

## Clinical prognosis of optimal medical therapy after percutaneous coronary intervention in patients with coronary heart disease

Jing-Yan Hao<sup>1</sup>, Jian Zhang<sup>2</sup>, Rui Jing<sup>2</sup>, Jing-Jing Liu<sup>2</sup>, Cheng-Ye Di<sup>2</sup>, Yu-Jie Lu<sup>2</sup>, Peng Gao<sup>2</sup>, Ya-Jie Wang<sup>2</sup>, Rui-Fei Yang<sup>2</sup>, Wen-Hua Lin<sup>2</sup>

<sup>1</sup>College of Clinical Cardiovascular Disease, Tianjin Medical University, Tianjin 300070, China;

<sup>2</sup>Department of Cardiology I, TEDA International Cardiovascular Hospital, Tianjin 300457, China.

*To the Editor:* Revascularization, regardless of whether it is percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), is still the dominant treatment of severe coronary heart disease (CHD). The long-term clinical outcome of revascularization is unpredictable because of the progression of atherosclerosis continuing after surgery.<sup>[1]</sup> Many studies and trials have proven that optimal medical therapy (OMT) with or without revascularization is critical for decreasing the incidence of adverse events and improving quality of life.

In recent years, patients from China with higher adherence to medical therapy have shown a lower incidence of adverse events at 1 year after PCI.<sup>[2]</sup> However, there have been no large clinical trials or observational studies for accurate understanding of maintenance of medical strategies in patients with CHD in China. Therefore, the present study aimed to investigate the use of OMT and evaluate its association with the clinical prognosis after PCI.

We prospectively collected data of patients with CHD who underwent PCI at the TEDA International Cardiovascular Hospital between October 2016 and September 2017. The study was approved by the Institutional Ethics Board of the TEDA International Cardiovascular Hospital (No. [2020]-1021-1). Given the retrospective nature of the study, the requirement of written informed consent was waived. Participants were included if they were treated by standard PCI following the Chinese PCI Guidelines (2016) after a coronary angiography examination. All patients were followed up after discharge either via an outpatient service or via telephone when the service was not feasible. Exclusion criteria were contraindications or intolerance to specified drugs of OMT, tumor or <1-year life expectancy, immune system disease, the presence of renal failure found during hospitalization, incomplete clinical or coronary

angiography records, and death before discharge. Demographic and clinical characteristics of the patients were obtained from the TEDA International Cardiovascular Hospital Database, and they included age, sex, body mass index (BMI), highest degree, payment method, tobacco use, diagnosis, and complications of CHD.

As previously described,<sup>[3]</sup> the definition of OMT was a combination of dual antiplatelet therapy (DAPT) (ie, aspirin and a P2Y<sub>12</sub> antagonist), statins,  $\beta$ -blockers, and angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs). The clinical endpoint of the study was major adverse cardiovascular events (MACE), which comprised all-cause mortality, hospitalization for non-fatal myocardial infarction (MI), and stroke. The follow-up lasted 1 year after discharge unless the endpoint was observed.

Categorical variables are described as the count with percentage (%) and continuous variables are expressed as mean  $\pm$  standard deviation. Differences between groups (OMT and non-OMT groups) were analyzed by the Pearson  $\chi^2$  test for categorical variables and the two independent samples *t*-test for continuous variables. To examine the effect of using OMT and each individual agent on the risk of the endpoint after PCI, unadjusted and adjusted hazard ratios (HRs) from Cox proportional hazards models were established as follows. There were four covariate models for each specific medication class, and these were adjusted for age, BMI, a history of MI, PCI, and heart failure (HF), the number of coronary artery lesions, the medication status for each agent at hospitalization, and the use of the other three classes of drugs at 1 year after discharge. Another model for OMT was adjusted for age, BMI, a history of MI, PCI, and HF, the number of coronary artery lesions, and OMT at hospitalization. Unless an additional statement was noted, each variable that was identified with univariate analysis

### Access this article online

Quick Response Code:



Website:

www.cmj.org

DOI:

10.1097/CM9.0000000000001720

**Correspondence to:** Wen-Hua Lin, Department of Cardiology I, TEDA International Cardiovascular Hospital, Tianjin 300457, China  
E-Mail: linwenhua@sina.com

Copyright © 2021 The Chinese Medical Association, produced by Wolters Kluwer, Inc. under the CC-BY-NC-ND license. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 3.0 License, where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially.

Chinese Medical Journal 2021;134(16)

Received: 09-03-2021 Edited by: Ning-Ning Wang

( $P < 0.050$ ) or previous clinical consideration was selected for inclusion in the adjusted multivariate models described above. All data were analyzed using IBM SPSS version 22.0 (IBM Corp., Armonk, NY, USA). All statistics were two-tailed and  $P < 0.050$  was considered significant.

We recruited 3812 patients after completing PCI and 224 patients were excluded (154 individuals refused follow-up and contact information was lost for 70). The final cohort consisted of 3588 patients at the end of follow-up, of whom 1299 (36.2%) persisted with OMT. Two-thirds of patients in this cohort had more than one comorbidity of CHD, which comprised hypertension, diabetes, hyperlipidemia, and tobacco use. Patients in the OMT group who received OMT at 1 year after discharge were more likely to have a college degree ( $P < 0.001$ ), medical insurance of employees ( $P < 0.001$ ), more coronary lesions ( $P = 0.003$ ), and a history of PCI ( $P = 0.019$ ) compared with those in the non-OMT group.

At hospitalization, 58.8% (2108/3588) of patients received OMT and the rates of DAPT, statins,  $\beta$ -blockers, and ACEIs/ARBs were 99.6% (3575/3588), 96.2% (3575/3588), 96.2% (3452/3588), 75.3% (2701/3588), and 75.0% (2692/3588) in hospital at baseline, respectively. At the 1-year follow-up, the treatment rate of DAPT and statins remained high ( $>85.0\%$ ) at 1 year after discharge, but the use of  $\beta$ -blockers was reduced to  $<60.0\%$  and that of ACEIs or ARBs was decreased by almost 30%. The use of  $\beta$ -blockers and ACEIs or ARBs showed a dramatic downward trend. At the end of the follow-up visit, only 36.2% of patients received OMT, which comprised all four classes of medications [Supplementary Table 1, <http://links.lww.com/CM9/A741>].

Table 1 shows the associations between MACE at 1 year after PCI and the use of OMT or each individual agent. Each class of OMT was associated with a significant reduction in MACE at 1 year, and a remarkable effect was observed using DAPT because of its higher rate of medication use (HR = 0.122, 95% confidence interval [CI]: 0.078–0.191,  $P < 0.001$ ). The use of statins (HR = 0.435, 95% CI: 0.279–0.677,  $P < 0.001$ ),  $\beta$ -blockers (HR = 0.614, 95% CI: 0.387–0.972,  $P < 0.038$ ),

ACEIs/ARBs (HR = 0.433, 95% CI: 0.281–0.667,  $P < 0.001$ ), and OMT (HR = 0.382, 95% CI: 0.244–0.599,  $P < 0.001$ ) were also significantly associated with a decrease in adverse events.

The benefits of statins and DAPT have been recognized in recent years, and DAPT improves clinical outcomes compared with aspirin alone in patients with acute coronary syndrome.<sup>[4]</sup> The use of  $\beta$ -blockers after acute coronary syndrome is indicated in clinical practice unless patients have severe complications, and is associated with a 30% lower rate of mortality or non-fatal MI. Similarly, the use of ACEIs or ARBs is recommended in patients undergoing acute coronary syndrome with HF or left-ventricular dysfunction.<sup>[5]</sup> However, data on the advantage of OMT remain limited. In our study, use of each individual agent was associated with a reduction in adverse events. However, OMT, which was a combination of DAPT, statins,  $\beta$ -blockers, and ACEIs/ARBs, showed better improvement of long-term outcomes compared with each agent alone.

In our study, the medication status in the long term remained suboptimal. The SYNERGY between percutaneous coronary intervention with TAXUS and cardiac surgery (SYNTAX) trial showed that the proportion of patients who received OMT was only 41.3% at discharge after revascularization (PCI, 50.2% vs. CABG, 31.2%) and nearly one-third at the 5-year follow-up (PCI, 39.6% vs. CABG, 35.7%).<sup>[6]</sup> Additionally, OMT was correlated with a remarkably lower hazard of death and the composite endpoint (death, MI, and stroke) in 5 years.<sup>[6]</sup> Therefore, essential measures should be taken to improve adherence to OMT in patients receiving revascularization surgically or interventionally.

OMT in this study played a crucial role in treating patients after PCI and should be recommended to all patients with complications. This recommendation is also supported by an analysis of almost 3000 patients after revascularization in the Project of Ex-vivo Vein Graft Engineering via Transfection (PREVENT) IV trial.<sup>[7]</sup> This trial showed that composite medication use, but not each individual agent (antiplatelets,  $\beta$ -blockers, ACEIs/ARBs, or lipid-lowering

**Table 1: Cox proportional hazards models for the associations between MACE and each individual agent and OMT.**

MACE 1 year	Unadjusted Cox proportional hazards models		Adjusted Cox proportional hazards models	
	HR (95% CI)	P	HR (95% CI)	P
DAPT	0.088 (0.059–0.131)	<0.001	0.122 (0.078–0.191)	<0.001
Statins	0.282 (0.191–0.416)	<0.001	0.435 (0.279–0.677)	<0.001
$\beta$ -Blockers	0.607 (0.426–0.865)	0.006	0.614 (0.387–0.972)	0.038
ACE inhibitor/ARBs	0.576 (0.402–0.827)	0.003	0.433 (0.281–0.667)	<0.001
OMT	0.563 (0.373–0.850)	0.006	0.382 (0.244–0.599)	<0.001

The HR for each specific drug was adjusted for age, BMI, a history of myocardial infarction, PCI, and HF, the number of coronary artery lesions, the medication status for each agent at hospitalization, and the use of the other three classes of drugs at follow up. The model for OMT was adjusted for age, BMI, a history of MI, PCI, and HF, the number of coronary artery lesions, and OMT at hospitalization. ACEIs: Angiotensin-converting enzyme inhibitors; ARBs: Angiotensin receptor blockers; BMI: Body mass index; CI: Confidence interval; DAPT: Dual antiplatelet therapy; HF: Heart failure; HR: Hazard ratio; MACE: Major adverse cardiovascular events; MI: Myocardial infarction; OMT: Optimal medical therapy; PCI: Percutaneous coronary intervention.

therapy), reduced the incidence of mortality or MI at a 2-year follow-up. However, a randomized clinical trial also showed that not all patients with newly diagnosed CHD benefited from  $\beta$ -blocker therapy.<sup>[8]</sup> This previous finding suggests that our advice may not be appropriate for patients with only a few comorbidities and more population-based research is required to investigate the effect of OMT on these patients.

Our study has some limitations. This was a monocentric, observational study in China, and therefore, the generalizability of our findings should be treated carefully. The use of drugs evaluated by patients' answers during the follow-up may not be reflective of their actual medication status. Moreover, we did not record specific reasons for the interception of OMT in the long term, including intolerance or contraindication of medication, and non-adherence in patients and physicians.

In conclusion, the use of OMT in patients with CHD undergoing PCI remains suboptimal. Adherence to OMT (DAPT, statins,  $\beta$ -blockers, and ACEIs/ARBs) is associated with a lower incidence of adverse cardiovascular events, including all-cause death, non-fatal MI, and stroke. OMT should be suggested to patients with CHD, especially those with comorbidities.

### Acknowledgements

The authors thank all the staff who participated in this study for their contributions to this study.

### Funding

This study was supported by grants from the Tianjin Science and Technology Committee (CN) (No. 16ZXMJJSY00080).

### Conflicts of interest

None.

### References

1. Pursnani S, Korley F, Gopaul R, Kanade P, Chandra N, Shaw RE, *et al.* Percutaneous coronary intervention versus optimal medical therapy in stable coronary artery disease: a systematic review and meta-analysis of randomized clinical trials. *Circ Cardiovasc Interv* 2012;5:476–490. doi: 10.1161/CIRCINTERVENTIONS.112.970954.
2. Hou Y, Yue Y, Zhao M, Jiang S. Prevalence and association of medication nonadherence with major adverse cardiovascular events in patients with myocardial infarction. *Medicine (Baltimore)* 2019;98:e17826. doi: 10.1097/MD.00000000000017826.
3. Ardati AK, Pitt B, Smith DE, Aronow HD, Share D, Moscucci M, *et al.* Current medical management of stable coronary artery disease before and after elective percutaneous coronary intervention. *Am Heart J* 2013;165:778–784. doi: 10.1016/j.ahj.2013.01.015.
4. Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, *et al.* Authors/Task Force Members. 2014 ESC/EACTS guidelines on myocardial revascularization: the task force on myocardial revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J* 2014;35:2541–2619. doi: 10.1093/eurheartj/ehu278.
5. Flather MD, Yusuf S, Kober L, Pfeffer M, Hall A, Murray G, *et al.* Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: a systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group. *Lancet* 2000;355:1575–1581. doi: 10.1016/s0140-6736(00)02212-1.
6. Iqbal J, Zhang YJ, Holmes DR, Morice MC, Mack MJ, Kappetein AP, *et al.* Optimal medical therapy improves clinical outcomes in patients undergoing revascularization with percutaneous coronary intervention or coronary artery bypass grafting: insights from the synergy between percutaneous coronary intervention with TAXUS and cardiac surgery (SYNTAX) trial at the 5-year follow-up. *Circulation* 2015;131:1269–1277. doi: 10.1161/CIRCULATIONAHA.114.013042.
7. Goyal A, Alexander JH, Hafley GE, Graham SH, Mehta RH, Mack MJ, *et al.* Outcomes associated with the use of secondary prevention medications after coronary artery bypass graft surgery. *Ann Thorac Surg* 2007;83:993–1001. doi: 10.1016/j.athoracsur.2006.10.046.
8. Andersson C, Shilane D, Go AS, Chang TI, Kazi D, Solomon MD, *et al.*  $\beta$ -blocker therapy and cardiac events among patients with newly diagnosed coronary heart disease. *J Am Coll Cardiol* 2014;64:247–252. doi: 10.1016/j.jacc.2014.04.042.

**How to cite this article:** Hao JY, Zhang J, Jing R, Liu JJ, Di CY, Lu YJ, Gao P, Wang YJ, Yang RF, Lin WH. Clinical prognosis of optimal medical therapy after percutaneous coronary intervention in patients with coronary heart disease. *Chin Med J* 2021;134:2003–2005. doi: 10.1097/CM9.0000000000001720