Survival of Patients with Acute Coronary Syndrome Who Receive Secondary Prevention Therapy: A Single-center Cohort Study

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Background and Purpose: Secondary prevention for patients with acute coronary syndrome is recommended by international guidelines; however, lifestyle intervention is an underutilized component. The purpose of this study was to determine the use of optimal secondary prevention therapy in a single-center and to assess how the survival and characteristics of patients correlate with optimal therapy. Methods: We included patients with acute coronary syndrome who underwent percutaneous coronary intervention from January 2012 to June 2013. Patients received dual antiplatelet therapy during follow-up, and they were allocated to an optimal or a suboptimal therapy cohort. The optimal therapy cohort received additional diet or exercise therapy. Data for clinical events, death, and patients characteristics were collected, and Kaplan-Meier survival analysis and a general linear model were used to determine differences in outcomes between cohorts. Independent t and chi-square tests were used to analyze baseline characteristics. Results: Younger (63±13.3 years of age) men (n=253, 79.1%) populated the optimal therapy cohort (n=320, 80.2%). There was no significant difference in clinical events and mortality rates (0.63% vs. 1.27%, respectively, \textit{p}=0.359) between cohorts. However, the rate of exercise therapy after discharge in the optimal therapy cohort was low (17.8%). Conclusions: Although we did not detect a significant difference in the rates of clinical events and mortality between cohorts, we believe that lifestyle intervention is insufficient. Further research should therefore focus on extended management after discharge to insure adherence to therapy. (FJPT 2014;39(4):223-230)

Key Words: Acute coronary syndrome, Secondary prevention, Cardiac rehabilitation

INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death and disability worldwide.\textsuperscript{1} Disease characteristics range from an asymptomatic state to potential sudden death. Acute coronary syndrome (ACS) comprises a constellation of acute clinical presentations linked to the rupture of an unstable atherosclerotic plaque, subsequent platelet aggregation, and

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thrombus formation that often completely occludes a coronary artery. Mortality during the first 30 days after onset exceeds 50%. The prognosis of ACS has improved over the past two decades because of significant advances in revascularization techniques. The use of evidence-based medical therapy contributes significantly to decreased cardiovascular morbidity and mortality in patients with ACS.

For secondary prevention, current international guidelines recommend life-style intervention to control risk factors through exercise and diet. Cardiac rehabilitation and secondary prevention therapies are associated with a 15%-25% reduction of all-cause and cardiovascular mortality.

Patients with ACS who engage in rehabilitation with healthy behavioral changes benefit from a 3-fold lower risk of death compared with non-participants and experience fewer unplanned and costly readmissions. Despite the robust class 1 recommendations of the guidelines, only 30% of patients treated for ACS benefit from the optimal therapy, including pharmaceutical and life style interventions.

There is a significant gap between the international guidelines and clinical implementation. A study of a large European cohort reported that only 43% of patients treated for ACS received complete optimal therapy during hospitalization and for 1 year afterwards. Exercise and diet programs were the least frequently used components of optimal therapy. The frequency of implementing optimal secondary prevention therapy in Taiwan is unknown. Therefore, the purpose of this study was to determine the use of optimal therapy after patient discharge and to evaluate its effects on mortality rate and patient characteristics.

METHODS

This is a retrospective cohort study that recruited patients diagnosed with ACS from January 2012 to June 2013. ACS was defined according to the American Heart Association and American College of Cardiology Joint Guidelines. All subjects underwent electrocardiography, tests for cardiac enzymes, and catheterization to confirm diagnosis. We included patients who underwent percutaneous coronary intervention (PCI) after admission and received dual antiplatelet therapy (DAPT) (aspirin and clopidogrel). We excluded patients who died during hospitalization.

Subjects were allocated to either an optimal or a suboptimal therapy cohort. Optimal therapy combined medication, diet consultation and/or exercise training. Patients received optimal therapy (optimal therapy group) uptake DAPT treatment after PCI and during follow-up period. Furthermore, one dietitian-delivered consultation during hospitalization and/or exercise interventions before discharge were given. Outpatient aerobic exercise training program, as phase 2 cardiac rehabilitation, followed AHA recommendation was applied by the physical therapist, and all patients were encouraged to participate enough sessions according to their risk classification. Each outpatient exercise training session included a 40-50 minutes individual moderate intensity aerobic exercise and education of risk factor modification especially for establishing exercise habit. Attendance of outpatient exercise training was defined as to attend at least once training session. Suboptimal therapy was defined as patients who only received DAPT.

Survival and clinical events were determined for each cohort from discharge until June 2013. Cardiovascular events were defined as long-term PCI (re-do PCI), stroke, myocardial infarction (MI), and death. All events were reviewed by medical chart and defined as diagnosis after current discharge. Heart function and physical activity (PA) level upon discharge and six months thereafter were also assessed. Left ventricular ejection fraction (LVEF) defined heart function, and patients’ PA level was determined using an international physical activity questionnaire (IPAQ). Demographic and clinical characteristics were acquired by reviewing hospital records. The Kaplan–Meier method and a general linear model were used to determine outcomes. Independent t and chi-square tests were used to evaluate patients’ baseline characteristics. Statistical significance was defined as p<0.05.

RESULTS

The characteristics of patients are summarized in Tables 1 and 2 and are briefly summarized as follows: mean age, 63.92±13.34 years; men, 76.4%; body mass index (BMI), 25.56±3.83 kg/m²; hypertension, 62.2%; hyperlipidemia, 49.6%; diabetes, 38.1%; DAPT, 100%; diagnosis of previous heart failure, 26.6%; previous PCI, 15%; MI, 9.3%; previous CABG, 6%; and previous stroke, 2.5%. Other medications are
shown in Fig 1.

Three hundred twenty patients (80.2%) were included in the optimal therapy cohort. Their most significant characteristics were as follows: younger age of 63±13.3 years; men 79.1% (n=253); and smokers 53.1% (n=170). The median duration of follow-up for mortality was 297.9±167 days. LVEF after PCI increased from 48.01±12.76% to 49.63±14.45% and from 49.63±14.45% to 50.09±14.13% for the optimal and suboptimal

Table 1. Demographics

<table>
<thead>
<tr>
<th></th>
<th>All (n=399)</th>
<th>Optimal therapy (n=320)</th>
<th>Suboptimal therapy (n=79)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63.92±13.34</td>
<td>62.96±13.30</td>
<td>67.78±12.81</td>
<td>0.004***</td>
</tr>
<tr>
<td>Males</td>
<td>305 (76.4%)</td>
<td>253 (79.1%)</td>
<td>52 (66.8%)</td>
<td>0.013†</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.56±3.83</td>
<td>25.53±3.84</td>
<td>25.70±3.81</td>
<td>0.731</td>
</tr>
<tr>
<td>Total follow-up duration (months)</td>
<td>10.1±5.5</td>
<td>10.1±5.4</td>
<td>9.9±5.7</td>
<td>0.625</td>
</tr>
<tr>
<td>DM</td>
<td>152 (38.1%)</td>
<td>127 (39.7%)</td>
<td>25 (31.6%)</td>
<td>0.187</td>
</tr>
<tr>
<td>Hypertension</td>
<td>248 (62.2%)</td>
<td>202 (63.1%)</td>
<td>46 (58.2%)</td>
<td>0.422</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>187 (46.9%)</td>
<td>157 (49.1%)</td>
<td>30 (38.0%)</td>
<td>0.077</td>
</tr>
<tr>
<td>Smoking</td>
<td>198 (49.6%)</td>
<td>170 (53.1%)</td>
<td>28 (35.4%)</td>
<td>0.005**</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD or No. of patients (%).

* p<0.05 compared between the optimal vs. suboptimal groups
BMI: body mass index; DM: diabetes mellitus

Table 2. Medical history

<table>
<thead>
<tr>
<th></th>
<th>All (n=399)</th>
<th>Optimal therapy (n=320)</th>
<th>Suboptimal therapy (n=79)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous MI</td>
<td>37 (  9.3%)</td>
<td>30 (  9.4%)</td>
<td>7 (  8.9%)</td>
<td>0.888</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>60 (15.0%)</td>
<td>51 (15.9%)</td>
<td>9 (11.4%)</td>
<td>0.311</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>24 (  6.0%)</td>
<td>16 (  5.0%)</td>
<td>8 (10.1%)</td>
<td>0.086</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>10 (  2.5%)</td>
<td>9 (  2.8%)</td>
<td>1 (  1.3%)</td>
<td>0.431</td>
</tr>
<tr>
<td>Heart failure*</td>
<td>106 (26.6%)</td>
<td>86 (26.9%)</td>
<td>20 (25.3%)</td>
<td>0.779</td>
</tr>
<tr>
<td>LM disease</td>
<td>52 (13.0%)</td>
<td>43 (13.4%)</td>
<td>9 (11.4%)</td>
<td>0.629</td>
</tr>
<tr>
<td>Multi-vessel disease</td>
<td>324 (81.2%)</td>
<td>261 (81.6%)</td>
<td>63 (79.7%)</td>
<td>0.711</td>
</tr>
<tr>
<td>Af</td>
<td>36 (  9.0%)</td>
<td>29 (  9.1%)</td>
<td>7 (  8.9%)</td>
<td>0.955</td>
</tr>
<tr>
<td>CKD³</td>
<td>99 (24.8%)</td>
<td>72 (22.5%)</td>
<td>27 (34.2%)</td>
<td>0.031†</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.63±2.05</td>
<td>1.48±1.87</td>
<td>2.27±2.61</td>
<td>0.002†</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>13.62±2.37</td>
<td>13.82±2.27</td>
<td>12.79±2.61</td>
<td>0.001†</td>
</tr>
<tr>
<td>COPD</td>
<td>9 (2.3%)</td>
<td>8 (2.5%)</td>
<td>1 (1.3%)</td>
<td>0.508</td>
</tr>
<tr>
<td>PAOD</td>
<td>4 (1.0%)</td>
<td>4 (1.3%)</td>
<td>0 (0%)</td>
<td>0.318</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD or No. of patients (%) unless otherwise indicated.

*Heart failure, LVEF< 40%
³CKD, chronic kidney disease, Creatinine> 1.4 mg/dL

p<0.05 compared between the optimal vs. suboptimal groups
MI: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; LM disease: left main coronary artery disease; Af: atrial fibrillation; COPD: chronic obstructive pulmonary disease; PAOD: peripheral artery occlusive disease
cohorts, respectively. Although we observed improvement in both cohorts, the difference between them was not significant.

Thirteen (3.26%) patients experienced at least one cardiovascular event during follow-up (Table 3), ten (3.13%) were patients of the optimal therapy cohort, and three (3.80%) were in the suboptimal therapy cohort. There was no significant difference between cohorts ($p=0.736$). All-cause death for all patients during the follow-up period was 0.75% (3/399), and two received optimal therapy. None died from a cardiovascular cause. The mortality rate was not significantly different between cohorts ($p=0.359$).

The rate of receiving exercise therapy after discharge of the optimal therapy cohort was 17.8% (57/320), and only six subjects (10.5%) attended more than 10 sessions. Major patients (36.8%, 21/57) attended only two sessions. The PA level determined using IPAQ ranged from 453.1±933.9 to 796.6±849.9 METs and from 386.8±419.8 to 814.1±1007.3 METs for members of the optimal and suboptimal therapy cohorts, respectively. Although both cohorts improved their PA level within six months of follow-up, the group-by-time interaction effect was not significantly different between them ($p=0.767$).

**DISCUSSION**

To the best of our knowledge, this retrospective observational cohort study of patients with ACS in Taiwan is the first to evaluate the influence on outcomes of exercise or diet as a component of optimal therapy. We focused on the survival of patients with ACS post-PCI who received DAPT with or without using lifestyle intervention. Eighty percent of patients received optimal therapy, which exceeds the frequency reported by a study of antiplatelet treatment observational registries.\(^{15}\) There were no significant differences between mortality rates and...
clinical events between the two cohorts studied here. The mortality rates were low in both cohorts (optimal, 0.63% vs. suboptimal, 1.27%), no cardiac mortality was noted, and clinical events were infrequent. All patients underwent early invasive PCI with better outcomes compared with a previous study\textsuperscript{13} that revealed coronary revascularization improves patient outcomes and reduces the frequencies of mortality and recurrent adverse events.\textsuperscript{19,20}

We assigned patients who received DAPT and lifestyle intervention to the optimal therapy cohort regardless of their use of other medications. Nevertheless, patients in the optimal therapy group used more of the recommended medications (Fig 1) compared with those in the suboptimal therapy cohort. We found that patients in the optimal therapy cohort were younger, predominantly men, and smokers. The patients in the suboptimal therapy cohort experienced more frequent chronic kidney disease. Patients in the optimal therapy cohort experienced fewer complications, and their socioeconomic status was more favorable, which may indicate that they were in greater compliance with the treatment protocol. A study of patients residing in Malaysia found that advanced age and renal failure predict mortality among patients with ACS post-PCI.\textsuperscript{21} Although there was no difference in mortality between the cohorts of the present study, we will continue follow-up with particular focus on the suboptimal therapy cohort.

Only 17.8% of the members of the optimal therapy cohort received exercise therapy after discharge, which was the least used element of the therapy regimen. Moreover, 91% attended exercise sessions only once or twice during follow-up, which is much less than the recommendations according to their risk classification.\textsuperscript{22} Exercise therapy for cardiac rehabilitation is associated with a 26% reduction in cardiac mortality in patients with CAD.\textsuperscript{5} Nevertheless, exercise therapy is underutilized for patients post-ACS in Taiwan, although it is a class I recommendation of the international guideline.\textsuperscript{5,6} Some possible reasons for the underutilization may include short hospitalization duration for the complete lifestyle interventions and lack of referral by physicians. An efficiently automatic referral system for post-ACS patients might be the key point for this issue, and further study was needed.

Here, we show that LVEF improved in both cohorts after PCI, indicating progress in the improvement of in-hospital ACS care such as reperfusion therapies and evidence-based medical therapy independent of outpatient exercise therapy. All patients included in this study received education regarding cardiac rehabilitation education before discharge, and the PA level increased at least until six months of follow-up (Fig 2). However, there was no significant difference between cohorts. Although this increase may be explained by the quality of education before discharge,\textsuperscript{23} only 10.5% of participants attended more than 10 sessions.

Multidimensional cardiac rehabilitation programs are an important cornerstone in the educational process of ACS care.\textsuperscript{9,24} Participation in rehabilitation or attendance at a sec-

Fig 2. Physical activity levels of patients in optimal therapy and suboptimal.
IPAQ: International Physical Activity Questionnaire.
ondary prevention clinic improves patient adherence with the overall therapeutic regimen. Lifestyle intervention, an important part of the rehabilitation program, should start from predischarge education and should be managed long-term. The Australian CHOICE study found that brief patient-centered lifestyle and behavior intervention significantly improved the control of risk factors after 1 year with sustained benefits for 4 years. Because these interventions are underutilized in Taiwan, we recommend the appointment of a coordinator to organize the present resource system. For example, after their discharge from the hospital, patients can be encouraged to adhere to a healthy lifestyle by consulting with physical therapists and dietitians.

A limitation of our study is that the experience at a single center and the short duration of follow-up may not represent the general population of patients with ACS. A second limitation is that the optimal therapy cohort did not receive both exercise and dietary intervention. The quality of optimal therapy is not perfect; a complete secondary prevention should combine medication, diet and exercise. A third limitation is that non-ST-segment or ST-segment elevation MI and variables such as stent design, medication, and other complications that influence survival were not studied. Further studies are required that include a longer follow-up that accounts for specific variables related to mortality and cardiovascular events.

Secondary prevention of ischemic events post-ACS requires a multi-target approach that includes treatment with evidence-based medication, modification of coronary risk factors, and adoption of recommended dietary and lifestyle changes. Greater focus should be placed on medium and long-term ACS management and adherence to therapies after discharge.

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REFERENCES


接受次級預防治療之急性冠心症病患的生存分析—單中心世代研究

許青翎¹ 林郁珊¹ 林維萱¹ 郭俐艷¹ 黃心怡¹,*

背景與目的：國際治療指引已建議急性冠心症病患接受次級預防治療計畫，而其中生活型態治療是未被充分利用的。本研究為一單中心世代研究，目的在觀察理想的次級預防治療被使用的狀況，以及參與與否之生存率以及相關臨床特徵。方法：本研究收集2012年1月至2013年6月間急性冠心症接受經皮冠狀動脈介人，並服用雙重抗血小板藥物治療之病患。定義接受雙重抗血小板藥物治療與生活型態治療（加入運動或飲食介入）為理想治療，僅接受雙重抗血小板藥物治療為次理想治療，並收集臨床事件、死亡、與病患特徵，利用Kaplan–Meier法與一般線性模式進行生存率與相關臨床資料分析，比較接受理想治療與次理想治療之情況。結果：有320位病患（80.2%）接受理想治療，此族群相較次理想治療者為年輕（63±13.3歲），男性較多（79.1%）。兩族群之臨床事件與死亡率（0.63% vs.1.27%，p=0.359）沒有顯著差異，而理想治療中於出院後維持參與運動治療的比例相當然低（17.8%）。結論：僅管理理想治療與次理想治療之臨床事件與死亡率沒有顯著差異，仍發現生活型態治療是未被充分利用的。未來研究應著重急性冠心症病患中長期追蹤，強調出院後次級預防之治療順應性。（物理治療 2014;39(4):223-230）

關鍵詞：急性冠心症、次級預防、心臟復健

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