

Is it worth to explore the contralateral side in unilateral childhood inguinal hernia?

A PRISMA-compliant meta-analysis

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Abstract

Background: It is still not clear if the contralateral side should be explored in children with unilateral inguinal hernias. The primary aim of the present study was to assess the incidence of metachronous contralateral inguinal hernias (MCIHs) in the pediatric population. The second aim was to assess factors associated with increased risk of MCIH development.

Methods: Prospective studies including patients from 0-19 years undergoing unilateral inguinal hernia repair without surgical exploration of the contralateral side between 1947 and April 2020 with a minimal follow-up of one year were searched. Searches included EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials.

Results: Seven studies involving 1774 children (1452 boys (82%) and 322 girls (18%) were identified. Overall the incidence of MCIH was 6%. Incidence of MCIH development was significantly higher in children with initial left-sided (9%) versus right-sided (3%) hernia (OR 2.55 with 95% CI from 1.56 to 4.17; P = 0.0002), in female (8%) versus male (4%) children (OR 1.74 with 95% CI from 1.01 to 3.01; P = 0.0469) and in patients with open (14%) versus closed (3%) contralateral processus vaginalis (CPV) (OR 4.17 with 95% CI from 1.25 to 13.9; P = 0.0202). There was no significant difference in MCIH development depending on follow-up duration (follow-up of ≤ 2 years (i.e. 1–2 years): calculated MCIH incidence 5% (95% CI from 0.00 to 0.11%; 3 studies; 569 patients), follow-up of ≥ 3 years (i.e. 3–4 years): 6% (95% CI from 0.03 to 0.09; 3 studies, 983 patients)) or patients' age (MCIH incidence in children <1 year: 6.9%; older children: 4.5%; OR 1.87 with 95% CI from 0.97 to 3.62; P = 0.0618).

Conclusions: Overall incidence of MCIH development is 6%. Initial left-sided hernia, female gender and open CPV are risk factors for MCIH development.

Abbreviations: CI = confidence interval, CPV = contralateral processus vaginalis, MCIH = metachronous contralateral inguinal hernia, OR = odds ratio.

Keywords: children, contralateral, inguinal hernia, meta-analysis, metachronous, unilateral repair

1. Introduction

The risk of a contralateral metachronous inguinal hernia in children following unilateral repair ranges from 5.8% to 15.8% in the literature.^[1–8] Despite inguinal hernia repair being one of the most often performed procedures in the pediatric^[9] and adult population,^[10,11] it is still debatable if a contralateral exploration

should be performed in a child with unilateral inguinal hernia. On the contrary, some surgeons laparoscopically assess the contralateral side and close a patent processus vaginalis, others only explore clinically evident inguinal hernias.^[12] If the risk of exploring the contralateral side (complications, pain, longer operation time) outweigh the risk of leaving an asymptomatic

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side intact (secondary anesthesia, potential incarceration of the contralateral asymptomatic side, inconvenience of the patients and parents, and reduced costs) is still not clear.^[8,13] Several risk factors of metachronous contralateral inguinal hernia (MCIH) development have been shown in the literature including younger patient's age, initial left-sided hernia, and CPV.^[1,3,4,8] The primary aim of the present meta-analysis was to assess the overall incidence of MCIH. A 2nd aim was to assess factors associated with increased risk of MCIH development.

2. Materials and methods

The present study reflects an update of the meta-analysis published in 2015 by our group.^[8]

2.1. Eligibility criteria

Only prospective studies with minimum follow-up time of 1 year were included. Only patients aged 0 to 19 years without contralateral groin exploration were included. Studies in English or German were included. Retrospective studies and/or studies with follow-up times of <1 year were excluded.

2.2. Literature search

Table 1

The literature search included the electronic databases MED-LINE (1966 to April 10th 2020), Embase (1947 to April 10, 2020) and the Cochrane Central Register of Controlled Trials (the Cochrane library Issue 4 of 12, April 2020).

The following search terms were used for MEDLINE search: "(Infant OR Child OR Adolescent) AND ("inguinal Hernia" OR "processus vaginalis") AND (Incidence OR "Treatment Outcome" OR Recurrence OR Laparoscopy OR contralateral OR Surgery OR Examination) AND (english[Language] OR german[Language])."

The Embase search included the following terms: "('infant'/exp OR 'child'/exp OR 'adolescent'/exp) AND ('inguinal hernia'/exp OR 'patent processus vaginalis'/exp) AND ('incidence'/exp OR 'treatment outcome'/exp OR 'recurrence'/exp OR 'laparoscopy'/ exp OR contralater- al OR 'surgery'/exp OR 'examination'/exp) AND ([english]/lim OR [german]/lim) AND [humans]/lim AND [embase]/lim."

The CENTRAL search was performed using: "(Infant OR Child OR Adolescent) AND ('inguinal Hernia' OR 'processus vaginalis') AND (Incidence OR 'Treatment Outcome' OR Recurrence OR Laparoscopy OR contralateral OR Surgery OR Examination)."

2.3. Study selection

Duplicate publications were removed prior to screening using the reference software EndNote. Using the study title and abstract, a decision was made to include or exclude studies based on our eligibility criteria. Hereby excluded studies were either clearly not relevant (i.e., not assessing MCIH), or clearly failed on one or more of the inclusion criteria (i.e., follow-up of <1 year, retrospective study design, contralateral exploration, etc). Full text PDFs were then automatically retrieved using the reference management software EndNote. This process was performed independently by 2 authors (RFS and RNF) and disagreements were discussed between reviewers.

2.4. Data collection

Data extraction was performed by 2 authors (INB and RNV).

2.5. Outcomes

Primary outcome was the calculated MCIH incidence. Secondary outcomes were incidence of MCIH in males vs females, in children <1 year compared to older patients, in children with initial left- vs right-sided inguinal hernia, in patients with open vs closed contralateral processus vaginalis (CPV), and in studies with minimum follow-up time of ≤ 2 years vs ≥ 3 years. Further data assessed are given in Tables 1 and 2.

2.6. Risk of bias in individual studies

Included studies were analyzed for risk of bias according to the Cochrane ROBINS-I Risk of Bias Tool,^[14] including risk of bias in individual studies and risk of bias across studies.

2.7. Data synthesis and analysis

Proportions were compared using odds ratios (ORs), and random-effects meta-analyses were performed.^[15–17] A funnel plot was designed to assess for possible publication bias.^[15,18] Statistics were executed using R (http://www.R-project.org/).

Patient characteristics.								
Study	Tepas 1986 ^[14]	Nassiri 2002 ^[15]	Maddox 2008 ^[16]	Kalantari 2009 ^[17]	Koivusalo 2009 ^[18]	Hoshino 2014 ^[13]	Kaneda 2015 ^[19]	
All patients with MCIH	2/179 (1.11%)	19/521 (3.65%)	15/222 (6.76%)	28/301 (9.30%)	6/89 (6.74%)	23/357 (6.44%)	11/105 (10.48%)	
Male	2/179 (1.11%)	16/466 (3.43%)	13/211 (6.16%)	n.a./270	3/66 (4.55%)	12/213 (5.63%)	4/47 (8.51%)	
Female	0/0	3/55 (5.45%)	2/11 (18.18%)	n.a./31	3/23 (13.04%)	11/144 (7.64%)	7/58 (12.07%)	
Right-sided	n.a.	7/344 (2.0%)	8/142 (5.63%)	n.a./213	2/54 (3.70%)	7/192 (3.65%)	4/54 (7.41%)	
Left-sided	n.a.	12/177 (6.78%)	7/80 (8.75%)	n.a./88	4/35 (11.43%)	16/165 (9.70%)	7/51 (13.73%)	
Prematurity	n.a.	n.a.	n.a.	6/30 (20%)	0/0	n.a.	n.a.	
Age range	0.5-2 yrs	1 mo-12 yrs	1 d-19 yrs	1 mo-12 yrs	8 mo-15 yrs	28 d–13 yrs	5 d–13 yrs	
CPV								
Closed	n.a.	n.a.	4/97 (4.12%)	n.a.	0/35 (0%)	n.a.	n.a.	
Open	n.a.	n.a.	6/53 (11.32%)	n.a.	3/12 (25%)	n.a.	n.a.	
Cleft	n.a.	n.a.	3/35 (8.57%)	n.a.	n.a.	n.a.	n.a.	
Positive family history	n.a.	n.a.	5/21 (23.81%)	n.a.	n.a.	n.a.	n.a.	
Increased IAP	n.a.	n.a.	4/48 (8.33%)	n.a.	n.a.	n.a.	n.a.	

CPV=contralateral processus vaginalis, IAP=intra-abdominal pressure, MCIH = metachronous contralateral inguinal hernia, n.a. = not applicable.

Table 2

Study	Tepas 1986 ^[14]	Nassiri 2002 ^[15]	Maddox 2008 ^[16]	Kalantari 2009 ^[17]	Koivusalo 2009 ^[18]	Hoshino 2014 ^[13]	Kaneda 2015 ^[19]
Follow-up ≥ 2 yrs	n.a.	19/521 (3.65%)	15/222 (6.76%)	n.a.	6/89 (6.74%)	23/357 (6.44%)	11/105 (10.48%)
Minimal follow-up	1.5 yrs	4 yrs	30.1 mo	12 mo	2 yrs	3 yrs	3 yrs
Follow-up modality	Not given	Annual evaluation" not further specified	Visit and phone call	Visit and phone call	Visit and phone call	Visit, phone call, letter, or e-mail	Visit, phone call, letter, or e-mail
Exclusion criteria	Female patients	Suspected high intra-abdominal pressure	Not given	Severe ascites, collagen disease	Male patients without completely descended testes	Not given	Not given
Dropouts	Not given	56/577 (10%)	64/286 (22%)	Not given	Not given	15/372 (4%)	0

Ethical approval and informed consent were not necessary for the present study, as no patients' data were assessed.

at initial presentation (9%; CI 0.06–0.11%) vs initial right-sided hernia (3%; CI 0.02–0.05) (Fig. 5).

3. Results

3.1. Results of the search

The search resulted in 8506 hits (Embase: 4732 references, MEDLINE: 3271 references, CENTRAL: 503 references). After exclusion duplicates, abstracts were screened as described above and full-text analysis of n=23 studies resulted in n=7 studies meeting the inclusion criteria.^[13,19-24] A total of 1774 patients were included in the present meta-analysis in total (Fig. 1). About 1452 (82%) were males and 322 (18%) were females, 999 (56%) had an initial right-sided hernia, and 596 (34%) had an initial left-side hernia. The hernia site was not given by 179 (10%) patients. Minimum follow-up ranged from 12 months^[20] to 48 months^[24] with 3 studies having a minimum follow-up of ≤ 2 years^[19-21] and 3 studies having a minimum follow-up of ≥ 3 years.^[13,22,24]

3.2. Overall incidence of MCIH

Calculated overall incidence of MCIH was 6% (95% confidence interval [CI] 0.03–0.08) ranging from $1.1\%^{[19]}$ to $10.5\%^{[14]}$ (Fig. 2) resembling 104 out of 1774 patients from 7 studies.^[13,19–24] Heterogeneity was significant (Tau²=0.0008; df=6 [P <.0001]; I^2 =82.56%). There was no evidence for publication bias (Fig. 3).

3.3. MCIH in females vs males

Five studies reported on MCIH events in male and female children separately.^[13,21-24] Kalantari and co-workers^[20] did not report MCIH incidence separately by gender, and Tepas et al^[19] did not include any females in their analysis. Hence, 1294 children (1003 males [77.5%] and 291 females [22.5%]) were analyzed. MCIH incidence in females was 8% (95% CI 0.05–0.11) vs 4% in males (95% CI 0.02–0.06) and was significantly higher in female children (OR 1.74; 95% CI 1.01–3.01; P=.0469) (Fig. 4).

3.4. MCIH following initial left- vs right-sided hernias

Five studies (including 1294 patients) differentiated on MCIH event numbers by side of the initial hernia.^[13,21-24] Hence, 786 (61%) right-sided hernia and 508 (39%) left-sided hernia were analyzed. Incidence of MCIH was significantly higher (OR 2.55; 95% CI 1.56–4.17; P=.0002) in children with a left-sided hernia

3.5. MCIH depending on open vs closed CPV

Assessment of the CPV was only documented in 2 studies.^[21,23] Heterogeneity was not significant (P=.1988), therefore a fixed effect model was used. The OR for a MCIH were significantly higher in patients with an open CPV (13.8%; CI 6.5–24.7%) compared to children with a closed CPV (3%; CI 0.8–7.6%). The estimated OR was 4.17 (95% CI 1.25–13.93, P=.0202) (Fig. 6).

3.6. MCIH depending on age

In 3 of the included studies, $^{[13,21,24]}$ the MCIH per age group was reported separately and could be included in this subgroup analysis. Heterogeneity was not significant (*P*=.4309), accordingly, a fixed effect model was used for analysis. The OR for a MCIH in children <1 year were larger (6.9%; CI 3.8% to 11.2%) compared to older children (4.5%; CI 3.1–6.2%). The estimated OR was 1.87 (95% CI 0.97–3.62, *P*=.0618) (Fig. 7).

3.7. MCIH depending on follow-up duration

According to the inclusion criteria minimum length of follow-op of included studies was 12 months. Minimum follow-up duration ranged from 12 months^[20] to 48 months^[24] (median: 31.1 months). Calculated MCIH incidence in studies with a minimum follow-up of ≤ 2 years (i.e., 1–2 years) was 5% (95% CI 0.00– 0.11%; 3 studies; 569 patients)^[19–21] (Fig. 8). MCIH rate in studies with a minimum follow-up of ≥ 3 years (i.e., 3–4 years) was 6% (95% CI 0.03–0.09; 3 studies, 983 patients).^[13,22,24] There was no significant difference between groups (minimum follow-up of ≤ 2 years vs minimum follow-up of ≥ 3 years) (Fig. 9).

3.8. Risk of bias in included studies

Overall risk of bias in included studies was low. As depicted in Table 3, risk of bias due to selection of participants was moderate in the report from Koivusalo et al,^[21] as only patients older than 8 months were included and high in the study from Tepas, as only males aged 0.5 to 2 years were included (and younger children had bilateral explorations). Risk of bias was high in the report from Maddox, as 13 patients with a contralateral patent processus vaginalis underwent bilateral repair due to contralateral swelling or palpable crepitus. Risk of bias due to missing data was moderate in the studies from Maddox and Smith^[23] and Nassiri with dropout rates of 22% and 10%, respectively.

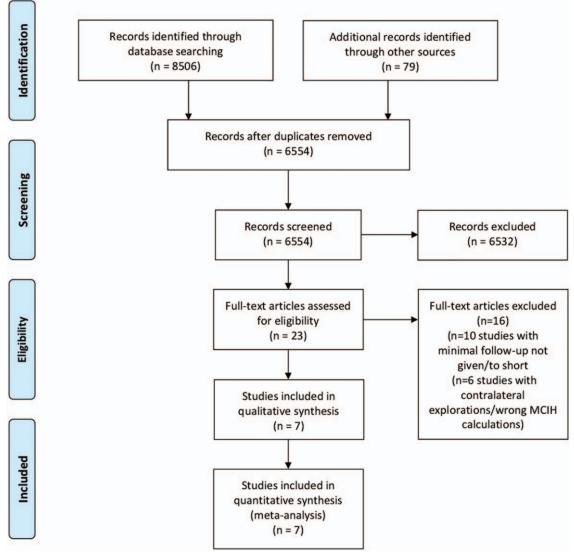
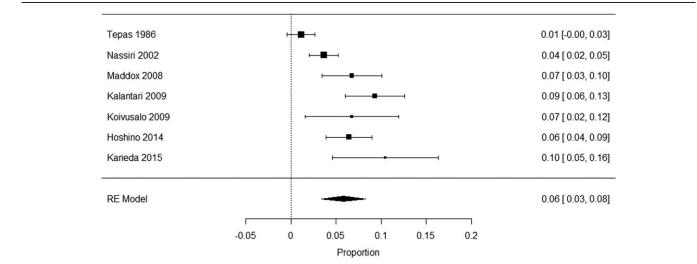
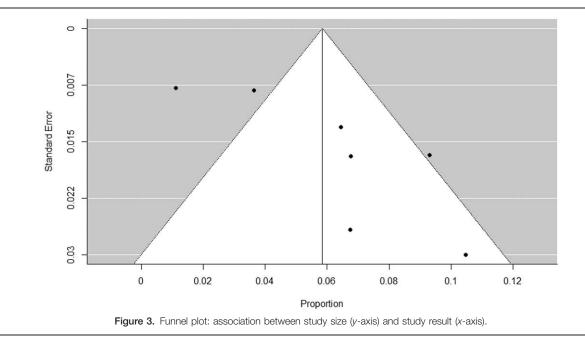


Figure 1. Literature search. Adapted after Zamakhshardy et al.^[25] MCIH = metachronous contralateral inguinal hernia.







Furthermore, risk of bias due to missing data was unclear for the studies from Tepas, Kalantari, and Koivusalo, as the drop-out rate was not given. Despite the fact, that assessment of a MCIH was different between and within reports ranging from phone calls to annual visits, we rated the risk of bias due to measurement of outcomes as low in all reports, as an inguinal bulging in a child with a history of an inguinal hernia and repair is well visible and easy to diagnose, both for health care providers and for caregivers.

4. Discussion

Seven prospective studies with a minimum follow-up of 1 year were included in the present meta-analysis.^[19–24] These included 1774 patients. Overall MCIH rate was 6%. MCIH incidence was higher in patients with left-sided hernias at initial presentation

(9%), in females (8%) and in patients with open CPV (14%).^[8] Length of follow-up (≤ 2 vs ≥ 3 years) and patients' age had no effect on MCIH development.

Inclusion and exclusion criteria varied among included studies possibly leading to sampling bias between the studies: age restrictions were different with minimum age of included patients ranging from 1 day^[23] to 8 months^[21] and maximum patient's age ranging from 2 years^[19] to 19 years.^[23] Whereas some studies did not report exclusion criteria,^[13,22,23] others excluded females,^[19] patients with suspected high intra-abdominal pressure,^[24] ascites and/or collagen disease,^[20] or males without completely descended testes^[21] (Table 2). Similarly, outcome data were different among included studies: Dropouts were not reported by 3 out of 7 studies^[19–21] and ranged from 0%^[22] to 22%^[23] in the remaining 4 reports. Similarly, the follow-up modality ranged from visit and phone call^[20,21,23] to "annual

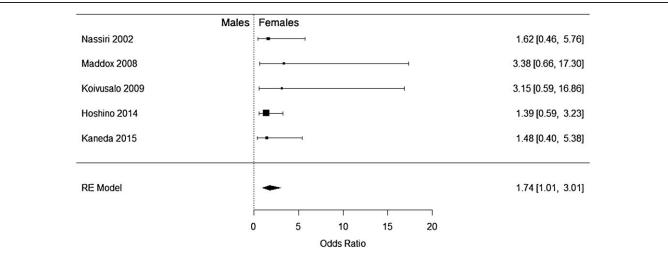


Figure 4. Forrest plot: metachronous contralateral inguinal hernia incidence in females vs males (minimum follow-up: 1 year).

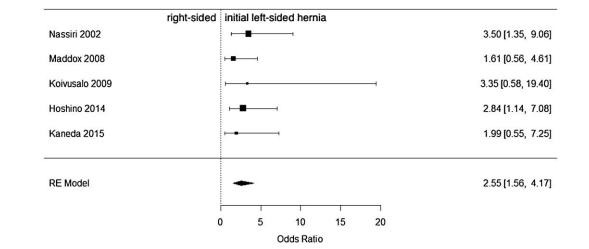


Figure 5. Forrest plot: metachronous contralateral inguinal hernia incidence in children with initial left- vs right-sided hernia (minimum follow-up: 1 year).

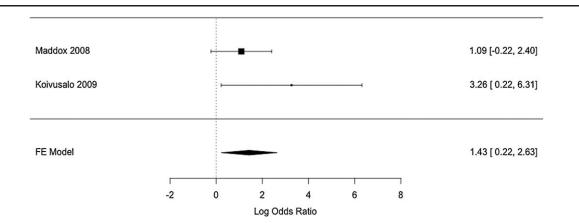


Figure 6. Forrest plot: metachronous contralateral inguinal hernia incidence in patients with an open contralateral processus vaginalis compared to children with a closed contralateral processus vaginalis.

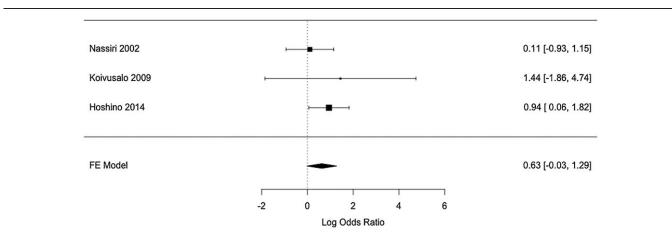


Figure 7. Forrest plot: incidence of metachronous contralateral inguinal hernia in children <1 year compared to older children.

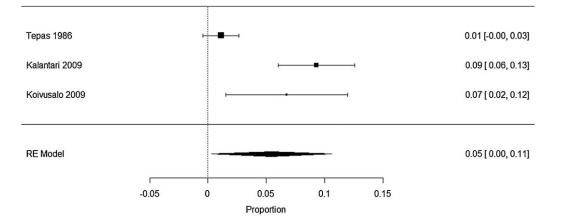
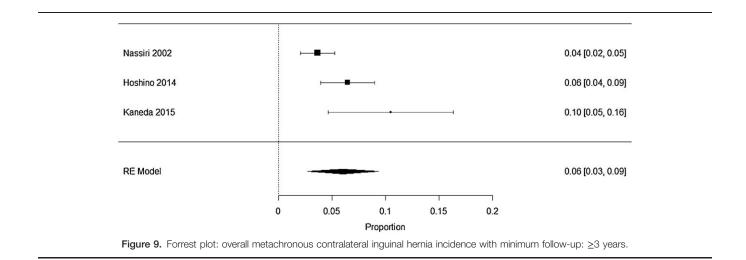


Figure 8. Forrest plot: overall metachronous contralateral inguinal hernia incidence with minimum follow-up: <2 years.



evaluation" not further specified^[24] to visit, phone call, letter, or e-mail.^[13,22]

Minimum length of follow-up ranged from 12 months^[20] to 4 years^[24] among included studies. Since less than half of MCIH seem to occur within 12 months,^[3,21,25] the follow-up duration of included studies may have affected our present findings. Nevertheless, in our previous meta-analysis, MCIH incidence was not higher in the subgroup of studies with a minimum length of follow-up of 2 or 3 years, respectively.^[8] Comparing the MCIH incidence in studies with a minimum follow-up of 2 years

or less vs \geq 3 years in the present meta-analysis similarly showed no significant difference. Furthermore, MCIH incidence for subgroups of pediatric patients (e.g., initial left-sided hernias) was not reported by all included studies. Hence, only a part of included patients were available for subgroup analyses. Finally, the 2 patient cohorts from Hoshino et al^[13] and Kaneda et al^[22] likely represent patients treated by the same group of surgeons at the same institution at 2 different time points (April 2006 until March 2009^[13] and April 2009 until March 2010^[22]). Older studies (published before 1990) might be under-reported, since

Table 3							
Risk of bias in included studies.							
	Selection of	Classification of	Deviations from	Missing	Measurement	Selection of	
Confounding	participants	interventions	intended interventions	data	of outcomes	reported results	Overall

	Confounding	participants	interventions	intended interventions	data	of outcomes	reported results	Overall
Tepas et al (1986)	Low	High	Low	Low	Unclear	Low	Low	Low
Nassiri et al, (2002)	Low	Low	Low	Low	Moderate	Low	Low	Low
Maddox et al, (2007)	Low	High	Low	Low	Moderate	Low	Low	Low
Kalantari et al, (2008)	Low	Low	Low	Low	Unclear	Low	Low	Low
Koivusalo et al (2015)	Low	Moderate	Low	Low	Unclear	Low	Low	Low
Hoshino et al (2014)	Low	Low	Low	Low	Low	Low	Low	Low
Kaneda et al (2015)	Low	Low	Low	Low	Low	Low	Low	Low

full articles were often not available for review. The quality of a meta-analysis depends on the quality of included studies. Metaanalyzing data from randomized controlled trials^[16,17,26,27] yields a higher evidence, then summarizing data from case series^[18] or even case reports. The incidence of a metachronous contralateral inguinal hernia cannot be addressed by randomized controlled trials, but only by observational studies.

Overall MCIH incidence of 6% was similar to meta-analyses of other systematic reviews published in the past 25 years (ranging from 5.8% to 7.4%),^[1–5] and unchanged from our own previous meta-analysis,^[8] but lower than older reviews published in the 1960s showing MCIH occurrences of 10% to 16%.^[6,7] To the authors' knowledge, there were no further systematic reviews published since 2015.^[8] The present meta-analysis used the same inclusion criteria (prospective studies, children with unilateral inguinal hernia, minimum follow-up of 1 year) as our previous study,^[8] but clearly differs from other meta-analyses by including only prospective studies and limiting the minimum duration of follow-up.

Left-sided inguinal hernia at initial presentation was associated with a significantly higher MCIH incidence (9%) than right-sided hernia (3%). This finding is in line with our previous metaanalysis,^[8] as well as with findings by other systematic reviews.^[1,3–5] It might reflect the fact that right-sided inguinal hernias are in general more common than left-sided hernias.^[28] Females (8%) are more likely to developed MCIH than males (4%), which was also reported by other meta-analyses,^[1,4] even though the systematic reviews by Miltenburg et al^[3] and Kokorowski and co-workers^[5] did not find an association of gender and MCIH incidence. The fact that gender was not a significant risk factor in our previous meta-analysis (but showed a clear trend that females were more likely to develop MCIH) might be reflective of the larger number of included patients in the present meta-analysis.

Open CPV was associated with significantly higher odds for MCIH (13.8%; CI 6.5–24.7%) compared to children with a closed CPV (3%; CI 0.8–7.6%). However, as reported by Zhong and Wang^[12] MCIH despite a closed CPV is possible, with a reported incidence of 1.31% in the Meta-Analysis from Zhong and Wang.^[12]

Children <1 year showed a nonsignificant trend to higher odds for development of MCIH (6.9%; CI 3.8–11.2%) compared to older patients (4.5%; CI 3.1–6.2%). This was confirmed in the studies from Ron and colleagues^[4] and Nataraja and Mahomed,^[1] while Miltenburg and colleagues reported gender and age were no risk factors for MCIH.^[3]

Incidences of MCIH in patients with open vs closed CPV and depending on age did not differ from our previous metaanalysis,^[8] as MCIH was not reported for these subgroups of patients in the additional study included in the present analysis.

Whereas the overall MCIH incidence was calculated separately for studies with a minimum follow-up duration of 2 and 3 years, respectively, in our previous meta-analysis, showing similar results to a follow-up period of 1 year,^[8] the present analysis compared MCIH occurrence in reports with a follow-up duration of ≤ 2 years vs ≥ 3 years, similarly showing no significant difference. It has been shown that MCIH rates increase with longer follow-up durations with highest incidence after about 10 years.^[4] The fact that MCIH rates decreased after even longer follow-up periods (>10 years) might be explained by the higher number of patients that were lost for follow-up. It has to be taken into account, that overall incidence of pediatric inguinal hernias ranges from 0.8% to $4.4\%^{[28]}$ The nonfinding in the present analysis might be reflective of a relative small difference in followup time (1–3 years) and of the small number of included studies and patients (due to the more restrictive inclusion criteria of the present systematic review).

5. Conclusion

Taken together, in the present meta-analysis the overall risk of MCIH was shown to be 6%. Patent CPV (MCIH: 14%), Leftsided inguinal hernia at initial presentation (MCIH: 9%) and female gender (MCIH: 8%) were identified risk factors of MCIH, whereas patients' age and the follow-up duration had no effect on MCIH rate. Other putative risk factors for MCIH (high intra-abdominal pressure, prematurity, connective tissue disease, etc) were not assessed in the present analysis. An overall MCIH of 6% implies a number needed to treat of 17 (overall MCIH=6%; 100/6=17), meaning that 17 contralateral explorations are necessary to prevent 1 MCIH. Bilateral repair should hence be offered to females with left-sided inguinal hernias and open CPV.

Author contributions

Acquisition of data: Ralph F. Staerkle, Isabella N. Bielicki, Stefan Gaukel, Raphael N. Vuille-dit-Bille.

- Analysis and interpretation of data: Ralph F. Staerkle, Laura C. Guglielmetti, Stefan Gaukel, Lukas Fink, Raphael N. Vuilledit-Bille.
- Critical revision: Ralph F. Staerkle, Laura C. Guglielmetti, Isabella N. Bielicki, Stefan Gaukel, Giovanni Frongia, Sarah Hilton, Lukas Fink, Raphael N. Vuille-dit-Bille.
- Drafting of manuscript: Ralph F. Staerkle, Laura C. Guglielmetti, Isabella N. Bielicki, Raphael N. Vuille-dit-Bille.
- Study conception and design: Ralph F. Staerkle, Raphael N. Vuille-dit-Bille.

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