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Renal stones in patients with autosomal dominant polycystic kidney disease, a treatment challenge?

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To the Editor

Autosomal dominant polycystic kidney disease (ADPKD) is a well-known cause for renal function decline, due to significant cyst formation and growth in both kidneys. Occasionally ADPKD patients may suffer from other, more acute complications, such as pain caused by cyst bleeding, cyst infection or renal stones.

Recently, Clinical Experimental Nephrology published an article by Xu et al. that evaluated the feasibility of laparoscopic ureterolithotomy, flexible ureteroscopic (fURS) lithotripsy and percutaneous nephrolithotomy (PCNL) for the management of renal stones in the upper urinary tract in ADPKD patients [1]. The authors start their article by stating that renal stones are one of the most common complications in ADPKD. In their retrospective design study, 45 patients in total were included, 13 patients underwent treatment of their urinary stones by a laparoscopic approach, 21 by fURS and 11 by PCNL. They concluded that all these approaches provided good outcomes regarding stone-free clearance and safety. Despite their clear and thoughtful overview, we have some doubts whether their results are an adequate representation of stone management in the ADPKD population.

The incidence of renal stones in ADPKD patients is estimated to be 5–10 times higher compared to non-ADPKD patients, due to abnormalities in anatomical renal structure and metabolic risk factors, such as hypocitraturia, hyperoxaluria, hyperuricosuria and low urine pH [2]. It should be noted however, that these incidence rates are based on

relatively small studies from the eighties and nineties, that indicated that up to 36% of the patients suffer from renal colic events, secondary to renal stones [3]. Results from our DIPAK observational cohort suggest that this number may be considerably lower. In this study, that was designed to investigate the natural course of ADPKD, 665 ADPKD patients were included, of which 65 (9.9%) patients had a medical history of renal stones. Only a relative small number of these patients needed an intervention for their renal stones, 14 patients underwent fURS and two PCNL, with good outcomes on stone-free clearance except for one patient who needed a re-intervention.

In the diagnostic approach of renal stones, CT imaging is the golden standard to determine whether renal stones are present. Intra-renal calcifications can be observed on CT scans in around 25% of ADPKD patients. It should be noted that in ADPKD, there is a frequent occurrence of parenchymal as well as cyst wall calcifications, which may lead to overdiagnosis of renal stones and may have caused a falsely high incidence rates in the aforementioned older studies, at a time when the resolution of imaging was not as granular as it is now.

In case of large or symptomatic stones, intervention is needed. Due to an abnormality in renal pelvic structure, electric shockwave therapy is not the preferred choice, because spontaneous passage after shockwave therapy is relative difficult. Therefore endoscopic options, such as fURS or PCNL, have been applied. Nowadays, fURS offers up to 270° deflections in both directions, resulting that most stones can be reached by an endoscopic approach and thereafter fragmented or extracted. In case the ureter is not accessible for fURS, pre-stenting with a JJ catheter may make introduction of the fURS feasible in a second session. Although also larger stones can be treated by fURS, this procedure is time-consuming and may, therefore, pose a greater risk for urinary tract infection. In patients with more sizable stones, PCNL could, therefore, be an attractive alternative. By the development of mini-PCNL and even ultra-mini-PCNL, the

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percutaneous approach may be a less harmful option for the renal parenchyma and could, therefore, also be executed in case of a limited stone load. Finally, in centers with specific expertise in treatment of kidney stones, a combined approach with fURS and PCNL can be offered, in which laser fragmentation is performed in a low-pressure system with a lower risk for urinary tract infection. It is our experience that since the fURS and PCNL techniques have been improved, the majority of renal stones in ADPKD can now be treated effectively with these techniques. We suggest, therefore, that the role for the more invasive laparoscopic treatment of renal stones in ADPKD should now be limited and only be carried out in selected patients.

After successful treatment of renal stones, it is important to prevent recurrence. The general preventive measures should be advised, including a low-protein diet and high water intake. For ADPKD specifically, recently some interesting articles were published in which it was shown that tolvaptan, a vasopressin V2 receptor antagonist that ameliorates the rate of renal function decline in ADPKD patients, may improve urinary lithogenic risk profile in ADPKD patients [4]. Whether tolvaptan use indeed results in less recurrence of renal stones is not yet known, but a post hoc analysis of a large-scale randomized trial with tolvaptan in ADPKD that we performed showed a 37% decrease in incidence of de novo kidney stones compared to placebo ($P < 0.001$) [5]. This drug may, therefore, be an attractive option to prevent renal stone recurrence in ADPKD patients, especially in those that are not able to adjust their dietary intakes out of their own initiative.

In conclusion, we are of the opinion that in ADPKD patients, literature may overestimate the incidence of renal stones and that endoscopic procedures for renal stone management, such as fURS and PCNL, should be the preferred treatment option instead of a laparoscopic approach. In addition, it should not be forgotten to advise measures to prevent recurrence, among which dietary changes and perhaps tolvaptan.

Compliance with ethical standards

Conflict of interest Prof. dr. R.T. Gansevoort received grant support and fees for serving on steering committees from Otsuka Pharmaceuticals, manufacturer of tolvaptan. The other authors have declared that no conflict of interest exists.

Ethical approval All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional research committee at which the study was conducted (IRB Approval Number METc2013/040) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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