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Objective—To determine whether mitral valve repair (MVR) under cardiopulmonary bypass would be an effective treatment for mitral regurgitation in small-breed dogs.

Design—Retrospective case series.

Animals—48 small-breed dogs (body weight, 1.88 to 4.65 kg [4.11 to 10.25 lb]; age, 5 to 15 years) with mitral regurgitation that underwent surgery between August 2006 and August 2009.

Procedures—Cardiopulmonary bypass was performed with a cardiopulmonary bypass circuit. After induction of cardiac arrest, a mitral annuloplasty was performed, and the chordae tendineae were replaced with expanded polytetrafluoroethylene chordal prostheses. After closure of the left atrium and declamping to restart the heart, the thorax was closed.

Results—Preoperatively, cardiac murmur was grade 3 of 6 to 6 of 6, thoracic radiography showed cardiac enlargement (median vertebral heart size, 12.0 vertebrae; range, 9.5 to 14.5 vertebrae), and echocardiography showed severe mitral regurgitation and left atrial enlargement (median left atrium-to-aortic root ratio, 2.6; range, 1.7 to 4.0). 45 of 48 dogs survived to discharge. Three months after surgery, cardiac murmur grade was reduced to 0/6 to 3/6, and the heart shadow was reduced (median vertebral heart size, 11.1 vertebrae, range, 9.2 to 13.0 vertebrae) on thoracic radiographs. Echocardiography confirmed a marked reduction in mitral regurgitation and left atrium-to-aortic root ratio (median, 1.7; range, 1.0 to 3.0).

Conclusions and Clinical Relevance—We successfully performed MVR under cardiopulmonary bypass in small-breed dogs, suggesting this may be an effective surgical treatment for dogs with mitral regurgitation. Mitral valve repair with cardiopulmonary bypass can be beneficial for the treatment of mitral regurgitation in small-breed dogs. (J Am Vet Med Assoc 2012;240:1194–1201)

Mitral regurgitation with DMVD is an acquired cardiac disease that occurs commonly in dogs.1–4 The exacerbation of DMVD is related to age, degree of MR (murmur and countercurrent jet), and degree of valvular degeneration.5,6,7 Degeneration of the mitral valve complex such as mitral valve prolapse, thickening, and tearing of the chordae tendineae is associated with deteriorating clinical signs and prognosis in patients with DMVD.7,8

When the compensatory function of the pulmonary vasculature fails in patients with MR, cough and dyspnea because of pulmonary congestion and pulmonary edema are observed. In affected dogs with dyspnea caused by severe pulmonary edema, treatment includes diuretics, supplemental oxygen, nitrates, cardiotonics, and vasodilators.9 Recently, a controlled clinical trial10 of pimobendan for the treatment of dogs with congestive heart disease indicated evidence that pimobendan improved quality of life and survival time in dogs with DMVD. However, the approximate survival time for dogs with DMVD or rupture of the chordae tendineae is <1 year.10,11 Because medical treatment for MR with cardiovascular drugs is palliative, MR is progressive and prognosis is poor. Reduction of MR requires surgical intervention.

For the surgical treatment of MR in humans, valve replacement or valve repair are performed.12–13 Newer methods for percutaneous valve treatment are in different stages of development in human medicine. These include a percutaneous edge-to-edge attachment technique involving the use a clip, deployment through trans-septal catheterization, or mitral annuloplasty with coronary sinus cinching.12,13 However, mitral repair via

Abbreviations

ACE Angiotensin-converting enzyme
CPB Cardiopulmonary bypass
CRI Constant rate infusion
DMVD Degenerative mitral valve disease
ePTFE Expanded polytetrafluoroethylene
MR Mitral regurgitation
MVR Mitral valve repair

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a conventional surgical approach currently confers improved long-term outcome with excellent durability in human patients with DMVD. Surgical repair of DMVD typically incorporates 2 components: a leaflet or chordal repair to correct prolapse and annuloplasty to restore normal annular geometry, increase leaflet coaptation, reduce tension on suture lines, and prevent future annular dilation. Artificial chordal replacement with ePTFE is an established technique for MVR with good long-term results. It is usually performed for prolapse of the anterior and posterior mitral leaflets.

A previous report describes the difficulty of open heart surgery with CPB in small-breed dogs. Mitral valve replacement with a mechanical valve has been attempted in dogs, but it is difficult to avoid thrombosis and mismatch of prosthetic heart valves sized for humans in small-breed dogs. A bioprosthetic valve with superior antithrombogenic properties has also been tested experimentally and applied clinically in few dogs. Given the excellent outcome of MVR in human patients, the purpose of the study reported here was to develop a safe method to perform CPB in veterinary patients, perform MVR with CPB in 48 small-breed dogs with mild to severe MR, and determine the early and intermediate term results of MVR under CPB in small-breed dogs with DMVD.

Materials and Methods

Dogs < 5 kg (11 lb) with MR referred to Nihon University Animal Medical Center Veterinary Cardiovascular Medicine and Surgery Unit between August 2006 and August 2009 were enrolled in the study. Physical examination, echocardiography, thoracic radiography (3 views), blood pressure measurement (by means of oscillographic methods), ECG, CBC, serum biochemical analysis, coagulation panel, and urinalysis were performed in all patients. Owners provided written informed consent for surgery.

General anesthesia and surgery were performed in the same manner for all dogs. Preanesthetic medications included atropine sulfate (0.025 mg/kg [0.011 mg/lb], IM), midazolam (0.3 mg/kg [0.14 mg/lb], IV), fentanyl (5 µg/kg [2.3 µg/lb], IV), and cefazolin sodium (20 mg/kg [9.1 mg/lb], IV). Each dog was then oxygenated with 100% oxygen, which was followed by face mask induction with 3% isoflurane and intubation with an endotracheal tube (internal diameter, 4 to 7 mm). Anesthesia was maintained with 2% to 3% isoflurane in oxygen at 1.5 L/min. During CPB, anesthesia was maintained by CRI of fentanyl (0.4 µg/kg/min [0.2 µg/lb/min], IV) and propofol (0.2 mg/kg/min [0.09 mg/lb/min], IV).

During the surgery, heart rate, respiratory rate, rectal temperature, esophageal temperature, arterial oxygen saturation, end-tidal CO₂, and isoflurane concentration were continuously monitored by use of a physiologic monitor system. The right femoral artery was catheterized for measurement of systolic, diastolic, and mean arterial blood pressures, and the femoral vein was catheterized for measurement of central venous pressure, both with a 22-gauge indwelling catheter. Complete blood count, Hct, total protein concentration, activated clotting time, and arterial blood gases were determined as necessary by use of blood samples obtained via the femoral artery catheter. A urinary catheter was placed to monitor urine volume.

Cardiopulmonary bypass was provided by a heart-lung machine with an extracorporeal circuit, 0.5-m² oxygenator, and heat exchanger. The CPB circuit was filled with 20% D-mannitol (5 mL/kg), 7% sodium bicarbonate (2 mL/kg [0.9 mL/lb]), heparin sodium (500 U), and acetate Ringer’s solution (120 to 170 mL). Fifty milliliters of whole blood was replaced with priming solution in dogs weighing < 4 kg (8.8 lb).

After a neck incision, the left carotid artery and external jugular vein were separated and secured with 3-0 nylon sutures. Next, a left thoracotomy was performed in the fourth or fifth intercostal space after incision of the left atrium. The cardioplegic solution was infused every 20 minutes. During CPB, arterial and venous blood pressure, the cardioplegic solution, and cardiac output were monitored.

Intracardiac procedures were performed via a left atriotomy approach. The ruptured mitral chordae tendineae of the septal and mural mitral valve were visualized via an incision in the left atrium. The first step for mitral annuloplasty was to make continuous sutures with pledgets at the cranial and caudal commissure of the mitral annulus to reduce the size of both commissure regions (Figure 1) because annular dilation at the septal and mural commissures was observed intraoperatively. Next, ePTFE strips (1.5 X 55 mm) were sutured to the mitral valve annulus with 5-0 sutures (Figure 2). Mitral annulus size was reduced to the size of the aortic sinus of Valsalva. The circumference of the aortic sinus of Valsalva was measured via echocardiographic evaluation at short-axis aortic level.
Artificial ePTFE chordae tendineae were sutured to the mitral valve and papillary muscles for chordae tendineae replacement (Figure 3). The ruptured mitral chordae tendineae of the septal and mural mitral valves were excised. Double needles attached to ePTFE chordae tendineae were pierced at S2 of the septal leaflet and were also pierced at the craniolateral papillary muscle. Then those needles were pierced at S1 of the septal leaflet, and knots were made. A second ePTFE chorda tendinea was sutured at S2 and S3 of the septal mitral valve and the caudomedial papillary muscle in the same manner. A third set of double needles of ePTFE chorda tendinea were pierced at M2 of the mural mitral valve and the caudolateral papillary muscle. These neochordae lengths were adjusted at mitral annulus level while avoiding tension to the heart and keeping a temporary Alfieri stitch, and knots were made. Then the temporary Alfieri stitch was removed.

The left atrium was closed with simple-interrupted and continuous 5-0 sutures. After closing the left atrium, the aortic clamp was released, and spontaneous sinus rhythm was observed. If ventricular fibrillation was observed, a defibrillator was used at 10 to 30 J. The duration of cardioplegia was 60 to 95 minutes. At the return of sinus rhythm, a dobu-
tamine CRI was started (1 to 5 µg/kg/min [0.45 to 0.23 µg/lb/min]), if needed. The body temperature was recovered to 37°C [98.6°F], and the CPB flow was gradually reduced before being completely shut down. Anesthesia was switched to maintenance with isoflurane inhalation.

After recovery from CPB, the catheter for cardioplegic infusion was removed from the aorta. The catheters were removed from the jugular vein and carotid artery. The carotid artery and jugular vein were closed with a continuous pattern by use of 7-0 suture material. The cervical wound was closed with a simple continuous pattern by use of 3-0 nylon. After the removal of catheters, protamine sulfate (6 mg/kg [2.7 mg/lb], IV) was administered over 30 minutes. Then, a thoracostomy tube was placed and the thorax was closed routinely after confirming that activated clotting time was < 200 seconds. The patients regained spontaneous respiration and reflexes 2 to 3 hours after the end of surgery. Isoflurane inhalation was discontinued, and the endotracheal tube was removed. The total duration of anesthesia was 4 to 6 hours.

After removal of the endotracheal tube, the patients were maintained in a cage filled with O₂ (25% to 35%) for 12 to 24 hours. Dalteparin sodium (25 to 50 U/kg [11.4 to 22.7 U/lb], SC) was administered when chest drainage fluid...
was reduced to a rate of < 1 to 2 mL/h. The chest tube was removed 24 h after surgery. Cefazolin sodium* (20 mg/kg, IV, q 8 h) was administered for 7 days. Laboratory tests were performed every day until discharge. Ozagrel hydrochloride† (10 mg/kg, PO, q 12 h), a thromboxane A synthase inhibitor, was administered for 1 month after surgery.

Statistical analysis—Statistical analysis of the data was performed with statistical software. The Shapiro-Wilk test was used to assess normal distribution. Values were expressed as median and range because data were not normally distributed. The Friedman test followed by the Dunn multiple comparison test were used to compare findings before and after MVR. Values of P < 0.05 were considered significant. Survival probability was estimated with the Kaplan-Meier method.

Results

Forty-eight small-breed dogs (body weight, 1.88 to 4.65 kg [4.11 to 10.25 lb]; age, 5 to 15 years) with MR were included in the study. Breeds of the dogs included Chihuahua (n = 19), Maltese (13), Pomeranian (5), Shih Tzu (4), Yorkshire Terrier (4), Toy Poodle (1), Miniature Dachshund (1), and mixed (1). Clinical signs included cough, pulmonary edema, exercise intolerance, cardiac syncope, and ascites. All dogs were graded for heart failure according to the International Small Animal Cardiac Health Council classification as follows: class II (n = 25 dogs), class IIIa (16), and class IIIb (8). Dogs were treated with ACE inhibitors (n = 34), furosemide (22), torasemide (12), pimobendan (28), digoxin (6), carvedilol (3), spironolactone (2), or sildenafil (1). Systolic murmur at auscultation, the chest wall thrill related to the cardiac murmur, first heart sound abnormality, and tricuspid regurgitation were identified on right parasternal long-axis views; moderate to severe MR and tricuspid regurgitation were identified on tendineae in right parasternal long-axis views; moderate to severe MR was diagnosed also measured by use of standard techniques. On the basis of these findings, moderate to severe MR was diagnosed and MVR under CPB was selected for treatment.

Two-dimensional echocardiography revealed an enlarged mitral area was auscultated and classified as grade 4/6 classified grade 1, 20 classified grade 2, and 11 classified grade 3 (Table 1). On the thoracic radiographs, the vertebral heart size was significantly decreased and improvement was confirmed through observations of reduced cardiac shadow, tracheal elevation, and pulmonary edema. Echocardiography showed that left atrial enlargement had decreased and MR was reduced remarkably. Left ventricular end-diastolic diameter was significantly decreased after MVR.

The clinical signs had essentially resolved by 1 month after surgery in all 45 patients, as had the tendency to reverse cardiac remodeling. The International Small Animal Cardiac Health Council classification was significantly improved. In addition, the number of medications prescribed to each dog, such as ACE inhibitors, furosemide, torasemide, carvedilol, pimobendan, sildenafil, spironolactone, and digoxin, decreased at 1 month after surgery. Twenty-nine dogs were no longer receiving medications. The survival probability was 93.3% at 38 months after MVR.

Discussion

In the present study, we successfully performed MVR with CPB in small-breed (body weight ≤ 5 kg) dogs, making this an effective surgical treatment for dogs with MR. Forty-five patients survived surgery and were alive at least 5 months after surgery. No annular

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before MVR (n = 48)</th>
<th>1 month (n = 45)†</th>
<th>3 months (n = 43)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>3.15 (1.88–4.62)</td>
<td>3.25 (2.00–4.98)</td>
<td>3.38* (2.15–5.50)</td>
</tr>
<tr>
<td>Cardiac murmur (grade)</td>
<td>5 (3–6)</td>
<td>2* (0–4)</td>
<td>2* (0–3)</td>
</tr>
<tr>
<td>Vertebral heart size (No. of vertebrae)</td>
<td>12.2 (9.5–14.5)</td>
<td>11* (8.7–13.5)</td>
<td>11* (8.2–13.0)</td>
</tr>
<tr>
<td>Left atrium-to-aortic root ratio</td>
<td>2.6 (1.7–4.0)</td>
<td>1.8* (1.4–2.7)</td>
<td>1.7* (1.0–3.0)</td>
</tr>
<tr>
<td>Left ventricular end-diastolic diameter (cm)</td>
<td>31.9 (23.4–41.5)</td>
<td>26.3* (18.5–30.7)</td>
<td>24.3* (17.6–34.9)</td>
</tr>
<tr>
<td>Left ventricular end-systolic diameter (cm)</td>
<td>14.4 (9.0–25.4)</td>
<td>14.6 (9.7–24.6)</td>
<td>14.9 (9.4–22.2)</td>
</tr>
<tr>
<td>Fractional shortening (%)</td>
<td>52.3 (37.7–68.1)</td>
<td>38.6* (24.2–60.5)</td>
<td>38.4* (22.2–60.3)</td>
</tr>
<tr>
<td>ISACHC classification</td>
<td>IIia (II–IIIb)</td>
<td>Ib* (Ia–II)</td>
<td>Ia* (Ia–II)</td>
</tr>
</tbody>
</table>

Values are expressed as median and range. *Indicates a significant difference from the preoperative value (P < 0.05). †One dog died during recovery from anesthesia because of hemorrhage, and 2 dogs died of thrombosis 5 and 8 days after surgery. ‡Two dogs did not undergo examinations 3 months after surgery because of owner constraints. ISACHC = International Small Animal Cardiac Health Council.
dilation or rupture of prosthetic chordae tendineae occurred in this series of patients. Annuloplasty by use of ePTFE and reestablishment of coaptation with prosthetic chordae tendineae are imperative considerations for MVR in dogs with mitral valve prolapse and DMVD. Prior to the series of patients in the present report, many patients in our hospital died undergoing this surgical procedure before we accomplished these results. We believe that operating room personnel need to be trained in the CPB procedures to achieve a good success rate. Similarly, surgeons need to be trained in the technique and have a high level of surgical skill and experience to successfully perform this surgery. Communication of the progress of the surgery among the surgeon, anesthesiologist, perfusionist, and other personnel reduces mistakes and shortens response time to changing circumstances. We suggest that the positive outcome for the present report is at least in part a result of a highly trained and motivated operating room team working regularly together over a long period of time.

Complications of open-heart surgery in small animals may be related to decreased circulation, thrombosis, hemodilution, and electrolyte imbalances. To reduce these risks, in the present study, we minimized the priming volume of the CPB tubing by using the shortest length possible and partially replacing the priming fluid with cross-matched whole blood in dogs weighing < 4 kg. Body temperature was lowered to 25°C to 30°C (77°F to 86°F) to minimize organ dysfunction in the event of low circulation or circulatory arrest during CPB. Additionally, heparin was required to prevent thrombosis during CPB and protamine was also used to antagonize heparin at the end of CPB. Protamine at high doses causes blood pressure to decrease. Because hypotension may lead to critical hypoperfusion, protamine should be administered slowly over 30 to 60 minutes. We believe that these procedures are important for successful CPB in small-breed dogs.

Mitral valve repair basically consists of annuloplasty and chordal replacement. In human patients, mitral annuloplasty has been stated to be the most important factor in maintaining the long-term durability of the mitral valve after MVR. The mitral annulus is saddle shaped, higher at the cranial and caudal segments, and lower at the commissures. The change in annular orientation indicates that the mitral annulus undergoes translational motion during systole. The mitral area is reduced from mid diastole to midsystole. This sphincter mechanism increases the depth of coaptation of the leaflets by contracting during systole and increases the annular orifice area during diastole. These physiologic motions of the annulus should be maintained in mitral annuloplasty.

Annular stabilization with prosthetic material enhances durability by increasing leaflet coaptation and preventing future annular dilatation. Jensen et al demonstrated that saddle-shaped annuloplasty rings provide superior uniform annular force distribution, compared with flat rings, and appear to minimize out-of-plane forces that could potentially be transmitted to leaflets and chords. The use of a mural annulus–shortening suture rather than a ring may preserve the natural shape of the annulus. In fact, hemodynamic performance of the mural annulus–shortening suture is reportedly superior to that of the rigid prosthetic suture, without increasing postoperative MR. However, we experienced suture annuloplasty detachment using this method in some patients prior to 2006 (data not shown), which has also been reported in humans. Therefore, soft prosthetic rings such as autologous pericardium or ePTFE may be a more feasible material for mitral annuloplasty. Because autologous pericardium is very thin in dogs, compared with that in humans, ring sutures are difficult to make. Therefore, the ePTFE soft prosthetic ring was selected for our procedure after 2006.

In the present study, we observed annular dilation at the septal and mural commissures. We previously experienced that even if prosthetic annuloplasty was performed with the ePTFE, the commissure areas could not achieve proper coaptation, leading to nontrivial MR in 4 dogs (data not shown). The cranial and caudal commissures may require closure of the commissure as described by Carpentier (ie, the so-called magic stitch) in those patients. To reduce regurgitation from both the cranial and caudal commissure areas, we performed mitral plication suture annuloplasty before prosthetic annuloplasty. The mitral plication suture and mitral annuloplasty may achieve good coaptation and reduce MR. Because the present study did not evaluate whether our surgical procedures result in the maintenance of physiologic leaflet and annulus motion and good leaflet coaptation, further 3-D echocardiographic evaluation of patients will be necessary to confirm durability and feasibility.

Popular techniques to treat mitral valve leaflet prolapse in humans include partial leaflet resection, chordal transfer, chordal shortening, and chordal replacement. Chordal replacement with ePTFE has gained increasing popularity because of its availability and long-term durability in humans and animals. Nevertheless, the main challenge with chordal replacement is the difficulty of adjusting artificial chordae to the appropriate length. If neochordae are too short, leaflet motion is restricted; if neochordae are too long, they are ineffective in controlling leaflet prolapse. In addition, the length of the neochordae must exactly match the length of the opposing chordae to make the opposing leaflets coapt at the same height. Several methods to ensure the optimal length of artificial chordae have been reported, which involve application of a caliper, transesophageal echocardiography, or multiple knots. Kasegawa et al described a method involving use of small tourniquets, and Ryu and Ruyra-Baliarda described a new surgical device that ensures the correct length of new mitral chords and helps surgeons to repair anterior leaflet prolapse. These techniques may be useful to adjust the length of chordae tendineae, but handling may become difficult when they are applied to the hearts of small-breed dogs. Morimoto et al described a temporary Alfieri stitch for anterior leaflet prolapse. This method maintained the visual field well and was able to maintain the coaptation of the leaflets. We used this method to prepare neochordae at S2 of the septal leaflet and M2 of the mural
leafflet because we experienced a tendency for chordal replacements at M2 of the mitral mural leafflet to shorten. The main challenge with chordal replacement is tying the ePTFE sutures, which are slippery. We made knots to adjust neochordae length at the mitral annulus level while avoiding tension to the heart and keeping a temporary Alfieri stitch.

All surviving dogs were able to run 1 month after surgery. Clinical condition, findings on echocardiographic examination, chest radiography results, and cardiac murmurs improved and cardiac medications decreased 1 month after MVR in all 45 dogs. Overall, the survival probability in the patients in the present study was 93.3% at 38 months after MVR. The approximate survival time with palliative treatment is <1 year, indicating that MVR is beneficial as a treatment for MR in dogs. The present study was limited by the small number of cases and the short follow-up period after surgery. Additionally, mitral regurgitant volume was not evaluated via quantitative methods. Future studies may provide more information.

Tribouilloy et al. reported that human patients who underwent surgery for organic MR with New York Heart Association functional class III or IV symptoms had increased mortality rates and morbidity after surgery, compared with those with class I or II symptoms, independent of age, left ventricular function, and other baseline characteristics. In the present study, older dogs and dogs with severe MR required treatment with an ACE inhibitor, pimobendan, or both after MVR. Because cardiac function is attenuated in older dogs and dogs with severe MR, cardiac medicine may be still required in these dogs. Therefore, early MVR may be a more beneficial treatment for MR.

References


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