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Re: Luke Harper, T. Blanc, M. Peycelon, et al. Circumcision and Risk of Febrile Urinary Tract Infection in Boys with Posterior Urethral Valves: Result of the CIRCUP Randomized Trial. Eur Urol. In press. <https://doi.org/10.1016/j.eururo.2021.08.024>

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Letter to the Editor

Re: Luke Harper, T. Blanc, M. Peycelon, et al. Circumcision and Risk of Febrile Urinary Tract Infection in Boys with Posterior Urethral Valves: Result of the CIRCUP Randomized Trial. Eur Urol. In press. <https://doi.org/10.1016/j.eururo.2021.08.024>

We wish to congratulate Dr. Sauvat's team for undertaking a randomized controlled trial looking at the role of circumcision in decreasing the risk of febrile urinary tract infections (UTIs) in boys with posterior urethral valve (PUV) [1]. At 2 yr, the risk of febrile UTI was 3% among boys undergoing circumcision (+ antibiotic prophylaxis), compared to 20% for the group receiving antibiotics alone, translating to a tenfold risk reduction and a number needed to treat of six. This effect was amplified further when a less stringent (and arguably more clinically relevant) definition of UTI was used. In addition, protocol-mandated scintigraphy also suggested a potential benefit in reducing renal scarring in the circumcision group. We would like some clarification for certain issues and highlight some pertinent points.

1. The authors do not clearly specify if undergoing primary valve ablation was an inclusion criterion or if boys undergoing vesicostomy/supravesical diversion were also included. One of the more interesting aspects was the presence of dilating (grade 3–5) vesicoureteral reflux (VUR) in more than half of all boys (~62% in the antibiotic only group vs ~50% in the circumcision + antibiotic group). The beneficial impact of circumcision would be even greater in PUV cases with VUR given their high propensity for febrile UTIs (at least until VUR resolves, which was >50% in the study), so the overall effect size in this study may in fact have been diluted by inclusion of non-VUR patients.
2. The authors state that it is usual practice in their country for all newborn boys with PUV to be on antibiotic prophylaxis (regardless of the presence of VUR), while starting anticholinergic treatment is not. A prior randomized study showed the efficacy of oxybutynin (0.2 mg/kg three times daily) in aiding resolution of hydronephrosis and VUR over 1-yr follow-up [2], although it did not significantly decrease risk of febrile UTI (30% vs 40%). The latter finding may be related to the small absolute numbers, discontinuation of oxybutynin (~20%), or lack of routine circumcision or antibiotic prophylaxis in the study. It is unclear in the current study whether any patients received anticholinergic therapy and the potential impact on UTI.

3. As the authors point out, most of the febrile UTIs happened over the first year of follow up. The febrile UTI incidence of ~20% despite continuous antibiotic prophylaxis (control arm) remains a cause for concern. It would be interesting to see the resistance patterns for patients who had febrile UTIs or antibiograms from the authors' institution/region, especially given the rising resistance of uropathogens to extended-spectrum penicillin and first- and second-generation cephalosporins among children with congenital anomalies of the kidney and urinary tract [3].

In summary, this was a very well-conducted study providing objective evidence for what was generally believed to be intuitively true. We posit that children with PUV and dilating VUR/hydronephrosis are at the greatest risk of UTI. Given the emergence of resistant organisms, future studies assessing the benefit of circumcision, with or without anticholinergic or α -blocker therapy, may determine if there are groups for which prophylaxis can be eliminated.

Conflicts of interest: The authors have nothing to disclose.

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- [3] Isac R, Basaca DG, Olariu IC, et al. Antibiotic resistance patterns of uropathogens causing urinary tract infections in children with congenital anomalies of kidney and urinary tract. Children 2021;8: 585.

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