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Associations between increased body condition score, bodyweight, age and breed with urethral obstruction in male castrated cats



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ABSTRACT

Identifying potential risk factors for urethral obstruction in male cats may help in disease prevention. The aims of this study were to assess whether breed, pedigree status, age, bodyweight and body condition score (BCS) are risk factors for urethral obstruction in castrated male cats using a primary care population. Within this, a specific question was whether any increase in rate of urethral obstruction in male cats due to excess body condition is because of higher bodyweight. A retrospective hospital-based matched case-control study was performed using 195 cases of urethral obstruction in castrated male cats and 195 control consultations for cats presenting to a feline-only first opinion veterinary practice in Brisbane, Australia.

The incidence rate of urethral obstruction did not vary significantly with bodyweight but increased with BCS (incidence rate ratio 1.6; 95% CI 1.2–2.1; P < 0.001). The effect of BCS was not due to high BCS cats having higher bodyweights. The incidence was lower in Burmese cats compared to Domestic shorthair cats (incidence rate ratio 0.1; 95% CI 0.0-0.4; P=0.001), and higher in non-pedigree cats compared to pedigree cats (incidence rate ratio 2.8: 95% CI 1.7-4.6: P < 0.001). Incidence rate ratios increased with age to 2 to 4 years (the ages with highest incidences) then progressively declined with each additional year of age. Further research is needed to define why there is a positive association between BCS and rate of urethral obstruction. In the interim, clinicians should encourage owners of castrated male pet cats to ensure their cat's BCS is not high.

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Introduction

The most common causes of feline lower urinary tract disease (FLUTD) are feline idiopathic/interstitial cystitis (FIC) (55-57% of FLUTD cases) and urolithiasis (12-23%) (Gerber et al., 2005; Kruger et al., 1991; Sævik et al., 2011). Urethral obstruction has been reported in 18-58% of cats presenting with FLUTD (Gerber et al., 2005; Kruger et al., 1991; Lekcharoensuk et al., 2001; Sævik et al., 2011). Common underlying causes of urethral obstruction include urethral plugs, urolithiasis and idiopathic disease (Gerber et al., 2005; Kruger et al., 1991; Sævik et al., 2011). Short term case fatality rates of 8–9% have been reported (Gerber et al., 2008; Segev et al., 2011) and recurrence of urethral obstruction is common (22% of affected cats within 6 months (Segev et al., 2011), 36% within 2 years (Gerber et al., 2008)).

Many host-related and environmental factors have been implicated in the aetiology of FLUTD including age, bodyweight, breed, coat length, sex, neuter status, dietary factors, outdoor access, season and weather (Bernard, 1978; Buffington et al., 2006; Jones et al., 1997; Lekcharoensuk et al., 2001; Sævik et al., 2011; Sumner and Rishniw, 2017; Walker et al., 1977; Willeberg and Priester, 1976). Risk factors specifically for urethral obstruction have also been identified. Neutered male cats (Lekcharoensuk et al., 2001), cats between 2 and 7 years of age (Lekcharoensuk et al., 2001), those with greater bodyweights (Segev et al., 2011), those that spend more time indoors (Reif et al., 1977) and those fed diets with large proportions of dry food (Reif et al., 1977; Segev et al., 2011) are at greater risk. Burmese breed and cats <1 and >15 years old are at lesser risk of urethral obstruction (Lekcharoensuk et al., 2001). However, most risk factor studies investigating FLUTD and urethral obstruction have used referral or veterinary teaching hospital populations (Cameron et al., 2004; Lekcharoensuk et al., 2001; Reif et al., 1977; Segev et al., 2011; Willeberg and Priester, 1976). Selection bias due to referral patterns has long been recognised in studies of human diseases (Kokmen and Özarfati, 1996; Sackett, 1979) and results of risk factor studies



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conducted using primary care populations may be less prone to this bias. Accordingly, there is a need to assess whether age, breed and pedigree status are risk factors for urethral obstruction using primary care study populations.

Bodyweight has been shown to be risk factor for urethral obstruction (Segev et al., 2011). The normal lean weight of cats can vary greatly due largely to differences in body skeletal ('frame') size (Kienzle and Moik, 2011) but cats with greater bodyweights generally have higher percentage body fat (Biornyad et al., 2011: Shoveller et al., 2014). To our knowledge, no studies have investigated whether body condition score (BCS) is a risk factor for urethral obstruction independently of bodyweight. It is plausible that the relationship between bodyweight and urethral obstruction is better described using BCS because BCS more accurately represents adiposity (Bjornvad et al., 2011; Laflamme, 1997; Shoveller et al., 2014), and this may be more important as a cause of urethral obstruction than frame size and muscle mass. Risk of idiopathic cystitis is increased in both high bodyweight cats and high BCS cats (Defauw et al., 2011; Kim et al., 2017; Lund et al., 2016) but not all of the cats in those studies were non-obstructed, and estimated effects of bodyweight may have been confounded by BCS in these studies. Further, in all of these studies, body condition was assessed by owners. Owners' estimates of their cats' body condition commonly differ from experts' estimates (Cave et al., 2012; Colliard et al., 2009; Courcier et al., 2010), and owners in general underestimate body condition of cats with high BCS and overestimate body condition of cats with low BCS (Colliard et al., 2009: Courcier et al., 2010).

The aims of this study were to assess whether breed, pedigree status (pedigree or not), age, bodyweight and BCS are risk factors for urethral obstruction in castrated male cats using a primary care study population. Within this, a specific question was whether BCS is a risk factor for urethral obstruction in castrated male cats independently of bodyweight. We assessed BCS using a validated body condition scoring method (Laflamme, 1997) administered by veterinarians.

Materials and methods

Overview of study

A retrospective, hospital-based, matched case-control study with incidence density sampling was conducted within client-owned cats presented to The Cat Clinic Group, Brisbane, a feline-only first opinion (i.e. primary care) veterinary practice. Consultations where the cat was diagnosed with urethral obstruction (case consultations) were identified and one control consultation (i.e. a consultation at which urethral obstruction was not diagnosed) was selected for each case matched on date of consultation. Ethical approval was not required according to local ethics laws as this was a retrospective study, and thus, all cats were managed using clinical methods that were routine at the study site and unchanged by the study protocol.

Potential risk factors assessed

The cats' breeds, estimated ages (measured in years and parts of years), bodyweights (measured in kilograms and parts of kilograms) and BCS (on a scale from 1 to 9 where 1 is emaciated, 5 is ideal and 9 is extremely fat) (Laflamme, 1997) as recorded at the study consultation were then ascertained from hospital medical records. Ages were calculated as date of consultation minus recorded estimated date of birth. If bodyweight and/or BCS were not recorded at the study consultation date, data for these variables were used if they were recorded within 14 days before or after the study consultation at which the cat was selected. All BCS estimates had been allocated by veterinarians working at the practice and trained in the use of the nine-point BCS system. Pedigree status (pedigree or not) were determined from each cat's breed description. Pedigree breeds were those defined by The Australian Cat Federation 2017² and domestic shorthair, domestic longhair and pedigree cross cats were classified as non-pedigree cats.

Source population

The source population from which cases and controls were drawn was defined as castrated male cats not previously affected by urethral obstruction that would have presented to The Cat Clinic as a primary care consultation if they had developed urethral obstruction during the study period. Only consultations where the cat's BCS was recorded on the day of the consultation or, for consultations where that was not done, within 14 days before or after the study consultation, were eligible for inclusion.

Case definition and identification

Case consultations were those where a client-owned, male castrated cat was diagnosed with their first known occurrence of urethral obstruction when presented for a primary care consultation at The Cat Clinic from August 2005 to March 2018 inclusive. Diagnosis of urethral obstruction was made if the cat had a distended/turgid bladder on palpation in conjunction with either a recent history of signs of lower urinary tract disease, or clinical signs of lethargy or malaise with abdominal pain. Potential cases of urethral obstruction were identified by searching the computer database for invoices that included a urethral catheterization fee and/ or item charge for a urinary catheter. Records were then examined to identify case consultations that met these selection criteria. Cats that had been previously diagnosed with urethral obstruction at another clinic or were referral or second opinion feline patients were excluded. Consultations for both cats that were alive and those that were deceased at the time of data collection were eligible for enrolment. All eligible case consultations were enrolled.

Control selection

For each case, one matched control consultation was randomly selected from all other castrated male cats that had no record of previous diagnosis of urethral obstruction that had been presented to The Cat Clinic on the same date as the corresponding case consultation and did not have urethral obstruction at that consultation. This source population was open as potential subjects could enter the source population through being castrated (a requirement for enrolment), could leave through dving, and could enter or leave if their owner changed the veterinary practice that they used/would use for veterinary services. Accordingly we used incidence density sampling (Dohoo et al., 2009; Knol et al., 2008; Rothman et al., 2008; Vandenbroucke and Pearce, 2012). All eligible consultations on that date were allocated sequential numbers and one control consultation was selected using a computer-generated random number. Consultations were eligible only where the cat was presented to the clinic for reasons not thought to be associated with age, breed, bodyweight or BCS. For example, conditions reported to be associated with increased BCS include diabetes mellitus (Lund et al., 2005; Scarlett and Donoghue, 1998), oral disease (Lund et al., 2005), urinary tract disease (Lund et al., 2005), skin diseases (Lund et al., 2005; Scarlett and Donoghue, 1998), lameness not associated with cat fight wounds or fractures (Scarlett and Donoghue, 1998) and neoplasia (Lund et al., 2005). Conditions reported to be associated with lower BCS include diarrhoea (Scarlett and Donoghue, 1998) and chronic renal disease (Greene et al., 2014). Thus, control cats were eligible for selection if they presented for annual wellness checks, vaccination or for acute presentations of other conditions. As required under incidence density sampling, the same cat could be selected multiple times as controls and cats selected as cases were eligible for selection as controls before their case consultation but were not eligible to be selected as controls at consultations subsequent to their case consultation. For nine cases, no suitable control consultation was available on the date of the matched case consultation so a control consultation was selected randomly from eligible consultations on the previous day (six cats), following day (one cat) or two days prior (two cats).

Statistical methods

Associations between urethral obstruction and each of cat breed and pedigree status, and cat age, bodyweight and BCS were assessed using conditional logistic regression, conditional on pair where each case consultation and its matched control consultation constituted one pair. Age was calculated in years as estimated age in days/365.25. BCS was treated as both a continuous variable, as body fat % increases approximately linearly with BCS (Bjornvad et al., 2011; German et al., 2006; Laflamme, 1997) and as a categorical variable. Breeds were categorised, with Siamese, Burmese, and Persian cats placed in separate categories as these breeds have been found to be at increased (Persians) or decreased risk (Siamese) of FLUTD and Burmese have been found to have decreased risk of urethral obstruction (Lekcharoensuk et al., 2001).

Covariates for multivariable models were chosen based on our causal hypotheses for interrelationships between each of age, breed, bodyweight and BCS and both (a) each other and (b) with urethral obstruction. We hypothesised that each of age, breed, bodyweight, and BCS could directly affect the incidence of urethral obstruction. A direct effect is a causal relationship with no specified intervening variable that mediates the relationship (Dohoo et al., 2009; Greenland et al., 1999). For example, we hypothesised that there could be effects of breed, that are not mediated through age, bodyweight or BCS. Instead, any effects of breed were

² See: The Australian Cat Federation (2017) Breed Standards http://www.acf.asn. au/index.php?page=standards (Accessed 27 November 2018).

hypothesised as being mediated via other mechanisms collectively captured as a direct effect. We further allowed that, as well as the possible direct effect of BCS on urethral obstruction. BCS could also affect incidence of urethral obstruction indirectly via its effect on bodyweight. The total effect of an exposure variable is the combination of its direct effect and all indirect pathways (Dohoo et al., 2009). Thus, the total effect of BCS would be the sum of its direct effect on urethral obstruction and its indirect pathway mediated through bodyweight. We further hypothesised that each of age and breed do or could affect both bodyweight and BCS. Finally, to allow for the possibility of changes in breed preferences over time amongst people obtaining cats, we included a latent (i.e. unobserved) variable, calendar year that cat was obtained, that affected each of breed and age. These causal hypotheses were incorporated into a directed acyclic graph using DAGitty (version 2.3) (Textor et al., 2011). This software was used to identify minimal sufficient adjustment sets. A minimal sufficient adjustment set is a list of covariates that must by fitted in a multivariable regression model along with a specified exposure variable to ensure that the regression coefficient for that exposure variable correctly estimates the effect ('correct' given the specified directed acyclic graph). Minimal sufficient adjustment sets can differ between exposure variables, and between when estimating the total and direct effect of the same exposure variable. Separate regression models were fitted when estimating each of the total effects of breed, age, bodyweight and BCS, and the direct effect of BCS. To assess the associations between urethral obstruction and pedigree status, we removed breed from the multivariable model and instead fitted pedigree status.

The relationship between age and urethral obstruction was explored by fitting fractional polynomial exposure variables in the conditional logistic regression models. Relationships between bodyweight and urethral obstruction, and BCS and urethral obstruction were assessed in the same way with breed and the selected fractional polynomial variables for age fitted as covariates. These fractional polynomial exposure variables allowed exploration of a wide range of possible non-linear relationships by fitting various combinations of transformed values for age, bodyweight and BCS. Fractional polynomials were fitted in the conditional logistic regression models by using the –fp- and –stcox- commands in Stata (version 14, StataCorp, College Station, Texas, USA) in combination. From the linear term, the single non-linear term and the combination of the two terms, that with lowest deviance was selected. Odds ratios and associated 95% confidence intervals and *P*-values for various ages were calculated after fitting the final multivariable model using Stata's –lincom- command.

As odds ratios from rate-based case-control studies where incidence density sampling is used to estimate ratios of incidence rates (Greenland and Thomas, 1982) (in this context, incidence rate of urethral obstruction for exposed cats relative to that for non-exposed cats), we refer to these as incidence rate ratios throughout.

Results

Numbers of cases and controls

In total, 195 consultations met our case definition and all were enrolled. For each case consultation, one matched control consultation was selected. Thus, in total, 195 pairs (where each pair consisted of one case consultation and its matched control consultation) were enrolled. All were included in statistical analyses except where exposure data were missing as detailed below. Six cats contributed multiple consultations: 3 cats contributed a control consultation and subsequently a case consultation, and 3 cats each contributed two control consultations. Hereafter, for simplicity, the terms 'consultation' and 'cat' are used interchangeably. Control cats presented for a range of conditions; these were vaccination or wellness check (102), cat fight wounds/trauma (32), ocular disease (15), acute gastrointestinal disease (11), respiratory disease (8), ectoparasitism (5), fever (4) and other conditions (18).

Risk factors for urethral obstruction

Distributions of cases of urethral obstruction and control cats by breed, coat length, pedigree status, age, bodyweight and BCS are shown in Table 1 and incidence rate ratios are shown in Tables 2 and 3. Relative to domestic shorthair cats, the incidence rate was lower in Burmese cats (estimated incidence rate ratio 0.1; 95% CI 0.0-0.4; P=0.001). Non-pedigree cats were more likely than pedigree cats to have urethral obstruction (estimated incidence rate ratio 2.8; 95% CI 1.7-4.5; P<0.001).

Table 1

Distributions of cases of urethral obstruction and control cats by breed, pedigree status, age, bodyweight and body condition score; all cats were castrated males.

	Cases		Controls	
	No.	%	No.	%
Breed				
Domestic shorthair	115	59%	87	45%
Domestic longhair	32	16%	16	8%
Oriental, Siamese	2	1%	2	1%
Burmese	3	2%	27	14%
Chinchilla, Himalayan, Persian	8	4%	4	2%
Other	35	18%	59	30%
	195	100%	195	100%
Pedigree status				
Pedigree	33	17%	77	39%
Non-pedigree	162	83%	118	61%
	195	100%	195	100%
Age (vears)				
0.3 to <1	3	2%	15	8%
1 to <2	22	11%	16	8%
2 to <3	21	11%	20	10%
3 to <7	87	45%	60	31%
7 to <10	35	18%	38	19%
10 to 18.8	27	14%	46	24%
	195	100%	195	100%
Bodyweight (kg)				
1.3 to <4	2	1%	15	8%
4 to <5	26	13%	43	22%
5 to <6	63	32%	62	32%
6 to <7	54	28%	49	25%
7 to 10.1	49	25%	25	13%
Not recorded	1		1	
	195	100%	195	100%
Body condition score (1-9 scale)				
4	8	4%	21	11%
4.5 or 5 ^a	94	48%	114	58%
6	54	28%	44	23%
7	26	13%	13	7%
8 or 9	13	7%	3	2%
	195	100%	195	100%

^a BCS for one case and one control cat were 4.5; BCS for all others in this category were 5.

Based on the fractional polynomial analyses, age was appropriately modelled using a non-linear relationship determined by two terms (age⁻² and age¹; P=0.031 and 0.036 for coefficients for these terms, respectively), while bodyweight and BCS were appropriately modelled using linear terms. Incidence rate ratios increased with age to 2 to 4 years (the ages with highest incidences) then progressively declined with each additional year of age (Table 3). Relative to cats aged 3 years, estimated incidence rate ratios were 0.5 or less for both cats aged 1 year or less and cats aged 15 years or more (Table 3).

Incidence rate of urethral obstruction did not vary significantly with bodyweight (estimated incidence rate ratio 1.1; 95% CI 0.8-1.5, P = 0.633). In contrast, rate of urethral obstruction increased with BCS. The estimated incidence rate ratios for the total and direct effects of BCS, respectively, were 1.6 (95% CI 1.2–2.1; P < 0.001) and 1.5 (95% CI 1.0–2.2, P = 0.052). Results were similar when BCS was treated as a categorical variable (Table 3).

Discussion

The key results indicate that greater BCS is associated with increased rate of urethral obstruction, and this is not due to greater bodyweight, on average, in cats with high BCS. This latter conclusion is based on the similarity of the incidence rate ratios for the total and direct effects of BCS in increasing rate of urethral

Table 2

Estimated total effects of each of breed and	pedigree status on rate of urethral	obstruction in castrated male cats.

Variable	Adjusted incidence rate ratio ^a	95% CI	Р
Breed			
Domestic shorthair	Reference category		
Domestic longhair	1.5	0.7-3.5	0.298
Oriental, Siamese	1.5	0.2-11.2	0.711
Burmese	0.1	0.0-0.4	0.001
Chinchilla, Himalayan, Persian	3.1	0.7-13.1	0.119
Other	0.5	0.3–0.9	0.030
Pedigree status			
Pedigree	Reference category		
Non-pedigree	2.8	1.7–4.6	<0.001

^a Minimal sufficient adjustment set was age (to control confounding due to age).

Table 3

Estimated effects of each of age, bodyweight and BCS on rate of urethral obstruction in castrated male cats.

Age (years) ³ 0.05 0.05 0.0-0.8 0.037 1 0.5 0.3-1.0 0.062 2 1.0 0.9-1.1 0.349 3 Reference category	Variable	Adjusted incidence rate ratio	95% CI	Р
0.5 0.05 $0.0-0.8$ 0.037 1 0.5 $0.3-1.0$ 0.062 2 1.0 $0.9-1.1$ 0.349 3 Reference category $0.9-1.0$ 0.376 5 0.9 $0.8-1.0$ 0.205 10 0.7 $0.4-1.0$ 0.070 15 0.5 $0.2-1.0$ 0.054 18 0.4 $0.2-1.0$ 0.050 Bodyweight ^b 1.1 $0.8-1.5$ 0.633 BCS (continuous scale) ^{c.d} Total effect 1.6 $1.2-2.1$ <0.001 Direct effect 1.5 $1.0-2.2$ 0.052 BCS categorised ^d Total effect 1.5 $0.7-5.2$ 0.217 6 2.5 $0.9-6.9$ 0.089 7 4.6 $1.4-14.9$ 0.011 8 or 9 11.2 $2.0-62.9$ 0.006 Direct effect 0.006	Age (years) ^a			
1 0.5 $0.3-1.0$ 0.062 2 1.0 $0.9-1.1$ 0.349 3Reference category $$	0.5	0.05	0.0-0.8	0.037
2 1.0 $0.9-1.1$ 0.349 3 Reference category	1	0.5	0.3-1.0	0.062
3 Reference category 4 1.0 0.9-1.0 0.376 5 0.9 0.8-1.0 0.205 10 0.7 0.4-1.0 0.070 15 0.5 0.2-1.0 0.054 18 0.4 0.2-1.0 0.050 Bodyweight ^b 1.1 0.8-1.5 0.633 BCS (continuous scale) ^{c,d} Total effect 1.6 1.2-2.1 <0.001	2	1.0	0.9-1.1	0.349
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Bodyweight ^b 1.1 0.8–1.5 0.633 BCS (continuous scale) ^{c,d} Total effect 1.6 1.2–2.1 <0.001	18	0.4	0.2-1.0	0.050
BCS (continuous scale) ^{c,d} Total effect 1.6 1.2–2.1 <0.001	Bodyweight ^b	1.1	0.8–1.5	0.633
Total effect 1.6 1.2–2.1 <0.001 Direct effect 1.5 1.0–2.2 0.052 BCS categorised ^d Inoperation of the second s	BCS (continuous sc	ale) ^{c,d}		
Direct effect 1.5 1.0–2.2 0.052 BCS categorised ^d Total effect <	Total effect	1.6	1.2-2.1	< 0.001
BCS categorised ^d Keference category Value	Direct effect	1.5	1.0-2.2	0.052
4 Reference category 4.5 or 5 1.9 0.7–5.2 0.217 6 2.5 0.9–6.9 0.089 7 4.6 1.4–14.9 0.011 8 or 9 11.2 2.0–62.9 0.006	BCS categorised ^d			
4 Reference category 4.5 or 5 1.9 0.7-5.2 0.217 6 2.5 0.9-6.9 0.089 7 4.6 1.4-14.9 0.011 8 or 9 11.2 2.0-62.9 0.006	Total effect	-		
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7 4.6 1.4-14.9 0.011 8 or 9 11.2 2.0-62.9 0.006 Direct effect 1.2 1.2 1.2 1.2	6	2.5	0.9-6.9	0.089
8 or 9 11.2 2.0–62.9 0.006 Direct effect	7	4.6	1.4-14.9	0.011
Direct effect	8 or 9	11.2	2.0-62.9	0.006
	Direct effect			
4 Reference category	4	Reference category		
4.5 or 5 1.8 0.6–5.0 0.262	4.5 or 5	1.8	0.6-5.0	0.262
6 2.1 0.7–6.8 0.202	6	2.1	0.7-6.8	0.202
7 3.6 0.9–15.4 0.079	7	3.6	0.9-15.4	0.079
8 or 9 8.0 1.0-64.8 0.050	8 or 9	8.0	1.0-64.8	0.050

^a Estimated total effect of age; age was fitted as a non-linear relationship, and incidence rate ratios were estimated at the specific ages shown; minimal sufficient adjustment set was breed (to control for confounding due to breed).

^b Estimated total and direct effect of bodyweight expressed as incidence rate ratio for each additional kg bodyweight (as bodyweight was fitted as a linear term); minimal sufficient adjustment set: breed, age, and BCS (to control for confounding due to these variables).

^c Estimated incidence rate ratio for each additional unit of BCS (as BCS was fitted as a linear term).

^d Estimated total and direct effects of BCS expressed as incidence rate ratios; minimal sufficient adjustment set for total effect: breed and age (to control for confounding due to these variables); minimal sufficient adjustment set for direct effect: breed and age (to control for confounding due to these variables) and bodyweight (to remove from the regression coefficient any indirect effects of BCS on urethral obstruction mediated via bodyweight).

obstruction. This indicates that the effect of BCS is not due to the increased bodyweight caused by greater BCS, so is due to the direct effect of BCS. In this situation, the direct effect would consist of all causal mechanisms from BCS to urethral obstruction other than any effects of BCS on rate of urethral obstruction that are mediated

via bodyweight. As greater BCS is a risk factor for urethral obstruction independently of bodyweight. Further, our results indicate that the rate of urethral obstruction is similar in cats with low and high bodyweights provided those differences in bodyweight are not due to differences in BCS. Accordingly, owners of castrated male pet cats may be able to influence their cat's risk of urethral obstruction by ensuring its BCS is not high regardless of the cat's size. A larger study would be required to identify the optimal BCS to minimize rate of urethral obstruction but interestingly, our point estimates are consistent with lower incidence at BCS 4 relative to BCS 5 (a score considered to be ideal) (Laflamme, 1997). A recent study also demonstrated that less than ideal (BCS 3–4/9) cats were at decreased risk of certain conditions (atopic dermatitis and oral disease) compared to cats with BCS 5/9 (Teng et al., 2018).

The 9-point body condition scoring system used in the current study has been validated using dual-energy X-ray absorptiometry; this demonstrated that BCS is strongly and linearly associated with increasing adiposity (Bjornvad et al., 2011; Laflamme, 1997) and has been found to be repeatable and reproducible between scorers (Laflamme, 1997). However, it is partly subjective and multiple different veterinarians scored cats, so misclassification errors are probably moderately frequent in the current study. Assuming these errors are non-differential (i.e. independent of whether the cat had urethral obstruction or not), this will have resulted in underestimation of the strength of association between BCS and urethral obstruction, as occurs generally with non-differential misclassification (Dohoo et al., 2009). Thus, the true relationship is probably stronger than that observed in the current study.

Further studies are required to identify causal mechanisms for the association between BCS and rate of urethral obstruction. Increased BCS may directly or indirectly lead to urethral obstruction or common factors may cause both increased BCS and urethral obstruction in male cats. Cats fed dry food diet (Rowe et al., 2015), those with an indoor lifestyle (Robertson, 1999; Rowe et al., 2015; Teng et al., 2017), those whose owners underestimate their BCS (Cave et al., 2012; Colliard et al., 2009) and those whose owners have a close emotional attachment to their cat (Kienzle and Bergler, 2006). Some of these factors may directly or indirectly contribute to increased rate of urethral obstruction in male cats independently of BCS.

Our findings demonstrated that the incidence of urethral obstruction increases with age to 2 to 4 years (the ages with highest incidences) then progressively declines with each additional year of age.

Lekcharoensuk et al. (2001) also found that very young cats (<1 year) and very old cats (\geq 15 years) were at decreased risk of urethral obstruction relative to cats in intermediate ages, although their highest risk group was cats aged 4 to <15 years, an older range than in the current study. Segev et al. (2011) found that the mean

age of cats affected by urethral obstruction was significantly less than control cats (mean age \pm SD 51.7 months \pm 37.7 months vs. 75.7 months \pm 61.3 months) but this approach did not allow for a curvilinear effect of age. For both studies, only univariable associations were reported, and in the latter study, 24% of cases were recurrent (rather than first) episodes of urethral obstruction, which may have increased the mean age of affected cats compared to those in the current study. In the current study we did not attempt to diagnose the underlying causes of urethral obstruction. However FIC has been shown to be an important cause of urethral obstruction in male cats, estimated to be the underlying reason in 29-100% of cases (Gerber et al., 2005; Kruger et al., 1991; Sævik et al., 2011; Segev et al., 2011), and FIC incidences by age generally reflect our estimated effects of age on urethral obstruction. FIC is most commonly first diagnosed in young to middle aged cats; Defauw et al. (2011) reported that 70% of affected cats experienced their first episode of FIC when aged between one and six years, and Kim et al. (2017) found middle aged cats (3 to <9 years old) were at higher risk of FIC compared to cats aged <3 years. Many environmental stressors have been implicated as risk factors for cats developing FIC (Cameron et al., 2004; Defauw et al., 2011; Kim et al., 2017; Lund et al., 2016) and it may be that middle aged cats particularly once they have reached social maturity at 36-48 months of age (whereby cats have developed adult social behaviour, interactions with other cats including defence of territory (Landsberg and Ley, 2012)) may be more likely to develop FIC and urethral obstruction. It is possible that the lower rates of urethral obstruction in older cats reflect a selection effect whereby cats predisposed to urethral obstruction progressively become affected over time so that the old cats reflect a less predisposed population.

Burmese breed were at decreased risk of urethral obstruction, a finding consistent with that from a previous large epidemiological study (Lekcharoensuk et al., 2001). However, other studies assessing potential risk factors for FLUTD or FIC did not find any specific breed associations (Buffington et al., 2006; Defauw et al., 2011; Lund et al., 2016; Segev et al., 2011; Walker et al., 1977). In the current study, non-pedigree cats were at increased risk cats of urethral obstruction compared to pedigree cats. This is in contrast to results from a small study where pedigree cats were more likely to be affected by FIC (which included urethral obstruction) than non-pedigree cats (Cameron et al., 2004).

A key strength of the current study was careful selection of case and control consultations, including use of incidence density sampling. Incidence density sampling has not been used commonly in veterinary studies but is the appropriate method when cases and controls are drawn from an open source population, a common situation for veterinary studies. Risk-based designs have been used much more commonly in veterinary case-control studies but can yield biased results due to failure to account for differences in time at risk of the outcome event (Dohoo et al., 2009). As required under incidence density sampling, consultations were eligible only where the cat was presented to the clinic for reasons not thought to be associated with age, breed, bodyweight or BCS. In addition, covariates for multivariable models were chosen based on our causal hypotheses for interrelationships between each of age, breed, bodyweight and BCS and both (a) each other and (b) with urethral obstruction.

Conclusions

Male castrated pet cats with greater BCS are at increased rate of urethral obstruction compared to cats in lesser body condition while rate of urethral obstruction is similar in cats with low and high bodyweights provided those differences in bodyweight are not due to differences in BCS. Further research is needed to define why there is a positive association between BCS and rate of urethral obstruction. In the interim., clinicians should encourage owners of castrated male pet cats to ensure their cat's BCS is not high. This is particularly important for young to middle-aged nonpedigree cats as they are at increased risk relative to very young and older cats and pedigree cats.

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Conflict of interest statement

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References

- Bernard, M.A., 1978. Feline urologic syndrome: a study of seasonal incidence, frequency of repeat visits and comparison of treatments. Can. Vet. J. 19, 284– 288.
- Bjornvad, C.R., Nielsen, D.H., Armstrong, P.J., McEvoy, F., Hoelmkjaer, K.M., Jensen, K. S., Pedersen, G.F., Kristensen, A.T., 2011. Evaluation of a nine-point body condition scoring system in physically inactive pet cats. Am. J. Vet. Res. 72, 433– 437.
- Buffington, C.A., Westropp, J.L., Chew, D.J., Bolus, R.R., 2006. Risk factors associated with clinical signs of lower urinary tract disease in indoor-housed cats. J. Am. Vet. Med. Assoc. 228, 722–725.
- Cameron, M.E., Casey, R.A., Bradshaw, J.W., Waran, N.K., Gunn-Moore, D.A., 2004. A study of environmental and behavioural factors that may be associated with feline idiopathic cystitis. J. Small Anim. Pract. 45, 144–147.
- Cave, N.J., Allan, F.J., Schokkenbroek, S.L., Metekohy, C.A.M., Pfeiffer, D.U., 2012. A cross-sectional study to compare changes in the prevalence and risk factors for feline obesity between 1993 and 2007 in New Zealand. Prev. Vet. Med. 107, 121– 133.
- Colliard, L., Paragon, B.M., Lemuet, B., Benet, J.J., Blanchard, G., 2009. Prevalence and risk factors of obesity in an urban population of healthy cats. J. Feline Med. Surg. 11, 135–140.
- Courcier, E.A., O'Higgins, R., Mellor, D.J., Yam, P.S., 2010. Prevalence and risk factors for feline obesity in a first opinion practice in Glasgow, Scotland. J. Feline Med. Surg. 12, 746–753.
- Defauw, P.A.M., Van de Maele, I., Duchateau, L., Polis, I.E., Saunders, J.H., Daminet, S., 2011. Risk factors and clinical presentation of cats with feline idiopathic cystitis. J. Feline Med. Surg. 13, 967–975.
- Dohoo, I., Martin, W., Stryhn, H., 2009. Veterinary Epidemiologic Research. VER Inc., Charlettetown.
- Gerber, B., Boretti, F.S., Kley, S., Laluha, P., Muller, C., Sieber, N., Unterer, S., Wenger, M., Fluckiger, M., Glaus, T., Reusch, C.E., 2005. Evaluation of clinical signs and causes of lower urinary tract disease in European cats. J. Small Anim. Pract. 46, 571–577.
- Gerber, B., Eichenberger, S., Reusch, C.E., 2008. Guarded long-term prognosis in male cats with urethral obstruction. J. Feline Med. Surg. 10, 16–23.
- German, A.J., Holden, S.L., Moxham, G.L., Holmes, K.L., Hacket, R.M., Rawlings, J.M., 2006. A simple reliable tool for owners to assess the body condition of their dog or cat. J. Nutr. 136, 2031S–2033S.
- Greene, J.P., Lefebvre, S.L., Wang, M., Yang, M., Lund, E.M., Polzin, D.J., 2014. Risk factors associated with the development of chronic kidney disease in cats evaluated at primary care veterinary hospitals. J. Am. Vet. Med. Assoc. 244, 320-327.
- Greenland, S., Pearl, J., Robins, J.M., 1999. Causal diagrams for epidemiologic research. Epidemiology 10, 37–48.
- Greenland, S., Thomas, D.C., 1982. On the need for the rare disease assumption in case-control studies. Am. J. Epidemiol. 116, 547–553.
- Jones, B.R., Sanson, R.L., Morris, R.S., 1997. Elucidating the risk factors of feline lower urinary tract disease. N. Z. Vet. J. 45, 100-108.
- Kienzle, E., Bergler, R., 2006. Human-animal relationship of owners of normal and overweight cats. J. Nutr. 136, 1947S-1950S.
- Kienzle, E., Moik, K., 2011. A pilot study of the body weight of pure-bred clientowned adult cats. Br. J. Nutr. 106 (Suppl. 1), S113–S115.

- Kim, Y., Kim, H., Pfeiffer, D., Brodbelt, D., 2017. Epidemiological study of feline idiopathic cystitis in Seoul, South Korea. J. Feline Med. Surg. doi:http://dx.doi. org/10.1177/1098612X17734067.
- Knol, M.J., Vandenbroucke, J.P., Scott, P., Egger, M., 2008. What do case-control studies estimate? Survey of methods and assumptions in published casecontrol research. Am. J. Epidemiol. 168, 1073–1081.
- Kokmen, E., Özarfati, Y., 1996. İmpact of referral bias on clinical and epidemiological studies of Alzheimer's disease. J. Clin. Epidemiol. 49, 79–83.
- Kruger, J.M., Osborne, C.A., Goyal, S.M., Wickstrom, S.L., Johnston, G.R., Fletcher, T.F., Brown, P.A., 1991. Clinical evaluation of cats with lower urinary tract disease. J. Am. Vet. Med. Assoc. 199, 211–216.
- Laflamme, D., 1997. Development and validation of a body condition score system for cats: a clinical tool. Feline Pract. 25, 13–17.
- Landsberg, G., Ley, J.M., 2012. Kitten development. In: Little, S.E. (Ed.), The Cat: Clinical Medicine and Management. Elsevier, Missouri, pp. 182–190.
- Lekcharoensuk, C., Osborne, C.A., Lulich, J.P., 2001. Epidemiologic study of risk factors for lower urinary tract diseases in cats. J. Am. Vet. Med. Assoc. 218, 1429– 1435.
- Lund, E.M., Armstrong, P.J., Kirk, C.A., Klausner, J.S., 2005. Prevalence and risk factors for obesity in adult cats from private US veterinary practices. Int. J. Appl. Res. Vet. Med. 3, 88–96.
- Lund, H.S., Sævik, B.K., Finstad, Ø.W., Grøntvedt, E.T., Vatne, T., Eggertsdóttir, A.V., 2016. Risk factors for idiopathic cystitis in Norwegian cats: a matched casecontrol study. J. Feline Med. Surg. 18, 483–491.
- Reif, J.S., Bovee, K., Gaskell, C.J., Batt, R.M., Maguire, T.G., 1977. Feline urethral obstruction: a case-control study. J. Am. Vet. Med. Assoc. 170, 1320.
- Robertson, I.D., 1999. The influence of diet and other factors on owner-perceived obesity in privately owned cats from metropilitan Perth, Western Australia. Prev. Vet. Med. 40, 75–85.
- Rothman, K.J., Greenland, S., Lash, T.L., 2008. Case-control studies, In: Rothman, K.J., Lash, T.L. (Eds.), Modern Epidemiology. 3rd edn Lippincott Williams and Wilkins, Philadelphia pp 124-125.

- Rowe, E., Browne, W., Casey, R., Gruffydd-Jones, T., Murray, J., 2015. Risk factors identified for owner-reported feline obesity at around one year of age: dry diet and indoor lifestyle. Prev. Vet. Med. 121, 273–281.
- Sackett, D.L., 1979. Bias in analytic research. J. Chronic Dis. 32, 51-63.
- Sævik, B.K., Trangerud, C., Ottesen, N., Sørum, H., Eggertsdóttir, A.V., 2011. Causes of lower urinary tract disease in Norwegian cats. J. Feline Med. Surg. 13, 410–417. Scarlett, J.M.>Donoghue, J.M., 1998. Associations between body condition and
- disease in cats. J. Am. Vet. Med. Assoc. 212, 1725–1731. Segev, G., Livine, H., Ranen, E., Lavy, E., 2011. Urethral obstruction in cats:
- predisopsing factors, clinical, clinicopathological characteristics and prognosis. J. Feline Med. Surg. 13, 101–108.
- Shoveller, A.K., DiGennaro, J., Lanman, C., Spangler, D., 2014. Trained vs untrained evaluator assessment of body condition score as a predictor of percent body fat in adult cats. J. Feline Med. Surg. 16, 957–965.
- Sumner, J.P., Rishniw, M., 2017. Urethral obstruction in male cats in some Northern United States shows regional seasonality. Vet. J. 220, 72–74.
- Teng, K.T., McGreevy, P.D., Toribio, J., Raubenheimer, D., Kendall, K., Dhand, N.K., 2017. Risk factors for underweight and overweight in cats in metropolitan Sydney, Australia. Prev. Vet. Med. 144, 102–111.
- Teng, K.T., McGreevy, P.D., Toribio, J., Raubenheimer, D., Kendall, K., Dhand, N.K., 2018. Associations of body condition score with health conditions related to overweight and obesity in cats. J. Small Anim. Pract. doi:http://dx.doi.org/ 10.1111/jsap.12905.
- Textor, J., Hardt, J., Knüppel, S., 2011. DAGitty: a graphical tool for analyzing causal diagrams. Epidemiology 22, 745.
- Vandenbroucke, J.P., Pearce, N., 2012. Case-control studies: basic concepts. Int. J. Epidemiol. 41, 1480–1489.
- Walker, A.D., Weaver, A.D., Anderson, R.S., Crighton, G.W., Fennell, C., Gaskell, C.J., Wilkinson, G.T., 1977. An epidemiological survey of the feline urological syndrome. J. Small Anim. Pract. 18, 283–301.
- Willeberg, P., Priester, W.A., 1976. Feline urologic syndrome: associations with some time, space, and individual patient factors. Am. J. Vet. Res. 37, 975–978.