EXPERIMENTAL CARINAL AUTOTRANSPLANTATION AND ALLOTRANSPLANTATION

Grafting is required when a primary reconstruction of a carinal defect is not feasible. A series of experiments in 21 dogs was conducted to assess the possibility of carinal reconstruction with the use of carinal autografts and allografts, with or without omentopexy. Carinal autograft transplantations were done without omentopexy in group A ($n = 6$) and with omentopexy in group B ($n = 6$). In group C ($n = 9$), carinal allograft transplantations were done with omentopexy and FK 506 was administered after operation. Survival of grafts was seen in 50% of group A, 83% of group B, and 44% of group C dogs. Postoperative bronchoscopy revealed inflammatory changes in the surviving grafts; the changes resolved more rapidly in the dogs with omentopexy than in the dogs without omentopexy. These experiments suggest that omentopexy is an effective method of facilitating survival and healing in carinal grafts and that carinal reconstruction with carinal allografts with FK 506 is feasible. (J THORAC CARDIOVASC SURG 1995;110:762-7)

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In the past, carinal resection with reconstruction was usually directed toward carinal lesions, including malignancies or occasional inflammatory changes. Many attempts have been made to reconstruct the carina with an end-to-side or double-barrel anastomosis or with prosthetic materials.¹⁻² Cases in which major defects were created by resection of carinal lesions were subject to the postoperative complications of ischemia, stenosis, and disruption as a result of extensive mobilization of the trachea and tension on the anastomosis. On the other hand, prosthetic materials are not generally used to reconstruct the carina, although use of a bifurcated prosthesis has been reported in eight cases.² It would be ideal to perform a transplantation with a carinal allograft that contains native epithelium and possesses cartilaginous rings and to eliminate the complicated tension at the anasto-

motomic site and differences in the consistency of the trachea and bronchus.

With regard to graft viability, the use of devascularized carinal grafts necessitates revascularizing measures after separation from the donor. Morgan and associates³ reported revascularization of total ischemic bronchial autografts by the use of omental pedicled flaps. We also have reported that omentopexy is an effective method of facilitating neovascularization in tracheal autografts.⁴ Furthermore, it has been reported that omentopexy markedly improves healing of bronchial anastomosis.⁵⁻⁹ Therefore omentopexy was used as the method of revascularization for carinal grafts in the present study.

Our objective was to assess the utility of omentopexy in carinal grafting and the possibility of carinal reconstruction with the use of carinal allografts.

Material and methods

Twenty-one adult mongrel dogs weighing from 8 to 16 kg were divided into three groups. In group A ($n = 6$), carinal autograft transplantations were done without omentopexy. The dogs in group B ($n = 6$) underwent carinal autograft transplantation with an omentopexy. In group C ($n = 9$), carinal allografts were done with an omentopexy.

General anesthesia was induced and maintained with an enflurane and oxygen mixture administered via an endotracheal tube. The lungs were ventilated with a volume-limiting respirator. The animals were positioned on the operating table in the left semilateral position. An upper

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Fig. 1. After preparation of omental pedicled flap supplied by right gastroepiploic artery in groups B and C, autograft or allograft was interposed at carinal defect in recipient and sutured to left main-stem bronchus during right-lung ventilation (A). B and C, Trachea and right main-stem bronchus, in that order, were sutured during left-lung ventilation. D, Finally, omental pedicled flap was used to cover the graft, including anastomotic portions, in groups B and C.

midline laparotomy was done and an omental pedicled flap was created, based on the right gastroepiploic artery. A right posterolateral thoracotomy was then done at the fourth intercostal space.

After the azygos vein was ligated and divided, the carinal trachea was dissected and excised together with two tracheal rings: one ring of the right main-stem bronchus and two rings of the left main-stem bronchus. In groups A and B, these specimens were used as autografts. In group C, sized carinal allografts from the donors were interposed at the site of the carinal defect in the recipients. The grafts were secured to the recipient's left main-stem bronchus, trachea, and right main-stem bronchus with continuous 3-0 and 4-0 Prolene polypropylene sutures (Ethicon, Inc., Somerville, N.J.). The right and left lung ventilation was isolated at various points in the procedure (Fig. 1). The differences in caliber were adjusted at the membranous wall. About 30 or 40 minutes were required to finish all the anastomoses, starting from the excision of the autografts or allografts. All anastomoses were checked for air leaks by the sealing test.

The omental pedicled flap was pulled into the thoracic

cavity via an opening in the right hemidiaphragm. It was used to cover the graft, including the anastomoses, in the dogs in groups B and C. The omentum was tacked to the diaphragm and to the tracheal sheath.

All the animals received antibiotics for the first 5 postoperative days. The animals in group C also received the immunosuppressant FK 506^{10,11} (Fujisawa Pharmaceutical Co., Osaka, Japan) at an intramuscular dosage of 0.1 mg/kg per day. Thereafter, graft viability was assessed by bronchoscopy and scored according to graft status (Table I). In group B, revascularization from the omental pedicled flap was assessed by infusion of India ink into the right gastroepiploic artery.

All animals were cared for in accordance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources and published by the National Institutes of Health (NIH Publication No. 86-23, revised 1985).

Statistical method. Scores were expressed as mean plus or minus the standard error. Two-way analysis of variance

Fig. 2. Graft scores after carinal transplantation in groups A and B. Differences between groups A and B ($p < 0.05$) suggest that omentopexy is effective method of facilitating healing process in carinal grafts.

Table I. Scoring of bronchoscopic graft findings

Score	Findings
0	No abnormality
1	Low-grade inflammatory changes
2	High-grade inflammatory changes
3	Stenosis caused by granulation
4	Malacia caused by ischemia or inflammation

was used to assess the utility of omentopexy. Differences with values of $p < 0.05$ were considered significant.

Results

Adequate graft healing was seen in three (50%) of six dogs in group A, five (83%) of six dogs in group B, and four (44%) of nine dogs in group C (Table II). Of the dogs in group A, three (Nos. 1, 4, and 17) died of progressive wasting. The graft transplanted in dog No. 17 exhibited ischemic changes immediately after the operation, and thereafter mucosal desquamation and exposure of the tracheal cartilage ensued. In group B, only one dog (No. 5) died of progressive wasting. Despite omentopexy, this graft exhibited malacia almost identical in appearance to that seen in dog No. 17. In group C, six dogs died within 1 month of the operation (Nos. 9, 11, 13, 14, 15, and 19). Infection and malacia of the graft occurred in dog No. 11. The dog (No. 10) that survived longer than 1 month displayed evidence of infection on the first postoperative day, despite the additional administration of antibiotics. This infection eventually spread to the graft and contributed to the development of stenosis

Fig. 3. Bronchoscopic findings after carinal transplantation in dogs with (A) and without (B) omentopexy. A, Note restoration by day 14, showing same mucosal characteristics as those of native trachea and rapid healing of dehiscence of membranous wall (arrows). B, Note persistence of inflammatory changes 14 days after operation, indicating delay in restoration.

at the anastomotic site. In dog No. 16, the graft showed stenosis without malacia on postoperative day 76.

Generally, postoperative bronchoscopy of the grafts that healed well revealed ischemia on the first postoperative day, with the development of inflammatory changes centering around the membranous wall between the third and the fifth postoperative days. However, in the subsequent healing process, disappearance of inflammatory changes in the au-

Table II. Results of carinal autotransplantation and allotransplantation

<i>Dog No.</i>	<i>Graft</i>	<i>Omentopexy</i>	<i>Survival time (days)</i>	<i>Cause of death</i>	<i>Score</i>
Group A					
1	Autograft	—	6	Mediastinitis	4
2			82	Killed	1
3			51	Killed	0
4			6	Pneumonia	1
17			14	Mediastinitis	4
20			27	Wasting	3
Group B					
5	Autograft	+	15	Mediastinitis	4
6			54	Killed	0
7			14	Wasting	1
8			115	Killed	0
18			7	Killed	1*
21			14	Killed	0*
Group C					
9	Allograft	+	13	Killed	1
10			44	Killed	3
11			10	Mediastinitis	4
12			420	Alive	0
13			5	Pneumonia	2
14			7	Mediastinitis	2
15			20	Wasting	0
16			76	Killed	3
19			26	Wasting	0

*Infusion of India ink.

tografts with omentopexy was significantly more rapid than in those without omentopexy (Fig. 2). The inflammatory changes seen in grafts with omentopexy tended to decrease by day 7. Furthermore, these changes had almost disappeared in this group by day 14 (Fig. 3, A). On the other hand, the inflammatory changes seen in the dogs in group A persisted until postoperative day 14 (Fig. 3, B). In those dogs in which the grafts exhibited malacia, inflammatory changes were not seen after transplantation. However, bronchoscopy revealed mucosal desquamation and exposure of cartilage.

As for the time of revascularization to the graft, healing was confirmed by India ink injection through the right gastroepiploic artery in two dogs (Nos. 18 and 21). India ink infused through the right gastroepiploic artery was seen clearly in the submucosa on postoperative day 7, indicating revascularization of the graft at that time (Fig. 4).

In the dog that survived the longest (No. 12), the graft exhibited good healing beginning on the first postoperative day. This graft subsequently showed good adaptation 14 months after transplantation (Fig. 5).

Discussion

Carinal reconstructions are generally done by an end-to-side or double-barrel anastomosis. However, owing to the complicated tension at the anastomotic site and ischemia as a result of tracheal mobilization, combined with differences in the consistency of the trachea and the bronchus, postoperative complications at the anastomotic site are probable.¹ On the other hand, carinal reconstructions of major defects have been attempted with the use of bifurcated prosthetic material.² However, this is not generally used to reconstruct the carina at present, and prosthetic material lacks the epithelium that participates in physiologic function.

The most potentially promising method of solving this problem is carinal allograft transplantation. Carinal allografts contain native epithelium and possess cartilaginous rings to maintain a patent airway. Experimental tracheal allotransplantation in canine models has been described, with good results in tracheal reconstruction.^{12, 13} Furthermore, Ueda and Shirakusa¹⁴ have reported on the conditions for successful carinal transplantation. These reports suggest that carinal reconstruction by carinal allografts is feasible.

Fig. 4. Macroscopic appearance of carinal autograft in dog No. 18 on postoperative day 7. Note submucosal bleeding and India ink that was infused through right gastroepiploic artery (arrows).

Fig. 5. Adaptation of carinal transplant in dog No. 12 on postoperative day 420. This graft exhibited good healing characteristics beginning on first postoperative day.

However, carinal transplantations differ from other organ transplantations in that the graft is subject to total ischemia after transplantation. A method of facilitating revascularization of the carinal graft and anastomotic healing is therefore required. Several studies have shown that omentopexy is effective in promoting bronchial anastomotic healing and revascularization of ischemic bronchial autografts.^{3, 5-9} In a previous study, we reported that

omentopexy facilitates neovascularization in tracheal autografts.⁴ This study was designed for the purpose of exploring the utility of omentopexy in carinal grafting and the possibility of carinal reconstruction with the use of carinal allografts and to study neovascularization in carinal grafts.

In bronchoscopic findings, the inflammatory changes centering around the membranous wall of the graft, which were observed between the third and fifth postoperative days, seemed to be a sign of revascularization of the graft. The disappearance of these changes in the group without omentopexy was correlated with a delay in healing. In grafts with omentopexy, revascularization was confirmed on postoperative day 7 by the infusion of India ink through the right gastroepiploic artery. Bronchoscopy revealed submucosal vessels in this group by postoperative day 14. We have also previously reported that neovascularization was seen by the fourth postoperative day in tracheal autografts that were combined with omentopexy.⁴ It is conceivable that the differences in blood flow between grafts with and without omentopexy account for the observed differences in the disappearance of the inflammatory changes.

In groups A and B, graft malacia was attributed to ischemia as a result of the absence or inadequacy of omentopexy. The anastomosis in dog No. 21, which was covered by omentum, exhibited good graft survival characteristics despite dehiscence of the membranous wall (Fig. 3, A). This protection was

attributed to the effect of the omentopexy. In dog No. 10, characterized by graft malacia and stenosis, an infection was noted immediately after the operation, which may have been exacerbated by the use of immunosuppressants. The serious infections seen in other dogs in group C may also have been facilitated by the immunosuppressants. All reconstructions were done with use of a short carinal graft commensurate with the defect. The fact that the grafts showed adaptation in three dogs in group A can be related to the use of short grafts and the absence of rejection. Considering that ischemia or malacia was seen in half of the dogs in group A and in only one dog in group B and taking into account the inevitability of infection and the size of the defect, the importance of the omentopexy becomes obvious (Fig. 2). The efficacy of omentopexy in the prevention of infection and the promotion of revascularization is also clear from the bronchoscopic findings.

Technical aspects of the operative procedure that require close attention include the creation of an airtight anastomosis. Differences in the caliber of the graft and the recipient tracheal sections must also be taken into account. The maintenance of omental blood flow and the complete wrapping of the graft, including the anastomosis, are considerations of paramount importance when the omentum is pulled into the thoracic cavity.

It has been reported that good adaptation after tracheal transplantation can be obtained by short-term administration of immunosuppressants during the immediate postoperative period.¹² The fact that the grafts are highly susceptible to infection necessitates further study of an optimal immunosuppressant regimen for carinal transplantation.

In conclusion, the feasibility of carinal reconstruction with the use of carinal autografts and allografts with or without omentopexy has been demonstrated. The results suggested that omentopexy is an effective method of facilitating the survival and healing of carinal grafts and that carinal reconstruction with carinal allografts with FK 506 administration is feasible. Further studies will be needed to demonstrate the utility of longer grafts for the reconstruction of major defects that currently cannot be repaired.

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