

Journal of Ankara Health Sciences



e-ISSN: 2618-5989

Determination of the Effectiveness of Physiotherapy Techniques After Coronary Artery Bypass Graft Surgery

Koroner Arter Bypass Greft Cerrahisi Sonrası Fizyoterapi Programlarının Etkinliğinin Belirlenmesi

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Article Information	ABSTRACT
Received:	Aim: The aim of this study was to investigate the effects of incentive spirometer on respiratory muscle strength,
14.01.2021	exercise capacity and hemodynamic responses after CABG surgery. Subject and Method: Between June 2017 and
	December 2018, a total of 35 patients who underwent CABG surgery were included in this prospective randomized
Accepted:	controlled study. Patients were divided into incentive spirometer (IS) group and physiotherapy (PT) group. All
08.12.2021	patients received standard physiotherapy postoperatively. In addition, IS group received volume-oriented incentive
	spirometer. Respiratory muscle strength (mouth pressure device) on 2 nd and 5 th postoperative day, exercise capacity
	(6-min.walking test (6-MWT)) on 3 rd postoperative day, before and immediately after physiotherapy on the first post-
	operative day blood gases were assessed. Results: Demographic characteristics of the groups were similar in both
	groups. Statistically significant increases in maximal inspiratory pressure (MIP), maximal expiratory pressure (MEP),
	%MIP and %MEP values were observed in both groups ($p<0.05$) but there was no statistically significant difference
	between the groups ($p>0.05$). There were no significant differences in 6 MWT parameters between PT and IS group ($p>0.05$). No significant difference was found in arterial blood gas values on first postoperative day in both groups
	(p>0.05). Conclusion: Respiratory muscle strength was improved and blood gas values were maintained in both
	groups. There was no superiority of IS combined with PT in increasing respiratory muscle strength and in maintaining
	arterial blood gas results after CABG surgery. IS combined with physiotherapy could be used safely from the early
	period after cardiac surgery due to the nonappearance of adverse effects.
	Keywords: Coronary artery bypass graft surgery, exercise capacity, physiotherapy
Makale Bilgisi	ÖZ
Geliş Tarihi:	Amaç: Bu çalışmanın amacı, koroner arter bypass greft (KABG) cerrahisi sonrası insentif spirometrenin solunum
14.01.2021	kas gücü, egzersiz kapasitesi ve hemodinamik yanıtlar üzerine etkilerini araştırmaktı. Örneklem ve Yöntem: Haziran 2017 ve Aralık 2018 arasında KABG ameliyatı geçiren toplam 35 hasta bu prospektif randomize kontrollü çalışmaya
Kabul Tarihi:	dâhil edildi. Hastalar insentif spirometre (IS) ve fizyoterapi (PT) gruplarına ayrıldı. Tüm hastalara postoperatif
08.12.2021	standart fizyoterapi uygulandı. Ayrıca, IS grubuna volüm duyarlı insentif spirometre verildi. Solunum kas kuvveti
	(ağız basıncı cihazı) postoperatif 2. ve 5. günlerde, egzersiz kapasitesi (6-dakika yürüme testi (6-DYT)) postoperatif
	3. günde, kan gazları ameliyat sonrası ilk gün fizyoterapiden önce ve hemen sonra değerlendirdi. Bulgular: Grupların
	demografik özellikleri her iki grupta benzerdi. Her iki grupta da maksimal inspiratuar basınç (MIP), maksimal
	ekspiratuar basınç (MEP), % MIP ve % MEP değerlerinde istatistiksel olarak anlamlı artış gözlendi (p<0.05) ancak
	gruplar arasında istatistiksel olarak anlamlı fark yoktu (p>0.05). PT ve IS grubu arasında 6 DYT parametrelerinde
	anlamlı fark yoktu (p>0.05). Her iki grupta postoperatif birinci gün arteriyel kan gazı değerlerinde anlamlı fark
	bulunmadı (p>0.05). Sonuç: Her iki grupta da solunum kas kuvveti düzeldi ve kan gazı değerleri korundu. KABG
	ameliyatından sonra IS ile kombine edilmiş fizyoterapinin, solunum kas kuvvetinin artmasında ve arteriyel kan gazı sonuçlarının korunmasında üstünlüğü yoktu. Fizyoterapi ile kombine edilen IS, yan etki gözlenmemesi sebebiyle
	kalp cerrahisi sonrası erken dönemden itibaren güvenle kullanılabilir.
	har contait contait and and have a garone kananacini.
	Anahtar Kelimeler: Koroner arter bypass greft cerrahisi, egzersiz kapasitesi, fizyoterapi
doi: 10.46971/ausbid.860630	

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Introduction

Cardiovascular diseases, which are very common in developed and developing countries, are one of the leading causes of mortality and morbidity. It is possible to extend the life expectancy and increase the quality of life of patients with open heart surgery. CABG surgery is one of the most common methods of open heart surgery (Martínez-González et al., 2017). Angina, dyspnoea and patient's fatigue is reduced, health-related quality of life is improved, especially in terms of mental and physical functions with CABG (Ghavami et al., 2018). However, as in all surgeries, some complications may develop from this surgery. Conditions such as anaesthesia, type of surgery and previous health problems can cause a decrease in lung volume and compliance, inadequate cough strength, respiratory muscle weakness and phrenic nerve dysfunction after CABG surgery (Inönü et al., 2011).

As a complementary therapy, physiotherapy, in addition to medical treatment, is recommended in the early period to prevent and treat the complications (Hulzebos et al., 2003; Haeffener et al., 2008). Respiratory PT methods, such as deep breathing exercises, bronchial hygiene techniques, forced expiration techniques, manual hyperinflation, percussion, IS, intermittent positive pressure breathing (IPPB), continuous positive airway pressure (CPAP) and early mobilization, walking training and active/assistive exercises of the lower and upper extremities are applied in the early postoperative period of cardiac and abdominal surgery (Haeffener et al., 2008; Westerdahl et al., 2005; Patman et al., 2017). Eltorai et al., 2019 stated that IS was improved the patient adherence, atelectasis severity, noninvasive positive pressure ventilation use, ICU and length of stay. In a review aimed to compare the effects of IS for preventing postoperative pulmonary complications in adults undergoing coronary artery bypass graft surgery stated that despite its widely used of IS in CABG studies have been unable to demonstrate the superiority of IS over other techniques and also high methodological trials are needed to determine effects of IS (Freitas et al., 2007).

In post-surgical conditions IS is frequently used techniques for treatment of respiratory complications (Haeffener et al., 2008; Eltorai et al., 2019; Freitas et al., 2007). Although IS is used in many studies, studies with high evidence for efficacy have been rarely encountered in the literature, especially in the early postoperative period. Therefore, this study aimed to investigate the effects of incentive spirometer on respiratory muscle strength, exercise capacity and hemodynamic responses after CABG surgery. We hypothesized that IS improves respiratory muscle strength, exercise capacity and haemodynamic responses in the early postoperative period after CABG surgery.

Subjects and Methods

Selection and Identification of Cases

Between June 2017 and December 2018, a total of 53 patients underwent CABG surgery at the Hatay Mustafa Kemal University were enrolled. Patients who underwent CABG surgery over 18 were included in the study. We excluded patients with neuromuscular disorders, chronic obstructive pulmonary disease, prior open heart or pulmonary surgery, cardiovascular instability or an aneurysm, congestive heart failure, deep vein thrombosis. Patients were randomly allocated to either a IS group or a PT group. A computer-based program, MedCalc Statistical Software version 17.6. (MedCalc Software by, Ostend, Belgium; https://www.medcalc.org; 2017) was used for randomization. The IS group received IS and standard physiotherapy, and PT group received standard physiotherapy. The study was approved by the Ethics Committee

of the Hatay Mustafa Kemal University (25/05/2017/101) and performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients to participate in the study.

Measurements

Pre-treatment diagnosis, age, sex, body mass indexes, smoking status, intubation times, and number of arteries that have been changed were recorded.

Respiratory muscle strength was evaluated on the second and fifth post-operative day with a portable electronic mouth pressure measurement device (MicroRPM, Micro Medical UK) and performed according to the American Thoracic Society (ATS) and European Respiratory Society (ERS) criteria. Maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) were used for the assessment of respiratory muscles. MIP was measured at residual volume with rapid and deep inspiration, and MEP was measured from total lung capacity. Patients were encouraged verbally to achieve the best performance. If there was more than 5% or 5 cmH2O difference between the two best measured values, the measurement was repeated. The best measurements were chosen for analysis. The minimal clinical significance of MIP was 11 cmH2O. Respiratory muscle weakness (RMW) was defined according to calculations when MIP and/or MEP values were less than 70% (Laveneziana et al., 2019; Troosters et al., 2000).

Functional capacity was assessed by the 6-MWT on the third postoperative day. Patients rested for at least 30 min before starting the test according to ATS criteria. Heart rate, oxygen saturation, blood pressure, respiratory frequency, fatigue and dyspnoea were measured before and immediately after the 6-MWT. Patients were encouraged to walk as fast as possible (but without running) at their own walking speed for 6 min in a 30 m straight corridor. Distance covered was recorded. Reference values were used (Holland et al., 2014; Enright &Scherril, 1998).

On the first post-operative day arterial blood gases evaluated to determine acute effects of IS. Blood gases analyzed before and immediately after physiotherapy. Partial arterial oxygen pressure (PaO₂), partial arterial carbon dioxide pressure (PaCO₂), oxygen saturation (SaO₂), bicarbonate level (HCO₃), and arterial pH were analyzed with analyzer a blood gas (RAPIDPoint[®] 500 Siemens, USA).

Interventions

All patients received post-operative respiratory physiotherapy including breathing exercises (diaphragmatic breathing, thoracic expansion exercises, and pursed lip breathing), assisted cough and huffing techniques, active cycle of breathing techniques (ACBT), mobilization, and active exercises of the upper and lower limbs and thorax. Patients were mobilized as early as possible by the physiotherapist according to the ordinary routines. Patients walked 30 m in the intensive care unit on the first post-operative day. On the second day patients walked in the room at least 50 m. On the other days, patients walked freely in the corridor. The upper and lower limbs exercises were performed twice a day repeated 5 times starting from the first post-operative day. On the second day exercises were repeated 10 times twice a day.

IS group received standard physiotherapy and IS with volume-oriented incentive spirometer (Voldyne, Hudson RCI, Temecula, CA, USA). Patients were placed in sitting or high sitting positions. It was instructed to inhale slow and deep

breath followed by 3 second breath hold then to exhale passively. Patient performed 3 sets of 5 repeated deep breaths every waking hour in first postoperative day. On other days treatment was applied 3 sets 10 repeated deep breaths every waking hour (Restrepo et al., 2011).

Statistical Analysis

The Windows based SPSS 20 (IBM Corp., Armonk, New York, USA.) statistical program was used for statistical analysis. The suitability of the variables to normal distribution was examined by visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). In the descriptive analysis, mean and standard deviation values were given for normally distributed variables, and percentages (%) for variables specified by counting. The independent samples t test (Student's t test) was used to compare the pre-treatment values of the groups with a normal distribution of variables. The difference between the groups was given using mean \pm standard deviation and 95% confidence interval (95% CI). Non-distributed data were compared using the Mann-Whitney U test and expressed as medians (minimum-maximum). Nominal data were compared using the Chi-square test. In addition, two-way ANCOVA was performed to compare the change in respiratory muscle strength between the two groups accounting for any change in baseline variables. Post-hoc comparisons were analysed using the Bonferroni test. A p-value <0.05 was considered statistically significant. Using the G*power sample size calculator, it was calculated that a sample size of 11 subjects for each group with a power of 80% (α =0.05) to detect 11 cm H2O differences in maximal inspiratory pressure. We estimated a 20% drop out rate among the participants, the sample size was determined as 26 (13 in each group).

Results

Fifty-three patients who underwent CABG surgery were consulted. Thirteen patients were excluded because of various reasons. Forty clinically stable patients with bypass surgery were included in the study. Standard medical treatments were applied to all patients during their time in the intensive care unit (ICU). Forty patients were systematically randomized and divided into two groups: the PT group and the IS group. Three patients in the IS group and two patients in the PT group were excluded from the study (Figure 1). Demographic characteristics of the groups were similar in both groups. Intubation time, the number of arteries that have been changed were not significantly different in the two groups (Table 1) (p>0.05).

Table 1. Comparison of Demographic Characteristics of Physiotherapy and Incentive Spirometer Groups

	Physiotherapy group (n=18)	Incentive spirometer group (n=17)	
Variables	X±SD	X±SD	р
Age (years)	62.35±8.37	58.23±9.75	0.1
Length (cm)	165.88±11.67	$167.00{\pm}6.90$	0.5
Body weight (kg)	76.23±15.26	80.14±13.94	0.4
Body mass index (kg / m2)	28.08±6.99	28.78±4.89	0.6
Intubation time	11.29±3.77	9.66±4.53	0.1
Smoking (pack-years)	26.06±19.04	20.38±14.37	0.4
Number of arteries have been changed	3.17±0.80	3.06±0.77	0.7
Male/female, n/%	13/82.4 %; 5/17.6 %	14/72.2 %; 3/27.8	0.4

Fisher's exact chi-square test, p<0.05

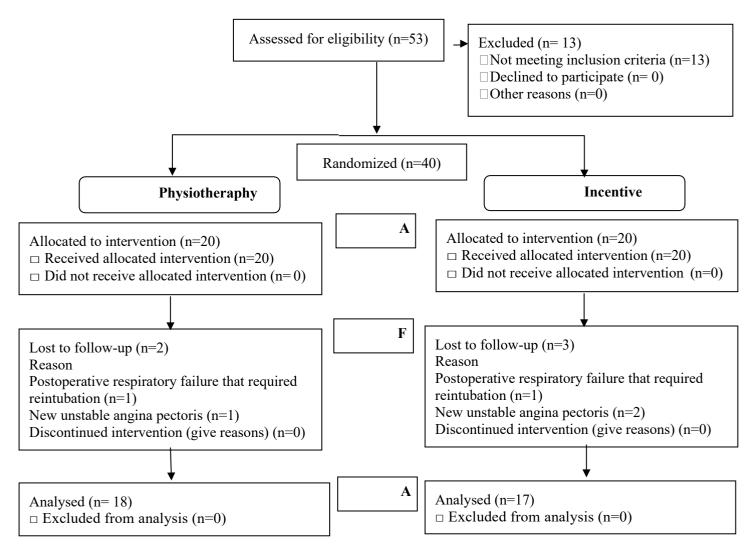


Figure 1. Flow Diagram of the Patients with CABG.

Statistically significant increases in MIP, MEP, %MIP and %MEP values were observed in both two groups (p<0.05) but there was no statistically significant difference between the groups (p>0.05) (Table 2). MIP was significantly increased in IS group (10.50 ± 15.31 cmH2O) and PT (9.17 ± 8.57 cmH2O) group. Also MEP was significantly increased in IS group (12.50 ± 18.93 cmH2O) and PT group (17.18 ± 15.85 cmH2O).

Table 2. Comparison of Respiratory Muscle Strength in Groups

	PT group (n=18)			IS g			
	Pre-treatment	Post-treatment	Within group	Pre-treatment	Post-treatment	Within group	Effect size
Respiratory muscle strength	X±SS	X±SS	р	X±SS	X±SS	р	р
MIP (cmH2O)	25.58±12.39	34±17.26	0.001	38.20±12.62	49.81±16.70	0.02	0.08
%MIP (%)	23.08 (14.67-49.76)	28.48 (17.12-70.81)	0.002	45.38 (15.34-59.33)	45.89 (30.69-83.24)	0.02	0.1
MEP (cmH2O)	36.93±15.49	53±21.12	0.001	52.60±13.21	64.93±16.83	0.02	0.17
%MEP (%)	19.10±7.21	27.99±10.33	0.001	27.21±9.60	34.06±10.92	0.03	0.002
ANCOVA test, p<0.05							

There were no significant differences in 6 MWT parameters between PT and IS group (Table 3) (p>0.05).

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	PT group (n=18)	IS group (n=17)	Z/t		
6-MWT parameters	X±SS Median (min-max)	X±SS Median (min-max)	Z/t	р	
Resting heart rate (beats/min)	98(85-106)	93(71-110)	-0.3	0.7	
% Peak heart rate (%)	67.54(61.63-81.65)	67.61(56.96-94.94)	-0.2	0.7	
Δ Heart rate (beats/min)	11.88 ± 11.08	20±19.07	1.5	0.1	
Resting SBP (mmHg)	125±19.47	122.5±8.36	-0.4	0.7	
∆SBP(mmHg)	8.61±19.38	17.81±25.94	1.1	0.2	
Resting DBP (mmHg)	75(50-110)	72.5(60-90)	-0.2	0.8	
∆DBP (mmHg)	7.11±14.47	7.18±11.25	0.0	0.9	
Resting SpO2 (%)	95(88-98)	93(86-97)	-0.9	0.3	
∆SpO2 (%)	1.27±2.73	0.8±3.91	-0.4	0.6	
Resting RF (breath/min)	27(16-32)	24(16-36)	-0.8	0.3	
∆RF (breath/min)	4.11±6.33	6.73±5.81	1.2	0.2	
Dyspnoea at rest (0-10. (0-10, MBS)	0(0-5)	0(0-2)	-0.5	0.5	
∆Dyspnoea (0-10, MBS)	1(0-3)	1.5(0-3)	-0.5	0.5	
General fatigue at rest (0-10. (0-10, MBS)	2(0-8)	1.5(0-7)	-0.1	0.9	
Δ General fatigue rest (0-10, MBS)	2.05±1.78	1.90±2.02	-0.2	0.8	
Resting QF muscle fatigue (0-10, MBS)	0(0-4)	2(0-6)	-0.8	0.4	
Δ QF muscle fatigue (0-10, MBS)	2(0-8)	2(0-4)	-0.6	0.5	
6-MWT distance (m)	136.97±90.45	145.70±67.59	0.3	0.7	
% 6- MWT (%)	22.05±13.19	22.03±9.69	-0.0	0.9	

Table 3. Comparison of 6-MWT Results between Groups	5
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 $\overline{6}$ -MWT: Six-minute walk test, 6-MWT: Percentage of expected 6-MWTdistance, QF: Quadriseps femoris, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MBS: Modified Borg scale, SpO2: Oxygen saturation, Δ : Test end and initial difference values, RF: Respiratory frequency, Mann-Whitney-U test, Independent samples test, p<0.05.

Arterial blood gas values did not change significantly in both groups on first postoperative day (Table 4; p>0.05).

Table 4. Comparison of Blood Gas Values of Physiotherapy and Incentive Spirometer Groups before and immediately after

 Physiotherapy on the first Postoperative Day

	PT group (n=18)			IS group (n=17)			
	Pre-treatment	Post-treatment	р	Pre-treatment	Post-treatment	р	
РН	7.42 (7.35-7.50)	7.41 (7.35-7.46)	0.7	7.35 (7.00-7.46)	7.39 (7.30-7.58)	0.3	
PO2 (mmHg)	80.00 (71-105)	93.00 (73-110)	0.4	95.15 (73-105)	97.00 (72-106)	0.9	
PCO2 (mmHg)	40.00 (30-49)	39.00 (31-49)	0.9	36.10 (30.5-53)	38.50 (30-48)	0.9	
HCO3 (mmol/L)	25.38±2.63	25.51±3.27	0.9	22.47±3.12	23.01±2.82	0.1	
SO2 (%)	97.25±2.63	97.33±1.77	0.9	96.40±4.54	97.08±2.33	0.4	

Paired Samples t test, Wilcoxon, p<0.05

Discussion

In this study, standard physiotherapy and IS combined with standard physiotherapy improved respiratory muscle strength and maintained arterial blood gases. In addition, both groups showed similar effects on respiratory muscle strength, arterial blood gases and exercise capacity of patients after CABG surgery.

Many PT techniques, such as deep breathing exercises, coughing, early mobilization and IS, have been reported in the literature after CABG surgery (Haeffener et al., 2008; Westerdahl et al., 2005; Patman et al., 2017). However, it is not clear which method is the most effective (Freitas et al., 2007). In a Cochrane Review study, which included randomized controlled trials, the efficacy of using an incentive spirometer to prevent postoperative pulmonary complications after CABG surgery stated that there were no significant differences between IS and conventional PT or ACBT with regard to arterial oxygenation. Also they concluded that effectiveness of IS in reducing complications, improving pulmonary functions still undetected (Freitas et al., 2007). The acute effects of PT and IS on arterial oxygenation were evaluated with arterial blood gas in our study, and we found that there was no significant difference between the two groups, which is compatible with the literature. Arterial oxygenation was maintained in both groups after the treatment. In present study IS combined with standard physiotherapy had no superiority on arterial blood gases. We did not include patients with pulmonary diseases or high pulmonary risk after CABG.

There was a decrease in respiratory muscle strength (MIP and MEP) after CABG surgery. Diaphragmatic dysfunction was mostly observed 2–8 hours postoperatively. Diaphragmatic muscle strength returned to preoperative values in at least 2 weeks (Borges-Santos et al., 2012; Moreno et al., 2011; Siafakas et al., 1999). The decrease in diaphragmatic muscle strength reduces in relation to the surgical procedure, pain, paresis and/or diaphragmatic dysfunction that causes cephalic displacement of the diaphragm with reduction of MIP and accelerates pulmonary complications (Siafakas et al., 1999). Earlier a study showed that after CABG surgery MIP and MEP decreased significantly at first postoperative day (Renault et al., 2009). In current study we could not measure respiratory muscle strength at preoperative period. However, postoperative period inspiratory [MIP %: 28.48 (17.12-70.81) in PT group & 45.89 (30.69-83.24) in IS group] and expiratory muscle [MEP %:27.99±10.33 in PT group & 34.06±10.92 in IS group] weakness was observed.

In previous studies showed improvement in MIP and MEP by using IS and deep breathing exercise after CABG surgery (Renault et al., 2009; Romanini et al., 2007). The use of IS was thought to increase muscle strength by activating more motor units. MIP and MEP were improved after two training protocols, but there was no statistically significant difference between the two groups.

The functional capacity status of patients after cardiac surgery is an important issue discussed in the literature. The 6-MWT evaluates postoperative functional capacity in a simple and safe manner in CABG operations (Fiorina et al., 2007). It is stated in the literature that the 6-MWT distance is affected by factors such as surgical type, cardiopulmonary bypass time, functional independence scale, and BMI during postoperative discharge (Oliveira et al., 2014). Chen et al., 2018 found that the 6-MWT distance was 277.00±86.00 m in the early postoperative period after CABG surgery. In other study, the 6-MWT distance was 260.00±89.00 m similar to Chen et al., 2018. The 6-MWT distance was 141.21±79.12 m in our study. The 6-

MWT distance was lower in our study as compared with the studies in the literature. The 6-MWT was performed on the fifth postoperative day in the literature. However, the 6-MWT was performed on the third postoperative day in our study. The patients were mobilized early in the intensive care unit and transferred to the service in the earliest period Patients were walking along the corridor in the service. Therefore, 6-MWT was performed on the third day to determine the functional capacity. It was thought that the difference might be due to the test being performed on the third postoperative day and demographic (e.g., ethnicity, height, leg length, etc.) differences. Fiorino et al., 2007 reported that patients with lower functional capacity during discharge had a greater increase in 6-MWT distance after a phase II cardiac rehabilitation program. It is emphasized that these patients need a more intensive program. It was thought that patients should be referred to the phase II cardiac rehabilitation program after discharge and long-term 6-MWT results should be investigated.

Deep breathing exercises and early mobilization are the most commonly used PT methods after CABG surgery (Filbay et al., 2012). Hong et al., 2018 reported that in Australia and New Zealand, physiotherapists frequently used mobilization, basal expansion exercises, and ABTC in the first 4 days postoperatively. Although there is insufficient evidence about the effectiveness of IS (Freitas et al., 2007), it has been shown that only 6% of physiotherapists use it in their PT program (Hong et al., 2020). In a systematic review, it has been found that early mobilization after CABG surgery prevents postoperative pulmonary complications, increases functional exercise capacity and reduces hospital stay (Ramos et al., 2015; Ramos Dos Santos et al., 2017). In the study, early mobilization was performed in both the PT and IS groups. There were no falls, arrhythmias or syncope during the treatment programs.

Limitations

Some potential limitations are present in our study. The 6-MWT that evaluates functional exercise capacity is reliable and suitable for this patient group. However, the limitation of our study is the lack of the 6-MWT in the preoperative period. In order to evaluate the efficacy of PT and IS programs, functional exercise capacity should be evaluated in the preoperative and postoperative periods. Another limitation is we did not classified patients according to their pulmonary risk scores. In a study it was shown that in high-risk group patients showed faster recovery after physiotherapy following CABG. Also they stated that physiotherapy is more crucial in high-risk patients to achieve similar results like low-risk group (Çırak et al., 2015). Therefore, effect of IS could be investigated at different risk groups in further studies. Finally the long-term effects of IS should be investigated in the wider sample size group at different risk groups in CABG patients.

Conclusions and Recommendations

In conclusion, in both groups respiratory muscle strength improved, and arterial blood gases maintained. There was no superiority of IS combined with PT in increasing respiratory muscle strength and in maintaining arterial blood gas results after CABG surgery. Studies can be conducted to investigate the effectiveness of a PT program using different methods after CABG surgery. IS combined with physiotherapy could be used safely from the early period after cardiac surgery due to the nonappearance of adverse. Also according to patient's characteristics, intensity of physiotherapy should be determined. We are of the opinion that it is the first randomized-controlled study evaluating functional capacity as soon as possible and this study will contribute to the literature in terms of providing clinicians with a different perspective in determining the effective treatment program after CABG surgery.

Ethical Approval of the Study

The study was approved by the Ethics Committee of the Hatay Mustafa Kemal University (25/05/2017/101) and performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients to participate in the study.

Conflict of Interest

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Acknowledgements

We are thankful to the CABG patients who participated in the study.

Funding

This study was supported by Hatay Mustafa Kemal University Research Center (No: 18.M.012).

Author Contributions

Concept – IH, NK; Design – IH, IF, MG; Supervision – IH, NK; Materials; IH, NK, BY Data Collection and/or Processing –BY, ET; Analysis and/or Interpretation – IH, NK, ET; Literature Research – BY, IH, MG; Writing Manuscript – IY, MG, IH; Critical Review – MG, IF.

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