Urethral Sphincter Mechanism Incompetence in Dogs: An Update

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ABSTRACT

Urethral sphincter mechanism incompetence (USMI) is the most common cause of acquired urinary incontinence in dogs. The pathogenesis of USMI is multifactorial and complex. Studies have shown variable results regarding the effects and timing of sterilization on the incidence of USMI. Diagnosis of USMI is often based on history, physical examination, and elimination of other differentials. Treatment options for USMI include medications, such as α-adrenergic agents and estrogen products, minimally-invasive urethral bulking procedures, surgical procedures (e.g., indwelling urethral occluders), or combination therapy. The overall prognosis for USMI is typically fair to good with long-term therapy.
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Introduction

Urinary incontinence, with a prevalence in dogs ranging from 5.1 to 20%, is particularly important because of the impact it can have on human-animal interactions and specifically on relinquishment or euthanasia of a pet.[1–4] A study evaluating causes of relinquishment of pets presented to an animal shelter identified that, in dogs, soiling in the house was the sole reason for 9.5% of relinquishments and a primary contributor to a multifactorial set of causes in 18.5% of cases.[4] Urinary incontinence may be congenital or acquired. Acquired etiologies may be neurogenic (e.g., lower-motor neuron, upper-motor neuron, detrusor-urethral dyssynergy, primary bladder atony) or non-neurogenic (e.g., urethral sphincter mechanism incompetence [USMI], secondary bladder atony, detrusor instability or urge incontinence, urovaginal fistula).[5,6] The most common cause of acquired urinary incontinence is USMI, which affects up to 60% of all dogs with acquired incontinence.[6–8]

Brief Review of Relevant Anatomy

Key anatomy of the lower urinary tract includes the detrusor muscle of the urinary bladder, the smooth muscle of the internal urethral sphincter, the skeletal muscle of the external urethral sphincter, and the ureterovesicular junction. Urine retention is under sympathetic nervous control through the hypogastric nerve and concurrent inhibition of the parasympathetic nervous system, whereas micturition is under parasympathetic nervous control through the pelvic nerve. Somatic sensory control is via the pudendal nerve (**Figure 1**).[1,9–11] Urinary incontinence in patients with USMI is defined as the involuntary leakage of urine during the storage phase.[11]

Pathophysiology/Etiology of USMI

Urethral sphincter mechanism incompetence has been associated with sterilization given the higher prevalence among spayed female dogs and responsiveness of some dogs to estrogen supplementation.[2,3] The method of sterilization (ovariohysterectomy [OHE] versus ovariectomy) does not alter the risk of developing USMI.[12] Structural, functional, and hormonal differences are present within a dog post-OHE as compared with pre-OHE, and may contribute to abnormal urine storage. However, the etiology is complex. A cohort study of 269 dogs found no difference in long-term (2-yr) urinary continence rates between spayed and intact dogs.[13] Additionally, USMI can occur in male dogs and has been reported in both male and female intact animals.[14,15]

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DES (Diethylstilbestrol); FSH (follicle-stimulating hormone); GnRH (gonadotropin analogues); HO (hydraulic occluders); LH (luteinizing hormone); OHE (ovariohysterectomy); PO (*per os*); PPA (phenylpropanolamine); USMI (urethral sphincter mechanism incompetence)

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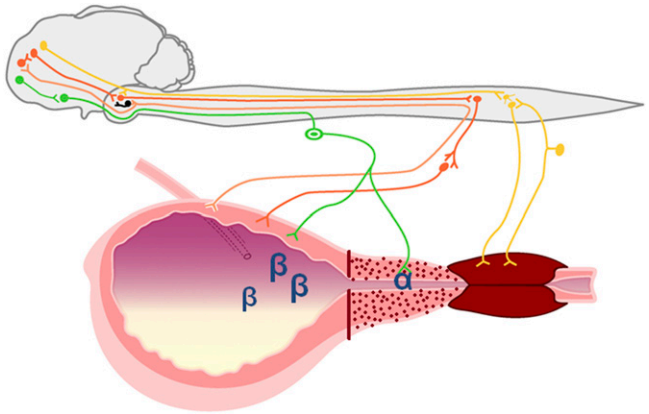

FIGURE 1 *Graphic representation of nervous control of micturition with innervation, receptors, and associated muscles denoted. Nervous control (*Green*) Sympathetic innervation via hypogastric nerve. Targets β receptors of detrusor muscle and α of the internal sphincter. (*Orange*) Parasympathetic innervation via pelvic nerve. Targets Ach receptors of detrusor muscle. (*Yellow*) Somatic nervous system via pudendal nerve. Targets skeletal muscle of the external urethral sphincter under conscious control. Musculature (*Pink*) Detrusor muscle. (*Brown Stippled*) Internal urethral sphincter. (*Solid Brown*) External urethral sphincter.*

The exact pathophysiology of USMI is unknown, but it appears to be multifactorial. Proposed mechanisms include hormonal (e.g., decreased estrogen levels altering urethral tone, increased gonadotropin levels, decreased local cyclooxygenase-2 expression), structural (e.g., altered collagen and smooth muscle, shortened urethra, intrapelvic bladder), and functional (e.g., altered urethral pressure profiles) abnormalities.[11,16]

Timing of Sterilization

There is conflicting evidence for USMI development and OHE in relation to the time of the first heat. There are numerous reports of decreased incontinence in dogs sterilized prior to the first heat cycle as compared with those sterilized later in life.[17,18] In contrast, dogs undergoing OHE at less than 3 mo of age in one study had greater incontinence compared with dogs undergoing the procedure after the first heat cycle.[3] Several studies found no association with USMI and timing of OHE.[3,19] A recent systematic review of 1853 records included only 3 articles on this topic and concluded that there was neither consistent nor strong enough evidence to make recommendations on the effect of OHE or age at the time of OHE for the development of USMI.[20]

Hormonal Abnormalities: Estrogen Deficiency and Gonadotropins

One of the most strongly hypothesized contributors to USMI is that estrogen deficiency impacts sphincter competence. Estrogen receptors are prominent in the urethra and increase the sensitivity of α-receptors to catecholamines, which improves urethral tone.[21] Alterations in urethral tone are observed both with normal estrus and iatrogenically-induced alterations in estrogen levels. However, intact female dogs only have elevated estrogen levels twice per yr; at other times, plasma estrogen levels are similar to those in sterilized female dogs.[22–24] Additionally, clinical experience supports that not all incontinent dogs improve with estrogen supplementation. Therefore, it is unlikely that estrogen alone is the sole factor for the development of USMI.

Elevations in luteinizing hormone (LH) and follicle-stimulating hormone (FSH) following OHE have been hypothesized to play a role in the development of USMI. Administration of gonadotropin analogues (GnRH) to down-regulate pituitary expression of gonadotropin receptors and subsequently suppress LH and FSH production has been effective in some dogs.[25] However, a relationship between gonadotropin expression and changes in urethral pressure profile changes has not been appreciated, and the impact of OHE on urinary tract receptor expression is controversial.[21,25,26] Gonadotropin analogues may have direct effects on the lower urinary tract to improve bladder capacity, which may explain why some dogs with USMI benefit.[27]

Gonadotropins may also induce prostaglandin synthesis. Prostaglandins play a role in regulating bladder tone and modulating micturition reflexes, and are cytoprotective for uroepithelium.[28] Decreased cyclooxygenase-2 expression in the lower urinary tract of sterilized dogs may impair normal function and contribute to development of USMI.[28]

Structural Abnormalities

Post-OHE, dogs develop increased collagen to muscle ratio in the bladder and urethra.[29] Different collagen composition of pelvic floor soft tissues results in altered tensile strength, contractility, and neuronal transmission.[30] Shorter urethral lengths found in sterilized dogs compared with their intact counterparts may contribute to an intrapelvic bladder and modified urethral pressure profiles.[18,21,31,32] Anatomical changes associated with tail docking, and obesity with intra-abdominal fat deposition have also been associated with USMI.[17,33]

Functional Abnormalities

There is decreased urethral closure pressure within 1 yr of OHE even in dogs that remain continent. If the urethral closure pressure drops below a certain threshold, the sphincter becomes incompetent and incontinence develops.[21,22,32]

Clinical Features

Signalment

Affected dogs are typically young to middle-aged spayed female dogs. Medium to large-breed dogs (>15 kg) are commonly affected, with

one study showing that of a population of spayed female dogs (n = 566), 9.12% of the dogs >15 kg were incontinent, whereas 1.37% of those <15 kg were incontinent.[3,34] Predisposed breeds include Doberman pinschers, Old English sheepdogs, springer spaniels, boxers, rottweilers, Weimaraners, giant schnauzers, and Irish setters.[11,26,35] Of the small-breed dogs, miniature poodles are the most common breed affected.[17] Most dogs develop incontinence within 3 yr of OHE or neuter, but clinical signs may be seen immediately or delayed up to 10 yr.[11,26] Males may also develop incontinence secondary to USMI. A retrospective analysis identified 54 cases of USMI out of 121 incontinent male dogs and showed that the condition follows a similar pattern of presentation and signalment to females, with larger, middle-aged, and castrated dogs most affected.[14]

History and Physical Exam

Animals with USMI may have intermittent or continuous urinary incontinence of varying degrees of severity. Generally, incontinence is worse when recumbent or during periods of increased abdominal pressure (e.g., barking, coughing, excitement).[17] There are no physical exam findings specific to USMI, but particular attention should be given to bladder size, tone, and location; urethral and prostatic palpation on rectal examination; neurologic assessment; and examination of the external genitalia.[11,17]

Diagnosis

The diagnosis of USMI is based on signalment as described, history of intermittent incontinence (particularly while relaxed or resting), and exclusion of other causes of incontinence.[11] Complete blood count and chemistry panel are generally unremarkable, but should be performed to rule out underlying systemic disease. Urinalysis with urine specific gravity and urine culture with antimicrobial sensitivity via cystocentesis are recommended as part of the minimum database for urinary incontinence to screen for concurrent polyuria/polydipsia or urinary tract infections that may be contributing to the severity of the urinary incontinence. Abdominal radiographs and ultrasound are typically normal in dogs with USMI. However, abdominal imaging is very important in helping to rule out concurrent urinary tract calculi or neoplasia and should be included in the minimum database for the diagnostic workup of urinary incontinence. If a strong clinical suspicion for USMI remains after the minimum database is collected, then a trial of medical therapy is an acceptable diagnostic and therapeutic step.

Definitive diagnosis of USMI requires urodynamic studies. However, these tests require specialized equipment and are generally not widely available except at some universities and referral centers, including University of California Davis School of Veterinary Medicine and The Ohio State University College of Veterinary Medicine.[36] Urethral pressure profiles measuring pressure along the length of the urethra are required to document decreased urethral tone.[36] There is wide interindividual variation, and the test is affected by sedation, movement, and muscle activity. Briefly, a transurethral urethra pressure profile catheter is placed and connected to a transducer. The transducer then records pressures within the urethra as fluid is slowly infused and the catheter slowly withdrawn. The maximal urethral pressure recorded in this procedure is compared with baseline as well as the normal for the patient demographic. Cystometrogram is also helpful in evaluating bladder storage function and determining if there are concurrent detrusor abnormalities.[36]

Treatment

Medical Management

Medical management is always recommended prior to considering more invasive surgical options. Medical therapies include α-adrenergic agonists, estrogens or testosterone, GnRH analogues and immunization, and, uncommonly, anticholinergic drugs.

Alpha-adrenergic Agonists

Alpha-adrenergic drugs, such as the nonselective α-agonist phenylpropanolamine (PPA), are the frontline treatment for USMI. These drugs are effective because of their sympathomimetic effects on the bladder neck and urethra.[37] Response rates in female dogs range from 86 to 97%, although efficacy may decrease over time.[22,26,38,39] The cause for decreased efficacy in some dogs with prolonged treatment is unknown; desensitization of the α-receptors has been hypothesized, but remains controversial.[40] The response rate in male dogs to PPA is lower: approximately 44%.[14]

Based on FDA recommendations in the United States, the starting dose of PPA is 2 mg/kg twice daily.[41] A study evaluating once-daily PPA in which continence was achieved in 8/9 dogs suggests that once-daily therapy at 1.5 mg/kg can also be considered.[40] Clinical improvement is expected within the first 3–4 wk after starting therapy; maximal urodynamic effects of PPA are observed by 7–14 days.[15,42] Generally, PPA is well tolerated at prescribed doses. Potential side effects, especially with overdose, include cardiovascular (e.g., arterial hypertension, tachycardia), neurologic (e.g., seizures, muscle tremors, ataxia, behavioral changes), gastrointestinal (e.g., vomiting, nausea), generalized anxiety, and malaise.[40,43] Most dogs with PPA toxicosis develop clinical signs within 2–8 hr, although some dogs show signs as early as 30 min. Most dogs recover within 24 hr with supportive care, but fatalities have been reported.[43] Ephedrine (1–2 mg/kg *per os* [PO] *q* 12 hr) is an alternative α-adrenergic and pseudoephedrine is a stereoisomer of ephedrine.[26] Phenylpropanolamine is considered superior because dogs treated

with ephedrine and pseudoephedrine tend to develop more adverse effects (in particular, nervousness and excitability), with decreased efficacy. Reported response rates to ephedrine and pseudoephedrine are only 25–75%.[44]

Estrogens and Testosterone

Estrogen supplementation may improve continence for female dogs who do not respond fully to PPA because estrogen and α-adrenergic drugs are synergistic and estrogens increase the number of and sensitivity of α-receptors.[14] Estrogen supplementation is not recommended for administration to cats or male dogs regardless of the underlying disease being treated because of potential side effects of pancreatic, hepatic, and cardiac lesions; and feminization, respectively.[45]

Diethylstilbestrol (DES) has historically been one of the most commonly used drugs in this class, with 60–80% of dogs showing improvement in their incontinence when DES is administered as a sole therapy.[11] There are, however, several considerations with DES. Diethylstilbestrol is a long-acting synthetic estrogen. Estrogens can cause bone marrow suppression through a poorly understood mechanism.[45,46] Bone marrow suppression specific to DES has been cautioned historically,[47] and data on estrogen-induced myelosuppression in general makes it a reasonable concern.[48] However, despite the association of estrogens with myelosuppression, there is not literature to support myelosuppression as a common side effect of DES at the recommended dose and dosing schedule in dogs. Long-acting estrogens can also increase the potential risk of mammary and reproductive neoplasia in rodent models, but the risk in dogs with long-term use has not been established.[49–52] Diethylstilbestrol is no longer commercially available because of carcinogenic and teratogenic effects in humans, but can be acquired through veterinary compounding pharmacies. A recommended dose is 0.1 mg/kg PO *q* 24 hr for 3–5 days, then a weekly dose of up to 1 mg per dog.[45]

In 2011, the FDA approved estriol[a] for the treatment of USMI in dogs within the United States; estriol has been used in Europe for much longer. Compared with longer-acting estrogens, estriol is theorized to be less likely to cause bone marrow suppression due to altered metabolism[53,54] Dose-related vulvar hyperplasia, as noted with estrogens in general, is possible.[45] The FDA-recommended dose is 2 mg/dog PO *q* 24 hr with subsequent dose titration to the lowest effective dose based on clinical efficiency, often reaching doses as low as 0.5 mg/every other day.[55] Estriol should be used cautiously in intact bitches because of increased risk of pyometra.[46] A pilot study using a dosing regimen starting at 0.5 mg/dog once daily, increasing to 1.0 mg/dog if no response within 1 wk, and, after 2 wk, increasing to 2.0 mg/dog if no response revealed complete continence in 65% (13/20) of dogs using estriol, but response rates including partial responses were up to 93%.[54] Another study in which 129 intact bitches received an initial dose of 2 mg estriol per day for 1 wk followed by weekly reduction in dose to the lowest-tolerated dose and transition to every other day dosing as tolerated showed an 83% improvement in incontinence, with 61% being fully continent and the remaining 22% showing improvement in continence. Of the 129 dogs, 12 were classified as nonresponders. The final dose of estriol ranged from 0.25 mg/dog to 3 mg/dog, and 65% of these dogs received their dose daily with the remainder every other day.[46]

Testosterone supplementation may be considered in male dogs who do not respond favorably to PPA. Response rates tend to be poor, with one report showing that 4 of 5 dogs who were administered testosterone for USMI did not have a clinical response.[14] Additionally, testosterone is administered via an injection and is associated with infrequent but significant side effects, including aggression, perianal adenomas, perineal hernias, and prostatic disorders.[56]

GnRH Analogues and Immunization

Suppression of FSH and LH with GnRH analogues or vaccination against GnRH may improve continence in some dogs.[25,57] No adverse effects have been reported. Unfortunately, a major limitation of these therapies is decreased availability in the United States. Human-approved GnRH are often cost prohibitive, and an approved drug for domestic animals, deslorelin acetate, is strictly reserved for use in ferrets.[57] Additionally, commercial GnRH immunizations are currently off the market.[57]

Other Therapies

Detrusor instability and bladder hyperactivity may contribute to USMI in some dogs and should be considered when the disease is difficult to manage traditionally.[2,58] Anticholinergic drugs, such as oxybutynin, may be helpful in reducing detrusor muscle spasm.[59]

Minimally Invasive Urethral Bulking

Urethral bulking improves continence because injection of bulking agents into the urethral submucosa increases muscle fiber length and subsequently increases urethral closure pressure.[60] This procedure is well tolerated and minimally invasive, and dogs are generally continent within 2–3 days.[61] Reported response rates with bulking alone are approximately 60–70%, and an additional 15% of dogs will become continent with the addition of an α-agonist.[61,62] One of the biggest disadvantages to urethral bulking is the poor long-term response. Efficacy decreases over the first 12 mo, and repeated injections are often required in up to 40% of cases.[61]

Another major disadvantage at this time is the decreased availability of an acceptable bulking agent. Bovine collagen has been considered the historical gold standard product for this procedure.[63] Various other bulking agents, including polyethylene glycol carboxymethyl cellulose hydrogel, teflon, carbon-coated zirconium oxide beads, ethylene vinyl, calcium hydroxyapatite, and hyaluronic acid/dextrantomer copolymer have been investigated, but none have replaced the gold standard.[62,64] The most promising is polydimethylsiloxane[b], which performed well in a recent clinical trial in which 21/22 dogs became continent after bulking.[63]

Intraurethral injection of autologous muscle stem cells has shown promise both in direct application in human stress-induced incontinence as well as in a canine model of incontinence currently being translated to human medicine.[65,66] The objective of the injection is to restore urethral sphincter function, as well as restore the adnexal structures including blood supply and innervation to the urethral sphincter.[65] A clinical trial was recently completed at North Carolina State University.

All bulking agents are placed similarly via cystoscopy. While the cystoscope is positioned at the proximal urethra, an injection needle containing the bulking agent is passed through the operating channel and visualized at the end of the cystoscope. The agent is injected submucosally at the 2-, 6-, and 10-o'clock positions until a bleb extending to the midline of the urethra is created. The goal at the end of the procedure is for the blebs to just close the urethral lumen when at rest (**Figures 2A, B**).[64] However, there is evidence to suggest that this level of apposition may not be necessary to achieve continence.[61] Urine retention is the most concerning short-term complication, but this is typically transient and self-limiting. Acute allergic reaction has been associated with some bulking agents.[63]

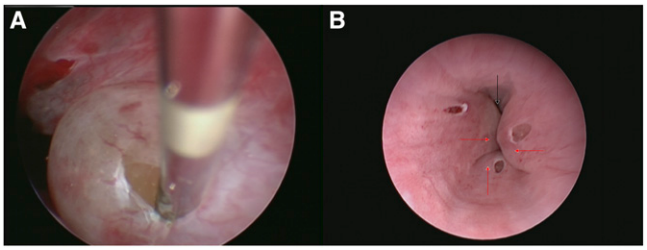

FIGURE 2 *(A) Cystoscopic view of injecting bulking agent at 3-, 6-, and 9-o'clock positions in the urethra. (B) Cystoscopic view after injection of bulking agent at completion of procedure. Red arrows identify collagen blebs and black arrow identifies the urethral lumen.*

Surgical Management

The goals of surgery for USMI are to increase urethral pressure, either by creating mid-urethral tension or cranial repositioning of the bladder neck, or to increase urethral length.[67] Over the last decade, surgical placement of urethral occluders has gained popularity and is an excellent option for dogs who fail medical management. Traditional surgical techniques including colposuspension, urethropexy, and cystourethropexy generally result in fair short-term, but poor long-term, continence.[68]

Urethral Occluders

Patient-controlled artificial urethral sphincters have been used for the treatment of refractory incontinence in human medicine for decades. In 1989, the first veterinary artificial urethral sphincter-like device used was a Dacron-impregnated Silastic band placed to encircle the proximal urethra and mechanically increase urethral resistance with subsequent continence.[69] Since that time, percutaneously adjustable urethral hydraulic occluders (HO) have become popular, and high continence rates (>90%) have been reported with their use in dogs.[67,70] Additionally, unlike other treatment options, response appears durable long-term; dogs from the initial pilot studies (n = 4 dogs) were continent at their last follow-up at >2 years.[67]

Urethral occluders are placed surgically via a ventral caudal median celiotomy. An in-depth surgical discussion is beyond the scope of this paper and has been published elsewhere.[67,70] Briefly, an inflatable silicone cuff is placed around the urethra and connected via tubing to a subcutaneous access port (**Figures 3A–C**). Approximately 30–45% of dogs may be continent following placement of the HO device alone because of passively increased urethral tone from the implant.[67,70,71] The addition of α-agonist or estrogen is recommended for animals who remain incontinent 2 wk postoperatively.[70] In the largest clinical study, 61% (n = 11/18) of dogs were continent after the placement of the HO in combination with medical management.[70] If refractory incontinence persists at 6–8 wk postoperatively, then saline may be injected in 0.1–0.2 mL increments into the subcutaneous access port using a noncoring Huber needle to inflate the silicone cuff.[70,71] Continence scores increased with HO placement for all cases in the literature.[67,70,71] Minor reported complications of HO include urinary tract infections (>4 mo after HO placement), temporary (<5 day) dysuria following HO placement and inflation, transient pain at the site of the subcutaneous port, and prolonged duration of urination.[67,70,71] Urinary obstruction is a major complication, which likely requires HO removal, and has been reported 1.5–23 mo postoperatively. Two dogs required urethral stenting to treat extraluminal urethral strictures in one report.[70] Although not yet reported in dogs, urethral atrophy secondary to chronic pressure on the pelvic urethra has been reported in humans with HO.[67,71]

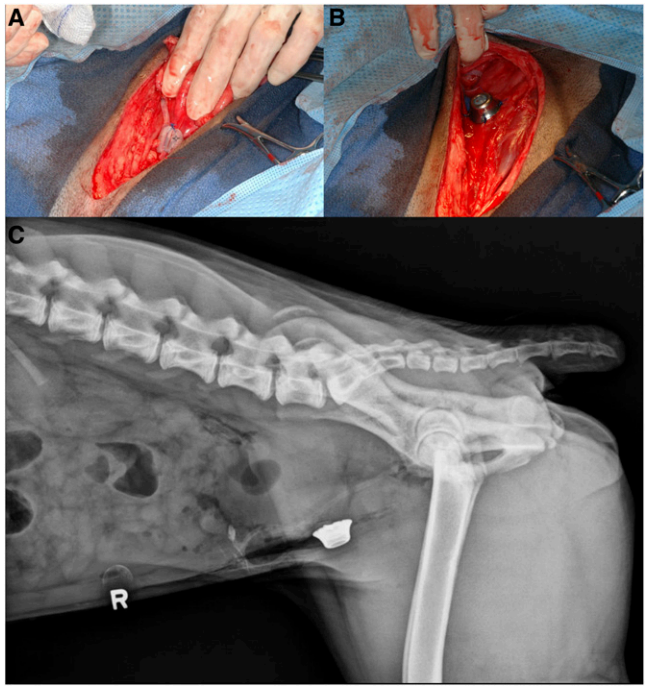

FIGURE 3 *(A) Intraoperative urethral occluder placement in a 14 mo old female spayed rottweiler with urethral hypoplasia. The cuff (*black star*) is in place around the urethra (*red arrow*) and tubing is exiting the body wall. (B) Intraoperative view of the subcutaneous port attached to the urethral occluder. (C) Postoperative radiograph showing placement of the subcutaneous port.*

Colposuspension

Colposuspension has historically been one of the most commonly performed surgical procedures for USMI.[72] In this surgery, the vagina is attached to the ventral abdominal wall with sutures that travel through the prepubic tendon to entrap the urethra.[72] In addition to advancing the bladder neck and proximal urethra cranially, the vagina cradles the urethra in a position over the pelvic brim to apply external compression. This procedure achieves short-term continence in 50–60% of dogs, but unfortunately, long-term continence is poor, with only 14% of dogs continent at 1 yr.[72,73] Transient dysuria may occur postoperatively, but complete urinary obstruction is uncommon. However, removal of the colposuspension sutures may be required if there is persistent obstruction that does not improve with conservative treatment.[72,73]

Urethral sling procedures have been combined with colposuspension to provide external urethral compression. Slings are created with either seromuscular bladder wall flaps or synthetic mesh material. However, combining these procedures with colposuspension does not improve outcome.[72] Colposuspension cannot be easily performed in dogs with intrapelvic bladders. Urethral lengthening has been performed in a small number of dogs with severe urethral hypoplasia and an intrapelvic bladder. Good results were reported in 7/8 dogs.[72]

Surgical techniques for male dogs that move the bladder neck cranially include vas deferens pexy and prostatopexy. Vas deferens pexy requires castration, which may worsen incontinence, and the pexy may become unstable over time.[74] Therefore, prostatopexy, suturing the prostatic capsule to the prepubic tendon, has been attempted to provide more stability. Unfortunately, results have been fairly disappointing. In a small study with nine male dogs undergoing prostatopexy, five dogs had improvement, but only one dog had complete resolution of incontinence; four dogs had no improvement.[74]

Urethropexy and Cystourethropexy

Similar to colposuspension, urethropexy or cystourethropexy move the bladder neck and proximal urethra to an intraabdominal position.[72] These procedures involve tacking the urethra or urethra and bladder neck, respectively, to the ventral abdominal wall. Unlike colposuspension, however, these pexy procedures reduce urethral luminal diameter and subsequently increase resistance to urine flow.[72,75] In a prospective study of 100 dogs, 87% of dogs improved after urethropexy. However, similar to other surgical techniques, the incontinence worsened with time, and long-term continence dropped to 56%.[35] Postoperative complications, including dysuria and anuria, were seen in approximately 20% of dogs.[35] Cystourethropexy was evaluated in a small 10-dog study and continence with surgery alone was only 20%.[75]

Conclusion

Incontinence, specifically USMI, is a relevant veterinary concern that impacts long-term well-being of both owners and pets. Etiology of USMI is multifactorial and complicated. Treatment options include medical and surgical management, or combination therapy. Medical management including α-adrenergic agents ± estrogen therapy is recommended for most cases of urinary incontinence. Minimally invasive urethral bulking and/or surgical urethral occluder placement may be considered for cases that are refractory to these medications. Some degree of lifelong medication is likely required even after urethral bulking is performed. Single-therapy surgical approaches, such as colposuspension, are currently out of favor.

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FOOTNOTES

[a] Incurin; Merck Animal Health, Summit, New Jersey

[b] Macroplastique; Uroplasty Cogentix Medical, Minnetonka, Minnesota

REFERENCES

1. Lappin MR, Barsanti JA. Urinary incontinence secondary to idiopathic detrusor instability: cystometrographic diagnosis and pharmacologic management in two dogs and a cat. *J Am Vet Med Assoc* 1987;191:1439–42.
2. Spain CV, Scarlett JM, Houpt KA. Long-term risks and benefits of early-age gonadectomy in dogs. *J Am Vet Med Assoc* 2004;224:380–7.
3. Forsee KM, Davis GJ, Mouat EE, et al. Evaluation of the prevalence of urinary incontinence in spayed female dogs: 566 cases (2003–2008). *J Am Vet Med Assoc* 2013;242:959–62.
4. Salman MD, Hutchison J, Ruch-Gallie R, et al. Behavioral reasons for relinquishment of dogs and cats to 12 shelters. *J Appl Anim Welf Sci* 2000;3:93–106.
5. Noël S, Claeys S, Hamaide A. Acquired urinary incontinence in the bitch: update and perspectives from human medicine. Part 1: The bladder component, pathophysiology and medical treatment. *Vet J* 2010;186:10–17.
6. Acierno MJ, Labato MA. Canine incontinence. *Compendium* 2006;28.
7. Krawiec DR. Urinary incontinence in dogs and cats. *Mod Vet Pract* 1988.
8. Holt PE. Urinary incontinence in dogs and cats. *Vet Rec* 1990;127:347–50.
9. Lane IF. Diagnosis and management of urinary retention. *Vet Clin North Am Small Anim Pract* 2000;30:25–57.
10. Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. *Nat Rev Neurosci* 2008;9:453–466.
11. Fischer J, Lane IF. Micturition disorders. In: Bartges J, Polzin DJ, eds. *Nephrology and Urology*. Chichester (UK): Wiley-Blackwell; 2011:755–77.
12. van Goethem B, Schaefers-Okkens A, Kirpensteijn J. Making a rational choice between ovariectomy and ovariohysterectomy in the dog: a discussion of the benefits of either technique. *Vet Surg* 2006;35:136–43.
13. Howe LM, Slater MR, Boothe HW, et al. Long-term outcome of gonadectomy performed at an early age or traditional age in dogs. *J Am Vet Med Assoc* 2001;218:217–21.
14. Aaron A, Eggleton K, Power C, et al. Urethral sphincter mechanism incompetence in male dogs: a retrospective analysis of 54 cases. *Vet Rec* 1996:139:542–6.
15. Power SC, Eggleton KE, Aaron AJ, et al. Urethral sphincter mechanism incompetence in the male dog: importance of bladder neck position, proximal urethral length and castration. *J Small Anim Pract* 1998;39:69–72.
16. Noël S, Claeys S, Hamaide A. Acquired urinary incontinence in the bitch: update and perspectives from human medicine. Part 2: The urethral component, pathophysiology and medical treatment *Vet J* 2010;186:18–24.
17. Holt PE. Urinary incontinence in the bitch due to sphincter mechanism incompetence: prevalence in referred dogs and retrospective analysis of sixty cases. *J Small Anim Pract* 1985;26:181–90.
18. Arnold S, Arnold P, Hubler M, et al. [Urinary incontinence in spayed female dogs: frequency and breed disposition]. *Schweiz Arch Tierheilkd* 1989;131:259–63 [in German].
19. Thrusfield MV, Holt PE, Muirhead RH. Acquired urinary incontinence in bitches: its incidence and relationship to neutering practices. *J Small Anim Pract* 1998;39:559–66.
20. Beauvais W, Cardwell JM, Brodbelt DC. The effect of neutering on the risk of urinary incontinence in bitches–a systematic review. *J Small Anim Pract* 2012;53:198–204.
21. Reichler IM, Pfeiffer E, Piché CA, et al. Changes in plasma gonadotropin concentrations and urethral closure pressure in the bitch during the 12 months following ovariectomy. *Theriogenology* 2004;62:1391–402.
22. Richter KP, Ling GV. Clinical response and urethral pressure profile changes after phenylpropanolamine in dogs with primary sphincter incompetence. *J Am Vet Med Assoc* 1985;187:605–11.
23. Schulze H, Barrack ER. Immunocytochemical localization of estrogen receptors in the normal male and female canine urinary tract and prostate. *Endocrinology* 1987;121:1773–83.
24. Hamaide AJ, Verstegen JP, Snaps FR, et al. Influence of the estrous cycle on urodynamic and morphometric measurements of the lower portion of the urogenital tract in dogs. *Am J Vet Res* 2005;66:1075–83.
25. Reichler IM, Hubler M, Jöchle W, et al. The effect of GnRH analogs on urinary incontinence after ablation of the ovaries in dogs. *Theriogenology* 2003;60:1207–16.
26. Reichler IM, Hubler M. Urinary incontinence in the bitch: an update. *Reprod Domest Anim* 2014;49(suppl 2):75–80.
27. Reichler IM, Barth A, Piché CA, et al. Urodynamic parameters and plasma LH/FSH in spayed Beagle bitches before and 8 weeks after GnRH depot analogue treatment. *Theriogenology* 2006;66:2127–36.
28. Ponglowhapan S, Church DB, Khalid M. Expression of cyclooxygenase-2 in the canine lower urinary tract with regard to the effects of gonadal status and gender. *Theriogenology* 2009;71:1276–88.
29. Coit VA, Gibson IF, Evans NP, et al. Neutering affects urinary bladder function by different mechanisms in male and female dogs. *Eur J Pharmacol* 2008;584:153–8.
30. Byron JK, Graves TK, Becker MD, et al. Evaluation of the ratio of collagen type III to collagen type I in periurethral tissues of sexually intact and neutered female dogs. *Am J Vet Res* 2010;71:697–700.
31. Wang KY, Samii VF, Chew DJ, et al. Vestibular, vaginal and urethral relationships in spayed and intact normal dogs. *Theriogenology* 2006;66:726–35.
32. Salomon JF, Gouriou M, Dutot E, et al. Experimental study of urodynamic changes after ovariectomy in 10 dogs. *Vet Rec* 2006;159:807–11.
33. Holt PE, Thrusfield MV. Association in bitches between breed, size, neutering and docking, and acquired urinary incontinence due to incompetence of the urethral sphincter mechanism. *Vet Rec* 1993;133:177–80.
34. Okkens AC, Kooistra HS, Nickel RF. Comparison of long-term effects of ovariectomy versus ovariohysterectomy in bitches. *J Reprod Fertil Suppl* 1997;51:227–31.
35. White RN. Urethropexy for the management of urethral sphincter mechanism incompetence in the bitch. *J Small Anim Pract* 2001;42:481–6.
36. Goldstein RE, Westropp JL. Urodynamic testing in the diagnosis of small animal micturition disorders. *Clin Tech Small Anim Pract* 2005;20:65–72.
37. Ek A. Adrenergic innervation and adrenergic mechanisms: A study of the human urethra. *Acta Pharmacol Toxicol (Copenh)* 1978;43(suppl 2):35–40.
38. Scott L, Leddy M, Bernay F, et al. Evaluation of phenylpropanolamine in the treatment of urethral sphincter mechanism incompetence in the bitch. *J Small Anim Pract* 2002;43:493–6.
39. White RA, Pomeroy CJ. Phenylpropanolamine: an alpha-adrenergic agent for the management of urinary incontinence in the bitch associated with urethral sphincter mechanism incompetence. *Vet Rec* 1989;125:478–80.
40. Claeys S, Rustichelli F, Noël S, et al. Clinical evaluation of a single daily dose of phenylpropanolamine in the treatment of urethral sphincter mechanism incompetence in the bitch. *Can Vet J* 2011;52:501–5.
41. FDA. Oral Dosage Form New Animal Drugs; Phenylpropanolamine. Federal Register Rules and Regulations 2012;77:53.

42. Carofiglio F, Hamaide AJ, Farnir F, et al. Evaluation of the urodynamic and hemodynamic effects of orally administered phenylpropanolamine and ephedrine in female dogs. *Am J Vet Res* 2006;67:723–30.
43. Peterson KL, Lee JA, Hovda LR. Phenylpropanolamine toxicosis in dogs: 170 cases (2004–2009). *J Am Vet Med Assoc* 2011;239:1463–9.
44. Byron JK, March PA, Chew DJ, et al. Effect of phenylpropanolamine and pseudoephedrine on the urethral pressure profile and continence scores of incontinent female dogs. *J Vet Intern Med* 2007;21:47–53.
45. Plumb DC. Diethylstilbestrol. In: Plumb DC, ed. *Plumb's veterinary drug handbook*. Ames: Blackwell Publishing; 2005:357–9.
46. Mandigers R, Nell T. Treatment of bitches with acquired urinary incontinence with oestriol. *Vet Rec* 2001;149:764–7.
47. Krawiec DR. Diagnosis and treatment of acquired urinary incontinence. *Comp Anim Pract* 1989;69:17–24.
48. Sontas HB, Dokuzeylu B, Turna O, et al. Estrogen-induced myelotoxicity in dogs: A review. *Can Vet J* 2009;50(10):1054–8.
49. Meites J. Relation of prolactin and estrogen to mammary tumorigenesis in the rat. *J Natl Cancer Inst* 1972;48:1217–24.
50. Russo IH, Russo J. Mammary gland neoplasia in long-term rodent studies. *Environ Health Perspect* 1996;104(9):938–67.
51. Bocchinfuso WP, Korach KS. Mammary gland development and tumorigenesis in estrogen receptor knockout mice. *J Mammary Gland Biol Neoplasia* 1997;2:323–34.
52. Cavalieri EL, Kumar S, Todorovic R, et al. Imbalance of estrogen homeostasis in kidney and liver of hamsters treated with estradiol: implications for estrogen-induced initiation of renal tumors. *Chem Res Toxicol* 2001;14:1041–50.
53. Hoeijmakers M, Janszen B, Coert A, et al. Pharmacokinetics of oestriol after repeated oral administration to dogs. *Res Vet Sci* 2003;75:55–9.
54. Janszen B, van Lear P, Bergman J. Treatment of urinary incontinence in the bitch: A pilot field study with incurin®. *Vet Q* 1997;19(suppl 1):42.
55. FDA. Oral Dosage Form New Animal Drugs; Estriol. Federal Register Rules and Regulations 2011;76:242.
56. Plumb DC. Testosterone. In: Plumb DC, ed. *Plumb's veterinary drug handbook*. Ames (IA): Blackwell Publishing; 2005:1309–12.
57. Donovan CE, Gordon JM, Kutzler MA. Gonadotropin-releasing hormone immunization for the treatment of urethral sphincter mechanism incompetence in ovariectomized bitches. *Theriogenology* 2014;81:196–202.
58. Nickel RF. Studies on the function of the urethra and bladder in continent and incontinent female dogs. *Vet Q* 1998;20(suppl 1):S102–3.
59. Tsuchida S, Nishizawa O, Noto H, et al. [A comparative study of the effects of propiverine, terodiline, oxybutynin on the lower urinary tract function in the decerebrate dog]. *Hinyokika Kiyo* 1990;36:915–9 [in Japanese].
60. Klarskov N, Lose G. Urethral injection therapy: what is the mechanism of action? *Neurourol Urodyn* 2008;27:789–92.
61. Byron JK, Chew DJ, McLoughlin ML. Retrospective evaluation of urethral bovine cross-linked collagen implantation for treatment of urinary incontinence in female dogs. *J Vet Intern Med* 2011;25:980–4.
62. Barth A, Reichler IM, Hubler M, et al. Evaluation of long-term effects of endoscopic injection of collagen into the urethral submucosa for treatment of urethral sphincter incompetence in female dogs: 40 cases (1993-2000). *J Am Vet Med Assoc* 2005;226:73–6.
63. Bartges J, Callens A. Polydimethylsiloxane Urethral Bulking Agent (PDMS UBA) Injection for Treatment of Female Canine Urinary Incontinence- Preliminary Results. In: Proceedings from the American College of Veterinary Internal Medicine Forum; 2011; Denver, CO.
64. Bartges J. Urethral bulking for urinary incontinence. In: Bartges J, Polzin PD, eds. *Nephrology and Urology of Small Animals*. Chichester (UK): Wiley-Blackwell; 2011:379–82.
65. Staack A, Rodríguez LV. Stem Cells for the Treatment of Urinary Incontinence. *Curr Urol Rep* 2011;12(1):41–6.
66. Eberli D, Aboushwareb T, Soker S, et al. Muscle precursor cells for the restoration of irreversibly damaged sphincter function. *Cell Transplant* 2012;21(9):2089–98.
67. Rose SA, Adin CA, Ellison GW, et al. Long-term efficacy of a percutaneously adjustable hydraulic urethral sphincter for treatment of urinary incontinence in four dogs. *Vet Surg* 2009;38:747–53.
68. Claeys S, Noël S, Hamaide A. Acquired urinary incontinence in the bitch: update and perspecitves from human medicine. Part 3: The urethral component and surgical treatment. *Vet J* 2010;186:25–31.
69. Dean PW, Novotny MJ, O'Brien DP. Prosthetic sphincter for urinary incontinence: results in three cases. *J Am Anim Hosp Assoc* 1989;25:447–54.
70. Currao RL, Berent AC, Weisse CW, et al. Use of a percutaneously controlled urethral hydraulic occluder for treatment of refractory urinary incontinence in 18 female dogs. *Vet Surg* 2013;42:440–7.
71. Delisser PJ, Friend EJ, Chanoit GP, et al. Static hydraulic urethral sphincter for treatment of urethral sphincter mechanism incompetence in 11 dogs. *J Small Anim Pract* 2012;53:338–43.
72. McLoughlin MA, Chew DJ. Surgical treatment of urethral sphincter mechanism incompetence in female dogs. *Comp Cont Edu Vet* 2009;360–73.
73. Rawlings C, Barsanti JA, Mahaffey MB, et al. Evaluation of colposuspension for treatment of incontinence in spayed female dogs. *J Am Vet Med Assoc* 2001;219:770–5.
74. Holt PE, Coe RJ, Hotston Moore A. Prostatopexy as a treatment for urethral sphincter mechanism incompetence in male dogs. *J Small Anim Pract* 2005;46:567–70.
75. Massat BJ, Gregory CR, Ling GV, et al. Cystourethropexy to correct refractory urinary incontinence due to urethral sphincter mechanism incompetence. Preliminary results in ten bitches. *Vet Surg* 1993;22:260–8.