Computed tomography (CT) is a powerful tool for generating clinically useful information. Iodinated contrast medium (ICM) is usually used to enhance the imaging intensities and the tissue contrast, anyway it can cause a variety of adverse reactions. Ionic ICMs are associated with more serious reactions than non-ionic ICMs, but the Bureau of National Health Insurance only pays for the use of ionic ICM with CT in Taiwan, except for certain specific indications. The goal of our study is to develop a real-time method for monitoring patients who received rapid intravenous injection of ionic ICM during CT examination.

Sixty-seven patients were enrolled in this study (aged 48±13 years, mean±SD), comprising 38 males (aged 47±11 years) and 29 females (aged 48±14 years), who received CT examinations with intravenous bolus injection of iothalamate meglumine. A standard pulse oximeter was used to detect the heart rate (HR) changes that were considered to represent the response to the ionic ICM. The results showed that the HR per minute rose rapidly to peak and then returned to baseline slowly. Patients felt much discomfort when there was rapid increase in HR or when the HR-recovery time is longer. Moreover, the HR-increase after intravenous injection of ionic ICM is greater in younger patients under 50 years than in older patients.

We conclude that an oximeter can be used to reliably monitor the pathophysiologic condition of patients and the discomfort related to tachycardia during a rapid intravenous injection of ICM for CT.

Computed tomography (CT) is a powerful tool for revealing anatomy, detecting abnormality, and staging of diseases. An intravenous iodinated contrast medium (ICM) is frequently used to enhance the tissue contrast and clarify the disease characteristics during CT examination. Rapid bolus intravenous injection of ICM by using a power injector is mandatory to take full advantage of the rapid acquisition time of multidetector CT [1].

The use of ICM can cause a variety of adverse reactions such as nausea, vomiting, vasovagal reaction, urticaria, respiratory distress, chest tightness, and even anaphylactic shock [2-6], which makes it important to monitor the patient’s condition during CT examinations. Ionic ICMs are associated with more serious adverse reactions than non-ionic ICM, but the Bureau of National Health Insurance only pays for the use of ionic ICM with CT in Taiwan, except for certain specific indications. Traditionally the patients are monitored by a video camera during CT scanning. However this does not monitor their physiological condition. The heart rate (HR) is usually increased during rapid bolus intravenous injection of ICM. The ionic ICM carries electrical charges, and the heart function could be affected [7]. The HR response had been used to estimate the heart function [8-10]. Therefore, in this study, we
used a standard pulse oximeter (SpO₂) during CT examinations to monitor the HR, which may indicate the physiologic condition of patients. The study was designed to evaluate two factors for which there is no related data: (1) the normal HR increase pattern during a rapid bolus intravenous injection of ionic ICM and (2) the timing of alert during the scanning with oximeter monitoring the patients.

**MATERIALS AND METHODS**

The study period was from December 2005 through June 2006. The enrolled patients were those who accepted an intravenous injection of iothalamate meglumine for CT scan, and signed the informed consent. There was a total number of 67 patients (aged 48 ± 13 years, mean ± SD), comprising 38 males (aged 47 ± 11 years) and 29 females (aged 48 ± 14 years). With the patient lying on the CT couch, we applied the SpO₂ probe (SA200, Rosmax, Taiwan) to the finger or toe and recorded the SpO₂ plethysmograph waveform. We marked the SpO₂ plethysmograph waveform when the power injector (Meorao Viston CT injection system) for the rapid intravenous injection of contrast medium started. The patient lay on the couch for 5 minutes after the CT examination, with the SpO₂ plethysmograph waveform recording continuously. A total volume of 90-95 ml of iothalamate meglumine (conray, 282 iodine mg/ml, 1400mOsm/kg at 37°C) was injected at a rate of 2.5-3.5 ml/second, depending on the age of the patient and the accessibility of the vein. The degree to which the patient felt uncomfortable during the iothalamate meglumate injection was assessed by a nurse with questionnaire, based on the five symptoms of palpitation, chest tightness, dyspnea, torridness, and nausea/vomiting, with each symptom scored as severe (9 scores), moderate (6 scores), mild (3 scores) or none (0 score). The degree of physical discomfort was based on the summed values of all the symptoms experienced. We categorized the patients into two groups. The discomfort group included patients who experienced uncomfortable with a score greater than 3.

The sampling rate of the SpO₂ monitor was 250 Hz, and data were transferred to the computer via its serial port. We used the infrared plethysmograph waveform to extract the HR. HR data were extracted from plethysmograph waveforms, 120- and 300-second before and after injection, as an indicator of the physiological responses to iothalamate meglumine. Because the plethysmograph waveform contains two minor peaks in a single period, moving-average filters were applied twice to reduce the high-frequency fluctuations and merge the minor peaks into a sinusoidal waveform [11]. Then, the positive-peak detection was used to determine the positive peaks of plethysmograph waveform. The moving-average filter was defined as

\[
H(z) = \frac{1}{70} \sum_{k=0}^{69} z^{-k}.
\]  

(1)

Then, the raw data, \(x[n]\), were filtered twice,

\[
X2(z) = X1[z]H[z],
\]  

(2)

and

\[
X1[z] = X[z]H[z],
\]  

(3)

then

\[
X2[z] = X[z](H[z]H[z]).
\]  

(4)

For positive-peak detection, first, define \(p[n]\) as follow:

\[
p[n] = \sum_{i=1}^{m} x2[n+i] \quad n = 1 \cdots m
\]  

(5)

where \(n\) is the sample point. If \(p[n]>p[n-1]\) and \(p[n]>p[n+1]\), then positive-peak, \(r[k] = n \quad k = 1 \cdots l - 1\),

(6)

where \(l\) is the number of beats. The HR interval can be explored as

\[
HR[k] = r[k+1] - r[k] \quad k = 1 \cdots l - 1.
\]  

(7)

Figure 1 illustrates how the HR is extracted from the plethysmograph waveform, in which the raw plethysmograph waveform is \(x[n]\), \(x1[n]\) is filtered once, \(x2[n]\) is filtered twice.

There were many investigations suggesting the correlation between heart function and HR response [12-14], and hence in this study we assessed the correlation between the HR response and the degree to which patients felt uncomfortable during CT examinations. Figure 2 presents a typical HR response during a CT examination, and shows the following time checkpoints that we defined to describe the HR response: injection (point A), HR increase (point B), maximum HR response (point C), and recovery (point D). The reference HR was defined as the average HR at 2 minutes before injecting the ionic ICM. The HR-transient time, \(T_{AB}\), was defined as where the HR increased by 5% relative to the reference HR; HR-increase time, \(T_{RC}\), was defined as where the HR increased from point B to point C; and
Iothalamate meglumate induced tachycardia

HR-recovery time, $T_{CD}$, was where the HR decreased from point C to point D. Moreover, the HR-response time was $T_{BC}$, and HR-total response time was $T_{AB} + T_{BC} + T_{CD}$. HR$_{BC}$ was HR-increase from point B to point C. HR-increase ratio was the ratio of HR at point C over HR at point B ($HR_C / HR_B$). Student’s t-test was used for statistics and a p value less than 0.05 was considered statistically significant.

RESULTS

After rapid intravenous injection of iothalamate meglumine, the HR will rise rapidly to peak and then return to baseline slowly. The distribution of severity of each symptom induced by the ionic ICM injection was listed on Table 1. The comfort group comprised 32 patients (aged 49 ± 11 years) and the discomfort group comprised 35 patients (aged 46 ± 14 years). The values of the parameters defined in Fig. 2 are listed in Table 2 as well as the comparison between these two groups. The HR-response time of discomfort group (155 ± 52 seconds) was greater than that of the comfort group (126 ± 36) ($p < 0.05$). In addition, the HR-increase of discomfort group (27 ± 12.2 beats/minute) was greater than that of the comfort group (18 ± 9.9) ($p < 0.005$).

We also compared between a younger group ($n = 41$, aged 37 ± 7.0 years) and an older group ($n = 26$, aged 57 ± 8.0 years), using a cutoff age of 50 years. We found that the young group has a larger HR-increase than the older group. Table 3 indicates that the HR-increase for younger and older groups, were 27 ± 13 and 19 ± 10 beats/minute ($p < 0.05$), respectively. But, in the HR-recovery time or HR-response time, we couldn’t find difference between these two groups.

Figure 1. Extraction of the HR from the raw plethysmograph waveform.

Figure 2. A typical HR response during a CT examination. Points A: injection; point B: HR increase; point C: maximum HR response; point D: HR recovery. $T_{AB}$: HR-transient time; $T_{BC}$: HR-increase time; $T_{CD}$: HR-recovery time; $T_{AB} + T_{BC} + T_{CD}$: HR-response time; $T_{AB} + T_{BC} + T_{CD}$: HR-total response time; $HR_{BC}$: HR-increase.

Table 1. The distribution of severity of each symptom induced by ICM injection.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Severe</th>
<th>Moderate</th>
<th>Mild</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpitation</td>
<td>1</td>
<td>4</td>
<td>17</td>
</tr>
<tr>
<td>Chest tightness</td>
<td>1</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>1</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Torridness</td>
<td>0</td>
<td>0</td>
<td>64</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>0</td>
<td>0</td>
<td>11</td>
</tr>
</tbody>
</table>

DISCUSSION

The prevalence of immediate type of mild
The discomfort rate is 52% (35/67)
of appetite, taste disturbance, headache, fatigue, fever, chills, flu-like symptoms, joint pain,
Other reported non-specific adverse reactions of ICM are fever, chills, flu-like symptoms, joint pain, and thus our data are more representative of the
adverse reactions of ionic ICM and non-ionic ICM is 3.8-12.7% and 0.7-3.1%, respectively, and the corresponding prevalence of severe immediate reactions is 0.1-0.4% and 0.02-0.04%. Although the adverse reactions observed with the nonionic ICM are usually less severe than the reactions induced by the ionic ICM, the associated death rates for the two types of ICM are not significantly different. The mortality rate has been estimated to be in the range of 1 in 100,000 examinations [15]. Some adverse reactions of ICM are idiosyncratic with unclear pathogenesis, such as hives, itching, facial/laryngeal edema, bronchospasm, and anaphylactoid shock. Other reported non-specific adverse reactions of ICM are fever, chills, flu-like symptoms, joint pain, loss of appetite, taste disturbance, headache, fatigue, depression, abdominal pain, constipation, and diarrhea [2-5, 15]. The discomfort rate is 52% (35/67) in our study. The discomfort rate in our study did not represent adverse reaction since it just indicates physiological discomfort felt subjectively by the patients.

Ionic ICM can decrease cardiac function and induce rhythm disturbance in many ways. The additional electrical charges of an ionic ICM can disturb the generation and conduction of these delicate electrical currents of the heart. An ionic ICM carries negatively charged ions, which bind to the positively charged calcium ions, resulting in decreased pumping action of the myocardium and decreased cardiac contractility. In contrast, since non-ionic ICM does not carry electrical charges, they have less effect on the conduction system and cardiac contractility. In addition, the high osmolality of the intravenous ionic ICM will cause a rapid water influx into the vascular space, resulting in an increased volume load and workload of the heart. Also, the hyperosmolality and chemotoxicity of an ionic ICM can induce peripheral vasodilatation, which will also affect the HR. These combined effects all contribute to the HR change directly or indirectly via autonomic feedback during and after intravenous ionic ICM injection [7].

The resuscitation for patients with life-threatening adverse reactions of ICM is urgent. Our design of apply an oximeter to patients during CT scanning in an attempt to detect the physiological change as soon as possible. The audible alarms, from the oximeter before and after the injection of an ionic ICM, provide information on the physiologic response of the patients. After the rapid injection of an ionic ICM, the HR will rise to peak rapidly and then return slowly to baseline. It was found that the patient discomfort was most strongly (and positively) related to the HR-increase after the rapid injection of an ionic ICM. We also found that a longer HR-recovery time will result in much discomfort. In addition, the HR-increase was more prominent in patients under 50 years. The exact reason why younger patients have greater HR-increase is unclear, but our results suggest younger patients response to the intravenous ionic ICM injection much strongly and suffer more discomfort.

One issue that should be emphasized is that we extracted the HR from the raw data of the oximeter, and thus our data are more representative of the instantaneous HR. In contrast, the HR displayed on the commercially used oximeter is a calculated averaged value, and therefore the displayed HR changes are smaller than the actual condition. None of our patients suffered from severe adverse reaction of ionic ICM during the course of the study, and thus

<table>
<thead>
<tr>
<th>Table 2. Comparison between comfort and discomfort groups.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time checkpoint</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>HR-transient time</td>
</tr>
<tr>
<td>HR-increase time</td>
</tr>
<tr>
<td>HR-recovery time</td>
</tr>
<tr>
<td>HR-response time</td>
</tr>
<tr>
<td>HR-total response time</td>
</tr>
<tr>
<td>HR-increase</td>
</tr>
<tr>
<td>HR-increase ratio</td>
</tr>
</tbody>
</table>

* p < 0.05, ** p < 0.005.

<table>
<thead>
<tr>
<th>Table 3. Comparison between younger and older groups.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time checkpoint</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>HR-transient time</td>
</tr>
<tr>
<td>HR-increase time</td>
</tr>
<tr>
<td>HR-recovery time</td>
</tr>
<tr>
<td>HR-response time</td>
</tr>
<tr>
<td>HR-total response time</td>
</tr>
<tr>
<td>HR-increase</td>
</tr>
<tr>
<td>HR-increase ratio</td>
</tr>
</tbody>
</table>

* p < 0.05.
Iothalamate meglumate induced tachycardia

we do not know whether such an event would result in a different curve of HR variability.

In summary, we conclude that an oximeter can be used to monitor the physiologic condition of the patient reliably during a rapid intravenous injection of ionic ICM for CT. The HR will rapidly increase to a peak and then return slowly to baseline. Patients with a greater HR-increase and a longer HR-recovery time suffer more discomfort, and in younger patients than in older patients the peak HR-increase is usually greater.

REFERENCES

4. Morcos SK, Thomsen HS. Adverse reaction to iodinated contrast media. European Radiology 2001; 11: 1267-1275
7. Schild HH. To See or Not to See—Everything about The Contrast Media. Schering AG 2002; 20-22
8. Desai M, Pena-Almaguer ED, Mannings F. Abnormal heart rate recovery after exercise as a reflection of an abnormal chronotropic response. Am J Cardiol 2001; 87: 1164-1169
14. Desai MY, Pena-Almaguer ED, Mannings F. Abnormal heart rate recovery after exercise as a reflection of an abnormal chronotropic response. Am J Cardiol 2001; 87: 1164-1169
快速靜脈注射 Iothalamate Meglumine 引起的短暫性心跳加速及病人不舒服度的探討

楊石崇 1  劉省宏 2  張剛鴻 3

林新醫院  放射診斷科 1
元培科學科技大學  醫學工程系 2
亞洲大學  電腦與通訊學系 3

電腦斷層對於檢查病患而言，是一種非常強而有力的工具。它對於顯示人體解剖結構、發現疾病、顯示疾病分期等，既方便又有效率。在電腦斷層檢查過程中，常會經由靜脈注射含碘顯影劑，以增強組織的對比度，突顯出病兆的特徵。在多排偵測器電腦斷層（MDCT）時代，常常更必須配合使用高壓注射器（power-injector）迅速且大量地經靜脈注射含碘顯影劑，以充分发挥多排偵測器電腦斷層快速掃描的優點。離子性含碘顯影劑的副作用遠多於非離子性含碘顯影剝，但除少數適應症外健保局目前只給付離子性含碘顯影劑的費用。本研究的目的在建立電腦斷層快速靜脈注射離子性含碘顯影剝的生理即時監測系統，以及早發現病人的不舒服。

在電腦斷層快速靜脈注射離子性含碘顯影剝 Iothalamate Meglumata 時，我們利用血氧濃度偵測器與雙波長脈波感測器即時監測病人心跳變異。我們共收集了 67 個案例（平均年齡 48 ± 13 歲）。結果顯示靜脈注射離子性含碘顯影剝後，每分鐘心跳數會急速上升而後緩下降。心跳回復時間較慢者或心跳加速較多者會感覺較不舒服，不舒服與舒服兩群間的數據差異具有統計學上的意義。小於 50 歲的族群心跳加快顯著高於大於 50 歲的族群。

在電腦斷層快速靜脈注射離子性含碘顯影剝時，利用血氧濃度偵測器與雙波長脈波感測器即時監測病人病理生理變化是一個可靠的方法，可讓我們及早發現病人的不舒服。