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Original Article

Myocardial Performance Index Predicts Mortality in Lung Resection Surgery

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ABSTRACT

Objective: Cardiac and pulmonary involvement affects morbidity and mortality after lung resections. Studies have shown that patients have increased pulmonary artery pressure (PAP) and right ventricular (RV) dilatation after resection. Myocardial performance index (MPI) is a numerical value obtained using cardiac time intervals. It has a prognostic importance independent of heart rate changes in different clinical situations. The main purpose of this study is to show the prognostic value of MPI in predicting mortality and morbidity.

Methods: This prospective study included 44 patients who applied to the thoracic surgery department between October 2014, April 2015 underwent lung resection. In the early postoperative period, pulmonary, cardiac functions of the patients were evaluated using non-invasive methods.

Results: The mean age was 59.1±6.3 years, (39male- 5female). Lobectomy was performed in 37 patients and pneumonectomy was performed in 7 patients. Prolonged air leak, atrial fibrillation, pneumonia, hemorrhage requiring re-thoracotomy, bronchovascular fistula, cerebrovascular infarction were recorded as postoperative complications. Average hospital stay was 8.8±3.6 days. When the effects of gender, age, echocardiography reports on morbidity and mortality were examined, mortality was found to be significantly higher in patients with a change of MPI in the first week more than 0.11 (p=0.022).

Conclusion: In our study, the amount of change in MPI in the early period after lung resection was found to be an important and independent variable in predicting mortality and probability of cardiovascular events of patients. Future studies are needed to test these results in larger populations.

INTRODUCTION

Lung cancer is the cancer type with the highest mortality rate in the whole world and is, due to the natural course of the disease, mostly diagnosed at an advanced stage. Most of the patients, therefore, cannot find a chance for surgical treatment.[1] The patients with the best survival in lung cancer are the early-stage patients undergoing surgical treatment.[2] The morbidity and mortality of surgical procedures have decreased significantly with the minimally invasive techniques developed recently.[3] Early detection of changes in cardiac functions following pulmonary resection, is predicted to affect the morbidity and mortality of these patients. In the preoperative preparation, no additional tests are routinely performed except for the electrocardiogram in those without a history of cardiac disease. Acute reduction in lung volume is obvious toe affect right-heart structures. As is known, cardiovascular complications are the most common in the early postoperative period, and there is no gold standard test by which these complications can be predicted. This study was, therefore, designed in patients with non-small cell lung cancer (NSCLC) undergoing resection, considering that the MPI value, which can be evaluated by non-invasive methods without being affected by cardiac rate, may enable us to detect these patients early.

MATERIALS AND METHODS

The study was approved by the institutional review board (Date: 18/11/2013 No:13104) and was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Selection

Between October 2014 and April 2015, 82 patients underwent NSCLC-caused anatomic resection. Before obtaining the approval of the ethics committee from our hospital and the consent form from the patients, inclusion criteria for the study were determined as 1) performing anatomical resection for lung cancer (lobectomy, pneumonectomy), 2) being between 50 and 70 years old, and 3) consenting to participate in this study. Exclusion criteria from the study were also determined as 1) presence of a known cardiac disease (right or left heart failure, uncontrolled hypertension, uncontrolled diabetes mellitus, and uncontrolled hyperlipidemia), 2) having undergone an open-heart operation, 3) having undergone wedge, 4) receiving neoadjuvant therapy, and 5) failing to comply with the postoperative follow-up periods. Forty-four patients conforming with the above-mentioned criteria were evaluated prospectively. After taking a medical history and performing the physical examination of the patients in the preoperative period, their blood tests (blood count, glucose, renal function tests, liver function tests, electrolytes, sedimentation, thyroid function tests, and coagulation parameters), pulmonary function tests, posterior-anterior chest X-rays, and electrocardiography were evaluated. The operability decision was made, considering the results of the analysis, together with the chest diseases specialist, internal diseases specialist, cardiologist, and anesthesiologist. The decision for resectability and operability was made using thorax computed tomography (CT), brain magnetic resonance imaging, whole-body positron emission tomography (PET-CT), and fiber optic bronchoscopy. While calculating the variables affecting complications and mortality, certain cut-off values were determined from age, gender, type of operation, and echocardiography (ECHO) examinations, and groups were formed. The age was evaluated as one group between 50-60 years old and the other group between 61-70 years old, close to the mean value. Gender was divided into two groups: Male and female, operations was divided as lobectomy and pneumonectomy.

In the ECHO examination, the MPI, a more objective value in the evaluation of right-heart functions, was divided into two groups considering the preoperative and postoperative 1st week and 1st month mean change values.

Echocardiographic Assessment

Transthoracic echocardiographic examination was performed in the preoperative (T1) and the early postoperative period (1st week -T1- and 1st month -T2-) while the patients were continuing their routine treatment. A 1.8 MHz probe was used with the GE Vivid P3 (GE Healthcare, Wauwatosa, USA) model device. Left ventricle (LV) and right ventricle (RV) diameters were measured with the parasternal long axis with M-mode. Right atrium (RA) transfer, left atrium (LA) transfer, pulmonary artery (PA) diameters, and aortic root was measured with 2-D mode. In this manner, the diameters of the left ventricle during diastole and systole were clearly seen. End-diastolic and end-systolic inner diameters were measured from the endpoints of the endocardium, and left ventricular ejection fraction was calculated using the Teicholz method. The images with the smallest and largest left ventricle during systole and diastole were detected. Pulsed Wave Doppler (PWD) recordings were obtained from the sample volume placed under the aortic valve using the apical long-axis image for left ventricular outflow tract and sample volume placed on the mitral valve in the apical four chambers for mitral valve diastolic flow. In each cycle, typical early diastolic filling (E wave), diastasis period, and atrial contraction (A wave) periods were obtained. Isovolumic contraction, relaxation, and ejection times were determined. MPI was calculated by dividing the sum of the isovolumic periods obtained with these measurements by the ejection time. All measurements were repeated with the same practitioner and device.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) 20 program was used to analyze the data. For the analysis of quantitative data, conformity to normal distribution was examined with the Kolmogorov-Smirnov test, and parametric methods were used in the analysis of variables with normal distribution and homogeneous variances, and nonparametric methods were used in the analysis of variables without normal distribution and homogeneous variance. Quantitative data were shown as mean ± std. (standard deviation) values in the tables while categorical data were as N (numbers) and percentages (%). The data were analyzed at the 95% confidence level, and the p-value was considered significant if it was less than 0.05.

RESULTS

Of the 44 patients included in the study, 39 (88.6%) were male, and 5 (11.4%) were female. The mean age of the study population was calculated as 59.1±6.3. Lobectomy was performed in 37 patients (25 upper and 12 lower lobectomies), and pneumonectomy was performed in the remaining seven patients. Complications related to the operation were detected in 24 of the patients. These were prolonged air leak (PAL), atrial fibrillation (AF), pneumonia, bleeding requiring re-thoracotomy, cerebrovascular infarction, and bronchovascular fistula (Table 1). PAL was

Table 1. Description of complications

Variables	n	%
PAL	14	58.3
AF	4	16.6
Pneumonia	2	8.33
Hemorrhage	2	8.33
Bronchovascular fistula	1	4.16
Cerebrovascular infarction	1	4.16

PAL=Prolonged Air Leak, AF=Atrial Fibrilation.

Table 2. Evaluation of the effect of myocardial performance index on mortality

Variables	Mortality		p-Value
	No n (%)	Yes n (%)	
MPI pre			
0.01-0.350	25 (96)	1 (4)	0.059
0.351-0.60	14 (78)	4 (22)	
MPI T1			
0.01-0.11	27 (100)	-	0.022
0.111-0.3	14 (83)	3 (17)	
MPI T2			
0.01-0.17	26 (96)	1 (4)	0.290
0.171-0.4	15 (88)	2 (12)	

MPI: Myocardial performance index, T1 First week change value, T2 first month change value.

Table 3. Variables affecting change of MPI in the first week

Variables	0.01-0.11 n (%)	0.111-0.3 n (%)	Sum n (%)	p-Value
Age				
50-59	15 (61)	9 (39)	24 (100)	1.00
60-70	13 (63)	7 (37)	20 (100)	
Gender				
Female	2 (40)	3 (60)	5 (100)	0.352
Male	25 (65)	14 (35)	39 (100)	
Side				
Right	13 (66)	6 (34)	19 (100)	0.750
Left	14 (58)	11 (42)	25 (100)	
Operation				
Lobectomy	26 (71)	11 (29)	37 (100)	0.008
Pneumonectomy	1 (14)	6 (86)	7 (100)	

MPI: Myocardial performance index.

the most common, and it was thought to be caused by the structure of the parenchyma depending on the patient factor as well as open surgical techniques. The mean length of stay (LOS) was found to be 8.77±3.55 days, and the mean drain using time was 7.32±2.78 days. The postoperative 30-day mortality rate of the patients was detected as 11.36% (5 of the patients).

The change in MPI greater than 0.111 in the first week was found to have a significant effect on mortality (p=0.022) (Table 2). Only pneumonectomy within these variables was determined to have a significant effect on the change in MPI in the first week greater than 0.111 (p=0.008) (Table 3).

DISCUSSION

Surgical treatment of lung cancer was first started by Evarts Graham in 1932, by performing pneumonectomy.[4] Besides the development of operation methods over the years, choosing the right patient in the preoperative evaluation is still one of the most crucial factors determining the treatment prognosis.

The respiratory system and the cardiovascular system are two structures of the body closely interconnected. Based on this fact, the slightest change in one of the systems can be said to affect the other system as well. Studies on the right ventricle (RV), the subject of many studies, have shown that it plays a minor role in maintaining cardiac output. RV performance has been, however, observed to play a crucial role in general cardiac functions in the following periods. Deterioration in RV functions has been shown to be an important pathophysiological factor in many cardiac morbidities.[5]

Clinical studies on early and late RV morphology and function after major lung resections have provided crucial information about adaptation. Interventional hemodynamic measurements before, during, and after pulmonary

resection come up with reliable and precise results, but because of their invasiveness, they impair patient comfort and increase the risk of complications. Doppler echocardiography, a widely used and noninvasive method in the evaluation of cardiac functions, has gained popularity in recent years to evaluate RV morphology and function in patients undergoing pulmonary resection.

Global MPI, reflecting both systolic and diastolic function of the myocardium, was first described by Tei et al.[6] It has been found to be associated with morbidity and mortality in cardiovascular diseases, is easy to calculate, and has a narrow range in normal healthy individuals. These intervals can be easily calculated by Doppler echocardiography. The calculated index is easily measured from Doppler traces obtained from mitral and aortic flows, not affected by heart rate, ventricular structure, and afterload. Using PWD echocardiography, the MPI value is calculated by dividing the sum of the isovolumic relaxation time (IVRT) and contraction times (IVCT) of the heart by the ejection time (Fig. 1).

In a study conducted by Poulsen et al.,[7] the MPI value was found to be 0.40±0.04 in healthy subjects. As a result of the study with healthy subjects performed by Moller et al.,[8] the normal value of MPI was determined to be 0.34±0.04, and this value increased in cases with myocardial infarction. In another study, its value was 0.39±0.05 in healthy people and 0.59±0.10 in patients with dilated cardiomyopathy.[6] MPI for RV should be considered, especially in patients with pulmonary hypertension. MPI is the strongest variable to distinguish individuals with primary pulmonary hypertension from normal individuals (0.93±0.34 vs. 0.28±0.04).[9] The major shortcoming of MPI is that it cannot be used in patients with atrial fibrillation. The postdiastole isovolumic contraction time of the heart cannot be determined in atrial fibrillation since the atrial A wave is not present. There is a linear correlation between age and MPI. This correlation is due to the increase in IVRT between the ages of 16-80. The diastolic function has been previously shown to be impaired in many individuals with normal systolic function with increasing age. It is, hence, known that IVRT and MPI, which are components of diastolic functions, will also change with age.[10]

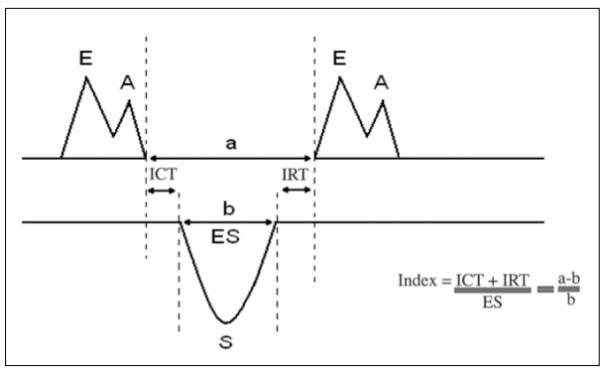

Figure 1. Myocardial Performance Index with pulsed doppler. E: Early diastolic wave; A: Late diastolic wave, S (systolic wave); a: Duration between late diastolic and early diastolic waves, b and ES (systolic ejection time), ICT (isovolumetric contraction time), IRT (isovolumetric relaxation time).

In various studies, early and late RV functions after lobectomy or pneumonectomy were investigated either with interventional methods or with echocardiographic methods. In the current study, cardiac functions were evaluated using transthoracic echocardiography, a non-invasive method, by calculating MPI before the operation, after surgical resection, at the 1st week, and the 1st month.

Techniques such as magnetic imaging and radionuclide ventriculography used for quantitative calculation of right ventricular ejection fraction (RVEF) are invasive, relatively expensive, time-consuming, and affected by the complex geometry of the right ventricle. Therefore, it cannot be performed much in clinical practice. Echocardiography can be, on the other hand, used in the evaluation of RV functions as a technique that can be performed in a short time, is relatively inexpensive, non-invasive, and can be interpreted in a short time. However, there are limitations such as poor echogenicity and left ventricular geometry in the evaluation of systolic and diastolic functions with echocardiography. Moreover, the complex geometrical structure of the right ventricle surrounding the left ventricle in a crescent shape, its separate infundibulum, and prominent trabeculation cause its functional structure not to be evaluated.[11]

Considering the examination of the right-heart pressure changes using right-heart catheterization after pneumonectomy, there was found an increase in mean pulmonary artery pressure. Therefore, publications have recommended using echocardiography to control right-heart pressure after pneumonectomy. An increase in pulmonary artery pressure after pulmonary resection, particularly after pneumonectomy, has also been detected using Doppler echocardiography.[12] However, in the same study, no significant increase was found in right atrial diameter and pressure after lobectomy or pneumonectomy. In another study, right ventricular enlargement and respiratory failure were observed in a small group of patients developing echocardiography after lobectomy and pneumonectomy. The researchers gave the measurement results up to the 2th postoperative day.[13] Thus, there is a need for new studies that can be useful in determining long-term prognosis. Since the number of patients undergoing pneumonectomy was limited in our series, no significant difference was found.

In our study, which was prepared with the thought that MPI could be used in the evaluation of systolic and diastolic functions after lung resection, an increase in atrial and ventricular diameters, a decrease in EF, and an increase in thickness of the interventricular septum (IVS) were found in our patients in the echocardiographic evaluation. However, when MPI measurements were taken into account to evaluate cardiac functions, the increase in MPI in the first week postoperatively was determined to be more than 0.11 had a significant effect on mortality (p=0.022). The

MPI change of more than 0.11 was detected to be affected by the presence of pneumonectomy (p=0.022).

Limitations

The main result of this study is that we demonstrated the cardiac workload affected after lung resections with a non-invasive method in the early period. Whether this is an indicator of morbidity and mortality should be, however, supported by larger series. Besides, not performing echocardiography in patients without cardiac history in routine preoperative evaluations will be a limitation for daily use.

Conclusion

The amount of change in the MPI in the early period after lung resection was found to be a significant independent variable in predicting mortality and cardiovascular morbidity of patients. In the current study, important parameters such as age, gender and operation type were established not to have a significant effect on mortality and morbidity. MPI is a newly used method evaluating systolic and diastolic functions together. It can be easily calculated without being affected by heart rate, left ventricular geometry, and afterload. The effects of atrial fibrillation and preload, on the other hand, limit the use of MPI. Routine use in postoperative patients may provide an advantage to the patient and specialists. Further and comprehensive studies are, however, needed for the standard use of MPI as a prognostic factor after lung resections.

Ethics Committee Approval

The study was approved by the Izmir Dr. Suat Seren Pulmonoloy and Surgery Hospital Ethics Committee (Date: 18.11.2013 , Decision No: 13104).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: E.Y., A.U., S.Y., S.G.; Design: E.Y., A.U., S.Y.; Supervision: E.Y., S.Y., S.G.; Fundings: E.Y., A.U., S.Y., S.G.; Materials: E.Y., A.U., S.Y., S.G..; Data collection &/or processing: E.Y.; Analysis and/or interpretation: E.Y., A.U., S.Y., S.G.; Literature search: E.Y., S.G.; Writing: E.Y., A.U., S.Y., S.G.; Critical review: E.Y., A.U., S.Y., S.G.

Conflict of Interest

None declared.

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Akciğer Rezeksiyonu Uygulanan Hastalarda Miyokart Performans İndeksinin Prognostik Değeri

Amaç: Akciğer rezeksiyonlarından sonra, kardiyak ve pulmoner etkilenme, morbidite ve mortaliteyi etkilemektedir. Yapılan araştırmalarda, rezeksiyon sonrası hastalarda pulmoner arter basıncında (PAB) artma ve sağ ventrikülde (RV) dilatasyon olduğu gösterilmiştir. Miyokart performans indeksi (MPI), kardiyak zaman aralıkları kullanılarak elde edilen sayısal bir değerdir. Kalp hızı değişikliklerinden bağımsız, farklı klinik durumlarda, prognostik değere sahiptir. Bu çalışmanın temel amacı, mortalite veya morbiditeyi öngörmede, MPI prognostik değerini göstermektir.

Gereç ve Yöntem: Prospektif olarak planlanan bu çalışmada Ekim 2014 – Nisan 2015 tarihleri arasında göğüs cerrahisi bölümüne başvuran ve akciğer rezeksiyonu yapılan 44 hasta dahil edildi. Hastaların erken postoperatif dönemde, pulmoner ve kardiyak fonksiyonları, non-invaziv yöntemler kullanılarak değerlendirildi.

Bulgular: Çalışma popülasyonunda 39 erkek ve beş kadın hastanın yaş ortalaması 59.1±6.3 (49-70) idi. Otuz yedi hastaya lobektomi, yedi hastaya pnömonektomi uygulandı. Uzamış hava kaçağı, atriyal fibrilasyon, pnömoni, retorakotomi gerektirecek hemoraji, bronkovasküler fistül ve serebrovasküler infarkt, postoperatif komplikasyon olarak kaydedildi. Ortalama hastanede kalış süresi 8.8±3.6 gündü. Hastaların cinsiyet, yaş, ve ekokardiyografi değerlerinin morbidite ve mortalite üzerine etkisi incelendiğinde, MPI'nın ilk hafta değişimi 0.11'den fazla olan hastalarda mortalite anlamlı olarak fazla bulundu (p=0.022).

Sonuç: Akciğer rezeksiyonu sonrası, MPİ' nın erken dönemde değişim miktarı, hastaların mortalite ve kardiyovasküler olayları öngörmede önemli bir bağımsız değişken olarak bulunmuştur. Bu sonuçları daha büyük popülasyonda doğrulamak için, gelecekteki çalışmalara ihtiyaç vardır.

Anahtar Sözcükler: Ekokardiyografi; miyokart performans indeksi; pnömonektomi.