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Pulmonary embolism: a frequent cause of acute fatality after lung resection

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Abstract Between 1975 and 1993, lung resections were performed in 1735 patients because of malignancies, with an early postoperative mortality of 7.2% (125 patients). Early postoperatively acute cardio-respiratory failure was experienced by 32 patients (1.85%), of whom 26 died despite immediate resuscitation measures. In 20/26 patients autopsy was performed revealing central pulmonary embolism as the cause of death in 19 of them. In one patient a rupture of the free posterior left ventricular wall following transmural myocardial infarction was found. Two patients who could be resuscitated successfully were operated on with extracorporeal circulation after pulmonary angiography had been performed to confirm the diagnosis; however they died 2 days later of right heart failure. Of the survivors three cases had myocardial infarctions, one patient had arrhythmias of unknown etiology. Immediate embo-

lectomy with the use of extracorporeal circulation was performed in two patients, only on the ground of suspected pulmonary embolism and without further diagnostic measures. Both patients survived. Of the 23 cases, with proven pulmonary embolism 17 were still under postoperative prophylaxis with heparin. Six patients were already fully mobilized. We conclude that massive pulmonary embolism is a frequent early postoperative fatal complication after lung resections, which cannot be safely prevented by postoperative heparinization. The only successful life-saving measure in the case of central pulmonary embolism is immediate pulmonary embolectomy, if necessary without further diagnostic measures. [Eur J Cardio-thorac Surg (1996) 10:242–247]

Key words Lung resection · Pulmonary embolism · Embolectomy

Introduction

Patients with malignant disease frequently suffer from coagulation abnormalities [25] causing deep venous thrombosis and thromboembolic events despite normal routine clotting tests [6, 20]. Inversely it could be demonstrated retrospectively [21] as well as prospectively [18] that patients suffering from deep vein thrombosis can have a malignant disease not yet diagnosed [1, 16, 19]. This associ-

ation between tumors and thromboembolic events is also known for patients with lung cancer [7, 12, 13, 22]. Nevertheless most of them can maintain normal hemostatic function [29] and venous thrombosis as well as thromboembolism cannot be predicted with certainty [4, 6]. The reduction of the cross-section of pulmonary arteries after lung resections holds an increased risk of serious complications in the case of minor pulmonary embolism and will lead to fatal cardiorespiratory failure more often compared to that in individuals with normal lungs [24, 30].

In order to clarify the significance of thromboembolic events as causes of early postoperative deaths we performed a retrospective study of nearly 2,000 patients operated because of pulmonary malignancies in our department during the past 18 years.

Patients and methods

Patient population

In 1735 patients who underwent lung resections between 1975 and 1993, early postoperative mortality was 7.2% (Table 1). The majority of the patients who died had a prolonged, complicated postoperative course ending fatally. The largest group, with 54 cases, included patients suffering from pneumonia which, as a result of the reduced amount of lung parenchyma, led to respiratory failure or right heart failure. In 20 cases, after pneumonectomy bronchus stump insufficiency occurred which led secondarily to septic problems. In 19 patients with advanced tumors, intraoperative or postoperative hemorrhaging could not be controlled. In seven cases other causes led to death, e.g. free wall rupture of the left ventricle due to myocardial infarction, cerebral damage or abdominal problems. The remaining 25 cases are part of a group of 32 patients with cardiorespiratory failure, possibly caused by pulmonary embolism as described in this study.

With respect to the duration of surgery, blood loss, transfusion requirements as well as anesthesia, all patients were comparable as far as tumor stages, operative procedures and histological types of bronchogenic carcinomas were concerned. Of all patients, 93% had a history of smoking.

Thromboembolic prophylaxis

The preoperative routine coagulation profile, consisting of activated partial thromboplastin time (APTT), prothrombin time and thrombocytes, showed normal values in all patients except in three cases, where moderately elevated numbers of thrombocytes between 450, and 500,000/ μ l were recognized, and in one patient who had 657,000/ μ l thrombocytes.

Only three of these patients had already been hospitalized for longer times before the lung resections. They were under treatment with $3 \times 7,500$ I.U. heparin/day subcutaneously. All other cases were outpatients coming to the hospital 1 or 2 days before the operation

Table 1 Causes of early postoperative death after lung resection ($n = 125$ of 1,735 = 7.2%)

Diagnosis	<i>n</i>	Autopsy (<i>n</i>)
Pneumonia with respiratory failure	54	46
Proven pulmonary embolism (autopsy or embolectomy)	21	19
Suspected pulmonary embolism (no autopsy)	4	
Complications after bronchus Stump insufficiency	20	12
Intraoperative or postoperative hemorrhage	19	10
Other cause	7	6
	125	93 (74.4%)

without any evidence of deep vein thrombosis. They had no medication for prophylaxis preoperatively. The thromboembolic prophylaxis was started on the morning of the 1st postoperative day as a continuous intravenous application of heparin with a dosage of 5 I.U./kgBW per h and was changed in the 2nd postoperative day to subcutaneous application of 7,500 or 10,000 I.U. every 8 h depending on the body weight of the patient, if they could be mobilized. Otherwise the continuous intravenous application was maintained and the dosage was chosen following the results of the APTT. All patients were mobilized on the 1st postoperative day if possible. Patients with varicose veins or known previous deep vein thrombosis were routinely provided with compression stockings. No antiplatelet drugs, warfarin or low molecular weight heparin were used as prophylactic agents in the early postoperative course.

Results

Out of the whole cohort of 1735 patients, 32 (1.85%) experienced non-predictable, acute cardiorespiratory failure within the first 2 postoperative weeks, which made resuscitation necessary (Table 2). All of these 32 patients had acute dyspnea followed by cardiac arrest, ventricular fibrillation or severe hemodynamic deterioration with systolic blood pressure below 70 mmHg, which did not rise despite the administration of adrenalin and worsened within the next minutes. Out of these 32, 26 patients died despite the resuscitation measures while 6 of them survived. In three out of these six cases, myocardial infarctions had taken place. In one case arrhythmias of unknown etiology were responsible for the acute event. In two patients who had experienced such situations, we performed immediate pulmonary embolectomy only on the grounds of suspected pulmonary embolism. The time lapse between the onset of symptoms and start of the operation did not exceed 60 min. Both patients survived the procedure, although in one case a major neurologic deficit had already occurred despite the immediate onset of resuscitation. The other patient had an uneventful postoperative course and was discharged from the hospital 2 weeks after the event.

Two patients out of the 26 who did not survive could be initially resuscitated and seemed to be in stable condition under appropriate medication. Pulmonary angiography was performed confirming the suspected diagnosis of pul-

Table 2 Causes of unexpected, acute cardiorespiratory failure after lung resection (within the first 2 p.o. weeks) ($n = 32$)

	<i>n</i>	Died
Massive pulmonary embolism (proven by autopsy or surgery)	23	21
Massive pulmonary embolism (clinically suspected)	4	4
Myocardial infarction	4	1
Arrhythmias of unknown etiology	1	0
	32	26

Table 3 Data of patients with pulmonary embolism after lung resection (proven by autopsy or surgery) (*n* = 23)

Age (years):	46–79 (mean 62)	
Sex:	m 18, f 5	
Diagnosis:	Squamous cell carcinoma	17
	adenocarcinoma	6
Tumor stage:	I	7
	II	5
	IIIA	9
	IIIB	1
	IV	1
Operation:	left pneumonectomy	4
	right pneumonectomy	10
	lobectomy	8
	segmental resection	1
Duration of operation:	70–340 min (mean: 180)	
Substitution of blood:	0–2000 ml (mean: 600)	

Table 4 Time interval between lung resection and onset of symptoms postoperatively (*n* = 23)

	<i>n</i>
0–12 h	0
13–24 h	6
25–48 h	6
49 h– 4 days	8
5–12 days	3

monary embolism. During the diagnostic procedures and until the onset of surgery with extracorporeal circulation, gradual hemodynamic deterioration occurred. The central pulmonary emboli could be removed successfully during the operation, but in both cases the overstrained right ventricle did not recover and the patients died within the first 48 h postoperatively. In these patients no additional autopsy was performed.

In 20 cases out of the 26 dying despite resuscitation, autopsy was performed, revealing central pulmonary embolism as the cause of death in 19 of them. In addition, in 10 of these cases deep vein thrombi were found. One patient had a rupture of the free posterior left ventricular wall following transmural myocardial infarction (this case is included in the group of „other causes“ in Table 1). In the four cases where autopsy was refused, the course of events strongly suggested that death was based on massive pulmonary embolism. Thus, it was proven by surgery or autopsy in 23 patients that pulmonary embolism had taken place, two patients survived after embolectomy. In four cases pulmonary embolism can only be suspected.

Data of the group of 23 patients with proven pulmonary embolism can be seen in Table 3, while Table 4 shows the time interval between the operation and the onset of symptoms postoperatively.

Discussion

The majority of the 125 patients who died early postoperatively after lung resections in our group of 1735 operated cases suffered from complications concerning the remaining lung or from problems directly related to the operation (118 out of 125 patients = 94.4%). Pulmonary embolism is the second most frequent cause of fatal outcome during the early postoperative course. There were 21 proven and 4 suspected cases in our cohort of patients. Only seven patients had various other problems not related to the lung operation. The clinically suspected reasons for death could be strengthened by autopsy in 93/125 cases (74.4%). In two cases, where no autopsy was performed, the massive pulmonary embolism was proven by angiography and surgery.

With regard to the histological type of bronchogenic carcinoma, we found a predominance of squamous cell carcinoma. The relation of squamous cell carcinomas to adenocarcinomas was 74%/26% in the patients dying from pulmonary embolism (see Table 3). This was not quite consistent with the whole study population: there were no patients with undifferentiated large cell carcinomas or with small cell carcinomas who had pulmonary embolism. This group amounted to 23% of the whole group of 1735 patients. This is in contrast to the publication by Ziomek et al. where adenocarcinoma was the more frequent type of carcinoma of the lung in patients with thromboembolism after pulmonary resection [31].

Most patients with lung cancer have normal routine clotting tests preoperatively [23, 29], as was the case in our patients where only four cases showed moderately elevated values of thrombocytes. Despite the existence of very sensitive tests demonstrating activation of coagulation as well as fibrinolysis in cancer patients [8, 23, 27], thromboembolic events are not predictable [4, 15, 17]. On the other hand, patients with malignant diseases have a higher incidence of venous thromboses and subsequent thromboembolism, as reported by Trousseau in 1868 [28] and confirmed by other studies [5, 31].

Compared to other groups of postoperative patients, e.g. in orthopedics or gynecology, the patients in thoracic surgery are supposed to be at lower risk of deep venous thrombosis and subsequent thromboembolism [3, 10, 12, 14]. This could possibly be explained by the fact that lung surgery bears a higher overall risk for severe complications, so that the number of thromboembolic complications means only a smaller percentage in the complete risk profile.

In our patients deep venous thrombosis and subsequent thromboembolism represented the second most frequent reason for early postoperative death and it even occurred under the condition of postoperative prophylaxis with heparin. All our patients after lung resections receive intravenous heparin from the morning of the 1st postoperative day with a change to subcutaneous application on the 2nd or 3rd postoperative day, as previously described, until they are completely mobilized [11].

Patients having pneumonectomies are at higher risk of fatal outcome with respect to thromboembolic events for three reasons: they often suffer from tumors in advanced stages, which are supposed to be connected with elevated clotting activity [23, 25, 31]. In addition, the major reduction of the cross-section of pulmonary vessels puts them into higher jeopardy when emboli reach the remaining pulmonary arteries. And third, if the stump of the pulmonary artery has been left too long after ipsilateral pneumonectomy, it might predispose to thrombus-formation and cross-embolization to the contralateral artery. In our study, in ten right-sided pneumonectomies only seven were performed with intrapericardial ligation of the pulmonary artery. In the remaining three cases the longer stump of the artery may have contributed to pulmonary embolism, although there was no evidence for this at autopsy. These facts must be considered in prophylaxis, which should be started even preoperatively in these patients with advanced tumors and planned pneumonectomy, and continued immediately following surgery as long as no bleeding complications occur.

The time between the lung resection and the onset of symptoms, indicating the major pulmonary embolism, was 48 h or less in 12 patients, in another 8 cases the event took place on the 3rd or 4th postoperative day. When the acute event occurred, 17 out of the 23 cases were still under postoperative anticoagulation with heparin (Table 4). The remaining six patients were already fully mobilized and prophylactic medication had been discontinued. Only three patients experienced embolism in the later postoperative course, i.e. between days 5 and 12. This is in agreement with the report by Gebitekin et al. where lethal cardiorespiratory arrest due to pulmonary embolism was also a major cause of death in the very early postoperative course [9].

This raises the question of if and when deep venous thrombosis could have developed in these patients and whether improved prevention could have inhibited it. Except for three, all cases in our study were outpatients, only one patient was not fully mobilized, because he was on a thoracic draining tube. These three patients were on prophylaxis with subcutaneous heparin. None of the 23 patients with postoperative thromboembolism had clinical signs of deep venous thrombosis preoperatively, however in 10 cases deep vein thrombi were found at autopsy. Thus it can be suspected that the thrombosis had already developed during the operation or in the first hours thereafter [23] or had grown on an incomplete asymptomatic thrombosis which had existed previously [31]. The course of events with the majority of pulmonary thromboembolisms during the first days after the operation and under prophylaxis with heparin supports this suspicion, though it has not yet been proven.

Because of possible bleeding complications, we did not give heparin during surgery, which consisted not only of lung resection but also of extensive lymph node dissection.

For the same reason thrombolytic therapy, as the most simple and effective therapeutic regimen, cannot be performed immediately after lung resections.

If major pulmonary embolism occurs postoperatively, the prognosis of these patients with reduced lung parenchyma and cross-sections of their pulmonary arteries is very poor [9]. Therefore, even the suspicion of major pulmonary embolism justifies operative embolectomy [26]. A delay caused by additional diagnostic procedures will worsen the prognosis, at least in those cases where mechanical and medical resuscitation measures have been necessary to bring the patient to a reasonably stable condition.

As extracorporeal circulation can be used at any time in our department for thoracic and cardiovascular surgery, we prefer to perform the operation with the use of the heart lung machine. Since extracorporeal circulation is not available in every department for general thoracic surgery, the emergency operative approach with pulmonary embolectomy during normothermic circulatory arrest performed by clamping the venae cavae might be chosen as an alternative [2, 26], when the high mortality of these patients without intervention is taken into account. In our group of 125 patients who died early postoperatively, proven acute pulmonary embolism was responsible for nearly 20% of the fatalities after lung resections. As the autopsy rate in this group was as high as 75%, this number of 20% gains additional significance.

In conclusion, pulmonary embolism is a frequent cause of death in patients after lung resections for malignancies. Unrecognized deep vein thrombosis seems to exist preoperatively in some patients or to develop intraoperatively or very early postoperatively and thus cannot be prevented by early postoperative anticoagulation. *In patients with advanced tumor stages requiring pneumonectomies a more aggressive prevention and anticoagulation by means of pharmacological prophylaxis should be recommended.* Finally, the only life – saving measure for these patients seems to be rapid pulmonary embolectomy. If resuscitation measures have been necessary the outcome is very unfavorable, and embolectomy only on the grounds of suspected pulmonary embolism could be justified in these cases.

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Discussion

Dr. F. Vermeulen (*Nieuwegein, The Netherlands*): Maybe I didn't get it exactly, but were there any of those patients, as you were coming from a cardiovascular and thoracic surgery department, where you considered doing a pulmonary embolism but postponed it? In fact, a large proportion of the patients with this diagnosis were discovered only at autopsy.

Dr. Kalweit: This was only a retrospective study of patients dying acutely within the 1st days after lung resections in the years from 1975 to 1993. During this time we performed four pulmonary embolisms in such patients. Certainly an embolism was taken into account in some other cases but was not undertaken due to the fast deterioration of the patient's condition. And before we did this study we were really not

aware that massive pulmonary embolism was responsible for almost 20% of all perioperative deaths. Although this incidence is higher than we thought before, it is nevertheless an acute event taking place only a very few times in a year and decision-making is not easy in this acute situation. You must know the data mentioned above to choose the more aggressive approach.

Dr. Vermeulen: And because they all die, those with apparently massive decompensation, those that are brought to your attention, the incidence of pulmonary embolus might be higher, of course, but clinically they are not known, not detected.

Dr. Kalweit: Yes. And it is the aim of this publication to point out the importance of pulmonary embolism as a cause of acute death after lung resections, because when you are aware of it you are more likely to take a pulmonary embolectomy into account.

Dr. Vermeulen: This is not a study aimed at looking at the incidence of pulmonary embolism and how many patients die.

Dr. Kalweit: Exactly. The incidence of pulmonary embolism is certainly higher, but small emboli may cause a complicated postoperative course, as has been published previously, but do not lead to death.

Dr. Vermeulen: Could you comment on the incidence of this phenomena in patients operated for non-malignancy?

Dr. Kalweit: No. We did not look at that.

Dr. A. Murday (London, England): Your recommendation is that patients who you believe have a pulmonary embolus should undergo immediate pulmonary embolectomy. Clearly there is a risk. If you operate on patients who are ill for another reason, post-thoracic surgery, and they haven't had a pulmonary embolus, then they are likely to do badly. Have you had that experience? Have there been any patients that have undergone pulmonary embolectomy in this circumstance and not had pulmonary embolus? And, secondly, although you recommend not performing angiography, presumably you must have very strict criteria for rushing in on these patients.

Dr. Kalweit: Recently we had a young patient who had a polytrauma some days before and who was put forward for embolectomy by our anesthesiologists after he had had acute cardiorespiratory failure apparently caused by massive pulmonary embolism. He was under ongoing resuscitation and we undertook the emergency operation without further diagnostic measures. In this patient we found no emboli. This may happen. So you are right in claiming strict criteria for this procedure. Our criteria are that the patient must have had acute cardiorespiratory failure making resuscitation necessary. Myocardial infarction or postresectional pulmonary edema must be ruled out. And, in addition, we must be convinced that any further delay of time caused by diagnostic procedures will worsen the prognosis of these patients, which is rather poor anyway.