World J Urol (2016) 34:577–583
DOI 10.1007/s00345-015-1645-x

ORIGINAL ARTICLE

# Differences between intrinsic and extrinsic ureteropelvic junction obstruction related to crossing vessels: histology and functional analyses

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Received: 14 March 2015 / Accepted: 15 July 2015 / Published online: 29 July 2015


**Abstract**
*Purpose* In children, ureteropelvic junction obstruction (UPJO) is mostly caused by intrinsic factors (IUPJO); extrinsic UPJO are rare and often due to crossing vessels (CVs).
*Methods* We retrospectively reviewed all data of children with UPJO that underwent surgery in our institution from 2004 to 2011. Analyses included age at surgery, gender, preoperative and postoperative results of ultrasound and renal scans [differential renal function (DRF); signs of obstruction], and pathology reports. Available histological specimens of cases with CV were compared to a random selection of intrinsic cases in a blinded fashion. After additional Masson's trichrome staining, the specimens were scored for fibrosis, muscular hypertrophy, and chronic inflammation.
*Results* Out of 139 patients with UPJO, 39 cases were associated with CV. Median age at surgery was 68 months (range 2–194) in the CV group and 11.5 months (range 0–188) in IUPJO group. Laparoscopic dismembered pyeloplasty (LDMP) was carried out in 134 and open DMP in five patients. Preoperative ultrasound identified 28/39 cases with CV. DRF below 40 % was more frequently seen in CV patients ($p = 0.020$). Histological analyses revealed no differences between the CV and IUPJO specimens in total. CV patients with higher grades of muscular hypertrophy had lower preoperative DRF, compared to those with higher preoperative DRF ($p = 0.026$). Functional recovery after (L)DMP was excellent in both groups.
*Conclusion* We could not find any significant histological differences between CV and IUPJO in children. To obtain excellent functional recovery, surgical procedures with a definite correction of the UPJ should be preferred in paediatric patients with CV.

**Keywords** Crossing vessels · Hydronephrosis · Ureteral obstruction · Child · Hydronephrosis

## Introduction

Most cases of ureteropelvic junction obstruction (UPJO) in children are caused by intrinsic factors (IUPJO), such as an aperistaltic ureteral segment, infoldings of the ureteral wall or true strictures. Differing histological changes in the constricted segment in relation to outcome and differential renal function (DRF) or degree of obstruction have been described [1–6]. The rare cases of extrinsic UPJO in children are due to fibrous bands or crossing vessels (CVs). These vessels may arise from the renal vessels, aorta, vena cava, or iliac vessels that supply the lower pole of the kidney. CVs are found in 20 % of adult patients with normal UPJ and in up to 38–71 % in patients with UPJO, whether causative or coincidental [7, 8]. Treatment of choice is surgery in case of flank pain, loss of DRF, or relevant obstruction in dynamic renal scans. The dismembered pyeloplasty (DMP) is the gold standard to successfully treat both intrinsic and extrinsic UPJO in children; recently published reports proved comparable results for laparoscopic, one trocar-assisted, or robotic-assisted dismembered pyeloplasty (LDMP, OTAP, RDMP), even in small infants [9, 10]. Furthermore, in adults, nondismembered pyeloplasty

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(YV-plasty) and DMP have gained advantage over laser pyelotomies in extrinsic UPJO [11].

However, in cases with crossing vessels, some authors promote vascular hitch procedures in order to avoid dissection and anastomosis of the ureteropelvic junction [12, 13]. Cases of failed vascular hitch and redo surgery with DMP or endopyelotomy have been described [14, 15]. The aim of this study was to compare clinical, functional, and histological aspects of IUPJO and UPJO–CV.

## Methods

We retrospectively analysed all patients undergoing dismembered pyeloplasty (DMP) in our department between 2004 and 2011. Preoperative assessment consisted of colour Doppler ultrasound (US) and diuretic renal $^{99m}$Tc-MAG3-scan (DRS). Indications for surgery were: significant impairment of differential renal function (DRF, below 40 %); more than 10 % loss of DRF in follow-up DRS; signs of obstruction in DRS with less than 50 % tracer clearance 20 min after furosemide application (TC20 min%); and half-time tracer clearance (½TC) over 20 min after furosemide application. LDMP was performed as previously described [16],

Postoperative follow-up included clinical evaluation once a year as well as DRS and colour Doppler ultrasound (US) after 3 months. Cases with IUPJO and UPJO–CV were compared regarding age, gender, pre- and postoperative courses, pre- and postoperative DRFs, TC20 min%, and reoperations.

For histopathologic comparison, first, the histological reports were compared concerning mention of fibrosis, muscular hypertrophy, and signs of chronic infection. Furthermore, the available histological haematoxylin- and eosin (HE)-stained specimens of cases with CV (24 specimens) were compared to a randomly selected control group of IUPJO (26) specimens. Additionally, a Masson's trichrome (MT) staining was realized for better assessment of fibrosis (Fig. 1). The specimens were graded for fibrosis, muscular hypertrophy, and inflammation from 0 to 3, as follows: grade 0: no alterations; grade 1: mild alterations; grade 2: moderate alterations; and grade 3: severe alterations. The stained sections were examined by light microscopy and rated independently by two observers blinded to patient information and to each other. To assess intraobserver variability, the same observers performed each method again without knowing the initial data. In case of incongruent results, specimens were rejected from the study. The project was approved by the Independent Ethics Committee (IEC, Project No. 566/2014R).

Statistical analysis was performed using SPSS version 22.0. Shapiro–Wilk test, and D'Agostino's K-squared test was performed to proof for parametric distribution. Descriptive statistics show the median, interquartile range (IQR) of nonparametric data, and mean and standard deviation (SD) of parametric data. For nonparametric data differences between patient' demographics and for correlation of DRF/TC20 min% with histological results, a two-sided

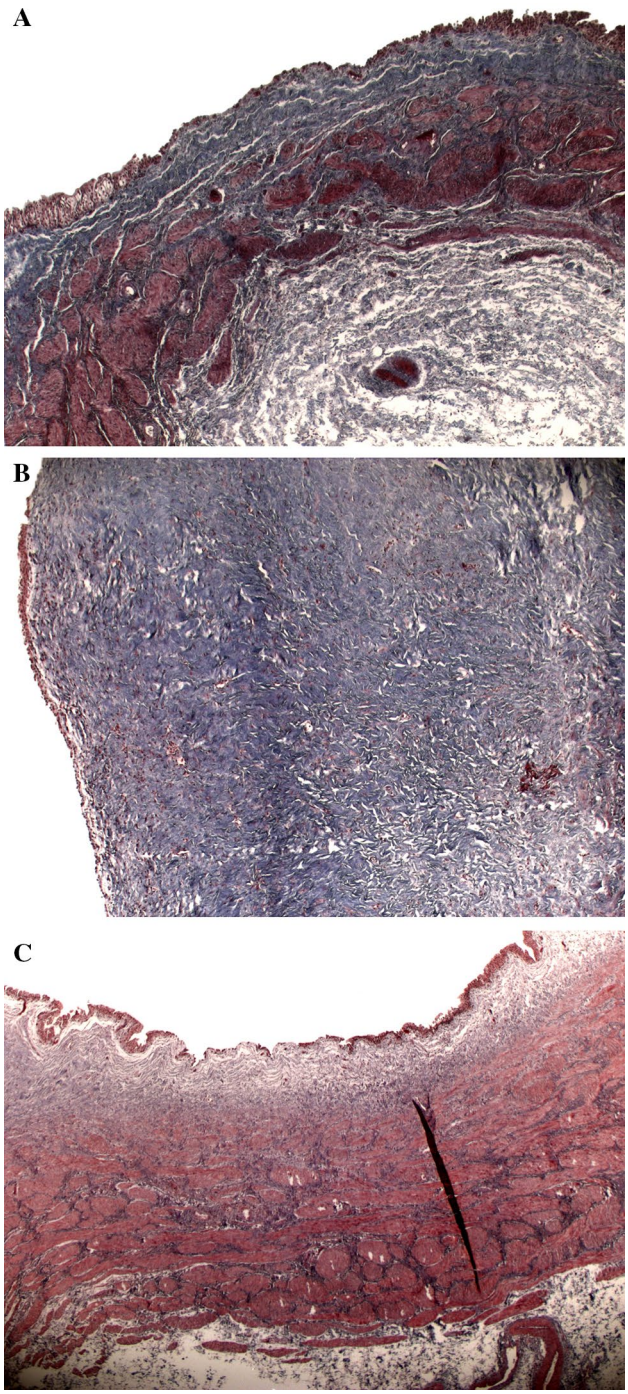


**Fig. 1** MT-stained specimen with **a** normal ureteral wall, fibrosis, and muscular hypertrophy grade 0, **b** muscular hypertrophy grade 3, **c** fibrosis grade 3 (×5)

**Table 1** Characteristics of the study population and comparison of the pathology reports

| All patients | Total ($n = 139$) | IUPJO ($n = 100$) | CV ($n = 39$) | $p$ value |
|---|---|---|---|---|
| Median age at surgery [months] (IQR) | 18 (0–194) | **11.6 (0–188)** | **68.0 (2–194)** | **0.000** |
| Male patients [no. (%)] | 102 (73.4) | 76 (76) | 26 (67) | 0.289 |
| Median DRF pre-op [% (IQR)] | 46.0 (39.0–50.0) | 46.0 (40.0–50.0) | 46.0 (33.0–50.0) | 0.463 |
| Median DRF post-op 3 months [% (IQR)] | 49.0 (42.5–51.0) | 49.0 (44.5–51.0) | 48.0 (38.0–51.0) | 0.654 |
| Median DRF post-op 1 year [% (IQR)] | 49.0 (40.5–52.0) | 49.0 (43.0–52.0) | 47.0 (39.0–52.0) | 0.524 |
| DRF pre-op <40 % [no. (%)] | 37 (26.6) | **21 (21)** | **16 (41)** | **0.020** |
| DRF post-op 3 months <40 % [no. (%)] | 27 (19.4) | 16 (16) | 11 (28) | 0.150 |
| DRF post-op 1 year <40 % [no. (%)] | 20 (14.4) | 13 (13) | 7 (17.9) | 0.435 |
| Median TC20 min pre-op [% (IQR)] | 15.0 (5–25) | 14.0 (1–25) | 16.0 (5–28) | 0.428 |
| Median TC20 min post-op 3 months [% (IQR)] | 84.5 (70.8–90.3) | **84.0 (69.0–90.0)** | **89.0 (78.0–95).0** | **0.030** |
| Median TC20 min post-op 1 year [% (IQR)] | 88.9 (70.8–95.0) | 86.5 (68.8–94.3) | 90.0 (81–95) | 0.193 |
| Pathology reports | Total ($n = 132$) | IUPJO ($n = 96$) | CV ($n = 36$) | $p$ value |
| Fibrosis [no. (%)] | 105 (79.5) | 78 (81.3) | 27 (75.0) | 0.487 |
| Muscular hypertrophy [no. (%)] | 45 (34.1) | 32 (33.3) | 13 (36.1) | 0.839 |
| Inflammation [no. (%)] | 40 (30.3) | 30 (31.3) | 10 (27.8) | 0.833 |

Significant $p$ values (<0.05) are indicated by bold values

Mann–Whitney $U$ test was used. Contingency analyses were performed to calculate differences between histological aspects using a two-sided Fisher's exact test. Significance was assumed for p below 5 % (*). Because the number of cases was not high enough, equivalence tests concerning the histological findings were not possible.

## Results

From 2004 to 2011, 139 patients (102 males, 73.4 %) were operated on because of UPJO. In 83 cases (59.7 %), UPJO was located on the left side; in 4 cases, it was bilateral (2.9 %, CI 0.7–7.2). The clinical and disease-specific characteristics of our study population are listed in Table 1. The median follow-up period was 37 months (12–190). In 134 patients, a laparoscopic dismembered pyeloplasty (LDMP) was carried out, in three of them on both sides. In five patients, an open DMP was performed. These latter patients (median age 2.5 months, IQR 0–3 months, 1 case with CV) were operated on open during our early observation period (2005) when our experience in laparoscopy in small infants was still growing. During surgery, CVs were associated with obstruction in 39 cases (28.1 %). The remaining 100 patients had IUPJO. Preoperative ultrasound identified 28 cases of the 39 CV cases; in 11 cases, CV was not described in preoperative ultrasound reports. In the IUPJO cases, ultrasound reports described CV in 12 cases that were not verified intraoperatively. This means a sensitivity of 71 %, a specificity of 88 %, a positive predictive value of 70 %, a negative predictive value of 88 %, and an accuracy of 84 % of US for depicting CV in our institution. There was no significant difference between the groups concerning the median DRF before and after surgery. However, focusing on preoperative DRF below 40 %, there were significantly more patients in the group of CV ($p = 0.020$). Postoperatively, this difference was no longer evident. There was no difference between patients with CV and IUPJO regarding signs of obstruction as expressed in preoperative TC20 min%. However, in the CV group, the obstruction recovery was significantly higher than in the IUPJO group ($p = 0.030$). Reoperation (re-LDMP) for re-stenosis was necessary in three cases (2.1 %) after 5, 6, and 24 months, respectively. In two patients (LDMP, IUPJO), complete loss of renal function (patient 1, early postoperative peritonitis, sepsis, and renal tubular necrosis; patient 2, prolonged loss of renal function after 5 years) led to nephrectomy (1.4 %). There was no significant difference between CV and IUPJO cases.

Standard pathological results were available in 132 cases. In these, there was no difference between the groups (Table 1). Out of 39 cases with CV, 26 histopathologic specimens were available for evaluation. These were compared to a randomly picked cohort of 26 IUPJO specimens. Because of incongruent findings in two specimens of the CV group, these cases were excluded from further histological evaluation. The clinical and disease-specific characteristics of the subgroup are listed in Table 2. Grading of HE and MT-stained specimen for fibrosis, muscular hypertrophy, and chronic inflammation did not reveal any difference between CV and IUPJO (Table 2).

**Table 2** Characteristics of the histologically reviewed patients and comparison of histopathologic aspects after additional staining and grading

| | IUPJO ($n = 26$) | CV ($n = 24$) | $p$ value |
|---|---|---|---|
| Histo review patients | | | |
| Median age at surgery (months [IQR]) | **15.6 (2–164)** | **58.0 (21–163)** | **0.000** |
| Male patients [no. (%)] | 18 (69) | 20 (83) | 0.757 |
| Median DRF pre-op [% (IQR)] | 47.5 (44.8–51.0) | 46.0 (33.0–50.0) | 0.213 |
| Median DRF post-op 3 months [% (IQR)] | 50.0 (47.0–51.0) | 49.0 (42.0–53.0) | 0.335 |
| Median DRF post-op 1 year [% (IQR)] | 50.0 (48.5–52.5) | 48.5 (44.3–52.0) | 0.450 |
| Median TC20 min pre-op [% (IQR)] | 20.0 (7.5–36.0) | 20.0 (5.0–28.0) | 0.407 |
| Median TC20 min post-op 3 months [% (IQR)] | 88.0 (74.3–95.0) | 83.3 (70.0–95.0) | 0.636 |
| Median TC20 min post-op 1 year [% (IQR)] | 91.0 (85.5–95.5) | 85.0 (74–93) | 0.349 |
| Histological grading results | | | |
| Fibrosis grade 0 [no. (%)] | 1 (3.8) | 1 (4.2) | 0.547 |
| Fibrosis grade 1 [no. (%)] | 8 (30.8) | 8 (33.3) | |
| Fibrosis grade 2 [no. (%)] | 12 (46.2) | 13 (54.2) | |
| Fibrosis grade 3 [no. (%)] | 5 (19.2) | 2 (8.3) | |
| Muscular hypertrophy 0 [no. (%)] | 1 (3.8) | 0 (0) | 0.781 |
| Muscular hypertrophy 1 [no. (%)] | 5 (19.2) | 5 (20.8) | |
| Muscular hypertrophy 2 [no. (%)] | 15 (57.7) | 13 (54.2) | |
| Muscular hypertrophy 3 [no. (%)] | 5 (19.2) | 6 (25.0) | |
| Inflammation 0 [no. (%)] | 11 (42.3) | 11 (45.8) | 0.698 |
| Inflammation 1 [no. (%)] | 15 (57.7) | 13 (54.2) | |

Significant $p$ values (<0.05) are indicated by bold values

Differing between lower (0–1) and higher (2–3) grades of muscular hypertrophy, higher grades of muscular hypertrophy had significantly lower preoperative DRF in CV cases ($p = 0.026$) and significantly lower preoperative TC20 min% in IUPJO cases ($p = 0.030$). Details are shown in Table 3. In the postoperative analyses, there were no such differences.

**Table 3** Comparison of functional aspects and histology

| | Median DRF pre-op [% (IQR)] | Median TC20 min% pre-op [% (IQR)] |
|---|---|---|
| CV | | |
| Fibrosis 0–1 | 47.0 (34.5–49.8) | 20.5 (1.3–29.5) |
| Fibrosis 2–3 | 39.5 (32.0–50.0) | 20.0 (5.0–24.0) |
| $p$ value | 0.497 | 0.871 |
| MH 0–1 | **49.5 (45.3–50.8)** | 20.0 (5.0–29.0) |
| MH 2–3 | **40.0 (30.0–47.0)** | 18.0 (10.5–40.5) |
| $p$ value | **0.026** | 0.753 |
| Infl. 0 | 47.0 (42.0–50.0) | 22.0 (12.5–32.3) |
| Infl. 1 | 39.0 (30.0–49.3) | 9.5 (5.0–21.0) |
| $p$ value | 0.109 | 0.078 |
| IUPJO | | |
| Fibrosis 0–1 | 49.0 (45.0–51.0) | 26 (12.0–37.5) |
| Fibrosis 2–3 | 45.0 (37.5–49.0) | 20 (0.5–28.0) |
| $p$ value | 0.279 | 0.173 |
| MH 0–1 | 49.5 (43.0–51.0) | **34.5 (25.3–40.3)** |
| MH 2–3 | 46.5 (45.0–50.0) | **20.0 (5.0–34.0)** |
| $p$ value | 0.561 | **0.030** |
| Infl. 0 | 48.0 (45.0–52.0) | 25.0 (20.0–38.0) |
| Infl. 1 | 47.0 (40.0–50.0) | 17.5 (4.0–36.0) |
| $p$ value | 0.361 | 0.309 |

Significant $p$ values (<0.05) are indicated by bold values

## Discussion

There is still an ongoing discussion whether CVs are even able to cause UPJO or whether they become trapped by an expanding renal pelvis in patients with intrinsic obstruction [17]. IUPJO is often diagnosed very early in live or even prenatally due to the widespread use of prenatal ultrasound. CV cases present at an older age [18]. Our findings confirm the late presentation of CV. Although the reliability of US has greatly improved with higher technical resolution, in our cohort the correlation between CV and preoperative US in intraoperative findings was not as good as described in other reports and the US reliability did not improve over the years [19].

Based on the fact that a CV exists from the beginning, but starts to present varying symptoms sometimes later in life, it is an important consideration of how the

**Table 4** Literature reports on outcome of paediatric patients with CV

| Annotation | Time period | CV | Median age range (mean age range) [months] | VH | Y-V | DMP | Median follow-up; range (mean follow-up; range) [months] | REC DRF (%) | REC OBS (%) | Re-stenosis with re-op (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Pesce [12] | 1972–1997 | 111 | (127.2; 12–240) | 61 | 0 | 50 | (58.8, 24–96) | 24/112 (21) | 112/112 (100) | 1/61 (1.6) |
| Nouralizadeh [30] | 2001–2009 | 117 | (327; 84–828) | 42 | 0 | 0 | (29, 3–84) | N/A | 38/42 (90) | 2/42 (4.7) |
| Gundeti [29] | 2004–2007 | 20 | (150; 84–192) | 20 | 0 | 0 | (22, 12–42) | N/A | 19/20 (95) | 1/20 (5) |
| Singh [32] | 2004–2008 | 19 | 119; 70–83 | 19 | 0 | 0 | (6, n.a.) | N/A | 18/19 (95) | 0/19 (0) |
| Godbole [28] | N/A | 13 | 122; 84–192 | 13 | 0 | 0 | 6, 3–18 | N/A | 12/13 (92.3) | 1/13 (7.7) |
| Schneider [31] | 2007–2011 | 8 | 114; 24–207.6 | 8 | 0 | 0 | 12, 6–50.7 | N/A | 4/4 (100) | 0/8 (0) |
| Schneider [31] | 2007–2011 | 11 | 122.4; 24–196.8 | 0 | 0 | 11 | 3.8, 2.8–50.7 | N/A | N/A | 0/8 (0) |
| Subotic [33] | 1997–2010 | 29 | 130; 5–192 | 0 | 16 | 13 | 69, 14–142 | 25/29 (86.2) | | 4/29 (13.8) |
| El-Ghoneimi [27] | 1999–2002 | 9 | 126; 22–180 | 0 | 0 | 9 | (12.7) | N/A | n.a. | 0/9 (0) |
| This study 2014 | 2004–2011 | 39 | 68.0; 2–194 | 0 | 0 | 39 | 27, 0–98 | 35/39 (87.7) | 39/39 (100) | 0/39 (0) |

*VH* vascular hitch, *Y-V* YV-plasty, *DMP* dismembered pyeloplasty, *REC* recovery, *OBS* obstruction

development of the ureteral wall is impaired by a pulsating and compressing CV. In theory, the alterations of the ureteropelvic segment caused by a CV are part of an individually ongoing process, depending on how long and how high the affecting pressure by the vessel is. One of our more recent cases with CV showed persistent signs of severe obstruction after a vascular hitch procedure. After secondary LDMP, the resected ureteral specimen showed histological signs of intrinsic stenosis (muscular hypertrophy and fibrosis). Comparable cases of failed vascular hitch and redo surgery have been previously described [14, 15]. In IUPJO, differing findings of histopathologic changes have been described: increased intermuscular and intramuscular connective tissue, or increased collagen that acts as an inelastic collar hampering ureteral peristalsis [1, 6]. Alterations of innervation [20, 21], muscular hypotrophy [2, 3], or hypertrophy have also been reported [4] as causative or resulting alterations of the ureteral wall. Surprisingly, in our reviewed CV specimens, we did not find any lower scores for the so-called intrinsic alterations such as muscular hypertrophy, fibrosis, and chronic inflammation. Only few other reports compared histomorphological aspects of ureteral segments in IUPJO with those of CV patients [22–25]. In most of them, significant differences between IUPJO and CV specimens have been described with fewer or even no intrinsic alterations of the ureteral wall in CV patients [23–25]. However, studies were limited because of very low numbers of analysed patients (four–nine patients) [23, 25] or did not deal with paediatric patients [23, 24]. Other limitations were the lack of grading the pathologic features [24]. One study observed findings similar to our results with muscular hypertrophy in two-thirds and muscle atrophy in one-third of all cases [22].

While the exact pathogenetical mechanisms of intrinsic obstruction remain unclear, some correlations of histopathologic findings with the grade of obstruction or renal impairment have been previously described: a lower collagen-to-muscle ratio was associated with a better renal function recovery after surgery [3]. Decreased preoperative DRF in children younger than 12 months was associated with higher grades of muscular hypertrophy and fibrosis; a postoperative significant recovery of DRF correlated with higher grades of inflammation [5]. We also found significantly lower preoperative DRF in CV patients with higher grades of muscular hypertrophy, respectively, lower preoperative TC20 min% in IUPJO patients in association with higher grades of fibrosis.

The findings of a higher amount in the CV patients with more severe impairment of preoperative DRF (below 40 %) and higher grades of muscular hypertrophy in CV patients with lower DRF should be of great interest in further studies.

Our study provides data of functional recovery concerning both DRF and obstruction not only 3 months but also 1 year after surgery. Whereas there are several reports, meta-analyses, and even one Cochrane review concerning the safeness and effectiveness of laparoscopic or robotic-assisted dismembered pyeloplasty in children [26], and the advantage of definitive procedure like NDMP and DMP over endopyelotomies in adults with extrinsic UPJO [11], only few reports about vascular hitch procedures in children are available (Table 4) [12, 27–33]. However, even in some of these reports, the analysed patient' cohorts consisted of mixed ages—children and adults [12, 29, 30]. In most of these studies, functional recovery was defined as recovery of obstruction in renal scans. One study described the poorer outcome of CV patients compared to IUPJO

after YV-plasty or retroperitoneal DMP [Subotic], but did not give information about DRF and obstruction recovery rates in detail. However, only one study mentioned the DRF recovery rate after vascular hitch with a rate of only 21 % [12]. We could show that LDMP offers an appropriate therapy in children with CV with high rates of functional recovery, especially DRF recovery of 87.7 %. Taking together reports on failed vascular hitch procedures [14, 15], missing information about DRF recovery after vascular hitch procedures in children, and our current findings of "intrinsic" histopathologic changes in CV patients, we favour pyeloplasty as standard procedure for both extrinsic and intrinsic UPJO in children.

In conclusion, our data revealed no significant differences between CV and IUPJO patients concerning the pathologic features of fibrosis, muscular hypertrophy, and inflammation in paediatric patients. Functional impairment is worse in cases with higher grades of fibrosis and muscular hypertrophy. Functional recovery after LDMP is excellent in both groups.

**Author contribution** V. Ellerkamp, J. Fuchs: Protocol/project development; V. Ellerkamp, R.R. Kurth S. Zundel: Data collection or management; V. Ellerkamp, R. R. Kurth, E. Schmid: Data analysis; V. Ellerkamp, S. W. Warmann, E. Schmid: Manuscript writing/editing.

**Compliance with ethical standards**

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical standards** The project was approved by the Independent Ethics Committee (IRB-Votum, IEC, Project No. 566/2014R).

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