Septic peritonitis, a prospective study of VAC assisted drainage versus open abdominal drainage: a midway analysis of 8 cases.

Abstract
Septic peritonitis is a life threatening and challenging problem that requires emergency surgery. In human medicine VAC-therapy (vacuum assisted drainage) has been successfully used for the treatment of septic peritonitis. This technique has been adapted for veterinary medicine and is thought to be an effective alternative for the classic open abdominal drainage therapy. This study focuses on a mid-way analysis of an ongoing research, comparing the cost and effectiveness of vacuum assisted abdominal drainage to classic open abdominal drainage therapy. Results off 8 cases were gathered, including blood and peritoneal fluid parameters, and there was an inquiry with owners to determine the course of recovery after discharge. Current cases presented statistically significant differences in protein losses. The cost of vacuum assisted closure therapy is higher than the cost of the classic open drainage method.

Introduction

Septic peritonitis is a challenging problem in veterinary medicine and is a life threatening condition that asks for immediate surgical intervention. Septic peritonitis is the result of a bacterial contamination of the abdomen and has several causes including perforation with corpus aliena, neoplasia, dehiscence of previous surgical wounds, urogenital infection, haematogenous spread and pancreatic disease but can also be found as a primary problem. (Swayne et al., 2012, Buote and Havig, 2012) Septic peritonitis has a high mortality with a wide variation between 20 and 80% in dogs and requires a quick diagnosis and treatment. (Hosgood and Salisbury, 1988; Woolfson and Dulisch, 1986; Lanz et al., 2001; Levin et al., 2004)

Suspecting a diagnosis of septic peritonitis is based on several criteria. These include history, physical examination and clinical signs and can be confirmed using diagnostic imaging, cytology of peritoneal fluid and/or bacterial cultures and lactate glucose ratios measured in blood and peritoneal fluid. Conformation of the suspected septic peritonitis is based on one of three criteria: cytological presence of (intracellular) bacteria in aspired abdominal fluid, positive bacterial cultures of aspired abdominal fluid or confirmed contamination of rupture during surgical intervention or during post mortem examination. (Swayne et al., 2012)

Another purpose of the culture is to determine the microbial strain of the septic peritonitis. A faster way of diagnosing a septic peritonitis is the use of blood and abdominal fluid parameters with lactate and glucose in combination with cytology or bacterial culture being the most important. For the diagnosis of septic peritonitis using blood and peritoneal fluid lactate and glucose, a lactate concentration of >2,5mmol/L in the peritoneal fluid is considered 91% sensitive and 100% specific. A difference in blood and peritoneal lactate concentration of 2mmol/L is 63% sensitive and 100% specific. (Bonczynski et al., 2003) A difference between blood and peritoneal glucose concentrations of >20mg/dL is also considered 100% sensitive and 100% specific. (Levin et al., 2004)

The main goals of the therapy consist of rapid hemodynamic stabilisation and

control of the infection. To do so, surgical exploration is necessary to identify and eliminate the cause of the infection. The surgery includes a lavage and debridement of the abdominal cavity, mainly focussing on the underlying problem, for example a ruptured intestine. (Cioffi et al., 2012; Craft and Powell, 2012)

Whenever surgery provides insufficient decontamination, drainage of the abdomen is indicated. There is some dispute over the best method of abdominal drainage, which can be realised using open abdominal drainage or vacuum assisted abdominal drainage. Other methods for the management of septic peritonitis after surgery include primary closure and drainage using Penrose drains, multiple lumen sump drains or abdominal dialysis catheters. (Orsher and Rosin, 1984) This study will focus on the differences between open abdominal drainage and vacuum assisted abdominal drainage.

The classic approach of septic peritonitis consists of an open drainage therapy where part of the abdomen is left open to ensure that exudate leaks out of the abdomen. This technique requires labour intensive bandage changes that usually require sedation. (Hosgood, Salisbury and Denicola, 1991) This therapy provides ample drainage and provides easy access for re-exploration of the abdomen. (Staatz, Monnet and Seim, 2002)

Negative pressure therapy, also known as vacuum assisted closure VAC (as marketed by Kinetic Concepts Inc.), is used to temporarily close and drain the abdomen under a constant negative pressure resulting in fluid drainage. Vacuum assisted closure therapy was developed for use in delayed wound healing and has become a promising new technique in the management of contaminated, acute and chronic wounds. (Mouës et al., 2004) VAC was further developed in human medicine to prevent abdominal visceral injury, decrease bowel desiccation, minimize abdominal wall damage, reduce the risk of peritoneal contamination, and control leakage of the abdominal fluid. (Popovic et al., 2012) It has been in use for several years and is now being used in veterinary medicine (Cioffi et al., 2012; Mueller, Ludwig and Barton, 2001) The VAC therapy does not require bandage changes as in the open drainage method.

This report focuses on a midway analysis of the cost and effectiveness of the VAC drainage method compared to the traditional open drainage method. The ongoing study at the University of Utrecht will provide for a larger set of data; however this report will provide a retrospective insight into the current status of the research and a mid-way analysis of the currently acquired data.
The relevance of the study arises from the fact that there have been no comparative retro- and prospective studies comparing open abdominal drainage and VAC therapy in dogs.

Material and Method

Selection criteria

Most of the patients in the study have been admitted as emergency patients. Patients were selected for VAC or open drainage therapy through a blind pick. The minimal requirements for selection included; ultrasonic evaluation of the abdomen and degenerated neutrophils with extra cellular or intracellular bacteria seen on cytology of peritoneal fluid and a positive lactate/glucose ratio (blood and peritoneal fluid). As mentioned in the introduction, differences between blood an peritoneal fluid glucose/lactate parameters can be used as an indicator for septic peritonitis these can aid in selecting patients.

A positive culture of the initial peritoneal fluid was used to confirm a septic peritonitis. Patients that turned out to have underlying malignancies that could influence the outcome of postoperative parameters were excluded from the study.

Parameter collection

Before surgery blood and peritoneal fluids were taken. These have been used for some of the following parameters, as seen fit by the overseeing emergency veterinarian, depending of the case.

Peritoneal fluid:	**Bloodwork:**

• EDTA, cell types and count.
• Culture: Aerobic or anaerobic bacteria
• Antibiogram
• Glucose, Lactate, total protein, albumin, Na+, K, Cl, Lactate, Creatinine, Lipase, Amylase
	• CBC and platelets
	• Biochemistry:
	  ○ Glucose, Na, K, Cl
	  ○ Albumin, Total protein
	  ○ Ureum, Creatinine
	  ○ electrolytes
	  ○ Lactate
	  ○ ALT, AST, AF, bile acids
	  ○ Lipase, amylase
	• Coagulation panel + D-Dimers + Fibrinogen

After the collection of the blood and peritoneal fluid the first exploratory surgery was performed. During this first surgery tissue biopsies were taken from the abdominal wall and omentum of the patients. This was repeated during the closure of the abdomen. These biopsies will later be used for histology.
After the first exploratory surgery the patients were moved to the ICU. During the admission to the ICU the following parameters have been monitored as closely as possible:

Peritoneal fluid:	**Bloodwork (daily):**
• Glucose • Lactate • Quantitative cell count • Qualitative cell count • Cytology smear: degenerated neutrophils, intracellular bacteria /HPF • Quantitative bacterial count • Qualitative bacterial count • • Creatinine, potassium • Protein, albumin • Lipase, amylase	• Glucose Lactate • Ureum, Creatinine • Elekrolytes (Potassium, chloride, Natrium) • Protein • Albumin • CBC • Venous bloodgasses • Alt, Ast, Af, bile acids • Lipase, Amylase

In addition to these parameters there was constant monitoring of the patient. This included heart rate, fluid therapy and pain/discomfort by using the modified composite Glasgow pain scoring system. (Murrell et al., 2008) Finally, the duration of VAC/open abdominal drainage therapy and the duration of hospitalisation were registered.

VAC

In this study the ABThera TM. Open Abdomen Negative Pressure Therapy System was used. When using the ABThera system a spider shaped-dressing is placed in the abdomen between the organs and the abdominal wall during the first exploratory surgery. The dressing consists of two sheets of perforated plastic with a polyurethane layer in between. In the abdominal wound an additional piece of polyurethane foam is placed. This piece is in contact with the dressing and covers the abdominal dressing. Lastly the entire wound is covered with an adhesive polyurethane sheet (not perforated) to create an airtight seal. A negative pressure pump is attached to provide constant negative pressure of -125 mm Hg resulting in constant removal of exudate.

Follow up

To gain insight into the long-term recovery of the patients after their release from the clinic a telephone questionnaire was performed which was later scored.
Scores were based on a scoring system divided into 7 categories. Each category can get a score of 0 to 5 making the total a score of x/35. (table 1)

Criteria	***0 value***	***5 value***
Regaining appetite (food and water).	Immediate appetite after discharge	Still problems with appetite (6months +)
Changes (diet/housing).	No changes	Severe changes in diet, housing and care taking
Problems related to treatment.	No problems reported	Severe changes and hospitalisation or death
Other problems	No problems reported	Severe illness
Behavioural problems	No changes	severe aggression or severe angst.
Wound healing	Fast healing without complications	Difficult healing including desiccation and/or infection.
Endurance	no changes in endurance	Severe exhaustion, unable to go for walks.

***Table 1. Scoring criteria for** questionnaire.*

Statistical method

Using the program SPSS 16.0 blood and peritoneal fluid parameters will be analysed using the Independent-Sample T-Test. To do so, all the gathered parameters were entered into 1 sheet in SPSS. Interesting results could be tested on their significance. A significance level of 0.05 was used.

Results

The mean hospitalisation of patients (table 2) with open drainage therapy was 10.7 days and the mean for patients that received ABThera therapy was 10 days. The mean duration of open drainage therapy was 3 days and 3.75 days for ABThera therapy. It has to be taken into consideration that deceased patients were not used for the average of hospitalisation and therapy because there is no way of predicting the length of their hospitalisation. There was no significant difference in the duration of the therapy neither was there a significant difference in the duration of the hospitalisation. The p values for the duration of the therapy and hospitalisation were 0.24 and 0.88 respectively.

Casenr.	**Age (years)**	**Sex**	**Breed**	**Weight (kg)**	**Dure of Hospitalisation. (days)**	**Days of ABThera of open drainage therapy (days)**	**Etiology and surgery preformed**	**Alive after discharge**
Kancha (1)	5	Male	Crossbreed	20	12	4 (ABThera)	Corpus alienum in the jejunum, anestemose jejunum and exploratory surgery.	Yes
Bonnie (2)	10	Male	Beauceron	27,3	18	2 (ABThera)	Gastric dilatation volvulus , torsion of the spleen. Sleenectomy and exploratory surgery	Yes
Bobbie (3)	11,5	Male	West highland terrier	9,8	10	3 (Open)	Corpus alienum, entrotomy and exploratory surgery	Yes
Dot (4)	12	Female	Labrador retriever	32,	8	4 (ABThera)	Pyometra, OVHX and exploratory surgery	Yes
Ivar (5)	14	Mal	GoldenRetriever	34	2 (deeased)	2 (open)	Septperitonitis (unknown cause)	No
Kaya (6)	5	Female	Shetland Sheepdog	8,8	8	4 (open)	Rupture of the gallbladder, exploratory surgery	Yes
Noa (7)	5	Female	Australian Shepard	21	10	4 (ABThera)	Pierced by steel pin. exploratory surgery	Yes
Simba (8)	8	Female	German Shepard	29,1	6	3 (open)	Dehiscectie colotomie, exploratory surgery	Yes

***Table** 2. Summary of treated patients.*

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Patient		Duration VAC/Open drainage therapy (days)	Total protein before first surgery (g/L)	Total protein before after closure (g/L)	Albumin before first surgery(g/L)	Albumin after closure (g/L)	Total protein loss(g/L)	Albumin loss (g/L)	Average total protein loss per day(g/L)	Average albumin loss per day(g/L)
	Reference		*26-37g/L*	*26-3g/L*	*26-37 g/L*	*26-37g/L*				
Kancha		4 VAC	39.0	29.0	15.0	13.0	-10.0	-2.0	-2.5	-0.5
Bonnie		2 open	38.0	33.0	14.0	11.0	-5.0	-3.0	-2.5	-1.5
Bobbie		3 VAC	50.0	50.0	21.0	21.0	0.0	-0.0	0.0	-0.0
Dot		4 open	54.0	43.0	18.0	14.0	-11.0	-4.0	-2.7	-1.0
Ivar		2 open	63.0	39.0	20.0	13.0	-24.0	-7.0	-12.0	-3.5
Kaya		4 VAC	26.0	48.0	11.0	16.0	+22.0	+5.5	+5.5	+1.25
Noa		4 VAC	26.0	33.0	8.0	11.0	+7.0	+3.0	+1.75	+0.75
Simba		3 open	57.0	41.0	9.0	9.0	-16.0	0.0	-5.3	0.0

Table 3. Parameters for protein and albumin loss

Patient	Day 1			Day 2			Day 3			Day 4		
	GB	GP	Dif	GB	GP	Dif	GB	GP	Dif	GB	GP	Dif
Kancha				6.3	0	**6.3**	7	0	**7**	4.3	3.2	**1.1**
Ivar	3.5	0	**3.5**	4.1								
Bonnie				6.4	0	**6.4**					0	
Bobbie	6.9			15.2						8.1		
Dot	4.2	0.2	**4**	6.1	0	**6.1**	7.4	1.2	**6.2**	7.5	0	**7.5**
Kaya	3.0			6.8			6			6	6	0
Noa	7.4	2.4	**5**	8.3	6.8	**1.5**	7.5	6.1	**1.4**	5.5	4.7	0.8
Simba	4.6	0	**4.6**	5.3	5.3	0	7.9	6.4	**1.5**			

Table 4: GB= Blood glucose in mmol/L, GP= Peritoneal fluid glucose in mmol/L, Dif= Difference between blood and peritoneal fluid glucose in mmol/L. Underlined values are indicative of septic peritonitis according to Levin, 2004 . Blank spaces represent measurements not taken and/or recorded.

Analysis of blood parameters

The mean total protein of dogs with septic peritonitis before the first exploratory surgery was 44.13 g/L and 14.5 g/L for albumin. Open drainage patients had a mean total protein of 39.0 g/L and a mean of 11.75 g/L albumin upon closure. Patients treated with the VAC therapy had a mean total protein of 40g/L and a mean of 15.25 g/L albumin upon closure. Mean losses of total protein and albumin consisted of 14g/L total protein and 3.5g/L albumin in patients with open drainage. Patients receiving VAC therapy had an average mean gain of 4.75 g/L total

protein and 1.5g/L albumin.
The average loss per day in open drainage patients was 5.63g/L total protein and 1.50g/L albumin, while there was a gain of 1.19g/L total protein and 0.38g/L albumin in patients with VAC therapy. (Table 3) No significant difference in daily loss of albumin was found with a P value of 0.065.There was a significant difference in the loss of total protein with a P value of 0.050.

Blood/peritoneal fluid glucose ratios

Blood and peritoneal fluid glucose was measured in the values shown in table 4. Coagulation times were also measured and have been recorded in table 5.

		aPTT	**PT**	**Fibrinogeen**
	REF	**13,2-18,2**	**7,2-9,9**	**1,0-2,7**
		sec	sec	g/L
Kancha		54.8	16.8	4.0
Bonnie		26.7	11.6	2.0
Bobbie		10.6	41.8	4.4
Dot		16.9	9.7	2.8
Ivar		18.7	14.5	3.0
Kaya		36.0	15.0	2.0
Noa		129.0	18.5	2.3
Simba		62.2	8.9	1.2

Table 5: PT, aPTT and fibrinogen before first exploratory surgery.

	Regaining appetite (food and water)	**Changes (dieet/housing)**	**Problems related to treatment**	**Other problems**	**Behavioral problems**	**Wound healing**	**Endurance**	**Total score**
Patient								
Bobbie	<3 weeks (3)	Hypoallergenic dieet (1)	none reported (0)	Hyperthereody, deaf (3)	Abandonment issues (3)	2 weeks (2)	Little slower, owner thinks age related. (1)	12
Bonnie	2 weeks (2)	No longer eats whole bones (0)	Veins in neck were infected after removal of the feeding tube (2)	Old neck hernia, problem with cruciate ligament (3)	none (0)	Good and fast, no problems, closed in <2days after discharge (0)	No change (0)	7
Dot	3 days (1)	none (0)	none reported (0)	none reported (0)	none reported (0)	Fast < 1 week (0)	No change (0)	1
Kaya	2 days (1) (increased appetite)	Sensetivity control dieet (1)	none reported (0)	Infection of outer ear (1)	none reported (0)	Bit of scar tissue is still visible. (3)	No change (0)	6
Noa	6 months + (still not returned to normal) (5)	Used less actively for sports (1)	Anaemia lasted several weeks (2)	none reported (0)	none reported (0)	Good and fast, a little scar tissue, but this has disappeared (1)	Less edurance, less strenght (3)	12

Table 6. Results of the questionnaire

Questionnaire

The main parts of the questionnaire consisted of digestive problems, clinical problems found by veterinarian preforming check-up and/or during removal of stitches after surgery, behavioural problems, wound healing and endurance. For this questionnaire 5 owners have been successfully contacted. Four of these owners had dogs that were treated with VAC-therapy and only one had received open abdominal drainage therapy. Results of the questionnaire are displayed in table 6.

Economics of the treatment.

Patients that were treated with the open abdominal drainage technique needed 1.08 bandage changes per day on average. The cost of one bandage change is €50.59,- (most recent pricing) contributing to an average of €50.95,- per day.
Patients that were treated with the VAC system needed only one bandage. On average these patients needed 0.29 bandages per day. The total cost of the VAC bandage is €420,-, this makes the average cost for the VAC bandage €121.80,- per day. However, this does not include the cost of the VAC machine which is currently a loan for the project. It does include labour cost for both techniques.

Discussion

Using the parameters from this ongoing study and several previously conducted researches we can come to several conclusions which will be discussed further on and try to and determine the value of these outcomes.

Protein loss has been reported in several studies as a problem during the treatment of septic peritonitis. (Lanz et al., 2001) In a study by Woolfson, evaluating 20 dogs and 5 cats with open peritoneal drainage as treatment for septic peritonitis, 25% of the cases presented with clinical manifestations such as oedema, due to hypoproteinaemia. (Woolfson and Dulisch, 1986) Currently this study only shows a significant difference in the loss of total protein. The study shows that there is a mean gain in protein when using the VAC – therapy. It shows a mean gain in protein levels in patients treated with VAC-therapy in comparison to the mean losses (5.63g/L of the total protein and 1.5g/L albumin) in patients with open abdominal drainage. This could become a favourable factor when choosing for VAC-therapy. This will have to be confirmed using a greater number of patients to be able to have stronger statistical confirmation. A greater number of patients might also show us whether the albumin losses will be significantly less, as this would back up the findings of significant reductions in the loss of protein when using the VAC – therapy in the treatment of septic peritonitis. This favourable outcome is backed up by the fact that humane patients are known to have significant protein losses during the treatment of an open abdomen and that losses should be kept to a minimum. (Friese, 2012) We can assume that less loss of protein is favourable in dogs as well. This could prove a very favourable property when choosing between open abdominal drainage therapy and VAC-therapy.

So far routine tests of PT and aPPT have not been proven useful in the prognosis of septic peritonitis. Although differences in the PT and aPPT between groups of surviving and non-surviving patients with septic peritonitis have been reported, they have not been found substantial enough to function as a prognostic factor. (Bentley et al., 2013) Other studies have failed to show the prognostic value of PT and aPPT as well. (Karamarkovic et al., 2005; Dhainaut et al., 2005) This suggests that the aPTT and PT should be of no influence to the outcome of the different therapies. Prolonged PT and aPTT are however linked to lowered plasma antitrombin activity(ATA). The lowered ATA on its turn has been connected to low

albumin and low PT and aPTT have been connected to a higher mortality rate. (Kuzi et al., 2010) This does show that PT and aPTT are a more general prognostic factors, it has however not been properly connected to the prognosis of septic peritonitis. So far no connection has been found in this study either. Due to the low number of patients, no comparison in survival, PT, aPTT and method of drainage can be made yet.

Blood to peritoneal glucose and lactate ratios can be used as a diagnostic tool for the diagnosis of septic peritonitis in dogs. (Levin et al., 2004; Bonczynski et al., 2003) However, this has also been questioned by Szabo in 2011 when the postoperative peritoneal fluid was studied in 10 healthy dogs with a closed suction drain. The study concluded that these values might not be as reliable as mentioned earlier. (Szabo et al., 2011) In the 8 patients in this study measurements of both peritoneal and blood glucose and lactate were possible before surgery, a mean difference in peritoneal to blood glucose difference of 4.13mmol/L (74.33 mg/dL) was found. This is consistent with the earlier findings that concluded that a blood to peritoneal fluid difference of >20mg/dL is 100% sensitive and 100% specific. (Levin et al., 2004)

MCV and MCHC can be used to determine the type of anaemia in patients. The main differentiation has to be made between regenerative and non-regenerative anaemia. Defining the type of anaemia will aid in the overall prognosis of the patient. (Fleischman, 2012) MCV and MCHC have been recorded in this study but cannot be used as a prognostic factor due to the low number of patients in which these have been recorded. Therefore there is no mention of MCV and MCHC in the results, but it can be taken into consideration when doing further research.

ALT and AST are considered good prognostic values when measuring the amount of liver damage. The largest increase of ALT is seen in dogs that have hepatocellular inflammation and necrosis. A decrease of 50% of ALT over the course of a few days in patients with inflammation of the liver is considered a good prognostic sign. (Center, 2007) These values can be used as a prognostic tool. For example in this study one patients passed away during the second day of treatment. His ALT and AST values were 594 U/L ALAT and 2169 U/L AST opposed to the normal values of <70 U/L ALT and <47 U/L AST. This has however only been documented in this case and could be used as a prognostic value in further study.

A study in 2002 revealed a significant mean difference in the days spend in the ICU when comparing primary closure to open abdominal drainage therapy. The time spend in the ICU was significantly lowered. (Staatz, Monnet and Seim, 2002) The mean duration of open abdominal drainage was reported at 3.5 days, this seems to be comparable to the duration of the open drainage therapy found in this study, which is 3 days. No significant difference was found in the hospitalisation or duration of the therapy in this study. The low number of patients cannot be conclusive in whether or not the VAC-therapy has a faster recovery then patients treated with the classic open abdominal drainage technique.

Comparing the duration VAC and open drainage therapy is useful, seeing that in human medicine the use of VAC therapy greatly reduces the duration of therapy. (Suliburk et al., 2003) Although in this study no significant difference was found in the duration of therapy, it is feasible that this could be found when comparing more patients.

In the original plan for this study it was planned that the modified composite Glasgow pain scoring system would be used to measure the level of discomfort in patients. This could be of great importance when choosing for the VAC- Therapy. This has however not been done during hospitalization of the patients in the ICU. It is strongly advised that this is implemented in further research as to see whether differences can be found in the level of discomfort in the patients. Currently patients that need to undergo bandage changes are sometimes sedated for this procedure. It is also not uncommon that they have to be turned

several times during the day. At this point this is purely speculation because there are no measurements that can be compared.

When looking at cost of the different therapies a clear difference can be seen. Assuming that prices of the bandage changes include working hours, the VAC therapy averages a price of € 121.80,- per day and the open drainage therapy only costs € 50.95,- per day. At this point in time not many conclusions can be made because of the low number of patients. It does however seen clear that VAC therapy is more expensive than open abdominal drainage. Further research with a greater number of patients has to be conducted to determine the cost effectiveness of VAC therapy. However the patients that are treated using the VAC therapy do not need bandage changes and can thus be left to rest. To be able to determine the level of discomfort that the patients undergo during both treatments pain scores have to be noted so that this factor can be used in further research.

Currently the results of the follow up questionnaire cannot be used for statistical analyses because only 5 of them have been conducted successfully. In this group of 5 patients 4 were treated with the VAC therapy and it is thus not possible the compare the outcomes of the questionnaire. It does however provide a start for research into the follow-up of the patients. The scoring system that is used in this study has a lot of room for interpretation. This is mainly because of the wide verity of answers that were expected from the owners. This could be narrowed down further by using the answers that were given during this questionnaire as to build a better and more precise scoring system that could be used in further research.

Another problem is that it seems to be very difficult to realise a good standardisation for the procedures that the patients undergo. The problem lies in the different aetiologies for septic peritonitis that these dogs are presented with and the different treatments that they need. Each patient needs different treatment and is treated by another team of surgeons and supporting staff. Uniform documentation seems to be a problem as this is mostly done by different students. It is important to realise that the complexity, rarity of patients and different aetiologies cause for a lot of variables in the study. It would help this study if more standardised measurements would be taken, following a very clear protocol that every staff member follows. It is, for example a problem that there is a lot of data missing in, for example, the fluid production of the dogs.

In conclusion it can be said that at this stage of the study no definitive conclusions can be made about the survival and the well-being of the animals that have been treated. The current price of the VAC therapy does seem to be higher but to be able to make conclusions about the benefits more research is needed and more parameters have to be collected on a regular and structured basis.

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