

Canine spaying: the positives and negatives

Can we make evidence-based recommendations about neutering dogs, asks Kathryn Pratschke MVB MVM CertSAS DipLECVS MRCVS RCVS, European specialist in small animal surgery, UK

Although medical/chemical options exist to suppress hormone production without physically removing the gonads, most commonly in veterinary practice 'neutering' refers to surgical removal of the ovaries/testes. In recent years, partly thanks to the Internet and social media, there has been rising concern among owners and breeders about the potentially undesirable effects of neutering, above and beyond the known surgical/anaesthetic risks. Anecdotally, few veterinary practices have a practice neutering policy, with individual veterinary surgeons being free to give their own opinion and recommendations to clients. If you go to the literature to see what the current evidence recommends, it is not a straightforward exercise.

This article will review the main evidence currently available for various neutering practices in pet dogs – issues such as population control and early neuter (<24 weeks) that pertain more to rescue shelters and feral animal management programmes will not be covered.

One of the problems when it comes to assessing the evidence base for neutering is the variability in the strength of the evidence. It's all well and good to say that a recommendation is 'evidence-based', but if the evidence is actually quite flimsy then the term 'evidence-based' means little or nothing. Many, if not most, of the published studies in the veterinary literature are retrospective, so this intrinsically means a high risk of inconsistent data and recall bias. When you read the detail about study populations you often find selection bias, and a suitable control group may or may not have been selected (if there is a control group at all). Veterinary studies often contain numbers that are simply too small for any reliable statistical analysis, although this doesn't stop us from generating numbers and significant/non-significant statements.

The situation is complicated further by the fact that many veterinary papers ignore confounding factors that will skew the result; and there are cases where the fundamental study design is flawed. In terms of considering the evidence it's also important to understand the difference between an observed 'potential association' (ie. there might be an association but we don't know whether A causes B) and an established causal relationship (ie. the data shows that A causes B). The majority of the veterinary publications regarding neutering practices and health risks only show potential associations, but the information is often presented as though a causal relationship has been proven.

THE BENEFITS OF NEUTERING – WHAT CAN WE SAY? POPULATION CONTROL

The question of population control relates more to rescue

centre animals than to individual client-owned animals. That said, there is no question that clients bear responsibility for unwanted litters that might result from unplanned or accidental mating of intact dogs. There is also the not inconsiderable inconvenience of dealing with oestrus episodes – this applies to the owners of male as well as female dogs.

RISKS ASSOCIATED WITH BREEDING AND PREGNANCY

Brucella canis, a breeding-associated infection, is not endemic in Ireland or the UK but it has been identified sporadically in many European countries and in North America (von Kruedener 1976, Corrente et al 2010, Holst et al 2012, Carter and Johnson 2012). Two cases have recently been confirmed in the UK, both in dogs brought in from rescue groups in other parts of Europe. With the increasing tendency for people to bring their pets with them when travelling, and to rescue dogs through overseas agencies, there is an increasing risk that such 'new' infections will be seen. *B canis* is predominantly a cause of infertility and genitourinary tract infection in dogs, but, it is also zoonotic, so there are public health concerns and, in some countries, it is a notifiable disease.

In terms of pregnancy-related complications, dystocia is the main one of veterinary concern. Although rates of dystocia are low in many breeds (<5%), they are reportedly as high as 80-85% in those with large and/or brachycephalic skulls (Bergstrom et al 2006, Forsberg et al, 2007). Dystocia carries morbidity and mortality risk for both dam and offspring, and if Caesarean section is required there could be significant cost implications.

PREVENTION OF CANCER

Cancer prevention is one of the more commonly cited reasons for neutering dogs. The effect on the incidence of mammary tumours, in particular, has historically been a strong argument in favour of neutering female dogs. Many veterinary surgeons are familiar with the figures of 0.5% risk of mammary tumours for bitches spayed before their first season, 8% for those spayed after one season and 26% for those spayed before the third season (Schneider et al, 1969). This study involved only 87 bitches, all in Alameda County in California, selected from submissions to the Animal Neoplasm registry between 1963-1966, so a long time ago and in a very specific population of dogs. The control group was a selection of bitches of broadly similar age and breed that had non-neoplastic lesions submitted during the same time period, and almost a quarter were

not breed matched at all. No other factors were taken into account. Given all of this, it is not really that surprising that a more recent systematic review of the literature on this subject found that overall the literature supports there being a protective effect from neutering, but whether it reduces the risk as dramatically as suggested in earlier studies is open to question (Beauvais et al, 2012). It's reasonable, therefore, to advise of a protective effect, but not to overstate the scale of the effect. For male dogs, obviously the risk of testicular tumours is removed through neutering, but there is no evidence that it reduces the incidence of malignant prostatic tumours and we do not know if it affects mammary cancer risk.

PREVENTION OF PYOMETRA

It's important to think about the magnitude and clinical impact of any given disease risk. In Sweden, where elective spaying is rarely practised, pyometra was documented in 25% of the bitches in their population by 10 years of age, ie. one in four, which is quite a high incidence (Egenvall et al, 2001). Another study carried out in charity hospitals in the UK (Gibson et al, 2013) documented an increase in the incidence of pyometra concurrent with a decrease in the rate of neutering in the population. While this UK study does not demonstrate causality, it raises a possible association between a decline in neutering and an increase in the incidence of pyometra. Although some cases can be managed medically and many cases with pyometra are successfully managed surgically, mortality rates between 4.2-17% are reported and comorbidities affecting other organ systems can be a problem (Johnston et al, 2001, Gibson et al, 2013). Even for straightforward cases there may be significant cost implications so it's something that should be discussed with owners who do not wish to neuter their dogs.

IMPACT ON BEHAVIOUR

The question of how neutering affects behaviour in dogs is very difficult to assess, but it is a subject about which people hold very strong views. Behaviour is the result of extremely complex interactions between numerous environmental and biological factors and the majority of veterinary studies are simply not constructed in a way that allows confounding variables to be removed. There are, however, some consistent patterns that emerge, for example most studies show a disproportionate number of intact male dogs involved in aggression-related problems, particularly relating to other dogs and to more aggressive attacks (Gershman et al, 1994, MacKenzie 2010). Although there are studies that describe an increased problem with aggression in spayed females, these studies have no control groups for comparison and provide insufficient information about the population from which the data was actually collected. As a result, the reliability of any findings should probably be considered open to debate.

In the absence of robust prospective well-structured studies on this topic, veterinary surgeons should realise that they are advising owners based on opinion and anecdotal evidence rather than from a strong evidence base.

THE DISADVANTAGES OF NEUTERING – WHAT CAN WE SAY?

Some of the more commonly raised concerns include neutering and neoplasia, neutering and orthopaedic disease, neutering and behavioural problems, neutering and urinary incontinence, and neutering and obesity.

DOES NEUTERING INCREASE THE RISK OF CANCER?

The idea that neutering a pet dog might increase their risk of cancer is clearly an emotive one for owners and where there are breed-specific implications breeders may hold very strong opinions. It's a difficult question to answer; the evidence currently available for review does suggest the possibility of an increased risk for certain types of neoplasia in at-risk breeds if animals are neutered. How strong a risk exists is not so clear. The issue of 'relative risk' compared to 'absolute risk' is important, as relative risk will always tend to exaggerate potential benefit and harm. 'Relative risk' reported in a clinical study refers to the risk level identified in that specific population of animals compared to whatever control group was selected, and under the conditions applied to the study. 'Absolute risk' is the risk in the population in general, and there is a tendency to assume that the two are the same, when in reality, they may be quite different, particularly with less well-constructed studies. We lack reliable epidemiological data regarding the true population incidence for most of the diseases in question and that is quite a big problem – what is an appropriate reference or control group for increased risk when you don't actually know the baseline? We also need to consider that disease incidence may change over time with shifts in population genetics and that this may be a region-specific phenomenon. If the underlying disease only occurs in <0.2% for example, then even a two to threefold increase in risk still translates in real terms to a 'low risk'. Some breed-specific studies have contradictory findings, for example, two studies were published in the same year that documented both an increased risk (Torres de la Riva et al, 2013) and no increased risk (Hart et al, 2013) for haemangiosarcoma in neutered Golden Retrievers. However, these authors made no mention of the fact that there seems to have been an increase in haemangiosarcoma in Golden Retrievers in North America in the past decade or so, which could have impacted the results. A survey from North America, in 1988, did not show Golden Retrievers as over-represented but, by 2011, the Golden Retriever Club of America reported a nearly one-in-five risk of haemangiosarcoma within the breed. In contrast, a survey of insured breeds in the UK, from 2002, showed a lower incidence of haemangiosarcoma in Golden Retrievers than all other breeds pooled (Dobson et al, 2002). This information strongly suggests that geographic sub-populations within breeds may have significant differences in cancer risk and that this can change over time; this is another reason to be cautious about extrapolating information from one continent to another in terms of breed-specific reports.

In Vizslas, a retrospective owner questionnaire-based study carried out in North America suggested an increased risk of haemangiosarcoma, lymphosarcoma and mast cell tumours in animals neutered after 12 months (Zink et al, 2014). In some categories the increase in risk was seemingly very high – neutered females were nine times more likely to develop haemangiosarcoma compared with intact females, early neutered females had a six-fold increased odds ratio for haemangiosarcoma and late neutered females 11.5 compared with intact females. Late neutered males were five times more likely to develop haemangiosarcoma compared with intact males. However, despite these apparently hugely increased risk levels for a malignant and aggressive form of cancer that we know carries a high mortality rate and a relatively short survival time, there was no significant difference in longevity between neutered and entire dogs, ie. they lived just as long ($p=0.595$). This makes it difficult to interpret the increased risk numbers and true clinical impact. Another issue with this paper is that it was based on owner recollection, with no requirement for clinical confirmation of any diagnosis put forward by owners. Nonetheless, it would be prudent to discuss the possibility of an increased risk in a purebred Vizsla, albeit there is no information regarding disease risk in European populations as opposed to North American.

Neutered dogs have also been reported as at increased

risk of osteosarcoma, although the risk may depend on breed, with Rottweilers and other large and giant breeds considered at increased risk in two studies (Ru et al, 1998, Cooley et al, 2002).

Both studies were retrospective and contained moderate levels of bias. However, there is some experimental evidence to support a potential role for sex hormones in development of bone tumours so it would be reasonable to consider that neutering before maturity in an at-risk breed may increase the relative risk of osteosarcoma.

A link between castration and increased risk of prostatic carcinoma/adenocarcinoma has been suggested in male dogs but again there are problems with the evidence cited in support of this. Some of the studies that suggested the increased risk put dogs that were only neutered because of prostatic disease in the 'neutered' group, which brings in significant bias – if you include dogs that already have prostatic disease in the neutered group, you may well find an increased risk of prostatic disease in the neutered group! Most drew their cases only from patients attending referral/specialist centres (Obradovich et al, 1987, Bell et al, 1991, Bryan et al, 2007); it's hard to say how much you can extrapolate results from this type of population to the general population, or whether it will vary between countries where referral habits may be different. In the author's opinion, it would be hard to say that the available evidence strongly supports making any specific claims regarding the effect of neutering on the risk of prostatic neoplasia, although we can say that neutering reduces significantly the risk of other prostatic conditions such as abscessation and cysts (see Figure 2).

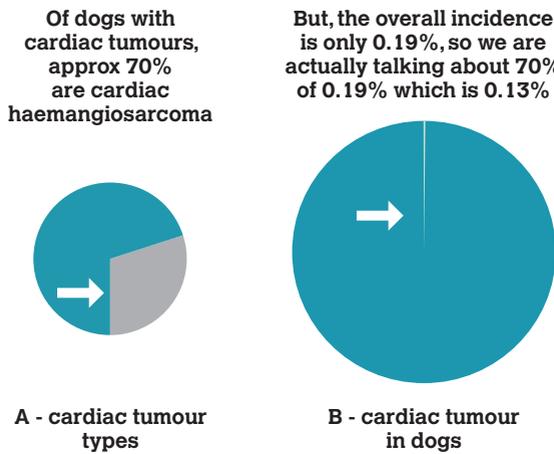


Figure 1: The situation with cardiac haemangiosarcoma is a good example of why we need to look not just at the numbers for increased risk of any particular disease, but also the incidence of that disease in the population and how severe the impact of that disease will be on any affected individuals. Cardiac haemangiosarcoma is without doubt a serious disease with a poor prognosis, and one that is devastating for owners and their pets. The overall incidence of cardiac tumours is estimated at 0.19%, with up to 65-70% being haemangiosarcoma – these figures are based on a study from North America published in 1999. If we take the higher figure for haemangiosarcoma of 70%, then 70% of 0.19 gives us a 0.13% incidence in the reported population. The population in question was dogs seen at referral centres in North America between 1982 and 1995. If we look at a pie chart based on cardiac tumour type (A) and say that neutering could increase the risk of haemangiosarcoma then this seems very concerning. If we look at a pie-chart for overall incidence of cardiac tumours, however (B) the visual impact is much less, ie. the way the data is presented influences how we react to it. Even with a three or even five-fold increase in risk, we are still realistically talking about less than 1%, and that is less than 1% of dogs that are referred for specialist investigations and management, not 1% of all dogs.



Figure 2: Prostatic cysts are associated with a range of clinical signs including dysuria, tenesmus, constipation, urinary incontinence, abdominal and perineal swellings. They carry a good prognosis with surgical treatment, but there are of course financial implications for clients (the star indicates where the prepuce is retracted beneath surgical swabs).

NEUTERING AND JOINT DISEASE

There are quite a number of studies looking at the question

of neutering and cranial cruciate ligament disease, and they have unfortunately produced contradictory and inconsistent results.

Overall, the preponderance of the evidence suggests an increased risk in some populations of neutered animals, but other factors, such as breed, bodyweight, conformation and so on do need to be taken into account (Duvall et al, 1999, Hart et al, 2013, Hart et al, 2016). A similar situation holds with hip dysplasia - some studies suggest an increased risk with neutering while others fail to show any difference in risk. The trend overall favours a link but it is unclear whether neutering is the primary cause, or a confounding factor (van Hagen et al, 2005, Witsbreger et al, 2008, Hart et al, 2013, Torres et al, 2013).

NEUTERING AND OBESITY

Obesity is a concern often cited by owners when discussing whether to neuter their dog, particularly with male dogs. Although most studies agree that neutered animals are more likely to be obese than intact animals, there is no agreement why this is the case. There is a tendency to assume that the metabolic rate will be lower in neutered animals, but this has not been conclusively proved.

There are so many factors involved in obesity in pet dogs – feeding habits, owner activity levels, husbandry and so forth – that it seems relatively unlikely neutering is of overwhelming importance *per se* (German, 2006).

Clients should probably be educated to the fact that obesity is eminently avoidable through appropriate diet and exercise levels, regardless of a dog's neuter status, i.e. neutering is not an excuse for letting your dog get fat!

NEUTERING AND URINARY INCONTINENCE

Canine acquired urethral sphincter mechanism incontinence (USMI) is often referred to colloquially as 'spay incontinence' due to the widespread belief that neutering is a significant risk factor, largely based on some relatively old studies that took no account of confounding factors, i.e. other factors that could also potentially increase the risk of USMI. Two more recent studies – one retrospective and one case control – found no significant association between neutering, or age at neutering, and USMI, although one did identify an increased risk of incontinence in bitches above 10kg bodyweight (de Bleser et al, 2009, Forsee et al, 2013). A systematic review of studies evaluating the effect of neutering on the risk of urinary incontinence in 2012 that concluded that while there is some evidence that neutering may increase the risk of incontinence, and earlier neutering may be more likely to do so than later neutering, overall, the evidence is weak and no firm statement on risk can be made (Beauvais et al, 2012). In 2016, a study looking specifically at German Shepherd dogs found a higher risk of incontinence in neutered females at 7% compared to 0% (Hart et al, 2016).

It seems likely, however, that this may not be a general neutering – USMI risk, however, in light of a study from this year (Byron et al, 2017) that identified body weight (expected adult bodyweight >25kg) as a significant factor,

with the hazard of USMI decreasing for every month's delay in neutering up to the first year of age.

CONCLUSIONS

The evidence to date, supports real potential benefits in disease prevention in neutered animals, particularly in females, and it's important not to forget this when considering potential negative factors. Some of these negative consequences need consideration (particularly in at-risk breeds), some are genuinely very low risk, some are unproven and some we do not know whether neutering is a primary cause or just one of many confounding factors. The volume of unregulated, complex and often ambiguous information available through the Internet and social media is enormous. Even if clients access reputable sources of information, there can still be problems with the fundamental strength of the evidence, as has been discussed in this article. Veterinary practices, as well as individual veterinary surgeons, need to appreciate and understand the relevant issues, including the fact that there is no single neutering policy that is 'right'.

Giving clients the best advice regarding neutering their individual dog involves weighing up the relative risks and benefits as we currently understand them, then giving judicious and well-informed recommendations that suits the individual client and pet.

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READER QUESTIONS AND ANSWERS

- 1: IN DOGS, THE MAIN PREGNANCY-RELATED COMPLICATION IS THOUGHT TO BE:**
- A** Pre-eclampsia
 - B** Dystocia.
 - C** Diabetes mellitus.
 - D** Chronic anaemia.
- 2: IN LARGE BREED FEMALE DOGS, NEUTERING BEFORE THE SECOND SEASON**
- A** Has no effect on incidence of malignant mammary tumours.
 - B** Lowers the incidence of urinary tract infections.
 - C** Has no impact on the risk of developing hip dysplasia.
 - D** May increase the risk of urethral sphincter mechanism incontinence.
- 3: A PAPER YOU READ TELLS YOU THAT FEMALE VISZLA'S NEUTERED EARLIER THAN SIX MONTHS HAVE AN INCREASED RELATIVE RISK OF SPLENIC TUMOURS. WHAT DOES THIS MEAN?**
- A** The risk in those neutered at less than six months was higher relative to the control population
 - B** The risk in those neutered at less than six months is

- high relative to current incidence levels
 - C** The risk in those neutered at less than six months is high within a specific geographical area
 - D** The risk in those neutered at less than six months is high relative to other closely-related breeds.
- 4: IN REGIONS WHERE IT IS UNUSUAL TO HAVE DOGS NEUTERED, SUCH AS DENMARK, WHICH OF THE FOLLOWING IS TRUE?**
- A** A higher mortality rate is associated with pyometra in female dogs over 10 years of age.
 - B** The incidence of pyometra may be as high as one in four by 10 years of age and above.
 - C** Pyometra is less likely to be a surgical disease and more likely to be managed medically.
 - D** The incidence of pyometra is roughly 20% with the majority having concurrent ovarian tumours.
- 5: MALE DOGS THAT ARE NEUTERED HAVE**
- A** An increased risk of prostatic neoplasia developing.
 - B** A higher metastatic rate with prostatic tumours.
 - C** A reduced risk of malignant mammary tumours.
 - D** No change in risk of developing splenic lymphoma.

ANSWERS: 1: B; 2: D; 3: A; 4: B; 5: D