

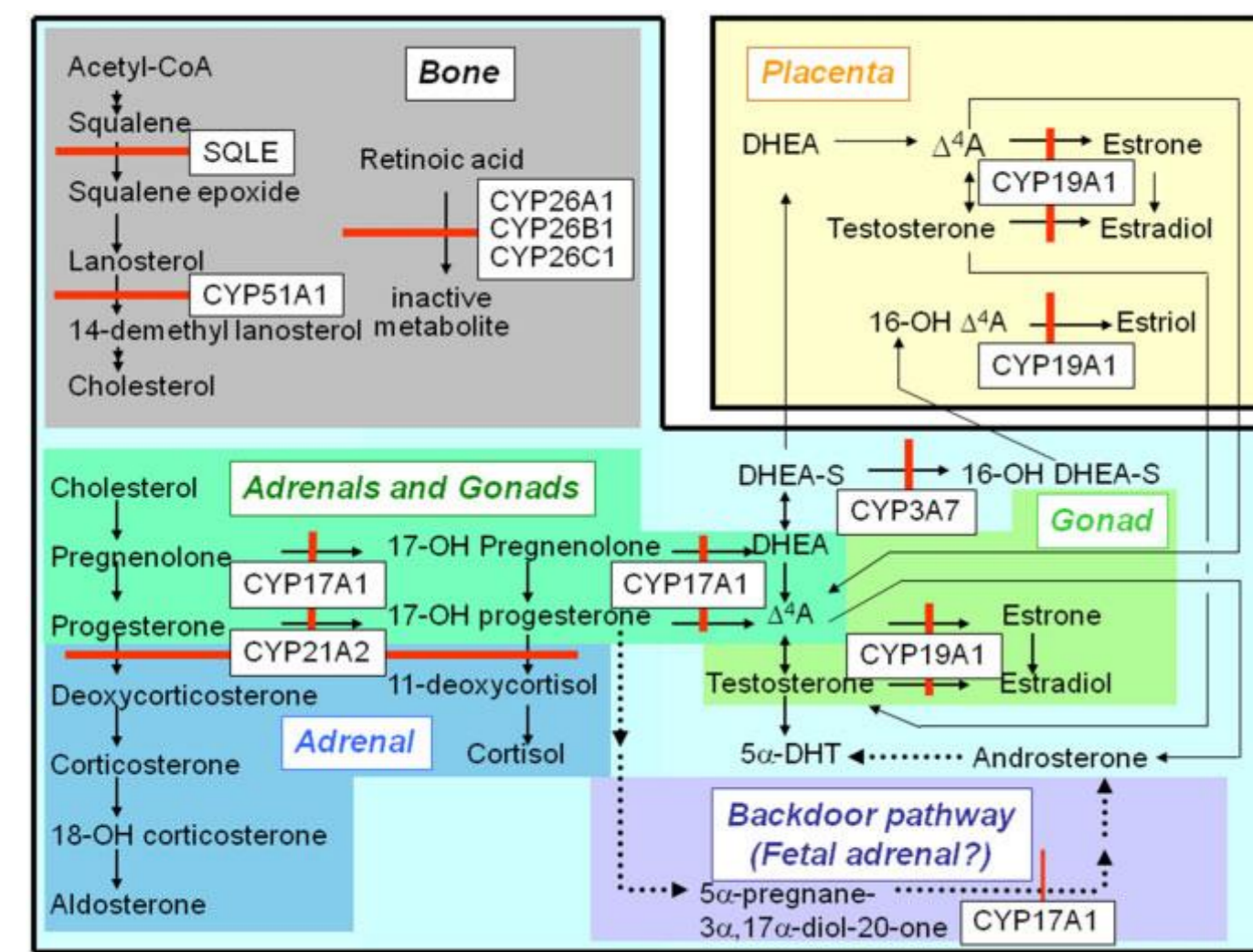
CLINICAL CHARACTERISTICS OF CYTOCHROME P450 OXIDOREDUCTASE DEFICIENCY: A NATIONWIDE SURVEY IN JAPAN

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INTRODUCTION^{1,2}

Cytochrome P450 oxidoreductase deficiency (PORD), which is caused by POR gene variants, shows broad clinical features including skeletal malformations, steroidogenic defects, and disorders of sex development (DSD).



AIM

- Genetic comprehensive analysis of PORD was reported in Japan¹, however, clinical symptoms at diagnosis and the clinical course of PORD have not been reported.
- To reveal clinical symptoms at diagnosis and the clinical course of PORD in Japan.

METHOD³

1st questionnaire in Sep 2018: 65 % response rate

183 of JSPE councilors

Q: Have you examined PORD patients?

A: 119 councilors answered

39 PORD patients were examined at 20 hospitals

2nd questionnaire: 77 % response rate

39 examined PORD patients at 20 hospitals

Q: clinical features at diagnosis and clinical courses

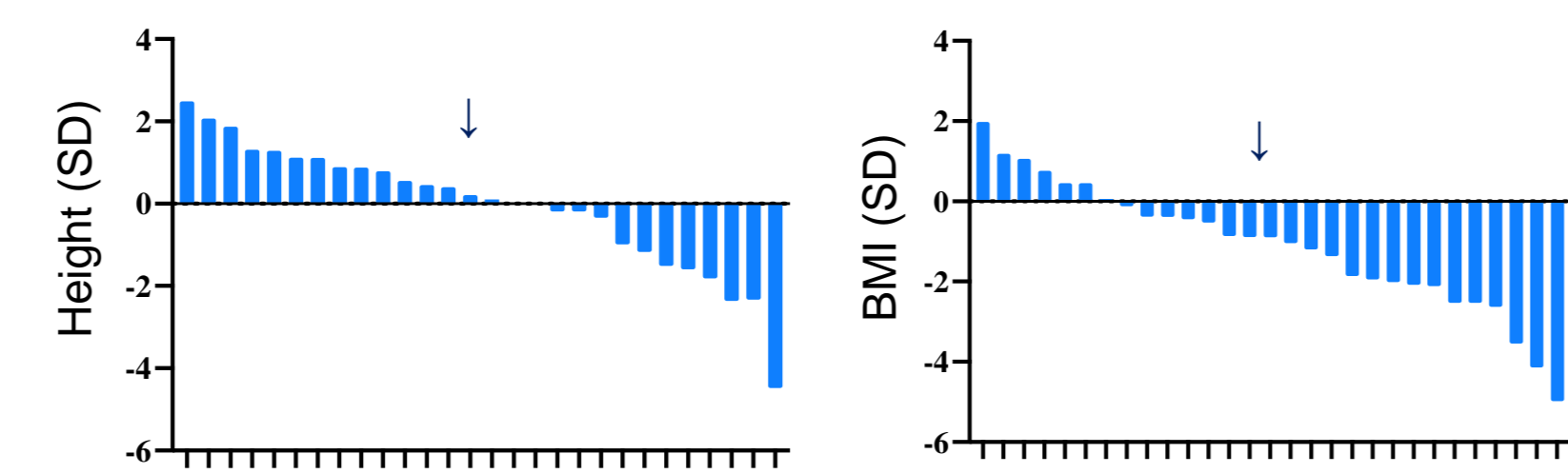
30 examined PORD patients (M:F = 13:17) at 18 hospitals

RESULTS³

1. Age, height and BMI

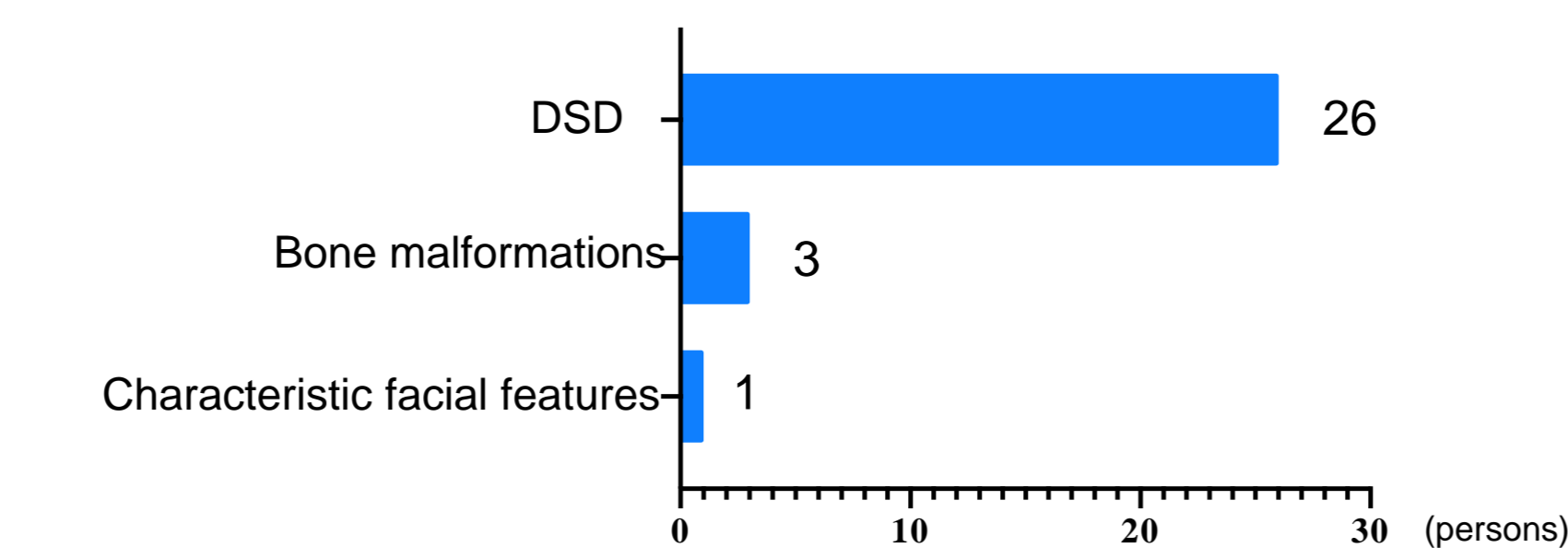
	Age (Y)	Height (SD)	BMI (SD)
At investigation	12.1 (0.7-46.1)	+0.16 (-4.5+2.5)	-0.9 (-5.0+2.0)
At diagnosis	0.21 (0-25)	x	x

mean (min to max)



→ No significantly different in height-SD.
Tendency for leanness.

2. Diagnosis determining symptoms

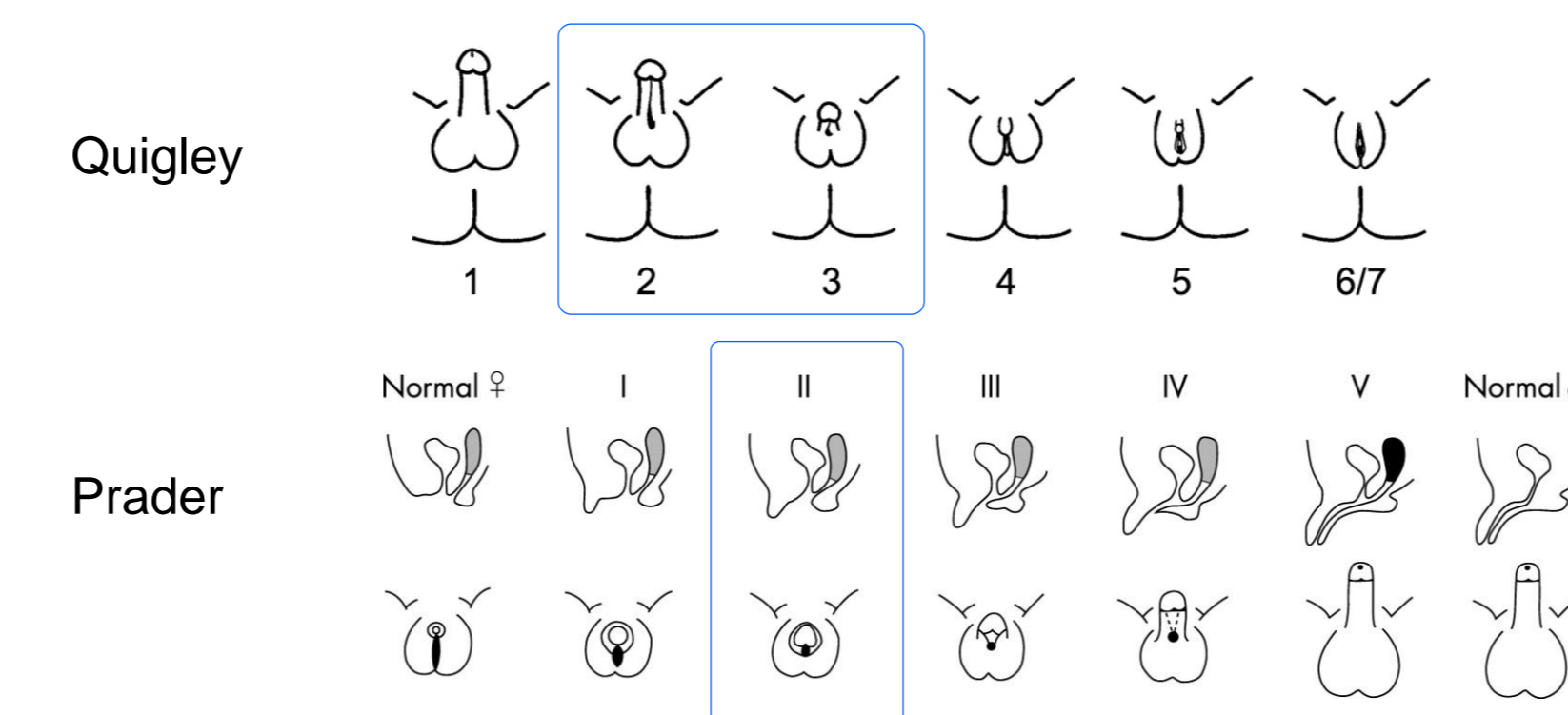


3. Urine steroid profile

20 PORD patients were performed.
All 20 PORD patients were suspected with PORD.

4. External genitalia at diagnosis

External genitalia at diagnosis	median	range
Quigley scale for male	2.5	1-3
Prader scale for female	2	2-5



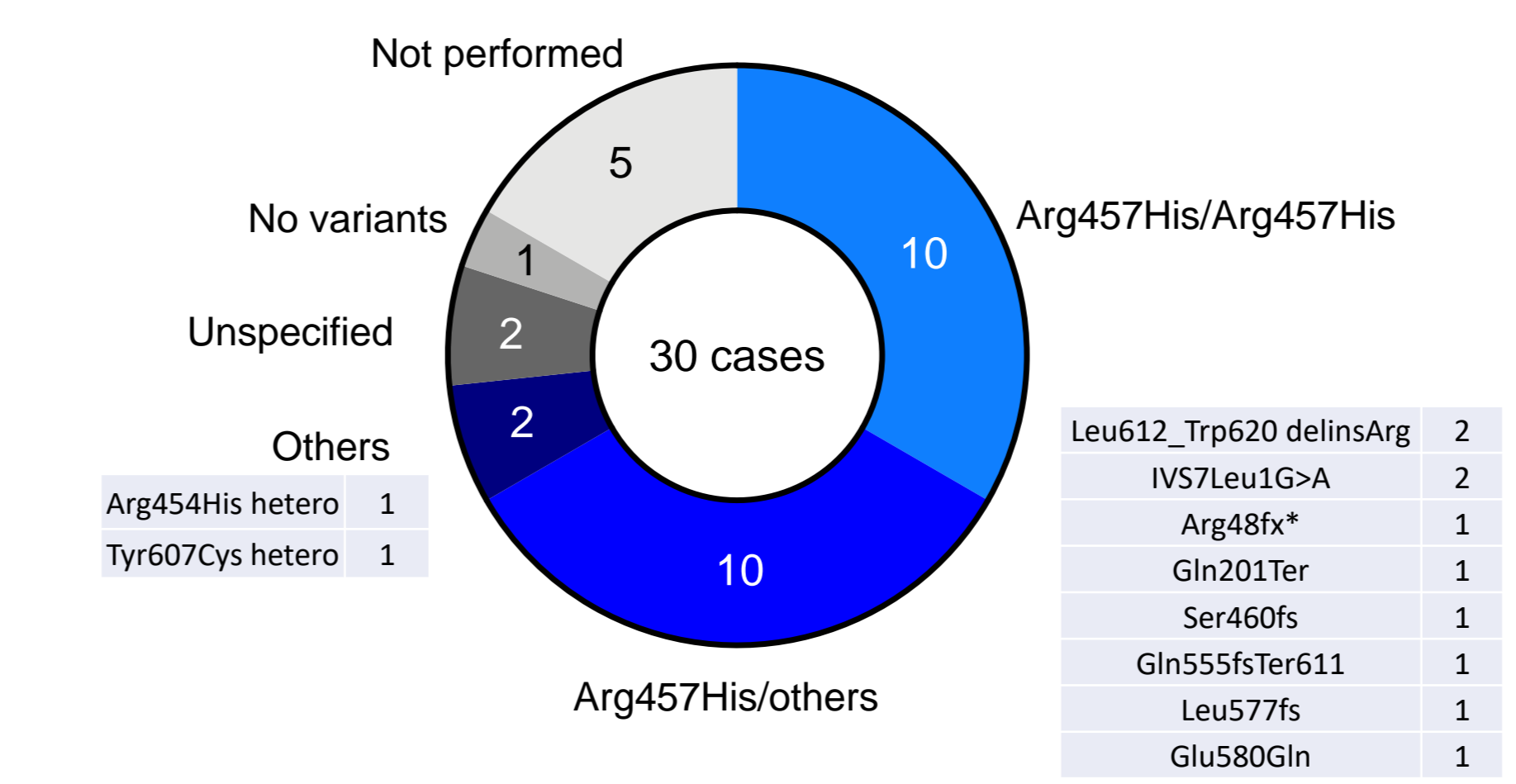
5. Plastic surgery for external genitalia and puberty

	persons	operations	years
Male	13	5 urethroplasty 2 orchiopexy	8.4 ± 7.4 1.1, 5.0
Female	17	9 vaginoplasty 7 clitoroplasty 6 labiaoplasty	3.6 ± 2.7 4.7 ± 4.4 2.4 ± 1.1
After puberty	15		
males	6		
androgen replacement	0		
females	9		
estrogen replacement	7		

External genitalia was more operated and earlier in females than males.

Hormone replacement therapy were more in females than in males after puberty.

6. POR genetic analysis



Japanese cases had many Arg457His variation as previously reported.

1. Fukami M, et al. J Clin Endocrinol Metab. 2009

7. Imaging tests

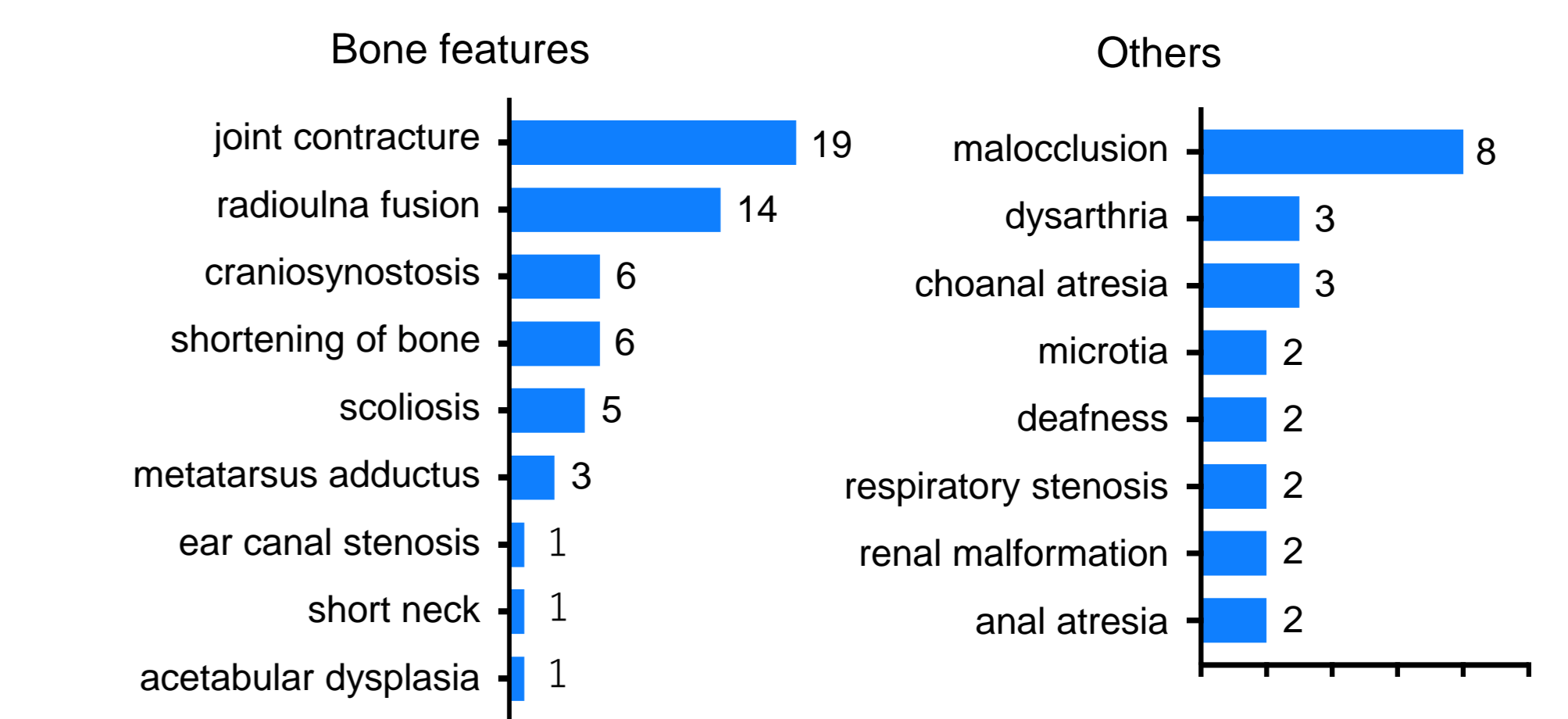
Abdominal ultrasounds 18 cases
median of performed age 0.17 years (0-18.3)

Abdominal MRI 9 cases
median of performed age 0.13 years (0.1-15.0)

8. Development

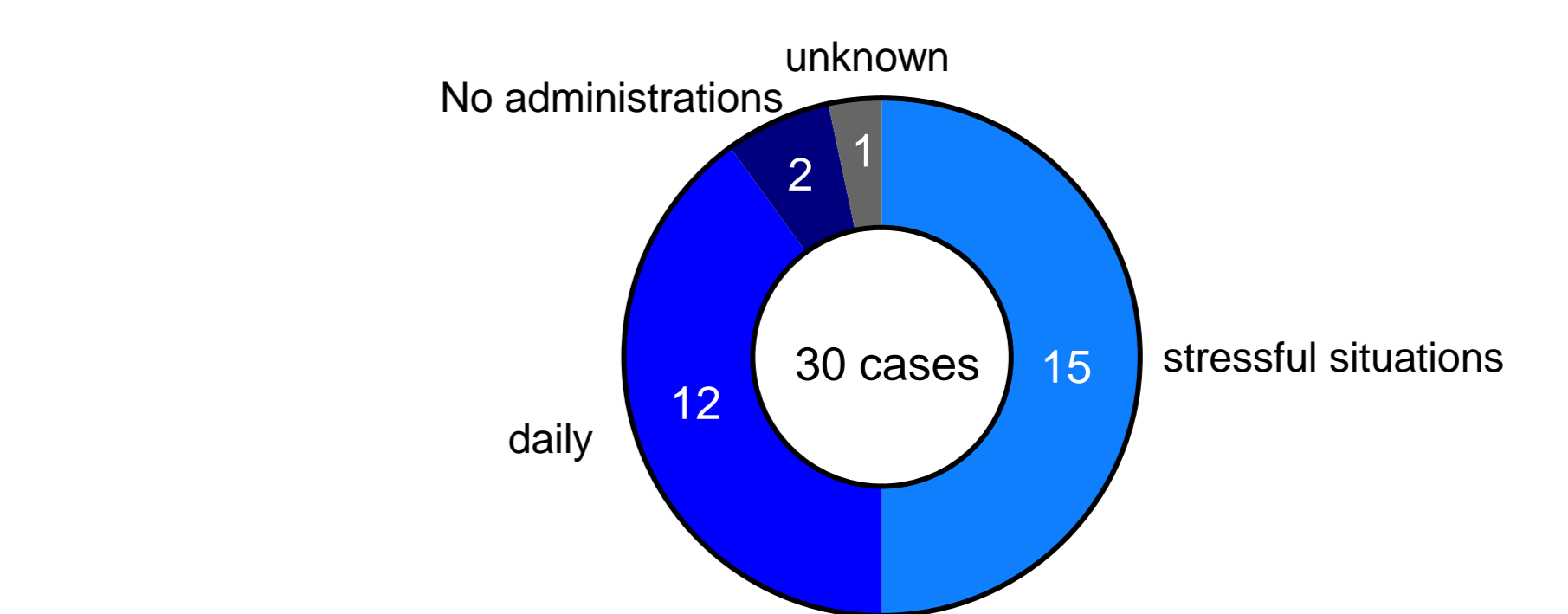
Developmental delay was seen in 5 of 29 patients. The Degree of developmental delay was unknown.

9. Bone features and others



10. Treatments

Hydrocortisone 26 cases
Prednisolone 2 cases



Evaluation of adrenal function is required to accumulate the POR cases.

CONCLUSIONS³

- Urine steroid profile is useful to diagnose PORD.
- Japanese cases had many Arg457His variation as previously reported.
- External genitalia in females may be more severe than in males, and sex hormone replacement in females was the majority in pubertal stage.
- Hydrocortisone was major for steroid therapy.
- Administration methods are controversial as a permanent or only stress.

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