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Editorial: Posterior urethral valves: advances in diagnosis, management, and long-term follow up

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Editorial on the Research Topic

Posterior urethral valves: advances in diagnosis, management, and long-term follow up

Posterior Urethral Valves (PUV) is a complex and fascinating condition that affects the urinary tract in boys. It represents the most common cause of congenital urinary outflow obstruction affecting approximately 1 in 3,000 to 8,000 male births (1).

Despite many recent advances in the understanding of PUV, there is still much to discover on the causes, evolution, and management of this condition, from the embryo up to adulthood. [Van der Zanden et al.](#) reviewed the files of more than 1,000 children (407 PUV and 814 controls) exploring potential maternal risk factors and identified that a family history of congenital anomalies of the kidneys and urinary tract (CAKUT) and maternal pre-existing hypertension as well as young maternal age seem to be associated with a higher risk of PUV development. This finding is in contrast with other reports that link increased maternal age (>35 years) as a risk factor for chromosomal anomalies (2) or urogenital defects, as shown by the recent systematic review published by [Ahn et al.](#) (3).

The quest for identifying genetic profiles and associated congenital defects is open and PUV is definitely an interesting condition to investigate (4). The association of PUV with genetic defects such as trisomy 21 has already been shown (5), but a more advanced exercise to explore the genetic association with PUV is represented by genome-wide association studies (GWAS). In 2022, [Chan et al.](#) identified TBX5 (T-Box Transcription Factor 5) and PTK7 (Protein Tyrosine Kinase 7) located in chromosomes 12 and 6, respectively, as candidate genes associated with PUV (6). Another GWAS for PUV, as well as a meta-analysis, was performed by [van der Zanden et al.](#) in four cohorts of patients and controls. They identified three suggestive loci in chromosomes 13, 16, and 20 but eventually found no definitive association, suggesting that more studies are needed to enable the identification of any possible significant association.

Over the years, the survival rate of foetuses with PUV has increased significantly. However, a large proportion of boys born with PUV will still face a degree of bladder and

renal deterioration and require multiple hospital admissions and interventions including, for the most severe cases, renal replacement. Multiple reports have previously suggested that nadir serum Creatinine is an accurate prognostic factor for mid and long-term renal function (7).

The meta-analysis performed by Meneghesso et al. reinforces this idea and they suggest a cut-off of 1 mg/dl to be significant.

The bladder represents a crucial player in the long-term outcome of boys born with PUV and this is being recognized more and more by clinicians and researchers, thus highlighting the need for more thorough investigations of its function, both in the short and long term. The paper from Pellegrino et al. shares their 30-year experience with PUV management and highlights the role of the bladder, including the association with Vesico-ureteric reflux (VUR) and Bladder neck dysfunction (BND), as well as the importance of long-term follow-up.

It must be said that the question of whether VUR and BND are both primary conditions associated with a structural anomaly of the urinary tract development or whether they are secondary to the bladder maldevelopment and caused by the high pressures developed during voiding and thickening of the detrusor muscle is both unanswered and fascinating (8).

On another level, the complex relationship between bladder pressure and renal function in the presence of venting mechanisms known as “pressure pop-off mechanisms” has been investigated for many years since the original description by Rittenberg et al. (9). More and more studies, however, have challenged the original belief that they would have a protective effect on the renal function and some teams have suggested that the presence of pop-off could actually represent a negative prognostic factor (10). The retrospective review published by Khondker et al. suggested no association between VURD and bladder dysfunction at 120 months of follow-up (11). In the study by Delefortrie et al., in a series of 137 PUV patients with a minimum of 5 years follow-up, the investigators found no significant difference in the mean renal function between boys with and without pop-off. They do, however, specifically question whether patients with and without pop-off mechanisms are truly comparable as we do not know why in the presence of high-pressure some will present a pop-off mechanism and why if they do, it will be in the form of VURD, urinoma, or a diverticula.

One of the factors that influence the long-term renal function in boys born with PUV is represented by the development of febrile urinary tract infections (fUTIs). The association between fUTIs and VUR is well known and a link with a higher risk of developing renal scarring has been clearly demonstrated (12).

In their secondary analysis of a multicentre randomised control trial, Harper et al. demonstrated this association in boys with PUV. Their data showed that the presence of high-grade VUR is associated with a 6-fold higher risk of presenting fUTIs, and, interestingly, they also identified the first 9 months of life as the more critical period in which boys have a higher risk of developing a febrile UTI. Circumcision plays a crucial role in mitigating the above risk and is, therefore, recommended, particularly in prenatally diagnosed cases (13).

It would be interesting to explore many other aspects of the long-term outcomes of boys born with PUV, including boys' psychological development, quality of life, and life achievements.

The complexity and low incidence of the condition make long-term outcomes of PUV scarcely reported in the literature, with most publications either reporting small series or including a very large time span (14).

The efforts of clinicians and researchers should therefore be focussed on identifying common guidelines and agreed pathways that will enable them to join and compare short and long-term results and enhance the quality of care for boys born with PUV.

Author contributions

All authors have contributed in writing the editorial. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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