Introduction

Hypothermia is common in dogs and cats undergoing coeliotomies and has been demonstrated in humans to occur due to vasodilatation, body surface area contact with conductive surfaces and increased surface area exposure to the atmosphere with heat loss by evaporation, convection and radiation from the surgical field.(Sessler 2000; Redondo and others 2012; Potter and others 2015)~~(Sessler 2000; Potter and others 2015)~~ Additionally anaesthetic agents disrupt the hypothalamic control of homeostatic temperature regulation mechanisms.(Sessler 2000) Factors affecting the development of hypothermia in surgical patients have been shown to include duration of the procedure, choice of anaesthetic agents and their method of administration, ambient temperature of the operating room, body condition score of the animal, size of the patient and~~,~~ the use of insulated bedding and warming aids, but likely additionally include other factors such as disease status and the nature of the surgical procedure itself. (White and others 1984; Sessler 2000; Redondo and others 2012; Potter and others 2015)~~(White and others 1984; Sessler 2000)~~

Multiple p~~P~~revious human and a single veterinary studies have documented increased anaesthetic recovery time and increased morbidity and mortality in hypothermic patients.(Kurz and others 1996; Schmied and others 1996; Lenhardt and others 1997; Beal and others 2000; Pottie and others 2007) This has driven the widespread use of heating aids in attempt to prevent hypothermia developing.(White and others 1984; Sessler 2000; Beal and others 2000; Sessler 2001; Janicki and others 2001; Machon and others 2004; Potter and others 2015) Heat loss begins from the periphery during the first

hour of anesthesia preceding heat loss from the core to the periphery.(Insler and Sessler 2006) Hence many warming aids aim to limit peripheral heat loss.

Following coeliotomy, the peritoneal cavity is commonly lavaged with balanced crystalloid solution to dilute contaminants and loosen debris prior to suctioning for removal. Warmed solution is recommended and is thought to help increase or maintain body temperature by conduction of heat from the lavage solution to the patient.(White and others 1984; Nawrocki and others 2005) While the practice of using warm lavage solution is commonplace, the therapeutic effects on an animal's core temperature have not been investigated in the clinical setting, although one experimental non-survivor study on dogs demonstrated that 15 minutes of intermittent lavage with a solution at 43±2ºC warmed patients compared to a room temperature solution.(Nawrocki and others 2005) The ideal safe temperature for lavage solution for use in the peritoneal cavity has not been identified. Fluids may be pre-warmed in purpose-designed cabinets, or warmed as required using hot water baths or microwave ovens and a qualitative check performed before use. In our experience a~~A~~ surgeon's perception of fluid temperature is ~~likely to be~~ highly variable and this ~~may~~ has the potential to ~~subsequently~~ impact on patient morbidity. Additionally, quantatitve temperature assessment of fluids taken from a purpose designed fluid warming cabinet set at 37ºC at the primary author's institution consistently results in the instillation of fluids which have reduced to between 34ºC and 35ºC.

The purpose of this study was to assess the efficacy of peritoneal lavage using fluid warmed to levels within a physiological range as a means of improving or maintaining body temperature in anesthetized cats and dogs during coeliotomy. Specifically we defined this physiological range to be that range of rectal temperatures recorded across

the population of small animal patients under the care of our specialist referral hospital, suffering a variety of disease states. It was hypothesized that an increase in temperature would be detected in dogs and cats receiving lavage solutions warmer than their body temperature.

Materials and Methods

The University of Nottingham, Ethics Committee, approved this study. Patients presenting to our specialist referral centre with body mass less than 10kg, undergoing coeliotomy for any surgical procedure between July 2014 and April 2015 were recruited pre-operatively, until a total of 20 cases were compiled based on a sample size calculation. Owners gave informed signed consent for inclusion in the study. Inclusion criteria required adherence to a strict anaesthetic protocol and procedural algorithm as detailed below. Any requirement for rescue analgesia outside of the protocol or divergence from the treatment algorithm resulted in exclusion from analysis. High American Society of Anaesthesiologists (ASA) grade was not an exclusion criterion in its own right. Patients were anesthetized by or under the direct supervision of board certified veterinary anaesthesiologists, and exclusion due to the restrictive anaesthetic protocol required for our study on patient safety grounds was at their discretion on a case-by-case basis.

Anesthesia Protocol

Intravenous [IV] pre-anaesthetic medication with methadone[a] (0.2mg/kg) was administered to each patient. Anesthesia was induced with propofol[b] IV given to effect and maintained with isoflurane[c] in oxygen administered via an endotracheal tube, with a heat and moisture exchange device connected, and a circle breathing system. Additional short-acting opioids were permissible for analgesia if required, but no other anaesthetic medications were administered. Non-steroidal anti-inflammatory drugs were given post-operatively at the clinicians' discretion. If these criteria were not deemed to be in the best interests of the individual patient then the protocol was immediately broken and the patient removed from the study. Patients were positioned in dorsal recumbency during

surgical preparation, maintained on a heat pad[d] set at 41˚C covered with an incontinence pad (soft non-woven cover, cellulose absorbent layer with a waterproof backing). Standard clipping and skin preparation protocols were followed. The patients were then transferred to the operating theatre, maintained in dorsal recumbency on a similar heat pad.

Either non-invasive oscillometric or invasive arterial blood pressure measurements were acquired, as well as continuous echocardiogram and capnography with recordings made at five-minute intervals for the duration of anesthesia using an anaesthetic monitor.[e]

Temperature Assessment

Patients were anaesthetized and prepared for surgery in the same surgical preparation room and transferred to the same operating room, with room temperature set at 21˚C. Rectal temperature was assessed prior to induction for each patient using a digital thermometer.[f] During patient preparation a temperature probe attached to the anaesthetic monitor was inserted into the oesophagus to the level of the eighth intercostal space. A second identical probe was placed 6 cm into the rectum, aiming to contact the rectal wall. Temperature measurements were recorded prior to induction of anesthesia (rectal only) and then every 5 minutes from induction using both the oesophageal and rectal probes. Both patient temperature probes were gauged against each other and the waterproof handheld thermometer prior to the start and following completion of the data collection period and found to have a maximum variability of 0.2˚C within the range of temperatures assessed.

Experimental Procedures

~~Patient species, breed, age, sex, body mass and body condition score were recorded preoperatively.~~ Patients were randomly assigned to treatment groups by coin toss by the primary investigator (who was not responsible for the patients assessment for anaesthesia). Blinding of treatment group allocation was not ~~possible~~practical as discussion of fluid requirements and measured fluid temperatures between surgeons, nurses and theatre technicians was required to ensure adherence to the study protocol and allow data recording. Following exploration and surgical treatment as required on a case-by-case basis, group 1 patients underwent peritoneal lavage with sterile isotonic saline at 34±1℃ and group 2 at 40±1℃. These temperatures were selected to be within what we perceived to be a physiological range, and within the working range for the thermometers and temperature probes used for assessment (32-43℃). Fluid heating was standardized using a microwave oven[g] applying settings/timings determined by a pilot study, which investigated various durations of microwave heating and the resultant temperatures achieved for similar fluid bags. Five hundred millilitre bags of isotonic saline designed for intravenous administration[h] were heated individually within their sealed outer packaging on the microwave oven's maximum setting (800W) for either 45 seconds or 70 seconds to achieve the desired fluid temperatures. Fluid temperature was verified prior to use by immediately unwrapping and aseptically emptying the fluid bags into a sterile plastic bowel to ensure mixing and temperature was assessed using the same sterile, waterproof, handheld, digital thermometer. The peritoneal cavity was then immediately filled to capacity with lavage solution. The solution was maintained in the peritoneal cavity for 30 seconds, whilst being gently manually agitated, then evacuated using continuous suction via a Poole suction tip placed into the cranial and caudal left and right

abdominal gutters, by performing colonic and duodenal manoeuvres in turn. The process was repeated until 200ml/kg of lavage solution had been used for each patient, coordinating warming of additional fluid bags as required to maintain progression of the lavage process without delay to await fluid heating and without allowing lavage solution to cool prior to use. Each fluid bag underwent the same temperature check process prior to use as described above.

Temperature recordings were obtained from the rectal, and oesophageal probes every 60 seconds during the lavage period. Thereafter, peritoneal fluid was completely evacuated, and the abdominal incisions were closed routinely in 3 continuous layers (external rectus sheath, subcutaneous tissue and intradermal skin closure). Time for closure of the external rectus sheath was also recorded.

At the end of surgery, oesophageal temperature probes were removed, but rectal temperature assessments continued every 5 minutes until the patient's trachea was extubated. The surgical incision length was measured, as was the pubis-xyphoid length.

Statistical Analysis

A sample size calculation was performed to estimate group size, based on a difference in change of core body temperature of 1˚C between treatment groups, using a power of 80%. Continuous patient demographic data were assessed for normality using the D'Agostino and Pearson omnibus normality test and intergroup comparisons were made using an unpaired t-test where distributions were normal, or the Mann-Whitney test otherwise. Correlation between rectal and oesophageal temperatures were assessed using Pearson's product-moment correlation coefficient. Linear regression was performed to compare the effect of peritoneal lavage on oesophageal and rectal temperature during the lavage

period. The level of significance for all tests was set to $p<0.05$. A computer software package was used to perform all statistical analyses.[i]

Results

Patient demographics:

Group 1 consisted of six dogs (Two Border Terriers, and one each of: German Shepherd, West Highland White Terrier, Pug, crossbreed) and four cats (two Domestic Shorthair, one Domestic Longhair and one Tonkinese.) Group 2 comprised six dogs (Two Miniature Dachshunds, two crossbreeds, one Bichon Frisé and a Cavalier King Charles Spaniel) and four cats (two Domestic Shorthair, one Siamese and one Maine Coon.) Groups were similar with respect to patient age, mass, body condition and surgical incision length (Table 1.)

Procedural data:

Surgical procedures performed in group 1 patients, preceding peritoneal lavage included enterectomy, cholecystectomy, splenectomy, management of a colonic perforation following a gunshot wound, ileocolic intussusception, cellophane band attenuation of an extra-hepatic porto-systemic shunt (EHPSS), ureteronephrectomy, diaphragmatic rupture repair, adrenalectomy, liver lobectomy and ovariohysterectomy. In group 2 procedures included cellophane band attenuation of one EHPSS and full ligation of another, cystotomy, intestinal biopsies, resection of an insulinoma, removal of a jejunal foreign body, subtotal colectomy, resection of an ovarian remnant and management of septic peritonitis following a previous enterotomy. The duration of anesthesia, surgical procedures and peritoneal lavage was similar for both groups (Table 2.)

Temperature data:

Patients in both treatment groups had similar rectal temperatures at the time of induction of anesthesia (mean values of 38.2˚C and 38.0˚C for the two groups respectively). Two

patients were mildly pyretic at the time of induction of anesthesia, one cat with septic peritonitis due to a colonic perforation and one cat with hydronephrosis as the result of an iatrogenic ureteral ligation. Both these patients were randomly assigned to Group 1.

Following the case specific abdominal procedures, at the start of the lavage period, oesophageal temperatures were comparable between groups, however group 1 were significantly warmer as assessed by rectal temperature. This discrepancy was no longer apparent at the end of the lavage period, with the groups having similar temperature at this time point on both oesophageal and rectal assessments. Mean (SD) temperature of the peritoneal lavage solutions used ((34.1˚C(1.2) and 40.2˚C(0.9)) and the changes in body temperature associated with peritoneal lavage as assessed both by the oesophageal (-0.5˚C(0.3) and +0.9˚C(0.7)) and rectal (-0.5˚C(0.4) and +0.8˚C(0.8)) probes were significantly different between the two groups ($p<0.0001$ for all these comparisons)(Table3). Linear regression showed no significant change in oesophageal temperature over the duration of the lavage period for group 1 ($p=0.64$), but a significant increase for group 2 patients ($p<0.0001$). The same results were true for rectal temperature ($p=0.92$ and 0.045 respectively.) (Figure 1.) Group 1 patients were a mean of 0.6ºC(0.5) cooler at the end of anaesthesia than at the start of peritoneal lavage. Group 2 patients were a mean of 0.6ºC(0.7) warmer at the end of anaesthesia than at the start of peritoneal lavage. This important difference was significant ($p=0.0005$).

Assessing all rectal and oesophageal temperatures together, there was moderate correlation between measurements made at the two sites ($R^2=0.44$) with a tendency for oesophageal temperature to be greater than rectal measurements. There was a measurable difference (>0.1ºC) in paired rectal and oesophageal temperature assessments collected at

438 of the total 533 individual time points. This difference was greater than 1ºC at 31 time points, for which oesophageal temperature exceeded rectal temperature at 25/31.

Discussion

Peritoneal lavage with mildly hyperthermic crystalloid solution consistently warmed patients, whereas mildly hypothermic crystalloid solutions had no significant effect on patient temperature. This result has been previously demonstrated using a protracted lavage period and fluids of temperature outside of a range considered clinically safe (21±1˚C and 42±3˚C) in an experimental non-survivor study.(Nawrocki and others 2005) In the current study, fluids at temperatures at the extremes of what we considered to be a physiological range were used. The measurable differences in patient temperatures reached statistical significance even during a relatively short period of peritoneal lavage as appropriate in clinical situations.

The groups of patients undergoing coeliotomy in the current study were diverse in terms of species, breed, age and the surgical procedures for which they underwent anaesthesia, but broadly similar with respect to patient mass, body condition and surgical incision length relative to body size. These latter factors were important to be similar between groups, as it is known that these may affect the rate of cooling of human patients undergoing anaesthesia, with relative surgical incision length having a direct influence on patient surface area available for evaporative and convective heat loss.(Sessler 2000)

Our patients were mildly hypothermic prior to peritoneal lavage. The variability in initial rectal temperatures prior to induction of anesthesia was likely due to normal inter-patient difference, as well as pre-operative disease status, although may also have been affected by the passage of stools. Enemas or manual evacuation of the rectum was not routinely performed as there was no clinical indication, however, efforts were made in each case to ensure contact between the rectal wall and the thermometer / temperature probe. By the

start of the lavage period, patients had undergone an assortment of surgical procedures of different durations and involving variable degrees of abdominal organ exposure and manipulation and subsequently convective and evaporative heat losses, despite standardized anaesthetic protocols. Different disease processes will also likely have affected local vascular flow and may have contributed to temperature changes before commencing lavage.

Group 2 patients had a significantly lower mean rectal temperature at the time of initiating peritoneal lavage. This finding occurred as the result of the random allocation of patients to treatment groups and does not undermine the clinical significance of the findings of this study. In general rectal and oesophageal temperature measurements in this study were only moderately positively correlated. At ~~a handful~~4.7% of measured time points oesophageal temperature exceeded rectal temperature ~~measured~~ by more than 1ºC~~lower than oesophageal temperature~~. This may be explained by an increased tendency for the rectal temperature probe to be positioned within rectal contents and/or to be expelled with the stool, losing contact with the rectal wall and requiring replacement. There may be more of a direct cooling effect of coeliotomy procedures on the rectum and heating effect of the lavage solution compared to the probe in the oesophagus, which is more shielded from the direct effect of temperature changed from the surgical field. Oesophageal temperature may therefore be more appropriate for monitoring of patients undergoing coeliotomy procedures. Subjectively the rate of change of both the rectal and oesophageal temperatures was the same for our patients, however this may have been influenced by the frequency of data recording during the period of peritoneal lavage.

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There was no significant change in patient temperature for animals in either treatment group following the lavage period until the point of the end of anesthesia, although there was a minor reduction in temperature of mean 0.3˚C for group 2 patients and temperature remained unchanged for group 1 patients. These results suggest that the clinical patient benefit of performing peritoneal lavage with warmed solution does extend beyond the lavage period. No assessment was made on quality or timings of patient recovery, morbidity or treatment outcome due to variability in disease status and surgical treatment performed. Future investigations may choose to investigate the time required for re-establishment of normothermia with ongoing peritoneal lavage with warm saline, prior to anaesthetic recovery and the effect thereof on patient morbidity and outcome. However, this would require standardization of treatment groups to include patients with the same or similar disease processes undergoing similar procedures in a similar time frame, as these factors will also influence patient hypothermia, vasodilatation, morbidity and outcome. Additionally, the optimum temperature for peritoneal lavage for maximizing efficiency of patient warming without injury to the abdominal viscera has yet to be determined. We should reinforce at this time that use of hyperthermic isotonic crystalloid solution in the abdominal cavity is not without risk and temperature assessment is essential prior to use.

Limitations of our study include the variable underlying pathologies and procedures undertaken which likely affected individuals' baseline temperature at the start of anesthesia, as well as rate of cooling during surgery, and possibly rate of warming as a result of peritoneal lavage. However, it is important to note that our study was designed to reflect clinical practice and the temperature tended to improve in the higher

temperature lavage group compared to those patients undergoing peritoneal lavage with less warm saline. The duration of the lavage period was not standardized here, however, it was similar between treatment groups. Instead we elected to adhere as closely as possible to a typical clinical scenario, filling the peritoneal cavity to capacity, agitating the fluid therein and suctioning. We chose a standardized total fluid volume of 200ml/kg as has been recommended for reduction of bacterial burden in cases of septic peritonitis,(Seim 1995) in order to make the protocol applicable to the widest possible number of cases. The relative abdominal volumetric capacity varied greatly between patients and even between fillings of the same body cavity on consecutive fillings. This variability resulted in lavage period durations between 4 and 15 minutes in total, which again may have impacted the clinical impact of exposure to the lavage solution. Variability in abdominal capacity was likely due to depth of anesthesia, changes in muscle tone and vascular responses in association with the previous surgical intervention, mechanical strain of elevation of the rectus abdominis muscle at the ends of the incision and perhaps also due to the exposure to the warm or cool crystalloid solution, although no specific attempts were made to classify this response in this study. Temperature data were not recorded for all patients at all time points, as patient anaesthetic monitoring, safety and the surgical procedure being undertaken were prioritized over the collection of data for this clinical investigation.

The decision to choose peritoneal lavage solution temperatures of 34±1℃ and 40±1℃ was arbitrary, but chosen to be within the working range of the temperature probes and thermometers used and within what we considered a safe and physiological range, appropriate for use in clinical patients. Fluids of these temperatures would likely have

been accepted for clinical use prior to this study, without temperature assessment and instead only a qualitative check by the surgeon prior to use. Future studies may aim to assess the ideal peritoneal lavage protocol to optimize the quality of recovery from anesthesia and subsequently potentially improve wellbeing and outcome of small animal patients.

In conclusion the use of isotonic crystalloid solution for peritoneal lavage at a temperature of 40±1˚C significantly warms small animal patients, when applied in a clinical setting, compared to lavage solution at 34±1˚C. Fluid intended for peritoneal lavage should undergo a quantitative temperature assessment prior to use in clinical patients.~~use isotonic crystalloid solution for peritoneal lavage at a temperature of 40±1°C compared to fluid at 34±1°C may be beneficial following coeliotomy procedures in small animal patients in order to aid the restoration of normothermia.~~

299 **Footnotes**

300 [a] Comfortan; Eurovet Animal Health, Netherlands

301 [b] PropoFlo; Abbott Animal Health, IL

302 [c] IsoFlo; Abbott Animal Health, IL

303 [d] Hot Dog™, Hot Dog Patient Warming, MN

304 [e] T5 Beneview or PM-9000vet; Mindray, China

305 [f] Kruuse model 291103; Denmark

306 [g] Samsung M1736N; Korea

307 [h] Aquapharm No1; Animalcare, York, UK

308 [i] Prism 6 for Mac OS X, GraphPad Software Inc, La Jolla, CA

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Figure Legends

Figure 1: Comparison of oesophageal temperature changes during peritoneal lavage between treatment groups, plotted as mean values with standard deviation at each time point.

Tables

	Age (years, months)	Mass (kg)	Length from xyphoid to pubis (cm)	Incision length (cm)
Group 1	5y8m (5y11m)	6.4 (2.8)	23.7 (3.5)	17.0 (3.0)
Group 2	5y0m (4y5m)	5.4 (2.2)	21.3 (2.4)	14.3 (2.8)
p value	0.77	0.43	0.09	0.054

Table 1: Comparison of age, body mass, linea alba and incisional lengths between patients in our two treatment groups (Mean (SD))

	Total anaesthetic time (minutes)	Time from induction to start of surgery (minutes)	Duration of surgery (minutes)	Duration of peritoneal lavage (minutes)	Time from end of lavage to abdominal wall closure (minutes)
Group 1	113 (68 - 148)	53 (20 – 88)	43 (31 – 65)	6 (3 – 10)	6 (3 – 12)
Group 2	101 (60 – 163)	38 (25 – 80)	47 (28 – 71)	7 (4 – 15)	8 (3 – 12)
p value	0.85	0.61	0.38	0.36	0.47

Table 2: Comparison of anesthesia and surgical timings for patients in each of our treatment groups (Mean (SD))

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	Temperature (℃)	Induction	Start of lavage	End of lavage	Change due to lavage	Lavage fluid temperature	End of anesthesia	Change subsequent to lavage	Change between start of lavage and end of anaesthesia
Group 1	Oesophageal		36.3 (1.0)	35.9 (0.7)	-0.5 (0.3)	34.1 (1.2)			
	Rectal	38.2 (0.7)	36.6 (0.8)	35.9 (0.9)	-0.5 (0.4)		35.9 (0.9)	0.0 (0.5)	-0.6 (0.5)
Group 2	Oesophageal		35.4 (1.4)	36.3 (1.2)	+0.9 (0.7)	40.2 (0.9)			
	Rectal	38.0 (0.4)	35.4 (1.2)	36.2 (1.8)	+0.8 (0.8)		36.0 (1.6)	-0.2 (0.3)	0.6 (0.7)
p value	Oesophageal		0.12	0.38	<0.0001	<0.0001			
	Rectal	0.43	0.02	0.68	<0.0001		0.81	0.24	0.0005

371 Table 3: Comparison of temperature measurements (Mean ℃ (SD)) for each of our
372 treatment groups.