

**OBIETTIVI DELLO STUDIO**

- Individuare i **fattori di rischio** per la morte nei pazienti affetti da leishmaniosi
- Valutare l'impatto dei fattori di rischio sulla **sopravvivenza**



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**MATERIALI E METODI**

- Pazienti condotti a visita presso l'Ospedale Veterinario Universitario del Dipartimento di Scienze Mediche Veterinarie dell'Università di Bologna  
(Gennaio 2001 - Novembre 2016)
- Studio retrospettivo

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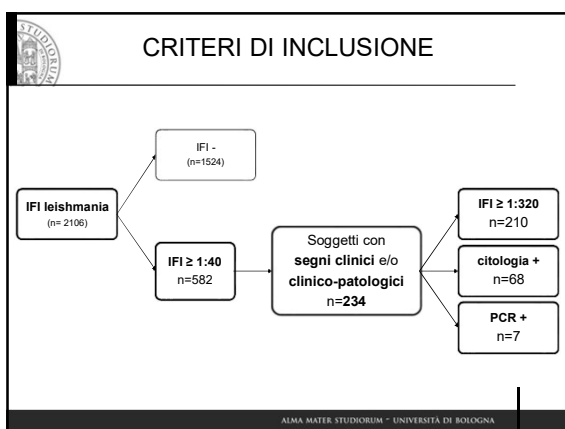
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### ANALISI STATISTICA

- Software per statistica medica MedCalc 16.8.4
- Analisi descrittiva
- Comparazione tra gruppo di studio e gruppo di controllo mediante **Kruskal-Wallis ANOVA**
- Analisi del rischio con regressione di **Cox univariata e multivariata**
- Analisi di sopravvivenza con il metodo **Kaplan-Meier**
- Significatività per valori  $P < 0,05$

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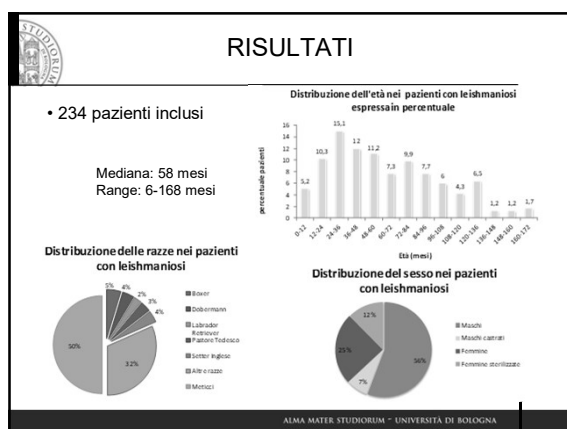
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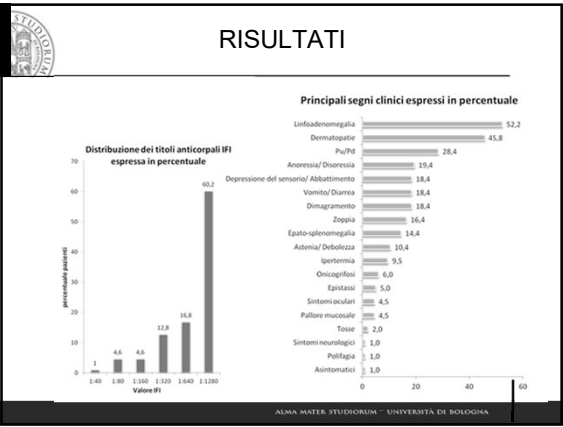
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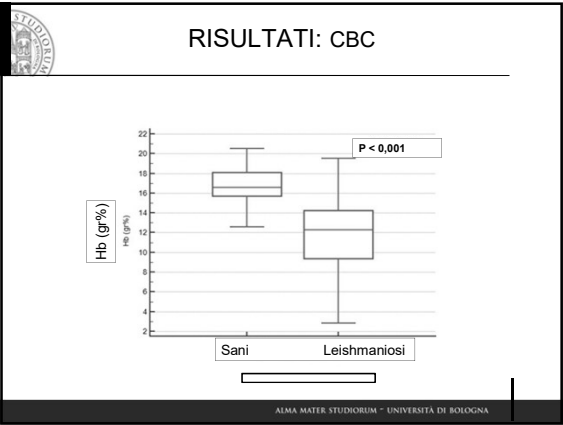
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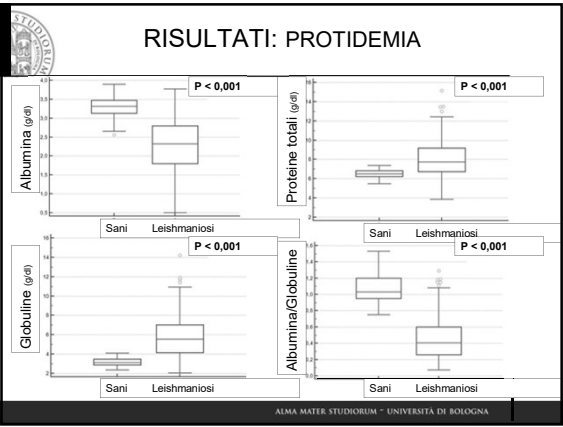
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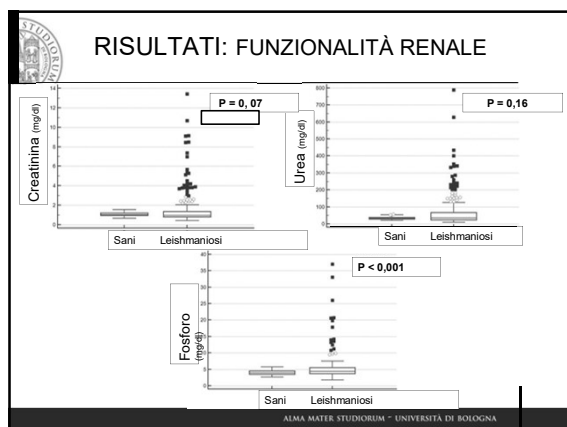
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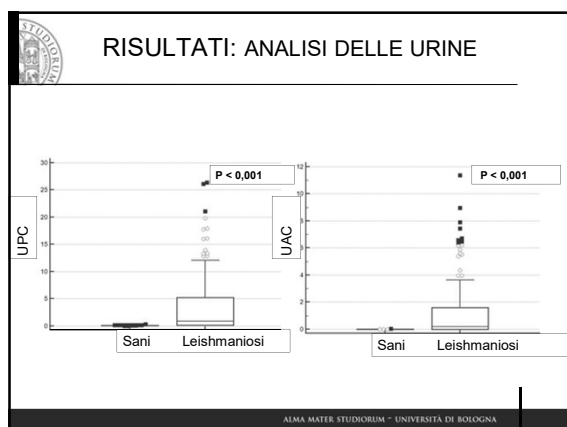
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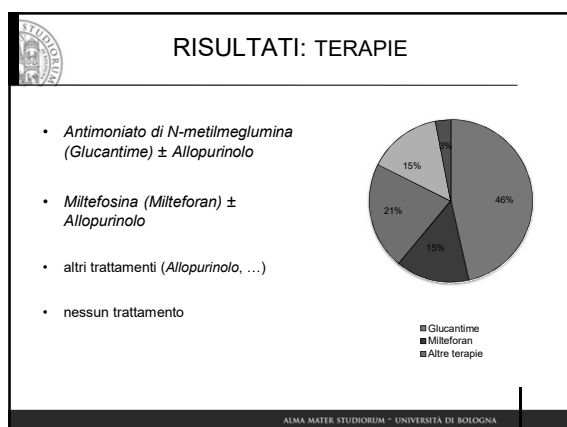
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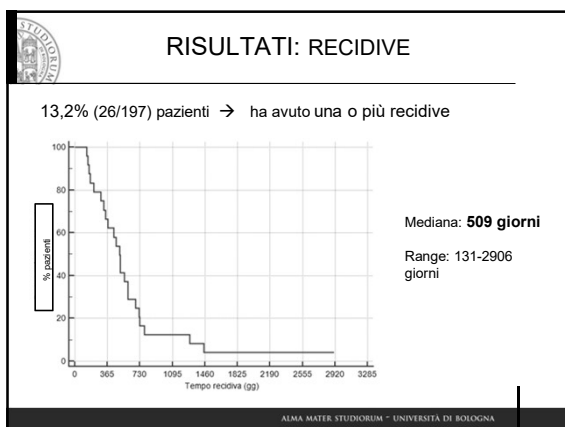
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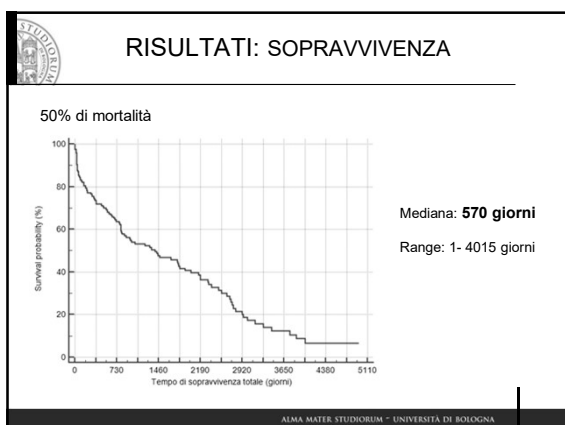
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**RISULTATI: REGRESSIONE DI COX UNIVARIATA E MULTIVARIATA**

Parametro	H.R.	I.C. (95%)	P	Parametro	H.R.	I.C. (95%)	P
Hct	0,9631	0,9446-0,9820	<0,01	Fosforo	1,1754	1,1314-1,2211	<0,01
RBC	1,0000	1,0000-1,0000	<0,01	Potassio	3,4468	2,3789-4,9940	<0,01
Hb	0,9019	0,8327-0,9549	<0,01	P.S	0,9642	0,9481-0,9807	<0,01
A/G	0,3044	0,1399-0,6822	<0,01	uPT	1,0005	1,002-1,008	<0,01
Albumina	0,4585	0,3421-0,6145	<0,01	uCrea	0,9935	0,9909-0,9951	<0,01
TIBC	0,9956	0,9922-0,9991	<0,05	UPC	1,0772	1,0447-1,1107	<0,01
Creatinina	1,2371	1,1530-1,3285	<0,01	UAC	1,2225	1,0277-1,2281	<0,05
Urea	1,0079	1,0081-1,0097	<0,01	Colesterolo	1,0041	1,0026-1,0057	<0,01

Parametro	H.R.	I.C. (95%)	P
Colesterolo	1,0076	1,0022-1,0130	< 0,01
uPT	1,0010	1,001-1,0019	
Urea	1,0067	1,0028-1,0107	

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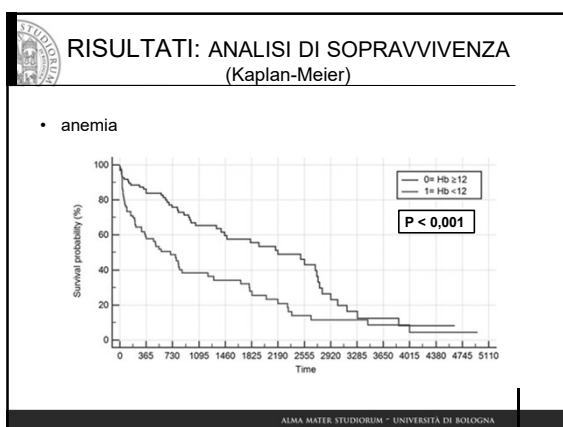
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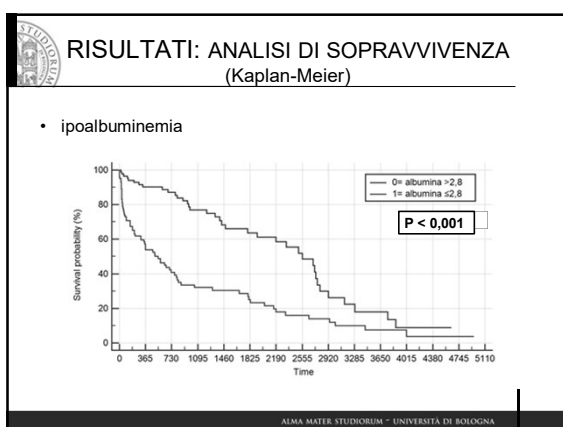
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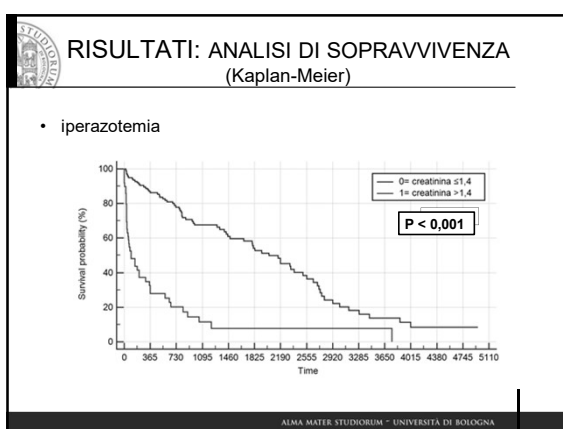
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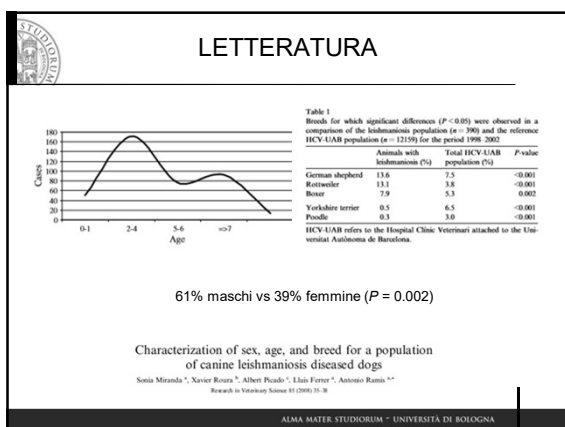
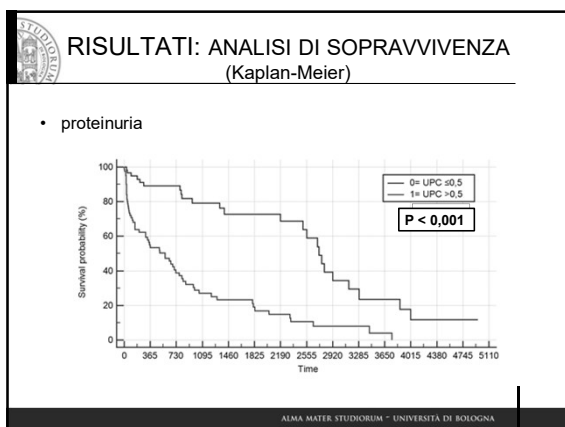
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**SEGNI CLINICI**

Linfoadenomegalia	62 – 90 %	52 %
Dermatopatia	81-89 %	46 %
Polidipsia / poliuria	40 %	28 %
Anorexia	32 %	19 %
Depressione del sensorio	67 %	18 %
Perdita di peso	64 %	18 %
Diarrea / vomito	26 - 30 %	18 %
Zoppia	37 %	16 %
Epato-splenomegalia	10 – 53 %	14 %
Astenia	67 %	10 %
Ipertermia	4 – 36 %	9 %
Onicofrosi	20 – 31 %	6 %
Epistassi	6- 15 %	5 %
Oculopatie	16 – 81 %	4 %
Epistassi	6- 15 %	5 %
Starnuti/ tosse	10 / 6 %	2 %

Baneth D. and Solano-Gallego (2012).  
Leishmaniasis. In  
Greene, *Infectious disease of the dog and cat* (p. 734-749).

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### ALTERAZIONI CLINICO-PATOLOGICHE

Iperproteinemia	63,3-72,8 %	60 %
Iperglobulinemia	76-100 %	84 %
Ipoalbuminemia	68-94 %	54 %
Diminuito rapporto A/G	76 %	75 %
Iperazotemia	16-45 %	25 %
Aumento fosfatasi alcalina (SAP)	16-51 %	
Aumento alanina amino transferasi	16-61 %	
Proteinuria	71,5-85 %	58 %
Anemia	60-73,4 %	47 %
Leucocitosi	24 %	
Leucopenia	22 %	
Trombocitopenia	29,3-50 %	
Positività anticorpi anti-nucleari	31-53 %	
Positività test di Coombs	21-84 %	

Baneth e Solano-Gallego, 2012. Leishmaniases. In Greene, *Infectious disease of the dog and cat* (p. 734-749)

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### RECIDIVE

- 86% soggetti entro 14 mesi (antimoniato+allopurinolo)  
(Ginel et al. 1998)
- 75% (3/4) soggetti 2-4 settimane dopo sospensione (allopurinolo)  
(Cavallero et al. 1999)
- 39% (7/18) soggetti 9-24 mesi (antimoniato + allopurinolo)  
(Marina et al. 2002)
- 60% (3/5) soggetti (antimoniato)  
(Guarga, J.L. et al. 2002)
- Nessuna recidiva (7 soggetti) durante 6 mesi di studio (antimoniato)  
(Kieda-Garcia, F.A. et al. 2007)
- 14% (4/28) soggetti entro 6 mesi (miltefosina + allopurinolo)  
(Marina et al. 2008)
- 13% (3/23) soggetti dopo 2 anni (antimoniato + allopurinolo),  
2/3 in terapia con allopurinolo  
(Torres et al. 2011)

relapse  
does not erase  
your sweeties

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CLINICAL STAGES	SEROLOGY*	CLINICAL SIGNS	LABORATORY FINDINGS	THERAPY	PROGNOSIS
STAGE I Mild disease	Negative to low positive antibody levels	Dogs with mild clinical signs such as solitary lymphadenopathy or papular dermatitis	Usually no hematological abnormalities observed. Normal renal profile. Creatinine < 1.4 mg/dL, non-proteinuria, UPC < 0.3	Specific regimen††† Monitoring of disease progression (see table II)	Good
STAGE II Moderate disease	Low to high positive antibody levels	Dogs, which apart from the signs listed in Stage I, may present other clinical signs such as effusive or symmetrical cutaneous lesions such as edematous dermatitis, mucopurulent ulcerations (granuloma nasale, forisetae), large proliferative, mucocutaneous junctional, generalized lymphadenopathy.	Disseminated dermatitis such as mild non-regenerative anemia, thrombocytopenia, hyperalbuminemia, severe hypercholesterolemia. <b>Subtle:</b> abnormal renal profile creatinine > 1.4 mg/dL non-proteinuria, UPC < 0.3 AC Creatinine < 2.4 mg/dL, UPC < 0.3-1	Allopurinol + meglumine antimoniate or miltefosina	Good to guarded
STAGE III Severe disease	Medium to high positive antibody levels	Dogs, which apart from the signs listed in Stages I and II, may present signs originating from immune complex lesions (e.g. uremia and glomerulonephritis)	Disseminated dermatitis listed in Stage II. Disseminated disease (DD): RBC stage with UPC > 0.4 per stage I creatinine > 2.4 mg/dL	Allopurinol + meglumine antimoniate or miltefosina Follow RBC guidelines for CQ††††	Guarded to poor
STAGE IV Very severe disease	Medium to high positive antibody levels	Dogs with clinical signs listed in Stage III. Pulmonary thromboembolism, anaplastic erythrocytes and stage renal disease	Disseminated dermatitis listed in Stage II. DD: RBC stage I creatinine > 2.4 mg/dL and stage II creatinine > 1 mg/dL or RBC stage II creatinine > 1 mg/dL proteinuria UPC > 1	Specific treatment should be initiated individually Follow RBC guidelines for CQ††††	Poor

\*High with negative to medium positive antibody levels should be confirmed as reflected with other stage nodes within 10 days such as lymph, kidney, liver, bone marrow and PCR. High levels of antibodies are indicative of a diagnosis of CL and are defined as a total increase of a well established laboratory reference value.

††High in Stage II (disseminated) are dogs to require less prolonged treatment with one or less combined drugs (allopurinol, miltefosina, meglumine antimoniate or miltefosina) or alternatively monitoring with the following. There is limited information on stage in this stage and therefore, treatment options remain to be defined.

LeishVet 4th Edition September 2008

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FATTORI PROGNOSTICI

TABLE 3: Factors significantly influencing overall survival time in treated dogs

		Median survival time (in days)	SD (in days)	95% CI (in days)	Level of significance (p)
Proteinuria					
Present	15	795	458	0-1613	<0.001
Absent	14	3664	0	-	
Ipoalbuminemia					
Present	15	731	445	0-1604	0.040
Absent	24	2037	571	916-3157	
Renal azotemia					
Present	10	148	111	0-346	<0.001
Absent	31	2327	443	1115-2719	
Lymphopenia					
Present	12	221	132	0-510	0.002
Absent	19	1948	424	916-3157	

Kaplan-Meier product limit method was used to assess inter-group differences in survival time. All deaths were considered events in this analysis. n, number of dogs.

Prognostic analytes in dogs with *Leishmania infantum* infection living in a non-endemic area

K. Gettemed, R. Maderley, C. Sauter-Rossi, K. Hartmann  
October 20, 2012 | Veterinary Record

	Mediana (g/dm3)	95% CI (g/dm3)
Proteinuria		
presente	570	300-772
assente	2729	2504-3148
Ipoalbuminemia		
presente	549	300-772
assente	2655	1927-3768
Iperazotemia		
presente	96	45-300
assente	2029	1481-2504

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IN CONCLUSIONE

Fattori prognostici:

- Anemia
- Ipoalbuminemia
- Nefropatia (glomerulopatia cronica)

Nessuna correlazione tra sopravvivenza e titolo anticorpale



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LIMITI DELLO STUDIO E PROSPETTIVE FUTURE

- Dati retrospettivi
- Terapie

✓ Fattori predisponenti le recidive della malattia

✓ Stabilire quali terapie leishmanicide e/o nefroprotettive migliorino l'outcome di questi pazienti



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**Ringraziamenti:**

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Erika Monari  
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Silvia Zamagni  
Alessandro Tirolo  
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Tutti i colleghi della UO di  
Nefrologia e Urologia

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