



Ordine dei
Medici Veterinari
della Provincia
dell'Aquila

Malattie virali emergenti e riemergenti dei piccoli animali

L'Aquila, 25 Marzo 2017



Morbillivirus del gatto: un nuovo virus di cui preoccuparsi?

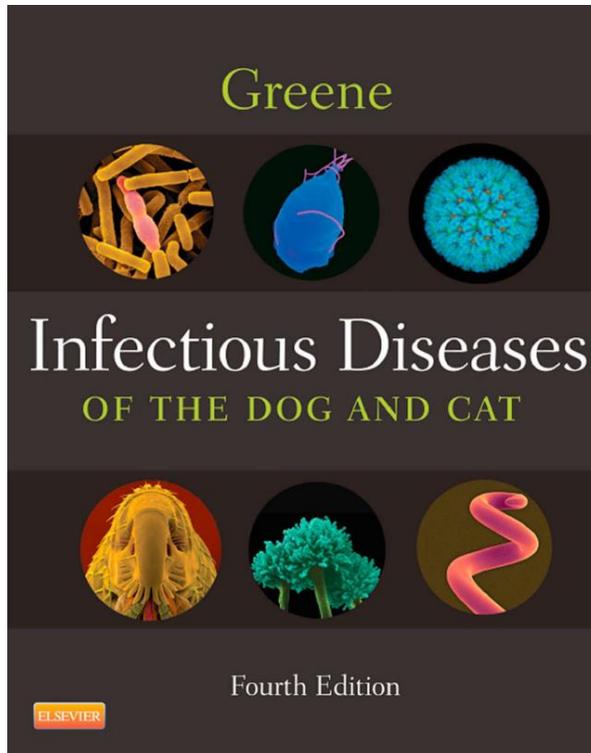
Dalla Clinica al Laboratorio

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OSPEDALE VETERINARIO
UNIVERSITARIO DIDATTICO FACOLTÀ MEDICINA VETERINARIA

Feline Paramyxovirus infections



Viruses of the family Paramyxoviridae (genera *Paramyxovirus*, *Morbillivirus*, and *Henipavirus* [containing *Nipah* and *Hendra* virus]) have been shown to cause infections in the central nervous system (CNS) of domestic and large exotic Felidae, although none of the viruses in this group are known to be primarily feline viruses.

- Virus della malattia di Newcastle (infezione sperimentale gatto)
- agenti Paramyxovirus-like (Tigre siberiana)
- CDV (grandi felidi selvatici – AB nel gatto domestico)
- Virus Hendra e Nipah
- parainfluenza 5 virus ???

Feline morbillivirus, a previously undescribed paramyxovirus associated with tubulointerstitial nephritis in domestic cats

Patrick C. Y. Woo^{a,b,c,d,1}, Susanna K. P. Lau^{a,b,c,d,1}, Beatrice H. L. Wong^b, Rachel Y. Y. Fan^b, Annette Y. P. Wong^b, Anna J. X. Zhang^b, Ying Wu^b, Garnet K. Y. Choi^b, Kenneth S. M. Li^b, Janet Hui^e, Ming Wang^f, Bo-Jian Zheng^{a,b,c,d}, K. H. Chan^b, and Kwok-Yung Yuen^{a,b,c,d,2}

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Edited* by Bernard Roizman, University of Chicago, Chicago, IL, and approved February 8, 2012 (received for review December 6, 2011)





First report of feline morbillivirus in Europe

Alessio Lorusso^{1*}, Morena Di Tommaso², Elisabetta Di Felice¹, Guendalina Zaccaria¹, Alessia Luciani², Maurilia Marcacci¹, Giovanni Aste², Andrea Boari² & Giovanni Savini¹

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Veterinaria Italiana 2015, **51** (3), 235-237. doi: 10.12834/VetIt.833.4136.2

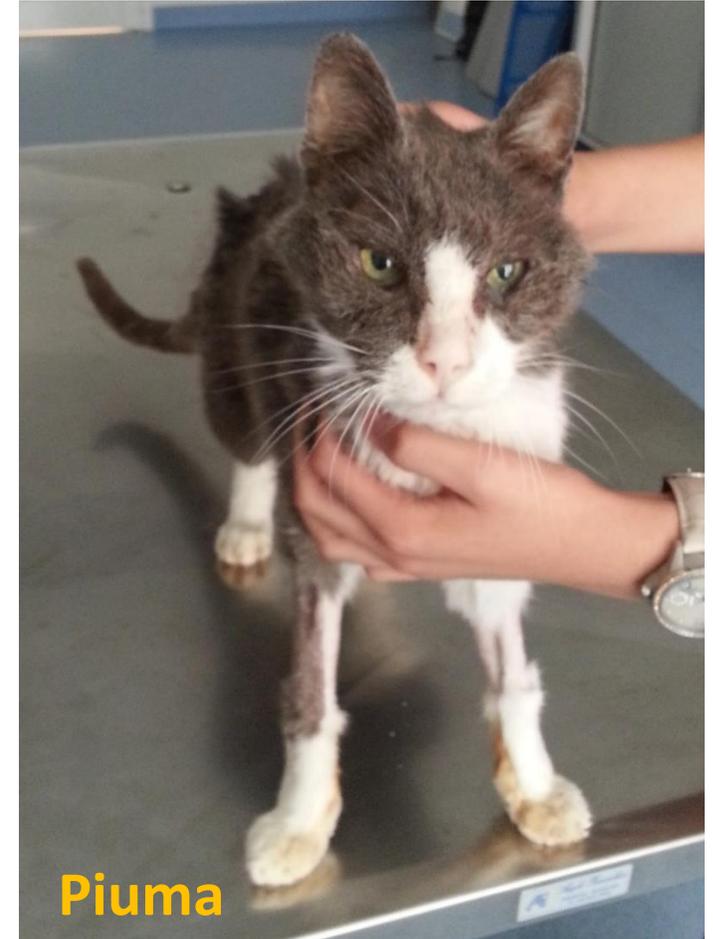
Accepted: 01.08.2015 | Available on line: 12.08.2015

Keywords

Cat,
Europe,
Feline morbillivirus,
Nephropathy.

Summary

Feline morbillivirus was detected in urine samples of a 15 year old cat suffering from severe nephropathy. Viral RNA was not detected in blood and faecal samples and also the most common pathogens associated to cat kidney failure were not found. This report describes the first evidence of feline morbillivirus in Europe.



Nefrite Tubulo-Interstiziale

	Positivi	Negativi	Bibliografia
Hong-Kong	7/12	2/15	Woo et al 2012
Giappone	26/29	44/71	Park et al 2016
Turchia	3/4	4/11	Yilmaz et al 2017
Italia	8/10	12/22	<i>Unpublished data</i>



Table 2 Detection of viral RNA, IgG and antigen

No. of cases	ID of cat	Degree of lesions	FmoPV RNA		Antibody titer in IF	IHC
			urine	tissue		
1 ^a	N010	++	P ¹	P	>20,480	***
2 ^a	N101	++	P	P	5120	***
3 ^a	N153	+++	P	P	640	***
4	N007	+	P	P	10,240	**
5	N110	+	P	P	1280	**
6	N134	++	P	P	160	**
7	N141	+	P	P	2560	*
8	N020	+	P	N ²	5120	*
9	N050	+++	P	N	640	**
10	N104	none	P	N	1280	**
11	N028	+++	N	P	5120	**
12	N040	++	N	P	1280	**
13†	N055	++	P	P	<40	***
14	N001	++	P	P	<40	**
15	N003	+	P	P	<40	**
16	N073	+++	P	P	<40	*
17	N076	none	P	P	<40	**
18	N109	++	P	P	<40	*
19	N140	+	N	N	640	*
20	N045	++	N	P	2560	none
21	N144	+++	N	P	640	none
22	N063	+	N	P	<40	none
23	N065	+	P	N	<40	none
24	N024	+	N	N	2560	none
25	N064	+++	N	N	2560	none
26	N131	+	N	N	320	none
27	N136	++	N	N	640	none
28	N138	none	N	N	320	none
29	N148	++	N	N	2560	none

RESEARCH ARTICLE

Open Access



Epidemiological and pathological study of feline morbillivirus infection in domestic cats in Japan

Eun-Sil Park¹, Michio Suzuki¹, Masanobu Kimura¹, Hiroshi Mizutani², Ryuichi Saito², Nami Kubota², Youko Hasuike², Jungo Okajima², Hidemi Kasai², Yuko Sato³, Noriko Nakajima³, Keiji Maruyama², Koichi Imaoka¹ and Shigeru Morikawa^{1*}

lesioni renali 26/29
 IHC
 titolo Ab in 7 gatti PCR negativi



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Frequency, clinicopathological features and phylogenetic analysis of feline morbillivirus in cats in Istanbul, Turkey

Huseyin Yilmaz¹, Bilge K Tekelioglu², Aydin Gurel³, Ozge E Bamac³, Gulay Y Ozturk³, Utku Y Cizmecigil¹, Eda A Tarakci¹, Ozge Aydin¹, Aysun Yilmaz⁴, Eduardo Berriatua⁵, Chris R Helps⁶, Juergen A Richt⁷ and Nuri Turan¹

TIN

Table 3 Clinical and histopathological findings of dead cats. Kidney, liver and the lymph node from the samples (C3, C8, C11 and C11) were positive on immunocytochemistry stained with anti-morbillivirus guinea pig serum

Sample ID	Presence of FmoPV RNA	Antibody to FCoV	Clinical findings							IHC findings (staining with anti-morbillivirus guinea pig serum)			
			A	U	R	F	W	Di	De	Kidney	Liver	Lymph node	
C1		+	+	-	-	-	-	-	-	+	-	-	-
C2		+	+	-	-	-	-	-	+	+	-	-	-
C3	+	+	-	-	+	+	+	-	-	-	+	+	+
C4		-	-	-	+	+	-	-	-	-	-	-	-
C5		+	-	-	+	-	-	+	-	-	-	-	-
C6		+	+	-	-	-	+	+	+	-	-	-	-
C7		-	-	-	+	+	-	-	-	-	-	-	-
C8	+	-	-	+	+	-	-	+	-	+	+	+	+
C9		-	+	-	-	-	-	-	-	-	-	-	-
C10		-	-	-	-	-	-	-	-	-	-	-	-
C11	+	-	-	-	-	+	+	-	+	+	+	+	+
C12		+	+	-	+	-	+	+	+	-	-	-	-
C13		-	-	-	-	-	-	-	-	-	-	-	-
C14		+	+	-	-	-	-	+	+	-	-	-	-
C15	+	+	+	+	+	+	+	-	+	+	+	+	+

R = respiratory signs; F = fever; W = weight loss; Di = diarrhoea; De = depression; NE = not examined; A = anorexia; U = urinary signs; IHC = immunohistochemistry; FmoPV = feline morbillivirus; FCoV = feline coronavirus



OVUD TERAMO & IZSAM (2015-2017)

ORIGIN GROUP	ORGAN	RESULTS PCR-REAL-TIME
FEMV 9216 Batuffolo 2016	Kidney	+
	Bladder	+
	Spleen	+
	Brain	+
FEMV 9257 Monk 2016	Kidney	+
	Bladder	+
	Bladder epithelium	+
FEMV 12807 Arpio 2016	Kidney	+
	Bladder	+
FEMV 25873 Cassiopea 2016	Kidney	+ (assenza di lesioni)
FEMV 27447/3 2016	Kidney	+ (assenza di lesioni)
FEMV 24961 Margarita 2016	Spleen	+
	Mesenteric Lymph nodes	+
FEMV 28321 Pedro 2016	n.a.	
FEMV 29045 Chicco 2016)	Kidney	+
	Bladder	+
FEMV 1734 Luna 2017	Right Kidney	+
	Left Kidney	+
	Spleen	+
FEMV 11441 Athos 2016	Kidney	+



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TERAMO, 20-MAR-2017

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ANNO 2017 NRG 1355 Rapporto di prova completo
Rif. rapporto di prova parziale del: 03-FEB-2017

Si comunicano i risultati delle ricerche eseguite sul materiale inviato al nostro laboratorio in data 31-GEN-2017 ed esaminato dal 02-FEB-2017 al 16-MAR-2017

Campioni	Materiale	Specie	Data Prelievo	Proprietario	Indirizzo
1	CARCASSA	GATTO	31-GEN-2017	██ ██	██

RENE - Specie: GATTO

Identificativo	Accertamento	Risultato	Tecnica di Prova
Leone-3	Ricerca Immunoistochimica	Positivo per morbillivirus	Avidina/Streptavidina Biotina Complex
Leone-3	Morbillivirus: Ricerca agente eziologico	Negativo	RT-PCR

RENE - Specie: GATTO

Campione	Esame Istologico - Inclusione - Ematossilina-Eosina
Leone-3	Nefrite interstiziale caratterizzata da focolai di infiltrato infiammatorio linfocitario e tubulonefrosi; microlitiasi

Morbillivirus del gatto: un nuovo virus di cui preoccuparsi?

1. TROPISMO RENALE (TIN?)





Frequency, clinicopathological features and phylogenetic analysis of feline morbillivirus in cats in Istanbul, Turkey

Huseyin Yilmaz¹, Bilge K Tekelioglu², Aydin Gurel³, Ozge E Bamac³, Gulay Y Ozturk³, Utku Y Cizmecigil¹, Eda A Tarakci¹, Ozge Aydin¹, Aysun Yilmaz⁴, Eduardo Berriatua⁵, Chris R Helps⁶, Juergen A Richt⁷ and Nuri Turan¹



Table 2 Signalment, clinical, haematological and urological findings of the three morbillivirus-positive live cats

Signalment and clinical findings	Cat			Haematological findings			Urological findings				
	Cat 1*	Cat 2	Cat 3	Cat 1*	Cat 2	Cat 3†	Cat 1*	Cat 2	Cat 3		
Age (years)	4	12	0,2	White blood cells	H	N	H	Ketone	NP	NP	NP
Gender	M	F	F	Lymphocytic count	N	L	H	Blood	NP	NP	NP
Breed	Mix	Mix	Mix	Monocyte	N	N	H	Protein	H	NP	NP
Health status	Death	Unhealthy	Unhealthy	Granulocyte	H	H	H	Bilirubin	H	NP	NP
Household	No	No	Yes	Red blood cells	N	N	L	Nitrite	P	NP	NP
Renal disorder	No	No	No	Haemoglobin	N	N	L	Leukocyte	P	P	NP
Urological signs	Yes	No	Yes	Haematocrit	N	N	N	Glucose	P	NP	NP
Respiratory signs	Yes	No	No	Albumin	N	N	N	pH	6	6	5,5
Allergy	No	Yes	No	Globulin	H	N	N	Residue in urine	P	P	P
Anorexia	Yes	No	No	Alb./glob. ratio	N	N	N	Microleukocyte	P	P	P
Diarrhoea	No	Yes	No	Total protein	H	N	N	Bacteria	P	P	P
Vomiting	No	Yes	No	BUN	N	N	N	Trans epithelial	P	N	P
Weight loss	Yes	No	No	Urea	H	H	N	Renal epithelia	NP	NP	NP
Fever	Yes	No	No	Creatinine	H	H	H	Struvite	NP	NP	NP
Depression	Yes	No	No	ALT	H	N	H	Oxalate	NP	P	NP
Hair loss, dullness	No	No	No	ALP	H	N	H	Cystine	NP	NP	NP
Dermatitis	No	No	No	Bilirubin	H	N	H	Tyrosine	NP	NP	NP
Stomatitis	No	No	No					Ca phosphate	NP	NP	NP

*Cat 1 died later

†Blood was not available for cat 3

M = male; F = female; H = high; L = low; N = normal; P = present; NP = not present



Chronic Infection of Domestic Cats with Feline Morbillivirus, United States

Claire R. Sharp, Sham Nambulli,
Andrew S. Acciardo, Linda J. Rennick,
J. Felix Drexler, Bertus K. Rima, Tracey Williams,
W. Paul Duprex

Author affiliations: Tufts University Cummings School of Veterinary Medicine, North Grafton, Massachusetts, USA (C.R. Sharp); Boston University School of Medicine, Boston, Massachusetts, USA (S. Nambulli, A.S. Acciardo, L.J. Rennick, W.P. Duprex); University of Bonn Medical Centre, Bonn, Germany (J.F. Drexler); German Center for Infection Research, Bonn-Cologne, Germany (J.F. Drexler); The Queen's University of Belfast School of Medicine, Dentistry, and Biomedical Sciences, Belfast, Northern Ireland (B.K. Rima); Zoetis LLC, Kalamazoo, Michigan, USA (T. Williams)



- **RNA virale isolato in un gatto clinicamente sano a distanza di 15 mesi**



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Morbillivirus del gatto: un nuovo virus di cui preoccuparsi?

1. TROPISMO RENALE
2. SOGGETTI DI TUTTE LE ETA'
3. INFEZIONI CRONICHE





ISFM Consensus Guidelines on the Diagnosis and Management of Feline Chronic Kidney Disease



upper urinary tract obstructions, and potentially viral infections involving retroviruses as well as a recently recognised morbillivirus.^{8–12} Other specific causes of CKD sometimes recognised include amyloidosis, polycystic kidney disease, renal lymphoma, hypercalcaemic nephropathy and congenital disorders – some of these have breed associations.^{4,8,13}



Feline CKD



- Comune nei gatti anziani
- >30-40% dei gatti sopra i 10 anni
- Prima causa di morte nei gatti UK >5 anni
- Predisposizioni di razza?

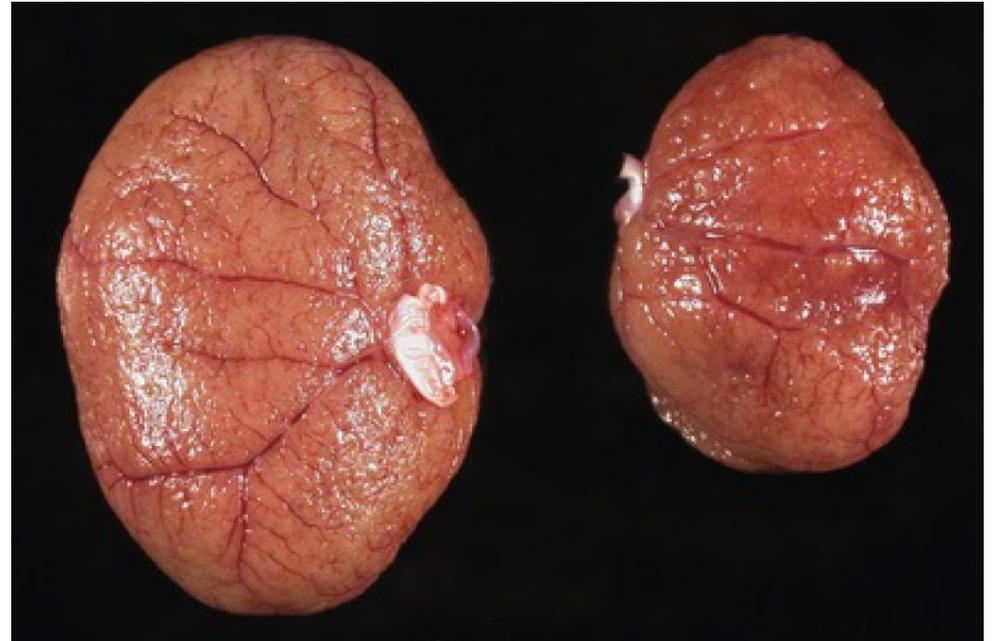
1 in **3**  will develop **kidney disease.**



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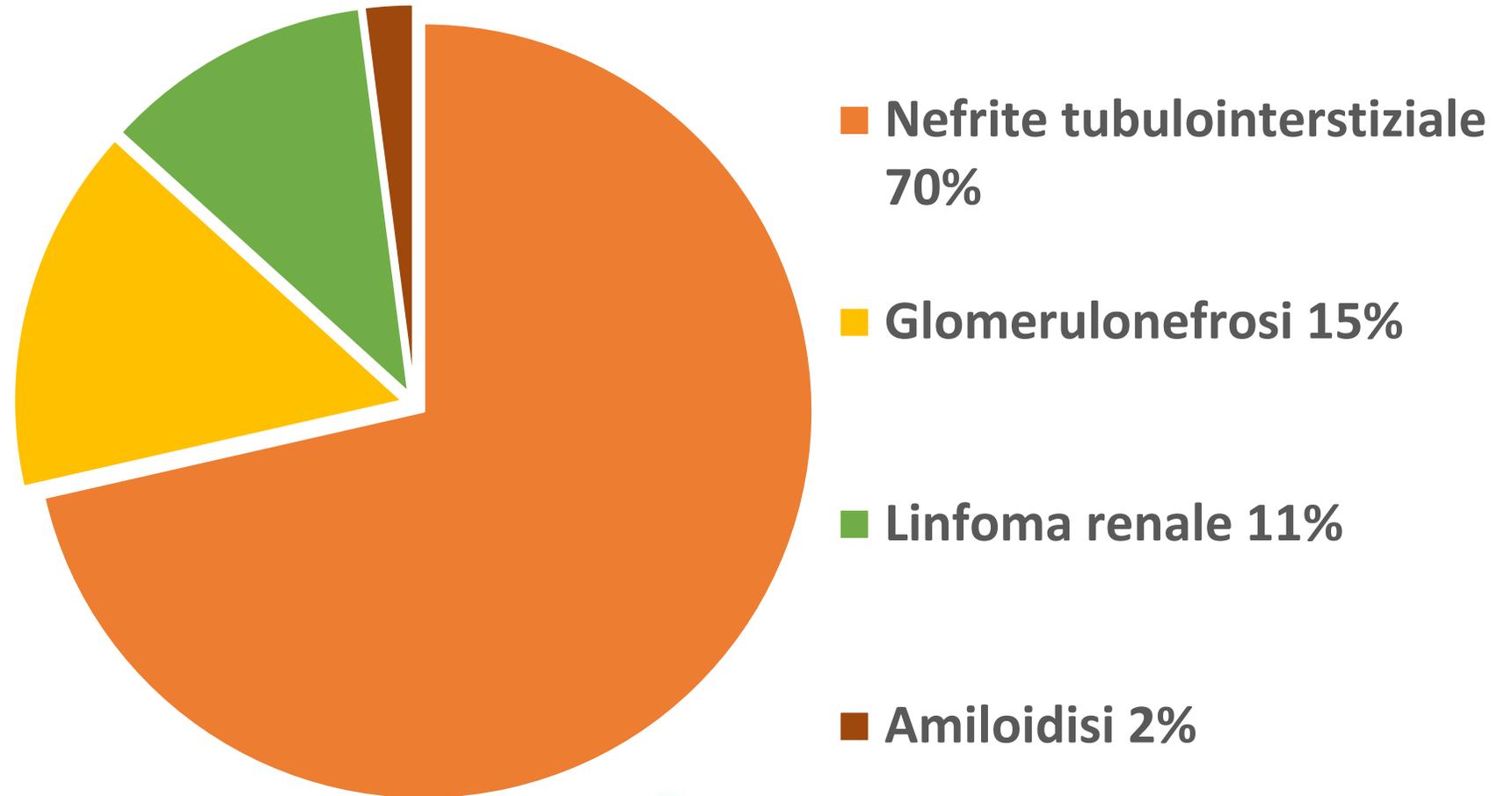
Feline CKD

- Condizione IRREVERSIBILE e PROGRESSIVA
- Progressione autonoma
- Iperfiltrazione -> *trade-off hypotesis*

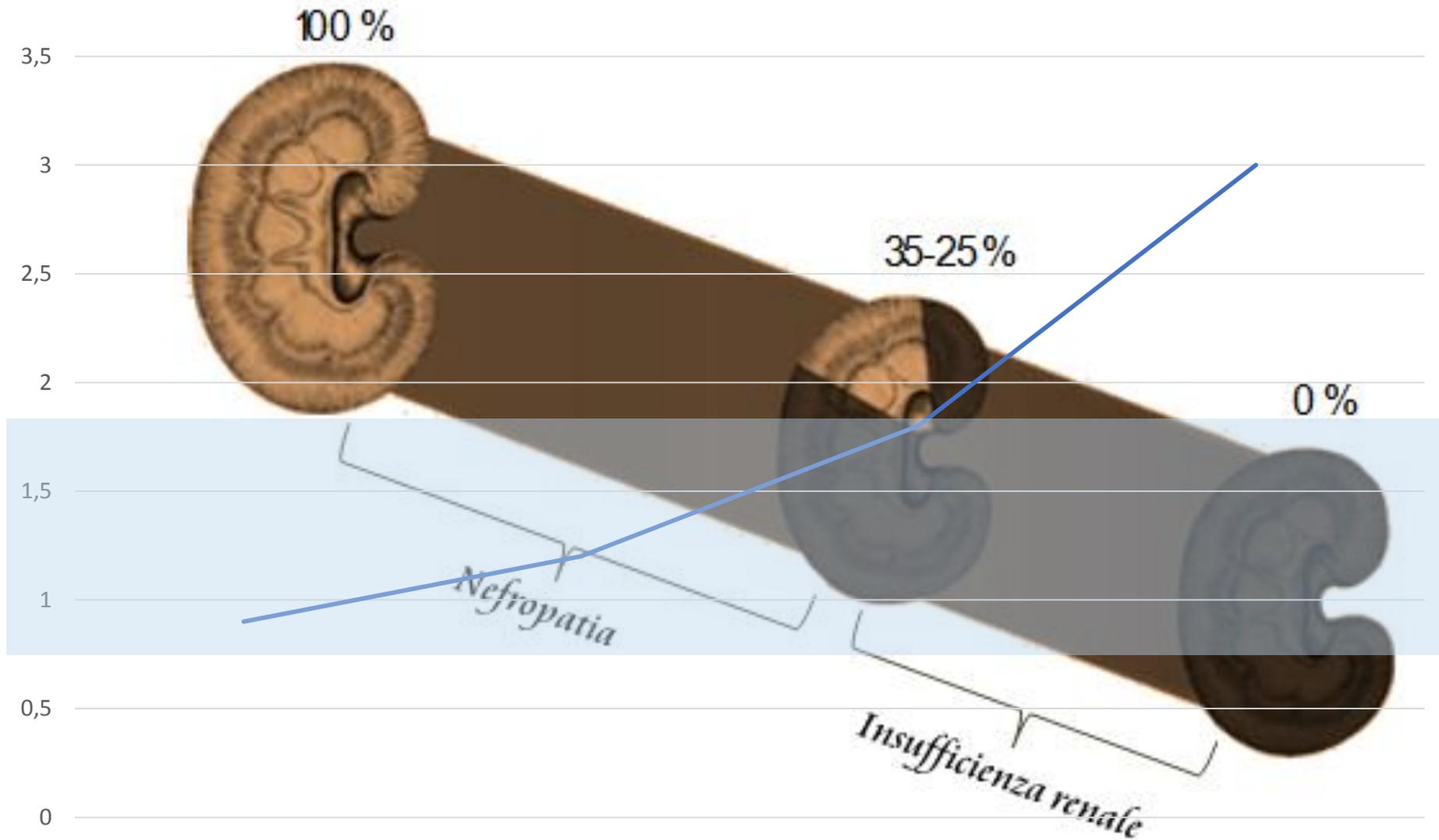


Feline CKD

Trigger rimane ignoto nella quasi totalità dei casi



Feline CKD



IRIS staging of feline CKD:

Based on fasting blood creatinine concentration, in a stable patient, measured twice

140 $\mu\text{mol/l}$
1.6 mg/dl

250 $\mu\text{mol/l}$
2.8 mg/dl

440 $\mu\text{mol/l}$
5.0 mg/dl

Stage 1

- ❖ Non-azotaemic
- ❖ Creatinine <140 $\mu\text{mol/l}$
- ❖ Some other renal abnormality present: known insult, abnormal palpation, poor concentrating ability, etc

Stage 2

- ❖ Mild azotaemia
- ❖ Creatinine 140–250 $\mu\text{mol/l}$
- ❖ Clinical signs usually mild (eg, PU/PD) or may be completely absent

Stage 3

- ❖ Moderate azotaemia
- ❖ Creatinine 251–440 $\mu\text{mol/l}$
- ❖ Many renal and extrarenal clinical signs may be present

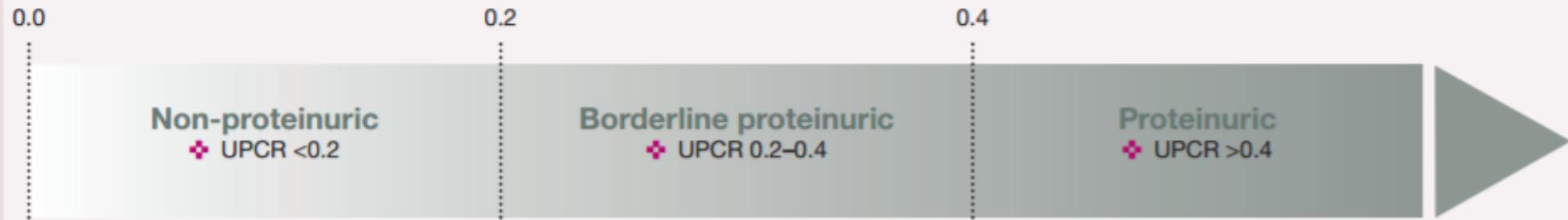
Stage 4

- ❖ Severe azotaemia
- ❖ Creatinine >440 $\mu\text{mol/l}$
- ❖ Increasing risk of systemic clinical signs and uraemic crises

>90% delle diagnosi in stadio 2 o 3



**IRIS substaging of feline CKD:
Based on proteinuria (urine protein:creatinine ratio [UPCR])**

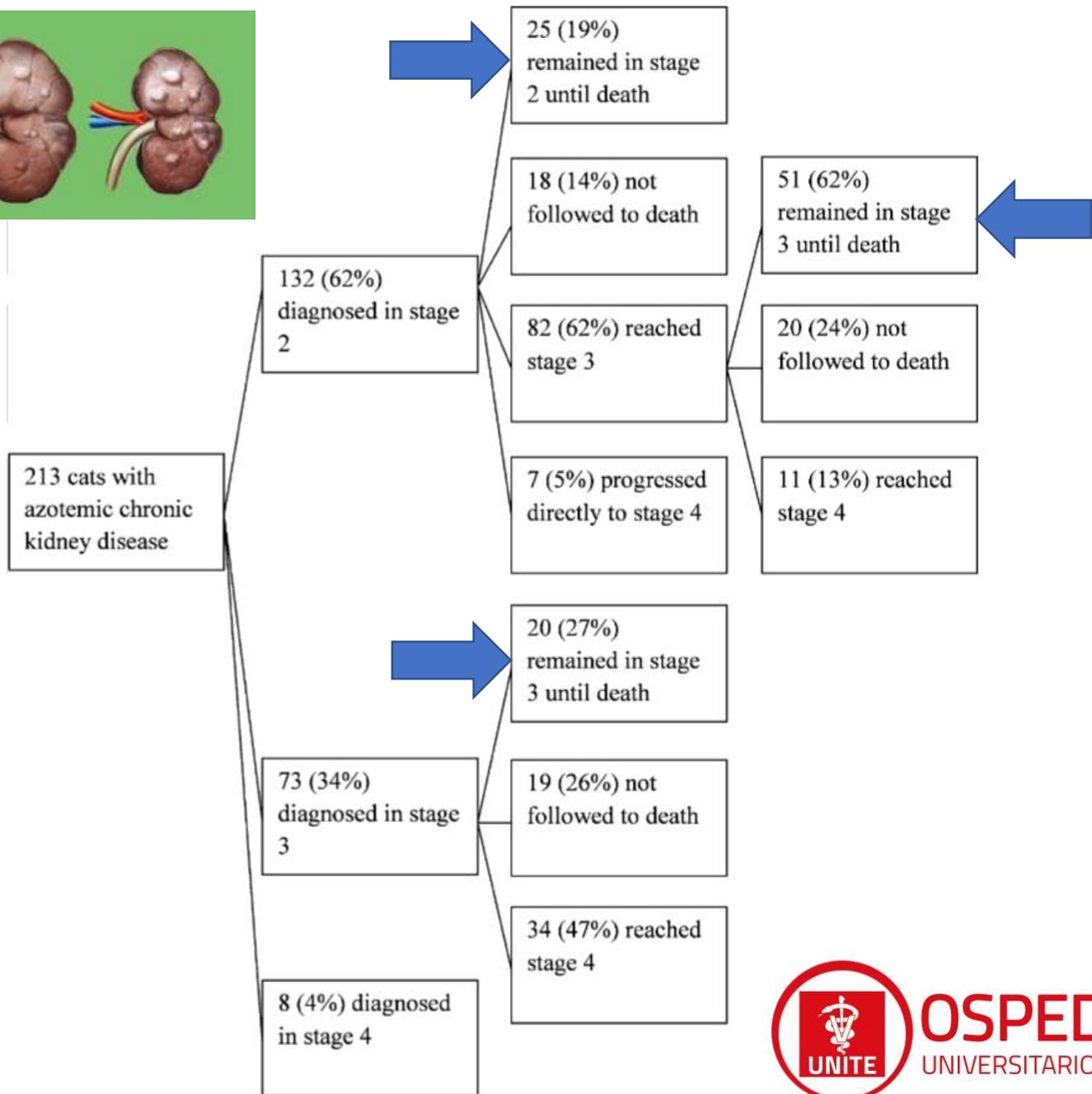
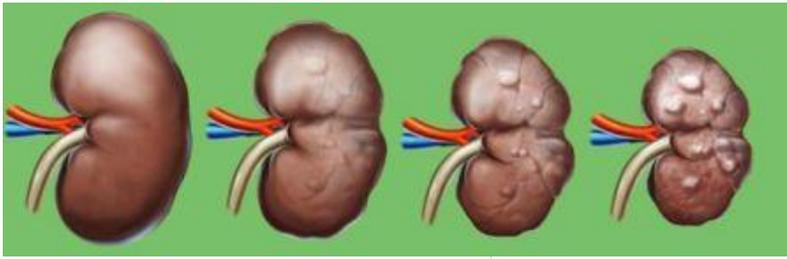


**IRIS substaging of feline CKD:
Based on measurement of systolic blood pressure (SBP)**



Adapted from www.iris-kidney.com.²⁷ IRIS = International Renal Interest Society; PU/PPD = polyuria/polydipsia; TOD = target organ damage





Clinicopathological Variables Predicting Progression of Azotemia in Cats with Chronic Kidney Disease

S. Chakrabarti, H.M. Syme, and J. Elliott

Table 1. Summary statistics for clinicopathological variables at diagnosis in cats with chronic kidney disease. Data presented as median (25th, 75th percentile) or prevalence (%).

Clinicopathological Variable	Stable (n = 112)	Progressive (n = 101)
Year of diagnosis	2004 (2000, 2007)	2003 (1999, 2006)
Age (years)	14 (11, 16)	14 (11, 16)
% Male	55	57
Weight (kg)	4.2 (3.5, 4.9)	3.9 (3.2, 4.5)
Plasma creatinine concentration (mg/dL)	2.5 (2.3, 3.0)	2.7 (2.4, 3.5)
Plasma urea nitrogen concentration (mg/dL)	49 (40, 60)	56 (45, 74)
Plasma inorganic phosphorus concentration (mg/dL)	4.4 (3.6, 5.2)	5.1 (4.0, 6.8)
Plasma total calcium concentration (mg/dL)	10.3 (9.9, 10.7)	10.2 (9.6, 10.8)
Plasma potassium concentration (mEq/L)	4.0 (3.7, 4.4)	3.9 (3.6, 4.3)
Plasma cholesterol concentration (mg/dL)	212 (162, 247)	204 (166, 250)
Plasma total protein concentration (g/dL)	7.7 (7.4, 8.2)	7.7 (7.3, 8.3)
Plasma albumin concentration (g/dL)	3.2 (3.0, 3.4)	3.1 (2.9, 3.3)
Plasma globulin concentration (g/dL)	4.5 (4.1, 4.9)	4.6 (4.1, 5.2)
Packed cell volume (%)	35 (32, 38)	31 (25, 35)
Urine protein to creatinine ratio	0.14 (0.08, 0.24)	0.27 (0.17, 0.68)
Urine specific gravity	1.020 (1.016, 1.024)	1.016 (1.014, 1.020)
% with urinary tract infection	11	5
Systolic blood pressure (mmHg)	147 (134, 164)	155 (132, 177)
% with systolic hypertension	29	40
Renal follow-up (days)	744 (576, 1014)	209 (99, 347)
Median survival with 95% confidence interval (days)	1021 [861, 1181]	264 [186, 342]



OVUD TERAMO & IZSAM (2015-2017)

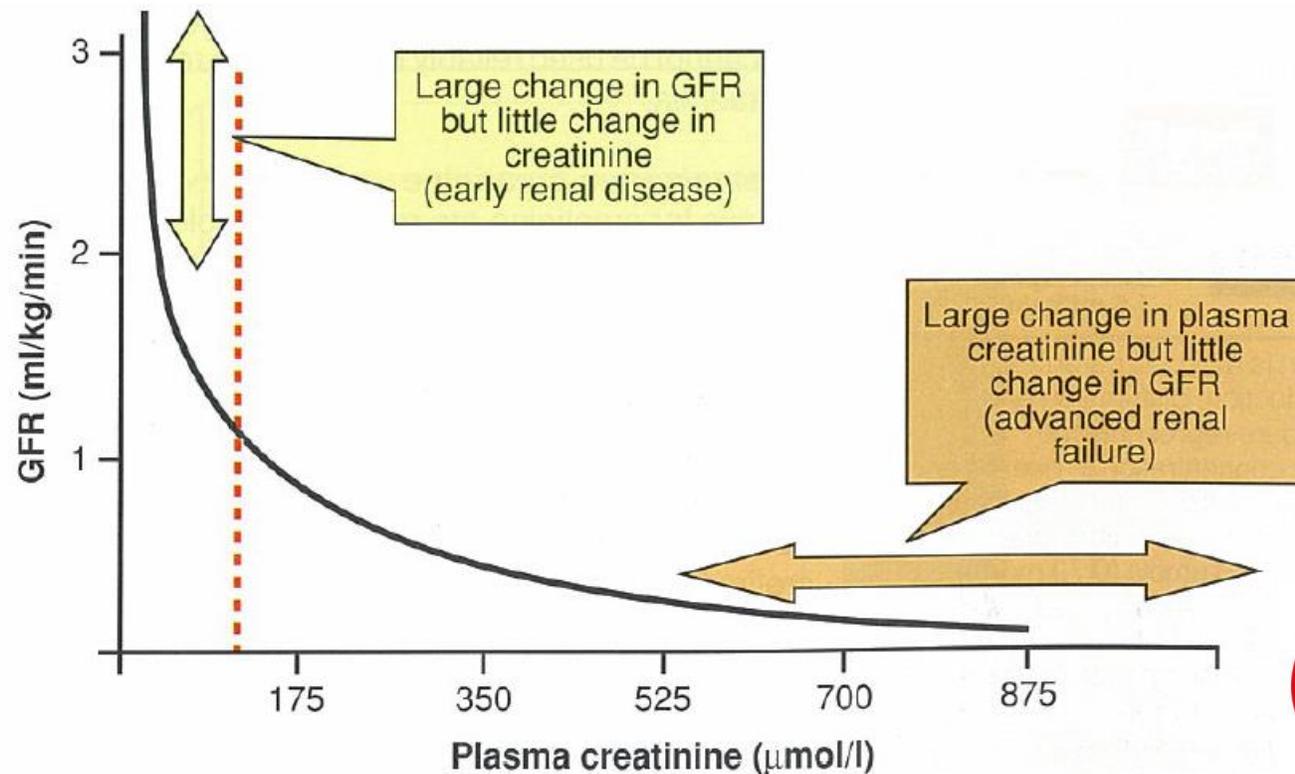
- 15 gatti con PCR positiva per FeMV
- Obiettivo: determinare la presenza di CKD
- Visita clinica, Emocromo, Biochimico, Elettroforesi, Esame delle urine, PU/CU, Ecoaddome



NESSUNA EVIDENZA DI CKD

Velocità di filtrazione glomerulare

- GFR misurazione diretta (inulina, iohexolo) **GOLD STANDARD**
- GFR stimata (creatinina sierica) **SCARSA SENSIBILITA'**



SDMA

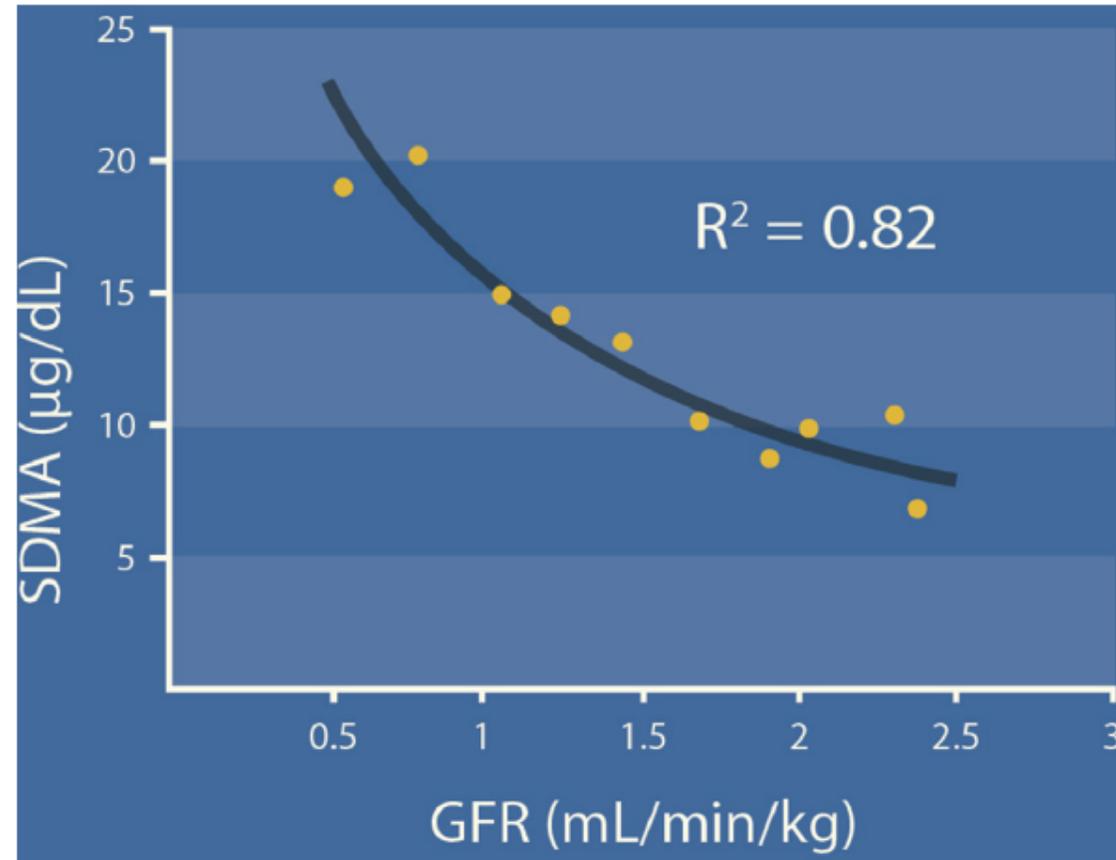
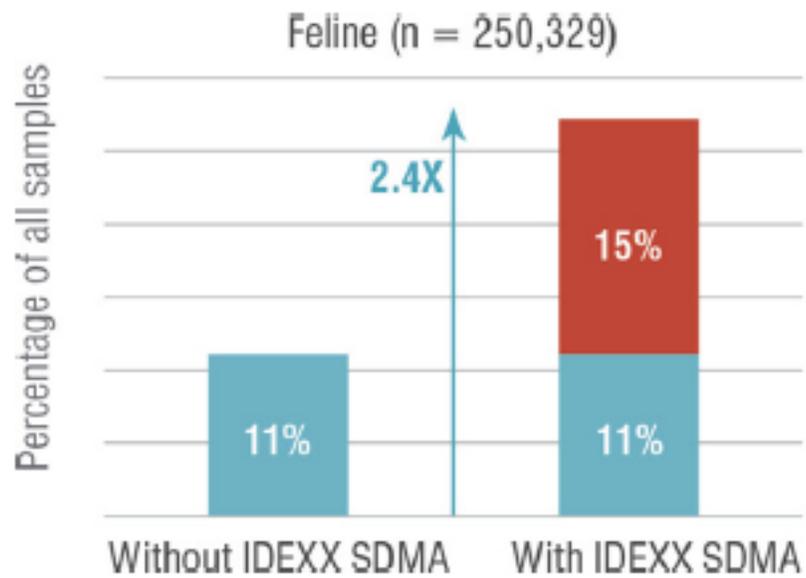


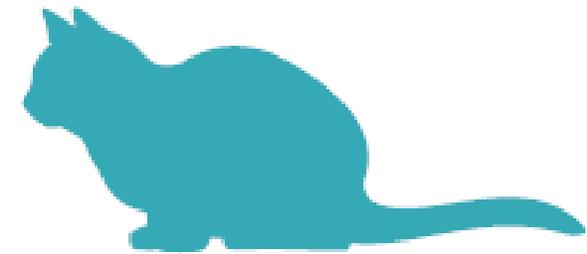
Fig. 4. The inverse relationship, with strong correlation ($R^2 = 0.82$; $P < .001$), between serum SDMA level (y axis) and GFR (x axis) in 10 client-owned cats with varied kidney function. (Data from Braff J, Obare E, Yerramilli M, et al. Relationship between serum symmetric dimethylarginine concentration and glomerular filtration rate in cats. J Vet Intern Med 2014;8:1699–701.)





Cats

- On average, 17 months earlier
- Up to 48 months earlier



Source: Hall JA, Yerramilli M, Obare E, Yerramilli M, Jewell DE. Comparison of serum concentrations of symmetric dimethylarginine and creatinine as kidney function biomarkers in cats with chronic kidney disease. *J Vet Intern Med.* 2014;28(5):1676-1683.



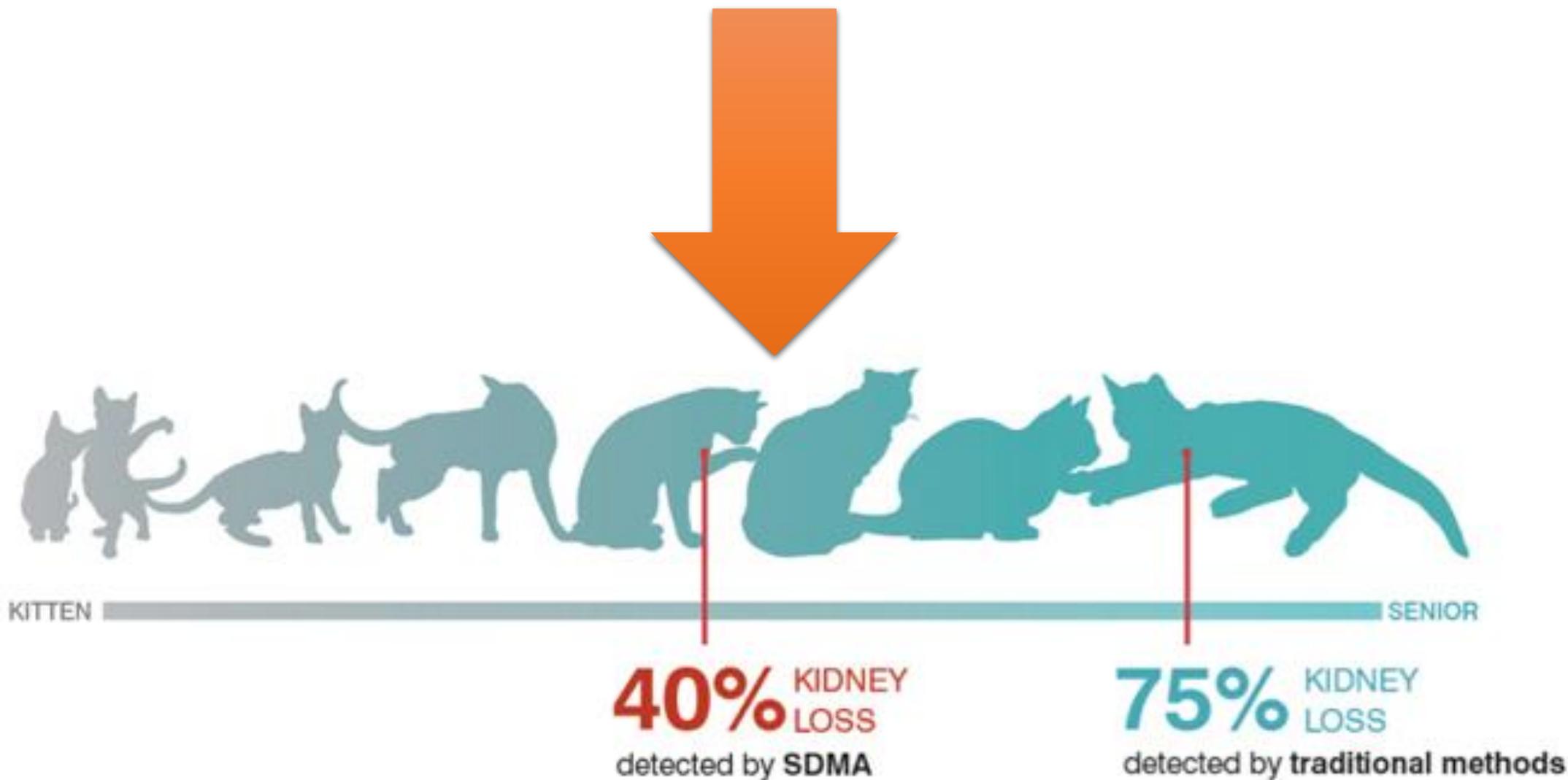
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ID	Segnalamento	CREA (0.7-1.8 mg/dl)	SDMA (0-14 µg/dl)
Claudio	2y, Mc	1,27	16
Santiago	3y, M	1.63	11
Pedro	4y, Mc	1.08	10
Peloponneso	1,5 y, M	0.72	15
Macchiolina	1 y, F	0.75	14
Nerina	1 y, F	0.72	9
Sofia	1,5 y, F	1.09	14
Ugo	4 y, Mc	0.83	20
Capitan harlock	2 y, M	0.68	12
Chicco	2y, Mc	0.73	14
Lamon	2 y, F	0.67	6
Antonio	5 y, M	1.15	8
Rossino	2 y, M	0.7	13
Felix	5 y, Mc	1.1	12
Regina	1 y, F	0.83	7

A persistent increase in SDMA above 14 $\mu\text{g}/\text{dl}$ suggests reduced renal function and may be a reason to consider a dog or cat with creatinine values <1.4 or <1.6 mg/dl , respectively, as IRIS CKD Stage 1.

In IRIS CKD Stage 2 patients with low body condition scores, SDMA ≥ 25 $\mu\text{g}/\text{dl}$ may indicate the degree of renal dysfunction has been underestimated. Consider treatment recommendations listed under IRIS CKD Stage 3 for this patient.

In IRIS CKD Stage 3 patients with low body condition scores, SDMA ≥ 45 $\mu\text{g}/\text{dl}$ may indicate the degree of renal dysfunction has been underestimated. Consider treatment recommendations listed under IRIS CKD Stage 4 for this patient.



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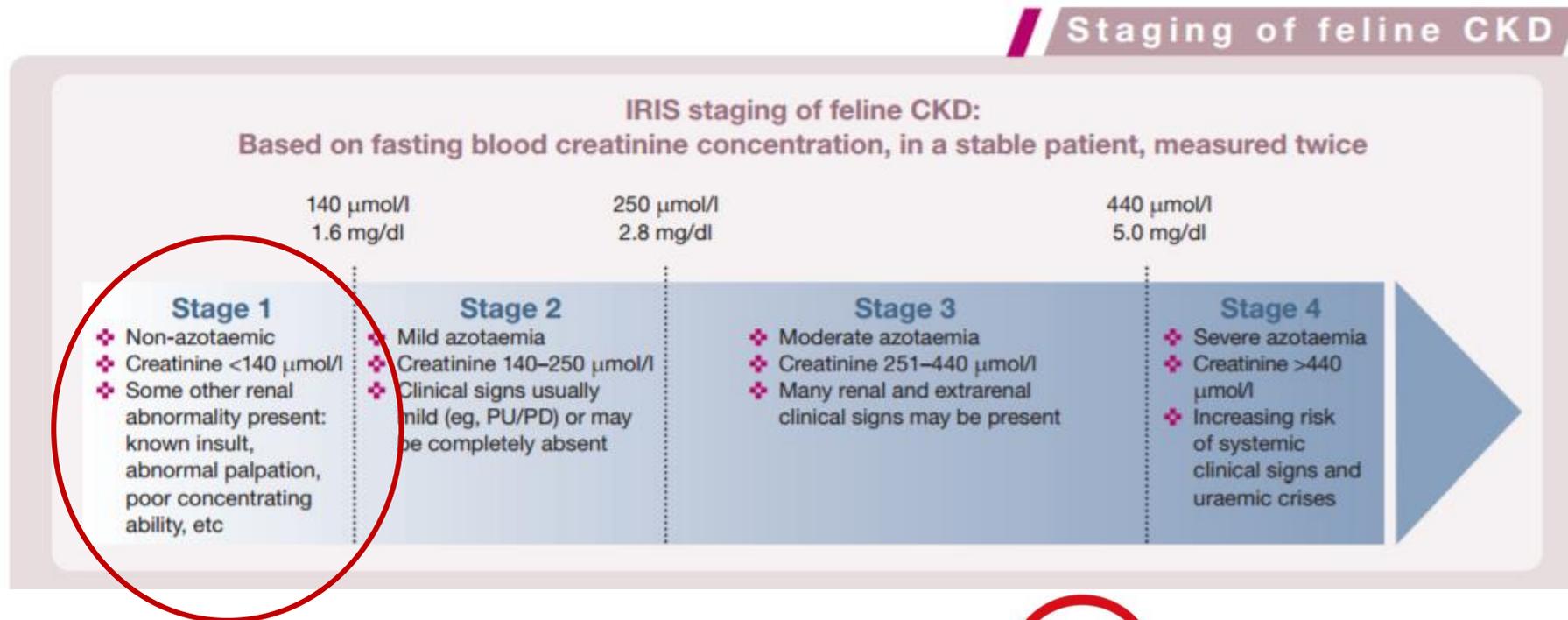
ID	Segnalamento	CREA (0.7-1.8 mg/dl)	SDMA (0-14 µg/dl)
Salciccio	2y, Mc	1,18	16
Roger	1y, M	0.77	16
Buffy	2y, Fs	0.86	11

PCR negativa

Titolo AB ?????

FeMV è causa di CKD nel gatto?

- presenza presunta dell'insulto
- SDMA



Feline Chronic Gengivo-Stomatitis



5/15

Immunocompromissione?

Azione diretta?

BIAS?

Morbillivirus del gatto: un nuovo virus di cui preoccuparsi?

1. TROPISMO RENALE
2. SOGGETTI DI TUTTE LE ETA'
3. INFEZIONI CRONICHE
4. RUOLO PATOGENO IGNOTO





- Ruolo patogeno IGNOTO
- Forte correlazione con presenza di lesioni renali
 - Elevata presenza TIN in gatti sani neg FeMV
 - *Shedding cronico*
- Considerare CKD stadio I ?
- Monitorare pazienti per insorgenza CKD (early diagnosis!!!!)



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