11 September 2013

Dear Editor,

Please find enclosed the edited full-text manuscript in Word format (file name ESPC Manuscript No: 4505.doc).

Title: Part I: Beta-blocker administration protocol for prospectively ECG-triggered coronary CT angiography

Author: Akmal Sabarudin, Zhonghua Sun

Name of Journal: World Journal of Cardiology

ESPS Manuscript NO: 4505

The manuscript has been improved according to the suggestions of reviewers:
1. Format has been updated
2. Revision has been made according to the suggestions of the reviewers:

- The authors reviewed beta-blocker administration for prospectively ECG-triggered coronary CT angiography. This review is well worth reading. I dare to raise my requests as the reviewer. 1) It is no doubt that intravenous administration of beta-blockers can achieve the target heart rate in a short period. However, I think that oral administration of beta-blockers has been widely used in the clinical setting, because of fewer adverse reactions. Therefore, the authors had better provide some information regarding oral administration of beta-blockers in the textbook and Figure 1 as possible. At least, in the present figure, the title should be changed to "Flow chart showing the intravenous administration of metoprolol protocol". Furthermore, the authors had better change the subtitle from "Administration of IV metoprolol" to another subtitle such as "Administration of beta-blockers and other alternative drug", because the contents regarding ivabradine were included in this section. 2) There were two disagreements of vocabulary. IV metoprolol vs. IV of metoprolol HR (page 6) vs. heart rate

Response: Thank you for your comments. Oral administration of beta-blockers has been added in the revised manuscript. Figure 1's title has been revised as suggested. IV metoprolol or IV of metoprolol HR has been corrected to make it consistent throughout the manuscript.

- In their paper entitled: - Beta-blocker administration protocol for prospectively ECG-triggered coronary CT angiography- Akmal Sabarudin and Zhonghua Sun illustrate a review about the role beta-blockers in prospectively ECG-triggered coronary CT angiography (CCTA). The manuscript is interesting and well made. I have only minor suggestions: Page 5, I suggest to change the title of chapter "Administration of IV metoprolol" in "Heart rate-lowering therapy" and to add the legend (table 1) in chapter Heart rate-lowering therapy. Page 7, I suggest to change: ? "Heart rate reduction is achieved approximately 10 beats per minute (bpm) at rest and during exercise at the recommended dosage (no more than 10 mg/day)" In "Heart rate reduction is achieved approximately 10 beats per minute (bpm) at rest

and during exercise at the recommended dosage (no more than 10-15 mg/day)" ? In general, beta-blockers are helpful in patients with irregular heart rate, either with premature atrial or ventricular contractions, supraventricular tachycardia and arrhythmias such as arterial fibrillation" ? In "In general, beta-blockers are helpful in patients with irregular heart rate, either with premature atrial or ventricular contractions, supraventricular tachycardia and arrhythmias such as atrial fibrillation" I suggest to consider the elimination of Trade name (manufacturer) in Table 1.

Response: Thank you for your comments. The subsection title on page has been revised as suggested. Trade name on table 1 has been removed.

- Comments This manuscript discussed the use of beta-blockers in the study of coronary CT angiography (CCTA). Authors have proposed a protocol for the administration of metoprolol before the CCTA. Besides, author also discussed the patient preparation before- and post-procedure care. It is well-known that heart rate has a major impact on the quality of the CCTA. Most centers have their own strategy and should be no difficulty to control heart rate before the procedure. Several important issues have not been addressed in this review: 1. Heart rate can be reduced by using oral β-blockers or calcium channel blockers a few days before the CCTA. Optimal heart rate control can be achieved in most patients with oral medications prior to the scan. If heart rate still >65 bpm approximately 1 hour prior to the scan, additional intravenous metoprolol may be helpful to achieve the optimal heart rate. Authors should add a paragraph mentioning the usefulness of oral medications in heart rate control. 2. A lot of CT angiographic literatures have reported that lower heart rates (<65 bpm) produce better-quality scans with improved visualization of all artery segments with more accurate stenosis detection. The definition of lower heart rate was 65 bpm in many previous articles. The paper from Pache et al [Ref. 1] even reported that optimal performance was observed in patients with heart rate below 70 bpm. This manuscript aim for 60 bpm, authors should discuss why they aim for such low heart rate. 3. Recently, advances in MDCT technology allow faster image acquisition or greater coverage so that an entire coronary data set can be acquired in one heartbeat. Given rapid enough image acquisition, heart rate control becomes less important for the acquisition of high-quality coronary CT. Quite a few papers have reported that the coronary CT angiography can be performed with 16-MDCT without hart rate control. I suggest authors provide a paragraph discussing the recent advance in the technology of this field. Ref. 1. Pache G, Saueressig U, Frydrychowicz A, et al. Initial experience with 64-slice cardiac CT: non-invasive visualization of coronary artery bypass grafts. Eur Heart J. 2006; 27(8):976-80.

Response: Thank you for your constructive comments. The usefulness of oral medications in heart rate control has been added. We agree to reviewer's comment on the technological developments on MDCT, in particular, dual-source CT and 320-slice CT, which enables acquisition of cardiac CT images, even in patients with high or irregular heart rates. This has been discussed in the revised manuscript. Furthermore, heart rate control is revised to less than 65 bpm.

Thank you again for publishing my manuscript in the *World Journal of Cardiology*.

Sincerely yours,

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