

# Analysis of the influence of respiratory disorders observed in preoperative spirometry on the dynamics of early inflammatory response in patients undergoing isolated coronary artery bypass grafting

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**Background:** Preoperative spirometry provides measurable information about the occurrence of respiratory disorders. The aim of this study was to assess the association between preoperative spirometry abnormalities and the intensification of early inflammatory responses in patients following coronary artery bypass graft in extracorporeal circulation.

**Material and methods:** The study involved 810 patients (625 men and 185 women) aged  $65.4 \pm 7.9$  years who were awaiting isolated coronary artery bypass surgery. On the basis of spirometry performed on the day of admittance to the hospital, the patients were divided into three groups. Patients without respiratory problems constituted 78.8% of the entire group. Restricted breathing was revealed by spirometry in 14.9% and obstructive breathing in 6.3% of patients.

**Results:** Inter-group analysis showed statistically significant differences in C-reactive protein (CRP) between patients with restrictive spirometry abnormalities and patients without any pulmonary dysfunction. CRP concentrations differed before surgery ( $P=0.006$ ) and on the second ( $P<0.001$ ), fourth ( $P=0.005$ ) and sixth days after surgery ( $P=0.029$ ). There was a negative correlation between CRP levels and  $FEV_1$ .

**Conclusion:** In our study, the most common pulmonary disorders in the coronary artery bypass graft patients were restrictive. Patients with abnormal spirometry results from restrictive respiratory disorders have an elevated level of generalized inflammatory response both before and after the isolated coronary artery bypass surgery. Therefore, this group of patients should be given special postoperative monitoring and, in particular, intensive respiratory rehabilitation immediately after reconstitution.

**Keywords:** pulmonary function, C-reactive protein, cardiac surgery

## Introduction

Among ~1 million cardiac surgeries performed in the world each year, the most common is coronary artery bypass graft (CABG) surgery. The prognosis of patient survival in cardiac surgeries is the result of many factors, such as indications for surgery and its scope, age and sex of the patient, and the severity of the disease. The type of surgery, experience of the surgical team, and the choice of anesthesia method may also play an important role.<sup>1-7</sup> In Europe, cardiovascular risk is most often assessed on the Euroscore scale. With regard to the respiratory system, this scale takes into account only chronic obstructive pulmonary diseases, defined as a “permanent intake of bronchodilators and/or steroids”. The risk associated with this condition is estimated

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at 0.8%. Measurable information about the degree of respiratory distress is provided by spirometry, which may also show an increased risk of postoperative complications.<sup>8</sup> Available literature does not describe the relationship between reduced vital capacity and the degree of inflammatory response. Reports concern only healthy subjects.<sup>9–16</sup> The increased rates of generalized inflammatory response may have many causes, including respiratory ones, such as primary lung disease and damage caused by infection or other external factors, or extracorporeal circulation.<sup>15,17–19</sup> Respiratory performance may also be reduced as a result of cardiovascular disease.<sup>15,20</sup>

The aim of this research was the evaluation of the relationship between preoperative respiratory dysfunction and increased inflammatory response in patients after coronary artery bypass surgery in extracorporeal circulation.

Detailed analysis of preoperative spirometry may be helpful in qualifying patients for surgery and predicting respiratory complications following CABG.

## Material and methods

### Study population and exclusion criteria

The study involved 1,169 patients with coronary artery disease admitted for CABG surgery at the Department of Cardiac Surgery, Szczecin, Poland, between January 2013 and December 2014. Out of these, 359 (30.7%) patients with angina at rest (class IV in the Canadian Cardiovascular Score, [CCS]) and those with acute myocardial infarction were excluded from the study. Subsequent analysis involved 810 (625 men and 185 women) aged  $65.4 \pm 7.9$  years. On the day of admission, spirometry tests were performed using an AsSPIRO D200 v.101. (ASPEL S.A., Zabierzów, Poland). The measurements were performed according to the recommendations of the American Thoracic Society and the European Respiratory Society.<sup>21–24</sup> All the patients provided written informed consent. The study was performed in accordance with the Declaration of Helsinki and approved by the Bioethics Committee of Pomeranian Medical University in Szczecin (KB-0012/121/14).

All the patients were interviewed for underlying diseases and concurrent symptoms. Symptoms were assessed using the CCS. In addition, information was gathered about concurrent and previous illnesses: diabetes mellitus, myocardial infarction, hypertension, renal disease, neoplasms, and neurological diseases. Blood pressure, body mass and height were measured. C-reactive protein (CRP) levels were assessed prior to surgery and on the second, fourth, sixth and eighth days after surgery.

All the patients had an isolated CABG with a sternotomy. The patients underwent standard postoperative management. Mechanical respiration was disconnected as quickly as possible. Rehabilitation proceedings were started in the preoperative period with clarification of the improvement methods. Positioning instruction was provided and training was provided for the assessment and prevention of postoperative pain in accordance with the “Painless Hospital” standards. Rehabilitation and education continued after the surgery in the intensive care unit and continued until the patients were discharged.

### Spirometry data

The spirometry test included the following parameters: FVC and  $FEV_1$ ,  $FEV_1/FVC$ , and peak expiratory flow (PEF). According to the recommendations of the Global Initiative for Chronic Obstructive Lung Disease,  $FEV_1/FVC$  values  $<0.7$  at  $FEV_1 < 50\%$  indicate acute respiratory obstruction,  $FEV_1$  between 50% and 80% indicates moderate obstruction, and above 80% indicates mild obstruction. Restrictive respiratory disorders were recognized when FVC was  $<80\%$ , while normal lung function was defined as  $FEV_1/FVC \geq 0.70$  and  $FVC \geq 80\%$ .<sup>25</sup> The patients were divided into three groups according to the spirometry score. The first group consisted of patients with normal lung function. The next two groups consisted of patients with respiratory disorders. The second group included patients with obstructive pulmonary disorders, and the third group comprised those with restrictive pulmonary disorders.

### Statistical analysis

Statistical analysis was conducted using licensed Statistica 12 software (StatSoft, Inc., Tulsa, OK, USA). The descriptive statistics mainly used mean and standard deviations. The normality of distribution was checked using a Shapiro–Wilk test. The uniformity of variance was assessed using a Levene test. Data analysis for two groups was performed using a Student's *t*-test or Mann–Whitney *U*-test, while for three groups, analysis of variance or Kruskal–Wallis tests were used. Tukey's post-hoc test was used to evaluate the differences between the groups. Friedman's test was used to evaluate the variables before and after surgery. For the noncontinuous variables, the  $\chi^2$ -test was used. Correlations between spirometry parameters and CRP levels for quantitative data were evaluated using the Pearson's correlation coefficient, and the Spearman's rank correlation coefficient for qualitative variables. The significance level was set at  $P \leq 0.05$ .

## Results

Of the 810 patients, no respiratory system disorders were observed in 638 (78.8%), while obstructive disorders were found in 51 (6.3%) and restrictive in 121 patients (14.9%). A total of 172 (21.2%) patients reported abnormalities in spirometry. Patients without respiratory distress exhibited better cardiovascular performance shown by significantly higher mean ejection fraction (EF) than the other patients ( $P=0.003$ ). Patients with respiratory disorders had higher mean CRP before surgery ( $P=0.012$ ), and on the second ( $P<0.001$ ), fourth ( $P=0.001$ ) and sixth days after surgery ( $P=0.009$ ). Also, on the eighth day after surgery, CRP level was higher in patients with respiratory disorders compared with those without respiratory disorders, but the differences were not statistically significant ( $P=0.57$ ). Among patients with respiratory disorders, 72 (41.86%) were being treated for diabetes, while in the group with normal respiratory parameters, 204 (31.97%) patients were being treated. Differences were statistically significant ( $P=0.015$ ).

Anthropometric and epidemiological data were analyzed in the three groups. The results are summarized in Table 1.

Then, the differences between the groups were compared by means of a post-hoc test. Detailed analysis showed a significantly higher body mass index (BMI) in patients with

restriction compared with the control group ( $P=0.018$ ) and patients with obstruction ( $P=0.005$ ). The lower EF was also shown in patients with restriction compared with patients with normal lung function ( $P=0.003$ ). Significant differences in CRP levels existed between patients with restrictive spirometry abnormalities and patients without any respiratory problems. The differences occurred before surgery ( $P=0.006$ ) and on the second ( $P<0.001$ ), fourth ( $P=0.005$ ) and sixth day after surgery ( $P=0.029$ ). Patients with obstructive pulmonary disease only showed significantly higher CRP levels, than patients without disturbances, on the fourth day after surgery ( $P=0.049$ ).

Multivariate analysis of the analyzed parameters showed statistically significant differences in age, respiratory dysfunction and CRP levels on the sixth day after surgery ( $P=0.024$ ). Another statistically significant difference was found for sex, respiratory disorders and CRP levels before surgery ( $P=0.001$ ).

Due to the observed significant differences in patients without disorders and with dysfunction of the respiratory system, CRP concentrations were assessed against other parameters assessed in patients. Table 2 summarizes the preoperative CRP levels and levels on the second, the fourth and the sixth day after surgery.

**Table 1** Analysis of variance of differences in mean values of the studied parameters, in patients without disturbances in respiratory function and those with obstructive and restrictive respiratory disorders

	Respiratory system			P-value
	No disorders (n=638)	Obstructive (n=51)	Restrictive (n=121)	
Age, years	65.17±7.91	67.27±7.10	65.64±8.32	0.174
Sex				
Female	139 (21.79%)	16 (31.37%)	30 (24.79%)	0.251
Male	499 (78.21%)	35 (68.63%)	91 (75.21%)	
BMI	29.10±4.20	28.07±5.70	30.14±4.98	<b>0.011</b>
ESL	4.26±5.28	5.94±5.58	4.54±3.70	0.237
EF%	49.21±9.97	47.25±11.02	46.31±10.01	<b>0.009</b>
Current smoking	216 (48.00%)	23 (54.76%)	60 (58.82%)	0.119
Years of smoking	32.88±10.35	35.47±11.67	35.74±11.69	0.157
Hypertonia arterialis	480 (75.24%)	39 (76.47%)	97 (80.17%)	0.506
Diabetes mellitus	204 (31.97%)	22 (43.14%)	50 (41.32%)	0.051
Renal failure	27 (4.23%)	0 (0%)	8 (6.61%)	0.146
Myocardial infarction	338 (52.98%)	27 (52.94%)	63 (52.07%)	0.983
CRP (mg/L)				
Admission	4.04±8.19	4.86±5.81	6.53±13.90	<b>0.023</b>
2 days after surgery	66.89±30.23	74.52±41.58	78.51±38.48	<b>&lt;0.001</b>
4 days after surgery	199.78±77.48	221.99±75.67	221.42±78.86	<b>0.005</b>
6 days after surgery	123.02±74.33	141.19±72.40	141.28±86.74	<b>0.034</b>
8 days after surgery	111.55±58.63	119.37±39.51	123.06±94.59	0.631
Hospital death	8 (1.25%)	2 (3.92%)	1 (0.83%)	0.245

**Notes:** Data in bold indicates statistical significance. Data presented as mean ± standard deviation or n (%).

**Abbreviations:** BMI, body mass index; ESL, Euroscore Logistic; EF, ejection fraction; CRP, C-reactive protein.

**Table 2** Descriptive statistics of preoperative CRP and mean postoperative CRP in study subjects

	CRP (mg/L) before surgery	P-value	CRP (mg/L) 2 days after surgery	P-value	CRP (mg/L) 4 days after surgery	P-value	CRP (mg/L) 6 days after surgery	P-value
Age, years								
<65 (n=385)	4.0±7.4	0.150	72.7±31.9	<b>0.003</b>	200.4±82.1	0.158	122.2±77.1	0.120
≥65 (n=425)	4.9±10.6		65.9±32.9		208.1±73.9		131.5±75.9	
Sex								
Female (n=185)	5.4±11.9	0.147	69.1±37.3	0.984	199.80±75.56	0.358	117.02±72.49	0.061
Male (n=625)	4.2±8.3		69.1±31.2		205.82±78.71		130.43±77.61	
BMI								
Underweight (n=3)	3.9±2.9	0.311	70.4±42.9	0.653	220.1±82.5	0.172	201.9±65.3	0.369
Normal (n=116)	5.9±13.7		72.6±31.2		204.8±80.9		135.1±74.2	
Overweight (n=365)	4.1±9.3		68.7±35.5		198.1±79.8		126.2±79.7	
Obesity (n=326)	4.4±6.7		68.3±29.6		211.2±74.6		125.1±73.7	
Hypertonia arterialis								
Yes (n=616)	4.9±9.8	0.284	68.9±30.9	0.855	203.4±76.5	0.518	124.7±73.2	0.138
No (n=194)	3.9±6.9		69.5±37.5		207.7±82.8		135.2±85.9	
Diabetes mellitus								
Yes (n=276)	4.2±7.5	0.496	65.6±31.5	<b>0.030</b>	214.4±78.8	<b>0.010</b>	133.8±80.8	0.108
No (n=534)	4.7±9.9		70.8±33.1		199.3±77.1		123.6±73.9	
Renal failure								
Yes (n=35)	3.9±6.5	0.712	61.6±27.8	0.165	209.9±82.8	0.680	131.9±91.3	0.730
No (n=775)	4.5±9.3		69.4±32.8		204.2±77.8		126.9±75.7	
Myocardial infarction								
Yes (n=428)	5.1±10.1	0.051	70.2±35.9	0.289	210.3±76.2	<b>0.024</b>	131.3±76.9	0.139
No (n=382)	3.8±8.1		67.8±28.6		197.9±79.5		122.3±75.8	

**Notes:** Data presented as mean ± standard deviation. Data in bold indicates statistical significance.

**Abbreviations:** BMI, body mass index; CRP, C-reactive protein.

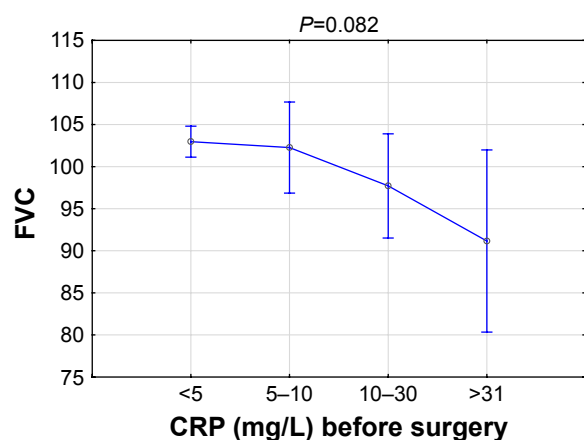
Figure 1 shows the FVC and preoperative CRP level. The worse the FVC parameter, the higher the preoperative CRP level. Figure 2 shows significantly lower FEV<sub>1</sub> values in patients with preoperative CRP levels exceeding 10 mg/L.

We also examined correlations between the results of spirometry and CRP level before surgery, and on the second, fourth and sixth day after surgery (Table 3). There was a negative correlation between FVC and FEV<sub>1</sub> parameters and all CRP values, which indicates the significant relationship

between the results of the spirometry and the inflammatory parameter. In the FEV<sub>1</sub>/FVC analysis, a significant negative correlation was only observed on the fourth day after surgery. In contrast, PEF was negatively correlated with CRP before surgery and on the fourth and sixth day after surgery.

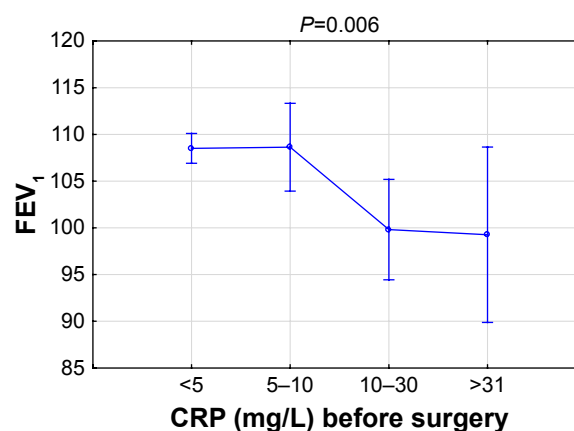
## Discussion

Unlike physical examinations and (to some extent) imaging studies, spirometry allows a quantitative evaluation of the respiratory system.



**Figure 1** FVC and preoperative CRP.

**Abbreviations:** CRP, C-reactive protein; FVC, forced vital capacity.



**Figure 2** FEV<sub>1</sub> and preoperative CRP.

**Abbreviations:** CRP, C-reactive protein; FEV<sub>1</sub>, forced expiratory volume in 1 s.

**Table 3** Correlation analysis according to spirometry parameters and preoperative and postoperative CRP

Spirometry parameters (n=810)	CRP (mg/L)				
	Admission	2 days after surgery	4 days after surgery	6 days after surgery	7 days after surgery
FVC (%)	-0.112 <b>P=0.005</b>	-0.095 <b>P=0.017</b>	-0.081 <b>P=0.041</b>	-0.1314 <b>P=0.001</b>	-0.1005 P=0.172
FEV <sub>1</sub> (%)	-0.152 <b>P&lt;0.001</b>	-0.107 <b>P=0.007</b>	-0.151 <b>P&lt;0.001</b>	-0.152 <b>P&lt;0.001</b>	-0.019 P=0.795
FEV <sub>1</sub> /FVC (%)	-0.013 P=0.737	-0.018 P=0.649	-0.105 <b>P=0.008</b>	-0.037 P=0.357	0.073 P=0.320
PEF (%)	-0.151 <b>P&lt;0.001</b>	-0.002 P=0.954	-0.141 <b>P&lt;0.001</b>	-0.079 <b>P=0.047</b>	0.027 P=0.716

**Note:** Data in bold indicates statistical significance.

**Abbreviations:** CRP, C-reactive protein; FVC, forced vital capacity; FEV<sub>1</sub>, forced expiratory volume in 1 s; FEV<sub>1</sub>/FVC, forced expiratory volume in 1 s% of vital capacity; PEF, peak expiratory flow.

In our study, patients with restrictive breathing who qualified for CABG surgery had elevated CRP levels before and after surgery compared with patients with no respiratory dysfunctions. Hancox showed higher inflammatory response in people with restrictive breathing compared with those with obstructive disorders, in a screening study on healthy individuals who were approximately half the age of patients in our study group.<sup>15</sup>

We observed a negative correlation between the initial spirometric parameters FVC, FEV<sub>1</sub> and FEV<sub>1</sub>/FVC, PEF, and CRP levels before and after surgery. A study by Yende et al on the elderly showed a negative correlation between FEV<sub>1</sub> and the systemic level of interleukin (IL)-6, which stimulates the production of CRP.<sup>26</sup> Another study on healthy and nonsmoking individuals by Aronson et al also showed a reverse correlation between CRP and the respiratory capacity parameters.<sup>9</sup> The negative correlation between FVC, FEV<sub>1</sub> and CRP was stronger in men in a study by Ólafsdóttir et al.<sup>27</sup> Hancox et al reported a correlation between respiratory distress and elevated CRP level. Increased values of CRP also correlated with low FVC.<sup>15</sup>

In our study, higher CRP level was observed in women with FEV<sub>1</sub> below 80%. This is contrary to the results of Rassmussen et al who reported higher CRP level in men, and Hancox et al who found no statistically significant differences between both the sexes.<sup>13,15</sup>

McAllister et al postulated that FEV<sub>1</sub> is a predictor for a longer patient stay in the hospital and increased mortality after cardiac surgery. They emphasized that the spirometry parameter FEV<sub>1</sub> should be added to the current Euroscore operational risk assessment for availability, ease of use and low cost of spirometry testing.<sup>1,28</sup>

In patients following coronary artery bypass, those with obstructive pulmonary disease are at a higher risk of respiratory tract infection compared with those without this disorder.<sup>29</sup> Grover et al report that a significant decrease

in FEV<sub>1</sub> (below 1.25 L) after CABG surgery was associated with increased postoperative mortality.<sup>30</sup> A relationship between obstructive pulmonary disorders and postoperative complications has also been described.<sup>31</sup> Patients after cardiac surgery have been reported to have a higher postoperative mortality when they suffered moderate-to-severe obstructive pulmonary disease. There was also a ten-times higher risk of death in these patients.<sup>32</sup>

In our study, the group was homogeneous and there was no relationship between respiratory disorders and mortality. The only observed relationship was found between the occurrence of obstructive disorders in the spirometry study and an elevated CRP level on the fourth postoperative day compared with patients with normal spirometry. Similar correlations were demonstrated between preoperative FEV<sub>1</sub>/FVC and CRP levels on the fourth day after surgery.

Our study has shown an increase in CRP in patients with an FVC below 80%. There was also a significantly higher BMI in this group. This has been confirmed by post-hoc testing comparing patients with obstructive respiratory disorders and those without any respiratory problems. Many reports suggest that obesity results in decreased FVC.<sup>33,34</sup> Leone et al show a decrease in spirometry parameters in patients with abdominal obesity, mainly in FVC and FEV<sub>1</sub>.<sup>35</sup> It is worth mentioning that out of many risk factors for ischemic heart disease, only a few are modifiable, one of them being a reduction in weight.

It is worth noting that the function of the respiratory system tested by means of spirometry allows an evaluation of the airflow through the lungs and also the strength of the skeletal muscles.<sup>36</sup> The described spirometry parameters should be included in the preoperative risk assessment. Information about pulmonary dysfunction prior to surgery may improve the patient's respiratory system faster and more efficiently and may be important in preventing complications following coronary artery bypass surgery.



## Conclusion

In our study, the most common pulmonary disorders in the CABG patients were restrictive.

Education of patients with preoperative respiratory disorders should also include education on the benefits of adopting a pro-health lifestyle, weight reduction, monitoring glycemic levels, any of which could lead to a lower risk of respiratory complications in these patients after surgery.

Patients with abnormal spirometry results from restrictive respiratory disorders have an elevated level of generalized inflammatory response both before and after the isolated coronary artery bypass surgery. Therefore, this group of patients should be given special postoperative monitoring and, in particular, intensive respiratory rehabilitation immediately after surgery.

## Limitations

Our study was limited by the number of patients with particular types of respiratory disorders. In order to obtain more representative results for the general population, the number of patients with obstructive ventilation should be increased in future research. Another significant limitation of this study was the difference in the number of women and men, which was due to the uneven number of patients qualified for CABG. In the future, spirometry should also be performed after CABG.

## Disclosure

The authors report no conflicts of interest in this work.

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