

CRP

在呼吸困難犬隻的臨床應用

盧大立/王文彥 獸醫師 

卷卷

- 13歲 馬爾濟斯 M/C
- Stage C 二尖瓣疾病
- 曾經肺積水過
- 目前藥物穩定控制中



3/13 晚

早上開始咳嗽咳不停，
咳血水，呼吸困難

你會做什麼？

- 理學檢查
- 拍X光
- 掃心超
- 給利尿劑
- 給抗生素
- 給類固醇

理學檢查

- 6級心雜音
- 右側crackle
- 脈搏弱
- 粘膜紫黑

處置

- Lasix 2_{mg/kg} SC
- ICU籠 50% O₂
- Lasix 0.5_{mg/kg/hr} CRI

呼吸 次數

入院	55 _{bpm}
Lasix SC	60 _{bpm}
Lasix CRI	66 _{bpm}
Lasix CRI加量	70 _{bpm}

Lasix沒效怎麼辦？

① 更高劑量

- Lasix 2–8_{mg/kg} IV bolus
- Lasix 1–3_{mg/kg/hr} CRI

Lasix沒效怎麼辦？

① 更高劑量

② 其他種利尿劑

- Torsemide 0.2–0.5_{mg/kg} PO
- Hydrochlorothiazide 0.5–2_{mg/kg} PO

Lasix沒效怎麼辦？

① 更高劑量

② 其他種利尿劑

③ 強心/升壓藥/血管擴張劑

③ 強心/升壓藥/血管擴張劑

- Pimobendan 0.3–1_{mg/kg} PO TID
- Dobutamine 5–20_{ug/kg/min} CRI
- Hydralazine 0.5–1_{mg/kg} PO/IV q1–3hr
- Nitroprusside 1–5_{ug/kg/min} CRI
- Milrinone 0.5–3_{ug/kg/min} CRI

Lasix沒效怎麼辦？

① 更高劑量

② 其他種利尿劑

③ 強心/升壓藥/血管擴張劑

④ 也許他不是肺積水!?



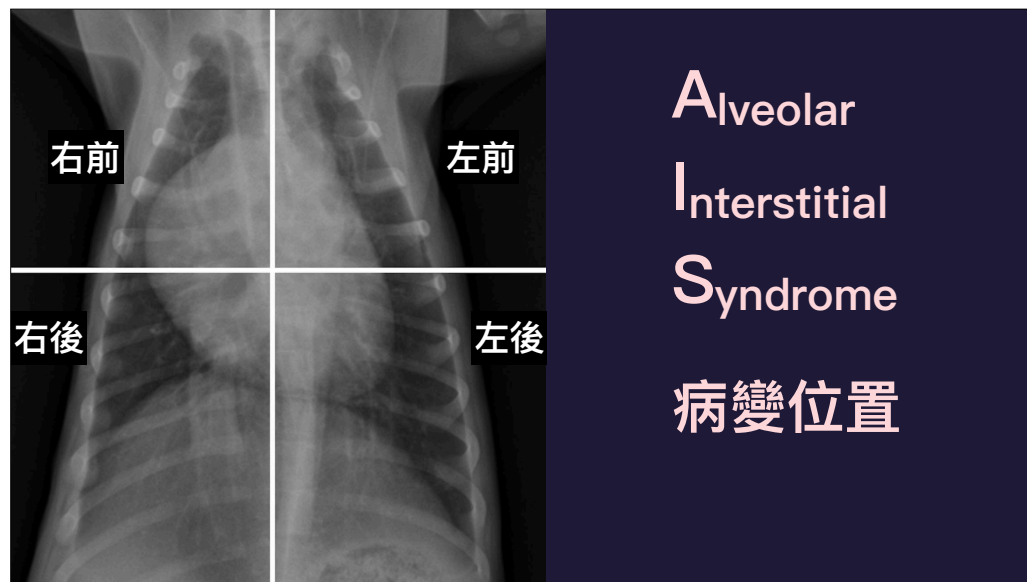
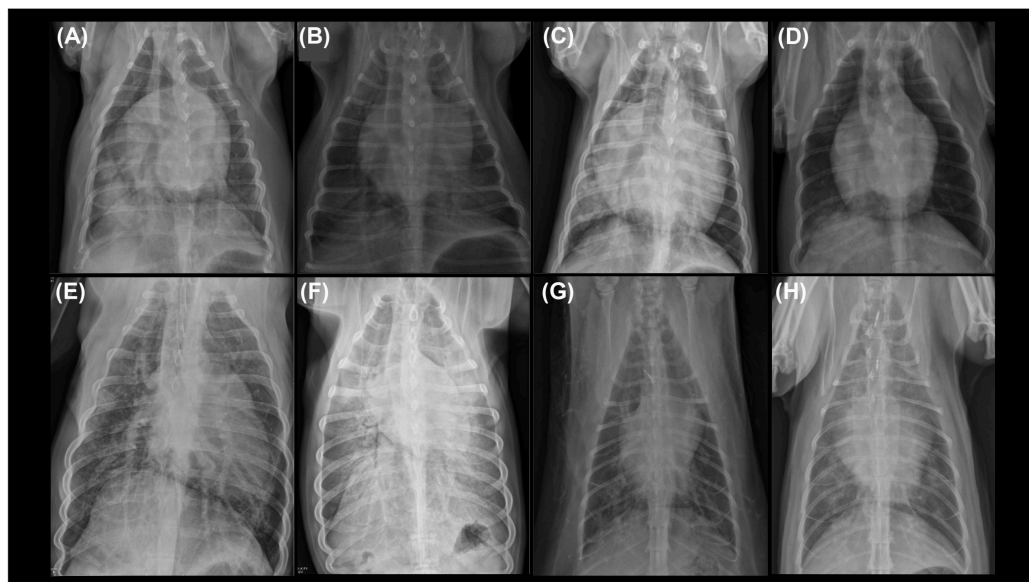
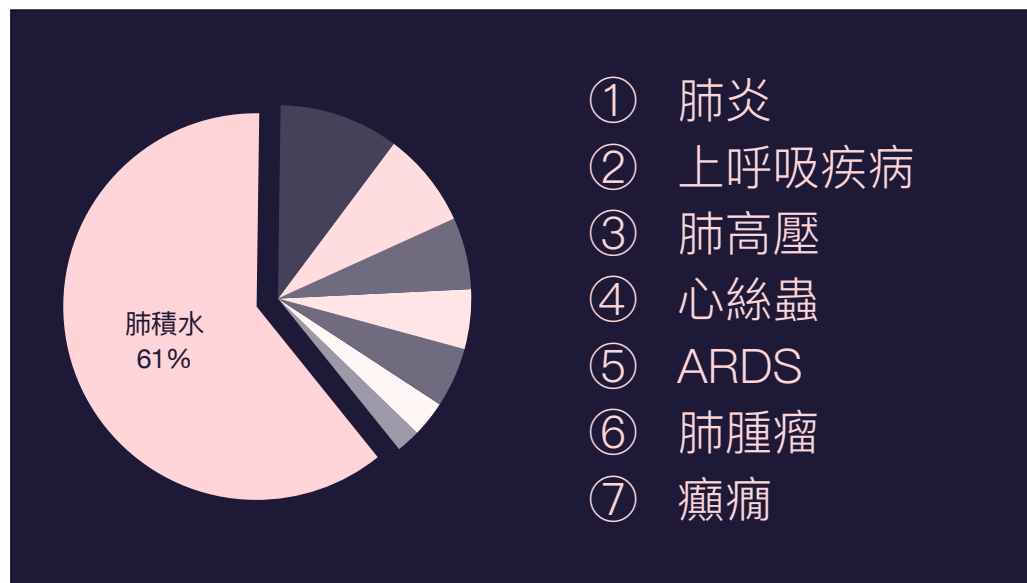
Original Study

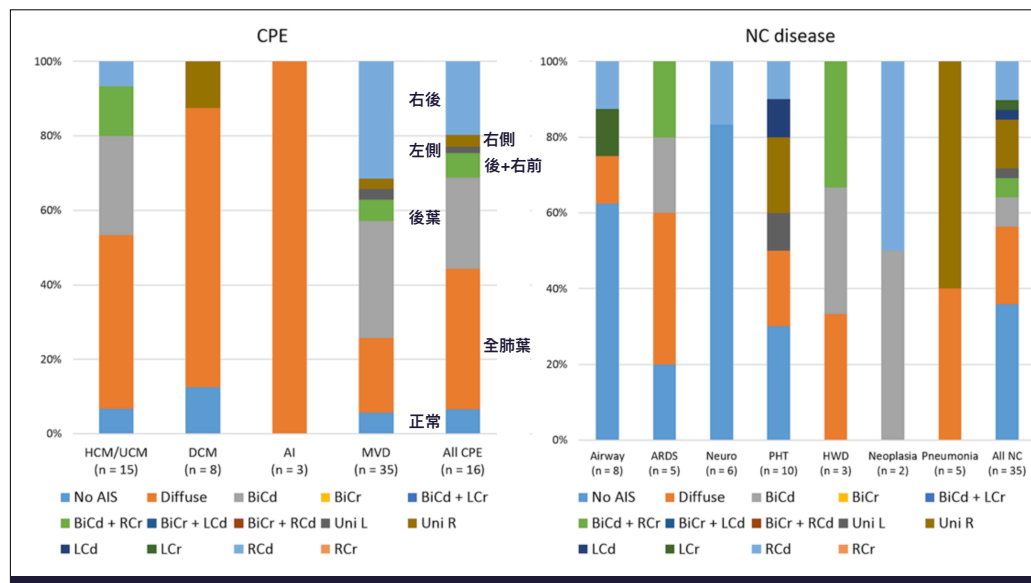
Journal of Veterinary Emergency and Critical Care 28(5) 2018, pp 415–428
doi: 10.1111/vec.12750

Distribution of alveolar-interstitial syndrome in dogs and cats with respiratory distress as assessed by lung ultrasound versus thoracic radiographs

Jessica L. Ward, DVM, DACVIM; Gregory R. Lisciandro, DVM, DACVECC and
Teresa C. DeFrancesco, DVM, DACVIM, DACVECC

100隻急性呼吸困難的狗貓

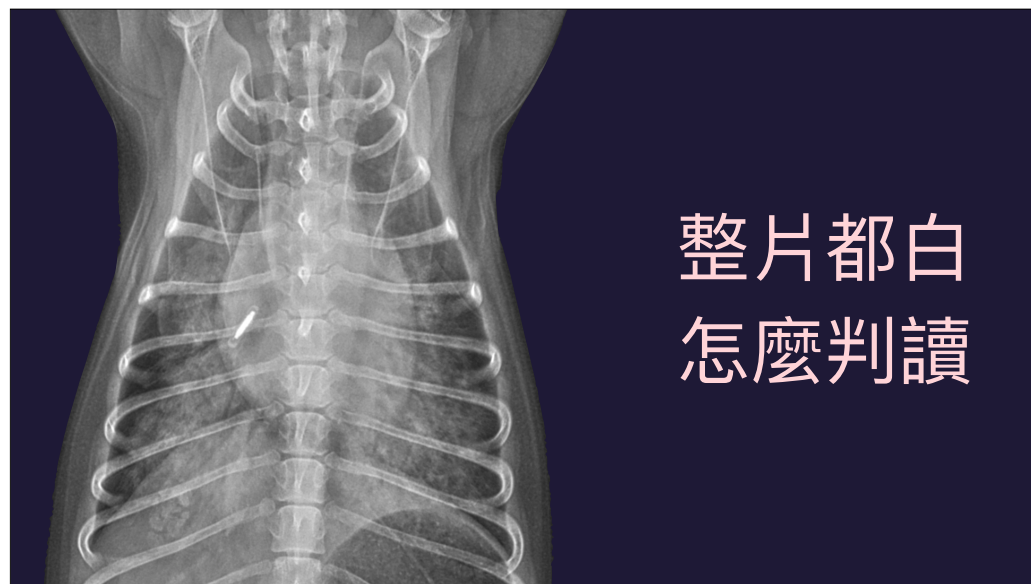




各疾病常見 X光下AIS病變區塊

- 心因性肺積水
- 肺炎
- 吸入性肺炎
- 腫瘤
- 肺高壓

全區/後/右後
全區/右
右中/左前/右前
後/右後
?



超音波

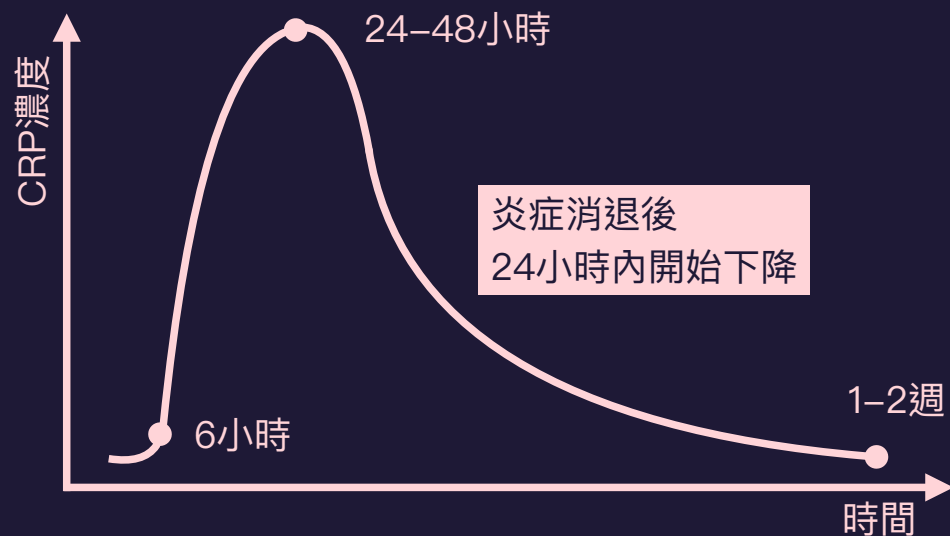
CRP

超音波

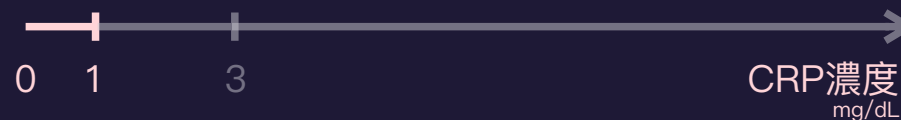
- ① 左心房大小 (LA/Ao)
- ② 肺靜脈大小 (Pv/Pa)
- ③ 左心房壓力 (E wave)

- C Reactive Protein
急性反應蛋白
- 由肝臟產生
- 評估/偵測 **系統性**
炎症反應的嚴重程度

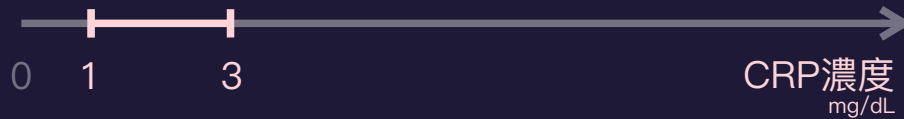
CRP



沒有系統性炎症反應



早期,輕度或正在緩解的炎症反應



嚴重系統性炎症反應
數值越高越嚴重



- 幫助區別診斷
- 追蹤疾病進展
- 評估治療效果/預後
- 不受年齡、性別、品種、緊迫或飲食、皮質類固醇、(NSAIDS)、腎上腺素、肝病、總蛋白的影響

CRP

- 無法指出炎症病因
- 無法偵測局部發炎
- 僅限於犬使用

CRP

在呼吸困難犬隻 的臨床應用

CRP

J Vet Intern Med 2014;28:84-91

Serum C-Reactive Protein as a Diagnostic Biomarker in Dogs with Bacterial Respiratory Diseases

S.J. Viitanen, H.P. Laurila, L.I. Lilja-Maula, M.A. Melamies, M. Rantala, and M.M. Rajamäki

Background: C-reactive protein (CRP) is a major acute-phase protein in dogs. Serum concentrations are low in healthy animals, but increase rapidly after inflammatory stimuli.

Objective: The aim of the study was to investigate CRP concentrations in various respiratory diseases of dogs and to determine if CRP can be used as a biomarker in the diagnosis of bacterial respiratory diseases.

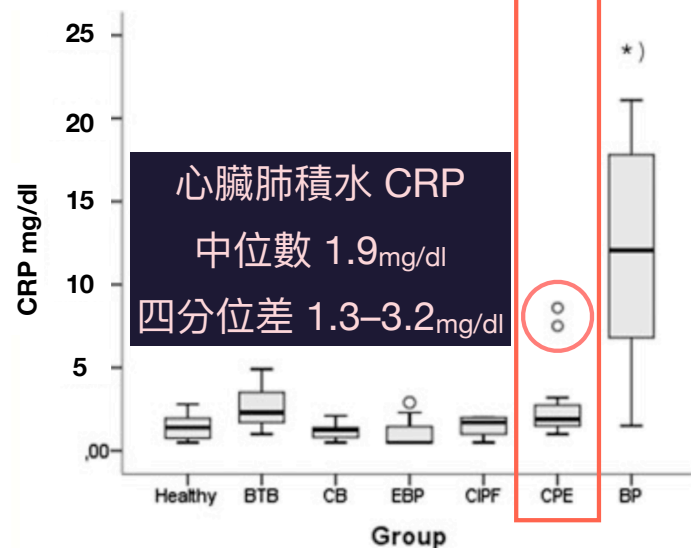
Animals: A total of 106 privately owned dogs with respiratory diseases (17 with bacterial tracheobronchitis [BTB], 20 with chronic bronchitis [CB], 20 with eosinophilic bronchopneumopathy [EBP], 12 with canine idiopathic pulmonary fibrosis [CIPF], 15 with cardiogenic pulmonary edema [CPE], and 22 with bacterial pneumonia [BP]) and 72 healthy controls.

Methods: The study was conducted as a prospective cross-sectional observational study. CRP was measured in serum samples. Diagnosis was confirmed by clinical and laboratory findings, diagnostic imaging, and selected diagnostic methods such as cytological and microbiological analysis of respiratory samples, echocardiography, and histopathology.

Results: Dogs with BP had significantly higher CRP concentrations (median, 121 mg/L; interquartile range, 68–178 mg/L) than dogs with BTB (23, 15–38, $P = .0003$), CB (13, 8–14, $P < .0001$), EBP (5, 5–15, $P < .0001$), CIPF (17, 10–20, $P < .0001$), or CPE (19, 13–32, $P < .0001$) and healthy controls (14, 8–20, $P < .0001$). Dogs with BTB had significantly higher CRP concentrations than dogs with CB ($P = .001$) or EBP ($P < .0001$) and healthy controls ($P = .029$).

Conclusion and Clinical Importance: These results indicate that CRP has potential for use as an additional biomarker, especially in the diagnostics of BP.

Key words: Acute-phase protein; Canine; Pneumonia.



Domanjko Petroc et al. Acta Vet Scand 2016;56:20
https://doi.org/10.1186/s13028-016-0372-4

Acta Veterinaria Scandinavica

RESEARCH

Open Access

Systemic inflammation in dogs with advanced-stage heart failure

Aleksandra Domanjko Petroc¹, Tajda Lukman, Barbara Verk and Anelka Nemec Svetec

Abstract

Background: Although human studies have shown that inflammation plays a role in the development of congestive heart failure, scarce information exists on white blood cell count (WBC) and differential cell counts in various stages of heart failure in man and dogs. A few studies demonstrated increased concentrations of C-reactive protein (CRP), a major acute-phase protein, in cardiac diseases in dogs. Our research aimed to investigate whether CRP concentration, WBC, and neutrophil count (NEUT), as markers of systemic inflammation, are elevated in canine cardiovascular patients. We also aimed to find out whether there is an association between CRP concentration and WBC, and NEUT, as well as associations between these inflammatory markers and selected echocardiographic parameters. Sixty-two client-owned canine cardiac patients and 12 healthy dogs were included in the study. The patients were classified into International Small Animal Cardiac Health Council classes (ISACHC I–III). The serum CRP concentration was determined using a canine CRP test kit. WBC and NEUT were determined using an automated hematology analyzer.

Results: Significantly higher serum CRP concentration, WBC, and NEUT were found in the decompensated stage of heart failure (ISACHC III) compared with healthy dogs and with patients in ISACHC group I and ISACHC group I. Serum CRP concentration significantly positively correlated with WBC ($r = 0.65$, $P < 0.001$) and NEUT ($r = 0.58$, $P = 0.002$) in the ISACHC III group, while no significant correlations were found in the ISACHC I and I groups. A significant negative correlation between serum CRP concentration and the left ventricular ejection fraction ($r = -0.49$, $P = 0.046$) and a significant positive correlation between CRP and the E wave velocity of the mitral valve inflow ($r = 0.52$, $P = 0.046$) were found in the ISACHC III group.

Conclusions: The CRP concentration, WBC, and NEUT were significantly increased in advanced-stage heart failure patients in comparison with compensated patients and healthy dogs, which indicate the presence of systemic inflammation. However, normal CRP concentration and normal WBC and NEUT can also be present in heart failure.

Keywords: Congestive heart failure, C-reactive protein, Dogs, Leukocytes, Neutrophils

Background Inflammation plays a role in the pathogenesis and progression of many forms of heart failure, and biomarkers of inflammation have become the subject of intensive investigation in human and veterinary medicine [1, 2]. In humans, C-reactive protein (CRP), measured using a high-sensitivity CRP assay (hsCRP assay), as a marker of inflammation has received the most attention [3–5]. Concentrations of CRP previously considered to be normal have been shown to predict future cardiovascular events independently in initially healthy individuals, as well as in human cardiovascular patients [6–8]. CRP is a major acute-phase protein in dogs that is characterized by a marked change in serum concentration consistent with systemic inflammatory activity [9–11]. It is produced primarily by the liver in response to proinflammatory cytokines, such as interleukin-1, interleukin-6 and tumor necrosis factor alpha [9, 12]. Several clinical studies have demonstrated significant alterations in some of the inflammatory markers in canine cardiovascular patients [13–18]. Increased concentrations of CRP have been demonstrated in acquired [14, 16–18] and congenital [19] cardiac disease in dogs.

*Correspondence: alexandra.domanjko@vetinst.hr
1Small Animal Clinic, Veterinary Faculty, University of Ljubljana, Ljubljana, 61100, Slovenia



© The Author(s). 2016. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

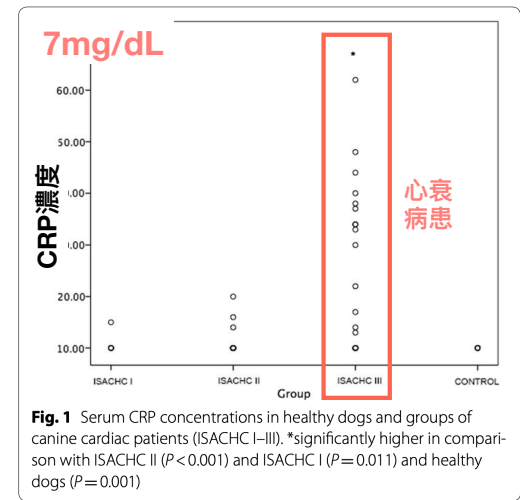
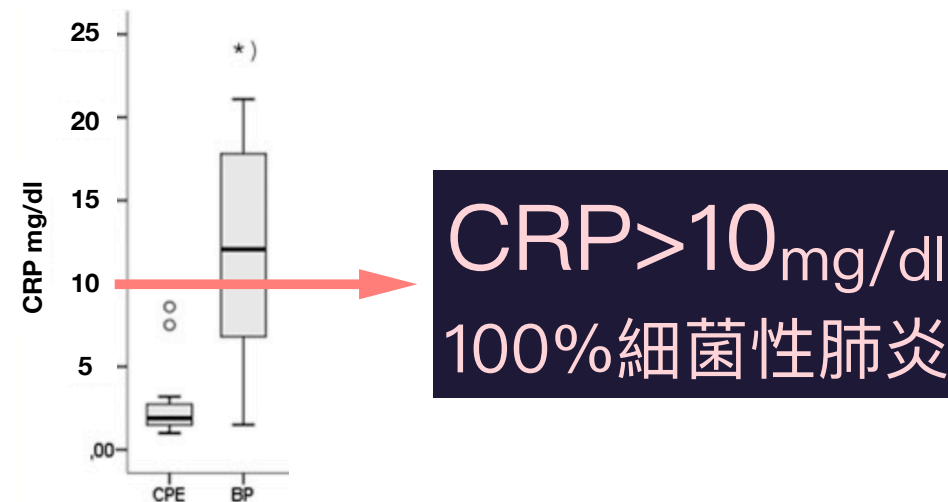
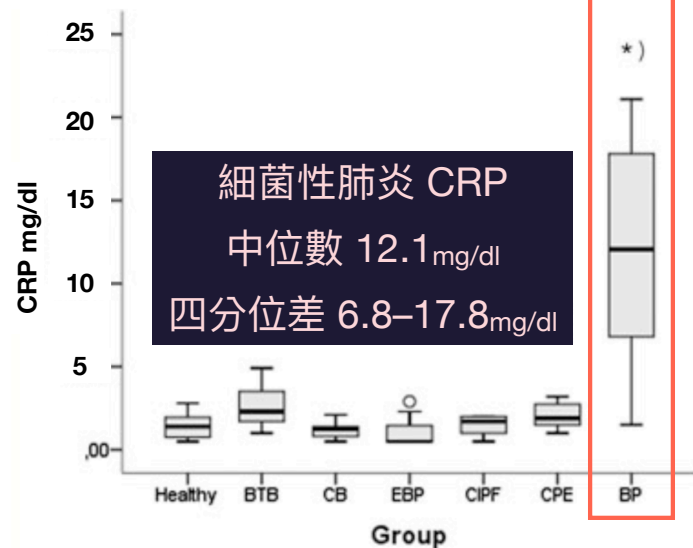


Fig. 1 Serum CRP concentrations in healthy dogs and groups of canine cardiac patients (ISACHC I–III). *significantly higher in comparison with ISACHC II ($P < 0.001$) and ISACHC I ($P = 0.011$) and healthy dogs ($P = 0.001$)



● 幫助區別診斷

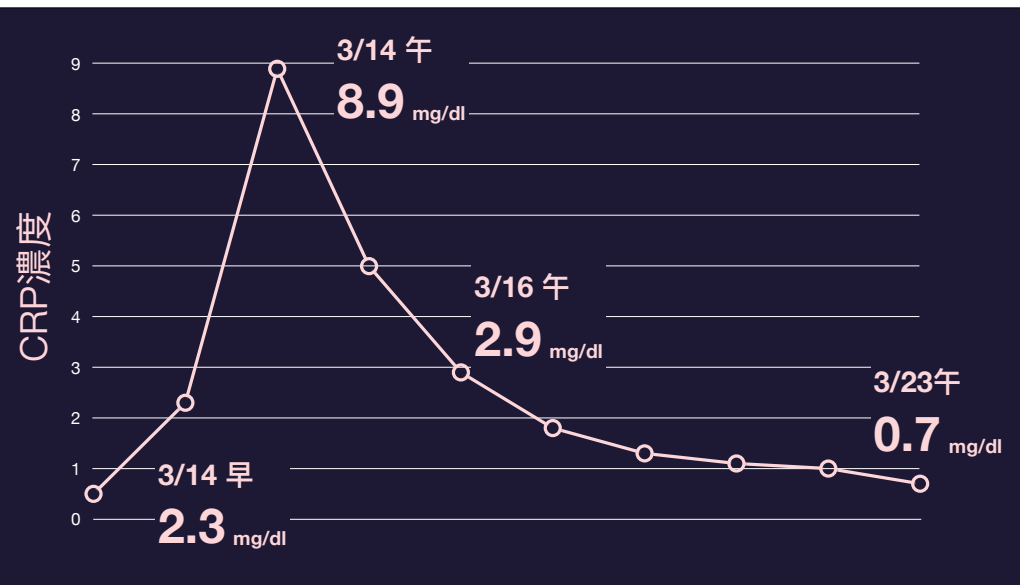
- ① CRP > 9-10 細菌性肺炎
- ② 肺積水 CRP 大多 < 5
- ③ 發病一天才達到最高值

CRP

● 追蹤疾病進展

- ① 每天追蹤一次
- ② 下降趨勢逐漸趨緩

CRP



● 追蹤疾病進展

- ① 每天追蹤一次
- ② 下降趨勢逐漸趨緩
- ③ 評估是否停藥

CRP

The Utility of Acute-Phase Proteins in the Assessment of Treatment Response in Dogs With Bacterial Pneumonia

S.J. Viitanen, A.K. Lappalainen, M.B. Christensen, S. Sankari, and M.M. Rajamäki

Background: Acute-phase proteins (APPs) are sensitive markers of inflammation, and serum C-reactive protein (CRP) recently has been shown to be a useful diagnostic marker in dogs with bacterial pneumonia (BP). In humans with community-acquired pneumonia, APPs also have great utility as follow-up markers aiding in the assessment of treatment response.

Objectives: The aim of our study was to investigate the applicability of APPs as markers of treatment response in dogs with BP.

Animals: Nineteen dogs diagnosed with BP and 64 healthy dogs.

Methods: The study was conducted as a prospective longitudinal observational study. Serum CRP, serum amyloid A (SAA), and haptoglobin concentrations were followed during a natural course of BP. Normalization of serum CRP was used to guide the duration of antibiotic treatment (treatment was stopped 5–7 days after CRP normalized) in 8 of 17 dogs surviving to discharge; 9 of 17 dogs were treated according to conventional recommendations.

Results: All measured APPs initially were significantly increased, but the magnitude of increase was not correlated to disease severity. C-reactive protein and SAA concentrations decreased rapidly after initiation of antimicrobial treatment. When normalization of serum CRP was used to guide the duration of antibiotic treatment, treatment duration was significantly ($P = .015$) decreased without increasing the number of relapses.

Conclusions and Clinical Importance: Serum CRP and SAA reflected the recovery process well and therefore may be used as markers of treatment response. According to the results, the normalization of serum CRP may be used to guide the duration of antibiotic treatment in dogs with BP.

Key words: Canine; C-reactive protein; Haptoglobin; Serum amyloid A.

抗生素使用天數中位數

傳統治療

35

CRP正常後
5–7天停藥組

21



Lasix沒效怎麼辦？

- ① 更高劑量
- ② 其他種利尿劑
- ③ 強心/升壓藥/血管擴張劑
- ④ 也許他不是肺積水!?

也許他不是肺積水!?

X光

CRP

超音波

病例分享



王文彥 獸醫師

2016 台大獸醫系畢業
2018 專心動物醫院
心臟科住院醫師訓練結業
2018 日本大學心臟內科外科診療見習
2019 日本 FASAVA研究發表
2019 日本動物循環器病學會研究發表
2019 心傳動物醫院主治醫師

病例一

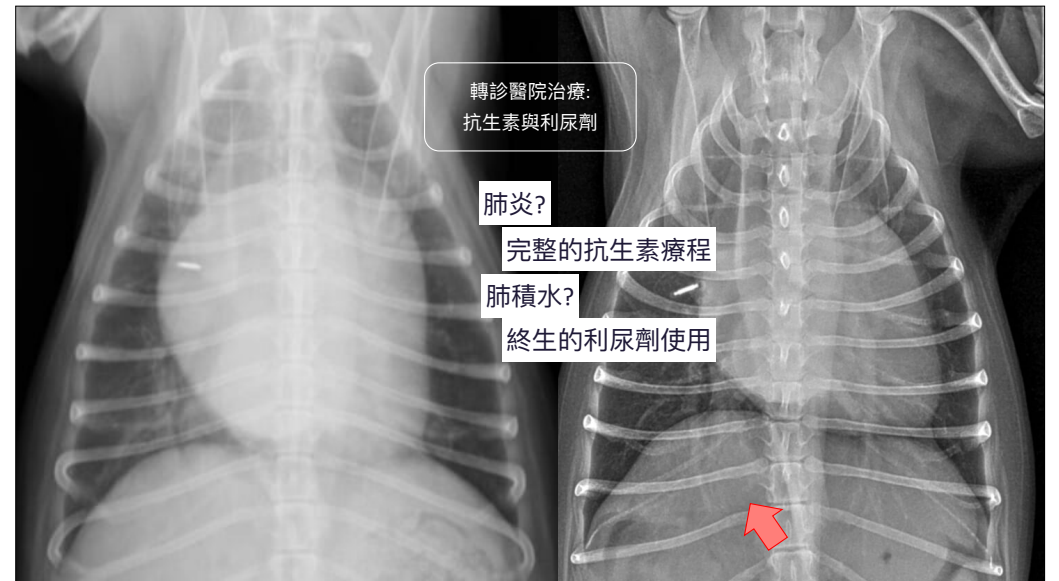
小乖, 12y/o, F/S, Poodle

2020/3 初診, 心臟檢查

C.C. Syncope and tachypnea

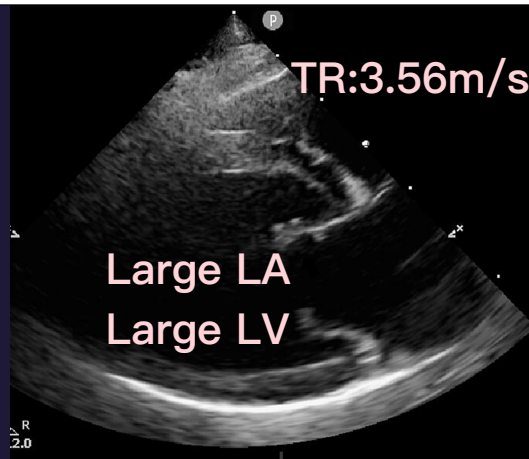


WBC:
20.53K/ μ L



Reference Intervals (Normal Values)			
WBC	19.33 K/ μ L	5.05 - 16.76	HIGH
NEU	12.64 K/ μ L	2.95 - 11.64	HIGH

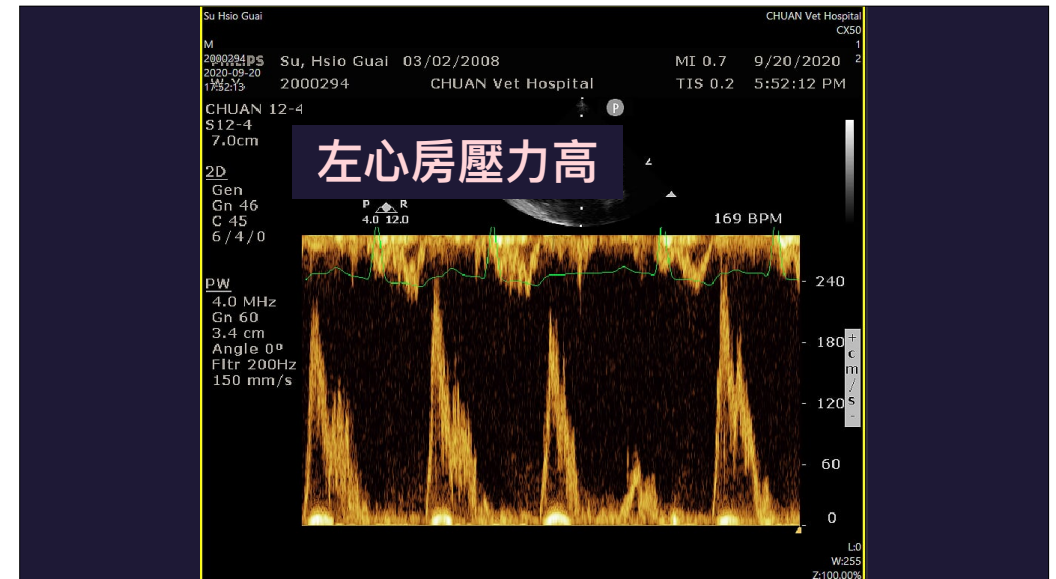
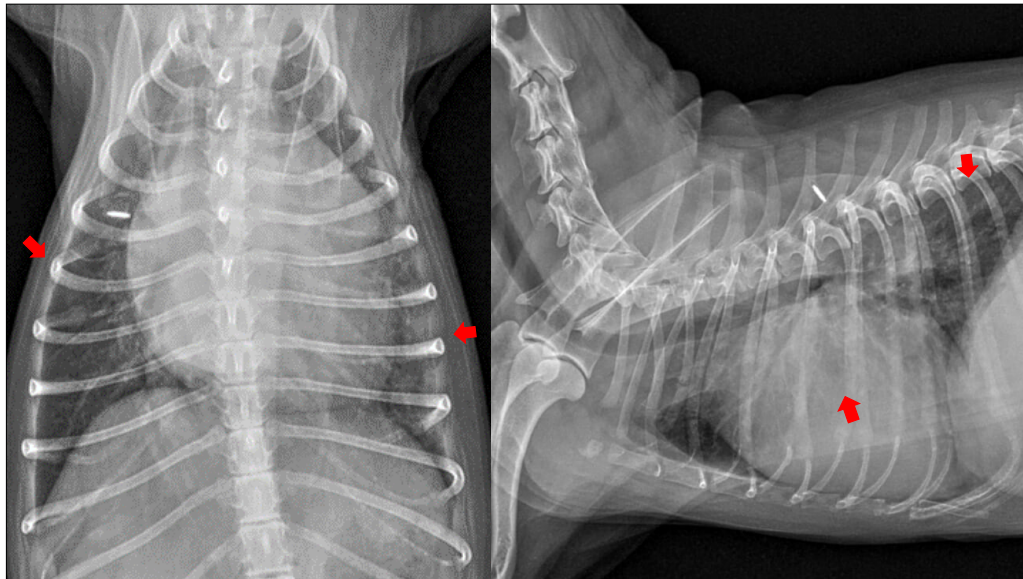
Reference Intervals (Normal Values)			
CRP	3.0 mg/dL	0.0 - 1.0	HIGH



Diagnosis

Mitral valve disease stage C
Moderate Pulmonary hypertension

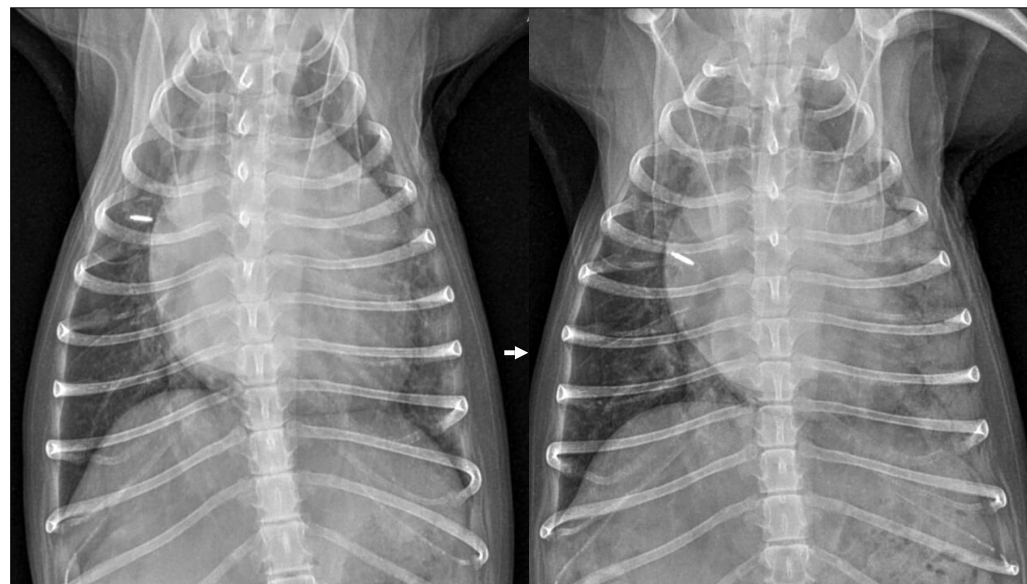
Treatment :
Pimobendan 0.35mg/kg BID
Furosemide 2mg/kg BID
Spironolactone 1.5mg/kg BID
Enalapril 0.3mg/kg BID



住院治療

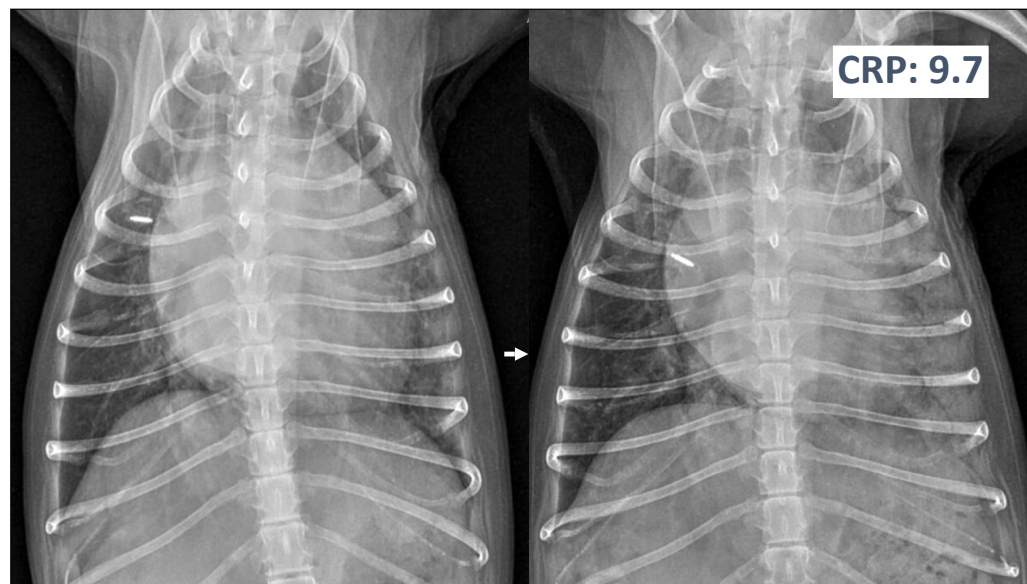
Lasix 1.66mg/kg/hr

ICU RA	小乘	0	0	00:00	00:30	01:00	01:30	02:00	02:30	03:00	03:30	04:00	04:30	05:00	05:30	06:00
BW																4.1
RR				60		66		64		48		52		60		40
狀態				側躺睡		正躺		躺睡		躺睡		躺醒		躺醒		躺睡
TDS				4		3		2		2		2		2		2
HR																150
BT																37.5
ABP																d 120 (2#)



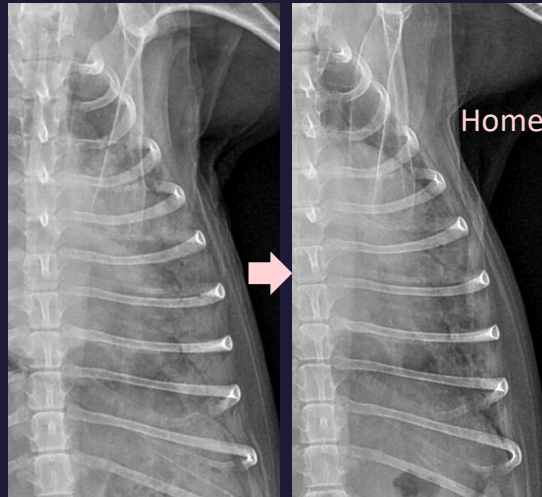
你的下一步驟？

1. 調高利尿劑劑量
2. 加入Torsemide
3. 給予Hydralazine 或Amlodipine
4. 排除其他肺部疾病



After xray and blood exam

Lasix CRI 0.66 - 1mg/kg/hr ↓
+ Enrofloxacin 10mg/kg IV SID
+ Ampicillin 25mg/kg IV TID



Treatment adjustment:

Pimobendan 0.55mg/kg BID
Furosemide 2.25mg/kg BID
Spironolactone 1.5mg/kg BID
Enalapril 0.3mg/kg BID
+Radi-K 0.3mEq/kg TID
+Augmentin 13.75mg/kg BID
+Baytril 5 mg/kg BID

出院後2天回診



出院後10天回診

Catalyst One (2020年10月3日 上午10:43)

CRP	1.7 mg/dL	0.0 - 1.0	HIGH
-----	-----------	-----------	------

C 反應蛋白 (C-Reactive Protein, CRP)

CRP 濃度 >3.0 mg/dL 指示具有顯著臨床意義的全身性發炎。

Catalyst One (2020年10月3日 上午10:29)

CREA	0.8 mg/dL	0.5 - 1.8	
BUN	34 mg/dL	7 - 27	HIGH
BUN/CREA	44		
Na	155 mmol/L	144 - 160	
K	4.3 mmol/L	3.5 - 5.8	
Na/K	37		
Cl	114 mmol/L	109 - 122	



Hints

- 治療反應不如預期時，應積極尋找其他病因
- 心因性肺積水導致CRP上升至極高值機會較低
- CRP可作為病程發展的監控工具，
配合影像協助臨床醫師決定停藥的時機點

病例二

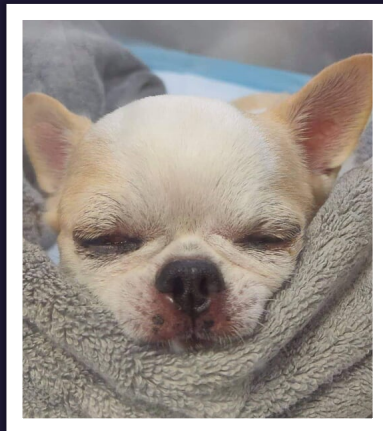
大大,
12y/o, M/I, Chihuahua

2020/8

C.C.

Dyspnea

Shocked when presented



CPR

Oxygen supply , IV catheter,...

Auscultation

HR>200, irregularly irregular rhythm, v/vi systolic heart murmur

ECG

Atrial fibrillation

Treatment

Lasix CRI 2mg/kg/hr

Diltiazem CRI 0.2–0.4mg/kg/hr, gradually tapered after HR slowing down

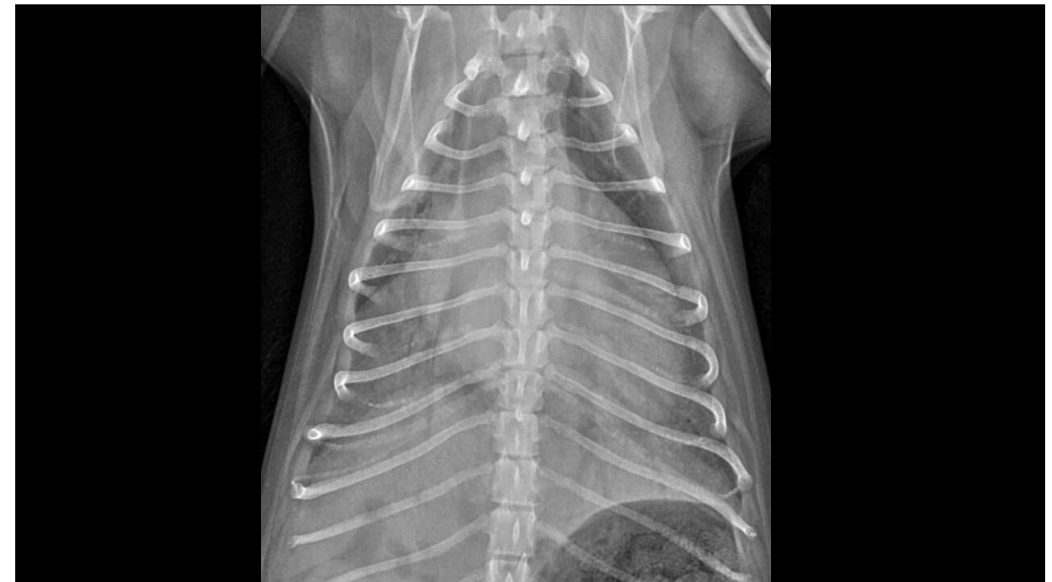
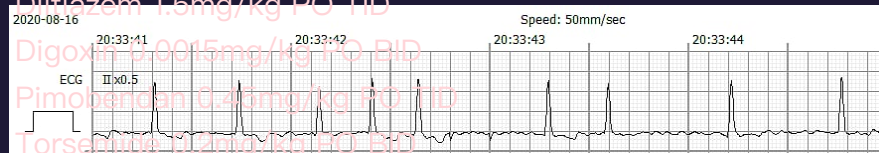
Diltiazem 1.5mg/kg PO TID

Digoxin 0.0015mg/kg q 12h BID

Pimobendan 0.45mg/kg PO TID

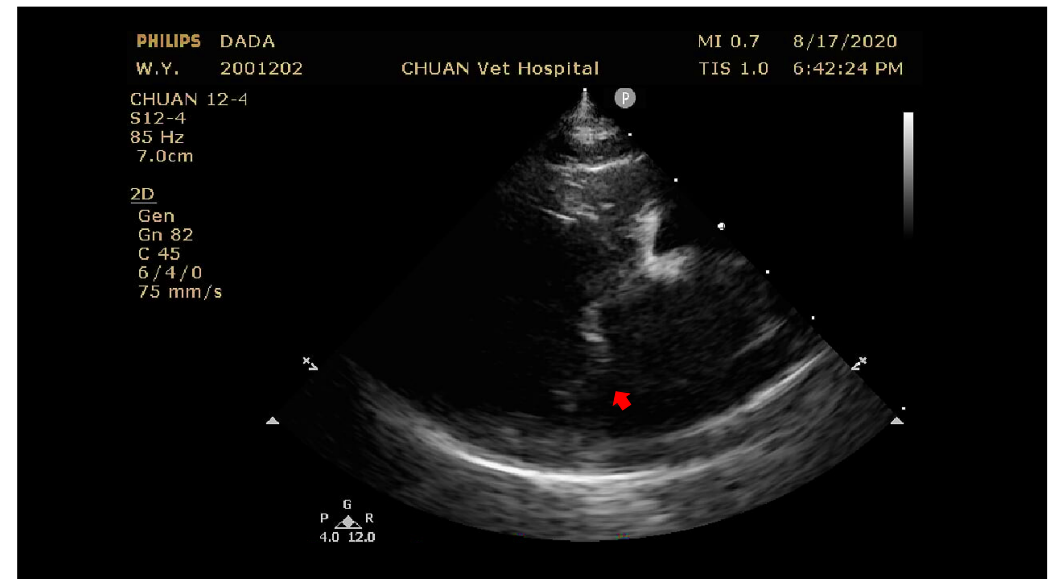
Torsemide 0.2mg/kg PO BID

K-plus PO



WBC	24.93 K/ μ L	5.05 - 16.76	HIGH
NEU	18.34 K/ μ L	2.95 - 11.64	HIGH

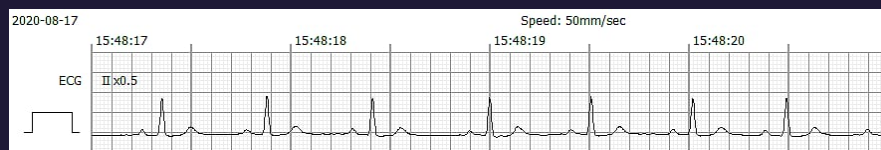
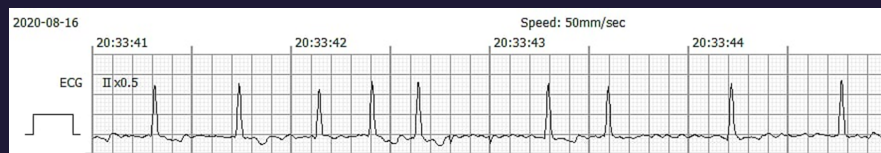
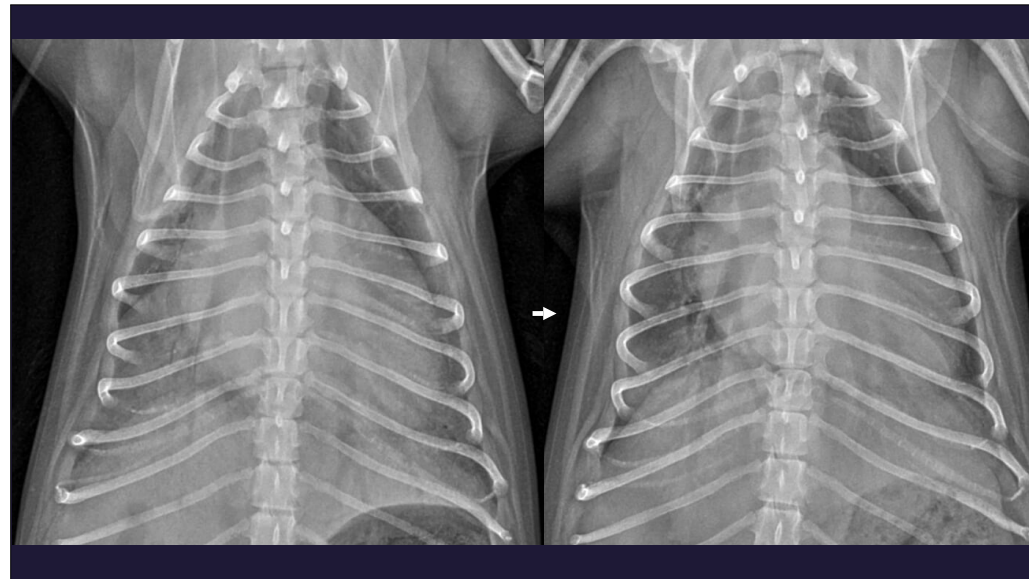
CRP	3.6 mg/dL	0.0 - 1.0	HIGH
-----	-----------	-----------	------



Diagnosis

Mitral valve disease <stage C>

Atrial fibrillation

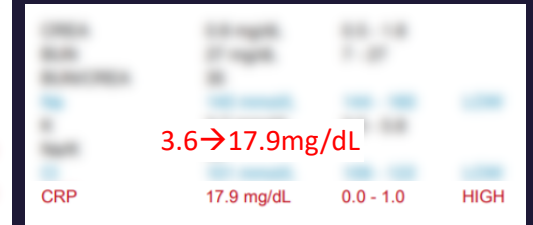
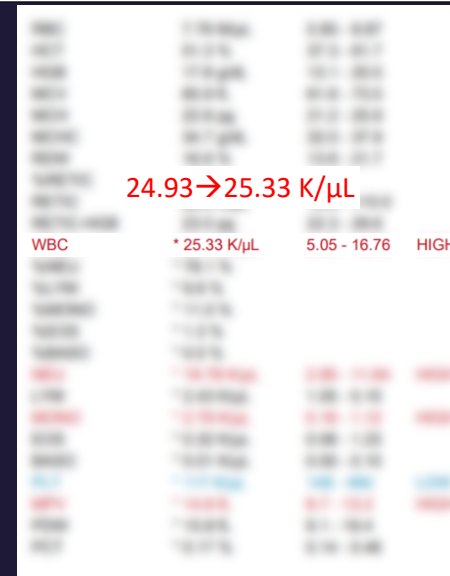


WBC	* 25.33 K/ μ L	5.05 - 16.76	HIGH
-----	--------------------	--------------	------

CRP	17.9 mg/dL	0.0 - 1.0	HIGH
-----	------------	-----------	------

CRP上升的可能原因？

1. 目前肺部的影像可能除了積水還有發炎性的問題
2. (因為休克造成)其他地方可能在發炎
3. 高CRP源自於昨日的嚴重積水
4. 心房震顫導致



Observe !



CRP

8/17
17.9

8/18
7.1

8/19
4.1

Hints

- CRP數值上升有反應期
- 任何部位的發炎都可能導致CRP上升，建議搭配其他診斷工具及臨床症狀做判斷

病例三

肉肉, 11y/o, M/I, Schnauzer

2020/9

C.C.

Increased respiratory effort for few days

Past history

Mitral valve disease stage B1

Moderate Pulmonary hypertension

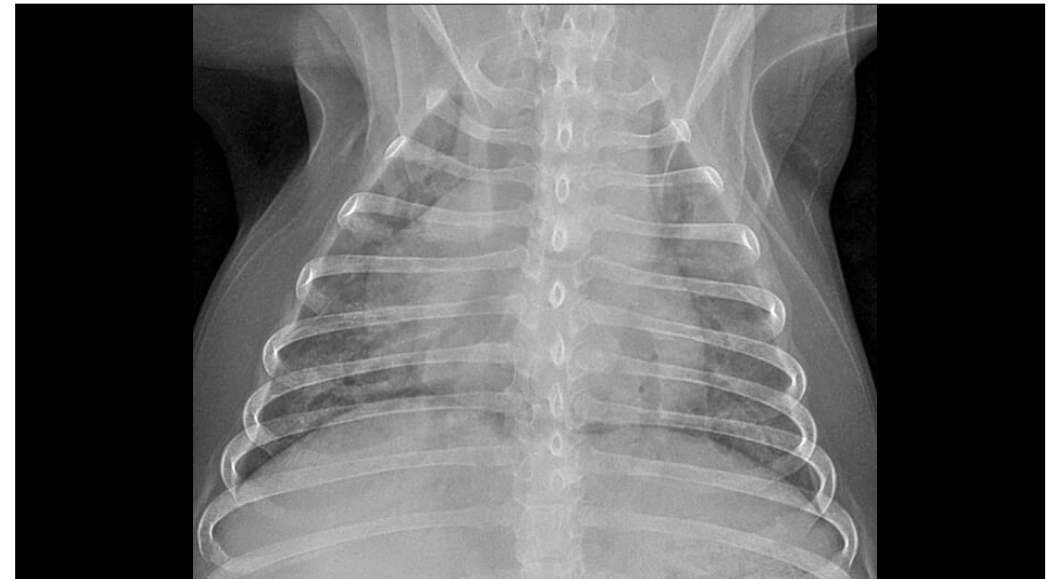
Pulmonary fibrosis suspected by NTU Respiratory clinic

2019/12 Dyspnea, responded to Doxycycline

ProCyte Dx (2020年9月12日 下午8:43)

RBC	6.05 M			
HCT	41.7 %			
HGB	15.7 g/L			
MCV	68.9 fL			
MCH	26.0 pg	21.2 - 26.9	HIGH	
MCHC	37.8 g/dL	32.0 - 37.9		
RDW	17.0 %	13.6 - 21.7		
%RETIC	0.4 %			
RETIC	24.2 K/uL	10.0 - 110.0		
RETIC-HGB	28.8 pg	22.3 - 29.6		
WBC	17.46 K/uL	5.05 - 16.76	HIGH	
%NEU	* 72.1 %			
%LYM	* 14.7 %			
%MONO	* 11.0 %			
%EOS	1.8 %			
%BASO	0.3 %			
NEU	* 12.59 K/uL	2.95 - 11.64	HIGH	
BAND	* 8.6 %			
LYM	* 2.57 K			
MONO	* 1.82 K			
EOS	0.33 K			
BASO	0.05 K			
PLT	* 287 K/uL			
MPV	16.3 fL			
PDW	— fL			
PCT	0.44 %			

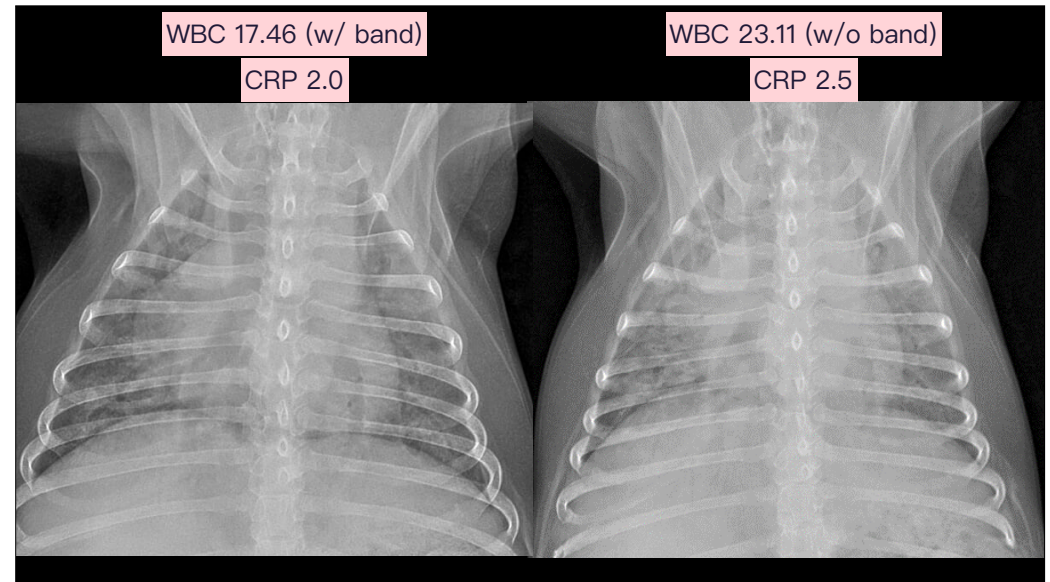
CRP 2.0 mg/dL 0.0 - 1.0 HIGH



Treatment

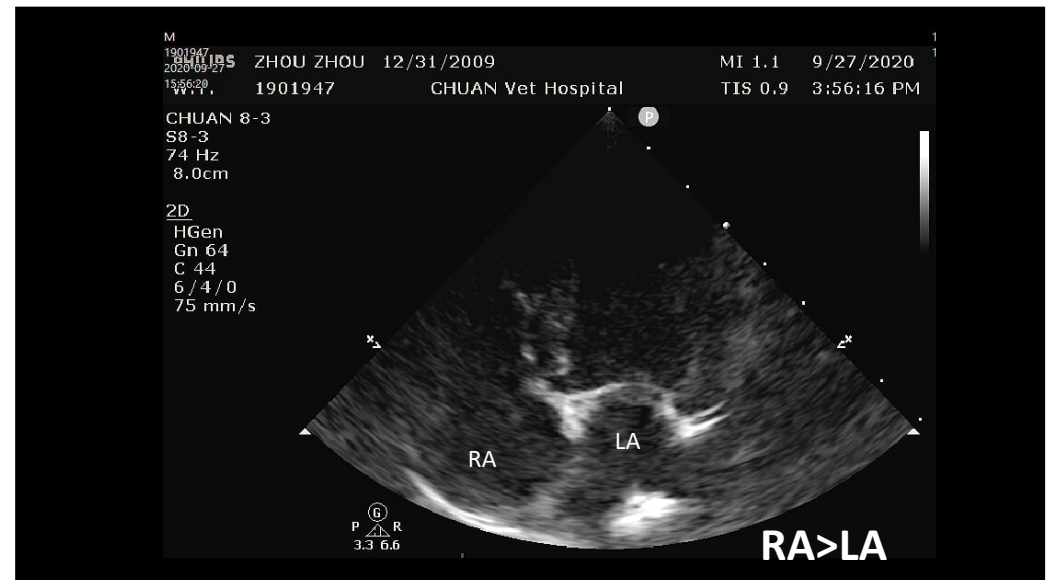
Doxycycline 5mg/kg BID

Acetylcysteine 15mg/kg BID



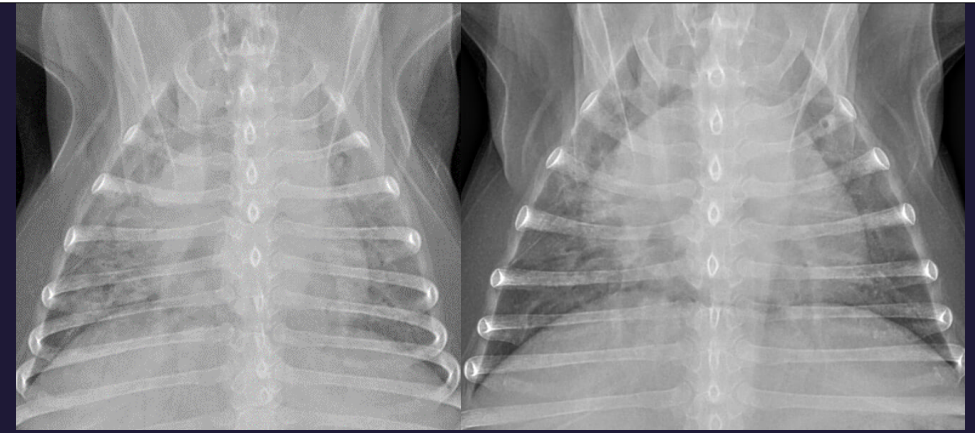
肺部影像惡化的原因？

1. 肺炎惡化
2. 肺纖維化惡化
3. 肺高壓惡化
4. 二尖瓣疾病惡化(肺積水)
5. 其他肺部疾病(建議呼吸道採樣等)



Treatment

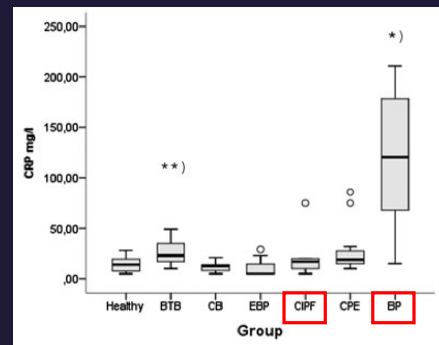
Acetylcysteine 30mg/kg BID
Prednisolone 0.25mg/kg BID
Augmentin 13.75mg/kg BID
Enrofloxacin 5 mg/kg BID
Sildenafil 2.5 mg/kg BID



WBC	17.46	20.44
CRP	2.5	0.7

Hints

- 肺纖維化的確診需依賴電腦斷層與組織病理診斷
- 血液檢查可能幫助尋找是否為其他病因
- 心臟超音波可作為輔助診斷的工具
- 目前無特異性的治療，用藥多為針對症狀或相關的併發症



Vitanen, S. J., et al. "Serum C-reactive protein as a diagnostic biomarker in dogs with bacterial respiratory diseases." *Journal of veterinary internal medicine* 25.1 (2014): 54-61.

感謝聆聽

