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RENAL DAMAGE IN ANCA-ASSOCIATED VASCULITIS IN INCIDENT AND RELAPSING PATIENTS - PATTERNS AND PROGRESSION USING REAL WORLD DATA

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ANCA-ASSOCIATED VASCULITIS – RENAL DISEASE IS COMMON AND ASSOCIATED WITH POOR CLINICAL OUTCOME

- ANCA-associated vasculitis is systemic small vessel disease in which renal disease is common
- Renal disease is a clinical challenge in both granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) – the hallmark renal lesion being a destructive pauci-immune necrotizing and crescentic glomerulonephritis
- Although clinical outcomes have improved, ANCA associated vasculitis leads to ESRD in approximately 25% of patients over 3 -4 years from diagnosis (1)
- Renal disease in ANCA-associated vasculitis could be the result of;
  - Active vasculitis with incident disease
  - Renal relapse
  - Progressive CKD without active vasculitis
- Early and sustained remission from vasculitis should be important in renal protection

(1) Lionaki et al Kidney Internation (2009) 76, 644-51

DELAY TO DIAGNOSIS AND TREATMENT HAS ADVERSE IMPACT ON RENAL OUTCOMES

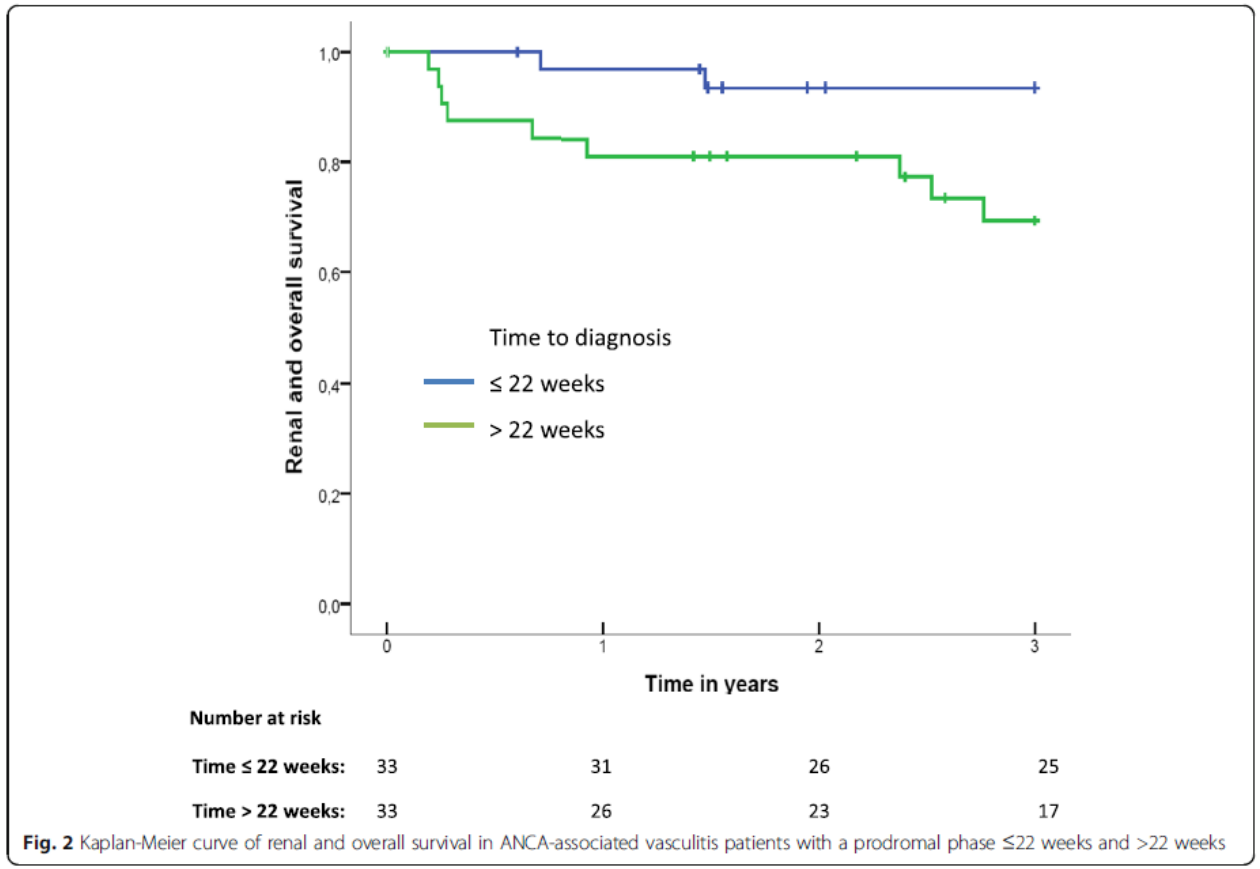


Fig. 2 Kaplan-Meier curve of renal and overall survival in ANCA-associated vasculitis patients with a prodromal phase ≤22 weeks and >22 weeks

Houben et al BMC Nephrology 2017; 18: 378

AIM OF THE STUDY

This study aimed to examine the patterns of renal disease and its progression in new and relapsing ANCA associated vasculitis patients in routine clinical practice in Europe.

METHODS

- Retrospective observational study involving 399 physicians (240 nephrologists, 120 rheumatologists and 20 internal medicine physicians (France, Germany, Italy and UK)
- Physician completed up to 3 online case report forms for ANCA associated vasculitis adult patients under their care. Patients had to fulfill the following criteria
  - Initiated on treatment for new or relapsing disease presenting between Nov 2014 and Feb 2017
  - Had at least 6 months of therapy including remission induction therapy
  - Under continuous care for 12 months

- Data was collected at baseline, 1 month, 3 months, 6 months and 12 months following the start of remission induction therapy

METHODS

Strengths

- 1100 patients
- Multi-centre and 4 countries
- Real world experience
- Contemporary cohort reflecting current guideline practice

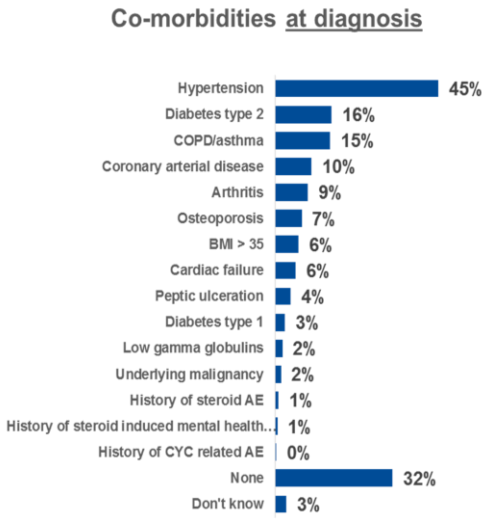
Weaknesses

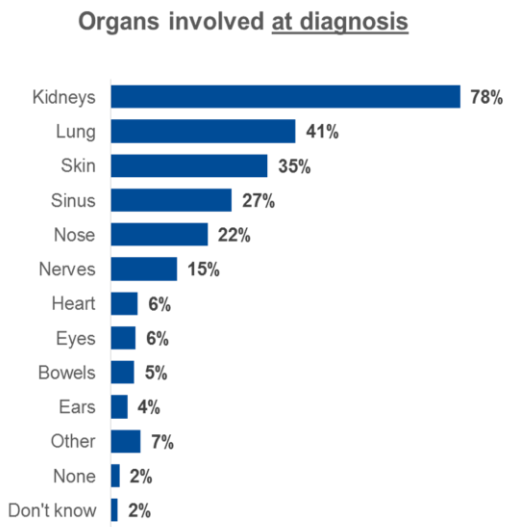
- Selection bias
- No monitoring of data quality

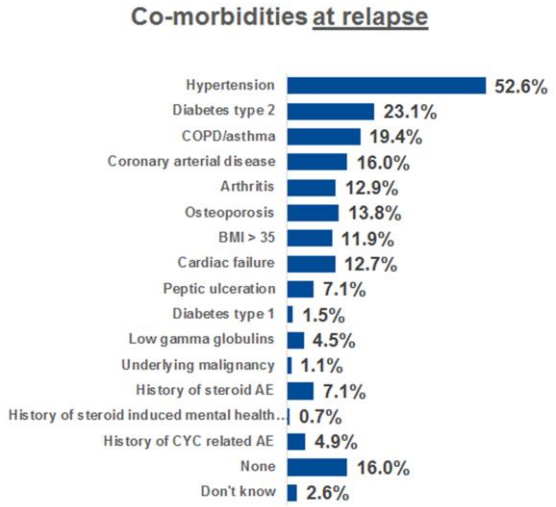
REAL WORLD SAMPLE IS REPRESENTATIVE WITH MOST PATIENTS HAVING MORE SEVERE DISEASE AND SYMPTOM DURATION OFTEN LONG BEFORE DIAGNOSIS

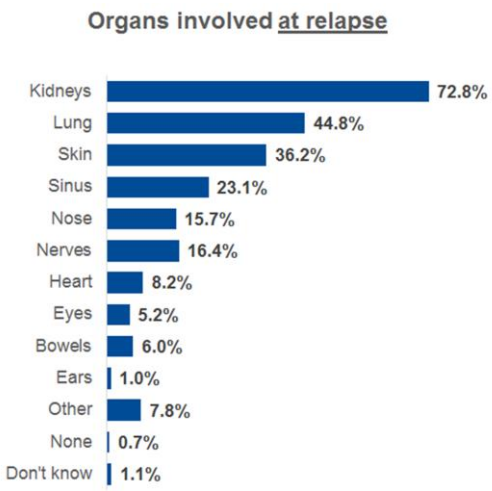
	Variable	Newly Diagnosed (N=929, 77.6%)	Relapse (N=268, 22.4%)
Age	Mean	56.8 ± 14.2	58.3 ± 13.1
Sex	Male (%)	53.7	60.1
Type of ANCA-associated vasculitis	MPA	45.6	45.9
	GPA	54.4	54.1
Antibody Status	MPO +	40.6	46.3
	PR3+	48.3	54.1
Disease severity level at diagnosis (BVAS reported in under 15%)	Mild	12.2	9.3
	Moderate	54.3	62.7
	Severe	33.6	28.0
Duration of symptoms prior to diagnosis	1-4 weeks	37.9	30.2
	5-8 weeks	24.4	15.7
	9-12 weeks	11.2	13.1
	>12 weeks	10.4	19.8
	Don’t know	10.7	21.3

RENAL INVOLVEMENT IS VERY COMMON AND MOST PATIENTS HAVE COMORBIDITY INCLUDING RISK FACTORS FOR CKD

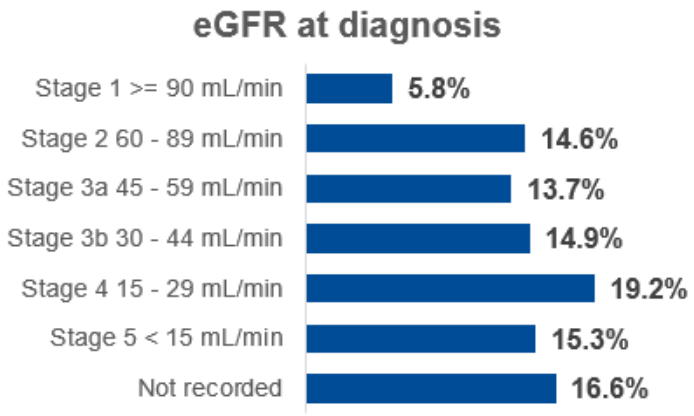


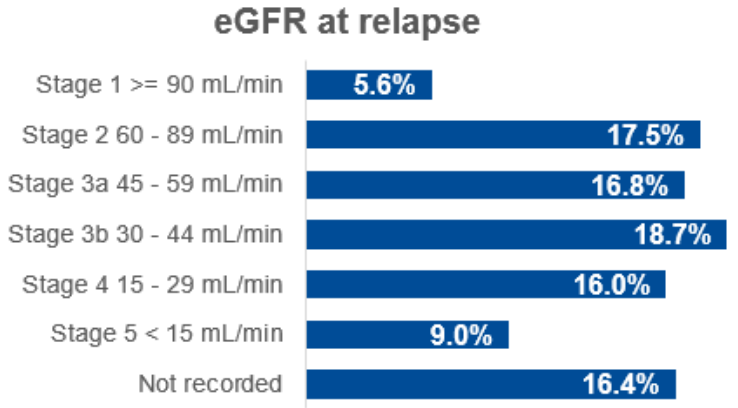


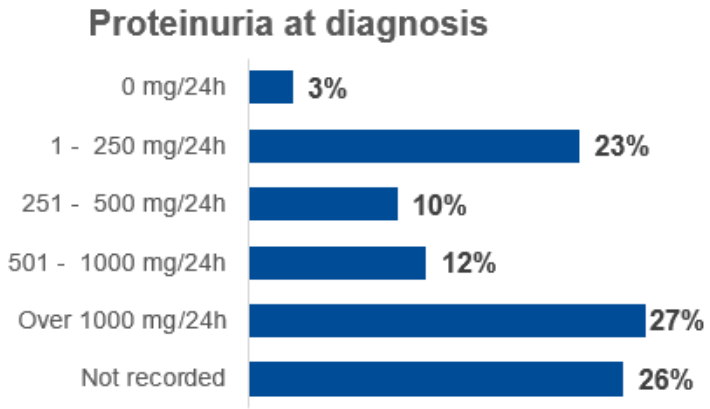


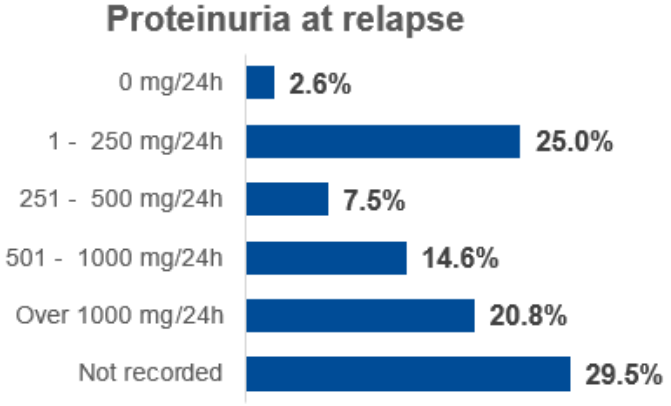


MANY INCIDENT AND RELAPSING PATIENTS HAVE LOW EGFR AND SIGNIFICANT PROTEINURIA







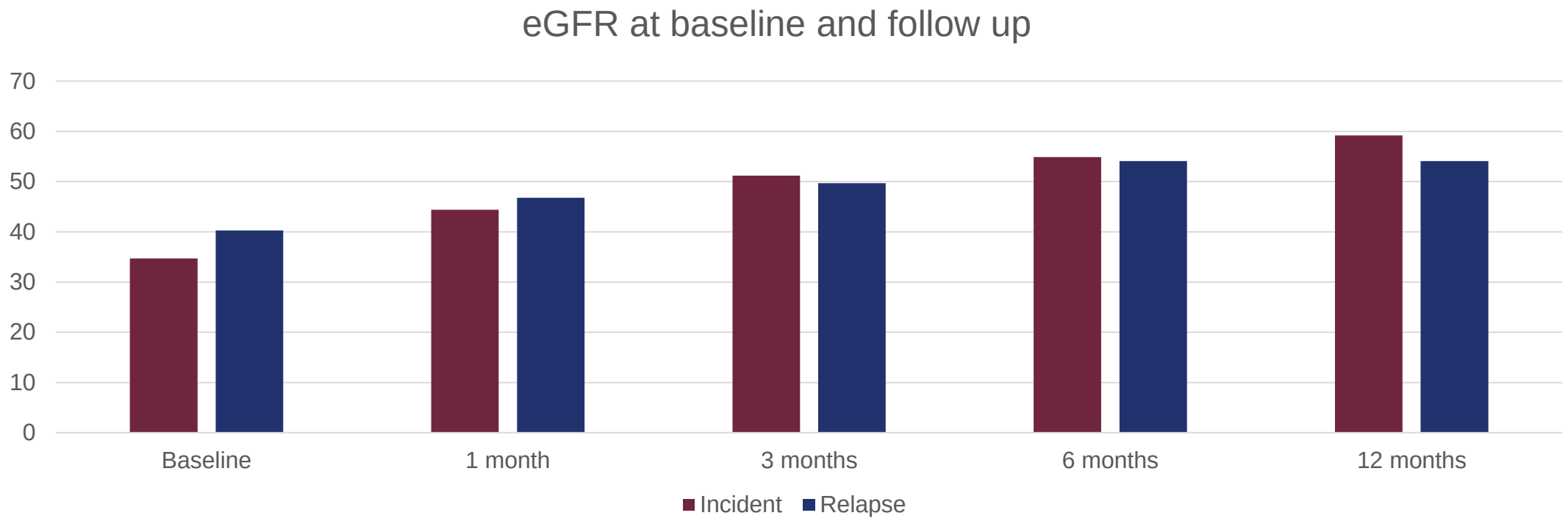


RENAL DAMAGE IS A PARTICULAR PROBLEM IN INCIDENT AND MORE SEVERE PATIENTS. TREATMENT VARIES AND PLASMA EXCHANGE IS OFTEN USED

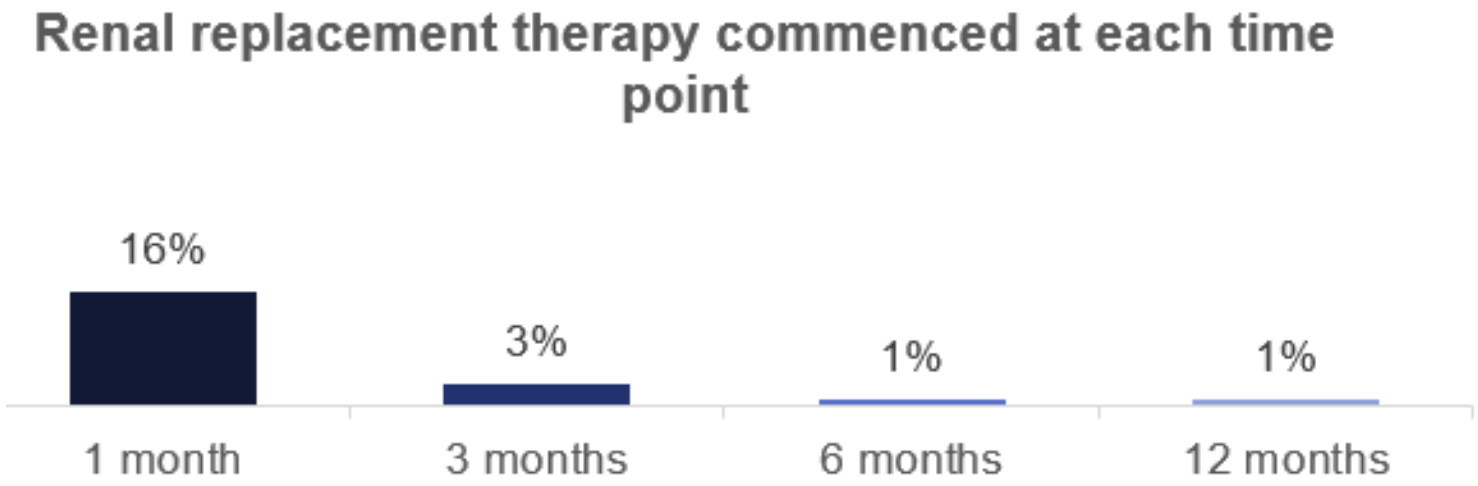
- Incident patients had more severe renal damage
  - Median eGFR – 34.7 vs 40.3 ml/min
  - Median urinary protein – 715.4 vs 545 mg/24 hours
- More severe vasculitis associated with more severe renal damage
  - Microscopic haematuria – 77% vs 29%
  - Median eGFR – 25.9 vs 71.4 ml/min
  - Median urinary protein – 1489.0 vs 348.3 mg/24 hours
- Renal biopsy was performed in 63.9% of incident patients
- Plasma exchange was used frequently – 23.4% incident and 16% relapsing

Medication	Incident	Relapse
Cyclophosphamide	59.2%	35.1%
Rituximab	24.4%	44.0%
Glucocorticoids	82.6%	76.5%
Azathioprine	6.50%	6.7%
Mycophenolate Mofetil	3.10%	7.5%
Methotrexate	6.40%	8.6%
Other	1.9%	0.7%

EGFR IMPROVES DURING REMISSION INDUCTION THERAPY – THE FIRST 3 MONTHS ARE IMPORTANT



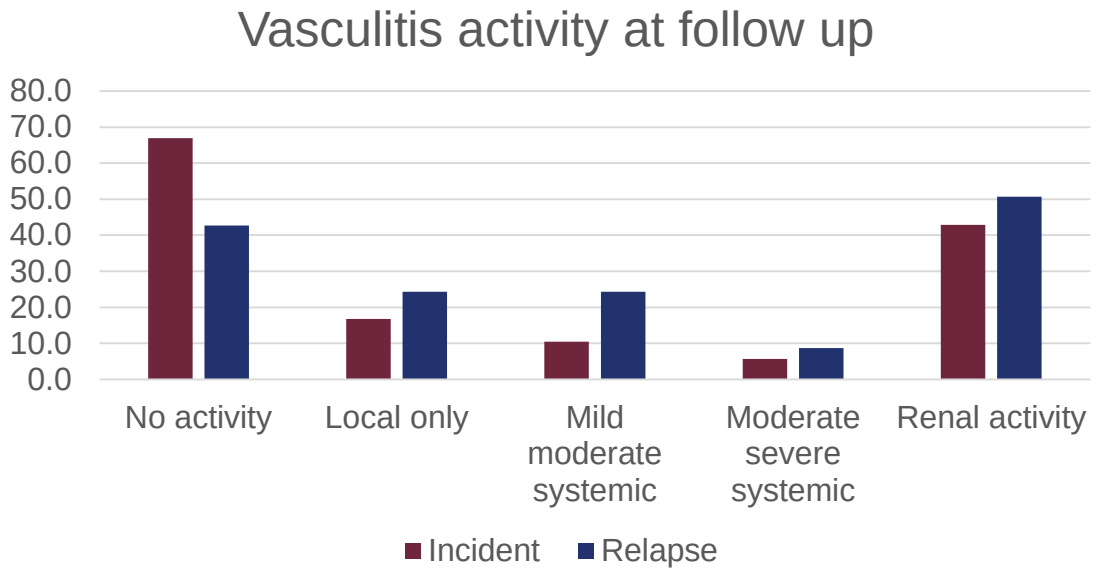
A SIGNIFICANT MINORITY OF PATIENTS REQUIRE RENAL REPLACEMENT THERAPY – INITIAL THERAPY COULD BE IMPROVED

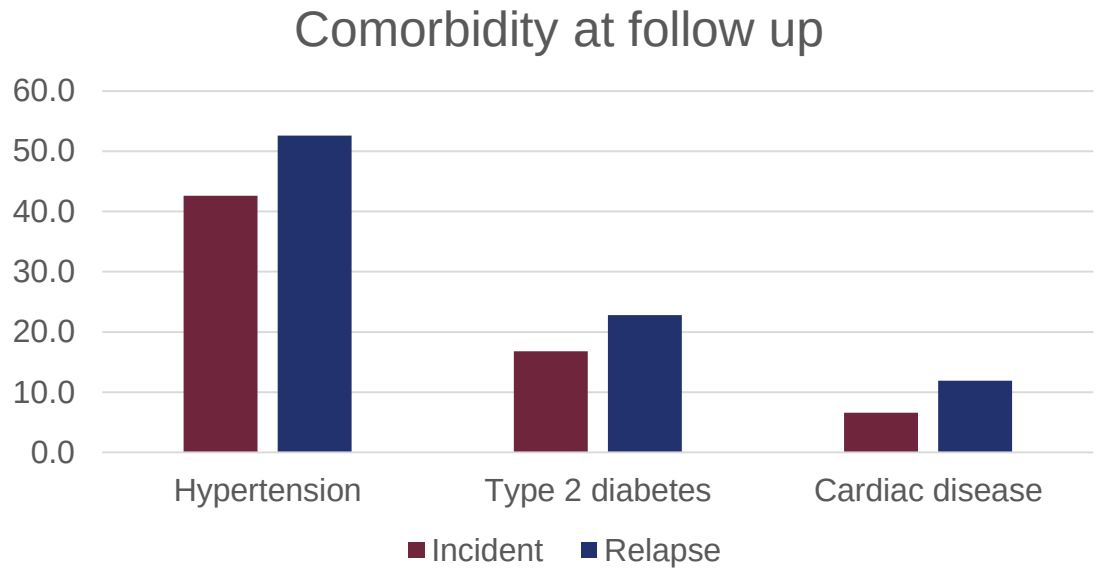


RENAL DAMAGE AND RISK WERE COMMON AT LAST PATIENT FOLLOW UP

Last patient follow up – 17.7 months for incident patients and 34.3 for relapsing patients

- Chronic renal replacement therapy – 12.6 % and 13.4%





SUMMARY

- Real world data from Europe has been gathered to show;
  - Renal involvement in ANCA associated vasculitis is common especially in incident patients and those with more severe disease
  - Patients invariably have important comorbidities which are relevant for treatment choices and outcomes

- Over 12 months of remission induction therapy although overall eGFR improves
  - More rapid and sustained improvement is still required
  - A significant minority of patients require renal replacement therapy in particular at the time of incident disease or relapse
  - Active ongoing renal inflammation as well as need for long term replacement therapy are longer term risks and unmet needs

RENAL DISEASE IN ANCA ASSOCIATED VASCULITIS - A CHALLENGING COMBINATION OF ACTIVE DISEASE, CUMULATIVE DAMAGE AND INCREASED RISK