

HCA Healthcare

Scholarly Commons

Nephrology

Research & Publications

3-26-2020

Case Series of ANCA Vasculitis as Prognostic Marker for Severity or Relapse of Glomerulonephritis.

Jake N. Cho

HCA Healthcare, Jake.Cho@hcahealthcare.com

Venkat Chitumalla

Ocala Kidney Group

Izuchukwu Nwakoby

Ocala Kidney Group

Follow this and additional works at: <https://scholarlycommons.hcahealthcare.com/nephrology>



Part of the [Cardiovascular Diseases Commons](#), [Female Urogenital Diseases and Pregnancy Complications Commons](#), [Internal Medicine Commons](#), [Male Urogenital Diseases Commons](#), and the [Nephrology Commons](#)

Recommended Citation

Cho JN, Chitumalla V, Nwakoby I. Case Series of ANCA Vasculitis as Prognostic Marker for Severity or Relapse of Glomerulonephritis. Poster presented at: NKF Spring Clinical Meeting; March 26-29, 2020.

This Poster is brought to you for free and open access by the Research & Publications at Scholarly Commons. It has been accepted for inclusion in Nephrology by an authorized administrator of Scholarly Commons.

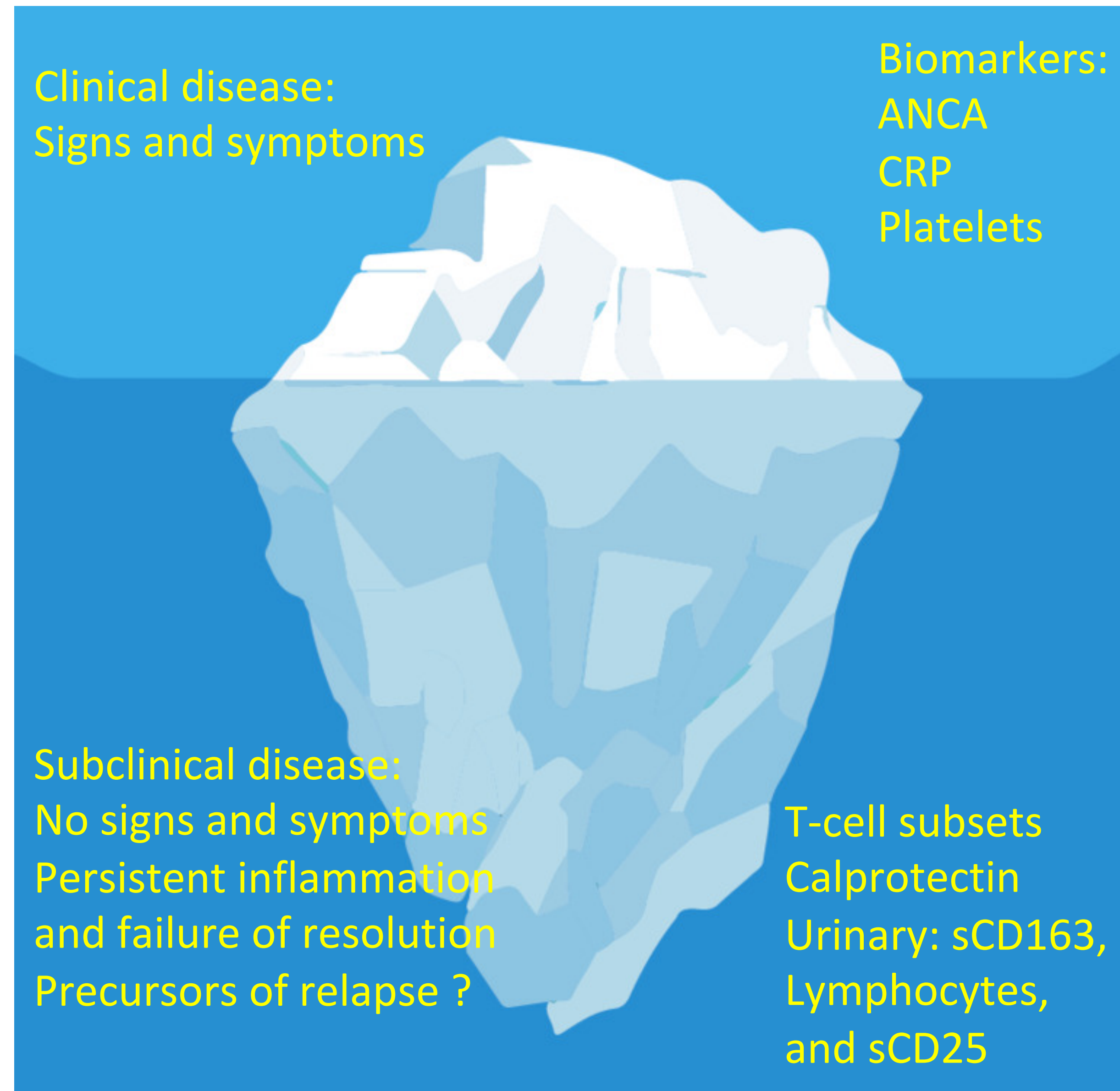
Dr. Jake Cho, M.D.^{1,2}, Dr. Venkat Chitumalla, M.D.^{3,4}, Dr. Izuchukwu Nwakoby, M.D.^{3,4}

1. University of Central Florida College of Medicine, Graduate Medical Education, Orlando, FL
 2. Ocala Regional Medical Center, Internal Medicine Residency Program, Ocala, FL

3. Ocala Regional Medical Center, Nephrology, Ocala, FL
 4. Ocala Kidney Group, Ocala, FL

Introduction

Antineutrophil cytoplasmic antibody (ANCA) associated vasculitides involve pauci-immune small vessel vasculitis that can lead to rapidly progressive glomerulonephritis. This case series examines the role of ANCA titers such as proteinase 3 (PR3) and myeloperoxidase (MPO) antibodies in assessing disease activity.



Clinically overt disease versus subclinical persistent inflammation in ANCA-associated vasculitis. Figure adapted from Salama (2020).

Case Presentations

Case 1 involves a 63 year old female with microscopic polyangiitis who developed pulmonary-renal syndrome requiring intubation, plasmapheresis and immunosuppression. Table 1 shows anti-MPO titer elevated to 80 U/ml with proteinuria and acute kidney injury.

Case 2 involves a 60 year old female with CKD stage 3 and focal segmental glomerulosclerosis in remission who relapsed and developed pauci-immune crescentic glomerulo-nephritis. In case 2, anti-PR3 titer was elevated (>100 U/mL) and associated with a 20-fold increase in the Protein/Creatinine ratio of 2343 mg/g. She eventually required peritoneal dialysis.

Case 3 involves a 78 year old female with CKD stage 3 and anti-MPO vasculitis in remission but developed AKI with a 6 fold increase in anti-MPO titer and 10 fold increase in proteinuria. She was managed conservatively with rituximab.

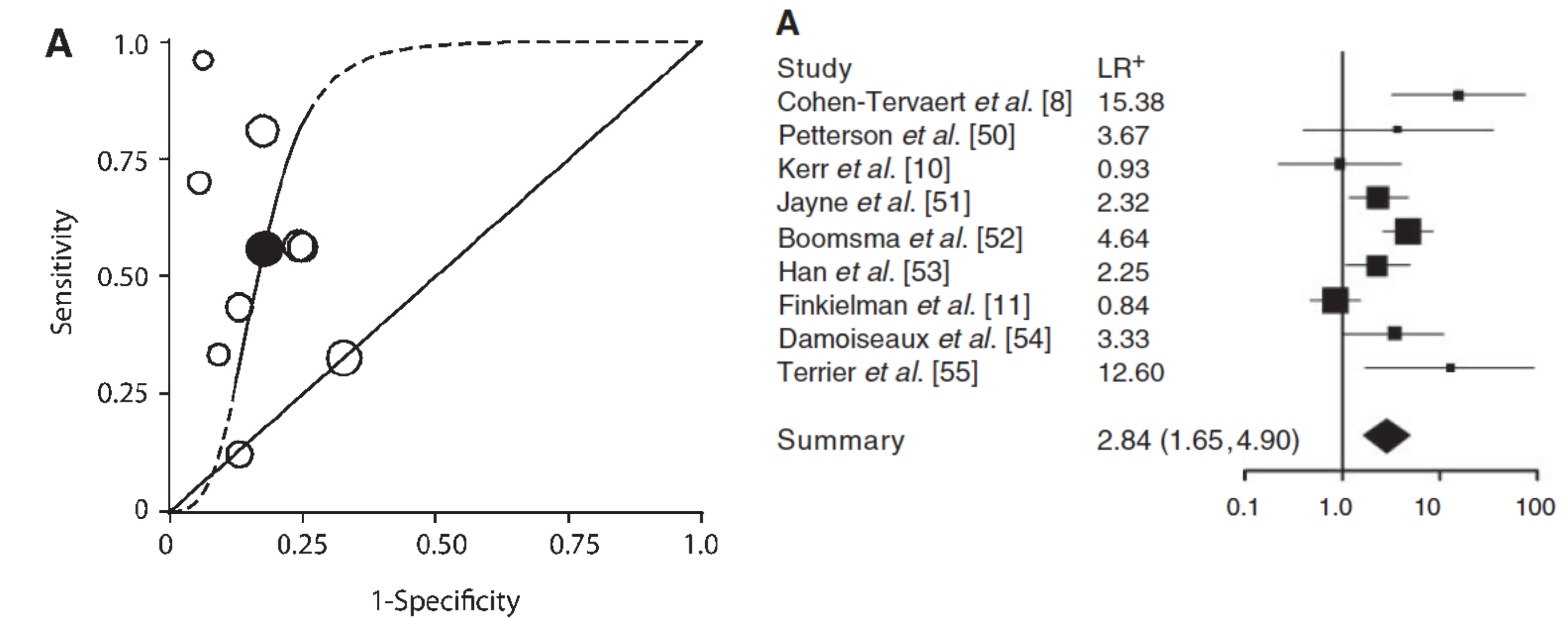
Table

Table 1. Case Series of ANCA vasculitis associated glomerulonephritis				
Case #, sex, age, diagnosis	Renal function at remission	Renal function at relapse	Special labs	Treatment course
Case 1: Female 63 year old, Microscopic Polyangiitis, Pulmonary-renal syndrome	Creatinine 0.90 to 1.70 mg/dL eGFR 30 ml/min	Creatinine 2.60 mg/dL eGFR 19 ml/min	• P-ANCA titer 1:80 (positive) • Anti-MPO 80 U/ml (ref. 0-9)	• methylprednisolone 250mg • plasmapheresis • cyclophosphamide • Mesna • hemodialysis catheter
Case 2: Female 60 year old, 2007, C-ANCA, anti PR3 positive, FSGS (biopsy) 2017, C-ANCA, anti PR3 positive, PICG (biopsy)	Creatinine 1.8 mg/dL eGFR 31 mL/min PR3 antibody 8 to 79 U/mL Prot/Crt ratio: 34 to 81 mg/g	Creatinine 3.90 mg/dL eGFR 11 mL/min PR3 Antibody >100 U/mL Prot/Crt ratio: 2343 mg/g	• Remission: ESR 8 to 16 mm/hr (ref. 0 – 20) • Flare: ESR 103 mm/hr (ref. 0 – 20)	• Rituximab 375 mg/m ² • methylprednisolone 250 mg • prednisone taper • peritoneal dialysis • kidney transplant list
Case 3: Female 78 year old, anti MPO positive, ANCA, glomerulonephritis	Creatinine 1.37 mg/dL eGFR 37 mL/min anti MPO 4.9 AI (ref. <1.0) Prot/Crt ratio: 263 mg/g	Creatinine 1.81 mg/dL eGFR 27 mL/min anti MPO 30 AI (ref. <1.0) Prot/Crt ratio: 2329 mg/g	• Remission: ESR 14 mm/hr (ref. 0 – 20) • Flare: ESR 111 mm/hr (ref. 0 – 20) • Weight loss BMI 18.67 to 16.36 kg/m ²	• kidney biopsy inconclusive • no steroids, osteoporosis • Rituximab 375 mg/m ² • Rituximab 500 mg maintenance to 24 months • Elderly BMI ref. 25–30

Abbreviations:
 ref. (reference), eGFR (estimated glomerular Filtration Rate), ESR (erythrocyte sedimentation rate), C-ANCA (cytoplasmic anti-neutrophilic cytoplasmic antibodies), P-ANCA (peri-nuclear anti-neutrophilic cytoplasmic antibodies), MPO (Myeloperoxidase), PR3 (Proteinase-3), PICG (Pauci immune crescentic glomerulonephritis), FSGS (Focal Segmental glomerulosclerosis), Crt (Creatinine), Prot (Protein), Prot/Crt ratio ref. < 160

Literature Review (Selected cases)

1. Tomasson meta-analysis (2012): 15 primary studies on the predictability of ANCA on relapse of disease, 9 with a total of 503 patients with a rise in ANCA and 9 with a total of 430 patients with persistently positive ANCA. Figures show analysis for Rise: (Left) Receiver operator curve for a rise in ANCA as predictor of relapse. Estimated sensitivity of 0.56 (95% CI 0.33, 0.79) and specificity of 0.82 (95% CI 0.75, 0.90). (Right) Positive likelihood ratio (LR+) of 2.84 (95% CI 1.65, 4.90) of a future relapse.



Serial ANCA measurements subject of controversy (Fussner 2016):

- The utility of ANCA testing has been widely accepted, but the clinical utility of ANCA as a biomarker of disease activity and predictor of relapses has remained a controversy:
- Published data on serial ANCA testing is heterogeneous with multiple variables possibly affecting the interpretation:
- Types of ANCA, the assays used, time intervals between measurements, definitions of rises in ANCA titres, inclusion of subgroups of patients with different disease manifestations and treatment chosen to induce or maintain remission.

Subgroup analysis (Kemna 2015):

Entire cohort, (hazard ratio HR 5.84; 95% CI, 3.44 to 9.92; P<0.001)

Rise is strongly related to a relapse in patients with renal involvement (HR, 11.09; 95% CI, 5.01 to 24.55; P<0.001)

Rise is only weakly associated with a relapse in patients with non-renal disease (HR, 2.79; 95% CI, 1.30 to 5.98; P=0.01).

The area up to a hazard ratio of 1 marks the border of significance.

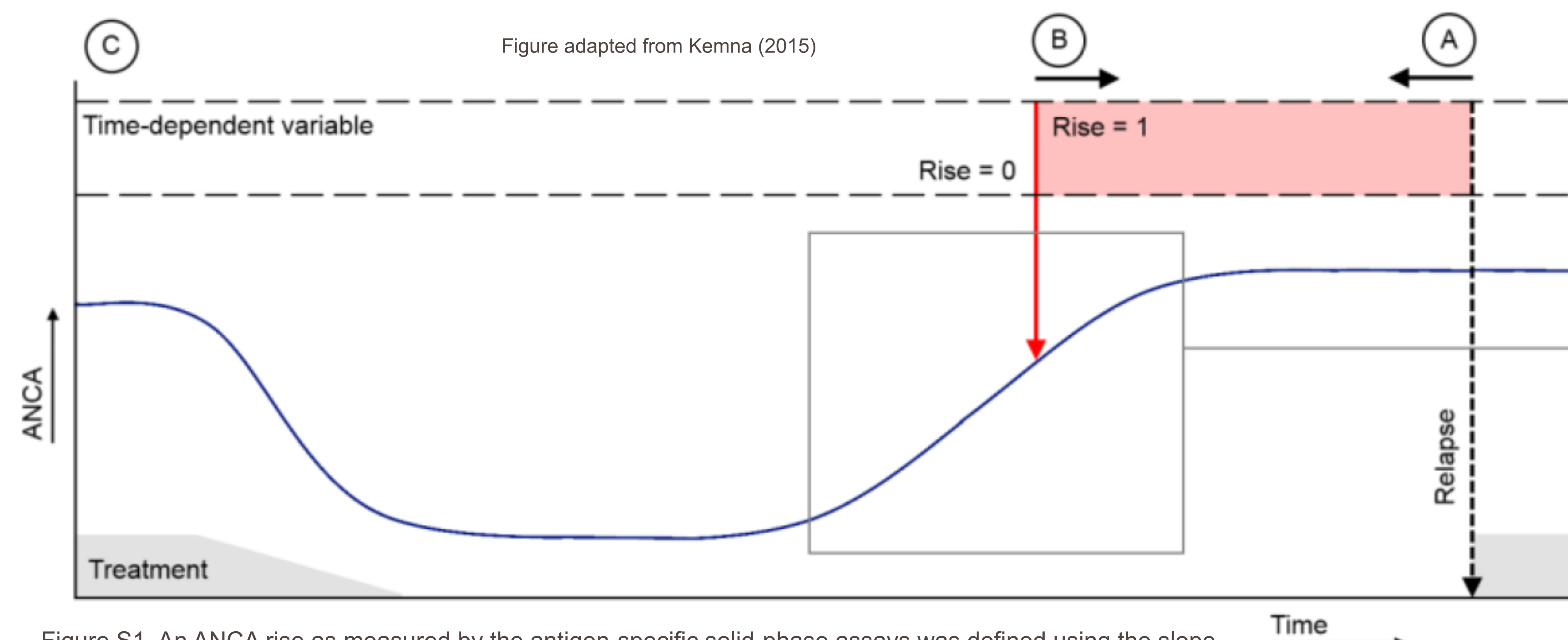
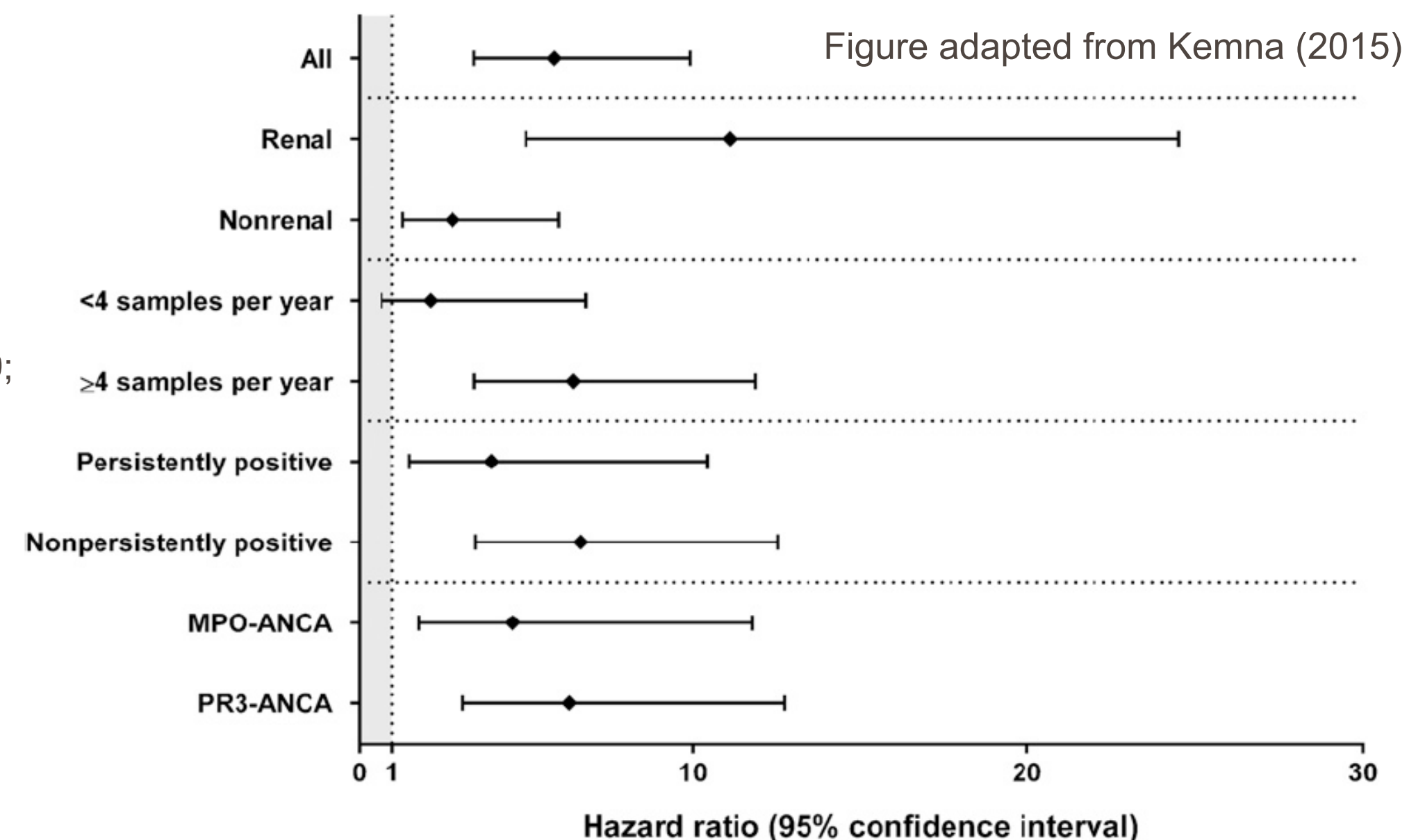


Figure S1. An ANCA rise as measured by the antigen-specific solid-phase assays was defined using the slope, but had to additionally constitute to a relative increase of at least 25%. Figure adapted from Kemna 2015.

Conclusion

- Although measuring ANCA to predict disease activity remains controversial, this case series demonstrates association between ANCA titers and severity of renal disease. ANCA titers may provide prognostic value that can be useful when discussing therapy options with the renal patient
- Understanding the pathophysiology of disease activity and remission to help define better biomarkers to positively affect adverse events and patient outcomes.

References

• Tomasson G, et al. Value of ANCA measurements during remission to predict a relapse of ANCA-associated vasculitis—a meta-analysis. *Rheumatology* 2012;51:100-109.
 • Salama AD. Relapse in Anti-Neutrophil Cytoplasm Antibody (ANCA)-Associated Vasculitis. *Kidney Int Rep* (2020) 5, 7–12.
 • Kemna MJ, et al. ANCA as a Predictor of Relapse: Useful in Patients with Renal Involvement But Not in Patients with Nonrenal Disease. *J Am Soc Nephrol* 26: 537–542, 2015.
 • Fussner LA, et al. Factors Determining the Clinical Utility of Serial Measurements of Antineutrophil Cytoplasmic Antibodies Targeting Proteinase 3. *Arthritis and Rheumatology*. Vol. 68, No. 7, July 2016, pp 1700–1710