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MANAGEMENT OF HAEMOPTYSIS: A RETROSPECTIVE ANALYSIS OF THE EFFICACY OF CURRENT TREATMENT MODALITIES.

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DECLARATION

I certify that this thesis is my own work. It has not been submitted previously to this or any other university.

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My family and friends within the Department of Cardiothoracic Surgery for their unwavering support

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ABSTRACT

BACKGROUND

Massive haemoptysis is a life-threatening condition that requires timeous and appropriate intervention. Bronchial artery embolisation (BAE) has been advocated as initial therapy, in preference over lung resection, in all patients presenting with massive and minor haemoptysis. This is despite the relatively high incidence of early recurrence of haemoptysis following treatment with BAE.

Though emergency lung resection for active massive haemoptysis has been associated with a high mortality, the literature has failed to detail the pre-operative evaluation which may have been inadequate and resulted in unsuitable surgical candidates. This has diminished enthusiasm for lung resection as a primary treatment modality for active massive haemoptysis.

METHODS

Case records from 01 January 2005 to 31 October 2007 of all patients admitted with haemoptysis, to the Department of Cardiothoracic Surgery, Inkosi Albert Luthuli Central Hospital were reviewed retrospectively and analysed.

The decision regarding the type of emergency treatment was at the discretion of the attending Cardiothoracic Consultant.

Following clinical examination and basic investigations patients were treated accordingly. Those who were haemodynamically stable were discussed at a Consultant forum and treatment was based on consensus.

RESULTS

Group 1 included 281 patients with massive haemoptysis and group 2 included 222 with minor haemoptysis.

Group one

15 of the 20 patients who were temporised with BAE (75%) had recurrent haemoptysis whereas 1 of the 41 patients (2.44%) who underwent lung resection without BAE developed recurrent haemoptysis (p-value < 0.0001).

In patients undergoing BAE and lung resection, there was 1 death and 2 patients developed a post resection empyema thoracis (5% mortality; 10% morbidity) compared to 2 deaths; 1 post resection empyema thoracis and 1 deep thoracotomy wound infection in patients' undergoing lung resection alone (4.88% mortality; 4.88% morbidity). This was not statistically significant (p-value 0.6736).

Group 2

7 of the 8 patients who were temporised with BAE (87.50%) had recurrent haemoptysis. None of the 44 patients who underwent lung resection alone, developed recurrent haemoptysis (p-value < 0.0001).

There were no deaths or surgical complications other than recurrent haemoptysis in patients who underwent BAE prior to lung resection. Though there were no deaths in patients who underwent lung resection alone, 2 patients developed a post resection bronchopleural fistula and 1 patient developed a post resection empyema thoracis (6.82% morbidity). This was not statistically significant (p-value 1.0000).

CONCLUSION

These preliminary data suggests that patients presenting with radiologically localised disease and massive haemoptysis, who are deemed suitable for surgery, should undergo emergency lung resection. This data also suggests that BAE is probably best utilised as a temporising measure in patients unsuitable for emergency lung resection.

This also appears applicable to patients presenting with minor haemoptysis. In this scenario however, lung resection may be electively undertaken.

Furthermore, this study emphasises the need for further prospective studies to clarify these issues.

INTRODUCTION

At present, bronchial artery embolisation is suggested as the initial form of therapy for all patients presenting with haemoptysis (*Mal, H., Rullon, I., Mellot, F., Brugière, O., Sleiman, C., Menu, Y., and Fournier, M., (1999); Andrejak, C., Parrot, A., Bazelly, B., Ancel, PY., Djibre, M., Khalil, A., Grunenwald, D., and Fartouk, M., (2009); Shigemura, N., Wan, IY., Yu, SC., Wong, RH., Hsin, MK., Thung, HK., Lee, TW., Wan, S., Underwood, MJ., and Yim, AP., (2009)*). This includes patients with massive haemoptysis with radiologically localised disease who are deemed suitable for lung resection following detailed evaluation thereof. Expeditious lung resection in selected patients is curative because it eliminates the risk of recurrent haemoptysis since the source of haemoptysis (diseased lung) is removed (*Knott-Craig, CJ., Oostuizen, JG., Rossouw, G., Joubert, JR., and Barnard, PM., 1993*).

The treatment regarding patients with: a) massive haemoptysis with non-localised disease; b) minor haemoptysis with localised disease and c) minor haemoptysis with non-localised disease; is also contentious. Therefore, by establishing treatment guidelines, based on this clinical review, best practice should be implemented.

At present, primary therapy for both massive and minor haemoptysis (irrespective of feasibility of lung resection) is bronchial artery embolisation (BAE). This may then, be followed by lung resection if it is deemed feasible or necessary, (*Fernando, HC., Stein, M., Benfield, JR., Link, DP., (1998), Knott-Craig et al; Andrejak, C., Parrot, A., Bazelly, B., Ancel, PY., Djibre, M., Khalil, A., Grunenwald, D., and Fartouk, M., (2009); Shigemura, N., Wan, IY., Yu, SC., Wong, RH., Hsin, MK., Thung, HK., Lee, TW., Wan, S., Underwood, MJ., and Yim, AP., 2009*).

BAE is either a temporising or occasionally, definitive intervention. When BAE is used as a temporising measure, followed by non-emergent lung resection (in appropriately selected patients), it is thought that this allows sufficient time for adequate resuscitation of the patient and clearing of blood from the bronchial tree. This improves lung function making lung resection feasible and post-operative complications associated with inadequate pulmonary reserve obviated. (*Fernando et al; Knott-Craig et al; Andrejak et al; Shigemura et al*).

Previous studies have shown a high morbidity and mortality associated with patients undergoing emergency surgery for massive haemoptysis (Gourin, A., Garzon, A., (1974). However, selection criteria for lung resection were vague and lung isolation techniques may have been inadequate.

Gourin et al had an overall mortality of 17%. When emergency surgery was undertaken in patients with active haemoptysis the mortality increased to 33%. However, lung isolation techniques were not ideal since 5 of 7 patients, who had spillage of blood into the normal bronchial tree, when a double lumen Carlens tube was used, demised. This improved when bronchial intubation and balloon catheters were introduced for lung isolation.

In addition, 31 of the 68 patients who underwent lung resection had no evaluation of pulmonary function. This is a major pre-operative omission since inadequate lung function is a significant predictor of post-operative morbidity and mortality.

Andrejak et al showed a post-operative morbidity of 71% and mortality of 35% in patients undergoing lung resection who were actively bleeding and in whom BAE was not undertaken or failed. However, no mention was made of the pre-operative evaluation

including pulmonary function tests. This is important since soiling of the airways with blood may have occurred in some patients. As a consequence, these patients may have had inadequate pulmonary reserve to justify surgery and this would have significantly contributed to the high morbidity and mortality.

Other treatment modalities for massive haemoptysis include ice cold saline lavage of the airways; instillation of vasoconstrictors into the bronchial tree; cellulose tamponade of the bronchi; cavernostomy (patients with cavitary lung disease with inadequate reserve for lung resection, undergo a thoracotomy whereby the lung cavity, which is the probable source of the haemoptysis, is surgically opened and packed, usually with surrounding muscle); radiotherapy in cases of massive haemoptysis from irresectable bronchial carcinoma or instillation of intravenous antifungal agents into mycetoma-containing cavities of the lung (*Jougon, J., Ballester, A., Delcambre, F., Mac Bride, T., Valat, P., Gomez, F., Laurent, F., and JF. Velly, JF., (2002) E. Hankanson, E., Kanstantinov, IE., Fransson, SG., Svedjeholm, R., (2002); Conlan, A., Hurwitz, S., (1980); Knott-Craig et al; Reisz, G., (2005); Haponik, EF., Fein, A., and Chin, R., (2000)*). These treatment modalities involved small cohorts and the results are not significant to warrant their routine use.

Lung resection in the presence of active tuberculosis is thought to be associated with a higher complication rate, especially that of bronchopleural fistulae and post-resectional empyema thoraces. Therefore, BAE is thought to be the best therapeutic modality in patients with massive haemoptysis with active TB, despite being suitable candidates for lung resection. These patients, like those with haemoptysis due to sequelar TB, have a

high risk of recurrent haemoptysis following BAE. This is despite the fact that there is no convincing evidence to suggest that there is a higher incidence of surgical complications in patients undergoing emergency lung resection for active massive haemoptysis and active TB (*Erdogan, A., Yegin, A., Gurses, G., and Demircan, A., (2005) Pomerantz, M., (2000); BJ Pomerantz, BJ., JC Cleveland, JC., HK Olson, HK., and M Pomerantz, M., (2001); Furak, J., Trojan, I., Szoke, T., Tizslavicz, L., Morvay, Z., Csada, E., and Balogh, A., (2001); Mouroux, J., Maalouf, J., Padovani, B., Rotomondo, C., and Richelme, H., (1996).*

OVERVIEW AND LITERATURE REVIEW

Massive haemoptysis is life-threatening and an extremely challenging condition that requires thorough and timeous intervention. Despite advances in treatment, this condition remains a serious threat to the well-being of the patient, since death due to asphyxiation and not exsanguination, is not uncommon.

DEFINITION

Haemoptysis is usually categorised into minor and massive, with massive haemoptysis being the major concern. The definition of massive haemoptysis may vary according to the quantity of blood expectorated or the clinical condition of the patient. The quantity may vary between 600ml to 1000ml in 24 hours, or more than 200ml to 250ml in a single bout. It may also include patients who are haemodynamically unstable with a haemoglobin <10g/dl, requiring intravenous inotrope infusions or ventilatory support. These patients are at high risk of spillage of blood into the normal unprotected lung. This is a more functional definition of massive haemoptysis since it necessitates invasive intervention to avoid death [Gourin, A et al; Jougon, J et al; Wong, ML., Szkup, P., Hopley, MJ., (2002); Andrejak, C., et al.].

Haemoptysis not meeting the above criteria is regarded as minor haemoptysis.

The aetiology of haemoptysis varies in both non-western and western countries. In non-western countries pulmonary tuberculosis, including tuberculous bronchiectasis is the most common cause. In western countries, bronchogenic carcinomas and chronic

inflammatory lung diseases due to bronchiectasis and cystic fibrosis are more prevalent. Other causes include lung abscess, pneumonia and both cardiac and pulmonary vascular abnormalities [Hankanson, E., Kanstantinov, IE., Fransson, SG., Svedjeholm, R., (2002)].

OUTCOMES

Massive haemoptysis has an extremely high mortality. Conservative management of massive haemoptysis has a mortality of 50-100% [Pomerantz, M., et al; Knott-Craig, CJ., et al]. Knott-Craig et al. showed that 36.4% of patients treated medically for massive haemoptysis had a recurrent bleed within 6 months. Of these 45% were fatal. No patients who underwent lung resection for massive haemoptysis had recurrent haemoptysis after 6 months [Knott-Craig, CJ., et al].

The cause of death is usually asphyxiation and not exsanguination. Mortality rates for surgery for massive haemoptysis vary between 7.1% and 18.2% [Knott-Craig, CJ., et al; Andrejak, C.; et al] which increases up to 40% when emergency surgery is undertaken [Gourin, A., et al; Knott-Craig, CKJ., et al; Andrejak, C., et al; Shigemura, N., et al]. Mortality is not affected by the aetiology, activity of TB, lack of therapy, age or sex of the patient [Gourin, A., et al]. The most significant factor influencing outcomes is soiling or aspiration involving the contralateral normal lung [Gourin, A., et al; Knott-Craig, CJ., et al].

TREATMENT OPTIONS

The main treatment modalities include lung resection, bronchial artery embolisation and medical therapy. Medical therapy includes anti-tuberculous drug therapy and broad spectrum intravenous antibiotics [Erdogan, A., et al; Knott-Craig, CJ., et al]. This form of

therapy is usually definitive for minor haemoptysis which is often due to an underlying lung infection.

Other treatment modalities include: ice cold saline lavage of the airways; instillation of vasoconstrictors into the bronchial tree; cellulose tamponade of the bronchi; cavernostomy; radiotherapy for irresectable bronchial carcinoma and instillation of intravenous antifungal agents into mycetoma-containing cavities of the lung.

1) SURGERY

Lung resection is the only definitive form of therapy and is curative [*Erdogan, A., et al*]. In general, due to the high mortality associated with emergency lung resection for active massive haemoptysis, surgery is usually undertaken in selected patients if other therapies, usually BAE, have failed [*Jougan, J., et al; Fernando, HC., et al; Mal, H., et al; Knott-Craig, CJ., et al; Andrejak, C., et al; Shigemura, N.,; et al*].

Therefore, due to the alarmingly high mortality associated with emergency lung resection for massive haemoptysis, a “cooling off” period is suggested. The patient is sedated and BAE undertaken to allow clearing of the bronchial tree if soiling of the lungs has occurred. This improves the pulmonary reserve and allows adequate resuscitation of the patient prior to surgery [*Knott-Craig, CJ., et al*], which is then usually undertaken 48-72 hours later.

All patients presenting with haemoptysis, either electively or as an emergency warrant detailed thoracic surgical investigations, prior to deciding on the feasibility of lung resection. Those patients presenting with massive haemoptysis require admission to a

high care facility and investigated as a matter of urgency following prompt and adequate resuscitation.

PRE-OPERATIVE INVESTIGATIONS

a) CLINICAL EVALUATION

The literature regarding the pre-operative nutritional assessment of those patients presenting with haemoptysis who require lung resection, is sparse at best. In addition, very little is mentioned regarding the analysis of pre-operative investigations to assess the feasibility of lung resection. These investigations include routine blood investigations, including full blood count (no specific values necessitating blood transfusion in this scenario have been cited), renal function and blood coagulation studies. Lung function parameters that have been used to permit lung resection in these cases include a vital capacity >40% predicted post-operative value and a FEV1 >40% predicted post-operative value [*Gourin, A., et al*]. However other aspects of lung function evaluation, including assessing lung parenchymal function and split-lung function studies have never been evaluated in this cohort.

b) RADIOLOGY

Radiological investigations are undertaken to assess the extent of the disease, localise the source of the haemorrhage and determine the possible aetiology.

The chest radiograph is the primary radiographic investigation. Where feasible, high resolution computerised tomography (HRCT), which more accurately depicts the extent

and location of disease, is undertaken. Lung resection is usually performed after careful review of the HRCT.

HRCT depicts five features of underlying lung disease: ground glass appearance, consolidation, cysts, nodules and septal thickening. Each feature has a wide differential diagnosis. Common conditions include TB, bacterial pneumonia, metastatic carcinoma, bronchiectasis and pulmonary oedema.

Abnormal features of lung disease on chest radiograph include: lung cavitation; secondary fungal infection of a lung cavity (ball-in-a hole); bronchiectasis; consolidation; bilateral round pulmonary opacities, which according to their size on radiological investigations may be termed miliary (1-3mm in diameter), mottling (3mm-5mm in diameter) or nodules (greater than 5mm but less than 1cm in diameter).

If a pulmonary arteriovenous malformation (PAVM) is suspected, pulmonary angiography is undertaken to confirm the diagnosis, determine the number and location of the PAVMs as well as the size and number of the feeding vessels. A pulmonary angiogram is also undertaken when the pulmonary artery system is suspected to be the source of the haemoptysis. In this instance, haemoptysis is best treated with emergency surgery since BAE is futile [*Jougon, J., et al; Andrejak, C., et al*].

However, CT findings may show a specific diagnosis in 50% of patients in whom flexible bronchoscopy is non-diagnostic and in 39-88% of patients with a non-diagnostic chest radiograph. Localisation of haemoptysis with CT and a chest radiograph is possible in 63% of cases [*Hankanson, E., et al*].

c) BRONCHOSCOPY

In instances of bilateral lobar disease, still within the physiological limits of lung resection, the dilemma arises in deciding which lobe to resect. Bronchoscopy, which may be either rigid or flexible, may allow localisation of bleeding [*Erdogan, A., et al; Jougon, J., et al; Hankanson, E., et al; Knott-Craig, CT., et al; Haponik, EF., et al; Shigemura, N., et al*]. Flexible bronchoscopy requires conscious sedation and thus avoids a general anaesthetic. It also allows the bronchoscopist to have a more detailed view of the bronchi and permits visualisation of secondary bronchi. This is not possible with rigid bronchoscopy [*Jougon, J., et al*].

Flexible bronchoscopy in patients with massive haemoptysis is certainly not without its pitfalls. Blood impairs vision, the airway is never secure, blood clots cannot be easily removed and adequate ventilation may require that the flexible bronchoscope be removed and replaced by an endotracheal tube. In addition, because this is done using conscious sedation, coughing may be provoked which may lead to a catastrophic haemorrhage. More importantly, definitive and possible life-saving treatment is delayed. Flexible bronchoscopy is efficacious in evaluating central bronchial lesions and is seen as a primary method of localising haemoptysis in 49%-92% of patients. The overall diagnostic accuracy in evaluating patients presenting with haemoptysis is 10%-43%.

Rigid bronchoscopy usually requires a general anaesthetic. Using this technique, blood clots within the airways are easily removed, the airway is secure and the source of haemoptysis is identified. There is no need to visualise the airways distal to the

secondary bronchi as lung resection usually involves a lobectomy at best. In addition, in the event of active haemoptysis during rigid bronchoscopy, spillage can be prevented by wedging the rigid bronchoscope into the main bronchus of the unaffected lung, permitting therapeutic procedures (ice-cold saline lavage, cellulose tamponade, instillation of vasoconstrictors into the bronchial tree, and insertion of Fogarty catheters or bronchus-blockers) to be undertaken. During this time, the airway is secure and the patient may be adequately ventilated using the rigid bronchoscope.

SURGICAL TECHNIQUE AND TIMING

Surgery is usually undertaken following a “cooling off” period. Lung isolation is imperative and is usually achieved with either a left or right sided double lumen endotracheal tube [*Erdogan, A., et al; Haponik, EF., et al*]. A left sided double lumen endotracheal tube is commonly used since correct placement is more easily obtained than a right sided double lumen endotracheal tube. The bronchial cuff of the double lumen endotracheal tube has to be proximal to the upper lobe bronchus to avoid occlusion of the upper lobe bronchus which may result in inadequate ventilation. The distance of the right upper lobe bronchus from the main carina is much shorter than that of the left upper lobe bronchus. This makes placement of a right sided double lumen endotracheal tube technically more difficult. This is especially important if a left pneumonectomy is necessary and the right lung requires ventilation. Insertion of a double lumen endotracheal tube is not an innocuous procedure and complications like bronchial rupture and malposition of the endotracheal tube resulting in inadequate ventilation and spill can occur.

Though not commonly used, a bronchus blocker or a Fogarty catheter is also an effective alternative for lung isolation [*Hankanson, E., et al*].

Surgery for haemoptysis predominantly involves lung resection (lobectomy; bilobectomy or pneumonectomy) and rarely includes cavernostomies and bronchial artery ligation. Cavernostomies are usually performed in instances of lung cavitation associated with massive haemoptysis and poor pulmonary reserve. These patients are usually not suitable for lung resection and a cavernostomy with cauterisation of the bleeding point may stop the haemoptysis. This procedure is usually complicated by a bronchopleural fistula, which may require definitive therapy with thoracoplasty.

The commonest cause of haemoptysis in Africa is inflammatory lung disease. This is usually due to active tuberculosis or its sequela form. The disease process is such that the lung firmly adheres to the chest wall, mediastinum and diaphragm. Freeing the lung from the thoracic cavity is necessary prior to undertaking lung resection. This may result in a significant amount of further blood loss. Therefore, maintaining adequate haemostasis during dissection is imperative, especially under circumstances where the indication for surgery is blood loss i.e. haemoptysis.

In instances of ongoing massive haemoptysis, during lung resection, it may be necessary to remove the bronchus prior to division of the hilar vessels. This will prevent soiling of the contralateral lung in cases of inadequate lung isolation and soiling of the ipsilateral lung during lobectomies.

COMPLICATIONS OF SURGERY

Two of the major post-operative complications following lung resection are bronchial stump dehiscence and a post-resectional empyema thoracis. Risk factors may be categorised into pre-operative risk factors (age > 70 years, chronic obstructive pulmonary disease, diabetes mellitus, collagen vascular diseases, malnutrition, prolonged steroid therapy, induction chemo/radiotherapy, active infection and resection through an empyema cavity); intra-operative risk factors (left pneumonectomy, extended or completion pneumonectomy, advanced malignancy, extensive nodal dissection, endobronchial disease, inadequate bronchial tissue for closure, residual cancer in bronchial stump, long bronchial stump and contamination of the pleural space during surgery) and post-operative risk factors (mechanical ventilation and haemothorax or empyema).

Muscle flaps, though not essential to prevent bronchial stump dehiscence, have been advocated in instances of pre-operative sputum positivity, the presence of a bronchopleural fistula prior to surgery, polymicrobial space contamination and anticipated space problems following lobectomy [*Pomerantz, M.; Pomerantz, BJ., et al; Furak, J., et al*]. Antibiotics (anti-TB therapy) should be continued for at least 12 to 24 months post surgery depending on bacteriologic and radiologic findings. If the antibiotics are stopped too soon, this may exacerbate resistance or increase mycobacterial spread [*Pomerantz, M., et al*].

Though there are variations in surgical techniques for bronchial stump closure i.e. staple versus suture closure, no comparative trials have been undertaken to show the

superiority of either. However, meticulous suture technique and preservation of the blood supply to the bronchial stump by minimising skeletonisation of the bronchial stump, helps prevent a bronchopleural fistula.

Post-resectional empyema thoracis is another fairly common complication occurring in about 13-45% of cases. The patient then requires a prolonged period of drainage and sterilisation of the pleural space and possibly further definitive surgical procedures in the form of either open drainage or thoracomyoplasty. The problem of a residual pleural space following lobectomy may be resolved intra-operatively by undertaking a myoplasty or a tailoring thoracoplasty.

Lung resection in the presence of active tuberculosis was associated with a high morbidity and mortality. Lung resection in the presence of active TB was thought to be associated with a morbidity of up to 12.5% and mortality of 5.5% [*Mouroux, J., et al*]. Furak, J., et al, reported morbidity rates of 22.9% in patients with active tuberculosis who underwent lung resection. Active tuberculosis is a risk factor for post lung resection empyema thoracis and bronchopleural fistulas. As such, lung resection for patients with active tuberculosis is recommended in instances, where feasible, for MDR TB or massive haemoptysis. As a consequence, patients presenting with haemoptysis with either confirmed or suspected active tuberculosis were treated definitively with BAE. However, patients with MDR TB who underwent lung resection after a minimum of 3 months of medical therapy were not always sputum negative at the time of surgery. Despite this, there was no evidence to show a higher surgical complication rate [*Pomerantz, M.*;

Pomerantz, B.J., et al; Furak, J., et al; Mouroux, J., et al]. In fact, the current approach is to adopt a more aggressive strategy for MDR TB. This follows the findings that in patients with MDR TB, early surgery in combination with medical therapy achieves higher cure rates than medical therapy alone [*Mouroux, J., et al*].

2) BRONCHIAL ARTERY EMBOLISATION

Bronchial artery embolisation (BAE) has become an important temporising and occasionally, definitive form of therapy for haemoptysis. Due to poor pulmonary reserve and other medical comorbid conditions most patients are not surgical candidates [Andrejak, C., et al]. BAE is effective in preparing patients for elective rather than high risk emergency surgery [Fernando, HC., et al; Knott-Craig, CJ., et al; Andrejak, C., et al; Shigemura, N., et al.].

TECHNIQUE

Massive haemoptysis usually occurs from the bronchial arteries (90%); pulmonary circulation (5%) and the rest (5%) from the aorta (e.g. aortobronchial fistula, ruptured aortic aneurysm) or the systemic arterial supply to the lungs (other than the bronchial arteries).

As a consequence of underlying parenchymal lung disease, particularly that of inflammatory lung disease, pulmonary circulation is decreased or occluded at the level of the pulmonary arterioles due to hypoxic vasoconstriction, intravascular thrombosis and vasculitis. Bronchial arteries then proliferate and enlarge to replace the pulmonary circulation. These arteries occur in an area of inflammation and are prone to rupture due to erosion by bacteria or elevated regional blood pressure [Jougon, J., et al]. The arterial blood, which is under systemic pressure, extravasates into the respiratory tree leading to massive haemoptysis.

BAE is a transcatheter technique, using the Seldinger technique to gain access into the femoral arteries in order to embolise the arterial source of haemoptysis [Mal, H., et al]. Arteries, other than the bronchial arteries that may be the source of the haemoptysis include: the intercosto-brachial trunk, subclavian artery, axillary artery and the internal mammary artery [Wong, ML., et al]. Embolic agents include gelfoam, polyvinyl alcohol particles, isobutyl cyanoacrylate, absolute alcohol and steel coils or steel spirals.

This procedure does not require a general anaesthetic but has to be undertaken in haemodynamically stable patients without active massive haemoptysis at the time of the procedure. The success rate of BAE ranges from 64 – 100% [Mal, H., et al; Shigemura, N., et al]. Recurrence usually occurs in the first 6 months in 20 -25% of patients which is due either to incomplete occlusion of the feeding vessels, recanalisation of previously embolised vessels, the development of new collaterals or inadequate treatment of the underlying pulmonary disease [Fernando, HC., et al; Mal, H., et al; Hankanson, E., et al]. The consequence of recurrent massive haemoptysis may be catastrophic. Death due to recurrent massive haemoptysis in patients who have undergone BAE, who are in the so called “cooling off period” and in whom lung resection is feasible, is unacceptable.

Repeat embolisation may be successful in those with recurrence. Failure to embolise bronchial vessels occurs in 13% due to non-bronchial artery collaterals [Mal, H., et al; Valipour, A., Kreuzer, A., Koller, H., Koessler, W., and Burghuber, OC., (2005)]. Complications, though uncommon, include spinal cord syndromes, bronchial stenosis,

bronchoesophageal fistulas, bronchial infarction and transient cortical blindness [*Wong, ML., et al*].

ANATOMY OF THE BRONCHIAL ARTERIES

Bronchial arteries supply the trachea, extra- and intrapulmonary airways, bronchovascular bundles, nerves, regional lymph nodes, visceral pleura, oesophagus and the vasa vasorum of the aorta, pulmonary artery and pulmonary vein.

Bronchial artery anatomy varies in origin, branching pattern and course. They originate directly from the descending thoracic aorta, usually between T5 and T6 vertebrae. Four classical branching patterns include: (i) two on the left and one on the right that represents an intercostobronchial trunk (ICBT)-40% of cases; (ii) one on the left and one ICBT on the right-21% of cases; (iii) two on the left and two on the right (one ICBT and one bronchial artery)-20% of cases; (iv) one on the left and two on the right (one ICBT and one bronchial artery)-10% of cases.

The right ICBT is most consistently seen on angiography (80% of patients) and usually arises from the right posterolateral aspect of the thoracic aorta. The right and left bronchial arteries arise from the anterolateral aspect of the thoracic aorta and the occurrence of both originating as a common trunk at angiography is rare.

Bronchial arteries originating outside of T5 and T6 vertebrae at the level of the major bronchi are anomalous and range from 8.3% to 35%. It may arise from the aortic arch, internal mammary artery, thyrocervical trunk, subclavian artery, costocervical trunk, brachiocephalic artery, pericardiophrenic artery, inferior phrenic artery or abdominal aorta.

Non-bronchial systemic collateral vessels enter the pulmonary parenchyma through the adherent pleura or via the pulmonary ligament. In addition these arteries do not course parallel to the bronchi.

Aberrant bronchial arteries can be distinguished anatomically and angiographically from non-bronchial systemic collateral vessels in that they extend along the course of the major bronchi and most originate from the aortic arch. It is usually present when a significant bronchial arterial supply to areas of abnormal pulmonary parenchyma is not demonstrated during angiography. Bronchial arteries of anomalous origin should be considered in patients with recurrent haemoptysis despite successful embolisation and in patients with parenchymal lung disease where the source of bleeding has not been detected.

Dorsal and ventral radicular spinal arteries arise from segmental spinal arteries and supply the dorsal and ventral roots. About eight anterior medullary arteries reinforce the anterior spinal artery which is the major source of spinal cord perfusion. The artery of Adamkiewicz, or greater anterior medullary artery, reinforces the circulation of lumbar enlargement of the spinal cord. This unilateral vessel has been observed to arise between T9 and T12 in 75% of cases.

Anterior medullary arteries have a characteristic "hairpin" configuration at angiography. Radicular arteries are often visualized during BAE. Unintentional embolisation of radicular arteries does not appear to cause clinical problems like spinal cord ischemia.

Therefore the presence of radicular arteries is not a contraindication for BAE. Anterior medullary arteries are rarely observed, but embolisation and repeat angiography should be avoided because spinal cord ischemia may occur with embolisation. Spinal arteries may arise from the intercostal branch of the right ICBT in 5%–10% of cases.

Normal adult bronchial arteries measure less than 1.5mm in diameter at their origin and 0.5mm at their point of entry into a bronchopulmonary segment. Bronchial arteries larger than 2mm at CT scan are usually abnormal. Contrast enhanced CT scans show hypertrophied bronchial arteries as enhancing nodular or tubular structures within the mediastinum and around the central airways, usually located in the retroesophageal area, retrotracheal area, retrobronchial area, posterior wall of the main bronchus and aortopulmonary window. Mediastinal lymph nodes, the azygous vein, and an enhancing oesophageal wall can mimic the bronchial arteries on CT scan.

The number and origin of the bronchial arteries are carefully evaluated to determine the optimal approach for embolisation. A thoracic aortogram is usually undertaken and is also useful to detect non-bronchial systemic arteries that supply pathological areas of the lung.

Cobra-type curved catheters are most commonly used for catheterisation of the bronchial artery. Other catheters include Simmons-1, Headhunter and the Yashigo-type. Microcatheters allow superselective catheterisation of vessels. This allows safe positioning of the catheter within the bronchial circulation, beyond the origin of the

spinal cord branches which helps prevent disastrous neurological complications. After catheterisation of the bronchial artery, bronchial angiography is performed with manual injection of contrast medium.

RADIOLOGICAL FEATURES OF THE CULPRIT VESSELS CAUSING HAEMOPTYSIS

Angiographic features of the blood vessels causing massive haemoptysis include hypertrophied and tortuous bronchial arteries, neovascularity, hypervascularity, shunting into the pulmonary artery or vein, extravasation of contrast medium, and bronchial artery aneurysms [*Fernando, HC., et al*]. Although extravasation of contrast is considered a specific sign of bronchial bleeding, this finding is rarely seen, and its reported prevalence ranges from 3.6% to 10.7%. Thus, determining which arteries are to be embolised should be based on a combination of the CT scan, bronchoscopy, angiography and clinical correlation. All angiograms, including intercostal arteriograms, must be carefully scrutinised for opacification of spinal arteries to avoid inadvertent embolisation.

MATERIALS FOR EMBOLOTHERAPY

Numerous embolic materials are used for BAE. Absorbable gelatin sponge is widely used because it is inexpensive, easy to handle, and has a controllable embolic size.

Disadvantages are its resolvability and lack of radiopacity. Its use may lead to recanalisation of the embolised artery and may sometimes be responsible for recurrent bleeding. Polyvinyl alcohol particles are nonabsorbable embolic materials, ranging from 350–500 µm in diameter and are the most frequently used materials. Its use may prevent

the early recurrence of haemoptysis due to recanalisation of the embolised artery [Wong, ML., et al].

It is essential to avoid the use of embolic materials that can pass through the bronchopulmonary vascular network which is usually about 325 µm in the human lung. Pulmonary infarction via bronchial artery–pulmonary artery shunts or systemic artery embolisation via bronchial artery–pulmonary vein shunts may occur when embolic agents less than 325 µm in diameter are used. It is important to avoid using embolic agents that produce distal occlusion to such an extent, that normal peripheral branches supplying the bronchi, oesophagus, or vasa vasorum of the pulmonary artery or aorta become occluded. This may lead to disastrous complications like bronchial, oesophageal, pulmonary arterial, or aortic wall necrosis. To avoid these complications, the use of polyvinyl alcohol particles with a diameter of 350–500 µm is recommended for BAE.

Liquid embolic agents like isobutyl-2 cyanoacrylate and absolute ethanol are not currently used because of the high risk of severe complications such as tissue necrosis. Stainless steel platinum coils are generally not used for BAE because they tend to occlude more proximal vessels and may preclude repeat embolisation if haemoptysis recurs. However, they may be used to occlude a pulmonary artery aneurysm and may occasionally be used in the internal mammary artery to prevent embolisation of a normal vascular territory and development of collateral vessels.

RESULTS OF BAE

BAE has been shown to be effective in controlling acute massive haemoptysis. The initial non-recurrence rates for BAE have been reported to be 73%–98% [*Mal, H., et al*], with a mean follow-up period ranging from 1 day to 1 month. As a consequence of the introduction of superselective embolisation and the refinement of embolic agents and techniques the immediate success rate of BAE has improved. However, the long-term success rate is still poor. Long-term recurrence rates have been reported to be 10%–52%, with a mean follow-up period ranging from 1 to 46 months. BAE is a palliative or temporising procedure that prepares the patient for elective surgery. However, it may be regarded as definitive in patients treated medically.

COMPLICATIONS OF BAE

Recurrent bleeding may be caused by recanalisation of embolised vessels, incomplete embolisation, revascularisation by the collateral circulation, inadequate treatment of the underlying disease, progression of the underlying lung disease or non-bronchial systemic arterial supply. Recurrence rates may also be influenced by the cause of the haemoptysis. Recurrent bleeding is more common in patients with chronic tuberculosis, aspergillomas, or neoplasms [*Mal, H., et al*]. Neoplasms receive its blood supply from multiple feeder vessels other than the bronchial artery and aggressively invade the bronchial vasculature.

Complications of BAE include chest pain (24%-91%), which is usually transient and is likely related to an ischaemic phenomenon caused by embolisation; dysphagia due to

embolisation of oesophageal branches (0.7%-18.2%) which usually regresses spontaneously; subintimal dissection of the aorta or the bronchial artery during BAE which occurs in 1%–6.3% of patients and is usually asymptomatic. The most disastrous complication of BAE is spinal cord ischemia due to the inadvertent occlusion of spinal arteries [Mal, H., et al]. The prevalence of spinal cord ischemia after BAE is reported to be 1.4%–6.5%. The visualisation of radicular branches on bronchial or intercostal angiograms is not an absolute contraindication for BAE. However, when the anterior medullary artery (artery of Adamkiewicz) is visualized at angiography, embolisation should not be performed.

Other rare complications that have been reported in the literature include aortic and bronchial necrosis, bronchoesophageal fistulae, non-target organ embolisation (e.g., ischemic colitis), pulmonary infarction, referred pain to the ipsilateral forehead and orbit and transient cortical blindness. It is postulated that cortical blindness develops because of embolism to the occipital cortex, either via a bronchial artery–pulmonary vein shunt or via collateral vessels between the bronchial and vertebral arteries.

Non-bronchial systemic arteries can be a significant source of massive haemoptysis, especially in patients with pleural disease from extension of the underlying lung disease. Missing the non-bronchial systemic arteries at initial angiography may result in early recurrent bleeding after successful embolisation of the bronchial arteries [Mal, H., et al]. In the presence of pleural thickening, non-bronchial systemic feeder vessels that originate from various arteries e.g. intercostal artery, branches of the subclavian and axillary arteries, internal mammary artery and the inferior phrenic artery may develop

along the pleural surface and become enlarged as a result of the inflammatory process. Pleural thickening seen on the plain chest radiograph negatively influences the long-term success rate of BAE. Following BAE, Wong et al. noted that 75% of patients had recurrent haemoptysis as an inpatient when bleeding occurred from non-bronchial systemic arteries and only 8% recurrence when the bronchial arteries were the source. *Mal et al.* assessed immediate and long term success of BAE for massive haemoptysis and showed an immediate success rate of 77% (43 of 56 patients). Long term control of bleeding (beyond 3 months) was achieved in 45% (25 of 56 patients).

CT may help predict the presence of non-bronchial systemic collateral vessels as a source of bleeding in patients with massive haemoptysis. Pleural thickening of more than 3mm and tortuous enhancing vascular structures within hypertrophic extrapleural fat seen on contrast-enhanced CT are suggestive of non-bronchial systemic arterial supply in patients with massive haemoptysis. Use of CT to predict the presence of significant non-bronchial systemic vessels resulting in haemoptysis may help in localising the site of bleeding and selecting systemic vessels for embolisation.

3) MEDICAL THERAPY

Conservative medical therapy using antibiotics is used to prevent further haemorrhage by preventing progression of disease [*Erdogan, A., et al*]. In Africa, haemoptysis is usually caused by inflammatory lung disease which includes tuberculosis (including its sequelae), lung abscess and bronchopneumonia. The organisms commonly responsible include; anaerobes (*bacteroides* species and *fusobacterium nucleatum*), gram-positive bacteria (*staphylococcal* species, *streptococcal* species and *haemophilus influenza*) and gram-negative bacteria (*klebsiella pneumonia* and *pseudomonas aeruginosa*).

OTHER TREATMENT MODALITIES

Life-threatening active massive haemoptysis may be treated using endobronchial therapies aimed at causing vasoconstriction of the bronchial arteries. Though not commonly used, these therapies may be useful when other modalities fail or are not feasible [Reisz, G., (2005); Andrejak, C., et al]. The arteries responsible for haemoptysis are similar to systemic arterial vessels in that the mural musculature is vasoresponsive, the exception being the pulmonary artery or its branches. Therefore, therapies causing vasoconstriction, decrease blood flow within these vessels causing thrombotic occlusion of the breached distal vessels.

a) ICE COLD SALINE LAVAGE

Rigid bronchoscopy and lavage of the bleeding lung is one such technique causing vasoconstriction of the culprit vessels. This is usually used as an emergency procedure where other treatment modalities have been unsuccessful or are not suitable [Conlan, A., Hurwitz, S., (1980); Knott-Craig, C.J., et al; Reisz, G.,].

Occasionally, this procedure has been used to stop haemoptysis and stabilise the patient prior to undertaking definitive therapy. A general anaesthetic is required. A rigid bronchoscope is introduced into the main bronchus of the non-bleeding side. This protects the underling lung from spillage and in addition allows ventilation with 100% oxygen. Thereafter, the bronchoscope is placed into the main bronchus of the pathological lung in order to evacuate blood clots and irrigate the airways with cold normal saline (4°C) in 50ml aliquots. This is then suctioned after about 30 seconds to a minute, the normal side re-intubated with the rigid bronchoscope and ventilation

continued. As bleeding slows, localisation of the haemorrhage from the airways is possible. On average, 500ml of normal saline is used to stop all bleeding.

b) VASOPRESSORS

Bronchial lavage using vasopressors (epinephrine; 1% adrenalin-saline solution) have also been used in an attempt to staunch haemoptysis. This is usually done after the blood clots have been removed from the airways and the haemoptysis has ceased with the use of ice cold saline lavage. This procedure cannot be undertaken with active bleeding since the vasopressor will not penetrate the site of haemorrhage because it will be diluted and flushed away by the blood.

Other pharmacological methods causing vasoconstriction of the bronchial arteries include intravenous vasopressin or aerosolised adrenalin. However, if these methods are used prior to undertaking BAE, there is a higher occurrence of technical failure because the offending arteries (bronchial or non-bronchial collateral arteries) undergo vasospasm which makes engaging these vessels, even with the microcatheters, more difficult.

The pulmonary artery wall is thin and is not as sensitive to vasoconstrictors as the bronchial arteries. Therefore, the methods described above to stop haemorrhage, will not be effective if haemoptysis occurs from the pulmonary arteries [*Jougon, J., et al*]. Bleeding from these vessels usually occur from ulceration of the vessel wall due to destruction from inflammation or malignancy. In this instance, haemorrhage is usually stopped by clot formation over the vascular tear. When the clot lyses or the tear

progressively enlarges, fatal haemorrhage may occur. Surgery in this instance is curative. Distinguishing bronchial from pulmonary artery haemorrhage is difficult. Clues inferring pulmonary artery haemorrhage include: radiological studies showing a fungal ball, lung abscess and a cavity that empties and refills.

c) ELECTROCAUTERY

Laser YAG electrocautery used when haemoptysis is due to carcinoma invading the airways is also undertaken with rigid bronchoscopy [*Jougon, J., et al*]. This is done once the bleeding has stopped through the use of other endobronchial control measures.

d) MECHANICAL TAMPONADE

The main or segmental bronchi on the side of the haemorrhage may be occluded using a topical haemostat, a double lumen endotracheal tube, fogarty catheter or a bronchus blocker [*Reisz, G. et al,*] to tamponade the haemorrhage.

Bronchoscopic guided topical haemostatic tamponade using oxidised regenerated cellulose mesh (ORC) has occasionally been used to successfully stop massive haemoptysis when other endobronchial therapies are unsuccessful [*Valipour, A., et al*]. This agent induces clot formation and tamponades bleeding.

A general anaesthetic and rigid bronchoscopy is undertaken to identify the site of haemorrhage. A flexible bronchoscope is then inserted through the rigid bronchoscope and the site of bleeding confirmed. Using a grasping forceps through the flexible bronchoscope, the mesh is placed as peripheral as possible into the bleeding bronchus. The mesh conforms and adheres to the airways and tamponades bleeding from the sub-

segmental to lobar bronchus level. Usually 4 to 10 layers of mesh are used to effect treatment and formation of thrombus. ORC has good tissue compatibility, is bactericidal and has a low incidence of promoting foreign body reaction. It is absorbed within 7 to 20 days, usually without evidence of a foreign body reaction.

Complications of this procedure include an obstructive bronchopneumonia, especially with tamponade of a lobar bronchus but this usually resolves with antibiotic therapy.

Lung isolation using a double lumen endotracheal tube, Fogarty catheter or bronchus blocker may also be used to salvage patients with active massive haemoptysis in whom first-line treatment modalities have failed. Once the site of haemorrhage is confirmed, lung isolation using the above methods may be used to maintain patency of the airways and control bleeding. The affected lung is isolated whilst the unaffected lung is adequately ventilated [*Erdogan, A., et al; Hankanson, E., et al; Knott-Craig, CJ., et al; Haponik, EF., et al*].

A double-lumen endotracheal tube may be used in severe cases of massive haemoptysis where urgent control of the airways is critical in order to prevent asphyxiation. However, placement can be challenging and the tube may easily be dislodged. This may lead to aspiration and death. In addition, blood clots causing airway obstruction cannot be easily removed with a flexible bronchoscope placed through the double lumen tube.

Fogarty catheters and bronchial blockers are easily placed (even at a segmental level) and are effective in tamponading bleeding. However, they are also easily dislodged and

complications include a post-stenotic pneumonia due to atelectasis of the occluded lung [Hankanson, E., et al].

Surgery for massive haemoptysis in appropriately selected patients has been accepted to be curative and the best modality of therapy for these patients. However, the timing of surgery is imperative. The general trend in these cases appears to favour BAE as a temporising measure prior to emergency lung resection since the mortality and morbidity is alarmingly high in patients who are actively bleeding at the time of surgery. This is most likely due to spillage and soiling of the normal bronchial tree resulting in inadequate ventilation. However, BAE commonly fails and often patients with adequate pulmonary reserve prior to BAE, have a repeat massive bout of haemoptysis, aspirate and may demise from asphyxia or become ineligible for lung resection now as a consequence of poor pulmonary function.

As the techniques for lung isolation and ventilation have improved, together with a more thorough and detailed pre-operative patient evaluation for lung resection, it stands to reason that the risks associated with this type of surgery would have diminished as well. However, this has never been appropriately evaluated. Instead, BAE has always been considered first-line therapy despite the risk of recurrent massive haemoptysis which can be fatal.

Patients presenting with minor haemoptysis have also been treated with BAE as first-line therapy. No previous studies have compared medical therapy to BAE or to lung resection for that matter. Therefore, case records of patients presenting with

haemoptysis (minor and massive) have been reviewed. Patients were treated either with medical therapy, BAE or lung resection as first-line therapies. Recurrent haemoptysis and procedural complications following one of the first-line treatment modalities will be regarded as treatment failure.

In view of the high risks associated with surgery for active massive haemoptysis, lung resection has not been contemplated even in suitable candidates. This should be challenged, since it is reasonable to assume that lung resection may be undertaken as a first-line treatment modality in appropriately selected patients, especially in an emergency.

Hence, a new protocol may be established, particularly regarding the indication for BAE as well as the timing and evaluation of lung resection.

AIMS

PRIMARY AIM

To compare the composite outcome of mortality, recurrent haemoptysis and procedural morbidity between surgery alone versus BAE plus surgery in patients who are amenable to surgery.

SECONDARY AIM

To suggest a treatment protocol for patients with haemoptysis based on the preliminary data of treatment outcomes

HYPOTHESIS

Emergency lung resection without BAE is the optimal treatment strategy in appropriately selected patients presenting with massive haemoptysis.

Elective lung resection without BAE is the optimal treatment strategy in appropriately selected patients presenting with minor haemoptysis

MATERIALS AND METHODS

Authorisation to access and review case records from 01 January 2005 to 31 October 2007 of all patients admitted with haemoptysis, to the Department of Cardiothoracic Surgery, Inkhosi Albert Luthuli Central Hospital and King George V Hospital, was granted by the Superintendants of each institution.

The decision regarding the type of emergency treatment was at the discretion of the attending Cardiothoracic Consultant. Patients, who were haemodynamically stable and not actively haemorrhaging, were discussed at a consultant forum and treatment was based on consensus.

All patients with active haemoptysis, or a history thereof, were included in the study and patients with other sources of bleeding mimicking haemoptysis e.g. haematemesis or bleeding from the upper airways, were excluded.

Depending on the quantity of haemoptysis, patients were grouped into either those presenting with massive or minor haemoptysis.

Each of the two groups was further subdivided according to the type of treatment undertaken, viz.

- a) Surgery
 - i) Temporised with BAE and
 - ii) no BAE
- b) Definitive BAE
- c) Medical therapy

A detailed history and examination was undertaken on all patients as a preliminary assessment of determining, not only the possible aetiology of the haemoptysis, but also the feasibility of lung resection.

PATIENT EVALUATION

MEDICAL HISTORY

Haemoptysis requires a detailed history and physical examination to establish the urgency of treatment. Important information required includes: quantity of blood expectorated, date of occurrence (especially if massive), number of episodes, reliable witnesses (health care professional), a history of blood transfusions as a consequence of haemoptysis, , previous episodes of haemoptysis and treatment thereof (inpatient or outpatient, BAE, surgery or medical).

Since tuberculosis is endemic in South Africa, it is not surprising that it is a major cause of haemoptysis in our patient population. Subsequently, a detailed history regarding tuberculosis is also imperative because this may impact on the type and timing of treatment. Further details include: if and how the diagnosis of TB was established, treatment regimen, treatment compliance, TB sensitivities, previous thoracic surgery for TB and the number of recurrences of TB.

The prevalence of HIV in sub-Saharan Africa is the highest in the world. Therefore, it was necessary to counsel patients to obtain consent regarding voluntary testing (where

necessary), information about their HIV status, anti-retroviral therapy, their current CD4 cell count and viral load if available.

The grade of the patient's effort tolerance (MRC-modified medical research council dyspnoea scale) was used as a crude assessment of pulmonary function. An effort tolerance greater than 2 was suggestive of impaired pulmonary function. This was used in association with more accurate methods of assessing pulmonary function in order to determine the feasibility of lung resection. Cardiac causes of dyspnoea were also excluded.

A careful review of the patient's symptoms and medical history may assist in determining the possible aetiology of haemoptysis. Common causes include:

- i) inflammatory lung disease (usually tuberculosis or its sequela forms – patients may present with an established diagnosis of active tuberculosis, constitutional symptoms or a history of previous tuberculosis)
- ii) pulmonary artery venous malformation-PAVM (history and examination may include a family history of a PAVM, epistaxis, cyanosis and a machinery murmur)
- iii) bronchial or metastatic carcinoma (history may include an established diagnosis of malignancy, loss of weight, loss of appetite and chest pain).

GENERAL EXAMINATION

This was an important part in the preliminary evaluation for lung resection. Important features on clinical examination included pallor (this may be an indication of chronic disease or severity of haemoptysis), temporal wasting (suggests poor nutrition), lymphadenopathy (scalene lymph nodes in the presence of bronchial carcinoma may indicate metastatic disease) and features of AIDS (generalised wasting and lymphadenopathy, oral thrush, etc.).

The respiratory and cardiovascular systems were examined for pertinent features to help in the assessment of both the severity of the haemoptysis and the extent of underlying lung disease. These features included: the oxygen saturation (using a pulse oximeter), respiratory rate, pulse and blood pressure and other features suggestive of hypovolaemia as a consequence of blood loss (decreased Glasgow coma scale, cool peripheries and decreased urine output).

INVESTIGATIONS

The timing of investigations depends on the severity of the haemoptysis and the patient haemodynamics. Massive haemoptysis requires emergency investigations.

Blood investigations included:

- i) Arterial blood gas

A PaO₂ >60mmHg and PaCO₂<45mmHg were usually the lower limits for lung resection. Blood gas analysis was also useful in assessing the risk of post-lung resection mechanical ventilation.

ii) Full blood count

A haemoglobin >10g/dl was usually necessary in patients with massive haemoptysis. Indicators of acute blood loss and chronic disease may also be seen on analysis.

iii) Clotting profile

This usually was normal but if not, treatment to correct this was undertaken prior to surgery or bronchial artery embolisation.

iv) Liver function and renal function

Patients suitable for surgery usually had an albumin>30g/dl (this was suggestive of adequate nutrition) and all patients should ideally have normal renal function. BAE requires contrast which is nephrotoxic and lung resection undertaken in patients with renal impairment is associated with a higher risk of post-operative morbidity and mortality.

v) HIV

The HIV status was usually only considered when lung resection for haemoptysis was elective and not life-saving (as in cases of active massive haemoptysis).

Currently, the Department of Cardiothoracic Surgery UKZN unit policy regarding surgery for HIV positive patients states that, patients with a CD4 cell count >200 cells/ul or an undetectable viral load in patients on anti-retroviral therapy, are suitable for surgery, provided other criteria for lung resection is satisfactory.

vi) Pulmonary function tests

This was only undertaken in patients who did not have active haemoptysis. Lung resection was usually undertaken when the ppoFEV1>40% and if necessary, a ppoDLCO>40% (ppo: predicted post-op FEV1: forced expiratory volume in the first second; DLCO: diffusing capacity for carbon monoxide).

vii) Radiology

A chest radiograph and HRCT of the chest (if feasible) was undertaken in all patients presenting with haemoptysis. These radiological investigations allow assessment of the extent of disease, possible aetiology and feasibility of lung resection. Following radiological review, localised lung disease was regarded as lung disease less than, or equivalent to, one lung. It stands to reason then that, extensive bilateral lung disease was lung disease greater than the extent of one lung.

viii) Sputum analysis for TB when feasible.

TREATMENT

Following detailed clinical evaluation, patients may require resuscitation. This may necessitate judicious fluid therapy with blood if necessary, oxygen supplementation, airway protection (using a double lumen endotracheal tube, usually in patients with active massive haemoptysis) and mechanical ventilation. Depending on the possible aetiology of haemoptysis, anti-TB therapy and broad spectrum intravenous antibiotics were usually commenced.

Thereafter, definitive treatment was undertaken based on the amount of haemoptysis, extent of lung disease, arterial blood gas, albumin, CD4 count, viral load and pulmonary function tests. Lung resection was undertaken in the presence of localised disease and if surgery was deemed suitable following detailed evaluation.

BAE was undertaken either as a temporising measure in those patients suitable for lung resection or as definitive therapy in patients declining surgery or who were deemed unsuitable for surgery. The decision regarding temporising surgical patients using BAE was at the discretion of the Consultant Cardiothoracic Surgeon on duty.

BAE was undertaken emergently by the on-call radiologist. Since the incidence of pleural disease is high in our patient population and if no contraindication exists, both bronchial and non-bronchial sources of haemoptysis are embolised. A pan-aortic radiological review to evaluate the culprit vessels was usually undertaken.

Unless suspected, no attempt was routinely made to assess for a possible pulmonary artery source of the haemorrhage. Polyvinyl alcohol sponges were the most commonly used materials for embolotherapy.

Patients with massive haemoptysis suitable for lung resection underwent surgery either emergently or urgently. Those with minor haemoptysis underwent elective surgery on the same admission.

Medical therapy alone was administered to all patients not suitable for surgery and/or BAE, those who refused surgery and/or BAE or had minor haemoptysis as a consequence of a specific aetiology which was then treated accordingly.

Recurrent haemoptysis and the complications of each modality of therapy was analysed in all patients prior to discharge. Where possible, patients were followed up at the out-patient thoracic clinic and their symptoms reviewed.

Patients who underwent lung resection were followed up for at least 1 month from their date of discharge. The other groups of patients' were followed up for a period of at least 3 months from discharge. Further review was subject to patient compliance, symptoms or complications.

RESULTS

DEMOGRAPHICS

TABLE 1	MASSIVE HAEMOPTYSIS n (%)			
	Surgery Alone	BAE and Surgery	BAE Alone	Medical Therapy
Median Age (yrs)	38	33	34	43
Male	28 (41) (n=68)	11 (20) (n=55)	120 (189) (n=63)	23 (32) (n=72)
Black	35 (41) (n=85)	19 (20) (n=95)	175 (189) (n=93)	26 (32) (n=81)
HIV positive	14 (41) (n=34)	11 (19) (n=58)	106 (189) (n=56)	23 (32) (n=72)
CD4 <200	4 (11) (n=36)	3 (10) (n=30)	78(119) (n=66)	10 (15) (n=67)
Active TB (histology)	19 (41) (n=46)	6 (20) (n=30)	29(58) (n=50)	1(5) (n=20)

p- values comparing columns 1 and 2 in Table 1 were all >0.05 and hence not significant

TABLE 2	MINOR HAEMOPTYSIS n (%)			
	Surgery Alone	BAE and Surgery	BAE Alone	Medical Therapy
Median Age (yrs)	44	40	38	45
Male	29 (44) (n=66)	6 (8) (n=75)	43 (75) (n=57)	60 (94) (n=64)
Black	37 (44) (n=84)	7 (8) (n=88)	66 (75) (n=88)	71 (94) (n=76)
Active TB (histology)	15 (38) (n=39)	3 (6) (n=50)	40 (75) (n=53)	56 (94) (n=60)
HIV positive	3 (14) (n=21)	0 (3) (n=0)	22 (33) (n=67)	30 (49) (n=61)
CD4 <200	11 (44) (n=25)	3 (8) (n=38)	11 (13) (n=85)	9 (21) (n=43)

p- values comparing columns 1 and 2 in Table 2 were all >0.05 and hence not significant

**COMPARISON OF OUTCOMES BETWEEN SURGERY ALONE VERSUS BAE AND
SURGERY**

TABLE 3	Massive Haemoptysis		
	Surgery Alone (n=41)	BAE and Surgery (n=20)	p- value
Recurrent Haemoptysis	1	15	<0.00001
Protocol Morbidity	2	2	0.5915
Mortality	2	1	1.0000
All complications	5	18	<0.00001

**COMPARISON OF OUTCOMES BETWEEN SURGERY ALONE VERSUS BAE AND
SURGERY**

TABLE 4	Minor Haemoptysis		
	Surgery Alone (n=44)	BAE and Surgery (n=8)	p-value
Recurrent Haemoptysis	0	7	<0.00001
Protocol Morbidity	3	0	1.0000
Mortality	0	0	1.0000
All complications	3	7	<0.00001

LUNG RESECTIONS UNDERTAKEN FOR MINOR AND MASSIVE HAEMOPTYSIS

TABLE 5	MASSIVE HAEMOPTYSIS		MINOR HAEMOPTYSIS	
	Surgery Alone	BAE and Surgery	Surgery Alone	BAE and Surgery
Right Pneumonectomy	2	3	7	
Left pneumonectomy	10	3	11	2
Right upper lobectomy	8	4	7	3
Left upper lobectomy	14	6	13	3
Right lower lobectomy	3	1	3	
Left lower lobectomy	2		1	
Right upper and middle lobectomy	1	1	1	
Middle lobectomy		1		
Middle and right lower lobectomy	1	1		
Other			1	

MULTIVARIABLE LOGISTIC REGRESSION FOR RECURRENT HAEMOPTYSIS

TABLE 6

ALL RECURRENT HAEMOPTYSIS			
RISK FACTOR	OR	95% CI	p-value
BAE and Surgery vs Surgery alone	457	31-6651	<0.001
HIV positive	4.4	0.47-42.4	0.196

COMPLICATIONS OF BAE AND MEDICAL THERAPY

TABLE 7	BAE		MEDICAL THERAPY	
	Massive haemoptysis n=189	Minor haemoptysis n=75	Massive haemoptysis n=32	Minor haemoptysis n=94
Recurrent haemoptysis	25 (13%)	11 (15%)	6 (19%)	7 (8%)
Protocol Morbidity (CVA)	2 (1%)	1 (< 1%)	0	0
Mortality	16 (9%)	2 (3%)	7 (22%)	9 (9.5%)

Results of the subgroups analysed were based on the intention to treat.

GROUP 1: MASSIVE HAEMOPTYSIS

a) SURGERY

An analysis comparing the occurrence of recurrent haemoptysis following treatment, morbidity, mortality and all complications (including recurrent haemoptysis, morbidity and mortality) between those patients temporised with BAE prior to surgery and those treated with surgery alone using the Fischer exact test, showed the following association between the 2 groups:

1) Recurrent haemoptysis

15 of the 20 patients who were temporised with BAE (75%) had recurrent haemoptysis whereas 1 of the 41 patients (2.44%) who underwent lung resection without BAE developed recurrent haemoptysis (p-value < 0.0001). Therefore, patients undergoing BAE prior to surgery have a statistically significant risk of recurrent haemoptysis when compared to patients having immediate surgery without temporising with BAE.

2) Morbidity and mortality

In patients undergoing BAE and lung resection, there was 1 death and 2 patients developed a post resection empyema thoracis (5% mortality; 10% morbidity) compared to 2 deaths; 1 post resection empyema thoracis and 1 deep thoracotomy wound infection in patients' undergoing lung resection alone (4.88%

mortality; 4.88% morbidity). This was not statistically significant (p-value 0.6736). Therefore there is no statistically significant risk for complications (disregarding recurrent haemoptysis) if surgery is undertaken without BAE used as a temporising measure.

3) All complications

Complications were noted in 18 patients (90%) in the BAE prior to lung resection group, compared to 5 patients (12.20%) who complicated in the group who underwent surgery alone (p-value<0.0001). There is a statistically significant risk for complications if BAE is undertaken prior to lung resection. This is predominantly due to the high risk of recurrent haemoptysis following BAE.

MORTALITY

1) MASSIVE HAEMOPTYSIS

a) SURGERY

i) TEMPORISED WITH BAE

The only death in this group was due to fulminant septicaemia from multi-drug resistant Gram negative Acinetobacter grown from blood cultures. This patient had ongoing massive haemoptysis despite successful BAE. Though preliminary investigations showed that he had AIDS (CD4 126 cells/ul which was ascertained following lung resection), a left pneumonectomy was undertaken as a life-saving procedure due to ongoing massive haemoptysis and following a second “successful” BAE. The patient required a massive blood transfusion and post-operative ventilation as a consequence of spill. Death

occurred 10 days after surgery despite maximum medical support. Histology of the left lung showed mycetoma with no evidence of active TB.

ii) SURGERY WITHOUT BAE

The first death, which occurred 9 days after surgery, was due to septic shock and multiple organ failure. This followed a post left pneumonectomy empyema thoracis due to a bronchopleural fistula. This was treated with closed-tube drainage. The patient eventually required mechanical ventilation. There were no significant risk factors for development of a bronchopleural fistula and the patient demised 3 weeks later. This patient had pre-operative anti-TB therapy for more than 3 months and histology of the left lung showed bronchiectasis and aspergilloma with no evidence of active TB.

The second death occurred suddenly on day 2, following lung resection. Prior to and during surgery there was active haemoptysis and surgery was undertaken as life-saving therapy. This patient had AIDS (CD4 127 cells/ul) and was not on HAART. He was ventilated overnight, resuscitated after lung resection and demised on day 2 in the high care unit while awaiting transfer to the general ward. The aetiology of his death was probably aspiration as a consequence of a bronchopleural fistula, but this was merely speculation as a post mortem was not undertaken. This patient was on anti-TB therapy for a month prior to emergency lung resection. Histology confirmed active TB which was sensitive to standard anti-TB therapy.

MORBIDITY

1) MASSIVE HAEMOPTYSIS

a) SURGERY

i) TEMPORISED WITH BAE

The first patient with a post resection empyema thoracis was HIV positive (CD4 283 cells/ul) and underwent an emergency right upper lobectomy for recurrent massive haemoptysis after “successful” BAE. Intra-operatively no mycetoma-containing cavity was breached and histology showed bronchiectasis with no evidence of active TB. He was treated with open drainage and was well upon discharge.

The second patient with a post resection empyema thoracis was HIV positive on HAART but a viral load (CD4 110 cells/ul-preoperative) was not obtained. Elective right pneumonectomy was undertaken about 2 months later to allow resolution of an associated bronchopneumonia, treated with oral antibiotics. BAE was undertaken as a temporising measure and there was no recurrence of haemoptysis during the period prior to lung resection. She was treated with open drainage and was well at the 3 month follow up. Histology showed aspergilloma with no evidence of active TB.

ii) SURGERY WITHOUT BAE

One patient developed a post right upper lobectomy empyema thoracis. Lung resection was undertaken due to ongoing massive haemoptysis and surgery was life-saving. This patient had AIDS (CD4 157 cell/ul) and was not on HAART. He was transfused with 7 units of packed cells peri-operatively. During surgery the aspergilloma-containing cavity

was breached resulting in soiling of the pleural space. Post-operatively he required a short period of ventilation due to hypothermia and acidosis resulting from prolonged surgery. The empyema thoracis was treated satisfactorily with open drainage and this patient was well at 3 months follow up. Histology showed bronchiectasis with no evidence of active TB.

A deep thoracotomy wound infection occurred in a patient who underwent an emergency left pneumonectomy for ongoing massive haemoptysis. Pre-operatively, following preliminary thoracic surgical evaluation, he had a haemoglobin of 8.6g/dl, albumin 28g/dl, was HIV positive with a CD4 cell count of 209 cells/ul and was diagnosed with active TB, 4 weeks prior to surgery. Intra-operatively the patient had a hypoxic arrest as a consequence of a blocked double lumen endotracheal tube and required a very short period of cardiopulmonary resuscitation. This patient required ventilation for a day. He was discharged in a fortnight and at 3 months follow up his wound had healed and he was well. Histology of the lung showed bronchiectasis with no evidence of TB.

b) BRONCHIAL ARTERY EMBOLISATION

189 patients underwent BAE as definitive therapy.

25 patients had recurrent haemoptysis following BAE (13.23%).

16 patients demised (8.47%). 13 patients (6.88%) died from recurrent massive haemoptysis (3 of these patients had failed BAE. In 2 of these procedures the catheters failed to engage the abnormal vessels and in 1 procedure the presence of spinal feeders contraindicated embolisation); 1 from contrast induced renal failure and 1 from a massive embolic cerebrovascular accident (CVA) following BAE. Another patient, who presented after a year with recurrent minor haemoptysis, following previous "successful BAE", was ineligible for BAE due to HIV associated nephropathy and subsequently demised from poor health.

2 patients developed post BAE embolic cerebrovascular accidents (CVA) (1.06%). One developed a right T6 and left T8 sensory level due to spinal cord ischaemia. No spinal feeders were noticed during the procedure. The other patient developed a right homonymous hemianopia. Spinal feeders were seen during the procedure and noted to be arising from the posterior intercostal vessels.

24 patients had a failed BAE (12.70%). There were a total of 28 BAE procedures undertaken. Of these, 16 showed spinal feeders which did not allow embolisation; 7 procedures undertaken did not permit catheters to engage abnormal vessels; 3 procedures failed to show abnormal vessels despite underlying lung disease and 2 procedures showed fistulae to the left pulmonary vein which contraindicated BAE.

c) MEDICAL THERAPY

There were 32 patients in this group. Of these, the majority included, 21 patients who had active or sequelar TB; 4 patients had irresectable bronchial carcinoma (confirmed either on sputum cytology or fine needle aspiration cytology and who were referred to the Department of Oncology for further treatment); 3 patients had a bronchopneumonia; 1 patient presented with cor pulmonale and in 3 patients no source of haemoptysis could be found despite detailed thoracic surgery and ear, nose and throat (ENT) investigations.

Recurrent haemoptysis occurred in 6 patients (18.75%). Of these, 5 patients had recurrent massive haemoptysis and demised (15.63%). The other patient had recurrent minor haemoptysis but refused any intervention (3.13%)

There were 7 deaths (21.88%), 5 of which resulted from recurrent massive haemoptysis, 1 from right heart failure (cor pulmonale) and 1 from generalised ill health as a consequence of extensive pulmonary tuberculous.

GROUP 2: MINOR HAEMOPTYSIS

a) SURGERY

An analysis comparing the occurrence of recurrent haemoptysis following treatment, morbidity, mortality and all complications (including recurrent haemoptysis, morbidity and mortality) between those patients treated with BAE prior to surgery and those treated with surgery alone using the Fischer exact test, showed the following association between the 2 groups:

1) Recurrent haemoptysis

7 of the 8 patients who were temporised with BAE (87.50%) had recurrent haemoptysis. None of the 44 patients who underwent lung resection alone, developed recurrent haemoptysis (p-value < 0.0001). Therefore, patients undergoing BAE prior to surgery were shown to have a statistically significant risk of recurrent haemoptysis following BAE, when compared to patients having emergency surgery alone.

2) Morbidity and mortality

There were no deaths or surgical complications other than recurrent haemoptysis in patients who underwent BAE prior to lung resection. Though there were no deaths in patients who underwent lung resection alone, 2 patients developed a post resection bronchopleural fistula and 1 patient developed a post resection empyema thoracis (6.82% morbidity).

This was not statistically significant (p-value 1.0000). Therefore there is no statistically significant risk factor for complications, if surgery is undertaken without BAE.

Both patients who complicated with a bronchopleural fistula had elective surgery for minor haemoptysis and were on anti-TB therapy preoperatively. Histology for one of these patients suggested active TB whilst the other showed features of sequela TB only. There were no other significant risk factors for a bronchopleural fistula in both patients, suggesting that flawed surgical technique was the probable cause. Successful surgical repair was undertaken in both patients using a muscle flap.

The third patient complicated with a post-lobectomy empyema thoracis. Following elective surgery, re-exploration for excessive post-operative haemorrhage was undertaken on the same day. Bleeding from a bronchial artery was seen and stopped. The patient required a blood transfusion with 6 units of packed cells. Histology of the left upper lobe showed bronchiectasis and aspergilloma with no evidence of active TB. An empyema thoracis developed within 2 weeks. A fortnight later, a decortication of the lung did not achieve a satisfactory result and an open drainage using a cut malecot catheter draining into stoma bag was opted for. After 6 months, the malecot catheter was removed following obliteration of the empyema space.

3) All complications

Complications were noted in 7 patients (87.50%) in the group who was temporised with BAE prior to surgery, compared to 3 patients (6.82%) who complicated in the group who underwent surgery alone (p-value<0.0001). Therefore there is a statistically significant risk for complications if BAE is undertaken prior to lung resection. This is predominantly due to the high risk of recurrent haemoptysis following BAE.

b) BRONCHIAL ARTERY EMBOLISATION

75 patients in this group underwent BAE as definitive therapy.

Recurrent haemoptysis occurred in 11 patients (14.67%). There were 2 deaths (2.67%) and both were as a consequence of recurrent massive haemoptysis. These fatal massive episodes occurred within 1 week and 2 months respectively of BAE.

The other 9 patients with recurrent haemoptysis had minor episodes of haemoptysis.

Other complications included 1 patient who developed a left sided embolic cerebrovascular accident (CVA), following BAE (1.33%).

8 patients had failed BAE (10.67%). There were a total of 9 BAE procedures undertaken. Of these, 3 showed spinal feeders contraindicating embolisation; 3 procedures did not permit catheters to engage abnormal vessels and 3 procedures failed to show abnormal vessels despite underlying lung disease. All of these patients had active or sequela TB.

c) MEDICAL THERAPY

There were 94 patients in this group. Of these, the majority included 56 patients with active or sequelar TB; 20 patients with irresectable bronchial carcinoma (confirmed either on sputum cytology or fine needle aspiration cytology and referred to the Department of Oncology for further treatment); 15 patients with bronchopneumonia; 1 patient with an eroding thoracic aortic aneurysm and in 2 patients no source of haemoptysis could be found despite detailed thoracic surgery and ENT investigations.

Recurrent haemoptysis occurred in 7 patients (7.45%), all of which were due to active or sequelar TB. 2 patients had recurrent massive haemoptysis and demised. 5 patients had recurrent minor haemoptysis.

There were 9 deaths (9.57%), 2 of which resulted from recurrent massive haemoptysis (2.13%), 4 from irresectable bronchial carcinoma and 3 from generalised ill health as a consequence of extensive pulmonary tuberculosis.

DISCUSSION

It is indisputable that in patients presenting with haemoptysis, lung resection is usually curative and BAE is a temporising measure. Simply stated, surgery is superior to BAE as a treatment option in these patients. Despite this, BAE has been advocated prior to surgery in all patients presenting with haemoptysis. Surprisingly, this also includes patients presenting with active massive haemoptysis who require little or no pre-operative preparation. This treatment strategy was borne from the high morbidity and mortality previously associated with emergency lung resection in patients presenting with massive haemoptysis. However, these results may have been as a consequence of poor surgical selection. With appropriate detailed pre-operative evaluation, this review has shown similar outcomes for both emergency and elective lung resection for massive haemoptysis without pre-operative BAE when compared to BAE prior to lung resection. BAE is a temporising measure which even if “successfully” undertaken still exposes these patients to recurrent and possible fatal haemoptysis. Therefore, by undertaking emergency lung resection without BAE in appropriate patients, the unnecessary risk of recurrent massive haemoptysis and possible death is avoided. This is contrary to current treatment methods for these patients.

Recurrent haemoptysis following BAE

Recurrent haemoptysis following BAE occurs in up to 20%-45% of patients at 1 month [*Fernando, HC., et al; Mal, H., et al; Andrejak, C., et al*]. This may be due to incomplete occlusion of the feeding vessels, recanalisation of previously embolised vessels, the

development of new collaterals or inadequate treatment of the underlying disease

[*Fernando, HC., et al; Mal, H., et al; Hankanson, E., et al*].

However, this high recurrence rate may be extremely hazardous since surgery may have to be undertaken in actively bleeding patients in whom BAE has failed. This poses an increased risk of soiling of the normal lung leading to an increased mortality even if lung resection is not undertaken.

In this review, 15 patients (75%) presenting with massive haemoptysis who were temporised with BAE prior to lung resection, had recurrent haemoptysis following BAE despite being suitable surgical candidates upon admission. Of these, 7 patients (46.67%) had bouts of recurrent massive haemoptysis following BAE. This necessitated emergency surgery. Furthermore of the 8 patients in this review, who underwent BAE for minor haemoptysis and who were deemed feasible for lung resection prior to BAE, 5 had recurrent haemoptysis (62.5%). Of these, 1 (20%) had recurrent massive haemoptysis requiring emergency surgery. This study has not shown significant morbidity and mortality associated with lung resection alone, albeit in selected patients presenting with massive haemoptysis. Therefore it can be reasonably deduced that BAE undertaken pre-operatively places these patients at an unnecessary risk of recurrent massive haemoptysis and possible death.

Recurrent haemoptysis following BAE is much higher compared to that following surgery. Lung resection is curative because the focus of the haemoptysis is excised. BAE,

on the other hand, is a temporising measure because it deals with the sequelae of pulmonary disease i.e. the pathological blood vessels.

Outcomes of Surgery for Haemoptysis

Patients with massive haemoptysis who are eligible for surgery, but who are treated medically, have a 78-85% [Knott-Craig, C.J., et al] mortality as a consequence of massive haemoptysis. This risk of death decreases to 10-35% if surgery is undertaken [Knott-Craig, C.J., et al; Andrejak, C., et al; Shigemura, N., et al].

Recurrent haemoptysis following surgery for massive haemoptysis may occur in up to 5% [Andrejak, C., et al]. This may be due to incomplete excision of the underlying diseased lung, progression or reactivation of disease or development of new lung pathology. In our series, 1 of 41 (2.44%) patients had recurrent haemoptysis following emergency surgery for massive haemoptysis. This was attributed to recurrent primary pulmonary tuberculosis which was successfully treated with anti-TB therapy.

From Table 3 it should be noted that the major outcome that differs between surgery alone versus BAE plus surgery is recurrent haemoptysis. Though morbidity and mortality between these 2 groups were insignificant in our preliminary data, a prospective study is deemed feasible further analyse the 2 groups.

This series assessed all-cause mortality. Analysis has shown a mortality of less than 5% in all patients undergoing emergency surgery for massive haemoptysis without pre-operative BAE, and about 5% in those patients undergoing surgery for massive haemoptysis following BAE. The difference in mortality between these 2 groups was not

significant in our preliminary data. This questions the previously held belief that BAE undertaken prior to lung resection improves outcomes especially in those patients presenting with active massive haemoptysis and suggests the necessity of a prospective study to further analyse morbidity and mortality.

In this series, complications of lung resection for massive haemoptysis following BAE included: 1 death (1/20; 5%), as a consequence of respiratory failure due to a post-lung resection bronchopneumonia and 2 patients (2/20; 10%) who developed a post-resection empyema thoracis.

Surgery for massive haemoptysis without BAE resulted in the following complications: 2 deaths (2/41; 4.88%) both as a consequence of respiratory failure exacerbated by post-resectional bronchopleural fistulae and 1 patient (1/41; 2.44%) who developed a post-resectional empyema thoracis.

These figures compare favorably to the current complication rates worldwide, which show an 18-30% occurrence of post-operative bronchopleural fistulae and post-resectional empyema thoraces in patients undergoing surgery for massive haemoptysis following BAE [*Shigemura, N., et al*]. Andrejak et al. showed a 5-11% occurrence of post-resection bronchopleural fistulae in patients undergoing emergency lung resection with active haemoptysis. This figure increased to 20% for planned resections i.e. patients with massive haemoptysis who were successfully temporised with BAE. Though not mentioned, this may be due to emergency lung resection undertaken in patients with

recurrent massive haemoptysis following BAE. These patients usually spill into the bronchial tree and surgery undertaken under these circumstances is associated with a higher risk of complications.

In this review, there were no complications in the group with minor haemoptysis who were temporised with BAE prior to surgery. 2 patients (2/44; 4.55%) in the group who had surgery for minor haemoptysis without BAE developed post-resection bronchopleural fistulae.

There was no mortality in our series in patients undergoing lung resection for minor haemoptysis even in patients having recurrent haemoptysis following BAE.

The surgical mortality from current experience worldwide is significantly higher than in this series. This may be due to suboptimal pre-operative evaluation, patient selection and timing of surgery in other centres.

This study suggests that emergency lung resection, without BAE, as the initial treatment modality, in appropriately selected patients presenting with massive haemoptysis and radiologically localised disease may be valid. This preliminary data would require a prospective study to confirm these suggestions. Nevertheless, at present, in our institution, all patients presenting with massive haemoptysis who are deemed suitable for lung resection, now undergo emergency surgery without the delay of BAE in order to avoid the risk of recurrent massive haemoptysis and soiling of the bronchial tree.

Multi-variable logistic regression analysis (Table 6) is limited in this study since the events per variable for other factors were too few. This preliminary data once again re-enforces the need for a prospective study.

HIV and Surgery

The literature deals extensively with surgery in the HIV positive patient. It is possible that HIV status may be affect recurrent haemoptysis following surgical intervention. In a post hoc analysis, the influence of HIV status on the treatment outcomes of the surgery alone group and the surgery and BAE group were analysed.

Following multivariable analysis, HIV status was not found to be significantly associated recurrent haemoptysis in both surgical groups i.e. surgery alone and BAE with surgery.

Outcomes of BAE

It is worthwhile repeating that, though BAE is essentially a temporising measure, it has to be regarded as definitive in those patients in whom lung resection is not feasible.

Studies show that BAE results in immediate cessation of haemoptysis in up to 77% [*Mal, H., et al*].

In our series, the rate of recurrent haemoptysis following treatment with BAE alone occurred in 13.23% (25/189) of patients presenting with massive haemoptysis and 14.67% (11/75) of patients presenting with minor haemoptysis. This compares favorably with current figures worldwide. However, these patients in this study were not eligible for lung resection and were discharged within 48 hours following BAE. In

addition, follow up of patients treated using non-surgical therapies was extremely poor. Besides the immediate outcomes of BAE, the short and long term outcomes of BAE in this study could therefore not be accurately reviewed. Therefore there is a bias in this sample since follow up was inadequate.

Common complications of BAE include: chest pain (24%-91%), dysphagia (0.7%-18.2%) subintimal dissection of the aorta or the bronchial arteries (1%-6.3%). As stated previously, the most disastrous complication of BAE is spinal cord ischaemia due to the inadvertent occlusion of spinal arteries [Mal, H., et al]. The prevalence of spinal cord ischemia after BAE is reported to be 1.4%-6.5%.

Complications of BAE in our series of 264 patients for both massive (189 patients) and minor (75 patients) haemoptysis included 1 patient with spinal cord ischaemia (demised), 2 patients with embolic strokes and 1 patient with contrast induced renal failure (demised).

13% of patients have non-bronchial collaterals as a cause of haemoptysis. Bleeding from non-bronchial collateral arteries should be suspected with radiological evidence of pleural thickening. Another important cause of failed BAE may result from vasoconstriction of the bronchial arteries especially when intravenous vasoconstrictors administered prior to BAE.

In our study, failed BAE occurred in 24 patients with massive haemoptysis. Of these, 8 patients had spinal feeders which contraindicated embolisation.

8 patients with minor haemoptysis had failed BAE. 2 of these patients had spinal feeders which contraindicated embolisation.

Though not considered an absolute contraindication, spinal feeders, can in experienced hands, be superselected and pathological vessels embolised using microcatheters.

Haemoptysis may occur from the pulmonary artery system in 5% of cases. In this review, this was only investigated if a pulmonary arteriovenous malformation was suspected. This did not include scenarios where despite the presence of haemoptysis in the presence of underlying pulmonary disease, no pathological systemic arterial vessels were identified as the source. This may be catastrophic in patients with massive haemoptysis originating from the pulmonary arterial system. As stated previously, in this instance, emergency surgery, if feasible is the only form of definitive therapy (BAE is contraindicated). Unfortunately, lung resection is rarely emergently undertaken in this instance, since the diagnosis is difficult and often not considered as the aetiology of the haemoptysis.

Patients with mycetoma-containing cavitary disease and extensive pleural disease are thought to have a higher risk of recurrent bouts of haemoptysis despite BAE or medical therapy.

Outcomes of Medical Therapy

In our series, patients treated medically also showed low rates of recurrent haemoptysis. Those with massive haemoptysis showed a recurrence rate of 18.75% (6/32) and 7.45% (7/94) in those with minor haemoptysis.

The low rate of recurrent haemoptysis following medical therapy is attributed to poor follow up, resulting once again in a bias sample.

Medical treatment (which may include antibiotics or radiotherapy based on the probable aetiology) for haemoptysis is only undertaken if BAE has failed (usually technical) or lung resection is not deemed feasible. This is especially so for patients with massive haemoptysis.

Of the 94 patients in our series treated medically for minor haemoptysis, 7 had recurrent haemoptysis. 2 of these patients had massive bouts of haemoptysis and demised. All 7 patients with recurrent haemoptysis had active or sequelar TB and BAE was not attempted in any of them. Therefore, patients with active or sequelar TB, presenting with minor haemoptysis and who are ineligible for curative lung resection, BAE is the treatment of choice. This is especially so if radiological investigations suggests a high risk for recurrent massive haemoptysis.

Outcomes of Surgery in patients with Active Pulmonary Tuberculosis

41 of 113 patients, who underwent lung resection, either electively or emergently for massive or minor haemoptysis, had active pulmonary TB confirmed either pre-operatively (usually on sputum analysis for acid-fast bacilli) or on TB analysis of the resected lung (histology or TB microscopy and culture). Of the 3 patients who died following lung resection, 2 patients had a bronchopleural fistula and only 1 of these patients was found to have active TB.

2 patients were treated with open drainage for a post lung resection bronchopleural fistula, 1 of which had active tuberculosis.

4 patients developed a post lung resection empyema thoracis. None of these patients had active TB following investigations for TB.

1 patient who developed a deep thoracotomy wound infection also did not show evidence of active TB following investigations for TB.

In summary, of the 41 patients with active TB, 2 patients had surgical complications. Of the 72 patients with no evidence of active TB, 8 patients had surgical complications.

In our study, active TB is not a statistically significant risk factor for complications following lung resection for patients presenting with haemoptysis. This includes patients presenting with active massive haemoptysis who require emergency lung resection.

Post Lung Resection Empyema Thoraces and Bronchopleural Fistulae

The *left bronchus syndrome* which as a consequence of the more horizontal plane of the left main bronchus, the decreased peri-bronchial space and the fact that the left main bronchus is 15% narrower, attempts to explain why left sided disease is more common. This was common to this review as well. The commonest operation was that of a left upper lobectomy followed by a left pneumonectomy.

One of the risk factors for a post-resection empyema thoracis or a post-resection bronchopleural fistula (BPF) includes a right pneumonectomy. However our series did

not show a significant association between a right pneumonectomy and post-resection empyema thoraces or a BPF.

All bronchial stumps were closed with interrupted Vicryl ® (Johnson and Johnson) absorbable sutures. Reinforcing the bronchial stump with a muscle flap was rarely used.

“Salvage Surgery”

Though not routinely recommended the concept of ‘salvage surgery’ is proposed in patients with extensive bilateral lung disease with symptoms of recurrent haemoptysis, despite numerous “successful” interventions with BAE. In this category of patients, despite extensive bilateral disease, the radiological investigations may suggest that the haemoptysis may be arising from a localised area of the diseased lung (e.g. cavity with mycetoma in a lobe). This should be confirmed by rigid bronchoscopy. Thereafter, if following detailed routine evaluation, lung resection is deemed suitable, this may be undertaken with the intention of cure. Though our series only included 2 such patients, this form of management should be considered, since surgery may be life-saving.

Study Limitations

The major limitation of our study was patient follow up. It should be realised that any study undertaken in an indigent population, which includes the vast majority of this study group, poor follow up, especially if patients are well, is inevitable. Inadequate transport facilities required to cover vast distances to reach a hospital and poverty are the main reasons for this. However, the main focus of this study was on patients presenting with haemoptysis who underwent lung resection with and without pre-operative BAE. The limitation of patient follow up did not affect this study group. All patients who

underwent successful lung resection were followed up for a minimum of 6 months and those who complicated with recurrent haemoptysis, bronchopleural fistulae or post-resection empyema thoraces were followed up beyond 6 months.

All patients treated with BAE alone were discharged within 2 days of treatment. All patients treated with medical therapy were discharged with 5 days of admission once assessment for other treatment modalities was complete.

It then stands to reason, that this retrospective study was not suitable to evaluate treatment outcomes of both BAE and medical therapy since both inpatient stay was short and patient follow up was very poor. The results tabulated in table 5 are therefore extremely biased. Furthermore, as we are a surgical unit with limited state resources, our primary concerns were patients who underwent lung resection. The other categories of patients are capably managed at base hospitals and for the overwhelming majority did not require further thoracic surgical opinions. It stands to reason that follow up of these patients is relatively non-existent.

Nevertheless, other studies have extensively evaluated BAE and medical therapy alone and the superiority of the addition of lung resection is not in dispute. It is for this reason this study focuses on surgery alone versus surgery following BAE. It is necessary to reiterate that all previous studies advocate BAE as a preliminary treatment method prior to lung resection even if upon admission patients are suitable for emergency lung resection. This is despite the fact that the risk of a possible fatal bout of recurrent haemoptysis following BAE is significantly higher than if lung resection is undertaken.

It is possible that the BAE plus surgery group had more chronic and complex disease which could have resulted in worse outcomes when compared to the surgery alone group. Again, a prospective study is required to evaluate this possibility.

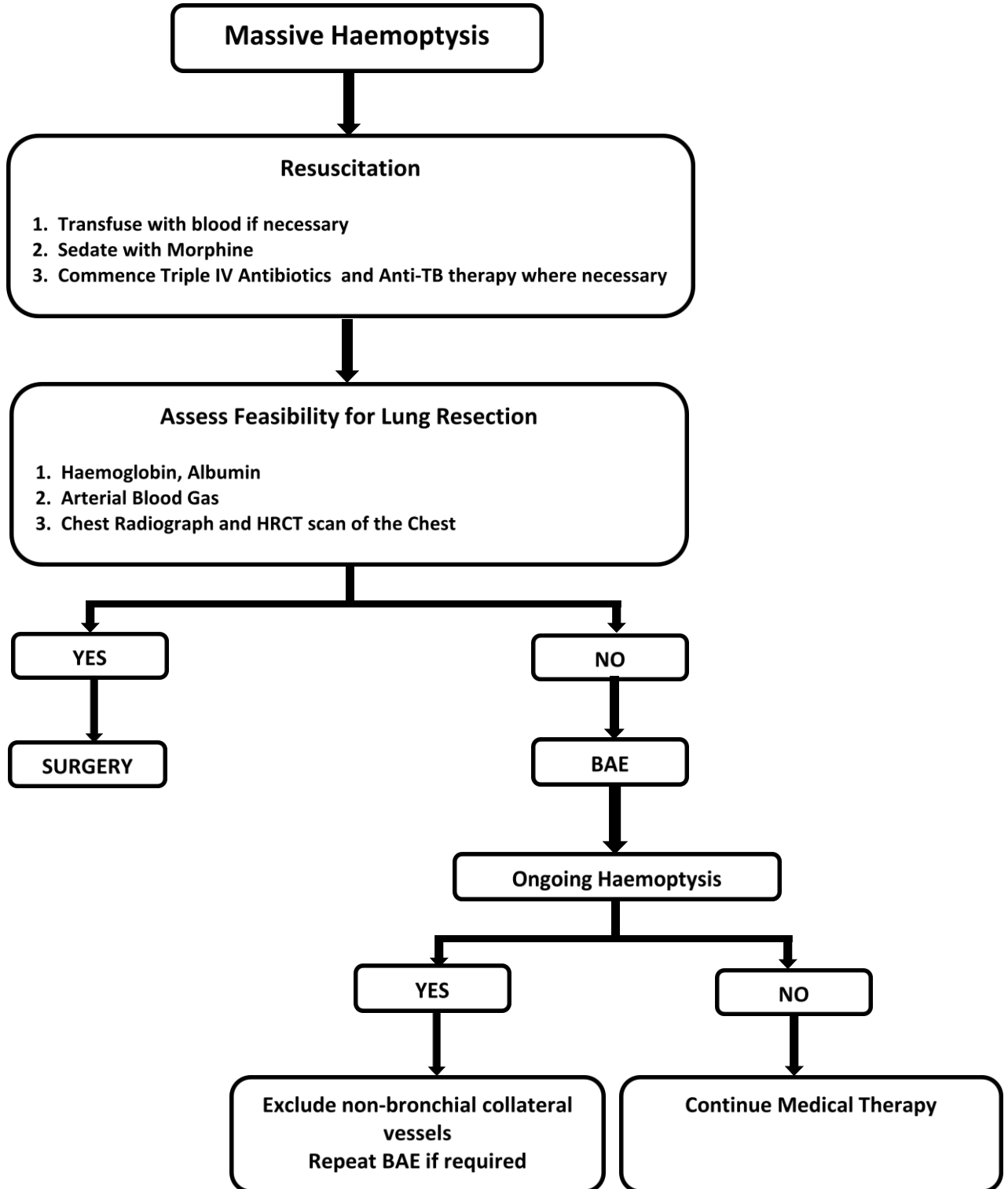
CONCLUSION

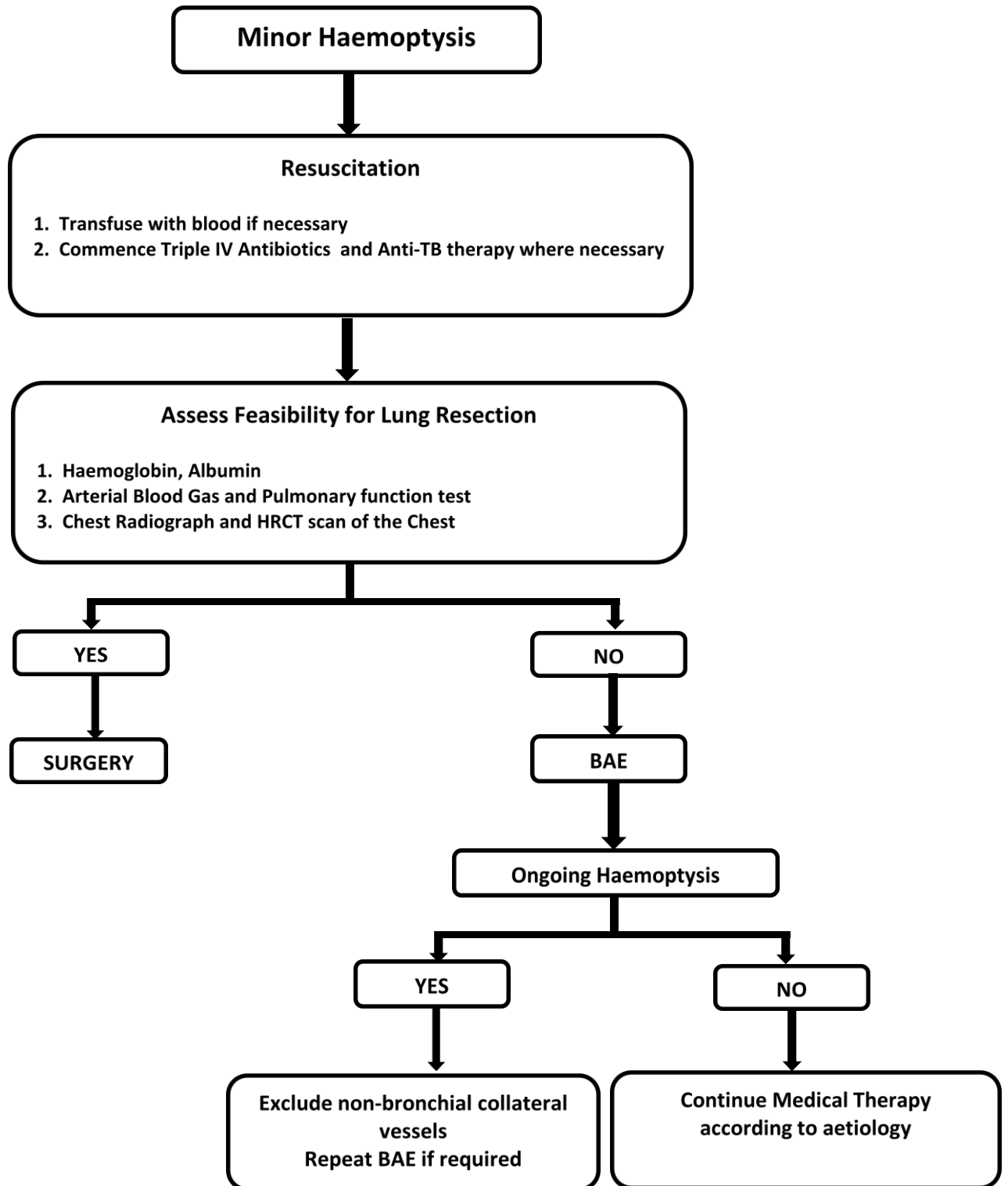
This retrospective review implies that all patients presenting with localised disease and massive haemoptysis, who are deemed suitable for surgery, should undergo emergency lung resection without undertaking BAE as a temporising measure. This is so, since this preliminary data shows a significant difference in recurrent haemoptysis if surgery is undertaken without BAE as a temporising measure. The previous belief of not undertaking emergency lung resection in patients with active massive haemoptysis because of the associated prohibitively high morbidity and mortality was not evident in our series. Therefore, BAE as a temporising measure in patients who are suitable for surgery should not be undertaken since delayed lung resection places the patient at an unnecessary risk of possible fatal recurrent massive haemoptysis.

Though prospective studies are required, it is suggested that BAE be reserved for patients who refuse or are deemed unsuitable for surgery.

Furthermore, it is also suggested that medical therapy alone should probably only be implemented if surgery or BAE is not feasible. This is especially so in patients with minor haemoptysis as a consequence of active or sequelar TB where there is radiological evidence suggestive of a high risk of massive haemoptysis. Patients presenting with minor haemoptysis due to other causes may be treated according to the possible aetiology of the underlying disease i.e. recurrent minor haemoptysis due to irresectable bronchial carcinoma may be treated with localised radiotherapy.

SUGGESTED TREATMENT PROTOCOL





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