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TITLE: Surgical treatment of pulmonic stenosis in dogs under cardiopulmonary bypass: outcome in nine dogs

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1 **Surgical treatment of pulmonic stenosis in dogs under cardiopulmonary bypass: outcome in 9 dogs**

2

3 **Objectives:** to describe the outcome for 9 dogs with pulmonic stenosis treated by open patch grafting using
4 expanded polytetrafluoroethylene under cardiopulmonary bypass.

5 **Methods:** data were collected from the hospital records of all dogs that had undergone right ventricular
6 outflow tract grafting with an expanded polytetrafluoroethylene patch under cardiopulmonary bypass
7 between 2006-2012 for the treatment of pulmonic stenosis. Echocardiographic images were reviewed and
8 the pressure gradient across the right ventricular outflow tract re-measured. Owners for dogs still alive at
9 the time of writing were invited to return to the hospital for reassessment.

10 **Results:** 9 dogs met the inclusion criteria. Median pressure gradient pre-operatively was 118 mmHg, (range 102
11 to 259 mmHg) reducing to a median of 20 mmHg (range 7-53 mmHg) at 48 hours post-operatively and 14
12 mmHg (range 10 to 70 mmHg), with a median percentage reduction of 89% (range 41 to 94%) at
13 long term follow-up. 8/9 dogs survived surgery, with 6/9 surviving to hospital discharge. Two dogs were still
14 alive over 6 and 8 years post-operatively. No long term deaths were believed to be attributable to pulmonic
15 stenosis.

16 **Clinical significance:** expanded polytetrafluoroethylene patch grafting of the right ventricular outflow
17 tract for treatment of severe pulmonic stenosis in dogs is feasible and can be an effective method to reduce
18 the severity of right ventricular outflow tract obstruction.

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29 **Introduction**

30 Pulmonic stenosis (PS) is caused by a narrowing or obstruction of the right ventricular outflow tract (RVOT) in
31 the region of the pulmonic valve. It has been reported to be the most common congenital heart disease in dogs,
32 accounting for 32% of congenital defects in one study (Oliveira et al. 2011) and is most frequently caused by a
33 valvular malformation (Oliveira et al. 2011, Ristic et al. 2001)¹. Balloon valvuloplasty (BV) is generally
34 considered to be the most appropriate first line treatment for valvular PS due to its safety and reportedly high
35 success rates (Johnson et al. 2004a). Surgical intervention is considered in dogs in which BV has failed to reduce
36 the pressure gradient (PG) within the RVOT, to relieve clinical signs, or in dogs considered to be poor
37 candidates for BV. The latter include dogs with deformed, dysplastic valve leaflets (type B valvular stenosis)
38 and hypoplasia of the pulmonic valve annulus (Bussadori et al. 2001, Locatelli et al. 2011), or those dogs in
39 which there is significant infundibular hypertrophy contributing to dynamic outflow tract obstruction (Johnson
40 et al. 2004b). For these dogs, the RVOT patching technique is considered more likely to be successful in
41 reducing the RVOT PG (Hunt et al. 1993, Orton et al. 1990).

42
43 Patch grafting of the RVOT was originally reported in the human literature for the treatment of tetralogy of
44 Fallot in 1956 (Lillehei et al. 1956). Since then a variety of patch materials and techniques have been described,
45 including aortic homografts (Longmore et al. 1966), autologous fascia lata composite grafts (Ionescu et al.
46 1970), autologous pericardial patch grafts (Yang et al. 2013), cryopreserved homografts (Youn et al. 2007),
47 polyethylene terephthalate (PET) (Breznock et al. 1976) and expanded polytetrafluoroethylene (ePTFE)
48 (Matsumoto et al. 2001, Orton et al. 1990). Similarly there has been a wide variety of techniques reported in
49 dogs. Initial reports in dogs describe variations of closed pericardial patch-grafting techniques, performed
50 without the need for cardiopulmonary bypass or total venous inflow occlusion (Breznock et al 1976, 1976,
51 Shores et al. 1985, Hunt et al 1993, Staudte et al 2004) . Collectively these studies report experience from a total
52 of 35 dogs, with a perioperative mortality rate of 11-17%.

53
54 A modified open technique has also been described using total venous inflow occlusion (TVIO) (Orton et al.
55 1990, Hunt et al 1993), incorporating an expanded polytetrafluoroethylene patch (ePTFE) or native pericardial
56 patch with or without concurrent hypothermia. More recently, open patch-grafting has been described using

57 bovine vena cava patch graft under cardiopulmonary bypass in 10 dogs (Tanaka et al 2009) and in 2 additional
58 dogs using glutaraldehyde-fixed canine tunica vaginalis (Fujiwara et al. 2012).

59
60 Collectively, these descriptive reports present the short term results of a range of techniques and patch graft
61 materials and document a range of follow up times, with a maximum follow-up time of 40 months. Notably
62 many of these reports predate the time when balloon valvuloplasty became an established and widely performed
63 procedure in dogs. Thus only a total of 12 dogs are reported that have undergone patch graft surgery under
64 conditions of CPB.

65
66 The purpose of the study reported here was to describe the short and long term outcome for 9 consecutive dogs
67 with pulmonic stenosis treated by open patch grafting using ePTFE under CPB, and to compare their outcomes
68 to those previously reported in the literature using alternative techniques.

69

70 **Materials and Methods**

71 Cases were selected for surgery if they had a diagnosis of pulmonic stenosis and had either undergone balloon
72 valvuloplasty without an adequate reduction in pressure gradient and/or clinical signs, or were considered at a
73 high risk of failing an attempted balloon valvuloplasty approach, as discussed above. Owners were carefully
74 counselled as to the emotional and financial commitment of the procedure and consented to surgery after full
75 consideration of the risks involved. Data were collected from the medical records of all dogs that had been
76 diagnosed with pulmonic stenosis that had undergone RVOT patching under CPB between 2006-2012. The
77 diagnostic criteria for PS was the generation of an estimated PG in the RVOT of greater than 20mmHg,
78 calculated from the modified Bernoulli equation, using the spectral Doppler derived peak blood flow velocity
79 (Bussadori et al. 2000) with concurrent typical 2D lesions; the latter included the presence of pulmonic valve
80 leaflet fusion and systolic doming, thickened or dysplastic leaflets or PA annulus hypoplasia. Dogs with 2D
81 lesions consistent with double chambered right ventricle or infundibular PS were excluded. Data collected
82 included signalment, clinical signs, previous and current medication, echocardiographic data, duration of
83 anaesthesia, duration of CPB and surgery, and pre- and post-operative complications. Long-term survival
84 outcome was determined by contacting the referring veterinarians. For dogs still alive, the owners were

85 contacted and asked to complete the FETCH questionnaire (Freeman et al. 2005). Owners were invited to return
86 to our centre for re-examination and a repeat echocardiogram. Minor complications were defined as those
87 requiring no surgical intervention and major as those requiring surgical intervention or resulting in death.

88
89 Echocardiographic studies were performed by a board-certified cardiologist or supervised cardiology
90 resident using the same ultrasound machine (Vivid 7 or Vivid E9, General Electric Medical Systems
91 Ultrasound). Standard echocardiographic views were obtained according to recommendations by the
92 Echocardiography Committee of American College of Veterinary Internal Medicine (Thomas et al. 1993).
93 Spectral Doppler tracings were also acquired to demonstrate flow across the stenosis (from either the right
94 parasternal short axis view or left cranial view, according to the view considered to optimise alignment
95 with the maximal flow velocity). Echocardiographic data collected included the PG within the RVOT pre-
96 balloon valvuloplasty (where applicable), pre-operative PG (PG_{pre}), the PG 48 hour post-operatively (PG_{48})
97 and the PG at the final assessment (PG_{final}). Pulmonic insufficiency was assessed and graded according to
98 Locatelli et al. (2011); the presence and severity of pulmonary valve insufficiency
99 pre- and post-operatively was assessed through colour flow mapping, considering the extension of the
100 regurgitating jet and its width at the origin. Any pulmonic regurgitant jet with a proximal width greater
101 than 50% of the right ventricular outflow tract diameter at that level was considered significant. If the jet
102 extended only into the outflow tract, the regurgitation was classified as mild. If the jet proceeded to the
103 tricuspid valve, the regurgitation was considered severe. Between both was considered moderate (Locatelli
104 et al. 2011). All stored images were reviewed by and re-measured by a single examiner (JS).

105
106 The protocols for anaesthesia and CPB used in this study were performed as previously described (Orton et al.
107 2001, Orton et al. 2002). All dogs had a right central venous line placed and invasive arterial blood pressure
108 monitoring was performed via a dorsal pedal arterial catheter or if unable to obtain cannulation at this site, via a
109 “cut down” to the right femoral artery. Perioperative antibiotic prophylaxis was with cefuroxime (Zinacef,
110 Galxosmith Kline) at 20mg/kg intravenously, every 90 minutes. A left 5th intercostal thoracotomy was
111 performed. The cardiopulmonary bypass circuit consisted of either a single one-stage or two-stage venous
112 drainage cannula placed through the right auricular appendage and into the right atrium/caudal vena cava, as

113 appropriate. In one dog with tricuspid valve dysplasia, bicaval cannulation was performed with one cannula
114 placed directly into the extracardiac cranial vena cava (CVC) and the caudal caval cannula placed across the
115 right atrium, via the right auricular appendage, with snares around the cranial and caudal cavae to create total
116 bypass and minimise the risk of air entering the circuit across the incompetent tricuspid valve. The arterial limb
117 of the circuit was completed with an arterial cannula in the left external carotid. An aortic root cannula was
118 placed through a pre-placed purse string suture of 5-0 Prolene. Following aortic cross-clamping, cold (4° C)
119 cardioplegia solution (Cardioplegia infusion – Martindale), combined with blood from the bypass circuit, was
120 infused into the aortic root through this cannula, in all but one dog who received no cardioplegia. Cardioplegia
121 was delivered at 20 minute intervals or whenever mechanical cardiac muscular activity was observed. An
122 incision was made across the valve from the main pulmonary artery extending into the ventricle, mid-way
123 between the paraconal interventricular branch of the left coronary artery and the right coronary artery. The
124 incision was extended two thirds of the way down the ventricular free wall towards the apex of the heart (Figure
125 1). The valve leaflets were examined and excised. A sheet of ePTFE was trimmed to the appropriate size in an
126 ovoid shape and sutured into the defect in the pulmonary artery using GoreTex® suture material (CV-5). This
127 was placed using a double armed suture with an ePTFE pledget started at the proximal end of the patch where a
128 knot was tied. A line of sutures was then placed in a simple continuous pattern at the caudal border, followed by
129 the same pattern with the other end of the suture at the cranial border. These were then knotted together with
130 addition of a second ePTFE pledget at the ventral extent of the patch (Figure 2). The hearts were de-aired as the
131 last sutures were placed in the patch. The dogs were re-warmed, the cross clamp removed and the dogs were
132 weaned from CPB once normal sinus rhythm or a regular epicardial paced rhythm was established. The dogs
133 were recovered from anaesthesia in the intensive care unit where their therapy was adjusted according to
134 perceived needs based on changes in arterial blood gas measurements, blood pressure, urine production and fluid
135 retrieved from the chest drain. Antiplatelet therapy (aspirin 0.5mg/kg PO q24 h) was instituted the day
136 following surgery and continued for three months.

137

138 Statistical analysis was performed using a commercially available software package (GraphPad Prism 6).

139 Descriptive statistics were performed and reported as median and range if not normally distributed and

140 mean and standard deviation if normally distributed. Continuous data (PG, weight, age, time of
141 anaesthesia, bypass and surgery) were assessed for normality using the Shapiro-Wilk Test.

142

143 **Results**

144 Nine dogs met the inclusion criteria. There were two Cocker spaniels and one each of Japanese Akita,
145 Bullmastiff, English Bulldog, Flat coated retriever, German Shepherd dog, Miniature Schnauzer and
146 Shetland Sheepdog. Seven dogs were male (four entire) and two were female entire. Body weight at time
147 of surgery ranged from 7 to 43.6 kg with three dogs weighing 15 kg or under. Age at the time of surgery
148 ranged from 7 to 38 months with 6 dogs less than one year old, (Table 1).

149

150 **Pre-operative data**

151 All dogs apart from one underwent balloon valvuloplasty prior to surgery. The 8 month old Shetland
152 Sheepdog did not undergo balloon valvuloplasty as she had severe infundibular hypertrophy and a very
153 hypoplastic pulmonary artery (with a main pulmonary artery:aortic diameter ratio of 1:2.35 and no
154 evidence of post-stenotic dilation), and the chances of success with BV were considered to be low. Time
155 from BV to surgery ranged from 56 to 454 days with a mean of 126 ± 57 days. The pre-balloon
156 valvuloplasty PG was available for 5 dogs and consistent with severe stenosis in all, with a median value of
157 164 mmHg (range 127-210 mmHg). After balloon valvuloplasty the median PG was 113 mmHg (range
158 108-167 mmHg).

159

160 Five dogs had clinical signs attributed to their cardiac disease pre-operatively; 2 had exercise intolerance,
161 one had a history of syncope, one was exercise intolerant and inappetent and another was polycythaemic
162 and cyanotic. Two dogs had experienced episodes of right sided congestive heart failure pre-operatively.

163 All dogs were receiving cardiac medications that included atenolol in all dogs (Teva, Tenormin;

164 AstraZeneca), furosemide (Frusedale; Dechra, Frusemid; Millpledge, Frusol; Rosemont), n=3, benazepril

165 (Fortekor; Elanco Animal Health or Benazecare; Animal Care Group plc), n=3 and spironolactone

166 (Prilactone; Ceva), n=2. Three dogs were receiving 3 medications with the remainder receiving one

167 (atenolol).

168

169 On echocardiography, 4 dogs had a patent foramen ovale (PFO), 3 of which were right to left shunting (the
170 direction of shunting was not confirmed retrospectively in one dog due to the lack of a bubble study). One
171 dog had a small (1.5mm) sub-aortic ventricular septal defect (VSD) with right to left systolic shunting (this
172 was the dog with severe infundibular hypertrophy and a very hypoplastic pulmonary artery). As well as
173 having a PFO, one dog also had tricuspid valve dysplasia, characterised by abnormal tethering of both
174 valve leaflets and the presence of tricuspid regurgitation. Tricuspid regurgitation was estimated to be
175 severe based on a subjective assessment of the size of the tricuspid regurgitation jet in relation to the size
176 of the right atrium. Median PG_{pre} was 118 mmHg, (range 102 to 259 mmHg). Pulmonic regurgitation was
177 able to be assessed in 4 dogs pre-operatively and was graded as moderate in 3 and as mild in 1.

178

179 **Intra-operative data**

180 Surgery was performed under CPB in all dogs, with one performed with the heart beating. In addition to patch
181 grafting of the RVOT, all dogs had partial/subtotal pulmonic valvectomy.

182

183 Intraoperative complications occurred in two dogs. One dog was euthanatised intra-operatively due to inability
184 to successfully wean from cardiopulmonary bypass; this dog had severe hypocalcaemia but the reason it could
185 not be weaned from bypass remains speculative. In the other dog, haemorrhage from the aortic root cannulation
186 site occurred and this was repaired with sutures.

187

188 Eight out of 9 dogs survived surgery. Median total anaesthesia time (n=6) was 404 minutes (range 294 to 531
189 minutes), median surgical time (n=6) was 273 minutes (range 180 to 366 minutes), and median CPB time (n=6)
190 71 minutes (range 27 to 168 minutes).

191

192 **Short term post-operative data**

193

194 **Complications**

195 Fatal complications in the immediate post-operative period occurred in 2/8 dogs. The dog that had bled intra-
196 operatively from the aortic root cannula site developed haemothorax within a few hours of cessation of
197 cardiopulmonary bypass, and during thoracocentesis the dog underwent cardiopulmonary arrest and died. One
198 dog developed profound hypotension of undetermined cause and despite aggressive supportive care, suffered a
199 fatal cardiac arrest. For the remaining dogs, median PG at 48 hours post-operatively (PG₄₈) was 20 mmHg
200 (range 7-53 mmHg). Pulmonic regurgitation had increased to severe in 2 dogs, remained as moderate in 1 and
201 was graded as moderate and severe in 2 further dogs who had no pre-operative measurement of pulmonic
202 regurgitation.

203

204 Three dogs experienced complications in the peri-operative period, none of which were fatal. One dog collapsed
205 7 days post-operatively and developed severe pyrexia with multiple joint effusions and joint pain. Investigations
206 revealed elevations in liver enzyme activity and hyperbilirubinaemia, in addition to thrombocytopenia, anaemia
207 and prolongation of clotting times. This dog recovered with supportive care including fluid therapy and
208 analgesia. A further dog developed hypoxia 4 days post-operatively. Radiographic evidence of an alveolar
209 pattern was present and the dog recovered with supportive care (oxygen supplementation and antibiotics). One
210 dog developed pleural and peritoneal effusions 72 hours post-operatively that resolved following diuretic
211 treatment. Therefore, six out of 9 dogs survived to discharge.

212

213 **Medium to long-term post-operative data**

214

215 **Echocardiographic data**

216 Medium to long-term post-operative data was available for all surviving dogs. Median time from surgery to last
217 echocardiographic exam was 1977 days (range 429 to 3098 days). The PG at final echocardiographic
218 examination (PG_{final}) was below 20mmHg in 62.5% of dogs (5/8). The median PG_{final} was 14 mmHg (range 10 to
219 70 mmHg), with a median percentage PG reduction of 89% (range 41 to 94%), (Figure 3). No dogs were
220 receiving cardiac medications at their final assessment.

221

222 **Survival data**

223 None of the dogs that survived to discharge were believed to experience a death related to PS. At the time of
224 writing 2 dogs were still alive at 6 years 9 months (Cocker Spaniel) and 8 years 7 months (German Shepherd)
225 post-operatively. Both dogs returned to our clinic for re-examination. At re-examination both dogs had normal
226 exercise tolerance and were considered well by their owners, with FETCH scores of 7/90 and 3/90 respectively
227 (higher scores indicate poorer quality of life). Pressure gradients across the RVOT were 35 mmHg and 14
228 mmHg respectively.

229

230 In three dogs that had died, the cause of death was one each: systemic mast cell disease (5 years post-
231 operatively), osteosarcoma (7 years post-operatively) and severe pancreatitis resulting in acute respiratory
232 distress syndrome (5 years 2 months post-operatively). One dog died with right heart failure 5 years post-
233 operatively, believed to be associated with concurrent tricuspid dysplasia. This was the dog diagnosed with
234 tricuspid valve dysplasia prior to patch grafting and his PG had decreased from 113 mmHg pre-operatively to 14
235 mmHg at the date of his last examination (429 days post-operatively).

236

237 **Discussion**

238

239 The data reported here comprises the largest number of dogs treated using an ePTFE graft under conditions of
240 CPB, and has the longest follow-up to date. In this population of dogs, ePTFE patch grafting of the RVOT under
241 CPB for treatment of severe PS was associated with a significant and sustained reduction in the RVOT PG and
242 excellent long-term survival in dogs surviving the peri-operative period. Although we were not able to obtain
243 final assessment echocardiograms from all dogs that survived to discharge, only one dog's death was related to
244 heart disease. This dog was evaluated by us with his death considered to be associated with the dogs pre-existing
245 tricuspid valve dysplasia since his pulmonic valve PG remained low at 14 mmHg and apart from the tricuspid
246 valve changes there were no other structural abnormalities in the heart. The PG remained markedly reduced in
247 all dogs at the time of their final echocardiographic assessment and no evidence of sub-clinical restenosis was
248 seen, further demonstrating the durability of this technique. Interestingly, two dogs had a PG of over 50 mmHg
249 which has been described above the limit for an optimal outcome (Locatelli et al. 2011), post-operatively yet still

250 had an excellent long term outcome. One dog had a PG of 70mmHg. We conclude, therefore, that this technique
251 gave sustained long term resolution of PS-related signs in those dogs that survived to discharge.

252

253 In the study reported here, one intraoperative fatality occurred and two dogs died in the immediate postoperative
254 period. The exact cause of death for these dogs is not clear although it is most likely one dog had fatal post-
255 operative intrathoracic haemorrhage. Because post mortem examination was not permitted, this cannot be
256 confirmed. The intraoperative death was associated with failure to successfully wean the dog from CPB.

257 Possible causes for this include myocardial ischaemia secondary to poor myocardial perfusion/protection with
258 cardioplegia, myocardial hypoperfusion (of the very thick right ventricle), coronary artery air embolization or
259 coronary artery obstruction by blood clot formation; all of which might prove difficult to confirm definitively
260 even with post-mortem examination. This dog's sustained hypocalcaemia may also have been a factor.

261

262 None of the previous reports are exactly alike in terms of patient selection criteria or surgical technique used.

263 The main technical differences are between the use of a closed technique without total venous inflow occlusion
264 (n=2) (Shores et al. 1985, Staudte et al. 2004), closed or modified open technique with TVIO (n=2) (Hunt et al.
265 1993, Orton et al. 1990), or an open technique under CPB (n=2) (Fujiwara et al. 2012, Tanaka et al. 2009).

266 There are a variety of reasons for each institution having reported the use of different techniques including
267 experience, cost, and availability of specialised equipment, such as that required to operate under CPB. The two
268 most recent reports use CPB, perhaps reflecting the increasing availability of this equipment and expertise, and
269 the success reported with its use for other conditions (Fujiwara et al. 2012, Mizuno et al. 2012, Orton et al.

270 2005, Uechi et al. 2012). In human patients that require surgical correction of PS caused by valve annulus

271 hypoplasia and fibrous valvular malformation (analogous to type B morphology in dogs), an open approach

272 under CPB is the standard of care, rather than surgery under TVIO, for reasons of safety, control and surgical

273 accuracy. Our reasons for using CPB were multifactorial: firstly, as previously mentioned, this is considered

274 preferable for surgical treatment of similar PS in humans. Secondly, use of CPB allows sufficient time to open

275 the heart and fully evaluate the source of obstruction and the pulmonic valve, thereby allowing the surgeon to

276 assess and accurately resect tissue likely to contribute to on-going obstruction. In addition, it allows accurate

277 sizing and suturing of an ePTFE patch so as to reconstruct the outflow tract in a way that minimizes risk of

278 residual or subsequent obstruction. Finally, we had already started using CPB for treatment of other surgical
279 conditions at our institution and therefore had some experience with the technique. In contrast, TVIO allows
280 only limited time to visualise and address abnormalities of the valve complex and so is described to facilitate
281 either “closed” or “semi open” valvotomy. These techniques are arguably more suited to dogs with fused valve
282 leaflets (type A) rather than type B PS. That is; a morphology of PS that would respond well to the much safer
283 BVP approach. It is difficult to make meaningful comparisons between the use of CPB and TVIO for surgical
284 treatment of PS in dogs given the small number of reports and low case numbers. Comparisons of mortality rate
285 are somewhat similar with 4/4 dogs surviving surgery in Orton et al.’s report with TVIO (1990), and 7/8
286 surviving in Hunt et al.’s (1993), (Hunt et al. 1993, Orton et al. 1990). Similarly with the use of a closed
287 technique, 8/9 survived (Staudte et al. 2004; Shores et al. 1985). With use of CPB 8/10 dogs survived surgery in
288 one report (Tanaka et al. 2009) and 8/9 dogs in a further report (Fujiwara et al. 2012), which is comparable to
289 our surgical survival rate of 8/9 dogs. In order to compare techniques in a meaningful way, a prospective
290 comparison of a larger number of dogs with similar disease status and selected for surgical intervention using
291 standard criteria, and with a long follow up time, would be needed.

292
293 As mentioned above, one advantage of the use of CPB is the increased time afforded to analyse and address the
294 cause(s) of the stenosis. This operation does, however create almost complete pulmonic valvular incompetence.
295 Pulmonic valvular incompetence is reported as a late (30 years after surgery) complication in humans that
296 undergo complete repair of tetralogy of Fallot (Therrien et al. 2000). This has led some surgeons to recommend
297 pulmonic valve replacement in this group of patients. The study reported here would suggest that pulmonic
298 valvular incompetence is well tolerated in this canine population; we accept that this is a small number of dogs
299 with limited follow-up, however in all dogs there was moderate to severe pulmonic insufficiency at the final
300 examination but this was not associated with long term clinically significant adverse remodelling, ventricular
301 arrhythmia or CHF. One dog did develop right sided CHF but this was the dog with tricuspid valve dysplasia.
302 It is possible that a complication that takes 30 or so years to develop in a human might not be a concern in the
303 context of a canine lifespan.

304

305 None of the dogs in our report died from heart disease directly related to their PS and both dogs with right sided
306 heart failure pre-operatively had resolution of this. However one dog died of heart failure six months post-
307 operatively in Hunt et al.'s study (1993) of patching under TVIO; and in Staudte et al.'s report of a closed
308 technique with use of a valvulotomy-ventriculotomy wire one dog died of heart failure at 16 months post-
309 operatively (Hunt et al. 1993, Staudte et al. 2004). In this latter report (Staudte et al. 2004), three dogs also
310 experienced syncope upon extreme exertion or exercise after surgery, whereas all dogs in the study
311 reported here remained free of clinical signs relating to PS (although, as mentioned, one dog did develop heart
312 failure secondary to TVD five years after surgery). The fact that previous reports of surgical treatment of PS
313 only contain relatively short term follow up mean that it is possible that recurrence of signs is an under reported
314 complication. Without larger patient numbers and a carefully controlled prospective study, it is impossible to
315 draw comparisons as to which technique may be superior.

316

317 Another difference in techniques to date is the use of differing materials for the patch with ePTFE, native
318 pericardium, bovine vena cava patch graft and glutaraldehyde fixed canine tunica vaginalis all previously
319 reported. Expanded polytetrafluoroethylene sheets are sterile "medical grade", "off the shelf" products with no
320 known adverse health and safety side effects for user or recipient. It is easy to handle and can be cut to size, as
321 needed. Because of the potential harmful effects of glutaraldehyde and the lack of availability of all natural
322 products other than native pericardium, and the fact that ePTFE had been previously described for this use, we
323 chose this in our dogs.

324

325 As in other reports of PS, some of our dogs had concurrent congenital cardiac abnormalities; VSD in one dog,
326 PFO in four dogs and TVD in one. The VSD was only 1.5 mm in diameter and in the subaortic position.
327 Surgical exposure of all of these defects would have been best achieved through a right atriotomy rather than the
328 right ventriculotomy incision required for the RVOT patch. The decision not to address the PFOs surgically was
329 based on the assumption that if the RVOT patch achieved the anticipated change in RV pressure, this would, in
330 turn reduce right atrial pressure to a level that would no longer favour right to left shunting of blood across the
331 PFO. This assumption was proved to be correct on follow-up echocardiography in one dog that had right to left
332 shunting prior to patching. We were not able to perform a bubble study at long term follow up to confirm the

333 absence of shunting in the second dog but one dog there was still evidence of right to left shunting on cardiac
334 echo. This dog, however, did not show any clinical signs associated with right to left shunting of blood. The
335 decision not to treat the TVD surgically in the dog with concurrent PS and TVD, was also based on the
336 presumption that the tricuspid regurgitation secondary to TVD would reduce once the PS had been treated as
337 well as the fact that there was no tried and tested surgical therapy for TVD at that time. Finally, the decision not
338 to surgically manage the VSD in the two dogs that had this lesion was based on the small size of the VSD and
339 the assumption that these would only have minor haemodynamic significance, once the PS had been treated. In
340 addition, they were relatively inaccessible via the right ventriculotomy. Again, this assumption proved to be
341 correct based on follow up echo studies and the long term survival. Indeed, only one dog developed clinical
342 signs relating to the concurrent cardiac abnormality (TVD) and this ultimately resulted in the death of the dog 5
343 years after surgery for PS. This dog still enjoyed a sustained period of a good quality of life following PS
344 surgery.

345

346 Based on our results, ePTFE patch grafting of the RVOT is an effective and durable treatment for severe PS, in
347 dogs that have failed BV. Whether it can also be an effective treatment for dogs who are not considered good
348 candidates for BV due to their concurrent congenital malformations remains to be seen.

349 The peri-operative mortality rate can be high but if dogs survive the peri-operative period then a significant
350 reduction in pressure gradient can be achieved with an excellent long-term prognosis. It is important to
351 recognize that the dogs reported here, along with a group of 9 dogs that underwent tricuspid valve replacement
352 and 3 dogs that underwent patching for double chambered right ventricle, represent the first 21 dogs operated on
353 by the bypass team at our institution and as such, represent the beginning of the “learning curve”. It is
354 anticipated, therefore, that further familiarity with these operative techniques, and refinements in patient
355 selection criteria, anaesthetic care and post-operative requirements, will result in significant reduction in short
356 term mortality and therefore improve overall outcome, as shown by another team with vast experience (Uechi et
357 al. 2012). Based on the small number of dogs reported here, open patch grafting under cardiopulmonary bypass
358 is feasible and results in durable reduction in PG along with long term relief from the clinical signs of PS,
359 providing the tricuspid valve function is good.

360

361 No conflicts of interest have been declared.

362

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