Medium term results of direct bronchial arterial revascularisation using IMA for single lung transplantation (SLT with direct revascularisation)\textsuperscript{1}

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Abstract

Objective: To describe a technique of direct revascularisation of the bronchial artery using the left IMA and assess its medium term results in patients undergoing left single lung transplant (SLT). Methods: Between March 1991 and September 1993, 22 patients who underwent direct bronchial revascularisation at the time of left SLT (20 pedicled IMA, one free IMA, and one direct anastomosis to the aorta) have been followed up for a minimum period of 1 year (mean 30 ± 12 months). Their mean age was 47.8 ± 9.6 and the original disease was emphysema in 19, lymphangioleiomyomatosis in two, and pulmonary fibrosis in one. The mean ischaemia time was 269.7 ± 23.4 min. Results: There was one early death (4.5%) and 3 patients were re-explored for bleeding. The actuarial survival at 1 and 3 years was 91 ± 0.4% and 82.6 ± 1%, respectively. Bronchial healing was excellent in all patients and angiographic studies showed patent vascular anastomosis in all 22 patients, with good run off in 20 and poor in two. One patient developed clinical obliterative bronchiolitis at 22 months (4.5%) during a period of follow up varying from 12 to 43 months (mean 30 S.D. 12). At last follow up the mean FEV1 was 1.4 ± 0.4 and the mean FVC was 2.2 ± 0.6. On average, each patient developed 1.5 ± 0.6 infection episodes and 1 ± 0.2 acute lung rejection. Conclusion: It is concluded that the medium term results of direct bronchial revascularisation are good. However the influence of this procedure on long term results needs further investigation. © 1997 Elsevier Science B.V.

Keywords: Complications; Lung transplantation; Revascularisation

1. Introduction

Single lung transplantation (SLT) is becoming the most common method of lung transplantation for non septic end stage pulmonary diseases. Despite the fact that the incidence of bronchial anastomotic complications have dramatically decreased, it is still one of the major causes of concern. In addition recurrent attacks of infection and acute lung rejections accounts for most of the associated morbidity and mortality of SLT [13,16]. Deterioration of the pulmonary function and

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paper we describe our technique and review the medium term results of this procedure.

2. Patients and methods

During a period of 5 years between March 1988 and September 1993, 153 SLT were performed in our hospital. In March 1991 we developed and used a technique of direct revascularisation of the bronchial arteries using the left IMA to the left lung. Until September 1993, 22 patients underwent SLT utilising this technique. This constitutes 50% of patients undergoing left SLT during this period. There were 12 male and 10 female patients with a mean age of 47.8 ± 9.6 years. The original disease was emphysema in 19, lymphangioleiomyomatosis in two, and pulmonary fibrosis in one. All patients were preoperatively in end stage respiratory failure. There were 13 (59.1%) in New York Heart Association functional class IV and nine (40.9%) in class III.

Our selection criteria for lung donors have been previously described [15]. The donor ages ranged between 16 and 42 with a mean of 26.3 (S.D. 4 years).

2.1. Harvesting technique

All lungs used were harvested by our team using cardiopulmonary bypass [15] and the mean ischaemia time was 269.7 ± 23.4 min. The thoracic organs were removed as a heart-lung block along with the descending thoracic aorta. We usually avoid opening or removing the oesophagus with the block to avoid contamination. The left bronchial arteries which are usually multiple and originate from the proximal portion of the descending aorta are preserved by carrying out the dissection very close to the spine and the anterior wall of the oesophagus with inclusion (if necessary) of muscle fibres from the oesophageal wall. When en-bloc double lung transplantation (DLT) is planned the right bronchial arteries are also preserved and that requires the irrigation of the oesophagus with betadine solution and its removal with the mediastinal block. The descending aorta is then opened along its entire length using an incision along its lateral surface confining the incision to the area covered by parietal pleura to avoid injury to any of the branches. Choosing the bronchial artery or arteries most suitable for revascularisation is achieved by careful inspection of their origin from inside the aorta as well as their course which if necessary can be confirmed by gentle probing. The final decision is made during operation after establishing pulmonary arterial flow to the graft which usually (but not invariably) results in retrograde flow of collateral blood through the orifice of the main bronchial artery to the left lung.

2.2. Revascularisation technique

The recipient pneumonectomy is performed in the standard way for SLT. The left internal mammary artery (IMA) is prepared as for coronary bypass surgery carrying the dissection right up to the origin from the subclavian artery. Special care is taken not to injure the left phrenic nerve which could be vulnerable from this approach. After implanting the lung with the bronchial anastomosis first followed by the artery and the left atrial anastomosis, the position of the orifice of the bronchial artery to be anastomosed is confirmed by the back flow of the blood as mentioned before. Revascularisation is established by anastomosing the left IMA to the chosen orifice (or orifices) using 6/0 monofilament sutures on an 8 mm needle with appropriate orientation of the artery. This technique was used in 20 patients; in 1 patient due to damage of IMA the chosen left bronchial artery was preserved with a button of aorta which was Anastomosed to the recipient aorta directly. In another patient, the IMA was used as a free graft. This revascularisation procedure required an additional operative time of 42 min S.D. 9 (range between 30 and 65 min).

2.3. Post operative management and evaluation

The immunosuppression regime consisted of double therapy using Azathioprine and Cyclosporin, routine steroids were not used. Bronchoscopy was performed around the 7th post operative day and thereafter when clinically indicated. IMA angiographic studies were performed in all patients at 7 to 10 days post-operatively and at yearly intervals thereafter. Full pulmonary function tests were performed routinely at twice weekly intervals during the first month, weekly up to 2 months, and then every 2 weeks during the following 6 months. At discharge a portable spirometer was given to each patient for daily use.

Diagnosis of rejection was based on the clinical symptoms of dyspnoea and cough with more than 10% drop in the FEV1. Febrile illness and radiological findings of alveolar infiltrate constituted additional diagnostic features. Transbronchial biopsy (TBB) was used to assess the presence, severity and occasionally resolution of rejection. Acute rejection was treated with high doses of steroids for 3 days followed by a period of enhanced immunosuppression using a tapering dose of oral prednisolone starting from a dose of 1/2–1 mg/kg and reducing to 0–10 mg/day depending on the severity and frequency of acute rejection during the preceding month. In infection episodes the routine use of bronchoalveolar lavage (BAL) for both viral and bacterial studies helped to differentiate from rejection.

Obliterative bronchiolitis was defined as late deterioration in respiratory functions in which airway obstruc-
tion predominated, in the absence of active infection or acute rejection.

DPTA inhalation scintigraphy which gives typical blotchy appearances in patients with OB was used to confirm the diagnosis. Histological evidence of OB was occasionally observed in TBB specimens. The annual evaluation included pulmonary function tests, exercise capacity with measurements of oxygen saturation and oxygen consumption at rest, anaerobic threshold and maximum exercise using the modified Bruce protocol [2]. The quality of life was assessed using the Nottingham Health Profile (NBP) through direct questionnaire performed annually [9]. Selective angiography of the IMA graft was performed to determine the patency of the graft and the distribution of the bronchial blood supply to the lung.

2.4. Statistical analysis

Survival curves were calculated using the Kaplan-Meier product limits method with 95% confidence interval. Statistical analysis was performed using the Student’s t-test with a P value of 0.05 or less considered significant.

3. Results

3.1. Survival

In this series there was one early death (4.5%), which occurred at 6 weeks postoperatively due to persistent chest infection and ARDS. During the period of follow up which ranged from 12 to 43 months there was an additional death at 6 months postoperatively due to multiorgan failure. The actuarial survival at 1, 3, and 5 years was 91% S.D 4%, 82.6% S.D. 1%, and 74.4% S.D. 2%, respectively (Fig. 1).

3.2. Post operative complications

Three patients required re-exploration of the chest for post operative bleeding. The bleeding site was identified to be from chest wall vascular adhesions in two and donor mediastinal tissue related to the IMA anastomosis in one (4.5%). One additional patient developed respiratory failure due to graft malfunction thought to be due to recurrent chest infections contributed to by phrenic nerve palsy. The patient underwent a right SLT 2 months after the first transplant with good post-operative recovery.

The average number of infection episodes during the first 6 months was 1.5 S.D. 0.6 (range between 0 to 5) and of acute rejection attacks was 1 S.D. 0.2 (range between 1 to 4).

3.3. Bronchial healing

At bronchoscopy all patients showed excellent bronchial healing. That was graded as grade 1 or 2A using the classification suggested by Couraud and his colleagues [6]. This meant the absence of any evidence of necrosis, ulceration, or granulation tissue and the presence of wide anastomosis with complete primary mucosal healing in 18 patients (grade 1) and with partial primary mucosal healing in four (grade

Late bronchoscopic examinations showed complete mucosal healing in all patients.
3.4. Angiographic findings

Angiographic studies of the IMA showed a patent vascular anastomosis (Fig. 2) in all 22 patients with good run off in 20 and poor flow in two. At 1 year 13 IMA studies were performed and showed patent anastomosis to the bronchial artery. At 3 years IMA was visualised in 5 out of 7 patients and showed good bronchial arterial flow. In the remaining 2 patients the IMA could not be visualised.

3.5. Late respiratory function

One patient (4.5%) developed deterioration of lung function presumed to be due OB which was not documented by histological examination. Redo right SLT was performed 18 months ago with marked improvement in her functional status. The other redo operation was performed for a patient with lymphangioleiomyomatosis due to hyperinflated native lung with recurrent infection. The second transplant was performed 19 months postoperatively with good outcome.

3.6. Exercise capacity and quality of life

At last follow up after a mean period of 30 months S.D. 12 months (range between 12 and 43 m) the mean FEV1 and FVC were 1.4% (± 0.4) and 2.2% (± 0.6), respectively. The improvement in FEV1 was maintained over the period of the follow up (Fig. 3). Exercise tests showed an average oxygen saturation at maximum exercise of 96%. 

The maximum oxygen consumption (VO2 max) was 18.3 S.D. 3 O2 ml/min per kg which is equal to 54% S.D. 7 of the average predicted value. Using the NBP the quality of life of the patients at last follow up showed no significant impairment when compared with the general population (Fig. 4).

4. Discussion

This study has shown that ‘long term’ bronchial revascularisation of SLT can consistently and safely be achieved. The medium term results have been encouraging.

During lung transplantation, the bronchus, pulmonary artery, and the pulmonary vein are anastomosed. However until recently the bronchial arteries have been neglected. The early and long term effect of not anastomosing the bronchial arteries remain largely
unknown. In these patients the bronchial wall and lung parenchyma rely on anastomotic channels from the pulmonary artery for their survival. As these channels can only supply a relatively small amount of desaturated blood under a low pressure, this could result in ischaemic damage which could manifest itself in a variety of ways.

Ischaemia of the bronchial wall particularly at the site of anastomosis can cause necrosis of the bronchial wall with resulting dehiscence, or excessive granulation which can progress to fibrous stricture. Although several surgical and pharmacological interventions have resulted in reduction in the incidence and severity of these complications, it continue to be a major cause of morbidity and mortality of SLT with an incidence up to 27.4% [11]. Some of the surgical procedures designed to increase the blood supply to the lung by indirect means have been shown to be ineffective. Colquhoun et al. in 1994 [4] reported an incidence of 10.6% (5/47) bronchial anastomotic complications (four stenosis and one dehiscence). This occurred despite the fact that they have used a bronchial wrap in 68.1% (32/47) of the cases. We have previously reported that wrapping the anastomosis with omentum or an internal mammary artery pedicle does not improve bronchial healing after SLT in a randomised prospective clinical trial [8]. The current study has shown that direct arterial bronchial circulation using the IMA virtually abolishes anastomotic problems.

In addition, under normal conditions the bronchial epithelium contributes to host defence through mucosal secretions and mucociliary action [12]. We have previously shown that following lung transplantation without bronchial revascularisation, these functions are impaired [12]. Direct bronchial revascularisation could maintain these functions. This is supported by our findings of infrequent bouts of infection following SLT in the present study.

OB, which is currently the main determinant of the medium and long term results of SLT, is a multifactorial disease [1,10,16]. The main three factors thought to contribute to its occurrence are immunological damage, recurrent infection (viral or otherwise) and ischemia of the bronchioli [1,16]. All these factors could be influenced by direct revascularisation of the bronchial artery. Immunological damage could be modulated by the fact that the bronchial arteries supply the donor hilar and intrapulmonary lymph nodes, therefore enhance their viability which in turn could increase the likelihood of the development of graft versus host disease and a mixed allogenic chimerism [2,14].

In this paper the potential benefits of direct revascularisation is supported by the low incidence of OB (4.5%), the maintained good respiratory function and the survival results (91 and 82.6% at 1 and 3 years, respectively) observed in our series. However a larger number of patients needs to be followed up for a longer period of time to make more definitive statements regarding this issue.

The incidence of other complications such as bronchomalacia or late stricture could also be reduced by direct revascularisation.

The technique has several important aspects. The small size and the variable anatomical course of the bronchial arteries require specific techniques during harvesting, removal of the recipient lung and the implantation of the donors lung. Schreinemakers et al. [12] in a cadaver study observed at least one constant left bronchial artery in 93% of the cases. In addition, selection of the conduit for bronchial artery revascular-
isation could have important implications with regard to long term function. It has been suggested to use the saphenous vein as a graft [3] but we believe the IMA to be the ideal graft for this purpose because of its ability to remain patent when anastomosed to small vessels and because of its proven excellent long term performance when used as a coronary bypass graft.

In conclusion this study has demonstrated the safety and efficiency of direct bronchial artery revascularisation using IMA after SLT in the medium term. We believe that this procedures deserve wider application and further assessment.

References


Appendix A. Conference discussion

Dr M. Eugene Baudet (Bordeaux-Pessac, France): Dr Couraud and myself, we congratulate the authors, and particularly Dr Yacoub, for their nice presentation and excellent results. As we already mentioned at the EACTS meeting in London, we have also developed, in en-bloc double-lung transplant with tracheal anastomosis, a technique of revascularisation of bronchial arteries using a saphenous vein graft interposed between the orifices of bronchial arteries and the recipient’s ascending aorta. This procedure allows to take in charge up to six ostia of bronchial arteries identified on the bench. Distal anastomosis is achieved and checked before organ transplantation.

We would like to briefly report our results on the 18 patients operated on between 1990 and 1993. There were within the 1st year three deaths due to paratnut or multiorgan failure or infection. At 1 and 2 years, overall survival was 83% and 87%, respectively. With a follow-up ranging from 2 to 4 years, 12 patients are currently alive (66%). Three of these 12 patients developed obliterative bronchiolitis and all three were verified to have late concomitant venous graft thrombosis. One of them underwent successful single-lung retransplant. In the other patients with long-term excellent functional respiratory results, recent angiographic control demonstrated in all but one patency of venous graft and current efficacy of bronchial artery revascularisation. None of these 9 patients with a follow-up of 2 to 4 years developed, until now, obliterative bronchiolitis. Thus, we may also assess, as the authors, that in the immediate postoperative course bronchial artery revascularisation allows perfect tracheal (or bronchial) healing. Furthermore, the absence of OBL in patients with long-term patent venous graft could support an hypothetic role of BAR for preventing this complication. However, the respective responsibility of chronic lung rejection and ischemia could be assessed only by longer follow-up and a larger number of patients with patent versus those with thrombosed grafts. I must say, in addition, that we didn’t switch from venous graft to IMA for technical reasons, among them the approach using a transverse bilateral thoracotomy.

Our question is whether the authors consider also that, in addition to the obvious beneficial effect on bronchial or tracheal healing, long-term, lasting revascularisation could be also beneficial for decreasing the incidence of obliterative bronchiolitis?

Dr K. Al Kattan (Harefield, UK): We have actually performed from 1989 around 38 double-lung en-bloc transplantations using a similar technique with direct revascularisation of the bronchial artery using the IMA, and also, although not reported, we have observed that among the survivors of this procedure, they have excellent functional results, they have a low incidence of both infection and rejection, and a low incidence of obliterative bronchiolitis. With respect to the use of the saphenous vein, we didn’t find any technical difficulties using the IMA.

Dr Magdi Yacoub (London, UK): I have one comment with regard to Professor Bashat’s comments and that is while we think that the internal mammary definitely has a longer survival time, if you like, we haven’t proven the point, because I think it was you or somebody made the point that it might be, and that might well be the case, that all that is needed initially is that critical for the development of collaterals, And if the saphenous vein were to bridge that gap over a
year or two, then adequate collateralisation might be just as good as the internal mammary. I’m just making a point that one cannot just make these generalisations, and it has to be tested, the hypothesis, that indeed the IMA is superior to the saphenous vein. It is still an open question.

Dr Eugene M. Baudet: I agree with you, Dr Yacoub, that as for coronary artery revascularization the IMA is obviously a better conduit than a saphenous graft, as far as long-term patency is concerned. But our first goal was the challenge of tracheal healing in en-bloc DLT, and thus, to ensure perfect healing because of bronchial artery revascularisation. Since the problem now is over that, perhaps it will be shown that the IMA could provide, if not a better, at least a more lasting blood supply to the lungs than a saphenous graft.

Dr Gosta Petterson (Copenhagen, Denmark): I enjoyed the paper very much, since I learned bronchial revascularisation at Harefield. I have now tried bronchial revascularisation in 63 patients en-bloc double lung, single lung, as well as heart/lung transplantation. My ambition has been to do complete revascularisation. I have been revascularising from one to four arteries in each patient. We have done mammary in 53 of these 63 patients. There are four failed revascularisation, three proven by antinio. Three failures were among the first 17 patients. We have repeated the anterigraphy after 2 years in 8 patients, and proven patency in all.

You have chosen to do only left lung revascularisation. Why have you not done revascularization of both lungs? That should be possible in about 75% according to the anatomical studies that we have done. Did you attempt revascularisation and later gave it up? En-bloc double lung is not going to work without successful revascularisation. Our failure rate in the double lung patients is in a situation when we had to be successful. We have not been backing out at any time.

Dr K. Al Kattan: As I said, we are performing this when we are doing double-lung en-bloc with direct revascularisation using the left IMA. As you know from the anatomy, there is a constant left bronchial artery, which is constant in 93% of the cases according to cadaveric studies. So it is more accessible. In addition to the anatomical course of using the right IMA for the right bronchial artery in doing a right single lung, we haven’t performed this, but, as we have had good results with the left single lung. I assume that would probably be encouraging to attempt revascularisation with each lung transplant procedure.

Dr Magdi Yacoub: And we haven’t failed in revascularising the left lung. Like you.

Dr Nitu V. Mandke (Bombay, India): You had 44 patients, and out of that, 22 were revascularised and 22 you did not. Did you find any statistical difference in these two groups of patients as far as their survival rate was concerned or in their bronchial healing? Was there any difference in their bronchial complications?

Dr K. Al Kattan: First, the 22 which were not revascularised during this period, it was either because they were a redo operation or because the bronchial artery was not reserved, as I said, during harvesting. So they are not really comparative groups. You noticed that 19 of the 22 cases of revascularisation were for emphysema. We have studied all of our experience with single-lung transplant for emphysema, and with a matched 19, none were revascularised. Although it is not in the manuscript, we have observed a significant difference in survival. The 5 year survival for the nonrevascularised group was 61% compared with 82.6% in the revascularised group. Again, the frequency of both infection and rejection was significantly different from the nonrevascularised group. This is in a matched group with the same primary disease which is emphysema.

Dr Severi Mattila (Heisinki, Finland): (Slide) We have used also the saphenous vein in six cases now. I would like to point out one technical issue. It is the bleeding, which may be a problem because you can’t check the back side when you have done the internal mammary artery anastomosis: if there are possible branches from the bronchial arteries on the other side. If you do the saphenous vein, distal an astomosis on bench, and then inject blood into the vein, you can see the bleeding points from the bronchial arteries and you can clip those before taking the block into the chest. So that may be the advantage of the saphenous vein. But, of course, the long-term patency rate is better with the IMA. I have here one angio which shows that these saphenous vein grafts can also be patent several months and I think they will work long enough to get bronchial collateral circulation to develop, as Magdi mentioned.

Dr Bernard A. Hausen (Hannover, Germany): Have you or any of the others who have used IMA for revascularisation noticed a reduced incidence of reperfusion injury in these lungs?

Dr Magdi Yacoub: Would you like to define reperfusion injury?

Dr Bernard A. Hausen: Well, I know it’s difficult, but edema, alveolar edema, chest X-rays, signs concomitant with reduction in A-aDO2.

Dr Magdi Yacoub: The quick answer is no.