

# Incidence, Clinical Presentation and Outcome in Patients with Long Asystole Induced by Head-up Tilt Test

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## Abstract

Long asystole during head-up tilt test is uncommon. When the duration is more than 5 seconds, it has been called "malignant". Although recent reports have demonstrated long asystole response is quite a benign course. Owing to most of these reports came from western countries, ethnic variation is possible. The clinical data about this subset of patients are reported herein. Head-up tilt test was employed for 604 patients with syncope of unknown origin. The protocol included 30min passive tilt test and 30min isoproterenol infusion which increased the heart rate up to 20% from baseline. The response patterns were analyzed and categorized. The prolonged asystole was searched. Follow up was made at the outpatient clinic or by phone during October 2004. Two hundred forty-two patients(40.1%) had positive response. 172 patients(71.1%) with the mixed type, 60 patients(24.8%) with the vasodepressive type and only 10 patients(4.1%) with the cardioinhibitory type. Three patients(1.2%) had prolonged asystole. One young girl and two elderly males with atrial fibrillation. The young girl received midodrine treatment and stop the medication 6 months later with only few recurrence of syncope. The two elderly received pacemaker implantation without syncope recurrence. The incidence of long asystole during head-up tilt test in our patients was much lower than that of western countries. Head-up tilt test may be an helpful tool for evaluation of syncope in elderly patients with atrial fibrillation. ( J Intern Med Taiwan 2005; 16: 134-138 )

**Key Words** : Head-up tilt test, Long asystole, Syncope

## Introduction

Head-up tilt test is documented a useful tool for diagnosing vasovagal syncope. The pathophysiolo-

gical mechanism underlying tilt-induced vasovagal syncope is still not completely known. Various physiopathological responses have been observed<sup>1</sup>. At present, vasovagal syncope is generally considered a

benign condition, although some authors have related it to rare events of sudden death<sup>2</sup>. Among patients developing bradycardia during the head-up tilt test, there is a subgroup in whom asystole occurs and on rare occasion has even required measures of cardiopulmonary resuscitation<sup>3</sup>.

By the American definition, when the duration lasts longer than 5 seconds, it is defined as malignant vasovagal syncope<sup>3</sup>. By the European definition, it is a vasovagal attack with so little warning as to render the patient at risk for sustaining an injury at the onset of syncope<sup>4</sup>. A recent study has demonstrated long asystole during head-up tilt test does not imply a malignant outcome and syncope recurrence is low<sup>5</sup>. Because most of these reports from western countries, ethnic variation is possible. Therefore, the aim of this paper is to present the clinical data of this subset of our patients.

## Methods

From November 1995 to September 2004, 604 patients with syncope of unknown origin received head-up tilt test at the Cardiology Section of our Hospital. All patients were studied after a protocol that at least included clinical history, physical examination, baseline 12-lead electrocardiogram (ECG), 24-hour ambulatory ECG monitoring and chest X-ray film. After informed consent was obtained, all patients underwent head-up tilt test off rugs. All tests were performed in the morning on the patients fasting at least 6 hours. Baseline heart rate and arterial pressure were measured after the patients had been in supine position for 15 min. During the test, the patients were monitored with ECG and the blood pressure was measured every 1 min with an automatic sphygmomanometer.

Patients were first tilted to 80 degrees for 30min, if no positive response then will lie down for 10min. Isoproterenol infusion then begin with 1  $\mu\text{g}/\text{min}$  and was adjusted to at least 20% increase in heart rate from baseline. The maximal dose used was 5  $\mu\text{g}/\text{min}$ .

This would continue till the positive response or 30min duration<sup>6</sup>. The positive response was defined as occurrence of syncope or presyncope (severe lightheadedness, severe weakness, transient graying of vision, or hearing loss with difficulty in maintaining postural tone). Abnormal test response is classified as the vasodepressive, cardioinhibitory and mixed type<sup>7</sup>. Patients with a prolonged asystole response were searched. Follow up was made at the outpatient clinic or by phone during October 2004.

## Results

Two hundred forty-two patients (40.1%) had positive response during head-up tilt test. The average age was  $41.7 \pm 16.9$  (from 15 to 78 years old). Sixty-five percent patients were female. The response was mixed in 172 patients (71.1%), vasodepressive in 60 patients (24.8%) and cardioinhibitory in only 10 patients (4.1%). In these 10 patients, 3 patients presented long asystole during the test. Their clinical presentations were quite unique as described below.

The first patient was a 68 years old male, a documented case of chronic atrial fibrillation, and regular followed up at the outpatient clinic. He began to suffer from syncope for four times in one month. Holter monitoring was first arranged but without significant pause, so head-up tilt test was performed. After tilted for 20 min, the patient lost consciousness and ECG monitoring showed pause for 8 seconds. He then received pacemaker implantation (VVIR form) in October 1998, with no syncope recurrence noted thereafter.

The second patient is a 15 years old female, experienced frequent attacks of syncope in recent days. In virtue of the frequency, they might appear even 2-3 times in one day. She was brought by her mother to our cardiology and neurology OPD clinic. A series of examinations including echocardiography, Holter monitoring, electroencephalography and even CT scan of brain. All revealed negative finding. Finally, head-up tilt test was performed. After tilted for 15

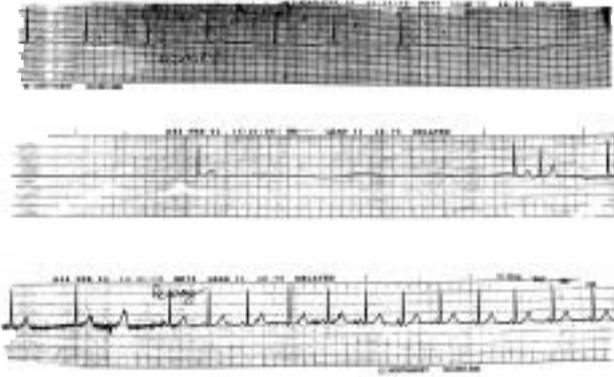


Fig. 1. Continuous ECG of 15 years old female during head-up tilt test showing an asystole last about 10 seconds



Fig. 2. Continuous ECG of 78 years old male during head-up tilt test showing a short pause followed by atrial fibrillation then long pause for 6 seconds

min, patient lost consciousness and ECG monitoring showed pasue for 10 seconds(Fig. 1). The patient was well educated on how to recognize syncope prodromes and was urged to sit down or lie down quickly. A therapeutic trial with midodrine 2.5mg per day was also given from February 2002, with no syncope recurrence. Follow up head-up tilt test was performed after 6 months treatment. The same episode of long pause 10 seconds remained. The medication was stopped in March 2003. But she suffered from only 2 episodes of syncope since then, and no attack in recent one year.

The third patient is a 78 years old male, he had past history of angina and hypertension for many years. He suffered from paroxysmal atrial fibrillation since September 2001. Coronary angiogram in October 2003 revealed only insignificant stenosis. But since then he experienced 5 times of syncope, and

Holter monitoring was arranged but with no pause or significant bradycardia., so head-up tilt test was implemented. After tilted for 12 min, the patient lost of consciousness and ECG monitoring showed atrial fibrillation and then 6 seconds pause(Fig. 2). He then received pacemaker implantation(VVIR form) in February 2004, with no syncope recurrence noted thereafter.

It was interesting to find that the youngest and oldest patient with head-up tilt test in our laboratory were both included in these three patients.

## Discussion

There were only three cases presenting as prolonged asystole during head-up tilt test in our laboratory in nearly ten years. The incidence was only 0.5% of the study patients and 1.2% of the patients with positive results. The incidence was quite low compared with previous reports which reported the incidence with a range from 4% to 33%<sup>8</sup>. There were a couple of possible reasons: (1) The first was the difference of the study protocol. Our protocol simply divided the test into two stages, passive head-up tilt test and test using isoproterenol. Most of the reports using protocol including nitrate provocation such as Italian protocol<sup>9</sup> or interrupted isoproterenol test such as protocol by Almquist et al<sup>10</sup>. According to the previous reports about tilt-induced long asystole, the incidence of tilt-induced long asystole was higher during nitrate provocation(21%) than during passive head-up tilt test(14%) and isoproterenol test(13%)<sup>8</sup>. It was also well known that isoproterenol, a beta stimulant, increases heart rate and, as such, it would be expected to reduce the occurrence rate of the cardioinhibitory response and that of ventricular aystole during head-up tilt test<sup>11</sup>. All our three cases occurred in the passive head-up tilt stage, and the ratio of positive response of cardioinhibitory type was also quite low. (2) The second possible reason might be in the timing of test termination. The test was operated by our technician, and physician was nearby. Thus the

test might be terminated much earlier due to patients frightening symptoms. It is amazing that the longest reported pause was 73 seconds<sup>12</sup> The first of our cases with 8 seconds pause, frightened our staffs and performed cardiac massage immediately. In general, the head-up tilt test is a safe procedure.(3) The final might be purely the ethnic variation. Most of these reports came from western countries, and rarely reported by Asian countries. To prove this, it need more large cohort of patients for comparison,. For our elderly cases, one had paroxysmal and the other had chronic atrial fibrillation. Both had recurrent syncope but during 24-hour Holter monitoring there was no long pause or persistent bradycardia to suggest the possibility of sick sinus syndrome. So under the suspicion of vasovagal syncope, they received the head-up tilt test and showed long pause. They both received permanent pacemaker implantation and had no recurrence of syncope thereafter. These two patients might be of sick sinus syndrome or so called "malignant vasovagal syncope" or even both. It had been reported that old age and accompanying atrial fibrillation were strong predictors of multiple potential causes of syncope. Such kind of patients had increased mortality among patients with syncope<sup>13</sup>. If Holter monitoring showed pause longer than 3 seconds, pacemaker implantation would be indicated for preventing syncope recurrence<sup>14</sup>. But when the Holter monitoring exhibited no abnormal finding, applying an implantable event recorder might be helpful but was impractical to use in these patients. Whether head-up tilt test is useful as an auxiliary test for syncope diagnosis. is unknown for this group of patients and may need a long-term prospective study for confirmation.

In conclusion, the incidence of long asystole during head-up tilt test in our patients was much lower than that of western countries. Head-up tilt test may be an helpful tool for evaluation of syncope in elderly patients with atrial fibrillation.

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# 傾斜床試驗所致長的心跳停止病患之發生率 臨床表現及結果

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## 摘 要

長的心跳停止發生於傾斜床試驗並不常見。若停止時間超過五秒就被稱為“惡性”。雖然近來一些報告顯示此一現象預後多為良性，但大多數的報告多來自西方國家，種族的差異是有可能的。所以我們於此呈現這類病患的資料。604位不明原因暈厥接受傾斜床試驗。其中包括30分鐘被動傾斜床試驗及30分鐘注射Isoproterenol使基本心跳至少上升20%。反應的型態皆加以分析及歸類並尋找有長的心跳停止者而於2004年十月於門診或電話做追蹤。242位病人(40.1%)為陽性反應，其中172位(71.1%)為混合型，60位(24.8%)為血壓下降型，而僅有10位(4.1%)為心跳抑制型。三位(1.2%)病人有長的心跳停止，包括一位年輕女性及二位有心房顫動之年長男性。年輕女性先接受midodrine治療，停藥後很少再復發，而兩位年長者則接受永久性心律節律器置放且再沒有暈厥發生。傾斜床試驗所致長的心跳停止於我們的病人發生機率比西方國家所報告低了許多。針對有心房顫動之年長男性發生不明原因暈厥時，傾斜床試驗或許可以做為輔助之診斷工具。