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Beta-blocker administration protocol for prospectively ECG-triggered coronary CT angiography

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INTRODUCTION

Prospectively ECG-triggered coronary computed tomography angiography (CCTA) is increasingly used in the diagnosis of coronary artery disease (CAD) due to its very low radiation dose with acceptable image quality[1-3]. This technique not only provides comparable diagnostic accuracy to that of conventional approach, retrospectively ECG-gated CCTA, but also shows superior advantage in reducing radiation dose (up to 83%), which is significantly lower than that from retrospectively ECG-gated protocol[1-4]. However, in order to ensure that image quality is acceptable for clinical diagnosis, prospectively ECG-triggered CCTA is restricted to patients with low (heart rates less than 65 bpm) and regular (HR variability < ± 5 bpm) during the scan[1,2,5].

With the advancements of computed tomography (CT) technology, the latest generation of multislice CT scanners enables customization of the scanning protocol to tailor individual patient’s condition such as using multiple heartbeat scanning modes or application of additional padding windows[5]. Thus, the prospectively ECG-triggered CCTA
Table 1 Beta-blocking agents

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Selectivity</th>
<th>Partial agonist activity</th>
<th>Lipid solubility</th>
<th>Onset</th>
<th>Hemodynamic effect</th>
<th>Plasma half-life</th>
<th>Elimination’s route</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-blockers</td>
<td>β1</td>
<td>Yes</td>
<td>Low</td>
<td>1-2 h</td>
<td>No</td>
<td>&gt; 24 h</td>
<td>No</td>
</tr>
<tr>
<td>Atenolol</td>
<td>β1</td>
<td>No</td>
<td>Low</td>
<td>1 h</td>
<td>1-2 min</td>
<td>24 h</td>
<td>No</td>
</tr>
<tr>
<td>Betaxolol hydrochloride</td>
<td>β1</td>
<td>No</td>
<td>Low</td>
<td>24 h</td>
<td>No</td>
<td>&gt; 24 h</td>
<td>No</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>β1</td>
<td>No</td>
<td>Low</td>
<td>1-4 h</td>
<td>No</td>
<td>24 h</td>
<td>No</td>
</tr>
<tr>
<td>Esmolol</td>
<td>β1</td>
<td>No</td>
<td>Low</td>
<td>No</td>
<td>1-4 min</td>
<td>No</td>
<td>5-10 min</td>
</tr>
<tr>
<td>Metoprolol tartrate</td>
<td>β1</td>
<td>No</td>
<td>Moderate</td>
<td>1 h</td>
<td>5-10 min</td>
<td>3-8 h</td>
<td>No</td>
</tr>
<tr>
<td>Metoprolol succinate</td>
<td>β1</td>
<td>No</td>
<td>Moderate</td>
<td>2-3 h</td>
<td>No</td>
<td>24 h</td>
<td>No</td>
</tr>
<tr>
<td>Nadolol</td>
<td>None</td>
<td>No</td>
<td>Low</td>
<td>1-2 h</td>
<td>No</td>
<td>24 h</td>
<td>No</td>
</tr>
<tr>
<td>Pindolol</td>
<td>None</td>
<td>Yes</td>
<td>Moderate</td>
<td>1-2 h</td>
<td>No</td>
<td>24 h</td>
<td>No</td>
</tr>
<tr>
<td>Propranolol hydrochloride</td>
<td>None</td>
<td>No</td>
<td>High</td>
<td>30 min</td>
<td>&lt; 1 min</td>
<td>6-12 h</td>
<td>4-6 h</td>
</tr>
</tbody>
</table>

PATIENT PREPARATION

There are several common indications for prospectively ECG-triggered CCTA inclusive of the CAD indications and non-CAD indications. CAD indications are inclusive of evaluation of coronary arteries in patients with new-onset heart failure to assess etiology, symptomatic patients at intermediate preset probability of CAD, patients with a chest pain syndrome regardless of acute or chronic with interpretable stress test. In certain circumstances, CCTA is required although non-CAD detection indications are presented such as suspected pulmonary embolism or aortic dissection or aneurysm, assessment of complex congenital heart disease, suspected coronary anomalies in asymptomatic patients, evaluation of pulmonary vein anatomy prior to atrial fibrillation radiofrequency ablation, evaluation of cardiac venous anatomy prior to biventricular pacing and evaluation of cardiac mass or pericardial condition when non-radiation imaging modalities are limited.

However, there are some contraindications to CCTA procedure which include pregnancy, severe anaphylactic contrast reaction, unable to comply with the scanning instructions such as fail to hold long breath-hold, renal insufficiency and clinically unstable patients. In addition, identification to contraindicated drug must be clarified before undergoing CCTA procedure inclusive of the pre-scan nitroglycerine such as severe aortic stenosis, hypertrophic cardiomyopathy and phosphodiesterase-5 (PDE-5) inhibitor and beta-blockers. For patients who are considered to undergo beta-blocker protocol, some guidelines have been suggested to avoid complications including screening contraindications to beta-blockers. The contraindications include sinus bradycardia, which is defined as a heart rate of < 60 bpm with systolic pressure of less than 100 mmHg; allergic to beta-adrenergic antagonists or its constituents; decompensated cardiac failure; asthma on beta-agonist inhalers; active bronchospasm; second or third-degree of atrioventricular (AV) block; Patients who are likely to have second- or third-degree AV block can be evaluated by generating a single-lead ECG strip.

Patient’s vital signs and pulse are also monitored and documented upon arrival. In patients with a sinus rhythm with heart rate < 65 bpm, no beta-blockers are required and therefore, the patient can be prepared for CCTA.
amination. In patients with irregular rhythm or/higher heart rate (≥65 bpm), the beta-blockers are given according to the protocol setting (Figure 1).

In addition, patients are required to follow all standard instructions for contrast-enhanced studies including fasting for at least 4 h prior to the scan, maintaining oral hydration with clear fluid up to 1 h before scan and need to hold metformin for a minimum of 48 h following the scan. Patients with non-severe anaphylactic contrast reaction in the past should receive pre-medication treatment to avoid the risk of current contrast reaction. A pre-medication protocol suggested as 50 mg of prednisone is administered orally 13, 7 and 1 h prior to scan with additional of 50 mg oral diphenhydramine (Benadryl) is taken 1 h prior to scan.

With regards to optimal heart rate control, caffeine product is not permitted within 12 h of CCTA. Moreover, severe hypotension can occur if PDE-5 inhibitors interact with nitrates. Therefore, patients are refrained from undertaking PDE-5 inhibitor drugs such as sildenafil (Viagra), vardenafil (Levitra) and tadalafl (Cialis) for at least 48 h before CCTA. Oral metoprolol might not be effective and other factors without proper scanning preparation, the effect of the oral metoprolol gives an advantage which may reduce the heart rate control with use of medications is necessary in 4- and 16-slice CT, but less common in 64- and post-64 slice coronary CT angiography due to improvement in temporal resolution. Pache et al. in their early study showed that 64-slice CT has high diagnostic accuracy in the assessment of coronary artery bypass grafts, despite the presence of irregular or high heart rates. Recent tech-

Most previous practices injected their first bolus of metoprolol once the patient is lying down supine on the CT examination table. Our practice suggests that first bolus administration of metoprolol (2.5 mg) is given before the patient is brought on the CT examination table; right after the IV line is set (pre-procedure). Then, the patient’s heart rate is monitored at the designated area under supervision of medically authorized personnel. This aims to avoid interruption of the procedure workflow and the delay time for beta-blockers to respond.

Although beta-blockers helped in lowering the heart rate, they also have negative inotropic effect and could decrease left ventricular contractility which may affect the assessment of ventricular function. However, ventricular function is only being evaluated by echocardiography or nuclear medicine studies and CCTA study is mainly performed for assessment of coronary arteries and degree of stenosis. Initially, two 2.5 mg doses of metoprolol are given with 5 min interval. Then two doses of 5 mg each are given 5 min apart with a total maximum dose of no more than 15 mg. Blood pressure and HR are monitored before each of the IV dose as stated in Figure 1. The beta-blockers’ administration is conducted under the supervision of the radiologists or cardiologists. Blood pressure and continuous ECG monitoring should always be used when giving IV metoprolol.

Ivabradine is another attractive option to reduce patient heart rate for CCTA procedure. Unlike metoprolol, ivabradine selectively inhibits if current in sinoatrial node cells that controls the spontaneous diastolic depolarization, resulting in the reduction of diastolic depolarization rate and heart rate. Therefore, it is useful in patients in sinus rhythm, but not in other rhythms such as atrial fibrillation. Ivabradine lowers heart rate at concentrations that do not affect other cardiac ionic currents. Therefore, ivabradine has no other direct cardiovascular effect. Therefore, the main pharmacodynamics of ivabradine in humans is a specific dose-dependent reduction in heart rate. Heart rate reduction is achieved approximately 10 beats/min (bpm) at rest and during exercise at the recommended dosage (no more than 10 mg/d) which leads to a reduction in cardiac workload and myocardial oxygen consumption. Ivabradine has a relatively short half-life of around 2 h and is currently only available as an oral preparation.

HEART RATE CONTROL-LESS COMMONLY APPLIED IN 64- AND POST-64 CT

Heart rate control with use of medications is necessary in 4- and 16-slice CT, but less common in 64- and post-64 slice coronary CT angiography due to improvement in temporal resolution. Pache et al. in their early study showed that 64-slice CT has high diagnostic accuracy in the assessment of coronary artery bypass grafts, despite the presence of irregular or high heart rates. Recent tech-
nological developments with the introduction of dual-source CT and 320-slice CT have overcome the limitation of early generation of multislice CT as the temporal resolution was significantly increased, thus image quality and diagnostic value of coronary CT angiography was less dependent on heart rates\cite{24,25}. It has been reported that dual-source coronary CT angiography shows improved diagnostic performance in patients with a wide range of different heart rates being included\cite{26,27}. Expansion of multislice CT systems from a prototype 256-slice to a 320-slice system has allowed for acquisition of whole heart coverage in one gantry rotation. Studies have shown that 320-slice coronary CT angiography demonstrated high sensitivity and specificity at per-patient, per-vessel and per-segment analysis in patients with atrial fibrillation\cite{28-30}. These results indicate that 320-slice CT has the potential to broaden the use of coronary CT angiography to more patients with high or irregular heart rates or those without responding well to the heart rate control.

**POST-PROCEDURE CARE**

All patients who are given IV metoprolol are observed for about 30 min once the scan is completed. If the patient presents with bronchospasm, an albuterol inhaler is given accordingly\cite{7,31}. If the patient’s heart rate drops to less than 45 bpm, administration of atropine is considered. However, if the patient is resistant to the atropine while the heart rate drops continuously, resuscitative measures and IV administration of beta-agonists need to be administered such as dopamine or epinephrine\cite{7}.

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. With atrial fibrillation, the negative chronotropic and dromotropic effects of the beta-blockers lengthen the diastolic portion of the

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### Figure 1  Flow chart showing the intravenous administration of metoprolol protocol in heart rate-lowering therapy.

CCTA: Coronary computed tomography angiography.
cardiac cycle\(^{[10]}\). In prospectively ECG-triggered CCTA, X-ray exposure occurs during a small portion of the cardiac cycle typically centered at mid-diastole at 75% of R-R interval\(^{[12]}\). Therefore, increasing diastole by beta-blockers would improve CCTA image quality. Previous studies showed that the vessel visibility was achieved with the single-segment reconstruction in patients with low heart rates (< 65 bpm) and with multisegment reconstructions in patients with high heart rates (> 65 bpm)\(^{[12,13]}\). Moreover, the visibility of right coronary artery also has been shown to improve significantly with the administration of beta-blockers. The proportion of the cardiac cycle spent in diastole increases as the heart rate decreases. Therefore, use of beta-blockers is suggested to increase the diastolic phase in the cardiac cycle\(^{[3]}\).

In conclusion, beta-blockers administration protocol has been discussed in this article with regard to its usefulness in preparing patient’s heart rate for prospectively ECG-triggered CCTA. Since use of medication is essential to ensure that coronary CT angiography will provide excellent diagnostic images with few artifacts, understanding the mechanism of beta-blockers in cardiac imaging will contribute to the efficient use of coronary CT angiography technique in clinical diagnosis.

REFERENCES


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