MEDIUM-TERM PATENCY AND ANATOMIC CHANGES AFTER DIRECT BRONCHIAL ARTERY REVASCULARIZATION IN LUNG AND HEART-LUNG TRANSPLANTATION WITH THE INTERNAL THORACIC ARTERY CONDUIT

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Objective: Our purpose was to study the 2-year patency of direct bronchial artery revascularization in lung transplantation. We wanted to clarify whether the revascularized bronchial artery system is functional after 2 years, whether bronchial artery vascularity changes with time, and whether posttransplantation bronchial artery disease is arteriographically evident after 2 years. **Methods:** Bronchial artery revascularization is performed by anastomosing the internal thoracic artery to as many bronchial artery orifices in the donor descending aorta as possible. Twenty-three patients surviving 2 years or more have had internal thoracic artery-bronchial arteriography performed 1 month and 2 years after transplantation. One-month and 2-year arteriograms have been compared. **Results:** Two-year patency of the internal thoracic artery conduit was 100%. The appearance of the bronchial arteries was unchanged after 2 years in 11 patients. A unilateral or bilateral increase in vascularity was found in two and seven patients, respectively. In three patients new vessels, not visible on the first arteriogram, had appeared. In four patients one or more small vessels visible on the first arteriogram had disappeared on the second arteriogram. We have found no arteriographic signs of bronchial artery disease, such as stenosis of the bronchial arteries, and no arteriographic evidence of arteriosclerotic disease in the internal thoracic artery. **Conclusion:** The internal thoracic artery is an excellent conduit for bronchial artery revascularization, with a 2-year patency of 100% in 23 patients. Only minor changes in the bronchial arteriograms have been found. (J Thorac Cardiovasc Surg 1997;114:326-31)

The lungs have a dual blood supply: the pulmonary arteries, which provide venous blood under low pressure, and the bronchial arteries, which provide oxygenated blood under arterial pressure. The bronchial arteries follow the bronchi far out into the lung parenchyma. Besides supplying the bronchi, they have been shown to contribute arterial blood supply to lung tissue, mediastinal tissue, esophagus, mediastinal and hilar lymph nodes, pericardium, medias-

tinal pleura, vagal and sympathetic nerves, and even, to a minor extent, to the myocardium.¹ Lung transplantation has stimulated an interest in the role and importance of the bronchial arteries.

The logical method to prevent bronchial and lung ischemia after lung and heart-lung transplantation (HLTX) is direct bronchial artery revascularization (BAR). The bronchial artery circulation has been shown to be beneficial in lung transplantation in laboratory animals, in addition to the improved healing of the airway anastomosis. Reduced ischemia-reperfusion injury by improved lung edema clearance has been demonstrated.^{2,3} Improved ability of the lungs to resist and fight infection seems probable.^{4,5} Mucociliary clearance has been shown to be decreased after bronchial devascularization and denervation in autotransplanted canine lungs.⁴ Finally, it has been proposed that ischemia could be a factor in the pathogenesis of obliterative bronchiolitis,⁶ and hopes have been expressed

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that BAR might reduce the prevalence of this condition.⁷⁻⁹

Inasmuch as early results have improved with lung transplantation without BAR since the frequency of airway problems has been reduced, most lung transplant teams have come to believe that transplanted lungs do well without BAR.¹⁰ Although short-term results may be considered acceptable or even good, long-term results after lung transplantation remain unsatisfactory.¹¹ According to our view, ischemia resulting from neglect of the bronchial arteries has not been excluded as a probable cause of problems and poor outcome after lung transplantation and HLTX.

BAR was introduced clinically in 1992 in Bordeaux^{12, 13} and in London,⁷ with the main purpose being to improve airway healing. Both centers performed en bloc double lung transplantation (DLTX). A saphenous vein graft was used as the conduit in Bordeaux and a left internal thoracic artery (ITA) was used as the conduit in London. These two series, as well as our own, have shown that BAR is possible with good early results.^{8, 14, 15}

In Copenhagen en bloc DLTX with BAR using the left ITA has been performed since 1992 as the preferred method of lung transplantation. In 63 cases (double lung [DLTX], single lung [SLTX], and heart-lung transplantation) with BAR we demonstrated an arteriographically monitored early success rate of 94%.¹⁵ The ITA was selected as the conduit because its patency was expected to be superior to that of the saphenous vein graft. If the beneficial effect of BAR in lung transplantation goes beyond primary healing of the airway anastomosis, long-term patency should be important. On the basis of a Kaplan-Meier survival proportion of 83% after 1 and 2 years in our patients having DLTX¹⁶ as compared with 1- and 2-year survivals of 66% and 57% in the total group of patients having bilateral or DLTX in the International Society for Heart and Lung Transplantation (ISHLT) statistics,¹¹ we have found it relevant to study the medium-term patency of the revascularized bronchial artery system and changes in the bronchial artery circulation with time after transplantation. Our aims were to clarify whether the revascularized bronchial arteries are still open after 2 years, whether bronchial artery vascularity changes with time, and whether a post-transplantation bronchial artery disease similar to posttransplantation coronary artery disease is arteriographically evident after 2 years. Furthermore, we have tested for significant correlations between

improved bronchial vascularity versus bronchiolitis obliterans syndrome, number of antibiotic treatments given, number of rejection episodes found at transbronchial biopsies, or number of rejection treatments given.

Patients and methods

In Copenhagen direct BAR with the left ITA used as the conduit has been performed in 58 en bloc DLTXs, 13 SLTXs, and 10 HLTXs from January 1992 to October 1996.

The revascularization is performed by anastomosing the distal end of the ITA to as many bronchial artery orifices in the descending aorta as possible. The aim is revascularization of all identified bronchial arteries, but revascularization of one large artery is considered acceptable.

All patients are routinely scheduled for cine ITA-bronchial arteriography, early (approximately 1 month) and 2 years after the transplantation. Patients in whom BAR had failed at the early examination were not reexamined.

So far, 23 of 27 consecutive 2-year survivors have been reexamined, 20 of 22 having DLTX, one of two having SLTX, and two of three having HLTX. The two patients having DLTX, one with complete BAR and one with incomplete bilateral BAR 1 month after transplantation, have refused to have the 2-year arteriographic examination performed. One patient having SLTX and one having HLTX have refused ever to have arteriography performed. No other surviving patient has been lost to follow-up.

The cine ITA-bronchial arteriogram is performed by means of the Seldinger technique. The tip of a 6F Cordis IM catheter (Cordis Corp., Miami, Fla., catalog No. 532 623) is introduced into the origin of the ITA under fluoroscopic control. By means of hand injection of 6 to 8 ml of contrast medium (Ultravist 370 mg iodine per milliliter), arteriograms are obtained in the anteroposterior, 45-degree left anterior oblique, and 45-degree right anterior oblique projections.

The surgical records and all cine films have been carefully studied, and schematic drawings of the vascular anatomy have been made in each case. The early and 2-year arteriograms were compared with the use of two cinearteriography projectors (Tagarno 35CX) simultaneously. Changes in the classification of BAR success, as well as disappearance, appearance, increase, and decrease in size of bronchial arteries between the first and the second arteriographic studies, have been recorded. In addition, the presence of bronchial artery disease, such as stenosis of the bronchial arteries or the ITA, has been carefully looked for.

Classification of the arteriographic findings.¹⁵ The following classification has been used for evaluation of the arteriograms: This classification applies to SLTX, DLTX, and HLTX with BAR.

Complete BAR: Clear visualization of bronchial arteries on the transplanted side(s) (DLTX, HLTX, SLTX); each lobe is supplied by at least one lobar ramus.

Table I. Arteriographic classification at arteriography approximately 1 month (1 to 5 months) and 2 years after transplantation

Patient No.	Classification		Notes	BOS	No. of infection episodes*	No. of rejection episodes†
	First arteriogram	Second arteriogram				
DLTX						
1	Incomplete bilateral BAR	Incomplete bilateral BAR	Bilateral hypertrophy, especially on the left side	No	1	1 (2)
2	Complete BAR	Complete BAR	Light bilateral hypertrophy	Yes	6	1 (0)
3	Incomplete hemilateral BAR	Incomplete hemilateral BAR	A few small irregular vessels on the left side have disappeared. One small subcarinal vessel has appeared.	Yes	11	2 (6)
4	Complete BAR	Complete BAR	Minor hypertrophy on the left side	No	0	1 (1)
5	Complete BAR	Complete BAR	Unchanged	No	0	1 (0)
6	Complete BAR	Complete BAR	Unchanged	No	2	3 (3)
7	Complete BAR	Complete BAR	Unchanged	Yes	3	2 (2)
8	Incomplete bilateral BAR	Complete BAR	Bilateral hypertrophy. Pouch at the anastomosis disappeared.	No	0	2 (1)
9	Incomplete bilateral BAR	Complete BAR	Bilateral hypertrophy	Yes	2	1 (0)
10	Incomplete hemilateral (+right) BAR	Incomplete Hemilat- eral BAR	Small subcarinal vessels have disap- peared. Basically unchanged.	Yes	1	3 (1)
11	Complete BAR	Complete BAR	Unchanged	No	3	1 (0)
12	Incomplete bilateral BAR	Incomplete bilateral BAR	Bilateral hypertrophy. One new vessel has appeared on the left side (previ- ously supplied only by collaterals from the right side).	No	2	1 (0)
13	Complete BAR	Complete BAR	Unchanged	Yes	2	1 (1)
14	Incomplete bilateral BAR	Complete BAR	Bilateral hypertrophy	No	4	2 (2)
15	Incomplete bilateral BAR	Complete BAR	Bilateral hypertrophy. One new vessel has appeared on the left side.	No	2	2 (1)
16	Complete BAR	Complete BAR	One small vessel for the right superior lobe has disappeared	No	0	1 (1)
17	Complete BAR	Complete BAR	Unchanged	No	1	2 (2)
18	Incomplete poor BAR	Incomplete poor BAR	One vessel prolonged 3 to 4 times. One very small vessel disappeared.	No	1	1 (0)
19	Complete BAR	Complete BAR	Unchanged	No	0	2 (2)
20	Complete BAR	Complete BAR	Unchanged	No	0	0 (0)
HLTX						
1	Incomplete bilateral BAR	Incomplete bilateral BAR	Unchanged	No	1	2 (1)
2	Incomplete hemilateral (left) BAR	Incomplete hemilateral BAR	Unchanged	No	1	2 (1)
SLTX						
1	Complete BAR	Complete BAR	Unchanged	Yes	1	1 (2)

BOS, Bronchiolitis obliterans syndrome, defined as a decrease in forced expiratory volume in 1 second of 20% or more from the maximum volume measured after the operation.

*Number of infection episodes as defined by number of antibiotic treatments given.

†Number of rejection episodes found at transbronchial biopsies. Number in parentheses indicates the number of rejection treatments given.

Incomplete bilateral BAR: Visualization of bronchial arteries on two transplanted sides but sparse on one and clear on the other side (DLTX, HLTX).

Incomplete hemilateral BAR: Clear visualization of bronchial arteries on only one of two transplanted sides (DLTX, HLTX).

Incomplete poor BAR: Sparse visualization of bronchial

arteries on one or two transplanted side(s) (SLTX, DLTX, HLTX).

Failed BAR: No visualization of bronchial arteries.

Bronchiolitis obliterans syndrome has been defined as an irreversible decline of forced expiratory volume in 1 second below 80% of the postoperative baseline

Fig. 1. A, Complete BAR 1 month after transplantation (patient 13, DLTX). B, The same patient 2 years after transplantation (complete BAR). Vascularity unchanged.

value, according to the working formulation of the ISHLT.¹⁷

Results

Twenty patients who underwent DLTX, one who had SLTX, and two who had HLTX and survived 2 years or more have had an ITA-bronchial arteriogram repeated after 2 years. The results are described in Table I. The ITA conduit and the revascularized bronchial arteries were patent in all patients reexamined after 2 years.

The appearance of the bronchial arteries was unchanged after 2 years in 11 patients (Fig. 1, A and B). Unilaterally or bilaterally increased vascularity was found in two and seven patients, respectively. In three patients new vessels, not visible on the first arteriogram, had appeared (Fig. 2, A and B). Four arteriograms primarily classified as showing incomplete bilateral BAR had improved to justify reclassification as complete BAR. In four patients one or more small vessels visible on the first arteriogram had disappeared on the second.

We have found no arteriographic signs of bronchial artery disease, that is, stenosis of the bronchial arteries, nor have we found any arteriographic evidence of arteriosclerotic disease in the ITA.

In patients in the DLTX group with improved vascularity (Table I, DLTX 1, 2, 3, 4, 8, 9, 12, 14, 15, and 18), the mean number of infections was 2.9 (0 to 11), whereas in those with unchanged vascularity the

mean number of infectious episodes was 1.2 (0 to 3). The difference, however, was not significant (Mann-Whitney U test). No statistically significant correlation was noted between improved vascularity and the number of histologic rejections, rejection treatments given, or occurrences of bronchiolitis obliterans syndrome.

The total incidence of bronchiolitis obliterans syndrome 24 months after transplantation was 35% in this series of patients.

Discussion

The 2-year BAR patency was 100%. The general impression is that vascularization has remained unchanged or has improved between 1 month and 2 years after transplantation. The appearance of new vessels may represent dilatation of vessels that were too small to be seen on the first arteriogram, or it may represent true neovascularization. The improved vascularization per se indicates a need for the bronchial circulation. In earlier experimental studies it has been observed that the bronchial arteries hypertrophy in the presence of infection.⁵ Such a vascular response to infection is normal in other tissues, and the same principle may apply to the lungs. Inasmuch as the bronchial arteries also supply the donor hilar lymph nodes, observed hypertrophy could be explained by increased activity in these nodes.

Another possible reason for improved vascularity could be development of collaterals to initially

Fig. 2. A, BAR classified as incomplete bilateral BAR 1 month after transplantation (patient 12, DLTX). Thin arrows mark pericardial vessels leaving the ITA before the ITA-bronchial artery anastomosis. B, The same patient 2 years after transplantation. The arteriogram still shows incomplete bilateral BAR, but with bilateral improvement in vascularity. One new vessel has appeared on the left side (bold arrow).

poorly perfused bronchial artery branches. Additional donor bronchial neovascularization on a level not possible to visualize arteriographically may actually be more important and common than what we have found with arteriography, although one would expect spontaneous revascularization to be less effective than direct surgical revascularization.

In patients undergoing HLTX, it is quite possible that the lungs have a better arterial blood supply than estimated from the ITA-bronchial arteriogram because of coronary collaterals.

The proportions of our patients who survived DLTX at 1 year ($n = 34$), 2 years ($n = 22$), and 3 years ($n = 7$) are, respectively, 83%, 80%, and 65%. When we compare these results with the ISHLT statistics,¹¹ our survival percentages are better than those of the pooled groups of ISHLT patients receiving two transplanted lungs. In the ISHLT statistics the 1-year survivals after bilateral ($n = 557$) and double lung ($n = 177$) transplantation are, respectively, 70% and 57%.

The only conclusion we draw from this fact is that we should continue to do lung transplantation with BAR and wait for the long-term results. In that context it is important to know that BAR has 100% medium-term patency.

It has earlier been stated that BAR is most important during the first 15 days after transplanta-

tion, allowing the airway anastomosis to heal.¹³ This is not necessarily true. It is our clinical impression and belief that the lungs' resistance to and management of pulmonary infections are the most important beneficial effects of BAR. The results of the present series support the view that long-term patency of BAR could be beneficial to the transplanted lung, but only a study comparing patients undergoing SLTX with and without BAR will show the effect of BAR per se. Comparison series from different centers will give imprecise information. Factors of importance after lung transplantation with BAR could be sustained mucociliary clearance, reduced mucosal bacterial adhesion, and improved lung fluid clearance, although this remains speculative.

The possible consequences of late BAR closure are still unknown. We believe collaterals will sustain viability of the bronchus, but this does not mean that BAR closure could not result in problems. To achieve more information, continuous follow-up is necessary.

In this study we have found no arteriographic evidence of posttransplantation bronchial artery disease similar to coronary artery disease seen after heart transplantation. This does not preclude the existence of this disease, and only longer follow-up will give the answer. We do not yet have sufficient autopsy material to study this histologically.

Conclusion

The ITA is an excellent conduit for BAR, with a 2-year patency rate of 100% in 23 patients. The general impression is that bronchial vascularity has remained unchanged or has improved 2 years after transplantation. Arteriographic evidence of post-transplantation bronchial artery disease has not been found.

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