Improved oxygen uptake efficiency slope in acute myocardial infarction patients after early phase I cardiac rehabilitation

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A predischarge submaximal exercise test is often recommended after acute myocardial infarction (AMI) as part of phase I cardiac rehabilitation. In this study, a submaximal exercise parameter, oxygen uptake efficiency slope (OUES), was used to monitor the benefit of early mobilization within 48 h after AMI. An early mobilization protocol within 48 h after AMI has been initiated since 1 September 2012 in our center. Patients with onset time of AMI within 1 year before and 1 year after initiation of the early mobilization protocol were recruited for comparisons. Sixty patients were analyzed on the basis of this criterion, and were subjected to predischarge submaximal exercise tests. The OUES calculated with 100% exercise duration ($OUES_{100}$) and calculated with the first 50% of exercise duration ($OUES_{50}$) were obtained and analyzed. Both $OUES_{100}$ and $OUES_{50}$ of the AMI patients with early mobilization were significantly higher than those without early mobilization ($P = 0.025$ and 0.007, respectively). The $OUES_{100}$ and $OUES_{50}$ were also highly correlated ($r = 0.891$, $P < 0.001$). The subgroup analysis using patients within 3 months before and 3 months after initiation of the protocol also showed a significant difference. OUES could be used to measure the exercise capacity and monitor the effect of phase I cardiac rehabilitation in patients soon after AMI. Early mobilization within 48 h following AMI significantly enhanced the patient's exercise capacity. ***International Journal of Rehabilitation Research*** **40:215–219 Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.**

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Introduction

The rates of short-term and long-term morbidity after acute myocardial infarction (AMI) have reduced in recent decades (Goldberg *et al.*, 2004; Bata *et al.*, 2006; Botkin *et al.*, 2006; Briffa *et al.*, 2009; Yeh *et al.*, 2010; Hardoon *et al.*, 2011; Smolina *et al.*, 2012; Cairns *et al.*, 2015; Hou *et al.*, 2016), attributed in part to the improvement of diagnostic and transferring systems, the growing accessibility of revascularization procedures, and more effective long-term secondary prevention. The initial management of AMI includes early oxygenation, early revascularization or fibrinolytic therapy, secondary prevention with antiplatelets and cardioprotective agents such as angiotensin-converting enzyme inhibitors or β-blockers, and cardiac rehabilitation for functional restoration. Previously, physicians tended to keep patients immobilized for days to weeks (Abraham *et al.*, 1975; Swan *et al.*, 1976) until the formation of a myocardial firm scar, which takes about 6 weeks (Mallory *et al.*, 1939). However, early mobilization has been found to provide noninferior outcomes in recent years (Rowe *et al.*, 1989; Herkner *et al.*, 2003; Lopes *et al.*, 2008; Cortes *et al.*, 2009; Asgari *et al.*, 2015), and some guidelines even suggest early ambulation on the first day following an uncomplicated ST-segment elevation myocardial infarction (Steg *et al.*, 2012).

According to the guidelines of the American College of Cardiology/American Heart Association, a submaximal exercise test should be performed among AMI patients for risk stratification before discharge (Gibbons *et al.*, 2002). Poor exercise tolerance indicates a poor prognosis and possible residual ischemia (Throux *et al.*, 1979; Krone *et al.*, 1985). These patients are at high risk for cardiac events and might need supervision while performing daily training. Although early mobilization and the submaximal exercise test have been suggested as possibilities to consider during the hospital stage following AMI, few reports had shown the presence of significantly increased exercise capacity after early mobilization. The reason for the nonsignificance is that the oxygen uptake (VO_2) measured at the submaximal endpoint is not the peak oxygen uptake ($VO_{2\,peak}$), which is usually beyond the set submaximal endpoint.

The oxygen uptake efficiency slope (OUES) is a submaximal parameter of exercise testing. It is proposed to be the prognostic factor of patients with coronary artery disease (Coeckelberghs *et al.*, 2015; Buys *et al.*, 2016) and

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Table 1 **Phase I cardiac rehabilitation protocol**

Step 1	Bed rest and ankle pumping
Step 2	Sitting with AROM exercise of the lower limbs (5–10 min, two times/day)
Step 3	Supervised walking in the room (target HR = baseline HR + 20, 5–10 min, two times/day)
Step 4	Independent walking or ergometry (target HR = baseline HR + 20, 5–10 min, two times/day)
Step 5	Independent walking or ergometry (target HR = baseline HR + 20, 10–15 min, two times/day) and climbing 6–10 steps of stairs

AROM, active range of motion; HR, heart rate.

chronic heart failure (Davies *et al.*, 2006; Myers *et al.*, 2008). The validity and reliability of the OUES have been verified in several previous studies (Laethem *et al.*, 2009; Bongers *et al.*, 2011; Williamson *et al.*, 2012). The OUES can be measured shortly after initiation of exercise, whereas the $VO_{2\,peak}$ can only be measured at peak work, which is usually not obtainable in a submaximal test. Therefore, we hypothesized that the OUES might be a better indicator than the $VO_{2\,peak}$ in AMI patients undergoing submaximal exercise testing.

The two aims of this study are to show the influence of an early mobilization program and to show the usefulness of OUES in predischarge submaximal exercise tests.

Patients and methods

Patients

All AMI patients who underwent phase I in-hospital cardiac rehabilitation after a percutaneous coronary intervention (PCI) in our center between 1 September 2011 and 31 August 2013 were recruited into this study. Each patient underwent a submaximal exercise test before discharge. Four patients were excluded because of incomplete data and the other 60 patients were enrolled for analysis. The clinical data of these patients were retrospectively collected from chart review. The Institutional Review Board at the Veterans General Hospital-Kaohsiung approved this study before initiation [15-CT7-05(150423-1)].

Cardiac rehabilitation programs

The acute managements for AMI including PCI, hospital care, and secondary prevention were performed by the cardiologists. Every cardiologist involved had at least 5 years of experience in PCI. The AMI patients without immediate complications after PCI were routinely consulted for cardiac rehabilitation. Patients started with long sitting, transferring, and then progressive walking as tolerated, with a target heart rate of baseline heart rate plus 20 beats/min.

To improve the caring quality of AMI patients, the cardiac rehabilitation team in our center revised the intervention protocol from 1 September 2012. Both the previous and the revised protocol shared the same concept of progressive phase I rehabilitation steps, but the revised protocol strictly focused on early mobilization (i.e. progression from steps 1 to3) within 48 h after the onset, whereas the previous protocol kept the patient at step one until about 3–5 days after AMI (Table 1). We retrospectively collected the data of all patients from the early mobilization group ($n=32$) from 1 September 2012 to 31 August 2013, and compared them with the data from the traditional group ($n=28$) from 1 September 2011 to 31 August 2012. All of the physiotherapists using this protocol had at least 3 years of experience. In addition, to minimize the confounding effect from the improvement of procedure and caring quality during these 2 years, we also carried out a subgroup analysis using data from between 1 June 2012 and 31 December 2012 (specifically, within 3 months before and 3 months after the initiation of the early mobilization protocol).

Cardiopulmonary exercise testing

The submaximal exercise test was performed using a MetaLyzer 3B (Cortex Biophysik GmbH Co., Leipzig, Germany) system, which included a leg ergometry, a gas analyzer, and an ECG monitor to measure the exercise capacity of the patients. Patients were asked for informed consent before the test. An incremental workload of 10 W/min was used and the submaximal endpoint was set at a heart rate of 120 beats/min, a workload of 75 W, or an oxygen uptake of 5 metabolic equivalents (METs). Patient VO_2 and carbon dioxide production were measured during the test breath by breath and the respiratory exchange ratio was calculated as the ratio of carbon dioxide production to oxygen consumption. The minute ventilation (VE) was estimated according to the volume of every single breath multiplied by breathing rate. The OUES was calculated by performing a linear regression between VO_2 and log (VE). Using the equation: $VO_2 = a \log(VE) + b$, the slope a was determined as the OUES. $OUES_{100}$ indicated the OUES calculated with 100% exercise duration, whereas $OUES_{50}$ indicated the OUES calculated with the first 50% of exercise duration.

Statistical analysis

Data were expressed as mean ± SD, numbers, or percentages as appropriate. The categorical variables including sex; the presence of Killip class of at least 2; the presence of ST-segment elevation myocardial infarction; the presence of stenotic vessels at least 2; the presence of comorbidities such as cerebral vascular accident, chronic kidney disease, diabetes mellitus, peripheral arterial occlusive disease; and the presence of 3-year cardiac-related rehospitalization were analyzed using Fisher's exact test. The continuous variables including age, BMI, left ventricular ejection fraction, resting diastolic blood pressure and heart rate, submaximal diastolic blood pressure and heart rate, and the submaximal oxygen uptake were confirmed to be normally distributed by the Shapiro–Wilk test and were compared using the independent Student's *t*-test. Other continuous variables were not normally distributed and were instead compared using the Mann–Whitney *U*-test. The subgroup analysis, using the data collected between 1 June 2012 and 31 December 2012, was carried out using the Mann–Whitney *U*-test. In addition, the relationship between the $OUES_{100}$ and the $OUES_{50}$ was analyzed with Pearson's correlation to support the hypothesis that the OUES value calculated shortly after the initiation of the exercise test could represent the one calculated with the entire exercise duration. All of the statistical analyses were carried out using SPSS, version 19 (IBM Corp., Armonk, New York, USA). A two-tailed *P*-value of 0.05 was considered significant.

Results

The clinical data of all of the patients involved in this study are shown in Table 2. No significant differences in the demographic data were found between the two groups and the severity of the two groups appeared to be similar.

The results of cardiopulmonary exercise testing (CPET) are shown in Table 3. Both the $OUES_{100}$ and $OUES_{50}$ of the early mobilization group were significantly higher than that of the traditional group ($P = 0.007$ and 0.011, respectively). Other parameters at rest and the submaximal endpoint were not found to be significantly different.

Figure 1 shows the $OUES_{100}$ and $OUES_{50}$ of the subgroups, consisting of the patients within 3 months before and 3 months after initiation of the early mobilization protocol. The $OUES_{100}$ of the early mobilization group was still significantly higher than that of the traditional group ($P = 0.045$).

The linear regression and Pearson's correlation of the $OUES_{100}$ and $OUES_{50}$, meanwhile, is shown in Fig. 2.

Table 2 Clinical data of the two study groups

	Early mobilization ($n = 32$)	Traditional ($n = 28$)	*P* value
Age (years)	58.4 ± 12.6	58.7 ± 8.9	0.912
Male/female (*n*)	31/1	26/2	0.476
BMI (kg/m^2)	25.38 ± 3.12	24.62 ± 3.43	0.379
Killip class ≥ 2 (*n*)	8	9	0.578
LVEF (%)	51.44 ± 6.59	51.89 ± 7.39	0.805
STEMI/NSTEMI (*n*)	27/5	20/8	0.225
Stenotic vessels ≥ 2 (*n*)	20	18	1.000
CVA (*n*)	2	2	1.000
CKD (*n*)	1	1	1.000
DM (*n*)	9	5	0.564
PAOD (*n*)	1	0	1.000
Hospitalization (days)	7.19 ± 3.50	6.11 ± 1.60	0.399
3-year rehospitalization (*n*)	17	16	0.799

CKD, chronic kidney disease; CVA, cerebral vascular accident; DM, diabetes mellitus; LVEF, left ventricular ejection fraction; NSTEMI, non-ST-segment elevation myocardial infarction; PAOD, peripheral arterial occlusive disease; STEMI, ST-segment elevation myocardial infarction.

Table 3 Cardiopulmonary exercise test of the two study groups

	Early mobilization ($n = 32$)	Traditional ($n = 28$)	*P* value
Rest			
SBP (mmHg)	122.4 ± 18.0	128.5 ± 17.5	0.173
DBP (mmHg)	72.3 ± 10.1	75.6 ± 12.7	0.270
HR (bpm)	80.6 ± 9.6	79.5 ± 14.9	0.755
Submaximal			
$OUES_{100}$	1.74 ± 1.42	1.10 ± 0.46	0.007
$OUES_{50}$	1.63 ± 1.25	0.96 ± 0.42	0.011
VO_2 (METs)	3.68 ± 0.86	3.64 ± 0.84	0.869
RER	1.11 ± 0.08	1.08 ± 0.12	0.032
SBP (mmHg)	157.3 ± 23.5	155.3 ± 29.2	0.402
DBP (mmHg)	76.9 ± 11.1	82.2 ± 13.9	0.109
HR (bpm)	112.6 ± 10.3	109.2 ± 14.7	0.312

DBP, diastolic blood pressure; HR, heart rate; MET, metabolic equivalent; $OUES_{100}$, oxygen uptake efficiency slope calculated with 100% of exercise duration; $OUES_{50}$, oxygen uptake efficiency slope calculated with the first 50% of exercise duration; RER, respiratory exchange ratio; SBP, systolic blood pressure; VO_2, oxygen uptake.

The $OUES_{100}$ correlated well with the $OUES_{50}$ ($r = 0.891$, $P < 0.001$), and the means of the $OUES_{100}$ (1.44 ± 1.12) and the $OUES_{50}$ (1.32 ± 1.01) were not significantly different ($P > 0.05$, paired *t*-tests).

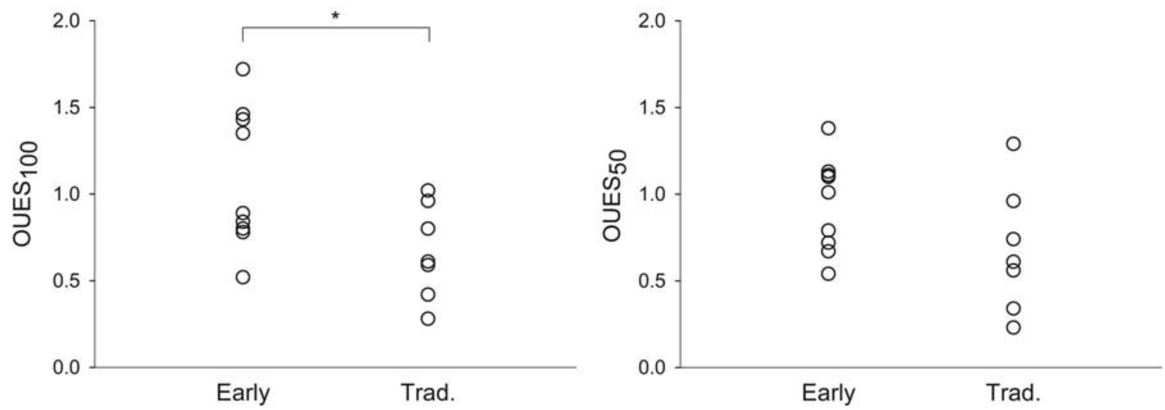
Discussion

The current study showed that early mobilization within 48 h after AMI could enhance the oxygen uptake efficiency in this population. Theoretically, the OUES might be more appropriate to evaluate the AMI patients, in whom a peak oxygen uptake is not usually obtainable

A submaximal CPET is routinely recommended in AMI patients before discharge (Gibbons *et al.*, 2002). Failure to reach a target METs level, or the presence of ischemic signs, typically signifies a significant increased potential for adverse cardiac events in the future (Arena *et al.*, 2007). In most cases, the commonly used threshold is 5 METs. However, a submaximal CPET ceased at a preset endpoint; thus, it could not differentiate the exercise capacity in the populations with a relatively good tolerance (e.g. those with $VO_{2\,peak} > 5$ METs). Therefore, theoretically, a submaximal parameter such as OUES should be more suitable to measure exercise capacity in this population. Previous studies have shown that OUES can be used to quantify exercise performance and predict $VO_{2\,peak}$ in patients with coronary artery disease (Defoor *et al.*, 2006; van Laethem *et al.*, 2006), but all of them used the symptom-limited CPET in the subacute outpatient training phase. The current study was the first to focus on the clinical use of OUES obtained from the predischarge submaximal CPET.

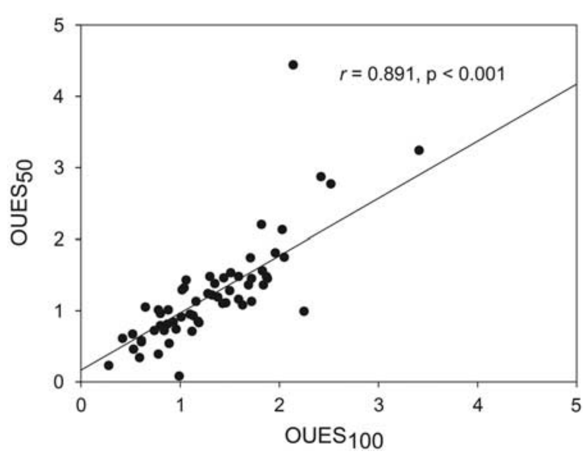
OUES is calculated with the VO_2 and the VE breath by breath during a period of exercise duration. Calculation of OUES using different parts of exercise duration will lead to different results. In a previous study that included adult cardiac patients, calculation of OUES with the first 75, 90, and 100% of exercise duration correlates with each other excellently (Baba *et al.*, 1999). However, in another

Fig. 1



The oxygen uptake efficiency slope calculated with 100% exercise duration ($OUES_{100}$) and the first 50% exercise duration ($OUES_{50}$) of the early mobilization and traditional groups, respectively. *$P < 0.05$, Mann–Whitney *U*-test.

Fig. 2



Linear regression and Pearson's correlation of the oxygen uptake efficiency slope calculated with 100% exercise duration ($OUES_{100}$) and the first 50% exercise duration ($OUES_{50}$) of all patients.

study on adult patients with congenital heart diseases, $OUES_{50}$ seemed to be lower than calculation with the last 50% of exercise duration (Giardini *et al.*, 2009). In the current study, the $OUES_{50}$ correlated highly with the $OUES_{100}$ and the values were not significantly different. Furthermore, the OUES appeared to be stable over the entire exercise duration in AMI patients. This feature supported the use of OUES in this population because the physicians tended to be more conservative in terms of these patients, and the exercise tests were often terminated prematurely because of presentation of relatively subtle symptoms. However, the OUES calculated shortly after initiation of the test might still be of clinical importance in such situations.

Very few studies have discussed the effects of early mobilization on functional capacity after AMI. In this study, a protocol of early mobilization within 48 h significantly enhanced the OUES in the predischarge submaximal CPET, making the OUES a potential indicator for monitoring recovery during phase I in-hospital cardiac rehabilitation. To the best of our knowledge, this was the first study to show that early mobilization clearly contributed toward a better exercise capacity, as measured with OUES.

Bed rest lasting more than 6–20 h is called prolonged bed rest (Cortes *et al.*, 2009), which can lead to a variety of complications including deep vein thrombosis, muscle wasting, and/or cardiac deconditioning. To compensate for the negative effects of bed rest, early mobilization after AMI is recommended currently (Steg *et al.*, 2012). A previous meta-analysis showed an increased trend of survival among AMI patients who received or were receiving early mobilization (Cortes *et al.*, 2009), likely through the reduction of the cardiac deaths following AMI, such as fatal arrhythmia. However, the nonfatal reinfarction rate was not reduced by early mobilization in this meta-analysis. In the current study, the 3-year cardiac-related rehospitalization rate was also not significantly different between the two groups, which is in agreement with the results of the previous meta-analysis. However, there was no short-term cardiac death for the two groups to compare, probably because of a small sample size.

The limitations of this study included a relatively small sample size and the nonrandomized design. However, because we retrospectively categorized these patients into two groups by a clear cut-off time, the only confounding factor was their onset time. Otherwise, the patients essentially had an equal chance of being categorized into the two groups. The different onset time might influence the results because of some reasons, such as the learning effect of the cardiologists performing PCI, or the different brands of medication being used. To minimize this confounding effect, we shortened the sampling duration to a period of 6 months in the subgroup analysis. Despite this, there was still a significant improvement in the OUES observed in the early mobilization group in the subgroup analysis. However, a randomized-controlled trial is still suggested for consideration in the future to further prove the effectiveness of early mobilization on functional capacity. In addition, there was no short-term cardiac death in any of the patients in this study, probably because of the small sample size. Further study of the relationships of the OUES and the short-term complications is also needed.

Conclusion

The early mobilization within 48 h following AMI could enhance a patient's exercise capacity, as measured with OUES. Theoretically, the OUES might be more suitable for AMI patients to evaluate the exercise capacity and monitor the effects of phase I cardiac rehabilitation because of its submaximal entity, especially in populations with a relatively fair exercise tolerance.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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