*p*
Rectoperineal fistula	52 (36.4 %)	3 (9.7 %)	0.0028
Rectourethral fistula	33 (23.1 %)	12 (38.7 %)	ns
Rectovesical fistula	5 (3.5 %)	3 (9.7 %)	ns
Rectovestibular fistula	28 (19.6 %)	7 (22.6 %)	ns
Cloaca	7 (4.9 %)	3 (9.7 %)	ns
No fistula	7 (4.9 %)	1 (3.2 %)	ns
Others	11 (7.7 %)	2 (6.4 %)	ns

Table 3 Comparison of the clinical and surgical outcome between the two study groups

	VACTERL− ($n = 143$)	VACTERL+ ($n = 31$)	p
Surgical complications	15 (10.5 %)	9 (29 %)	0.0174
UI	14 (9.8 %)	6 (19.3 %)	ns
Constipation	100 (70 %)	25 (80.6 %)	ns
Soiling	60 (42 %)	19 (61.3 %)	ns
Dietary/laxative treatment	80 (56 %)	29 (93.5 %)	<0.0001
BM	47 (32.9 %)	17 (54.8 %)	0.0251

UI urinary incontinence, *BM* bowel management

different type of ARM for each study group. Rectoperineal fistula was the more frequent ARM encountered, with significantly higher prevalence in patients not in the context of VACTERL association (36.4 vs 9.7 %, $p = 0.0028$). The prevalence of other ARMs was comparable in the two groups. Ten female patients had cloacal anomalies, with no difference in prevalence in the two groups (4.9 % vs 9.7 %, $p =$ ns).

Posterior sagittal anorectoplasty (PSARP) was the treatment in 129 (90.2 %) VACTERL–patients and 25 (80.6 %) VACTERL+, abdominal PSARP in 4 (2.8 %) VACTERL− and 3 (9.7 %) VACTERL+, total urogenital mobilization in 7 (4.9 %) VACTERL− and 3 (9.7 %) VACTERL+, posterior sagittal anorecto-vagino-urethroplasty in 3 (2.1 %) VACTERL−. Overall, a colostomy was performed in 111 patients, with a significant difference between the two groups (58 vs 90 % in VACTERL− vs VACTERL+, respectively; $p = 0.0004$). Table 3 shows the outcomes in the two groups. Prevalence of surgical complications (including intestinal obstruction, abdominal abscess, anorectoplasty dehiscence/prolapse/stenosis, wound dehiscence, laparocele, vaginal and urethral injury) was significantly higher in patients with VACTERL ($p = 0.0174$).

Results of telephone interview administered to families of both study groups, showed no difference between the two groups in terms of UI, constipation and soiling. A significantly higher prevalence of VACTERL+ patients required dietary/laxative treatment as compared to VACTERL− patients (93.5 vs 56 %; $p < 0.0001$). The need for bowel management was significantly higher in patients with VACTERL association ($p = 0.0251$), mostly in those with rectourethral fistulas ($n = 6$).

Discussion

Anorectal malformations are relatively common congenital anomalies. Patients with ARM are often affected by additional congenital anomalies, whose coexistence account for the high morbidity and mortality associated with this condition [3, 6]. In our population, we report an incidence of associated malformations and syndromes (at least 1) in 66 % of children with ARM, which is in line with what has been reported in the recent literature (20–70 %) [2, 3, 6–8]. It is of paramount importance for the pediatric surgeon to identify in these patients any associated anomalies both in the prenatal and postnatal period, to guarantee an optimal management and counselling for the families. In this study, we aimed to estimate the implications of VACTERL association on patients with ARM, in terms of clinical and surgical outcomes. In our population VACTERL association had a prevalence of 17.8 %, similar to what has been reported by Cuschieri et al. in their large sample population [8]. We divided patient in different subgroups, according to the Krickenbeck anatomic classification (Table 2). The distribution of the different type of ARMs was similar in the two groups except for the rectoperineal fistula, whose incidence was significantly higher in patients VACTERL -, like previously reported in the literature [9]. When we analyse the surgical outcome of the two study groups, patients with VACTERL association had a significantly higher prevalence of surgical complications ($p = 0.0174$). Complications were intestinal obstruction (4 in VACTERL− and 2 in VACTERL+), anorectoplasty dehiscence (2 in VACTERL− and 3 in VACTERL+), laparocele (1 in VACTERL− and 2 in VACTERL+), abdominal abscess (2 in VACTERL−), anorectoplasty stenosis (2 in VACTERL−), colostomy ischemia (1 in VACTERL−), colostomy prolapse (1 in VACTERL+), vaginal lesion (1 in VACTERL−), urethral lesion (1 in VACTERL−), seminal vesicle lesion (1 in VACTERL−) and NEC (1 in VACTERL+). This higher prevalence could be related to the anomalies associated to the ARM in these patients. However, no surgical complication seems to be the direct consequence of the associated anomalies. Therefore, other factors are probably responsible for this difference. Considering the two groups, colostomy was significantly more frequent in patients with VACTERL. In addition, patients in the VACTERL group required significantly more laparotomies for associated anomalies, such as duodenal atresia ($n = 3$), biliary atresia ($n = 1$) and choledochal cyst ($n = 1$) as compared to patients without VACTERL ($n = 0$) ($p < 0.0001$). Most of the complications may be laparotomy related.

We found that patients with VACTERL had a poorer clinical outcome in terms of need for dietary/laxative treatment and bowel management. The higher incidence of spinal anomalies ($p = 0.0215$) may play a role in the worse prognosis of these patients. In fact, it is well known that the presence of spinal anomalies has a bad influence on the functional prognosis of these patients [10, 11].

Conclusions

Our data clearly show that the coexistence of VACTERL association significantly impacts the clinical and surgical outcomes of patients with ARM. These patients have a worse surgical outcome and functional prognosis in terms of bowel management and dietary/laxative treatment. However, it is still not clear if this is due to the higher incidence of spinal anomalies or to the more complex general condition of these patients.

An exhaustive evaluation of all patients with ARM should be done, focusing with particular regard on the presence of associated anomalies. The clinician should be aware that the presence of associated anomalies dictates a strict dedicated follow-up and should acknowledge the families of these patients that they may have worse surgical and functional prognosis.

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