Management and treatment of glomerular diseases: Highlights of the 2020 KDIGO guideline

Jürgen Floege
University of Aachen
Germany
### Recommendations

**(GRADE-Approach*)**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Patients</th>
<th>Clinicians</th>
<th>Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1 “We recommend”</td>
<td>Most people in your situation would want the recommended course of action and only a small proportion would not.</td>
<td>Most patients should receive the recommended course of action.</td>
<td>The recommendation can be evaluated as a candidate for developing a policy or a performance measure.</td>
</tr>
<tr>
<td>Level 2 “We suggest”</td>
<td>The majority of people in your situation would want the recommended course of action, but many would not.</td>
<td>Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.</td>
<td>The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grade</th>
<th>Quality of evidence</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>High</td>
<td>We are confident that the true effect lies close to that of the estimate of the effect.</td>
</tr>
<tr>
<td>B</td>
<td>Moderate</td>
<td>The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.</td>
</tr>
<tr>
<td>C</td>
<td>Low</td>
<td>The true effect may be substantially different from the estimate of the effect.</td>
</tr>
<tr>
<td>D</td>
<td>Very low</td>
<td>The estimate of effect is very uncertain, and often will be far from the truth.</td>
</tr>
</tbody>
</table>

* Grading of Recommendations Assessment, Development and Evaluation
CHAPTER 1. GENERAL PRINCIPLES FOR THE MANAGEMENT OF GLOMERULONEPHRITIS

1.1. Kidney biopsy

Practice Point 1.1.1. The kidney biopsy is the “gold standard” for glomerular diseases. However, under some circumstances, a diagnosis may be made without a kidney biopsy confirmation of diagnosis.

Practice Point 1.1.2. The evaluation of kidney tissue should be thorough and adequate.

Practice Point 1.1.3. Repeat kidney biopsy should be performed if there is a need to potentially alter the therapeutic plan.
2020 KDIGO clinical practice guideline on glomerular diseases

CHAPTER 1. GENERAL PRINCIPLES FOR THE MANAGEMENT OF GLOMERULONEPHRITIS

Summary of Recommendation Statements and Practice Points

1.1. Key Practice Questions

1.1.1. What are the key questions about the management of glomerulonephritis?

1.1.2. How should the diagnosis of glomerulonephritis be made?

1.1.3. What is the role of imaging in the management of glomerulonephritis?

1.1.4. How should the treatment of glomerulonephritis be individualized?

1.1.5. What are the potential complications of glomerulonephritis?

Chapter 1. General Principles for the Management of Glomerulonephritis

Chapter 2. Immunoglobulin A Nephropathy/Immunoglobulin A Vasculitis

Chapter 3. Primary Membranous Nephropathy

Chapter 4. Nephrotic Syndrome in Children

Chapter 5. Minimal Change Disease in Adults

Chapter 6. Focal Segmental Glomerulosclerosis in Adults

Chapter 7. Infection-Related Glomerulonephritis

Chapter 8. Complement-Associated Glomerulonephritis

Chapter 9. Anti-neutrophil cytoplasmic antibodies (ANCA)-Associated Vasculitis

Chapter 10. Lupus Nephritis

Chapter 11. Anti-Glomerular Basement Membrane Antibody Glomerulonephritis
Glomerulonephritis-Types encountered in Europe

Kidney biopsy diagnoses in 2243 adult patients undergoing native kidney biopsy at the Division of Nephrology, Aachen University Hospital between 1990 and 2013.
2.2. Prognosis  

Practice Point 2.2.1. Considerations for the prognostication of primary IgAN:

- Clinical and histologic data at the time of biopsy can be used to risk assess the patient using the International IgAN Prediction Tool available at QxMD.
- The International IgAN Prediction Tool cannot be used to determine the likely impact of any particular treatment regimen.
- There are no validated *prognostic* serum or urine biomarkers for IgAN.

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**Research**

*JAMA Internal Medicine | Original Investigation*

**Evaluating a New International Risk-Prediction Tool in IgA Nephropathy**

Sean J. Barbour, MD, MSc; Rosanna Coppo, MD, FERA; Hong Zhang, MD, PhD; Zhi-Hong Liu, MD; Yusuke Suzuki, MD, PhD; Keiichi Matsuzaki, MD, PhD; Ritsuko Katafuchi, MD, PhD; Lee Er, MSc; Gabriela Espino-Hernandez, MSc; S. Joseph Kim, MD, PhD; Heather N. Reich, MD, PhD; John Feehally, FRCP; Daniel C. Catran, MD, FRCP; for the International IgA Nephropathy Network
IgA nephropathy

Practice Point 2.3.1. Considerations for treatment of all patients with IgAN

- The primary focus of management should be optimized supportive care.
- Assess cardiovascular risk and commence appropriate interventions as necessary.
- Give lifestyle advice including information on dietary sodium restriction, smoking cessation, weight control, and exercise as appropriate.

Level 1 Recommendations
- Control blood pressure (sitting systol. BP in the 120s)
- ACEI or ARB therapy (uptitrate + maybe combine)
- Avoid dihydropyridine type calciumchannel-blockers
- Control protein intake

Level 2 Recommendations
- Restrict NaCl- and fluid-intake, diuretics
- Non-dihydropyridine type calciumchannel-blockers
- Control all components of the metabolic syndrome
- Aldosterone antagonist, ß-blocker
- Stop smoking
- Low evidence: NaHCO₃ therapy, independent of metabolic acidosis

ALL

As many measures as possible

Floege & Eitner, JASN 2011  Floege & Feehally Nat Rev Nephrol 2013
Recommendation 2.3.2.
We recommend that all patients with proteinuria >0.5 g/24h, irrespective of whether they have hypertension, are treated with either an ACEi or ARB (1B).

Recommendation 2.3.3.
We suggest that patients who remain at high risk of progressive CKD despite maximal supportive care are considered for a six-month course of corticosteroid therapy.
The important risk of treatment-emergent toxicity must be discussed with patients, particularly those who have an eGFR below 50 ml/min/1.73 m² (2B).

Use extreme caution or avoided entirely if:

- eGFR < 30 mL/min/1.73 m²*
- Diabetes
- Obesity (BMI > 30 kg/m²) **
- Latent infections (e.g. hepatitis, TB)
- Secondary disease (e.g. cirrhosis)
- Active peptic ulceration
- Uncontrolled psychiatric illness
STOP-IgAN trial: Long-term Renal Outcomes

92% with longterm follow-up (median 7.4 yrs)

162 patients underwent randomization

STOP-IgAN randomized 3-year trial phase

Supportive therapy (n=80)
1 died
1 withdrew consent
2 lost to follow-up
76 completed trial phase

Supportive therapy + immunosuppression (n=82)
1 died
1 withdrew consent
2 lost to follow-up
78 completed trial phase

Long-term observation

70 with available data on ESRD and renal function
1 died
5 lost to follow-up
72 (90.0%) pts.

74 with available data on ESRD and renal function
2 died
2 lost to follow-up
77 (93.9%) pts.

Long-term endpoint (death, ESRD or eGFR-loss >40%)

Probability of event free survival

0.0
0.2
0.4
0.6
0.8
1.0

0 2 4 6 8 10

Time (years)

Supportive Care
Supportive Care plus Immunosuppression

+ Censored

Pts. with available EP information (i.e. death, ESRD and eGFR-loss >40%) at end of longterm observation

Rauen T, …. Floege J. Kidney Int 2020 in press
Membranous nephropathy

Practice Point 3.2.1. In patients with MN, use clinical and laboratory criteria to assess the risk of progressive loss of kidney function

<table>
<thead>
<tr>
<th>Low risk</th>
<th>Moderate risk</th>
<th>High risk</th>
<th>Very high risk</th>
</tr>
</thead>
</table>
| • Normal eGFR, proteinuria < 3.5 g/day and/or serum albumin > 30 g/L     | • Normal eGFR, proteinuria > 4 g/day and no decrease > 50% after 6 months of conservative therapy with ACE/ARB | • eGFR < 60 ml/min/1.73 m²<sup>a</sup>  
• Proteinuria > 8 g/day for > 6 months  
• PLA2Rab > 150RU/ml<sup>b</sup>  
• High LMW proteinuria  
• U IgG > 250 mg/day  
• Selectivity index > 0.20                                           | • Life-threatening nephrotic syndrome  
• Rapid deterioration of kidney function not otherwise explained  
• High LMW proteinuria in two urine samples collected with interval of 6–12 months |

<sup>a</sup> Estimated glomerular filtration rate

<sup>b</sup> Proteinuria and renal dysfunction often resolve with ACE/ARB therapy.
Membranous nephropathy

**Recommendation 3.3.1.**
For patients with MN and at least one risk factor for disease progression, we recommend using rituximab, or cyclophosphamide and steroids for six months, or tacrolimus-based therapy for at least six months, with the choice of treatment depending on the risk estimate (1B).
MENTOR: Rituximab vs. CyA in membranous GN

Rituximab or Cyclosporine in the Treatment of Membranous Nephropathy


MENTOR: Rituximab vs. CyA in membranous GN

Partial or full remission at 24 months

Cumulative Incidence (%)

End of therapy

No. at Risk
Rituximab 65 59 48 48 44
Cyclosporine 65 56 42 20 13

Practice Point 3.3.3. Longitudinal monitoring of PLA2Rab levels at three and six months after start of therapy may be useful for evaluating treatment response in patients with membranous nephropathy, and can be used to guide adjustments to therapy.

0 months
- Measure PLA2Rab
  - PLA2Rab: absent
    - RTX: no additional therapy
    - CP: withdrawal
    - CNI: continue
  - RTX: no change
    - PLA2Rab: increased
      - RTX: extra doses or add CP
        - CP: add RTX
        - CNI: add CP or RTX

3 months
- PLA2Rab: absent
  - Absent or low
    - Continue as per guideline

6 months
- PLA2Rab: moderately increased, stable or slowly increasing
  - Additional therapy with standard agents
- PLA2Rab: high titers, persistent or increasing
  - Evaluate and treat as resistant disease
Recommendation 5.3.1. We recommend high dose oral corticosteroids for initial treatment of MCD (1C).

Recommendation 5.3.1.1. We suggest cyclophosphamide, rituximab, calcineurin inhibitors, or mycophenolic acid analogs (MPAA) for the treatment of frequently-relapsing/corticosteroid-dependent MCD as compared to prednisone alone or to no treatment (1C).
Tacrolimus versus corticosteroid monotherapy for adult minimal change nephropathy

British multicenter trial, median eGFR about 100 ml/min, median proteinuria about 7 g/d
Tacrolimus 0.05 mg/kg twice daily (N=25) vs. prednisolone starting at 1 mg/kg/d (N=25)

**Primary end point:** Achievement of complete remission at week 8

Tapering of treatment over about 12 weeks (pred) or 20 weeks (tac) after remission
Secondary end point: Relapse rate in those who achieved full remission

Tacrolimus versus corticosteroid monotherapy for adult minimal change nephropathy

Adverse event rate comparable

<table>
<thead>
<tr>
<th>Weeks from complete remission</th>
<th>Prednisolone (number followed-up)</th>
<th>Tacrolimus (number followed-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>22 (23)</td>
<td>22 (22)</td>
</tr>
<tr>
<td>12</td>
<td>18 (23)</td>
<td>19 (22)</td>
</tr>
<tr>
<td>26</td>
<td>13 (23)</td>
<td>16 (22)</td>
</tr>
<tr>
<td>52</td>
<td>7 (21)</td>
<td>9 (22)</td>
</tr>
<tr>
<td>78</td>
<td>4 (21)</td>
<td>6 (22)</td>
</tr>
</tbody>
</table>

Medjer-L-Thomam NR et al, CJASN 15: 209–218, 2020
**Recommendation 6.2.2.1.** We recommend that high dose corticosteroids be used as the first line immunosuppressive (1D).
Recommendation 9.3.1. We recommend that corticosteroids in combination with cyclophosphamide or rituximab be used as initial treatment of new-onset AAV (1B).

Recommendation 9.3.1.1. We recommend maintenance therapy with either rituximab or azathioprine and low dose glucocorticoids after induction of remission (1C).
Pexivas: Plasmapheresis in severe ANCA vasculitis

- 704 patients
- 18% pulmonary hemorrhage, 9% severe
- Median s-creatinine 327 µmol/l, 20% dialysis dependent

* 60 ml albumin/kg body weight
7x during 14 days after randomization

Pexivas: Plasmapheresis in severe ANCA vasculitis

Plasma Exchange vs. No Plasma Exchange

- Plasma Exchange: 28% vs. 31% (p=0.27)
- 100/352 vs. 109/352

Years

Death or ESKD (% of patients)
Pexivas: Plasmapheresis in severe ANCA vasculitis


- Full dose steroid
- 50% dose steroid

- 26% vs. 28% p=n.s.
- 83/325 vs. 92/330
## Pexivas: Plasmapheresis in severe ANCA vasculitis

<table>
<thead>
<tr>
<th>Secondary Outcome</th>
<th>Plasma Exchange vs. No Plasma Exchange</th>
<th>Reduced-Dose vs. Standard-Dose Glucocorticoid Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from any cause</td>
<td>0.87 (0.58–1.29)</td>
<td>0.78 (0.53–1.17)</td>
</tr>
<tr>
<td>End-stage kidney disease</td>
<td>0.81 (0.57–1.13)</td>
<td>0.96 (0.68–1.34)</td>
</tr>
<tr>
<td>Sustained remission</td>
<td>1.01 (0.89–1.15)</td>
<td>1.04 (0.92–1.19)</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>1.21 (0.96–1.52)</td>
<td>0.95 (0.75–1.20)</td>
</tr>
<tr>
<td>Serious infections at 1 year</td>
<td>1.16 (0.87–1.56)</td>
<td>0.69 (0.52–0.93)</td>
</tr>
</tbody>
</table>

*effect size (95% CI)*
<table>
<thead>
<tr>
<th>Week</th>
<th>“Reduced-corticosteroid dose” in PEXIVAS trial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50 kg</td>
</tr>
<tr>
<td>1</td>
<td>50</td>
</tr>
<tr>
<td>2</td>
<td>25</td>
</tr>
<tr>
<td>3-4</td>
<td>20</td>
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<td>&gt;52</td>
<td></td>
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</tbody>
</table>

Investigators’ Local Practice
Recommendation 10.2.1.1. We recommend that patients with LN be treated with hydroxychloroquine or an equivalent antimalarial unless contraindicated (1C).
Recommendation 10.2.3.1.1. We recommend that patients with active Class III or IV LN, with or without a membranous component, be treated initially with corticosteroids plus either low dose i.v. cyclophosphamide or MPAA (1B).

Recommendation 10.2.3.2.1. We recommend that after completion of initial therapy patients should be placed on MPAA for maintenance (1B).