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ARTICLE

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Trends in the surgical management of vesicoureteral reflux in Finland in 2004–2014*

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ABSTRACT

Objectives: Previous data on the trends of surgical treatment of vesicoureteral reflux outside USA are scarce. The aim of this study was to clarify the national trends of operative treatment of vesicoureteral reflux (VUR) in Finland.

Methods: We analyzed national data from Finnish Care Register for Health Care on children (<16 years of age) surgically treated for VUR in 2004–2014.

Results: Endoscopic injections of the ureteral orifices were primarily performed for 1212 and open ureteral reimplantation for 272 children. The use of both types of surgery decreased during the study period ($p = 0.0043$ and $p < 0.001$, respectively). The median age at surgery for VUR was lower in those treated with open ureteral reimplantation than those with endoscopic injections of the ureteral orifices [3 and 4 years, respectively] ($p = 0.0001$). The length of hospital stay was significantly longer (median 9.9 days) with open ureteral reimplantation compared to that (median 1.3 days) with endoscopic injections ($p < 0.0001$) and did not change during the study period. Reoperations were significantly more common in patients who were primarily treated with endoscopic injections ($n = 146/1072$, 14%) than with ureteral reimplantation ($n = 7/230$, 3%) ($p < 0.0001$).

Conclusions: While the best treatment options for VUR remain debatable, operative treatment of VUR has become less common in Finland.

HIGHLIGHTS

- Recent data on the trends of treatment of vesicoureteral reflux outside USA are scarce.
- Surgical treatment for vesicoureteral reflux decreased in Finland during the study period.
- The length of stay was longer but reoperations were needed less often with ureteral reimplantation compared to endoscopic injections.

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KEYWORDS

VUR; deflux; reimplantation; surgery; pediatric

Introduction

Despite emerging high-quality analyses, the management of vesicoureteral reflux (VUR) seems controversial, especially regarding younger patients [1]. The treatment options of VUR are conservative treatment and antimicrobial prophylaxis, suburethral injection of bulking agents under cystoscopic guidance (referred to as endoscopic injections), and open or laparoscopic ureteral reimplantation. The emphasis in the management of VUR seems to be towards less invasive procedures [2]. While the traditional surgical treatment option of VUR has been open ureteral reimplantation, endoscopic injections seem to have gained ground as the preferred method of reducing the degree of VUR [3].

The best treatment option for VUR to inhibit renal scarring remains debatable [4,5]. It is known that VUR spontaneously resolves in some patients with increasing age [6]. The role of continuous antimicrobial prophylaxis has been questioned. However, some data on the advantages of antimicrobial prophylaxis in preventing renal scarring has been published [7]. Endoscopic injections have been reported to be effective with the first treatment in grade 4 and 5 VUR in 63 and 51% [8]. There are few reports on the effects of endoscopic injections on renal scarring with modest results [7,9].

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*Level III retrospective cohort study.

In open ureteral reimplantations, 92–99% VUR resolution rates have been reported depending on the technique used [8,10]. In addition, laparoscopic ureteral neoimplantation can be used with reports of 96-100% VUR resolution rate [11,12], although these studies also included patients with lower grades of reflux. Again, there is little evidence on the usefulness of ureteral reimplantation on renal scarring [1].

Data on the trends of treatment of VUR are scarce and there are no publications on the trends in Europe. In the USA, the rate of ureteral implantations remained stable from 2002 to 2004 while the rate of endoscopic injections for the treatment of VUR increased [13]. After that, a significant decrease in ureteral reimplantations (from 2003 to 2013) [14] and a decrease in the use of endoscopic injections for VUR (from 2004 to 2011) [15] has been reported in the USA. This decrease in both procedures in the USA has become more pronounced after the American Academy of Pediatrics urinary tract infection guidelines were released [16].

The aim of this study was to clarify the national trends of the operative treatment of VUR in Finland during the years 2004–2014. We hypothesized that there was a decrease in the overall operative treatment of VUR during the study period due to a decrease in both open ureteral reimplantation and endoscopic injection therapy.

Materials and methods

We included patients aged less than 16 years that were surgically treated by ureteral reimplantation or endoscopic injections of the ureteral orifices from January 2004 through to December 2014. Data were retrospectively collected from all hospitals surgically treating pediatric patients in mainland Finland by using the Finnish Care Register for Health Care (CRHC). CRHC is a nationwide obligatory-by-law register that includes data on all hospital admissions and day surgery visits in Finland. Surgical procedures were identified according to Nordic Classification of Surgical Procedures codes for ureteral reimplantation (open KBH20 and laparoscopic KBH21) or endoscopic injections of the ureteral orifices (KBV52). The corresponding diagnoses codes according to the 10th Revision International Statistical Classification of Diseases and Related Health Problems (ICD-10) were collected and analyzed. The length of hospital stay with primary surgery and the number of reoperations for VUR were recorded. The day of surgery and the day of discharge were included in the length of stay. We excluded patients with congenital malformations of the urinary tract (Q64.x), rectum or colon (Q42.x-Q43.0), and patients with neurogenic bladder dysfunction (N31.x).

Data on rehospitalizations and reoperations were collected for two years after the primary surgery for VUR for children born in 2004-2012. The complication of treatment was defined as Clavien–Dindo Classification grade IIIb complication [17] (i.e. a complication requiring rehospitalization with reoperation under general anesthesia). For the list of procedures considered as reoperations for VUR see Appendix 1.

Statistical analyses

Continuous variables were described in terms of median and interquartile ranges (IQR). Categorical variables were presented as frequencies and proportions (percentages). The number of VUR procedures were calculated relative to less than 16-year-old children at risk by using publicly available population data from Statistics Finland [18]. For differences in medians, the Wilcoxon rank sum test was used. For differences in proportions, Chi-squared test or Fisher's exact test was performed. All analyses were conducted using R version 3.6.1. p-Values less than 0.05 were considered statistically significant.

Ethics

The study was approved by the National Institute for Health and Welfare of Finland (permissions no: THL/143/5.05.00/2015). This was a retrospective register study and thus no informed consent was required and the participants were not contacted. The legal basis for the processing of personal data is public interest and scientific research (EU General Data Protection Regulation 2016/679 (GDPR), Article 6(1)(e) and Article 9(2)(j); Data Protection Act, Sections 4 and 6).

Results

A total of 1484 children were treated for VUR in mainland Finland during the study period, the majority of which in five university hospitals. Most children ($n = 1212$, 67% female) were primarily treated with endoscopic injections of the ureteral orifices, while open ureteral reimplantation for VUR was primarily performed for 272 children (57% female), and no laparoscopic ureteral reimplantations were performed. The numbers of open ureteral reimplantations and endoscopic injections performed per 100 000 children decreased during the study period ($p = 0.0043$ and $p < 0.001$, respectively). The annual reduction was 5.2% per year for ureteral reimplantations and 12.4% for endoscopic injections. During the study years, there were on average 954,901 (range 945,977 to 974,301) inhabitants aged 0 to 15 years per year in Finland. See Figure 1.

The median age of the patients at primary surgery for VUR was 3 years (IQR 1–6, range 0–12) for open ureteral reimplantation and 4 (IQR 2–6, range 0–15) for endoscopic injections of the ureteral orifices ($p = 0.0001$). The age for primary endoscopic injections decreased ($p < 0.0001$), but did not significantly change for open ureteral reimplantation ($p = 0.1116$) during the study period.

The length of hospital stay was significantly longer (median 9.9 days [IQR 8–11, range 3–24]) with open ureteral reimplantation compared to that (median 1.3 days [IQR 1–1, range 1–17]) with endoscopic injections ($p < 0.0001$). The length of stay did not significantly change during the study years with either procedure ($p = 0.2299$ for open ureteral reimplantation and $p = 0.0582$ for endoscopic injections).

Within 2 years after primary treatment of VUR, 164 patients were reoperated (13% of all those treated for VUR

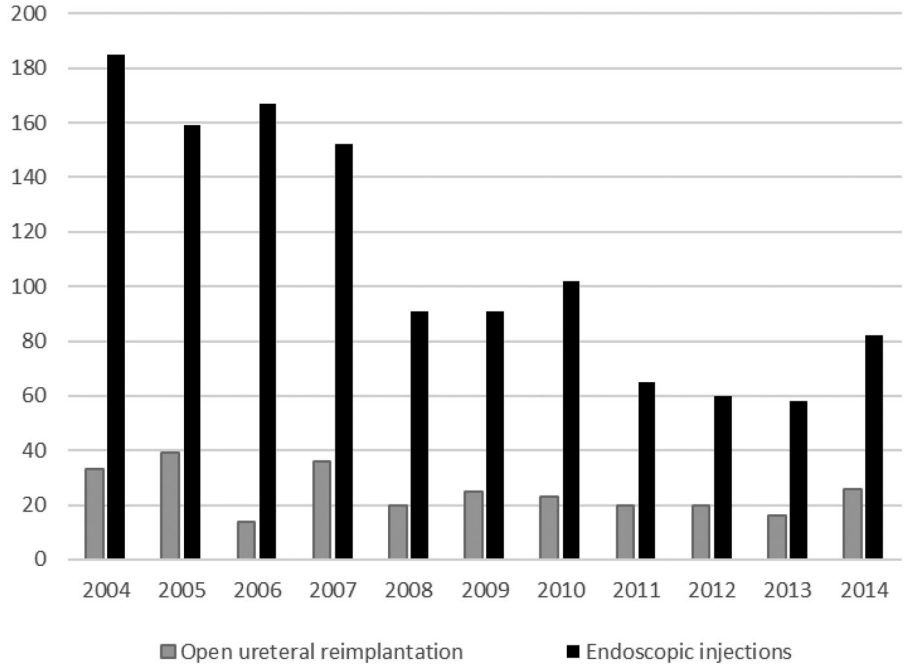

Figure 1. The number of primary procedures for vesicoureteral reflux in 2004–2014 in Finland.

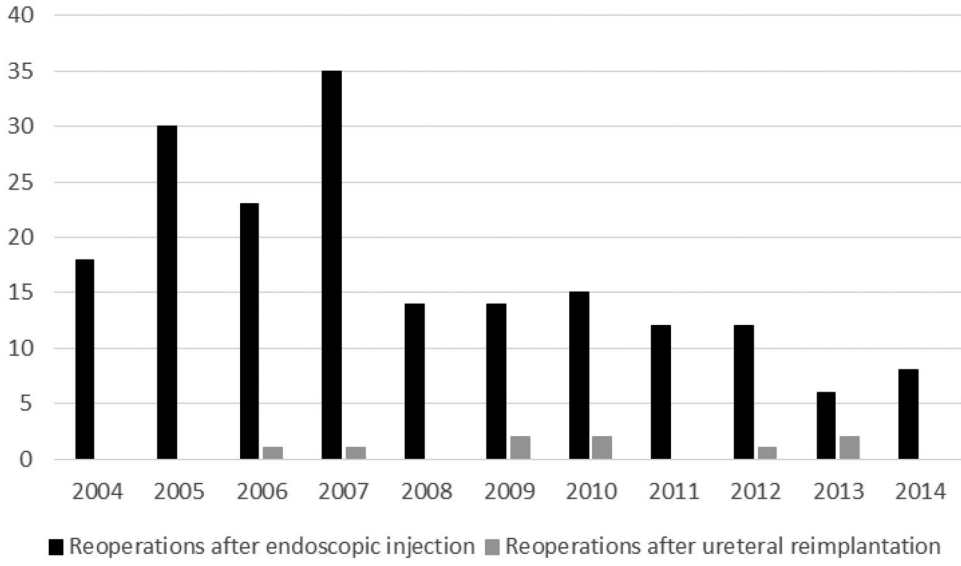

Figure 2. The number of reoperation within 2 years from the primary procedure (2004–2012) for vesicoureteral reflux according to the type of primary surgery.

from 2004 to 2012). Reoperations were significantly more common in patients who were primarily treated with endoscopic injections ($n = 146/1072$, 14%) than with ureteral reimplantation ($n = 7/230$, 3%) ($p < 0.0001$, see Figure 2). More than one reoperation was required in 55 and 0 patients, respectively. Altogether, 173 reoperations were required after endoscopic injections and 7 after ureteral reimplantation. The rate of reoperations did not significantly change during the study years ($p = 0.2238$).

Discussion

Operative treatment rates for children with VUR declined in Finland. Most children that were treated operatively underwent endoscopic injections, that was associated with shorter lengths of stay but more reoperations than open ureteral reimplantations.

We had access to national population-based data including all children that were hospitalized or operated on due to VUR in Finland. Virtually all VUR patients in Finland who require surgical treatment are treated in public hospitals, most of them in the five university hospitals. We were able to exclude major malformations of the urinary and gastrointestinal tract to be able to concentrate on primary VUR. However, we could not assess the grade of VUR or the rate of minor complications such as recurrent urinary tract infections or the rate of lower urinary tract dysfunction reliably from the registered data. Also, with recommendations to perform voiding cystograms less actively the diagnostic rate of VUR may have changed and assessed the true incidence of

VUR is not possible [19,20]. Since the Nordic Classification of Surgical Procedures has only one code (KBH20) for all types of open ureteral reimplantations. we did not have data on which open anti-reflux procedures were performed. However, we think it is safe to assume, that reimplantation a.m. Cohen was performed for most children that were operated for VUR since this is most commonly used in Finland for reimplantations and has the advantage of submucosal tunneling of the ureters effectively preventing VUR.

We showed that the use of endoscopic injections for VUR decreased and the age at endoscopic injection decreased parallel to the changes seen in the USA from 2004 to 2011 [15]. Similarly, the rate of ureteral reimplantations decreased as reported in the USA from 2003 to 2013 [14] and from 2009 to 2012 [21], even though the decrease was seen in our study in ureteral reimplantation procedures was not as apparent as that of endoscopic injections. In addition, the proportion of minimally invasive ureteral reimplantations was increasing in the USA [21] while laparoscopic ureteral reimplantations were not performed in Finland during the study period. It is likely that the incidence of VUR has not dramatically changed during the study period. With increasing recognition of the spontaneous resolution of VUR more conservative strategies with the imaging for reflux have been recommended [20] and the treatment strategies of VUR have become more conservative both in Finland and in the USA.

In line with international VUR guidelines, operative treatment is reserved for patients, who fail conservative medical management [5,22,23]. Spontaneous resolution of VUR is more common in children under a year of age than older children [6]. The median age of the patients in our study was 3 years for ureteral reimplantation and 4 years for endoscopic treatment. As the natural history of VUR is one of spontaneous slow regression or resolution for lower grades [6], it is evident that children identified in this study were of higher grade VUR. Patients treated in the USA for VUR [14] with ureteral reimplantations were slightly older than those in our study (median 4 vs 3 years, respectively), but the age at treatment was decreasing in the USA while the age of the patients treated with ureteral reimplantations in our study did not change during the study years.

The length of hospitalization with ureteral reimplantation continued to be significantly longer than with endoscopic injections (median 9.9 vs 1.3 days) and was longer than reported in previous studies from other countries with open ureteral reimplantation [24,25]. No decrease in the length of hospitalization was seen during the study period. It is possible that some of the patients with long hospital stay after an open procedure have visited home with the catheters and have then been officially discharged from the ward only after the catheter removal. Also, the one long hospital stays after endoscopic injections in our data are likely to be explained with comorbidity. However, it is important to discuss the length of stay as well as the possible discomfort due to urinary catheters, drains, and postoperative pain with the family before deciding on the mode of treatment for VUR.

Data on the complication rate of ureteral reimplantation are scarce. Although a straightforward procedure, ureteral reimplantation still encompasses the opening of the bladder and thus possibly affects the bladder function. While bulking agent injections are fairly well tolerated with low complication rates, the efficacy remains lower than with reimplantation [8,10]. In this study, we limited complication detection to Clavien-Dindo grade IIIb due to the technical limitations of the register study. On the other hand, also the difference in the length of stay between the procedure groups reflects the associated post-operative morbidity of the operations. We showed that the risk for reoperations is 14% for injection therapy and 4% for open ureteral reimplantations. While reoperations are here graded the same, converting to an open operation must be regarded as a more serious complication than a renewed injection therapy. Still, any reoperation involves a significant burden on the families involved. Health-related quality of life was not investigated in this register-based study but has previously been analyzed [26–28]. The results have been somewhat controversial since some have reported successful endoscopic treatment of VUR to be associated with improved quality of life [26,28]. On the other hand, one study showed the good quality of life in both those treated with antimicrobial prophylaxis and ureteral reimplantation [27].

Randomized controlled studies on the effect of endoscopic injections of VUR compared to no treatment are scarce [7]. According to the one study available [7], the number needed to treat (NNT) of VUR in scar prevention compared to no treatment was 17. The NNT for endoscopic treatment compared to continuous antimicrobial prophylaxis was also 17 according to the Swedish high-grade reflux trial published in 2017 [9]. However, the Swedish Reflux Trial published in 2010 [7] failed to show any advantage in scar prevention of endoscopic treatment compared to antibiotics.

VUR remains a multifaceted disease and the treatment needs to be tailored to the individual patients. Operative treatment usually opts after break-through infections. The current trend seems to evolve towards less invasive treatments with bulking agent injections, and the open ureteral reimplantations are diminishing. Still, open ureteral reimplantations need to be kept in the armoury for circumstances where non-operative treatment and bulking agent injections are deemed insufficient. The optimal treatment mode for higher grade VUR with regards to future renal parenchymal disease is controversial. The main goal of treatment still remains long-term renal health, while up to 20% of children with reflux nephropathy suffer from hypertension or end-stage renal disease [29]. Thus, operative treatment is not to be neglected in the treatment of VUR.

Conclusions

The rate of primary procedures for vesicoureteral reflux has declined during 2004–2014 in Finland. The length of hospital stay is significantly longer with open ureteral reimplantation than with endoscopic injection of ureteral orifices. However, reoperations are more frequent after endoscopic injection

therapy. While the best treatment options for VUR remain debatable, the treatment strategies of VUR seem to have become more conservative.

Ethical approval

The study was approved by the National Institute for Health and Welfare of Finland (permissions no: THL/143/5.05.00/2015). This was a retrospective register study and thus no informed consent was required and the participants were not contacted. The legal basis for the processing of personal data is public interest and scientific research (EU General Data Protection Regulation 2016/679 (GDPR), Article 6(1)(e) and Article 9(2)(j); Data Protection Act, Sections 4 and 6).

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Appendix 1

Complication of treatment for vesicoureteral reflux was defined as a complication requiring rehospitalization with reoperation (i.e. Clavien-Dindo Classification grade IIIb complication). The following procedures were considered reoperations after ureteral reimplantation or dextranomer/hyaluronic acid injections of the ureteral orifices in 2004–2014:

JAH00 laparotomy, JAH01 laparoscopy, JAP00 Freeing of adhesions in the peritoneal cavity, JFK10 Freeing of adhesions in intestinal obstruction, KAC00 Nephrectomy, KAD00 Partial nephrectomy, KAD10 Heminephrectomy, KCH96 Other reconstructive operation on bladder, KCW96 Other operations on bladder, UKC02 cystoscopy, UKD02 Urethroscopy, KBH20 Replantation of ureter, KBV52 Cystoscopic injection therapy for vesicourethral reflux.