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Safety and efficacy of intravenous esmolol before prospective electrocardiogram-triggered high-pitch spiral acquisition for computed tomography coronary angiography

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Abstract

Background   In order to acquire a high quality image with a low radiation dose, prospective electrocardiogram (ECG)-triggered computed tomography coronary angiography (CTCA) requires a stable heart rate (HR) < 65 beats/min. Esmolol has the advantage of reducing HR. The objective of this article is to assess the value of intravenous esmolol treatment before prospective ECG-triggered high-pitch spiral acquisition for CTCA. **Methods**   From March 2013 to June 2013, 313 patients underwent prospective ECG-triggered CTCA. Two hundred and thirty two of them received esmolol before angiography. We retrospectively analyzed clinical characteristics, esmolol dose, radiation exposure dose, and the change in HR and blood pressure in these 232 patients. **Results**   A total of 232 patients with a HR > 65 beats/min before CTCA examination received intravenous esmolol treatment (mean dose of 57.26 ± 15.39 mg). The mean initial HR (HR1), slowest HR (HR2), and the HR 30 min after HR2 (HR3) were 75.06 ± 5.59, 60.75 ± 4.00, and 75.54 ± 5.96 beats/min, respectively (HR1 *vs.* HR2, $P < 0.0001$; HR1 *vs.* HR3, $P = 0.377$). The mean time from esmolol administration to HR2 was 24.25 ± 4.97 s and the mean effective radiation dose was 2.28 ± 0.02 mSv. **Conclusions**   HR could be rapidly controlled at an optimum level with intravenous esmolol before prospective ECG-triggered high-pitch spiral acquisition for CTCA. Consequently, the patients received a very low radiation dose.

1   Introduction

As an established, non-invasive method, cardiac computed tomography angiography (CTCA) can evaluate coronary arteries with a high negative predictive value for excluding significant coronary artery disease (CAD).[1,2] However, high radiation doses with conventional retrospective electrocardiogram (ECG)-gating is a concern because of the use of slow helical pitches and the X-ray beam being on throughout the cardiac cycle.[3] To decrease the radiation dose, a prospective ECG-triggering method was developed. Prospective ECG-triggering, which combines step-and-shoot axial data acquisition and an incrementally moving table with adaptive ECG-triggering, represents the most

effective approach with a significant reduction in radiation dose by 60%–80% compared to retrospective ECG-gating.[4–6] Scanning in CTCA with prospective ECG-triggering is exclusively performed during the short diastole phase, so this technique requires a low heart rate (HR) to obtain good image quality.

Esmolol, a short-acting HR-lowering agent, has highly selective beta-1 blocking capabilities. This drug can rapidly reduce HR and is eliminated in several minutes. Similarly, some articles show that oral beta blockers are effective for reducing HR,[7,8] but the time to onset is very long; and patients need to wait 48 h before undergoing examination after receiving oral beta blocking treatment. Therefore, esmolol is an ideal agent for controlling HR before prospective ECG-triggering.

In this study, we not only observed the effects of intravenous esmolol for achieving optimum HR before prospective ECG-triggering scanning, but also the time to onset of intravenous esmolol and the time to HR and blood pressure recovery.

2 Methods

2.1 Patient preparation

A total of 232 patients referred for prospectively triggered CTCA received esmolol in this study. All of the patients gave written informed consent, and the study protocol was approved by the local ethical committee. Patients with atrial fibrillation, known arrhythmias, impaired renal function (serum creatinine >1.5 mg/dL), known allergy to contrast medium, pregnancy, baseline HR < 65 beats/min, left ventricular ejection fraction < 35%, blood pressure < 100/60 mmHg, other known contraindications to beta blockers, such as second- and third-degree atrioventricular block, congestive heart failure, severe peripheral vascular disease, or chronic obstructive pulmonary disease were excluded from this study. All patients were initially assessed in the outpatient clinic and baseline HR (HR1), systolic blood pressure (SBP1), diastolic blood pressure (DBP1), and a 12-lead ECG were obtained.

2.2 HR control

After obtaining informed consent, patients received their first dose of intravenous esmolol (0.8 mg/kg); 20 s later if the HR was still > 65 beats/min, another dose of 0.8 mg/kg was administered. If a patient's HR was still > 65 beats/min after the second administration, we did not administer any additional drugs, and the patient received ECG gating acquisition or coronary angiography retrospectively. The monitor recorded the slowest HR (HR2), the HR 30 min after HR2 (HR3), systolic blood pressure (SBP2, SBP3), and diastolic blood pressure (DBP2, DBP3) at the same time as HR2 and HR3.

2.3 Image acquisition

The patients were examined using a dual-source CT system (Somatom Definition Flash, Siemens Medical Solutions, Forchheim, Germany) with a tube voltage of 100 kV. Scanning began when the patients' HR was less than 70 beats/min. Contrast media were injected, 60–80 mL (scaled to body weight) of Ultravist (370 mgI/mL, Shering AG, Guangzhou, China), or Omnipaque (350 mgI/mL, GE Healthcare Limited, Shanghai, China), followed by a 40 mL saline bolus at a rate of 4.5–5.0 mL/s (scaled to venous condition) using a double-head injector (Medrad Stellant CT Injector System, Indianola, PA, USA).

Prospective ECG tube-current modulation was used at its maximum for 35%–75% of the R-R interval in all scans, triggered by the enhancement (100 HU) of the region of interest (ROI) in the ascending aorta with a delay of 10 s.

The estimated radiation dose using this CTCA protocol was approximately 2–4 mSv.

2.4 Statistical analysis

All continuous variables are presented as means ± SD and categorical variables as percentages. The independent Student's *t*-test was used to assess differences in continuous variables. $P < 0.05$ was considered indicative of statistical significance.

3 Results

The baseline characteristics of the patients are summarized in Table 1. The mean age was 56 (31–83) years, and 155 (67%) patients were males; 35 patients had diabetes, 76 patients had a history of smoking, 88 patients had hyperlipidemia, 110 patients had hypertension, and 11 (15%) patients had a previous old myocardial infarction (OMI). Fifteen patients (6%) had a history of coronary artery bypass graft (CABG). Twenty one patients (9%) had a history of percutaneous coronary intervention (PCI). Mean body mass index (BMI) was 24.27 ± 2.37 kg/m^2.

Table 1. Baseline characteristics of the patients ($n = 232$).

Mean age (range), yrs	56 (31–83)
Males	155 (67%)
Current smoker	76 (33%)
Patients with diabetes	35 (15%)
Patients with hypertension	110 (47%)
Patients with hyperlipidemia	88 (38%)
BMI (kg/m^2)	24.27 ± 2.37
Patients witn OMI	11 (5%)
Patients with previous CABG	15 (6%)
Patients with previous PCI	21 (9%)

Data are presented as *n* (%) or other, as indicated. BMI: body mass index; CABG: coronary artery bypass graft; OMI: old myocardial infarction; PCI: percutaneous coronary intervention.

3.1 HR

Esmolol effectively and rapidly reduced HR (Figure 1). It took a mean of 24.25 ± 4.97 s from esmolol administration to HR2 acquisition; HR was reduced from 75.06 ± 5.59 beats/min (HR1) to 60.75 ± 4.00 beats/min (HR2; $P < 0.0001$). After examination, the patients had a 30 min rest and HR3 returned to 75.54 ± 5.96 beats/min (HR1 *vs*. HR3, $P = 0.377$). Only five patients (2%) had a HR2 > 65 beats/min before CTCA. One patient (0.4%) had asymptomatic sinus bradycardia with HR < 50 beats/min.
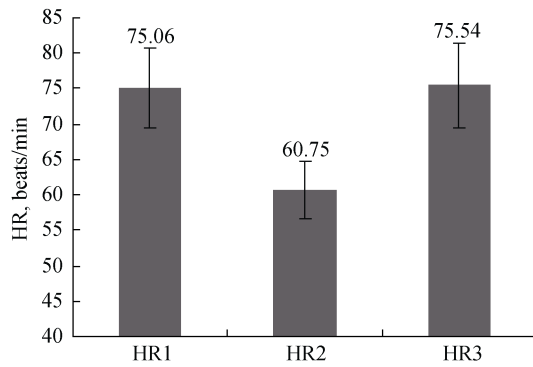
Figure 1. Variations in HR after intravenous esmolol treatment. A mean of 24.25 ± 4.97 s after intravenous esmolol, heart rate decreased from HR1 to HR2, (*P* = 0.000). Thirty minutes later, the heart rate increased to HR3 (HR1 *vs*. HR3, *P* = 0.377). HR: heart rate; HR1: initial heart rate; HR2: the slowest heart rate; HR3: heart rate 30 min after the slowest heart rate.

3.2 Blood pressure

Blood pressure also decreased significantly (Figure 2) with SBP falling from 131.91 ± 14.64 mmHg (SBP1) to 123.17 ± 14.76 mmHg (SBP2), *P* < 0.0001, and DBP falling from 82.13 ± 8.23 mmHg (DBP1) to 77.18 ± 7.1 mmHg (DBP2), *P* < 0.0001, Figure 3. Thirty minutes later, SBP3 returned to 132.7 ± 13.59 mmHg (SBP1 *vs*. SBP3, *P* = 0.728), and DBP3 returned to 82.53 ± 7.49 mmHg (DBP1 *vs*. DBP3, *P* = 0.575). One 82 year old patient (0.4%) felt dizziness after CTCA, and his blood pressure decreased to 88/50 mmHg and his HR was 63 beats/min. The patient laid down to rest and 20 min later his symptoms disappeared and his blood pressure returned to 121/67 mmHg.
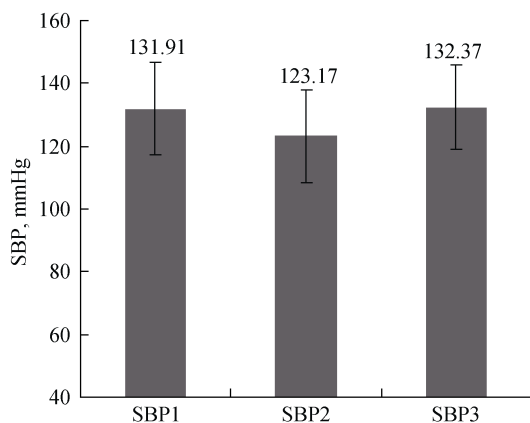

Figure 2. Variations in SBP after intravenous esmolol treatment. After esmolol administration, SBP1 decreased to SBP2 (*P* = 0.000). Thirty minutes later, HR increased to SBP3 (SBP1 vs SBP3, *P* = 0.728). HR: heart rate; SBP: systolic blood pressure; SBP1: initial SBP; SBP2:the lowest SBP; SBP3: 30 min after the lowest SBP.
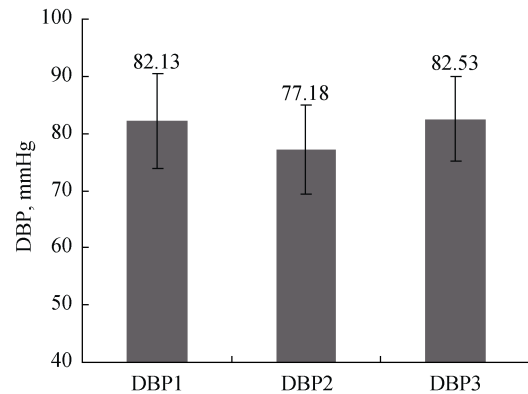

Figure 3. DBP variations after intravenous esmolol treatment. After esmolol administration, DBP1 decreased to SBP2 (*P* = 0.000). Thirty minutes later, DBP returned to pre-treatment levels (DBP3; DBP1 *vs*. DBP3, *P* = 0.575). DBP: diastolic blood pressure; DBP1: initial DBP; DBP2: the lowest DBP; DBP3: 30 min after the lowest DBP.

3.3 Esmolol and radiation dose

The patients received a mean esmolol intravenous dose of 57.26 ± 15.39 mg and a mean radiation dose of only 2.28 ± 0.02 mSv. No adverse reactions to the contrast medium were noted during or after CTCA in any patient.

4 Discussion

CTCA has emerged as an excellent non-invasive tool for the diagnosis of CAD.[9–11] Traditional CTCA is frequently performed using retrospective ECG gating, which can result in high radiation exposure exceeding 30 mSv.[12] In order to reduce radiation exposure, the prospective ECG-triggered high-pitch spiral acquisition method was developed. Average radiation doses of less than 5 mSv have been reported for prospective scan modes;[13–15] however, in order to acquire optimum image quality, prospective ECG-triggered high-pitch spiral image acquisition requires a stable HR of about 60–65 beats/min.

In this study, we found that most patients needed an intervention to maintain the desired HR for optimum image quality acquisition. Some studies have reported that oral beta-blockers can obtain this optimum HR, but the onset time, at about 48 h, is lengthy.[7,16] The half-life of oral beta-blockers is also long and this can have some potential side effects, such as sustained tachycardia. In this study using Chinese patients, we found that bolus doses of esmolol at 40–150 mg were well tolerated and effective for lowering the HR below 65 beats/min in 84.91% of patients after a mean of 24.25 ± 4.97 s. Because the HR was rapidly controlled to a suitable level, we could utilize prospective

ECG-triggered high-pitch spiral acquisition methods to acquire images with a very low effective radiation dose. Thirty minutes later, we examined HR and blood pressure again; HR and blood pressure both recovered to equivalent levels prior to esmolol administration. Only one patient, an 82 year old male, felt dizziness; no other adverse effects were noted.

Esmolol has the obvious advantage of generating the desire HR. It is also available for intravenous use, both as a bolus and as an infusion, and is metabolized via rapid hydrolysis by red blood cell esterases, which is not dependent on renal or hepatic function.[17] The prompt onset and offset of esmolol effects make it an appealing drug when short duration of HR and blood pressure control are desired. Patients who have a fast HR can receive CTCA immediately with a very low radiation dose after a bolus intravenous esmolol; however, patients would have to wait for a long time to the optimal HR if they took some oral drugs to control HR. With its short half-life, esmolol avoids possible prolonged side effects seen in oral beta-blockers. Esmolol has also been found to be relatively safe in patients with bronchospastic diseases.[18,19]

Intravenous esmolol still has some risks such as bradycardia, hypotension and tracheospasm, *etc.* In this study, One 82 year old patient felt dizziness after CTCA, and his blood pressure decreased to 88/50 mmHg and his HR was 63 beats/min. After having a rest and being given some fluid, his blood pressure returned to 121/67 mmHg. Because of the potential risks of intravenous esmolol, the radiologists prefer to administer orally ivabradine or metorprolol to patients as they have little experience to deal with the complications of intravenous esmolol.

4.1 Limitations

Due to the retrospective nature of this study, some baseline characteristics, such as echocardiography, are absent in some outpatients. Although some studies have shown that esmolol is safe for bronchospastic patients, chronic obstructive pulmonary disease was an exclusion criterion in this study.

4.2 Conclusions

Bolus intravenous esmolol is safe and effective for reaching optimum HR in patients before prospective ECG-triggered high-pitch spiral acquisition for CTCA. Through intravenous esmolol, doctors can acquire an optimal HR for CTCA and patients can receive lower doses of radiation.

Acknowledgment

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