Clinical Characteristics And Outcomes For Males With PAIS: An I-DSD Registry Study

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Introduction:

Partial Androgen Insensitivity Syndrome (PAIS) due to a mutation in the androgen receptor gene (*AR*) is the single largest cause of DSD in boys and is associated with a variable phenotype. *AR* mutations may be found in almost 30% of boys with XY DSD who have normal androgen synthesis. To date there are limited data on the outcomes for male adolescents with this condition and there is little evidence that identification of *AR* mutation is beneficial for long-term management.

Objectives:

The aims of this study were to determine the outcomes and clinical characteristics for 46,XY males reported as PAIS, using information from the International DSD (I-DSD) Registry.

Methods:

The I-DSD Registry was used to identify all male patients registered as having PAIS. Each of the centres who registered the patients was then contacted to obtain information regarding the clinical characteristics of these patients.

Results:

52 men from 9 centres met the inclusion criteria for this study. Most commonly they presented in the neonatal period (54%). Twenty nine (56%) of the men had an *AR* mutation, with 20 different mutations reported. *AR* –ve men were more likely to present at a younger age (p=0.02). Median external masculinisation score (EMS) at time of diagnosis was 8 (range 2-12). Median EMS at time of most recent presentation was 9 (range 3-12). Twenty two men (42%) received testosterone therapy at some point between first and most recent presentation with variable regimens used. Thirty one (60%) men required at least one surgical procedure, with *AR* +ve men being more likely to require multiple surgeries for hypospadias repair (p=0.004). All *AR* +ve men had gynaecomastia at time of most recent presentation compared to 9% of those who were *AR* –ve (p<0.0001). Six men had such significant gynaecomastia that mastectomy was required. Five (83%) of these men had *AR* mutations.

Conclusions:

Boys with PAIS with an identifiable mutation in *AR* are more likely to have a worse medical and surgical outcome in adulthood. Routine genetic analysis of *AR* in boys with XY DSD will guide prognosis and the need for expert input. The I-DSD Registry is a powerful tool for understanding clinical out[...] are conditions affecting sex development.
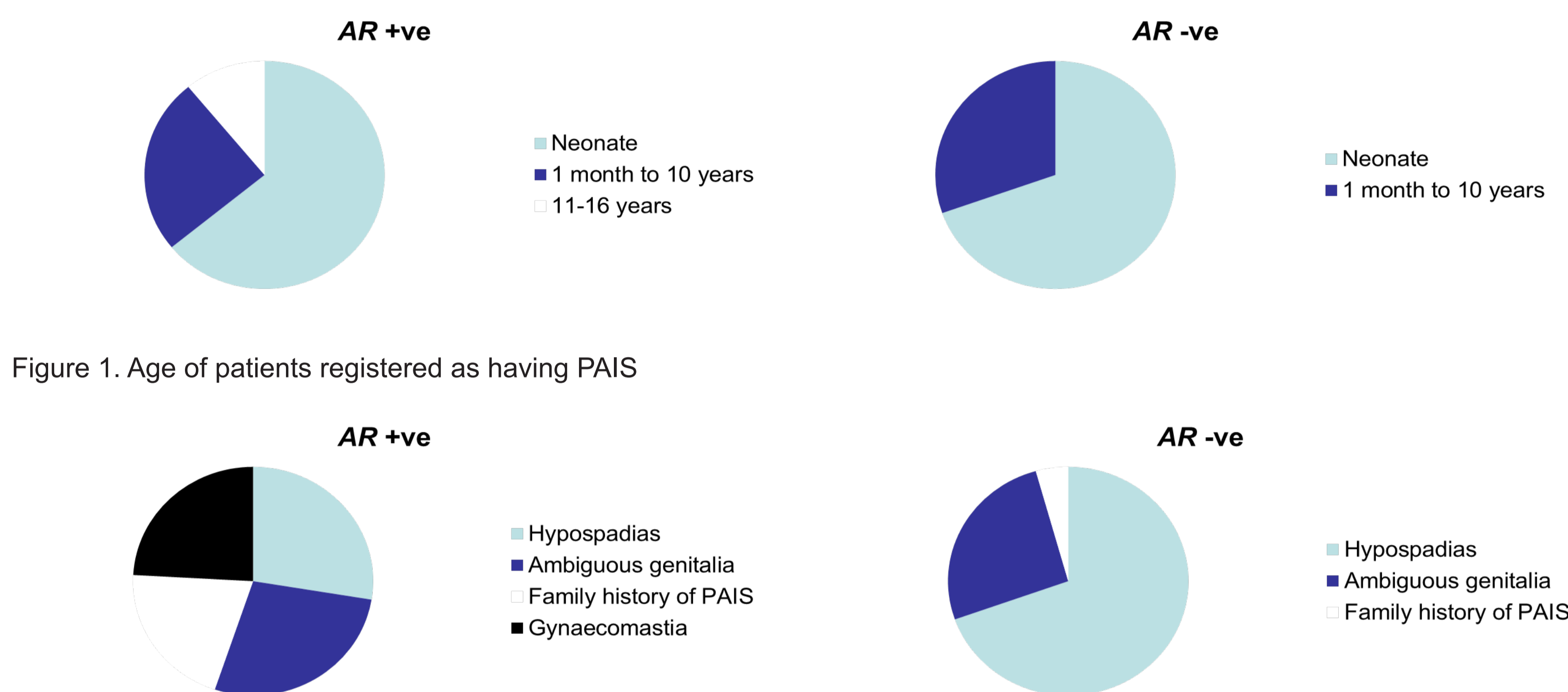

Figure 1. Age of patients registered as having PAIS

Figure 2. Presenting complaint of patients registered as having PAIS

	AR +ve n=29	*AR* –ve n=23	p
Median age at first presentation (range)	3m (0-16 years)	1m (0-10 years)	**0.02***
Median EMS at first presentation (range)	7 (2-12)	6 (2-12)	0.83
Median EMS at last presentation (range)	9 (3-12)	10 (7-12)	0.09
Number of men with hypospadias at first presentation	20 (69%) Proximal 15 (75%) Mid 2 (10%) Distal 1 (5%) Unknown 2 (10%)	20 (87%) Proximal 13 (65%) Mid 0 (0%) Distal 6 (30%) Unknown 1 (5%)	0.19 0.73 0.49 0.09 1.0
Number of men with hypospadias at last presentation	6 (21%)	1 (4%)	0.12
Number of men with 1 undescended testis at first presentation	2 (7%)	0 (0%)	0.49
Number of men with 1 undescended testis at last presentation	2 (7%)	0 (0%)	0.49
Number of men with BUDT at first presentation	7 (24%)	11 (48%)	0.09
Number of men with BUDT at last presentation	0 (0%)	0 (0%)	1
Number of men with micropenis at first presentation	13 (45%)	6 (26%)	0.25
Number of men with micropenis at last presentation	5 (17%)	1 (4%)	0.21
Number of men with gynaecomastia at first presentation	7 (24%)	0 (0%)	**0.01***
Number of men with gynaecomastia at last presentation	29 (100%)	2 (9%)	**0.00***
Median LH at first presentation (range) (IU/l)	4.5 (0.04-21.1)	3.3 (0.1-15)	0.27
Median LH at last presentation (range) (IU/l)	10.3 (1.78-57)	4.4 (0.1-27.4)	0.05
Median FSH at first presentation (range) (IU/l)	1.9 (0.1-39.8)	1.7 (0.5-5.2)	0.28
Median FSH at last presentation (range) (IU/l)	4.7 (1.15-89)	4.5 (0.3-27.4)	0.28
Median T at first presentation (range) (µg/l)	8.6 (0.1-60.8)	2.5 (0.1-12)	**0.03***
Median T at last presentation (range) (µg/l)	17.6 (4.6-68.3)	18.9 (0.9-23.4)	0.19

Table 1. Comparison of clinical and biochemical characteristics of *AR* negative and *AR* positive men at time of first presentation. EMS: External Masculinisation Score. T: testosterone. LH: luteinizing hormone. FSH: follicle stimulating hormone. BUDT: bilateral undescended testes.*p<0.05
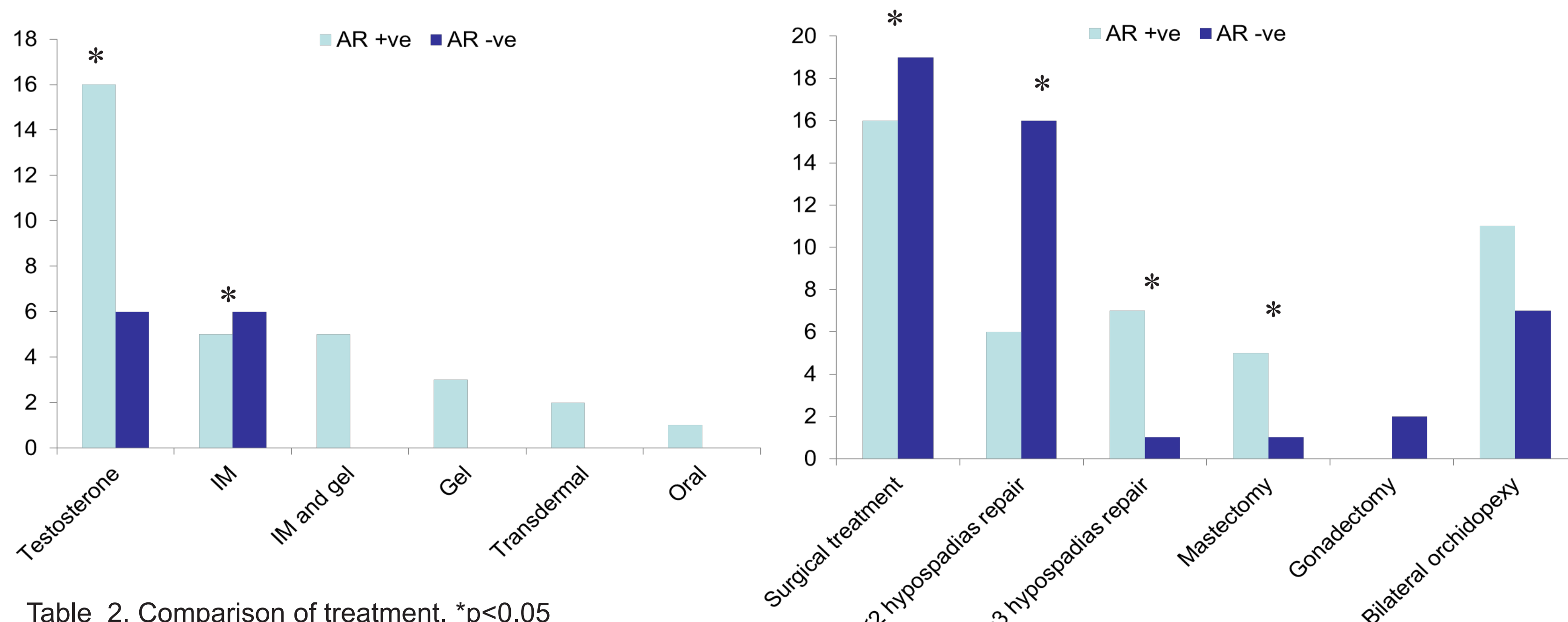

Table 2. Comparison of treatment. *p<0.05

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Sex Differentiation

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