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1. Introduction and Aim

Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) are a group of multisystem autoimmune conditions characterised by ANCA positive serology and small vessel inflammation.

Disease subcategories include Granulomatosis with polyangiitis (GPA), Microscopic polyangiitis (MPA), Eosinophilic granulomatosis with polyangiitis (EGPA) and renal limited ANCA vasculitis (RLV) [1]. Renal involvement occurs in more than 50% of GPA and 80% of MPA patients and often presents as RPGN [2-4]. ESRD is reported to occur in 20-40% of cases[5,6].

Renal transplantation remains the best renal replacement option for eligible patients with AAV and ESRD. The reported patient and graft outcomes following renal transplantation in AAV have been comparable to those with other primary renal diseases [5-7]. Most of this evidence came from case series studies and subsequently larger multicentre retrospective studies and registry data [7-9].

In this series, we present outcomes of patients with AAV who received a kidney transplant across the East of Scotland, followed by a literature review and a pooled analysis.

2. Materials and Methods

All patients who developed ESRD secondary to AAV and received at least one kidney transplant from June 1987 till July 2014 were included in this series. All patients were transplanted at the Royal Infirmary of Edinburgh (RIE) which is the sole kidney transplant centre for the east of Scotland and Inverness.

Patients included in this series were identified using the following search criteria for a primary renal diagnosis prior to transplantation:

- Positive ANCA assay with a positive MPO or PR3 titre together with a
- Kidney biopsy confirming the presence of pauciimmune glomerulonephritis

Renal relapse was considered in the presence of transplant dysfunction associated with an allograft biopsy showing necrotising glomerulonephritis.

Literature search was done using terms 'renal transplantation' and 'ANCA vasculitis' in the following medical databases: Medline, PubMed, Embase and Scopus.

3A. Results of our series

Table 1. Baseline characteristics of patients pre-transplant

Characteristic	n
Total number of patients	24
Total number of transplants	31
Female gender (%)	15 (62.5)
White European ethnicity (%)	24 (100)
ANCA+ at diagnosis (%)	24 (100)
PR3+ (%)	17 (71)
MPO+ (%)	7 (29)
Organ involvement at diagnosis:	
Kidney (%)	24 (100)
Lung (%)	10 (48)
ENT (%)	8 (38)
Joints (%)	8 (38)
Skin (%)	6 (29)
Eyes (%)	5 (24)
Neurology (%)	2 (10)
Induction treatment of vasculitis:	
Cyclophosphamide (%)	17/18 (94)
PEX (%)	7/18 (39)
Rituximab (%)	1/18 (5)
n/a	6
Maintenance therapy of vasculitis:	
Azathioprine (%)	16/18 (88)
Mycophenolic acid (%)	3/18 (16)
Methotrexate (%)	3/18 (16)
n/a	6
Relapse rate /patient years	0.12

Table 2. Patient characteristics and outcomes post-transplant

Characteristic / Outcome	n
Median age at transplantation; years (range)	51.5 (26-74)
Median time on transplant list; months (range) ^a	32 (3-96)
Cadaveric (%)	23 (74)
Live related (%)	8 (26)
ANCA+ at transplantation (%)	5 (24)
ANCA- at transplantation (%)	14 (67)
Equivocal (%)	2 (10)
ANCA status n/a	3
Basiliximab induction (%)	17 (55)
No induction (%)	11 (35)
Induction data n/a	3
Tacro/MMF/Pred (%)	20 (65)
Tacro/AZA/Pred (%)	5 (16)
Cyclo/AZA/Pred (%)	4 (13)
Maintenance data n/a	2
HAR (%)	1 (3.2)
TCMR (%)	12 (39)
ABMR (%)	2 (6)
Malignancy	1
Median creat at 1 year; μmol/l (range)	145 (74-257)
Median eGFR at 1 year; ml/min/1.73m ² (range)	44 (25-93)
Median creat at 5 years; μmol/l (range)	135 (99-247)
Median eGFR at 5 years; ml/min/1.73m ² (range)	45.3 (24-69)
Allograft survival at 1 year	93%
Allograft survival at 5 years ^b	56%
Patient survival at 1 year	92%
Patient survival at 5 years	87%

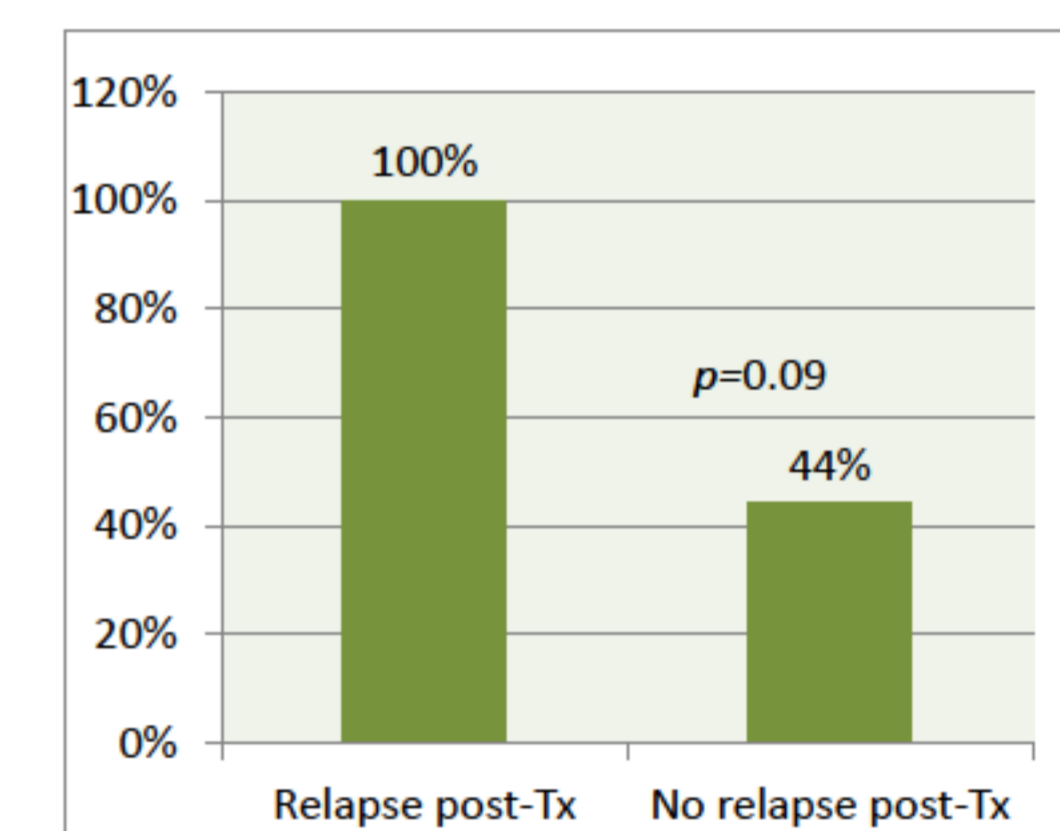
^aone patient had pre-emptive transplant
^bfour of the failing grafts belonged to one patient

Table 3. Characteristics of patients developing AAV relapse post-transplant

Characteristic / Outcome	n
Total ANCA-SVV relapse ^a (%)	4 (18.2)
Basiliximab induction	2
No induction	2
Graft rejection episodes	0
Relapse pre-transplant	4
Multi-organ involvement pre-transplant	4
ANCA sero-conversion	1
Time to relapse range (weeks)	7-780
Relapse rate /patient year	0.004
Renal + extra-renal relapse ^b	2 (9.1)
Extra-renal relapse only ^b	2 (9.1)

^adata available for 22 patients.
^bextra-renal relapse featured pulmonary and ENT involvement.

Figure 1. Comparison of pre-transplant relapse rates in patients developing and not developing AAV relapse post-transplant



3B. Results of pooled analysis

Table 4. Pooled analysis showing respective graft and patient survival in AAV

Study	Number of patients	AAV type: GPA/MPA	Graft survival	Patient Survival
Kuroos et al. 1981	9	9/0	100% at 47 mo	100% at 47 mo
Schmitt et al. 1993	20	20/0	95% at 48 mo	95% at 48 mo
Stegeman et al. 1994	9	2/3	100%	100%
Grotz et al. 1995	4	3/1	100% at 39 mo	100% at 39 mo
Frasaca et al. 1996	3	0/3	100%	100%
Nyberg et al. 1997 ^a	17	4/13	n/a	n/a
Roasting et al. 1997	8	3/5	87.5%	87.5%
Haubitz et al. 1997	18	15/3	65% (72-83%) at 10 yr	80% (71-85%) at 10 yrs
Allen et al. 1998	24	n/a	69% (70%) at 5 yr	85% (80%) at 5 yr
Nachman et al. 1999 UNC	15	3/11	71.5%	100%
Nachman et al. 1999 Lund	13	4/7	91%	63.4%
Briggs et al. 1999	227	115/112	MPA: 60%(69%) GPA: 70%(69%) at 3 yr	MPA: 77%(91%) GPA: 91%(86%) at 3 yr
Schmitt et al. 2002	378	378/	10 yr 65%	10 yr 80%
Elmedhem et al. 2003	9	5/4	100%	100%
Deegens et al. 2003	33	8/25	60%(56%) at 5 yr	77%(79%) at 5 yr
Moroni et al. 2007	19	10/9	84% (100%) at 10 yr	87% (90%) at 10 yr
Little et al. 2009	107	57/42	70% at 10 yr	65% (67%) ^b at 10 yr
Geetha et al. 2011	85	42/43	79% at 10 yr	67% at 10 yr
Tang et al. 2013	98	47/46	MPA: 50% GPA: 62% (70%) at 10 yr	MPA: 68% GPA: 85% (83%) at 10 yr
Marco et al. 2013	49	5/44	59%(52%) at 10 yr	64%(63%) at 10 yr

^athis study included vasculitis other than AAV
^bcontrol was a national graft survival

Figure 2. Pooled analysis showing respective AAV relapse rates

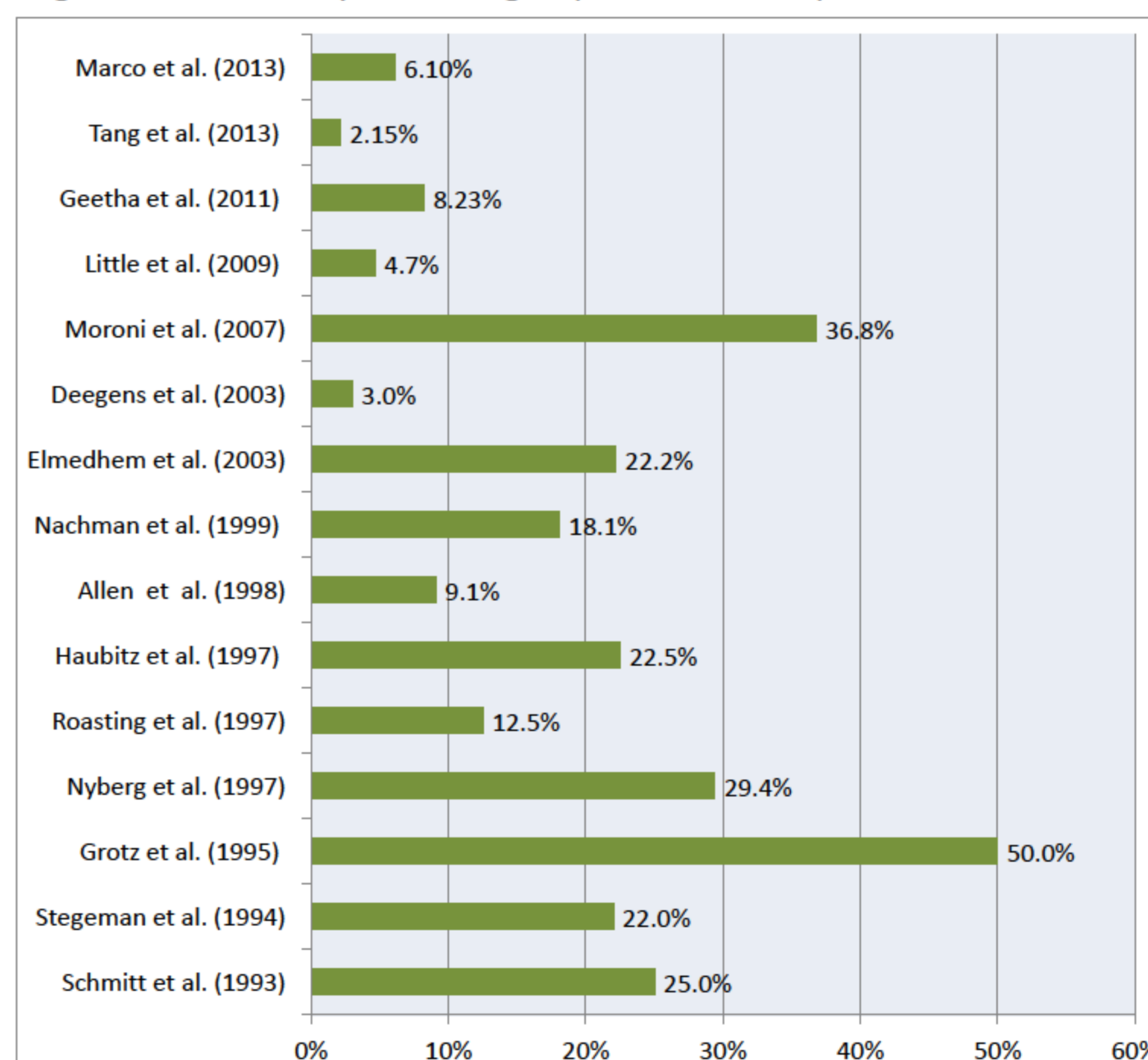


Figure 3. AAV relapse rate in GPA vs. MPA

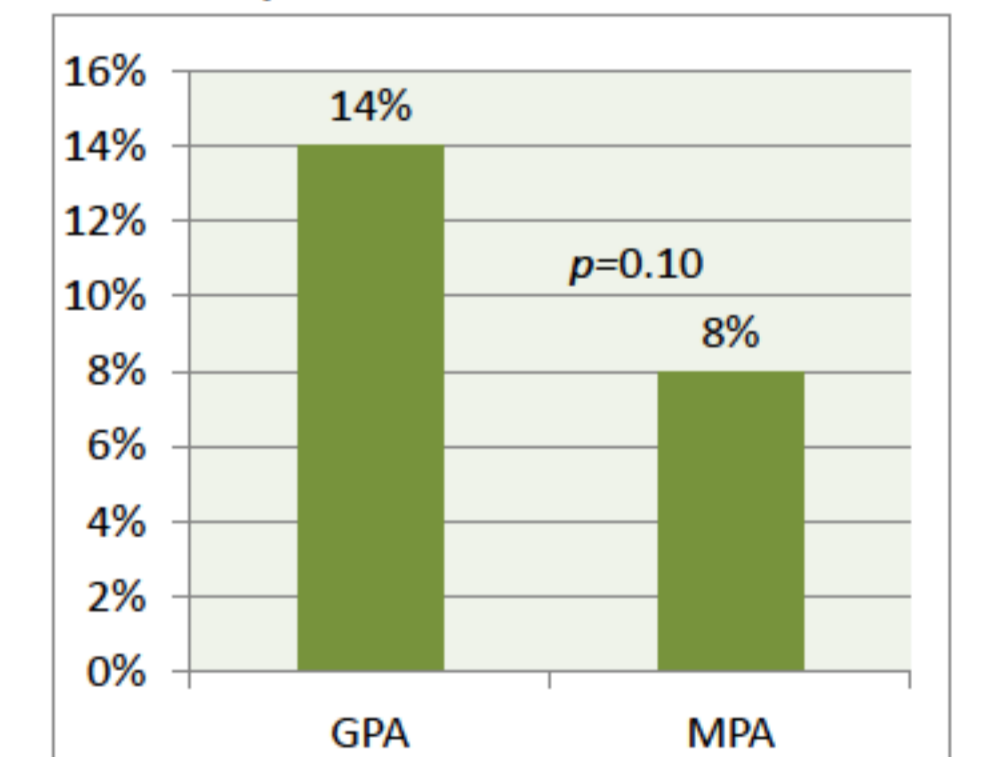
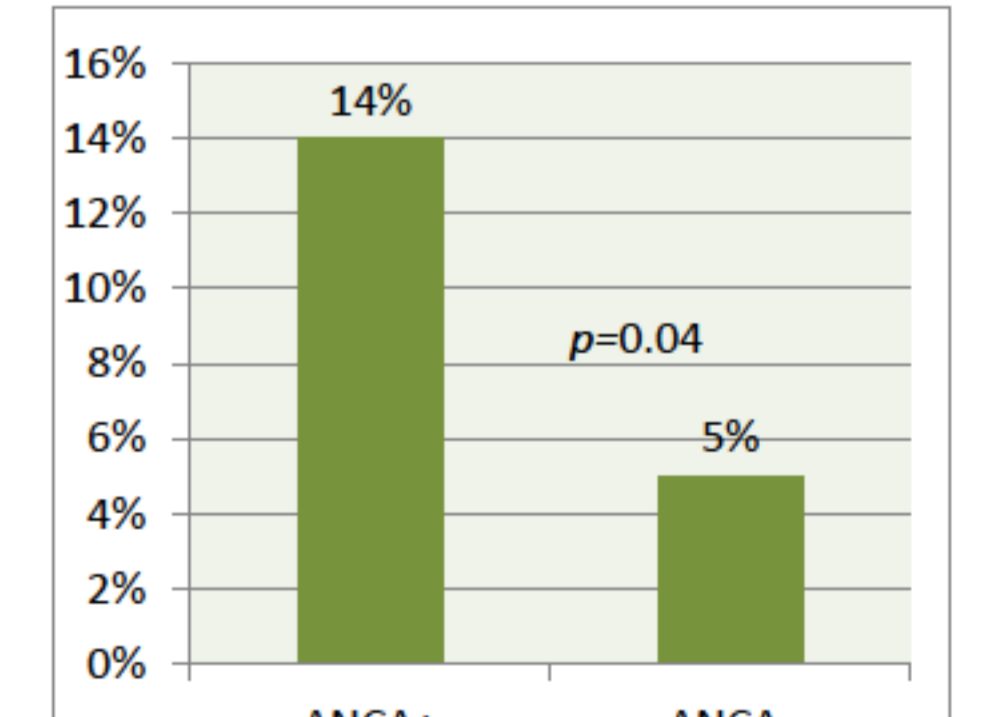


Figure 4. AAV relapse rate in ANCA+ vs. ANCA- at the time of transplant



4. Conclusions

- Our single center experience with renal transplantation in AAV shows that renal transplantation remains a safe option in AAV patients with ESRD.
- Disease relapse post-transplantation is rare and often manifest as extra-renal disease.
- Lower graft survival at 5 years post-transplantation cannot be explained by disease recurrence.
- Multicenter collaboration and large registry data are needed to define predictors of renal outcomes in rare diseases such as AAV.

5. References

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