4. Results

4.1. Results of section one: The clinical and prognostic significance of radiographic pattern, distribution and severity of thoracic radiographic changes in neonatal foals

4.1.1. Reproducibility of the equine neonatal radiographic scoring system

A total of 207 thoracic radiographs of 128 neonatal foals were evaluated by three independent and blinded interpreters to establish the reproducibility of the radiographic scoring system. The average measure intra-class correlation (ICC) between the three radiographic interpreters was highly reliable with a value of 0.97, 0.96 and 0.93 for the total score, corrected total score and "assessment" score, respectively. The following regional radiographic variables were also highly reliable (ICC > 0.90): regional score (sum), alveolar pattern and alveolar-interstitial sum within the caudodorsal (cd), caudoventral (cv) and the cranioventral (crv) lung region. These nine regional radiographic variables with an ICC > 0.90 (Table 8, I-III), as well as the "assessment" and corrected total scores of each radiograph (ICC = 0.96) were selected for further analysis in the study. A linear correlation analysis revealed that the corrected total score was linearly related to the "assessment" score ($R = 0.9$, $p<0.001$).

Table 8: Objective radiographic scores with an intra-class correlation coefficient (ICC) > 0.9

Radiographic Score	**ICC**
"assessment" score	0.93
corrected total score	0.96
I. Caudodorsal Region:	
cd regional sum (score of the cd lung region)	0.92
cd alveolar-interstitial sum (alveolar-interstitial score of the cd lung region)	0.90
cd alveolar score (alveolar score of the cd lung region)	0.90
II. Caudoventral Region:	
cv regional sum (score of the cv lung region)	0.93
cv alveolar score (alveolar score of the cv lung region)	0.92
cv alveolar-interstitial sum (alveolar-interstitial score of the cv lung region)	0.91
III. Cranioventral Region:	
crv regional sum (score of the crv lung region)	0.93
crv alveolar score (alveolar score of the crv lung region)	0.92
crv alveolar-interstitial sum (alveolar-interstitial score of the crv lung region)	0.91

4.1.2. Radiographic pattern distribution

A total of 75/128 (59%) neonatal foals in this study displayed radiographic changes upon presentation (corrected total score ≥ 1). An additional 14 patients (14/128; 11%) developed pulmonary infiltrates on follow-up films and 39/128 foals (30%) never showed radiographic changes.

We descriptively analyzed the 75 abnormal radiographs obtained upon presentation (Table 9-11). Concurrent radiographic abnormalities within the caudodorsal and caudoventral lung regions were most frequently observed (47/75, 63%). Radiographic changes involving all lung regions were noted in 17/75 (22.7%) foals. In contrast only 8/75 foals showed abnormalities which were limited to the caudodorsal region alone. Therefore, the total number of foals with any abnormalities involving the caudodorsal lung region added up to 72/75 animals (96%). Eighty-nine percent of patients [67/75] showed some form of caudoventral disease. Changes in the cranioventral lung region, however, were only observed in foals with diffuse radiographic disease [17/75]. The distribution of selected radiographic patterns is further described in Tables 10 and 11.

Table 9: Regional distribution of lung disease in 75 abnormal neonatal thoracic radiographs taken within 48 hours of admission

Distribution of radiographic abnormalities [(*)]	**No. (%) of foals affected** [(**)]	**No. (%) survivors**	**No. (%) non-survivors**	**Odds ratio of non-survival**	**95% CI**	**p-value**
caudodorsal (cd) [a] lung field only	8 (10.7)	7 (88)	1 (12)	-	-	-
caudoventral (cv) [b] lung field only	3 (4)	3 (100)	0	-	-	-
cranioventral (crv) [c] lung field only	0	-	-	-	-	-
cd + cv [d]	47 (63)	32 (68)	15 (32)	1.2	0.4 – 3.4	0.70
cd + crv [e]	0	-	-	-	-	-
cv + crv [f]	0	-	-	-	-	-
cd + cv + crv [g]	17 (22.7)	7 (41)	10 (59)	3.6	1 – 14.3	0.02
normal foals	39 [(***)]	28 (72)	11 (28)			

[*] Total number of foals with radiographic changes within in the following lung regions:

- caudodorsal region (a + d + e + g) = 72 (96 %)
- caudoventral region (b + d + f + g) = 67 (89.3 %)
- cranioventral region (c + e + f + g) = 17 (22.7 %)

[**] Total number of foals with radiographic respiratory disease, for which data was available = 75. Overall survival: 49/75 (65%)

[***] Number of foals without radiographic changes during their hospital stay

Table 10: Alveolar pattern distribution in 75 abnormal neonatal thoracic radiographs taken within 48 hours of admission

Distribution of radiographic abnormalities:	**No. (%) of foals affected** [(*)]	**No. (%) survivors**	**No. (%) non-survivors**	**Odds ratio of non-survival**	**95% CI**	**p-value**
caudodorsal (cd) lung field only	6 (8)	4 (67)	2 (33)	-	-	-
caudoventral (cv) lung field only	21 (28)	17 (81)	4 (19)	0.6	0.1 – 2.5	0.43
cranioventral (crv) lung field only	1 (1.3)	0	1	-	-	-
cd + cv	10 (13.3)	4 (40)	6 (60)	3.8	0.7 – 20.7	0.05
cd + crv	1 (1.3)	0	1	-	-	-
cv + crv	1 (1.3)	1	0	-	-	-
cd + cv + crv	5 (6.7)	2 (40)	3 (60)	-	-	-
no alveolar disease present	30 (40)	21 (70)	9 (30)	1.1	0.3 – 3.5	0.87
normal foals	39 [(**)]	28 (72)	11 (28)			

[*] Total number of foals with radiographic respiratory disease, for which data was available = 75. Overall survival: 49/75 (65%)

[**] Number of foals without radiographic changes during their hospital stay

Table 11: Alveolar-interstitial pattern distribution in 75 abnormal neonatal thoracic radiographs taken within 48 hours of admission

Distribution of radiographic abnormalities:	**No. (%) of foals affected** [*]	**No. (%) survivors**	**No. (%) non-survivors**	**Odds ratio of non-survival**	**95% CI**	**p-value**
caudodorsal (cd) lung field only	8 (10.7)	7 (87.5)	1 (12.5)	-	-	-
caudoventral (cv) lung field only	4 (5.3)	4 (100)	0	-	-	-
cranioventral (crv) lung field only	0	-	-	-	-	-
cd + cv	45 (60)	30 (67)	15 (33)	1.3	0.5 – 3.6	0.61
cd + crv	0	-	-	-	-	-
cv + crv	0	-	-	-	-	-
cd + cv + crv	17 (22.7)	7 (41)	10 (59)	3.6	1 – 14.3	0.02
no alv-interstitial disease present	1	1	0	-	-	-
normal foals	39 [**]	28 (72)	11 (28)			

[*] Total number of foals with radiographic respiratory disease, for which data was available = 75. Overall survival: 49/75 (65%)

[**] Number of foals without radiographic changes during their hospital stay

4.1.3. Results of part one: The association between selected clinical parameters and the type of pulmonary radiographic disease manifestation

The first part of section one of this study explored the association between 12 selected clinical parameters (Table 6, I-III) and 4 radiographic variables with an ICC ≥ 0.90 (corrected total score, regional cd, cv and crv scores), using a multiple stepwise linear regression analysis. This analysis served to investigate the impact of clinical findings on distribution and severity of radiographic changes in 75 foals, with radiographic abnormalities upon presentation (Table 12). The presence of tachypnea, a poor suckle reflex and fibrinogen concentration > 400 mg/dL were responsible for 31 % of the variability of the corrected total score ($R^2 = 0.31$, $p<0.0001$) in the final multiple linear regression model.

Individual regional radiographic assessment revealed that significantly higher cd regional scores were observed in tachypneic foals and patients with SIRS (Table 12). However, only 17% of the variability in the cd regional scores could be explained by these variables. Tachypnea was also related to significantly higher cv radiographic scores while a poor suckle reflex decreased scores within the caudoventral lung region. The presence of dyspnea, fibrinogen concentration > 400 mg/dL, and tachypnea were significantly related to radiographic changes within the cranioventral lung region. These clinical variables were responsible for 27% of the variability in the crv regional sum (Table 12).

Table 12: The association between selected clinical parameters and radiographic scores

Radiographic score	n[a]	Clinical variables[b] in the final multiple linear regression model	slope	95% CI of the slope	Sig.	R^2	p-value of R^2
corrected total score	65	Tachypnea	1.14	0.44 – 1.8	.002		
		Fibrinogen > 400 mg/dL	0.44	0.13 – 0.75	.006	.31	< .0001
		Poor suckle reflex	-0.6	(-1.22) – (-0.05)	.033		
cd regional sum	65	Tachypnea	1.2	0.25 – 2.1	.014		
		SIRS	0.9	0.11 – 1.6	.026	.17	.003
cv regional sum	65	Tachypnea	1.6	0.45 – 2.7	.007		
		Poor suckle reflex	-1.3	(-2.2) – (-0.3)	.011	.20	.001
crv regional sum	65	Dyspnea	1.5	0.5 – 2.4	.002		
		Fibrinogen > 400 mg/dL	0.5	0.1 – 0.8	.02	.27	< .0001
		Tachypnea	0.9	0.1 – 1.8	.038		

[a] Number of cases included in the final multivariate model (total: 75 foals with radiographic changes)

[b] Variables entered:

Poor suckle reflex, abnormal respiratory sounds, dyspnea, milk reflux from nares, tachypnea, fever, SIRS, upper airway pathology, immaturity, serum IgG ≤ 400 mg/dL, neutropenia, hyperfibrinogenemia

The term "SIRS" in this study was used to include patients with a modified sepsis score ≥ 11 (Brewer and Koterba 1988; Brewer, Koterba et al. 1988), a positive blood culture or a known focus of systemic infection. In 49/72 (68%) foals, SIRS was identified based on the presence of at least one inclusion criteria. Sixty-three percent of foals (45/71; no sepsis score performed in 4/75 foals) had a sepsis score ≥ 11, while 33% (17/51; no culture performed in 24/75 foals) had a positive blood culture. Both a blood culture and sepsis score could be evaluated in 50/75 foals. Of 34/50 (68%) foals with a sepsis score ≥ 11, thirteen patients also had a positive culture (13/34; 38%). The presence of septic arthritis was considered to be a

known focus of systemic infection and was observed in 10/75 (14.3%) foals with thoracic radiographic abnormalities upon presentation.

4.1.3.1 Arterial blood gas parameters

The association between five arterial blood gas parameters (Table 6, IV) and 4 radiographic variables with an ICC ≥ 0.90 (corrected total score, regional cd, cv and crv scores), was investigated in a subset of 50 foals with arterial blood gas results (67%, 50/75). The prevalence of any selected clinical or radiographic parameter was not significantly different between foals which did (50/75) or did not (25/75) have arterial blood gas results. In the multiple stepwise linear regression analysis, foals with an AG ≥ 20 mEq/L had significantly higher corrected total scores and cd regional scores (Table 13). However, only 11% of the variability in the corrected total scores and cd regional scores could be explained by the anion gap in foals with arterial blood gas results.

Table 13: The association between arterial blood gas parameters and radiographic scores (multiple linear regression analysis)

Radiographic score	**n[a]**	**Clinical variables[b] in the final multiple linear regression model**	**slope**	**95% CI of the slope**	**Sig.**	**R^2**	**p-value of R^2**
corrected total score	43	Anion gap > 20 mEq/L	0.84	0.1 – 1.6	.033	.11	.033
cd regional sum	43	Anion gap > 20 mEq/L	1.02	0.12 – 1.9	.027	.11	.027

[a] Number of cases included in the final multivariate model (total: 50 foals with arterial blood gases)

[b] Variables entered: pH, bicarbonate, P_aCO_2, P_aO_2, Anion Gap

4.1.4. Results of part two: The impact of pattern recognition, distribution, and severity of pulmonary changes on short-term survival

In the second part of section one of this study we investigated the outcome of 128 foals, which had thoracic radiographs taken within 48 hours of admission to TUSVM. A single thoracic radiograph was obtained from 70 patients, while a set of two and three consecutive studies was evaluated in 37 and 21 foals, respectively. Overall, 85/128 (66.5%) patients lived to be discharged, while 10/128 (8%) died naturally, 26/128 (20%) were euthanized and the mode of death was not differentiated in 7/128 (5.5%) animals. At the time of admission, only 75/128 (59%) foals showed radiographic abnormalities. Forty-nine of these 75 foals (65%) survived to be discharged, while 8/26 non-survivors died naturally and 14/26 were euthanized (4/26 unspecified). Fourteen foals (14/128, 11%) developed pulmonary infiltrates that were not evident upon presentation, but were detected on follow-up films. Therefore, only 39/128 foals (30%) never developed radiographic changes and a total of 89/128 animals (70%) were diagnosed with pulmonary radiographic abnormalities while hospitalized. Fifty-seven of these 89 foals (64%) lived to be discharged, while 32/89 (36%) died. Of the 39 normal foals, 28 (72%) lived and 11 (28%) died. The prevalence of any of the selected clinical or radiographic variables was not significantly different between euthanized animals and foals which died naturally. Therefore, for further analysis, the term “non-survival” included foals which had died and those that were euthanized.

Between 1990 and 1998, our neonatal unit also admitted 157 neonatal foals which did not obtain thoracic radiographs within 48 hours of admission. Eighty three percent (131/157) lived to be discharged. The survival rate was significantly different between the selected population of foals which underwent radiographic evaluation and foals which did not have radiographs taken ($p=0.001$). The reason for radiographic analysis was not always defined, but most likely related to a suspicion of respiratory disease.

The thoracic studies of 75 neonatal foals with radiographic evidence of respiratory disease upon presentation were further analyzed to explore the effect of radiographic pattern

and disease distribution on patient survival. The odds of dying were similar for patients with concurrent radiographic disease within the cd and cv lung regions and foals which retained normal radiographs throughout their hospital stay (Table 9). Foals with diffuse radiographic changes (cv + cd + crv), however, were 3.6 times more likely to die than radiographically normal patients (95% CI: 1-14.3; Table 9). Additionally, foals with concurrent alveolar disease within the cd and cv lung regions were 3.8 times more likely to die than normal foals (95% CI: 0.7-20.7; Table 10). The odds of non-survival were similar for animals without alveolar disease, foals with alveolar changes limited to the cv lung region and normal patients.

A univariate (Table 14) and subsequent multiple stepwise logistic regression analysis was performed to evaluate the association between outcome and 4 radiographic variables with an ICC > 0.90 (corrected total score, regional cd, cv and crv scores). Only one variable, the regional score of the caudodorsal lung field (cd regional sum), retained statistical significance in the final multivariate model (n=69). For every one unit increase in cd score, the odds for non-survival were increased by a factor of 1.7 (95% confidence interval: 1.2-2.6; p=0.007).

Table 14: The prognostic significance of radiographic infiltrates on survival of neonatal foals with evidence of pulmonary disease (continuous data; p<0.1):

Criteria [a]	**Non-survivors**		**Survivors**		**p-Value**
	n	mean	n	mean	
Concurrent evaluation of all lung regions:					
"Assessment" score	26	6.2	49	5.2	.028
Corrected total score	26	2.6	49	2.0	.022
Evaluation of individual lung region:					
cd regional sum	26	4.1	49	3.0	.002
cv regional sum	26	3.7	49	3.4	.516
crv regional sum	26	1.5	49	0.6	.023
Evaluation of radiographic changes over time					
Corrected score difference 2-1	15	.97	34	-.05	.004
Corrected score difference 3-1	6	2.4	14	-.82	< .0001
Corrected score difference 3-2	6	.88	14	-1.1	.001

[a] Total number of foals with radiographic respiratory disease upon presentation = 75

4.1.4.1. Radiographic changes over time

In order to describe the type of radiographic changes which developed over time, we analyzed all foals which were diagnosed with pulmonary radiographic abnormalities while hospitalized (89/128). Of these 89 foals, 75/89 animals showed radiographic abnormalities upon presentation, and an additional 14/89 foals developed pulmonary infiltrates that could only detected on follow-up films.

A total of 49/89 (77%) foals with radiographic abnormalities during their hospital stay, had sequential thoracic radiographs taken. The change in radiographic appearance over time was significantly associated with outcome in all patients (Table 14), with a positive corrected

score difference indicating progression of radiographic disease in the follow-up film. A negative corrected score difference determined the resolution of radiographic changes. Foals with a positive corrected score difference were significantly more likely to die than animals with a negative corrected score difference. The strongest association between changes in radiographic appearance and outcome was observed when comparing the final thoracic radiograph (rad3) to the initial thoracic radiograph (rad1) (corrected score difference 3-1, $p<0.0001$) although all comparisons (rad2 to rad1 and rad3 to rad2) obtained statistical significance ($p=0.004$ and $p=0.001$, respectively; Table 14).

We further evaluated the difference in radiographic patterns and disease distribution between rad 3 and rad1 (n=20). Foals with radiographic abnormalities upon presentation, showed improvement of the cd and cv lung regions over time, while radiographic abnormalities within the cranioventral lung region deteriorated. Similarly, the cd and cv alveolar patterns improved, while the crv alveolar pattern became more severe over time. Foals which were normal upon presentation but had radiographic abnormalities on follow-up films, showed more severe pulmonary infiltrates in all three lung regions on repeated radiographic evaluation. These increased opacities were most commonly related to more pronounced interstitial lung infiltrates. The most prominent changes were noted in the caudoventral lung region. Alveolar infiltrates did not change significantly in these foals over time.

Foals were hospitalized for a mean of 8.8 days (range: 0-38) in this study. A significant difference in the duration of hospitalization was observed between survivors (mean = 11 days) and non-survivors (mean = 4.8 days) (mean difference: 6.2 days, 95% CI: 3.5-8.8; $p<0.0001$), but not between foals that had died and those that were euthanized. On average, rad 1 and rad 2 were obtained 3.3 days apart, while a mean of 6.1 days elapsed between rad 2 and rad 3, in patients with repeated diagnostic imaging.

4.2. Results of section two: Risk factors and prognostic variables for survival of foals with radiographic evidence of pulmonary disease

A total of 163 neonatal foals had standing or recumbent thoracic radiographs taken within 48 hours of admission at TUSVM (1990-1998). 121/163 animals (74.2%) were diagnosed with pulmonary radiographic abnormalities while hospitalized. The prevalence of radiographic abnormalities was not significantly different between thoracic images obtained standing or in lateral recumbency of the patient.

4.2.1. Results of part one: Clinical variables, which may predispose neonates or indicate respiratory disease

The first part of section two of our study explored the association between selected clinical parameters (Table 7) and the incidence of pulmonary radiographic abnormalities, by comparing 121/163 patients with radiographic pulmonary disease (PD) to the foals without radiographic changes (no disease, ND: 42/163; Table 15). A diagnosis of upper airway disease was significantly associated with the presence of radiographic pulmonary abnormalities ($p=0.012$), while a respective correlation could not be established for patients with dyspnea ($p=0.074$). IgG concentrations $\leq$ 400 mg/dL were noted in 47/148 (31.8%) patients and were positively correlated with the presence of radiographic changes ($p=0.034$). The diagnosis of immaturity or patent urachus did not predict radiographic abnormalities, with $p=0.070$ and $p=0.074$, respectively. A complete blood count and chemistry profile was obtained from 150/163 (93%) foals at the time of admission. No single hematologic parameter, however, was significantly associated with radiographic evidence of lower respiratory disease.

Table 15: Univariate analysis of clinical & laboratory findings, as indicators of equine neonatal pulmonary disease [p < 0.1]

Criteria	n[a]	No. diagnosed (%) with criteria	No. of PD foals (%) with criteria	No. of PD foals (%) without criteria	p - Value
Dyspnea	163	17 (10.4)	16 (94.1)	105 (71.9)	.074 [b]
Patent urachus	163	17 (10.4)	16 (94.1)	105 (71.9)	.074 [b]
Upper airway pathology	163	15 (9.2)	15 (100)	106 (71.6)	.012 [b]
Immaturity	163	26 (16)	23 (88.5)	98 (71.5)	.070
IgG ≤ 400 mg/dL	148	47 (31.8)	41 (87.2)	72 (71.3)	.034

[a] Number of foals for which data was available.

Total number of foals equals 163 (121 with radiographic evidence of pulmonary disease, 74.2%).

[b] Fischer's exact test

A stepwise multiple logistic regression analysis was subsequently performed including all variables with data in more than 131/163 foals (80%) and a p-value < 0.1 in the univariate model: dyspnea, patent urachus, upper airway pathology, immaturity and an IgG concentration < 400 mg/dL. Only failure of passive transfer retained statistical significance in the final multivariate model (n=148). Foals with an IgG concentration < 400 mg/dL were 2.7 times more likely to show radiographic evidence of pulmonary disease (95% confidence interval: 1.0-7.2; p = 0.043), if all other parameters in the model remained equal.

4.2.1.1. Arterial blood gas analysis

An arterial blood gas (temperature corrected analysis) was obtained from 86/163 (52.8%) foals within 24 hours of admission. The prevalence of any selected clinical parameters (Table 7), including outcome and occurrence of lower respiratory disease, was not significantly different between foals which did (86/163) or did not (77/163) have arterial blood gas results.

The association between arterial blood gas parameters (pH, bicarbonate, P_aCO_2, P_aO_2, anion gap) and radiographic evidence of pulmonary disease was therefore explored using the subset of 86 foals with arterial blood gas analysis results. In the univariate analysis, only hypoxemia (P_aO_2, < 60 mmHg) was significantly associated with radiographic pulmonary disease (p=0.026). The subsequent multivariate analysis of arterial blood gas results in 75/86 foals, showed that hypoxemic patients were 4.9 times more likely to show radiographic evidence of pulmonary disease (95% confidence interval: 1.4 – 17.1; p = 0.01).

4.2.1.2. Systemic inflammatory response syndrome (SIRS)

Similar to section one the term "SIRS" in this study was used to include patients with a modified sepsis score ≥ 11 (Brewer and Koterba 1988; Brewer, Koterba et al. 1988), a positive blood culture or a known focus of systemic infection. In 93/163 (57%) foals, SIRS was identified based on the presence of at least one inclusion criteria. Fifty-one percent of foals (78/154; no sepsis score performed in 9/163 foals) had a sepsis score ≥ 11, while 32 % (34/106; no culture performed in 57/163 foals) had a positive blood culture. Both a blood culture and sepsis score could be evaluated in 104 foals. Of 57/104 (55%) foals with a sepsis score ≥ 11, 33% (19/57) also had a positive culture. The diagnosis of septic arthritis was considered to represent a known focus of systemic infection and was observed in 25/163 (15.3%) foals with radiographic evidence of pulmonary disease. A negative blood culture was obtained in 38% (8/21) of these patients.

4.2.2. Results of part two: Clinical variables, which may predict survival of foals with radiographic evidence of pulmonary infiltrates

The second part of section two of our study explored the potential role of selected clinical and laboratory variables (Table 16) as prognostic indicators for survival in 121 foals, with radiographic evidence of pulmonary disease. Sixty-nine percent (83/121) of all foals with radiographic abnormalities were discharged alive from the hospital. Of the 38 dead foals, 21

were euthanized, 12 died naturally and for five animals the type of death was not specified. The prevalence of any of the selected clinical and laboratory variables was not significantly different between euthanized animals and foals which died naturally. Therefore, for further analysis, the term "non-survival" included foals which had died and those that were euthanized.

Table 16: Univariate analysis of the association between survival and clinical and laboratory variables in neonatal foals with radiographic pulmonary disease [$p < 0.1$]

Criteria	**n**[a]	**No. diagnosed (%) with criteria**	**No. survivors (%) with criteria**	**No. survivors (%) without criteria**	**p - Value**
Dystocia	121	10 (8.3)	3 (30)	80 (72.7)	.011 [b]
Depression	121	45 (37.2)	26 (57.8)	57 (75)	.049
Poor suckle reflex	121	27 (22.3)	15 (55.5)	68 (72.3)	.098
Dyspnea	121	16 (13.2)	7 (43.8)	76 (72.4)	.022
SIRS	121	70 (58.9)	43 (61.4)	34 (77.3)	.079
Hyperkalemia [K > 4.7 mEq/L]	109	10 (10.9)	4 (40)	68 (68.7)	.086 [b]
Increased creatinine [Creatinine > 1.7 mg/dL]	109	23 (21.1)	9 (42.9)	63 (73.3)	.002
pH (arterial pH < 7.3)	67	12 (17.9)	4 (33)	38 (69.1)	.044 [b]
Anion gap [AG ≥ 20 mEq/L]	58	24 (41.4)	7 (29.2)	28 (82.4)	.000

[a] Number of foals for which data was available. Total number of foals = 121 (83 survivors; 69%).

[b] Fischer's exact test

Forty-two of 163 foals (26%) in this study did not show evidence of radiographic abnormalities during their hospital stay and served as controls. Seventy-four percent (31/42) of these patients lived to be discharged. The survival rate was not significantly different between controls and foals which radiographic evidence of respiratory disease.

Among the historical and physical examination parameters of foals with radiographic pulmonary disease, the presence of dyspnea, depression or dystocia were significantly associated with non-survival in the univariate model (Table 16, $p<0.05$). Evaluation of laboratory data showed that foals with an initial creatinine concentration above 1.7 mg/dL were significantly more likely to die than patients with a lower creatinine concentration.

The most common diagnosis in foals with thoracic radiographic abnormalities was SIRS (70/121, 58.9%), while failure of passive transfer (FPT, IgG concentration ≤ 400 mg/dL) was noted in 41/113 patients (36.3%; IgG concentration was not measured in 8/121 foals). Diarrhea (33/121, 27.3%), omphalitis (25/121, 20.7%), immaturity (23/121, 19%) and hypoxic ischemic encephalopathy (18/121, 14.9%) were observed with decreasing frequency. None of the above diagnoses, however, significantly predicted outcome. Sixty-five percent (79/121) of foals with radiographic pulmonary disease had multiple concurrent diagnoses (>1 additional diagnosis). The presence or absence of multiple concurrent diagnoses did not have a statistically significant impact on survival of foals with radiographic pulmonary disease. In 55/70 (79%) foals with SIRS and thoracic radiographic changes at least one of following five potential causes or sites of infection was identified: 33/70 (47%) patients had failure of passive transfer, 26/70 (37%) diarrhea, 17/70 (24%) omphalitis, 13/70 (19%) septic arthritis and 13/70 (19%) a patent urachus.

4.2.2.1. Multivariate outcome analysis

The stepwise multiple logistic regression analysis of outcome included all variables with data in more than 97/121 (80%) foals, and a p-value < 0.1 in the univariate model: Historical evidence of dystocia, depression, dyspnea, poor suckle reflex, SIRS, hyperkalemia (K > 4.7 mEq/L) and a creatinine concentration > 1.7 mg/dL (Table 16). Three variables retained statistical significance ($p<0.05$) in the final multivariate model (n=109): A history of dystocia ($p=0.036$), dyspnea ($p=0.023$) and a creatinine concentration > 1.7 mg/dL ($p=0.003$), were all associated with decreased survival rates (Table 17).

Table 17: Multivariate analysis of the association between survival and clinical & laboratory variables in neonatal foals with radiographic pulmonary disease

Variable	n[a]	Exp (B) [odds ratio]	95% Confidence interval	p - Value
Dystocia	109	5.0	1.1 – 22.7	.036
Dyspnea	109	3.9	1.2 – 12.8	.023
Creatinine > 1.7 mg/dL	109	4.9	1.7 – 13.6	.003

[a] Number of foals included in the multivariate analysis. Total foals with pulmonary disease = 121

4.2.2.2. The impact of arterial blood results and anion gap on survival

The association between arterial blood gas parameters (pH, bicarbonate concentration, P_aCO_2, P_aO_2, anion gap) and survival of foals with respiratory disease was explored in all foals with arterial blood gas results (67/121). The P_aCO_2 showed a negative linear correlation with arterial pH ($p<0.001$) and a positive linear correlation with arterial bicarbonate concentration ($p<0.001$). Subsequent descriptive blood gas analysis showed that 29/40 patients (72.5%) with primary acidemia had a respiratory acidosis with a $P_aCO_2 \geq 50$ mmHg, while a metabolic acidosis was noted in only 5/40 (12.5%) and mixed acid-base changes in 6/40 (15%) animals. Forty-six percent of patients with a primary respiratory acidosis (12/26,

no AG available in 3/29) also had an AG ≥ 20 mEq/L. All arterial blood gas analyses were obtained from foals over 6 hours of age.

An arterial pH < 7.3 was significantly related to non-survival (p=0.044). Increases in anion gap (AG ≥ 20 mEq/L), however, retained the highest statistical significance in the univariate outcome analysis (p<0.0001). 17/24 (71%) foals with an anion gap ≥ 20 mEq/L died, compared to 6/34 (18%) non-survivors with an anion gap < 20 mEq/L (p<0.001). The subsequent multivariate analysis of arterial blood gas results in 58/67 foals, showed that foals with an AG ≥ 20 mEq/L were 11.3 times more likely to die than foals with an AG < 20 mEq/L (95% confidence interval: 3.3 – 39.4; p < 0.0001), if all other parameters in the equation remained equal.

The presence of SIRS, dystocia and low pH were positively related to a high anion gap (p ≤ 0.05) within our study population. Additionally, hyperkalemia and a creatinine concentration > 1.7 mEq/L were significantly associated with an AG ≥ 20 mEq/L (p ≤ 0.05). Severe arterial hypoxemia (P_aO_2 ≤ 55 mmHg) was also related to an AG ≥ 20 mEq/L (p=0.058).