

**Comment on: European consensus-based recommendations
for diagnosis and treatment of immunoglobulin A
vasculitis—the SHARE initiative**

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| Absolute indications |
| Persisting severe proteinuria (UP:UC >250 mg/mmol for 4 weeks) |
| Persisting moderate proteinuria (UP:UC 100-250 mg/mmol for 3 months) |
| Acute kidney injury stage 1 or greater (serum creatinine >1.5x previous baseline (if known) or >1.5x upper limit of normal for age) |
| Nephrotic syndrome (clinical oedema, serum albumin below lower limit of normal for age, moderate/severe proteinuria) |
| Relative indications |
| Reproducible severe proteinuria (UP:UC >250 mg/mmol) at any time point |
| Serum creatinine above upper limit of normal |

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Comment on: European consensus-based recommendations for diagnosis and treatment of immunoglobulin A vasculitis—the SHARE initiative

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Key message (maximum 15 words): Standardising when to perform a renal biopsy in IgA vasculitis will assist with improving outcomes.

Dear Editor, We read with great interest the article published in September 2019 by Ozen et al. (1) entitled 'European consensus-based recommendations for diagnosis and treatment of immunoglobulin A vasculitis – the SHARE initiative'. Firstly, we would like to congratulate all members of the Single Hub and Access point for paediatric rheumatology in Europe (SHARE) initiative for developing such important recommendations for childhood IgA vasculitis (IgAV) as this is a disease that significantly lacks an evidence base to guide best practice. The recommendations were formulated as a result of a systematic literature review and a process of agreement among an expert group of European rheumatologists with a representative nephrologist and we acknowledge the extensive effort that this must have taken.

We are writing to inform you that a group of 10 nephrologists (9 paediatric, 1 adult) with an interest in IgAV nephritis (Henoch Schonlein purpura nephritis) met on 17th October, 2019 in Venice, Italy for an international workshop. The aim of the workshop was to discuss a much needed clinical trial for children with biopsy proven IgAV nephritis. As part of this workshop, we incorporated a session focused on when to perform a renal biopsy in these children and we are delighted to report that the SHARE recommendations were met with great enthusiasm. Generally, the attendees, who represented 9 different nephrology institutions from across the world, supported the recommendations however we did note areas that would benefit from clarification to improve their interpretation. This is particularly important as the renal monitoring for this disease is predominantly delivered by non-specialists. As a group we felt that changes in renal function would be better based on changes in creatinine values rather than the more complex estimated glomerular filtration rate to ease interpretation; this would be aligned with recent international efforts to standardise the definition of acute kidney injury (2, 3). Additionally, we felt that due to the increased risk of significant long term renal consequences in children with nephrotic and/or nephritic syndrome (e.g. up to 19.5%) (4-6), as is stated in the manuscript, it would be important to specifically state that the presence of nephrotic syndrome should also be an absolute indication to performing a renal biopsy. Finally the group acknowledged the importance of providing equivalent proteinuria thresholds if these recommendations are to become adopted into international clinical guidelines as reporting of creatinine or proteinuria concentrations vary in different countries. . We have therefore combined the SHARE recommendations with the suggested terminology improvements from our international workshop into a user friendly table (Table 1).

The next phase would be to receive input from our general paediatric colleagues on the suitability of these indications as we move towards incorporating them into management recommendations. Once again we would like to congratulate the SHARE expert group, as they have started the process of standardising an important aspect of management in childhood IgAV, as we work together to achieve the vision that no child with IgAV should get chronic kidney disease.

Table 1: Suggested absolute and relative indications for performing a renal biopsy in IgA vasculitis (adapted using (1, 2))

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| Absolute indications |
| Persisting severe proteinuria (UP:UC >250 mg/mmol for 4 weeks) |
| Persisting moderate proteinuria (UP:UC 100-250 mg/mmol for 3 months) |
| Acute kidney injury stage 1 or greater (serum creatinine >1.5x previous baseline (if known) or >1.5x upper limit of normal for age) |
| Nephrotic syndrome (clinical oedema, serum albumin below lower limit of normal for age, moderate/severe proteinuria) |
| Relative indications |
| Reproducible severe proteinuria (UP:UC >250 mg/mmol) at any time point |
| Serum creatinine above upper limit of normal |

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3 partnership with King's College London and King's College Hospital NHS Foundation Trust.

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6 7 **References (max 8)**

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9 1. Ozen S, Marks SD, Brogan P, Groot N, de Graeff N, Avcin T, et al. European consensus-based
10 recommendations for diagnosis and treatment of immunoglobulin A vasculitis-the SHARE initiative. Rheumatology
11 (Oxford). 2019.
12 2. Group KDIGOKAKIW. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney inter.
13 2012;Suppl.(2):1-138.
14 3. Excellence NifHaC. Acute kidney injury: prevention, detection and management of acute kidney injury up to
15 the point of renal replacement therapy. (Clinical guideline 169) 2013:<http://guidance.nice.org.uk/CG169>.
16 4. Narchi H. Risk of long term renal impairment and duration of follow up recommended for Henoch-Schonlein
17 purpura with normal or minimal urinary findings: a systematic review. Arch Dis Child. 2005;90(9):916-20.
18 5. Butani L, Morgenstern BZ. Long-term outcome in children after Henoch-Schonlein purpura nephritis. Clin
19 Pediatr (Phila). 2007;46(6):505-11.
20 6. Coppo R, Andrulli S, Amore A, Gianoglio B, Conti G, Peruzzi L, et al. Predictors of outcome in Henoch-
21 Schonlein nephritis in children and adults. Am J Kidney Dis. 2006;47(6):993-1003.
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