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Between a Rock and a Hard Place: The Uncertainties in Managing Renal Stones

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The management of renal calculi has evolved over the last few decades due to technological advances. Treatment options include shock wave lithotripsy, percutaneous nephrolithotomy (PCNL), or retrograde intrarenal surgery (RIRS), with the choice of intervention guided by stone location, size, composition, and anatomic factors [1], along with the availability of technical expertise and equipment. However there is considerable uncertainty regarding how these interventions compare with each other, a fact underlined by current clinical practice guidelines [1]. The systematic review and meta-analysis by De et al. [2] in this month's issue of *European Urology* represents a welcome attempt to clarify some of the uncertainties regarding PCNL and RIRS for the treatment of renal stones.

The review synthesised evidence based on a structured literature assessment. Outcomes assessed included stone-free rate (SFR), need for auxiliary procedures and complication rate, and process outcomes. Meta-analysis was planned on all outcomes irrespective of study design, and subgroup analysis was performed on PCNL subtypes. The review ultimately included 10 studies, 6 of which were retrospective observational studies. In the main analysis, the authors found PCNL had a significantly higher SFR (odds ratio [OR]: 2.19; 95% confidence interval [CI], 1.53–3.13) and a higher complication rate (OR: 1.61; 95% CI, 1.11–2.35) than RIRS, but no data on the need for auxiliary procedures were presented. In the subgroup analysis, standard PCNL had higher SFR than RIRS (OR: 4.32; 95% CI, 1.99–9.37), but there was no difference in complication rate or the need for auxiliary procedures. Conversely, RIRS had better SFR than minimally invasive percutaneous procedures (OR: 1.70;

95% CI, 1.07–2.70), but there was no difference in complication rate or the need for auxiliary procedures.

We commend the authors for attempting to address the prevalent uncertainties regarding the management of renal stones in a methodical and thoughtful manner. Reviews regarding surgical practice are rarely undertaken systematically [3], and high-quality systematic reviews concerning kidney diseases are lacking [4]. The merits of a high-quality systematic review, supplemented by a robustly undertaken meta-analysis, are undeniable [5]. The observed greater complication rate associated with PCNL compared with RIRS on meta-analysis is particularly striking, considering the consistency of magnitude and direction of effects across studies and lack of statistical heterogeneity, in spite of the inherent clinical and methodological heterogeneity that must surely be present due to the diverse types of included studies. This finding supports efforts to refine and innovate PCNL to minimise morbidity while maintaining its stone-clearing efficacy.

However, to interpret the findings of any evidence synthesis, especially in terms of its potential impact on clinical practice and clinical practice guidelines, a close scrutiny of its conduct and processes is mandatory. In this context, the work suffers from significant methodological limitations. The greatest concern relates to the authors' decision to combine unadjusted data from retrospective observational studies and randomised trials in performing their meta-analysis. This strategy is usually discouraged because it is difficult to control and account for biases, heterogeneity, and confounding, hence risking misleading or spurious findings [6]. The sum of multiple biases and uncertain estimates of individual studies are magnified

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when such data are combined while introducing new biases and errors in the analysis.

Second, the conduct of the review is generally poorly described. In particular, the patient or problem, intervention of interest, comparison, and outcome (PICO) elements are not clearly or adequately specified. Did the review include patients with all stone sizes and all stone locations? Did it matter if patients were first-time or recurrent stone formers? What about the composition of stones? Which group was considered the experimental intervention, and which was the control? What were the prespecified comparisons? The outcomes were also poorly specified in terms of the primary outcome, how it was defined (eg, were residual fragments allowed in the definition of stone-free clearance), and when it was measured. The risk of bias (RoB) assessment results were merely summarised; no detailed description was provided, and it was unclear which confounding variables were considered in the RoB assessment for observational studies.

All things considered, there was little evidence that the review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analysis framework [7]. The observation that only 16 articles of 30 000 abstracts were eligible for full-text screening is highly unusual, especially considering that nonrandomised and observational study designs were included. There was a clear imbalance in the number of participants between the two groups, with almost twice as many patients who had PCNL ($n = 727$) compared with RIRS ($n = 454$), which is typical of any synthesis involving retrospective observational studies. There was moderate to high statistical heterogeneity for virtually all outcomes except for complication rate, which seriously limits the reliability of most of the review findings. Why was subgroup or sensitivity analysis not planned on important confounders such as stone size and location, patient age, and gender to explore and account for such heterogeneity that must surely have been anticipated?

The authors used RoB assessment as a surrogate for quality of evidence. The quality of evidence for any research question is influenced by the interplay of many elements that extend far beyond the risk of bias of individual studies alone; these include inconsistency, imprecision and indirectness of effects, magnitude of effect, and the impact of opposing biases and confounders [8]. Consequently, the reported quality assessment is incomplete, which hinders any meaningful interpretation of the review findings.

Lastly, the authors conclude that RIRS should be recommended as standard therapy for stones <2 cm. Given

the considerable limitations of the review conduct and the uncertainties associated with its findings, this recommendation is at best misleading, and it is out of sync with present clinical practice guidelines [1].

In conclusion, although the review by De et al. [2] raises interesting points, the fundamental question of how PCNL truly compares with RIRS for the management of renal stones remains essentially unanswered. Ultimately, the paper does highlight the relative lack of reliable and good quality data in the evidence base concerning this clinically and economically important question. This emphasises the need for high-quality, robust, and well-designed prospective RCTs incorporating clinically meaningful outcomes that are important to patients, based on standardised definitions and measured using standardised outcome measures [9].

Conflicts of interest: The authors have nothing to disclose.

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