Journal of the Hong Kong College of Cardiology

Volume 10
Issue 1 *January*

Article 1

The First Whf Global Conference On Cardiovascular Clinical Trials

Journal of the Hong Kong College of Cardiology

January 2002
Volume 10, No. 1

Table of Contents

Guest Editorial

Appropriate Use of Clopidogrel

CYRUS R KUMANA, BERNARD MAN-YUNG CHEUNG, IJ LAUDER*

From Department of Medicine and Department of Statistics & Acturial Science*, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Clopidogrel (Plavix®) is an orally administered pro-drug, whose pharmacology and therapeutic role has been extensively reviewed in recent publications.[1-5] In essence, it results in selective and irreversible antagonism of ADP-induced platelet aggregation. Such aggregation normally results in the surface expression of platelet glycoprotein (GP) IIb/IIIa receptors, which facilitate fibrinogen binding as well as consequential further platelet aggregation – the final common pathway of vascular occlusion. Specific cytochrome P450 enzymes are thought to generate the responsible active metabolite (believed to persist transiently). However, dosage adjustment is not recommended in hepatic impairment (unless severe) and drug-drug interactions and co-administration with meals are believed to be unimportant.

Based on clinical trials of outcome, several orally administered anti-platelet drugs have proven efficacy (mainly for secondary prevention) in the context of coronary events, ischaemic strokes and peripheral vascular disease. These include: (1) aspirin, (2) dipyridamole (Persantin), (3) ticlopidine (Ticlid), and (4) clopidogrel (Plavix) all of which have important adverse effects.[6,7] Dipyridamole gives rise to headaches, postural lightheadness, and gastrointestinal symptoms (mainly diarrhea & nausea). The relatively common adverse effects of ticlopidine (neutropenia, thrombocytopenia, hepatitis and diarrhea) pose a problem. With clopidogrel, adverse effects are comparable to aspirin and certainly less frequent and less severe than with ticlopidine. However, it too has been linked to thrombotic thrombocytopenic purpura (even resulting in death).[8] Moreover, clopidogrel's long term safety has not been established, nor are the risks known among ethnic groups (including the Chinese) that are believed to be more prone to bleeding.

Only a few of the relevant clinical trials have compared different anti-platelet drug treatment intervention regimes to each other with respect to outcomes. In the multi-centre **CAPRIE (Clopidogrel v Aspirin in Patients at Risk of Ischaemic Events)** double blind randomised controlled trial, clopidogrel or aspirin (both 75 mg/day) were given to 19,185 atherosclerotic patients.[9] The protocol entailed randomisation to three groups viz: Stroke, MI & Peripheral arterial disease (PAD), and follow up for 1-3 years. The ensuing results are outlined below (Table 1).

Table 1. Primary outcome (myocardial infarction, ischaemic stroke or vascular death)

	Event ensued	No event	Total
Clopidogrel	939	8614	9553
Placebo	1021	8846	9546

The *relative risk reduction* **(RRR)** was 8.7% (adjusted) with a 95% CI of 0.3-16.5%; $P<0.05$. The more meaningful *absolute risk reduction* **(ARR)** amounted to 0.86% over an average of 1.91 years. The corresponding *number needed to treat* **(NNT)** to prevent one patient experiencing an adverse outcome event over that period was 115 (95% CIs 57-∞), which is equivalent to an **NNT/year** of 220. Unexpectedly the benefit was largely confined to patients with prior peripheral arterial disease and stroke.

That drugs such as clopidogrel, which inhibit ADP induced platelet aggregation may complement the antiplatelet activity of aspirin (a cyclo-oxygenase inhibitor) without unduly compromising safety, has kindled interest in using them in combination. In the multi-centre **CURE** (Clopidogrel in Unstable angina to prevent Recurrent Events) trial,[10,11] 12,562 patients taking aspirin (75-325 mg/day) ± heparin, β-blockers,

Opinions expressed are views of the authors and not necessarily the view of the editorial board or the Hong Kong College of Cardiology.

statins or calcium channel blockers – were randomised to treatment with clopidogrel (75 mg/day) or placebo for 3-12 (mean of 9) months. The **RRR** (for cardiovascular death, non-fatal stroke or MI) was 20% (adjusted) with a 95% CIs of 10-28%. The corresponding **NNT** was 47 or 35/year. Evidently, the relative risk **(RR)** of major bleeding was 1.38% (95% CIs 1.13-1.67), there being one such additional episode for every 99 patients treated with clopidogrel and aspirin (as opposed to aspirin alone) over this period of time (or 74/year). However, there was no excess in bleeds causing fatality, strokes or need for surgical intervention. Notably, for many of the patients undergoing revascularisation procedures, study medication was temporarily interrupted or given as open label therapy. In the overall analysis, it was estimated that for every 1000 patients treated for 9 months, 28 major events would be prevented at a cost of 3 patients having life-threatening bleeds and 3 more requiring transfusions.[12]

In 2001, clopidogrel was among the Hong Kong Hospital Authority's top 20 items of expenditure on pharmaceuticals, having increased in popularity dramatically over the last year. Compared to aspirin, currently it is many orders of magnitude more expensive. Thus, substituting clopidogrel for aspirin, treatment of 220 patients for 1 year would be expected to prevent 1 of them from suffering an ischaemic event, but depending on which formulation was replaced - corresponding drug costs could increase by between 46 to 205 fold (Table 2). In mitigation, use of clopidogrel may involve cost-savings in terms of slightly reduced numbers of patients having revascularisation procedures and the associated use of much more expensive drugs (GP IIb/IIIa receptor blockers).

Hitherto the conventional indications for prescribing clopidogrel were mainly confined to: (1) cover (together with aspirin) for patients undergoing angioplasty and/or stenting procedures, and (2) as a substitute for aspirin for individuals in whom the latter drug was contraindicated or poorly tolerated. If the daily cost of clopidogrel treatment (currently up to 205 fold that of aspirin) is not an issue, it may also be reasonable to use it: (3) instead of aspirin in all ischaemic cardiovascular disease states, and (4) in combination with aspirin for patients with unstable angina. However, the long-term safety of this agent is not known.

Table 2. Drug acquisition costs

Drug	Typical dosage/day	HK$ (Nov 2001)
Clopidegrel	75 mg	12.30
Ticlopidine	250 mg	7.25
Dipyridamole	25 mg	0.09
	75 mg	0.20
Aspirins		
Asprin	80 mg	0.06
Dispersable aspirin	300 mg	0.27
Cartia	100 mg	0.23
SR Cardiprin	100 mg	0.18

References

1. Zusman RM, Chesebro JH, Comerota A, et al. Antiplatelet therapy in the prevention of ischemic vascular events: literature review and evidence-based guidelines for drug selection. Clin Cardiol 1999;22:559-73 (review).
2. Gorelick PB, Born GV, D'Agostino RB, et al. Therapeutic benefit. Aspirin revisited in light of the introduction of clopidogrel. Stroke 1999;30:1716-21 (review).
3. Folts JD, Schafer AI, Loscalzo J, et al. A perspective on the potential problems with aspirin as an antithrombotic agent: a comparison of studies in an animal model with clinical trials. J Am Coll Cardiol 1999;33:295-303 (review).
4. Jarvis B, Simpson K. Clopidogrel: a review of its use in the prevention of atherothrombosis. Drugs 2000;60:347-77 (review).
5. Hankey GJ, Sudlow CL, Dunbabin DW. Thienopyridines or aspirin to prevent stroke and other serious vascular events in patients at high risk of vascular disease? A systematic review of the evidence from randomized trials. Stroke 2000;31:1779-84.
6. Review. Antiplatelet drugs in cardiovascular prevention: take adverse effects and costs into account. Prescrire Int 2000;9:82-3.
7. Review. Drug-induced thrombotic thrombocytopenic purpura. Prescrire Int 2001;10:50-1
8. Bennett CL, Connors JM, Carwile JM, et al. Thrombotic thrombocytopenic purpura associated with clopidogrel. N Engl J Med 2000;342:1773-7.
9. CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). Lancet 1996;348:1329-39.
10. Mehta SR, Yusuf S. The Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) trial programme; rationale, design and baseline characteristics including a meta-analysis of the effects of thienopyridines in vascular disease. The Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) Study Investigators. Eur Heart J 2000;21:2033-41.
11. Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. The Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators. N Engl J Med 2001;345:494-502.
12. Mitka M. Results of CURE trial for acute coronary syndrome. JAMA 2001;285:1828-9.

The Long-term Clinical Prognosis in Patients with Anterior Wall and Non-anterior Wall Acute Myocardial Infarction Referred to Primary Percutaneous Transluminal Coronary Angioplasty

MINGZHONG ZHAO, DAYI HU, TIANCHANG LI, SANQING JIA, MING YANG, YUYUN XU

From Department of Cardiology, People's Hospital, Beijing University, Beijing 100044, China

ZHAO ET AL.: ***The Long-term Clinical Prognosis in Patients with Anterior Wall and Non-anterior Wall Acute Myocardial Infarction Referred to Primary Percutaneous Transluminal Coronary Angioplasty. Objective:*** *To investigate the long-term clinical prognosis in patients with anterior wall acute myocardial infarction (AW-AMI) and non AW-AMI (NAW-AMI) referred to primary percutaneous transluminal coronary angioplasty (P-PTCA).* ***Methods:*** *287 patients with AMI who underwent P-PTCA were divided into AW-AMI group (142 cases) and NAW-AMI group (145 cases) according to different sites of AMI. The baseline characteristics and coronary artery lesions of patients were analysed. The primary end points were in-hospital mortality and the major cardiovascular events (MACE) during a mean 17.3±9.8 months follow-up including the occurrences of non-fatal myocardial infarction, non-fatal congestive heart failure, revascularization of target vessels and overall cardiac-related death.* ***Results:*** *The peak values of CK and CK-MB were significantly higher (3533±2888 U/L vs 2322±1638 U/L, 158±197 U/L vs 95±64 U/L, all P<0.01), and left ventricular ejection fraction decreased (0.55±0.13 vs 0.61±0.12, P<0.05) and in-hospital mortality increased significantly (4.1% vs 0, P<0.05) in AW-AMI group than in NAW-AMI group. At a follow-up of mean 17.3±9.8 months, the incidences of non-fatal heart failure, in-hospital mortality, total cardiac-related mortality and combined end points in AW-AMI group increased significantly than those in NAW-AMI group (all P<0.05). Multivariate analysis revealed that anterior location of myocardial infarction and proximal left anterior descending (LAD) coronary artery lesion were associated with the occurrence of cardiac-related death in patients with AMI after procedure of PTCA (all P<0.05).* ***Conclusions:*** *The present study shows that anterior location of myocardial infarction is associated with a higher incidence of MACE. The long-term clinical outcomes are poorer in patients with AW-AMI than NAW-AMI referred to P-PTCA. (J HK Coll Cardiol 2002;10:3-6)*

Acute myocardial infarction, angioplasty, percutaneous coronary, prognosis, transluminal

摘要

目的：探討急性前壁心肌梗死(AW-AMI)與非前壁心肌梗死(NAW-AMI)患者直接經皮冠狀動脈腔內成形術(P-PTCA)後長期預後分析。方法：行P-PTCA的287例AMI患者根據梗死的不同部位分成AW-AMI組(142例)和NAW-AMI組(145例)，分析患者的基本臨床特徵和冠脈病變特點，觀察終點為住院期死亡率與隨訪期平均17.3±9.8個月的主要心血管事件(MACE)，包括非致命心肌梗死，非致命心力衰竭，靶血管血運重建及總心臟性死亡的發生率。結果：與NAW-AMI組比較，AW-AMI組的CK與CK-MB峰值顯著升高(3533±2888 U/L比2322±1638 U/L，158±197 U/L比95±64 U/L，P均<0.01)，左室射血分數降低(0.55±0.13 比 0.61±0.12，P<0.05)以及住院期死亡率增高(4.1% 比 0，P<0.05)。隨訪平均17.3±9.8個月，AW-AMI組的非致命性心力衰竭、總死亡率及複合終點事件發生率高於NAW-AMI組（P均

Address for reprints: Dr. Mingzhong Zhao
Department of Cardiology, People's Hospital, Beijing University,
Beijing 100044, China

Tel: (86) 010 68314422-4726, Fax: (86) 010 68792845

Received May 25, 2001; revision accepted January 14, 2002

＜0．05）。多變量分析顯示前壁心肌梗死和前降支近段病變與AMI患者直接冠脈介入治療後心臟性死亡發生相關（P均<0.05）。結論：前壁心肌梗死與主要心血管事件發生率增高有關，AW-AMI行直接PTCA患者的長期臨床預後較NAW-AMI行直接PTCA者差。

關鍵詞：急性心肌梗死　成形術　經皮冠狀動脈　預后　經腔

Introduction

During the treatment of acute myocardial infarction (AMI), early and effective recanalization of infarct-related artery (IRA) is a very important strategy. Primary percutaneous transluminal coronary angioplasty (P-PTCA) or intracoronary stenting can restore immediate TIMI 3 coronary flow of IRA. A few reports showed the advantages of P-PTCA over intravenous thrombolysis in the treatment of AMI. But, the different sites of myocardial infarction might affect the patients' clinical outcomes. The risk of patients with anterior wall AMI (AW-AMI) was higher than that of patients with non-anterior wall AMI (NAW-AMI) because of their greater myocardial infarction sizes.[1] In the present study, we investigated the effect of P-PTCA on the long-term clinical outcomes in patients with AW-AMI and NAW-AMI.

Methods

Patient Population

From January 1997 to December 2000, a total of 287 patients had taken emergency coronary artery angiography (CAG) at our hospital with AMI and suitable coronary anatomy for P-PTCA. The eligibility criteria of P-PTCA were documented by the following: (1) Persistent chest pain ≥30 min, with no relief by nitrates; (2) ECG showing 1 mm ST segment elevation in two contiguous limb leads or 2 mm ST segment elevation in two contiguous precordial leads; (3) Fewer than 12 hours from onset of symptoms; (4) AMI patients with recurrent ischemic symptoms or persistent ST segment elevation or CAG showing TIMI 0-II flow at 90 min after thrombolysis should undergo rescue PTCA. For patients meeting above criteria, written informed consents were obtained before they underwent PTCA in the catheterization laboratory.

According to the presentation of electro-cardiogram (ECG), AMI patients were divided into AW-AMI and NAW-AMI groups. The former group included 142 cases (male:110 cases and female:32 cases) and the latter group included 145 cases (male: 103 cases and female:42 cases).

Angiography and PTCA

AMI patients were sent directly to catheterization laboratory from Emergency Department. At first, CAG was performed with Judkins method, then primary PTCA or intracoronary stenting was decided according to the characteristics of coronary artery disease. Generally, we usually intervened with IRA during emergency procedure.

Follow-up

Patients were followed up within 1 to 41 months (a mean 17.3±9.8 months) for in-hospital mortality and major cardiovascular events (MACE), which included incidences of non-fatal myocardial infarction, non-fatal heart failure, need for target vessel revascularization (TVR) and total cardiac mortality.

Statistical Analysis

Continuous variables are expressed as mean±s; discrete variables are expressed as percentages. Differences between two groups were evaluated with the student t test or χ^2 test. The logistic regression analysis was used to investigate the changes of risk factors of cardiac death.

Results

Baseline Clinical and Angiographic Characteristics (Table 1)

The results showed the percentages of patients with angina before AMI or with Killip class II-IV, and the peak values of CK or CK-MB were higher in AW-AMI group than in NAW-AMI group (P<0.01). Angiogram indicated that left anterior descending (LAD) was the dominant IRA of patients with AW-AMI and right coronary artery (RCA) was the dominant IRA of patients with NAW-AMI.

The Results of Follow-up (MACE)

Stent was implanted in 91.6% and 86.9% of AW-AMI and NAW-AMI patients respectively (P>0.05). Out of 287 patients, 122 patients with AW-AMI and 117 patients with NAW-AMI were followed up. The incidences of non-fatal heart failure, in-hospital mortality, total cardiac death and combined end points were significantly higher in the AW-AMI group than in the NAW-AMI group (Table 2).

The Effect of IRA on Cardiac Death Rate (Table 3)

The mortality rate was higher in patients whose IRA were left main trunk (LMT) than those whose IRA were LAD, LCX or RCA. Proximal and non-proximal lesions in IRA were identified according to the different sites of coronary occlusion.[2] Compared with patients with non-proximal IRA lesions, the cardiac mortality was higher in patients with proximal IRA lesions in LAD (P<0.05).

Logistic regression analysis revealed that myocardial infarction sites (anterior wall) and proximal LAD lesion were associated with the occurrence of cardiac-related death in patients with AMI after PTCA procedure (all P<0.05).

Discussion

This report described that the enzyme leak, the Killip Class and left ventricular ejection were poorer in patients with AW-AMI than NAW-AMI. More patients with angina before AMI were presented in the AW-AMI group. The increased risk of patients with anterior wall AMI was associated with greater myocardial necrosis, as well as larger infarct expansion, which resulted in aneurysm formation, heart failure, mural thrombus formation and myocardial rupture.[3-5] CAG showed no difference between the 2 groups besides IRA. LAD was the dominant IRA in AW-AMI group, and RCA was the dominant IRA in NAW-AMI group. It was reported that AMI patients by occlusion of LAD had a higher risk and more importantly clinical significance than those by occlusion of LCX or RCA.[6]

The follow up data in this study showed that although there was no significant difference in rates of non-fatal myocardial infarction and TVR between the 2 groups, the incidences of non-fatal heart failure, in-hospital mortality and total cardiac mortality increased significantly in the AW-AMI group. The combined end point event was also higher in the AW-AMI group than

Table 1. Baseline clinical and angiographic characteristics

Characteristics	AW-AMI group (142)	NAW-AMI group (145)
Age	63.2±8.9	62.1±9.5
Hypertension	35.9 (51/142)	29.0 (42/145)
Hyperlipideremia	26.8 (38/142)	22.1 (32/145)
Diabetes	11.3 (16/142)	11.0 (16/145)
Smoking	38.0 (54/142)	45.5 (66/145)
Angina before AMI	59.9** (85/142)	35.2 (51/145)
Killip class II-IV	28.8** (41/142)	10.0 (15/145)
Duration from onset of symptom to reperfusion (min)	251±154	268±141
Rescue-PTCA	11.3 (16/142)	9.0 (13/145)
CK (U/L)	3533±2888**	2322±1638
CK-MB (U/L)	158±197**	95±64
LVEF	0.55±0.13*	0.61±0.12
Single vessel disease	52.8 (75/142)	41.4 (60/145)
Multivessel disease	47.2 (67/142)	58.6 (85/145)
LM	6.3 (9/142)	5.5 (8/145)
Infarct-related artery (IRA)		
LAD	95.8** (136/142)	2.8 (4/145)
LCX	0**	20.7 (30/145)
RCA	1.4** (2/142)	76.5 (111/145)
LM	2.8 (4/142)	0

LVEF, left ventricular ejection fraction; LM, left main; LAD, left anterior descending
*P<0.05, **P<0.01, patients with AW-AMI versus with NAW-AMI

Table 2. The incidence of MACE in the two groups

MACE	AW-AMI (n=122)		NAW-AMI (n=117)	
	case	%	cases	%
Non-fatal myocardial infarction	2	1.6	1	0.9
Non-fatal heart failure	18	14.8*	8	6.8
Target vessel revascularization	9	7.4	10	8.6
In-hospital mortality	5	4.1*	0	0
Total cardiac death rate	8	6.6*	2	1.7
Combine end points	37	30.3*	21	18.0

*P<0.05, patients with AW-AMI versus with NAW-AMI

Table 3. The effect of IRA on cardiac death rate

IRA	Cases	Cardiac mortality	
		cases	%
LAD	112	7	6.3*
proximal	54	6	11.1▲
non-proximal	58	1	1.7
LCX	30	0**	
proximal	21		
non-proximal	9		
RCA	93	2	2.2**
proximal	57	1	1.8
non-proximal	36	1	2.8
LM	4	1	25.0
proximal	1	1	100
non-proximal	3	0	

*P<0.05,**P<0.01, compared with patients whose IRA are LM; ▲P<0.05, compared with non-proximal at the same vessel

the NAW-AMI group. Furthermore, our study also showed the cardiac mortality rate was higher in patients whose IRA was LMT or proximal in LAD compared with other subgroups, but it should be further studied due to limited cases. The present study indicated that patients with AW-AMI was a high risk population, which was identical to the results that Zijlstra reported.[7] The patients with AW-AMI were likely to have a greater likelihood of a cardiac event at follow-up than NAW-AMI.[8] The multivariate analysis revealed that myocardial infarction sites (anterior wall) and proximal LAD lesion were associated with the occurrence of cardiac-related death in patients with AMI after the PTCA procedure.

Our results showed that anterior location of myocardial infarction was associated with a higher incidence of MACE. The long-term clinical outcomes were poorer in patients with AW-AMI than NAW-AMI referred to P-PTCA.

References

1. Sammel NL, Stuckey JG, Brandt PWT, et al. Comparison of enzymic with cineangiography. N Engl J Med 1981;305:297-302.
2. Principle Investigators of CASS. The National Heart, Lung, and Blood Institute coronary artery surgery study (CASS). Circulation 1981;63(suppl I):1-81.
3. Engelen DS, Gorgels AP, Cheriex EC, et al. Value of the electrocardiogram in localizing the occlusion site in the left anterior descending coronary artery in acute anterior myocardial infarction. J Am Coll Cardiol 1999;34(2):389-95.
4. Gaudron P, Eilles C, Kugler I, et al. Progressive left ventricular dysfunction and remodeling after myocardial infarction: potential mechanisms and early predictors. Circulation 1993; 87:755-63.
5. Eaton LW, Weiss JL, Bulkley BH, et al. Regional cardiac dilation after acute myocardial infarction: recognition by two-dimensional echocardiography. N Engl J Med 1979;300:57-62.
6. Klarich KW, Christina TF, Higano ST, et al. Variability of myocardium at risk for acute myo cardial infarction. Am J Cardiol 1999;83:1191-5.
7. Zijlstra F, Beukema WP, Hof AWJ, et al. Randomized comparison of primary coronary angioplasty with thrombolytic therapy in low risk patients with acute myocardial infarction. J Am Coll Cardiol 1997;29:908-12.
8. Welty FK, Mittleman MA, Lewis SM, et al. Significance of location (anterior versus inferior) and type (Q-wave versus Non-Q wave) of acute myocardial infarction in patients undergoing percutaneous transluminal coronary angioplasty for postinfarction ischemia. Am J Cardiol 1995;76:431-5.

Syncope in Children in Hong Kong

GEOFFREY CHI-FUNG MOK, RITA YN-TZ SUNG

From Department of Paediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong

MOK and SUNG: ***Syncope in Children in Hong Kong. Objectives:*** *Syncope is a common event in children. The objective of this study was to review the aetiologies and their relative frequencies in the paediatric patients in a general hospital in Hong Kong.* ***Methods:*** *This is a retrospective study of paediatric patients admitted to our hospital between 1987 and 1996 with a presenting complaint of syncope. Their hospital notes were retrieved and reviewed. The syncopal event and the circumstances together with the clinical assessment as well as the subsequent investigations were analyzed in order to establish the respective aetiology for syncope.* ***Results:*** *Altogether 146 patients were included in the study. The mean age was 10.4 years. Vasovagal syncope accounted for 54.1% of patients presented with syncope. Seizure disorder accounted for 25.3%, while cardiac cause accounted for another 3 patients (2.1%) with 2 patients having paroxysmal supraventricular tachycardia and 1 patient having frequent hypoxic spells due to complex cyanotic heart disease. In 13.7% of patients, the cause of syncope was unknown. One patient belonging to the seizure group died with autopsy finding revealing diffuse glioma at frontal region.* ***Conclusions:*** *Syncope is a common presentation in the paediatric population and vasovagal syncope accounts for over half of the cases. Although most cases of syncope are benign, it is important not to miss those cases in whom a life-threatening condition is present. (J HK Coll Cardiol 2002;10:7-10)*

Aetiology, children, syncope, vasovagal syncope

摘要

目的：暈厥是兒童常見的突發事件。本研究目的是複習暈厥的病因學及其在香港一所綜合醫院兒童患者中有關的發作頻率。方法：這是一個回顧性研究，患者為1987年至1996年間訴暈厥住院的兒童病人。我們檢索、複習了病歷記錄。分析了暈厥事件、環境因素、臨床評價以及隨訪結果以分別確立暈厥的病因學。結果：研究中包括146例患者，平均年齡10.4歲，迷走性暈厥佔54.1%，癲癇疾病佔25.3%，心原性疾病3人(2.1%)，其中2人有陣發性室上性心動過速，以及1人因紫紺型心臟病而有頻繁低氧症狀發作。有13.7%的患者的暈厥原因尚不清楚。1例診斷癲癇的患者死亡，屍檢顯示大腦前葉為瀰漫性神經膠質瘤。結論：暈厥在兒童人群中是一常見現象，迷走性暈厥佔一半多的病例。儘管大多數暈厥是屬良性的，但避免遺漏可能威脅生命的一些病例仍是十分重要的。

關鍵詞：病因學　兒童　暈厥　迷走性暈厥

Address for reprints: Dr. Geoffrey Chi-Fung Mok
Department of Paediatrics, 6/F, Clinical Sciences Building, Prince of Wales Hospital, Shatin, New Territories, Hong Kong

Tel: (852) 2632 2849, Fax: (852) 2636 0020

Received October 8, 2001; revision accepted December 20, 2001

Introduction

Syncope is a common presentation in the paediatric population. The reported incidence of paediatric syncopal episodes which received medical attention was 71.9-125.8 per 100 000 population.[1] However, the actual incidence of paediatric syncope is not known due to the lack of large-scale population-based study in children. It has been estimated that as many as 15% of children and adolescents experienced at least one episode of syncope prior to the end of adolescence.[2]

There are many causes of syncope. The most common one is vasovagal or neurally mediated syncope, which accounts for as much as 50% of the cases of syncope in children.[3-6] Neurally mediated syncope is presumably due to relative hypovolaemia leading to vigorous contraction of the heart, thus causing stimulation of C-fibres and sympathetic withdrawal.[7] Its clinical course is usually benign. However, it is important to exclude the minority of cases which have a more serious and treatable cause of syncope, such as epilepsy or underlying cardiac abnormality.

The objectives of this study were to review the aetiologies and their relative frequencies in the paediatric patients in a general hospital in Hong Kong.

Methods

This retrospective study included paediatric patients admitted between 1987 and 1996 with a presenting complaint of syncope who were identified from our department audit database.[8] Their hospital notes were retrieved and reviewed. Patients who were already known to have history of seizure attack or history of arrhythmia were not included in the study. Syncope is defined as the sudden, temporary and complete loss of consciousness with loss of postural tone and with spontaneous recovery.

Demographic information including the age at presentation and sex of the patient was noted. Clinical history was thoroughly reviewed with regards to the detailed description of the syncopal event and the circumstances under which syncope occurred. The investigation results were noted, with particular reference to the types of the blood tests performed, electrocardiography, and other more specific investigations including echocardiography, electroencephalography, Holter monitor as well as brain imaging. The cause of syncope was established based on the review of the clinical presentation as well as the relevant investigation results.

Diagnostic criteria for inclusion of cases in different categories were defined as below. Vasovagal syncope was defined as syncope that was preceded by periods of prolonged upright posture followed by prodromal symptoms of dizziness and diaphoresis prior to the syncopal event. Triggering factors such as emotional and stressful situations may be present. Seizure disorder was diagnosed when the electro-encephalogram showed epileptiform discharge or when the patient developed clinical seizure subsequently. Cardiac cause of syncope was diagnosed when there was history of heart disease that was known to predispose to syncope or when there were abnormalities detected on electrocardiogram or echocardiogram that could account for the syncope.

Results

Altogether 146 patients were included in the study over the 10-year period from 1987 to 1996. There were a total of 68 males and 78 females. The age ranged from 3 to 15 years old with a mean (±SD) age of 10.4±3.0 years. The results were shown in Table 1.

The majority of patients underwent the basic investigation for the causes of syncope including complete blood count, blood sugar, serum electrolytes level, electrocardiogram and electroencephalogram. Other more specific tests include echocardiogram, Holter monitor, electrophysiological study and computed tomography of the brain and the decision to use these depended on the individual clinical

Table 1. Causes of syncope

	Number	Male	Female
Vasovagal	79 (54.1%)	37 (54.4%)	42 (53.8%)
Seizure	37 (25.3%)	24 (35.3%)	13 (16.7%)
Cardiac	3 (2.1%)	0	3 (3.8%)
Psychological	2 (1.4%)	0	2 (2.6%)
Others	5 (3.4%)	0	5 (6.4%)
Unknown	20 (13.7%)	7 (10.3%)	13 (16.7%)
Total	146	68	78

presentation and indication. The relative frequencies of the investigations performed were shown in Table 2.

Over half of the study population were classified as having vasovagal syncope (54.1%). Seizure disorder ranked the second important group among the causes of syncope (25.3%). Psychological cause of syncope, such as hysteria, consisted of 1.4%. Cardiovascular cause of syncope accounted for 3 cases (2.1%) of the study population. Among the 3 patients, 1 patient had congenital complex cyanotic heart disease and had repeated hypoxic spells. Two other patients had paroxysmal supraventricular tachycardia. Other miscellaneous causes of syncope accounted for 3.4% of the study group and this included 2 patients with vestibular disorder, 2 patients with upper respiratory tract infection who were prescribed cough mixture and 1 patient with drug overdose. In 13.7% of the study population, no aetiology of the causes of syncope could be identified.

One patient in the study group subsequently died. The patient was a 14-year-old girl who initially presented with syncope. Her electroencephalogram showed abnormal sharp waves and was diagnosed as having epilepsy. This patient did not have a computed tomography of the brain performed before her second admission. She presented as status epilepticus two months afterwards and died within few hours after admission. She was found to have diffuse glioma at the frontal region at autopsy.

Discussion

There were a few published series describing the causes of syncope in childhood. Our study showed that vasovagal syncope accounts for over 50% of syncope in our paediatric population. This figure is consistent with other published data shown in Table 3.

Vasovagal syncope or neurally mediated syncope involving altered systemic vascular tone,[9] is a diagnosis mainly made based on the clinical history. However, not every patient with vasovagal syncope would present with the typical clinical features, thus occasionally making vasovagal syncope difficult to diagnose. Recently, the upright tilt testing has been increasingly used both as a diagnostic aid as well as a means to evaluate the various therapeutic measures for vasovagal syncope, but different studies have shown variable specificity, sensitivity and reproducibility which may be a result of the absence of a unified study protocol.[10,11] However, it is still considered to be a useful test in some patients with vasovagal syncope in whom the clinical presentation is less typical and a positive upright tilt test may help to establish the diagnosis. In addition, a positive tilt test in children was also found to be predictive of increased incidence of recurrent rate of syncope compared with those with negative tilt test.[12]

Cardiac cause of syncope accounts for only a small percentage of the study population when compared with Özme et al's report.[5] This may be due to the fact

Table 2. The relative frequencies of investigations performed on patients presenting as syncope

Investigation	Number of positive tests/Number of patients tested	% positive
Complete blood count	0/111	0
Serum Electrolytes	1/108	0.9
Serum Glucose	1/113	0.9
Electrocardiography	3/76	3.9
Electroencephalogram	11/59	18.6
Computed Tomography of Brain	2/5	40

Table 3. Aetiologies of syncope in other published series

	McHarg et al (1997)	Özme et al (1993)
Number of patients	108	80
Vasovagal	75%	33%
Seizure	8%	11%
Cardiac	6%	27.5%
Migraine	11%	0
Others	0	1%
Unknown	0	27.5%

that the study patients were from general paediatric wards rather than a cardiac centre. Our results are more comparable to a population-based study published by Driscoll et al,[1] which described that only 6% of the paediatric syncope was attributed to a pre-existing cardiac aetiology. Nonetheless, it is of utmost importance to look for any evidence of cardiac causes of syncope as they are potentially life-threatening. Attention needs to be paid to any possibility of arrhythmia and left ventricular outflow tract obstruction, and necessary investigations including Holter monitoring, stress electrocardiography and echo-cardiography should be performed if cardiac cause of syncope is suspected.[13] Electrocardiograms provide many valuable information as arrhythmia may be demonstrated, and the practice of measuring the QT_C interval is important as this may reveal the diagnosis of long QT syndrome as the cause of syncope.

It has always been suggested that the yield of a significant abnormality is relatively low if every child presenting with syncope were to undergo the whole series of comprehensive investigation and it would not be cost-effective as well. This statement is best exemplified in our study which showed that the basic investigations which were frequently included as part of the diagnostic workup for syncope had very low diagnostic yield compared with the more selective investigations such as electroencephalograms and computed tomography of brain. However, there is always the concern of the potential risk of missing the diagnosis of a potential life-threatening cause of syncope. It is thus important in the clinical assessment to identify those individuals in which case the suspicion of a potentially sinister cause of syncope is suspected, such as patients with atypical history, patients with a family history of sudden death, and patients with abnormal clinical examination. These patients would warrant further specific investigations accordingly for the establishment of the respective diagnosis.

The study has its limitation. The true incidence of syncope in children could not be estimated from the study since not all children with syncope would present to the hospital. In one emergency room series, syncope accounts for <1% of all visits.[3] In another study which resembled a population-based study as the region was served with a nearly uniform health care provider service, it was found that only about 0.1% paediatric patients came to seek medical attention for syncope.[1] Clearly, it would be interesting to know if there is any difference in the relative frequencies in the various causes of syncope in the general paediatric population compared with those who present themselves to hospitals. Another limitation is related to the retrospective nature of the study, in which the diagnostic criteria used in this study were not prospectively defined. Therefore, there may be potential error in their clinical diagnosis and this may account for a relatively low incidence of cardiac cause of syncope in the study population.

Conclusions

Syncope is a common symptom in the paediatric population and vasovagal syncope accounts for over half of the patients presenting with syncope. Although most cases of syncope are benign, it is essential not to miss those cases in whom a life-threatening cause could be identified, especially those patients with a cardiac cause of syncope or central nervous system pathology.

References

1. Driscoll DJ, Jacobsen SJ, Porter CJ, et al. Syncope in children and adolescents. J Am Coll Cardiol 1997;29:1039-45.
2. Ruckman RN. Cardiac causes of syncope. Pediatr Rev 9:101.
3. Pratt JL, Fleisher GR. Syncope in children and adolescents. Pediatr Emerg Care 1989;5:80-2.
4. McHarg ML, Shinnar S, Rascoff H, et al. Syncope in childhood. Pediatr Cardiol 1997;18:367-71.
5. Özme S, Alehan D, Yalaz K, et al. Causes of syncope in children: a prospective study. Int J Cardiol 1993;40:111-4.
6. Lerman-Sagie T, Lerman P, Mckamel M, et al. A prospective evaluation of pediatric patients with syncope. Clin Pediatr 1994; 33:66-70.
7. Sokoloski MC. Evaluation and treatment of pediatric patients with neurocardiogenic syncope. Prog Pediatr Cardiol 2001;13: 127-31.
8. Leung DT, Tseng RY, Davies DP. Setting up a clinical audit of paediatric morbidity in Hong Kong: some early experiences. Aust Paediatr J 1987;23:111-3.
9. Johnsrude CL. Current approach to pediatric syncope. Pediatr Cardiol 2000;21:522-31.
10. Kapoor WN, Smith MA, Miller NL. Upright tilt testing in evaluating syncope: a comprehensive literature review. Am J Med 1994;97:78-88.
11. Sung RYT, Yu CW, Ng E, et al. Head-up tilt test without intravascular cannulation in children and adolescents. Int J Cardiol 2001;80:69-76.
12. Salim MA, Ware LE, Bernard M, et al. Syncope recurrence in children: relation to tilt-test results. Pediatrics 1998;102:924-6.
13. Scott WA. Evaluating the child with syncope. Pediatr Ann 1991; 20:350.

The Clinical Observation of Biventricular Pacing in Patients with Congestive Heart Failure

WEI HUA, XIN CHEN

From Clinical Electrophysiology Laboratory, Fu Wai Hospital, Chinese Academy of Medical Sciences, Beijing, China

HUA and CHEN: ***The Clinical Observation of Biventricular Pacing in Patients with Congestive Heart Failure.*** *Congestive heart failure is one of the leading health problems in medicine. Intraventricular conduction delay is associated with contraction abnormalities, prolonged mitral regurgitation and a shortened left ventricular filling time in patients with conduction defects and dilated cardiomyopathy. Biventricular pacing is a promising new strategy for correcting the ventricular activation sequence and potentially improving myocardial function and clinical outcome in patients with congestive heart failure. Uncontrolled and controlled studies have shown that biventricular pacing could help to improve patients by at least one functional class, increases the 6-minute walk distance by 20-40%, and improves quality of life (as assessed by the Minnesota living with heart failure questionnaire) by 20-50%. Left ventricular lead implantation requires more time than implantation of traditional pacemaker leads. New technology and techniques are likely to reduce the time required for implantation in the future. (J HK Coll Cardiol 2002;10:11-16)*

Biventricular pacing, clinical observation, congestive heart failure

摘要

充血性心力衰竭是醫學領域面臨的主要問題之一。在充血性心力衰竭患者，心室內傳導延遲與心肌收縮不同步，二尖瓣返流延長及左室充盈時間縮短相關。雙心室同步起搏可糾正心室激動不同步，改善患者心功能，是一個有前途的治療方法。一些對照和非對照的臨床研究已經證明雙心室同步起搏可改善患者心功能一級，6分鍾步行距離 20-40%，以及生活質量20-50%〔明尼蘇達生活質量評分〕。植入左心室電極導線比植入傳統電極導線要更長時間，隨著技術的不斷改進，植入時間將減少。

關鍵詞：雙心室同步起搏　臨床觀察　充血性心力衰竭

Introduction

The aging of the population has made chronic heart failure (CHF) an increasingly important health problem. It is the leading medical cause of hospitalization and its economic cost continues to increase. In recent years, pharmacological treatment made considerable progress. Angiotensin converting enzyme (ACE) inhibitors and B blockers have significantly reduced mortality and morbidity in New York Heart Association (NYHA) class II-IV patients, while improving their quality of life. But that benefit is probably not permanent and will be limited in time. A variety of non-pharmacological approaches is available to treat these refractory heart failure patients. Heart transplant remains the best solution but can only be applied to a restricted number of patients.

Intraventricular conduction delay is associated with asynchronous ventricular contraction, even in patients without heart failure. Contraction abnormalities, prolonged mitral regurgitation and a shortened left

Address for reprints: Prof. Wei Hua
Clinical Electrophysiology Laboratory, Fu Wai Hospital, Chinese Academy of Medical Sciences, 167 Bei Li-shi Road, Beijing 100037, China

Tel: (86) 10 68314466-8290, Fax: (86) 10 68313012

Received June 7, 2001; revision accepted December 11, 2001

ventricular filling time have also been documented in patients with conduction defects and dilated cardiomyopathy.[1-4] Biventricular pacing is a promising new strategy for correcting the ventricular activation sequence and potentially improving myocardial function and clinical outcome in patients with heart failure.[5-8] Although large controlled clinical trials of biventricular pacing have yet to be completed, currently available data suggest that patients with advanced heart failure and ventricular conduction abnormalities may benefit from such therapy.

Intraventricular Conduction Delay and Biventricular Pacing

Wide QRS are frequently observed in patients with chronic heart failure associated with left ventricular (LV) systolic dysfunction. Some studies revealed a prevalence of intraventricular conduction delay (as defined by QRS duration >120 ms) in chronic heart failure patients, estimation at 27-53%.[9] These conduction abnormalities - intraventricular conduction delay in particular is considered to be an independently predictive factor of mortality. Thus in the Vesnarinone Trial (VEST) study,[10] the 6 years mortality rate in patients with chronic heart failure with altered LV function (LV ejection fraction <40%) was significantly higher in patients whose QRS duration exceeded 110 ms (65%) than in those where it did not (40%), regardless of the degree of LV impairment.

In addition, these conduction disorders have deleterious effects both on systolic function and on LV filling, and they can induce or enhance mitral "functional" regurgitation. Xiao and colleagues[11] demonstrated, in dilated cardiomyopathy (DCM) patients, that the presence of a left bundle branch block (LBBB) was associated with a more than 80% increase in LV pre-ejection contraction time and 60% increase in LV relaxation time; there was also a negative correlation between the QRS duration and the +dp/dt. So, the wider the QRS, the lower the contractility. In the same studies, analyzing the parameters of LV diastolic function revealed that the LV filling time was significantly reduced (by nearly 40%) in DCM patients in the presence of LBBB or a significant prolongation of the PR interval (>200 ms). In parallel, the quality of atrial contribution to LV filling was impaired, as reflected on transmitral Doppler by a single phase flow linked to E wave and A wave superimposition. Lastly, in patients with LV systolic dysfunction, the presence of an LBBB or prolonged PR interval is associated with an increase in the duration of mitral regurgitation. Incidentally, the presence of an LV-left atrial diastolic gradient-frequently found in patients with DCM and atrioventricular conduction disorders which can be the origin of diastolic mitral regurgitation.

The aim of multisite biventricular pacing is to correct not only the atrioventricular asynchrony but also the nonuniformity of ventricular activation, contraction and relaxation sequences. It is proposed primarily for patients with drug refractory heart failure with LV systolic dysfunction and wide QRS complex. In 1994 Cazeau et al[12] from France reported the remarkable benefit of biventricular pacing in a patient with drug-refractory CHF due to dilated cardiomyopathy, and left bundle-branch block (QRS=200 ms). The left ventricle (LV) and right ventricle (RV) were paced simultaneously to achieve a more physiologic depolarization sequence. Since this report, a substantial number of short-term studies have shown that biventricular pacing improves haemodynamics in CHF patients with severe left ventricular systolic dysfunction and major left sided intraventricular conduction disorders.[6,7,13,15,16] A longer spontaneous QRS complex may be predictive of a greater positive response to pacing. Intraventricular conduction delays cause an inefficient dysynchronous pattern of left ventricular activation with segments contracting at different times. The rationale of biventricular pacing is to improve the sequence of electrical activation (resynchronization) and create a more coordinated and efficient left ventricular contraction. Resynchronization may also reduce functional mitral regurgitation.[14-16] Reversal of left ventricular remodeling by synchronous biventricular pacing in heart failure was reported.[17]

Patients with chronic atrial fibrillation may also benefit. In this instance, continual biventricular pacing often requires radiofrequency ablation of the Atrial-ventricular (AV) junction to ensure control of ventricular depolarization by the pacemaker.[18] Optimized AV delay played an important role in improvement of hamodynomics particularly in patients accompanied by atrioventricular conduction delay. Shortening AV interval could reduce presystolic regurgitation and improve filling pattern of the left ventricle.[19]

Left Ventricular Pacing Technique

To achieve biventricular pacing, left ventricular lead placement is the most important part. The cardiac venous structures differ among individual patients, with wide variations in the location and size of the coronary sinus and its side branches. Consequently, adequate visualization of the venous anatomy is very important in transvenous left ventricular lead placement. The venous phase of the coronary angiogram sufficiently outlines the coronary sinus ostium and a number of its branches in about 20% of patients. Selective coronary sinus catheterization from the subclavian route undoubtedly provides better visualization of potential sites for lead placement. The use of an occlusive balloon enhances the quality of the images. AP, RAO, and LAO views of the coronary sinus will help in guiding the leads, and a knowledge of the position, angulations, and size of the side branches will assist in lead selection and placement.

The lead most commonly used for left ventricular pacing is the attain LV model 2187, a unipolar, polyurethane lead, available in 65 cm or 75 cm length, with a curved distal body and a soft tip. The tip can be straightened using the stylet. Withdrawal of the stylet alters the curve, allowing angulation of the lead to the desired location. Recently, the new transvenous over-the-wire and side wire (Figure 1) left ventricular lead system has been used in clinical practice.[20,21] The left ventricular lead is implanted via the subclavian vein and, ideally, placed in a vein in the posterolarteral or lateral wall of the heart, where the sensed endocardial signals occur late in the QRS complex. The right ventricular lead is then placed at a site anatomically remote from the left ventricular lead, with good electrical separation and, preferably, early in the QRS complex.

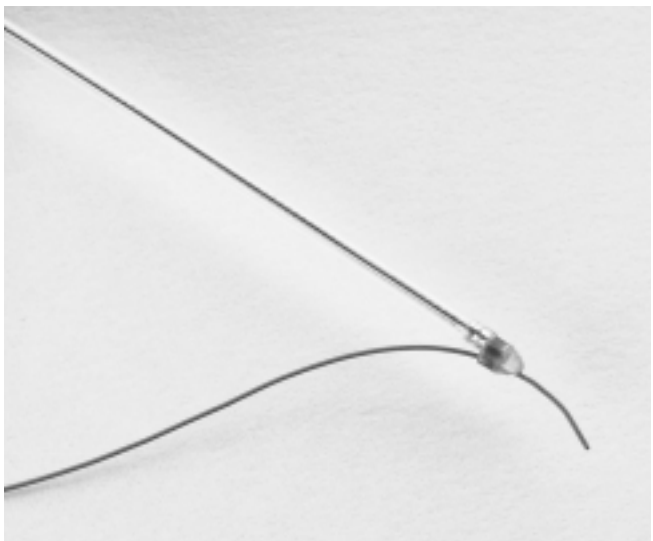

Figure 1. *Side-wire left ventricular lead system*

Successful transvenous ventricular lead implantation is defined as (1) a stable left ventricular lead position, (2) satisfactory pacing thresholds and (3) good electrical and anatomic separation of the right and left ventricular leads. The clinical experience shows that success rate for transvenous left ventricular lead implantation was 84-93%.[22,23] Left ventricular lead implantation requires more time than implantation of traditional pacemaker leads. New technology and techniques are likely to reduce the time required for implantation in the future.

Clinical Observation of Biventricular Pacing

Results from uncontrolled studies suggest that multisite pacing improves selected heart failure patients. One of the largest of these is the InSync study.[24,25] It comprised 103 patients with severe heart failure of mixed etiology. All patients had severe heart failure, NYHA functional class III-IV, and a QRS duration of at least 150 ms. Significant improvements by biventricular pacing were seen in most patients after 12 months of pacing compared to baseline with regard to NYHA class, 6-minute walk distance, and quality of life. Moreover, pacing reduced the QRS duration significantly and normalized the intraventricular delay as an indication that ventricular resynchronization had been achieved.

There are a number of randomized trials on the efficacy and safety of biventricular pacing, the results of some of them remain to be published (Figure 2). In the Pacing Therapies for Congestive Heart Failure (PATH CHF) trial,[26] patients with severe heart failure (120 ms) were included. After an extensive acute invasive evaluation performed during implantation, the patients were randomized during implantation, the patients univentricular mode - that is, right or left ventricular pacing only, no pacing, and biventricular pacing. The study enrolment ended in 1998 and included 54 patients. Interim results indicate a 40% improvement

in the 6-minute walk distance and a 50% improvement in quality of life after 1 month of the best univentricular mode cases constituted by left ventricular pacing, and 1 month of biventricular pacing.

The Multisite Stimulation in Cardiomyopathy (MUSTIC) study[22] involves 67 patients. Enrolment was completed in June 1999. This study includes only NYHA class III heart failure patients with a sinus rhythm, QRS duration of at least 150 ms. The patients were randomized in a single blind crossover fashion to 3 months each of biventricular pacing or fixed rate ventricular pacing at a rate of 40 beats per minute. The primary end points are the 6-minute walk distance and maximal oxygen uptake, with quality of life as a secondary end point. The result shows that the mean distance walked in 6 minutes was 23% greater with active pacing, the quality-of-life score improved by 32%, peak oxygen uptake increased by 8%, hospitalizations were decreased by two thirds, and active pacing was preferred by 85% of the patients.

The Multicenter Insync Randomized Clinical Evolution (MIRACLE) study[23] is a large prospective, randomized, double-blind, controlled trial designed to more definitively evaluated the clinical efficacy and safety of cardiac resynchronization for heart failure. Until July 2000, this study has being enrolled 370 patients with NYHA class III and IV systolic heart failure and QRS durations of 130 ms or more. The primary end points is defined the effects on functional status (quality of life, NYHA class, 6-minute hall walk distance) at 6 months. The result was presented in the North American Society of Pacing and Electrophysiology, 22nd Annual Scientific Sessions (NASPE 2001). The success rate for transvenous left ventricular lead was 93%. The 6-minute walk distance was 350 meters in active pacing and 300 meters during control phase. The quality of life score was improved 22%. The peak oxygen uptake was a trend to increase but no significant difference (p=0.056).

Biventricular pacing is a promising treatment in patients with severe heart failure with intraventricular conduction disturbances. It helps to improve patients by at least one functional class, increases the 6-minute walk distance by 20-40%, increases the oxygen uptake by 8-40%, and improves quality of life (as assessed by

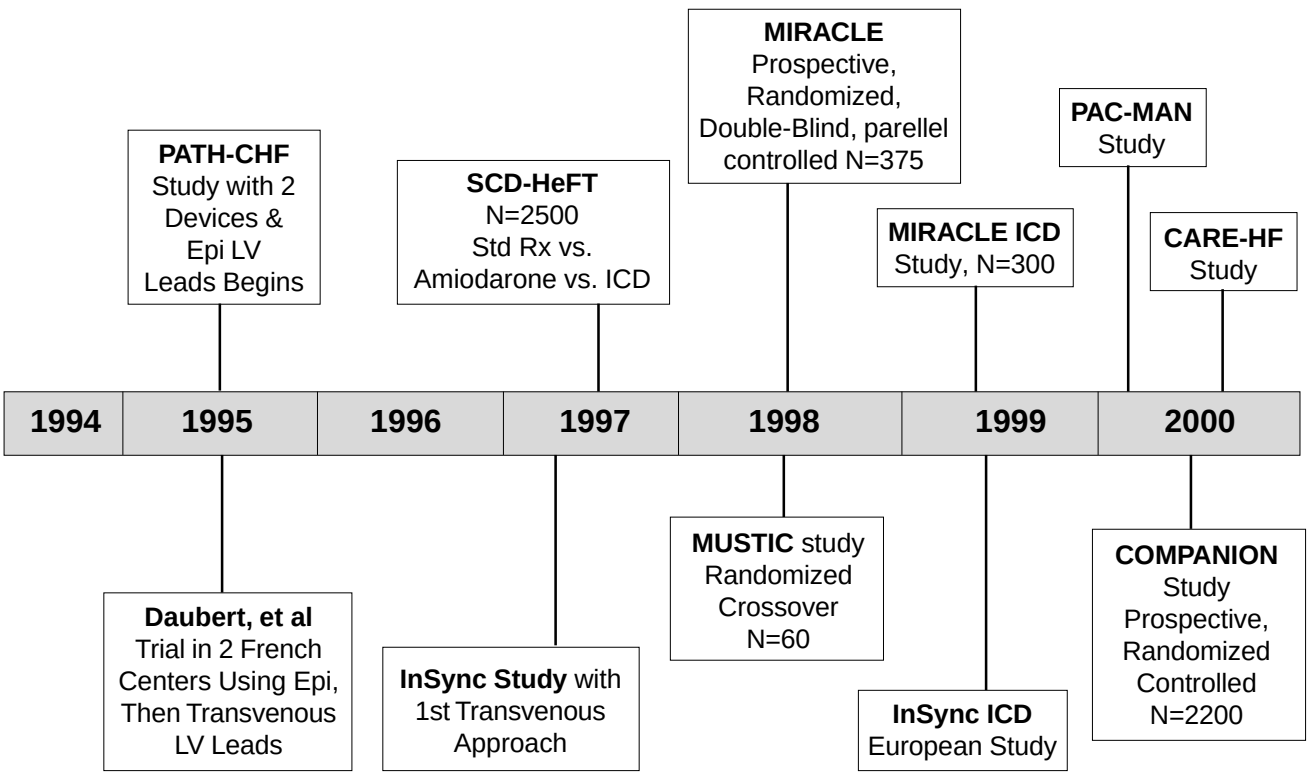

Figure 2. *Clinical studies about resynchronization therapy.*

the Minnesota living with heart failure questionnaire) by 20-50%. These figures are impressive. From uncontrolled and controlled studies it is also clear that not all patients respond to this treatment. Clinical, electrical or echocardiographic predictors of response to pacing are needed in view of the costs involved in pacemaker implantation and follow up. The ultimate success of the ambitious efforts to resynchronize cardiac activity in CHF will depend on defining its real benefit in a variety of circumstances by rigorous scientific evaluation and the development of new technology or further refinement of existing technology. For example, adjusted RV-LV stimulation delay - rather than simultaneous activation - may enhance the hemodynamic response. Left ventricular dual-site pacing seems to improve haemodynamics compare to single site left ventricular pacing. Implantable Cardioverter-Defibrillator (ICD) encompass the biventricular pacing could reduce episodes of ventricular tachyarrthmias by improve heart function in patients with intraventricular conduction delay.[27,28] Ongoing clinical studies (InSynch-ICD, CONTAKCD, COMPANION) will prove ICD combine biventricular pacing could further improve the quality of life and survivals.

References

1. Grines CL, Bashore TM, Boudoulas H, et al. Functional abnormalities in isolated left bundle branch block. The effect of interventricular asynchrony. Circulation 1989;79:845-85.
2. Xiao HB, Lee CH, Gibson DG. Effect of left bundle branch block on diastolic function in dilated cardiomyopathy. Br Heart J 1991;66:443-7.
3. Xiao HB, Brecker SJD, Gibson DG. Effects of abnormal activation on the time course of the left ventricular pressure pulse in dilated cardiomyopathy. Br Heart J 1992;68:403-7.
4. Xiao HB, Breaker JD, Gibson DG. Differing effects of right ventricular pacing and left bundle branch block on left ventricular function. Br Heart J 1993;69:166-73.
5. Gibson DG, Chamberlain DA, Coltart DJ, et al. Effect of changes in ventricular activation on cardiac haemodynamics in man. Comparison of right ventricular, left ventricular, and simultaneous pacing of both ventricles. Br Heart J 1971;33: 397-400.
6. Leclercq C, Cazeau S, Alonso C, et al. Multisite biventricular pacing in advanced heart failure: current status of the French Pilot Study. PACE 1999;22:733 (abstract).
7. Saxon LA, Kerwin WF, Cahalan MK, et al. Acute effects of intraoperative multisite ventricular pacing on left ventricular function and activition/constraction sequence in patients with depressed ventricular function. J Cardiovasc Electrophysiol 1998;9:13-21.
8. Hua W, Wang FZ, Zhang S, et al. Acute efficacy of three chamber biventricular pacing in patients with congestive heart failure. Chin J Cardiac Arrhyth 2000;5:38-40.
9. Aaronson K, Schwartz S, Chen T, et al. Development and prospective validation of a clinical index to predict survival in ambulatory patients referred for cardiac transplant evaluation. Circulation 1997;95:2660-7.
10. Venkateshawar K, Gottipaty K, Krelis P, et al. for the VEST investigators. The resting electrocardiogram provides a sensitive and inexpensive marker of prognosis in patients with chronic congestive heart failure. J Am Coll Cardiol 1999;33:145A (abstract).
11. Xiao HB, Gibson DG. Natural history of abnormal conduction and its relation to prognosis in patients with dilated cardiomyopathy. Int J Cardiol 1996;53:163-70.
12. Cazeau S, Ritter P, Bakdach S, et al. Four chamber pacing in dilated cardiomyopath. PACE 1994;17:1974-9.
13. Kerwin WF, Botvinick EH, O'Connell JW, et al. Ventricular contraction abnormalities in dilated cardiomyopathy: effect of biventricular pacing to correct interventricular dyssynchrony. J Am Coll Cardiol 2000;35:1221-7.
14. Baker P, Meijburg H, De Jonge, et al. Beneficial effects of biventricular pacing in congestive heart failure. PACE 1994; 17:820A (abstract).
15. Leclercq C, Cazeau S, Le Breton H, et al. Acute haemodynamic effects of biventricular DDD pacing in patients with end-stage heart failure. J Am Coll Cardiol 1998;32:1825-31.
16. Cazeau S, Ritter P, Lazarus A, et al. Multisite pacing for end-stage heart failure: early experience. Pacing Clin Electrophysiol 1996;19(11 Pt 2):1748-57.
17. Lau CP, Yu CM, Chau E, et al. Reversal of left ventricular remodeling by synchronous biventricular pacing in heart failure. Pacing Clin Electrophysiol 2000;23(11 Pt 2):1722-5.
18. Verlato R, Turrini P, Baccillieri MS, et al. Biventricular pacing and atrioventricular junction ablation as treatment of low output syndrome due to refractory congestive heart failure and chronic atrial fibrillation. Ital Heart J 2000;1:844-7.
19. Auricchio A, Stellbrink C, Block M, et al. Effect of pacing chamber and atrioventricular delay on acute systolic function of paced patients with congestive heart failure. Circulation 1999; 99:2993-3001.
20. Ppone C, Auricchio A, Schalij M, et al. Can tansvenous left ventricular leads be used as standard treatment for heart failure patients? The European experience with the first 1000 over-the-wire lead implantation. PACE 2001;24:619 (abstract).
21. Walker S, Levy T, Rex S, et al. The use of a "side-wire" permanent transvenous pacing electrode for left ventricular pacing. Europace 1999;1:197-200.
22. Cazeau S, Leclercq C, Lavergne T, et al. Effects of multisite biventricular pacing in patients with heart failure and intra-ventricular conduction delay. N Eng J Med 2001;344: 873-80.
23. Abraham W. Rationale and design of a randomized clinical trial to assess the safety and efficacy of cardiac resynchronization therapy in patients with advanced heart failure: The Multicenter InSync Randomized Clinical Evaluation (MIRACLE). J of Cardiac Failure 2000;6:369-80.
24. Gras D, Mabo P, Yang T, et al. Multisite pacing as a supplemental treatment of congestive heart failure: preliminary results of the

Medtronic Insync Study. PACE 1998;21:2249-225.
25. Grase D, Cazeau S, Mabo P, et al. Long-Term benefit of cardiac resynchronization in heart failure patients: The 12 month results of the InSync trail. JACC 2000;35230A.
26. Auricchio A, Stellbrink C, Sack S, et al. The Pacing Therapies for Congestive Heart Failure (PATH-CHF) study: rationale, design, and endpoints of a prospective randomized multicenter study. Am J Cardiol 1999;83(5B):130D-135D.
27. Pappone C, Salvatore C, Oreta G, et al. Can we optimize ventricular resynchronization by dual site left ventricular pacing? Acute haemodynamic findings in heart failure patients with left bundle branch block. PACE 2000;23:635.
28. Higgins SL, Yong P, Sheck D. Biventricular pacing diminishes the need for implantable cardioverter defibrillator therapy. Ventak CHF Investigators. J Am Coll Cardiol 2000; 36:824-7.

Update on the Treatment of Hypertension

BERNARD MAN-YUNG CHEUNG

From Department of Medicine, The University of Hong Kong, Hong Kong

CHEUNG: ***Update on the Treatment of Hypertension.*** *Despite recognition of the dangers of untreated and uncontrolled hypertension, it is still widely and persistently under-treated in the community. Universal screening of all adults for hypertension is essential, as the probability of hypertension in any randomly chosen person is considerable, especially from middle age onwards. The level of blood pressure, the presence of other risk factors, target organ damage and overt cardiovascular disease allow the physician to estimate the cardiovascular risk of a patient. The urgency of treatment depends on the degree of risk. It is now believed that the control of hypertension is the primary goal. This may necessitate changing the class of antihypertensive drug or using a combination of different classes. The choice of drug class is also determined by co-morbidities. The control of blood pressure to the point of normalisation of blood pressure is safe and beneficial, especially in diabetics. In patients with mild hypertension, non-pharmacological treatment through lifestyle modification has a definite place. (J HK Coll Cardiol 2002;10:17-20)*

Antihypertensive drugs, blood pressure, cardiovascular diseases, hypertension

摘要

儘管已認識到高血壓未治療或未得到控制的危險性，但社區中仍存在許多未得到持續性治療的高血壓患者。對所有成年人進行高血壓普查十分必要，因為在任何隨機抽取的人群中高血壓的概率比較大，特別是中年以上者。血壓水平、合併的其他危險因素、靶器官損害及明顯的心血管系統疾患有助於醫師評估患者的心血管危險性。治療的緊迫性有賴於疾病的危險程度。迄今得到認可的是高血壓的控制是首要目的。這有必要改換抗高血壓藥物的種類或採用聯合用藥。藥物種類的選擇同樣要受到伴發疾病的影響。把血壓控制在正常點是安全、有益的，尤其是糖尿病患者。輕度高血壓患者，通過改善生活方式的非藥物療法具有肯定的作用。

關鍵詞：抗高血壓藥物　血壓　心血管疾病　高血壓

Update on Hypertension

The risks of untreated hypertension are well known and well understood. Blood pressure has a direct relation with the risk of stroke and myocardial infarction. Hypertension may also lead to left ventricular hypertrophy, heart failure and renal failure. Despite recognition of the dangers of untreated and uncontrolled hypertension, it is still widely and persistently under-treated in the community. Many hypertensives remain undiagnosed. Of those who have been diagnosed, many of them are not on treatment. Of those who are on treatment, many are not well controlled. This "rule of halves" has been demonstrated in many countries around the world, including even the United States.[1] As hypertension is an asymptomatic disease, screening in apparently healthy individuals is warranted. The probability of hypertension in an individual in the general population is around 20%; this increases to as high as 50% in the elderly.[2] Universal screening of all adults for hypertension is essential, as the probability of hypertension in any randomly chosen person is considerable, especially from middle age onwards.

Address for reprints: Dr. Bernard Man-Yung Cheung
Department of Medicine, Queen Mary Hospital, 102 Pokfulam Road, Pokfulam, Hong Kong

Tel: (852) 2855 4768, Fax: (852) 2872 5828

Received August 29, 2001; revision accepted November 26, 2001

Screening for hypertension in first degree relatives is arguably mandatory in view of the clustering of hypertension in families due to shared genetics and environmental factors.

If high blood pressure is undesirable, we may ask what is the ideal blood pressure for normal people and what is the treatment target for hypertensives. We have little definite information on the former but we now have a partial answer for the latter. In the Hypertension Optimal Treatment (HOT) Study, an achieved diastolic blood pressure of 83 mmHg was associated with the lowest incidence of cardiovascular events (Table 1).[3] However, there was scarcely any difference whether the target diastolic blood pressure was <80, <85 or <90 mmHg. The results of HOT allow a dual interpretation; aggressive blood pressure reduction is justifiable as there is no harm, but cautious and cost-conscious prescribing is also justified as there is little additional benefit from lowering the diastolic blood pressure below 90 mmHg. Instead of increasing the dose or adding on another drug if the diastolic blood pressure is already below 90 mmHg, one might consider addressing other modifiable risk factors. There is one subgroup of hypertensives who should have aggressive reduction of blood pressure; these are the diabetics. In HOT and the UK Prospective Diabetes Study (UKPDS),[4] there were benefits in lowering the blood pressure beyond 140/90 mmHg. A target blood pressure of <130/85 mmHg is now recommended for diabetics.[5]

There is increasing recognition that elevated systolic blood pressure is of prognostic significance and treatment of systolic hypertension is beneficial, even if the diastolic blood pressure is normal as in isolated systolic hypertension. In the latest guidelines, a systolic blood pressure of 140 mmHg or above is considered abnormal.[1,5,7] However, a large proportion of the elderly has a systolic blood pressure higher than this. Thus, a large section of the elderly population is at risk from the complications of hypertension and requires a combination of lifestyle modifications and drug treatment.

The role of other additional medications for hypertensive patients is unclear. Aspirin was shown to be beneficial in HOT in terms of reduction of cardiovascular events, but the incidence of gastrointestinal bleeding is also increased, so the risks and benefits have to be worked out for each patient. Antioxidants are less promising than they have appeared to be; the Heart Outcome Prevention Evaluation (HOPE) did not show any cardiovascular benefit associated with vitamin E supplementation.[6]

The assessment of the overall cardiovascular risk for each patient is the cornerstone in the latest World Health Organisation (WHO) guidelines[4] as well as the British Hypertension Society guidelines[7] for the management of hypertension. As hypertension is only one of a number of risk factors for cardiovascular disease, it is desirable to address all these risk factors rather than to consider the level of blood pressure in isolation. Hence, in the new paradigm, the level of blood pressure, the presence of other risk factors, target organ damage and overt cardiovascular disease allow the physician to estimate the cardiovascular risk of a patient. The urgency of treatment depends on the overall degree of cardiovascular risk as well as the level of blood pressure. This new mode of thinking, although initially complicated, is an improvement on treating the blood pressure with disregard of actual cardiovascular risk. A pre-menopausal woman with mild hypertension, e.g. 150/100 mmHg, but no other risk factors has a very low immediate risk of cardiovascular events and should probably have lifestyle changes to lower blood pressure as far as possible. The same level of blood pressure in a 60-year-old male smoker with multiple risk factors requires treatment and aggressive modification of other risk factors to lower the cardiovascular risk. However, a major disadvantage of using cardiovascular risk in treatment decisions is that it makes no distinction between a cardiovascular event in the young and in the elderly. In the very elderly, treatment might only prolong life marginally whereas it is disastrous if a young person

Table 1. Recent major clinical trials

Trial objective	Name of Trial
Optimal blood pressure target	HOT[3]
Hypertension in diabetics	UKPDS[4]
CCB vs. placebo	Syst-Eur,[10] Syst-China[11]
CCB vs. other drugs	INSIGHT,[13] NORDIL[14]
ACEI vs. placebo	HOPE,[6] PROGRESS[18]
Comparing several drug classes	STOP-2,[12] ALLHAT[17]
Diet	DASH,[19,20] TONE[21]

has a debilitating stroke. It is therefore important to consider the potential benefits of treatment as well as the risks of no treatment.[8]

The relative merit of different classes of antihypertensive drugs is always a controversial area, not least because of commercial interests. The WHO,[5] British[7] and JNC-VI[1] guidelines have all attempted to address this issue. It is now believed that the control of hypertension is the primary goal. This may necessitate changing the class of antihypertensive drug or using a combination of different classes. Following some adverse findings about calcium channel blockers (CCBs) mainly from case control studies,[9] randomised controlled trials such as Systolic Hypertension in Europe (Syst-Eur),[10] Systolic Hypertension in China (Syst-China),[11] the Swedish Trial in Old Patients with Hypertension-2 (STOP-Hypertension-2),[12] the International Nifedipine GITS Study Intervention as a Goal in Hypertension Treatment (INSIGHT)[13] and Nordic Diltiazem (NORDIL) Study[14] have shown that this drug class also reduces cardiovascular events. This underlines the paramount importance of blood pressure control. However, two meta-analyses of hypertension trials have recently been published with somewhat conflicting conclusions regarding CCBs. One reported a significantly higher risk of myocardial infarction and heart failure associated with CCBs,[15] whereas the other regarded these differences to be of borderline significance.[16] In Asia, the incidence of stroke is higher than that of myocardial infarction. As CCBs are effective in lowering blood pressure and reducing the risk of stroke, they have an important place in the formulary.

The merits of alpha-blockers are put in doubt by the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), in which a higher rate of cardiovascular events, mainly heart failure and strokes, was observed in the alpha-blocker arm.[17] However, there was no difference in the primary endpoint, which was the occurrence of fatal and non-fatal myocardial infarction. Alpha-blockers may not be the first-line drug for the treatment of hypertension, but they remain useful for the control of blood pressure, especially in elderly male patients with prostatic symptoms.

The latest guidelines have also incorporated clinical trial evidence to support the use of certain classes in certain situations. For example, a hypertensive with angina should receive beta-blockers. ACEIs have emerged as an important drug class, preventing cardiovascular events in those who are at risk, as shown in the HOPE study.[6] On the other hand, both the STOP-Hypertension-2 and the UKPDS failed to show that ACEIs are superior to conventional antihypertensive agents.

In the HOPE study, subjects randomised to treatment with an ACEI had lower cardiovascular events even if they were normotensive.[6] It has been argued that the degree of blood pressure lowering did not fully explain the benefits observed. It was postulated that ACEIs might have a protective effect beyond blood pressure reduction. Interestingly, in the Perinodopril pROtection aGainst Recurrent Stroke Study (PROGRESS), a decrease in stroke rate was observed in normotensive as well as hypertensive patients randomised to treatment with an ACEI.[18]

The cost-effectiveness of antihypertensive medications varies enormously because of the tremendous differences in the price of drugs. At the same time, the efficacies of antihypertensive drugs are remarkably similar. Large clinical trials have shown that, in terms of cardiovascular outcome, the newer classes are not superior to beta-blockers and diuretics.[12,13,17] In patients at high risk from cardiovascular disease, use of expensive medications may be acceptable. Yet, in patients with mild hypertension and at low risk from cardiovascular disease, cost-effectiveness should not be ignored, especially in the public sector. Nevertheless, patients respond differently to antihypertensive medications and some may require newer and more expensive medications to control their blood pressure or to avoid side effects.

In the approach to treating patients with mild hypertension, non-pharmacological treatment has a definite place. Factors leading to hypertension in Hong Kong include ageing, family history, obesity and diabetes. The Dietary Approaches to Stop Hypertension (DASH) study showed that a healthy diet rich in fruits and vegetables and low in fat and sodium lowers blood pressure.[19,20] The Trial of Non-pharmacologic intervention in the Elderly (TONE) showed that weight loss and reduction in salt intake resulted in decreased blood pressure and need for antihypertensive medications.[21] We have also identified sodium intake as a strong determinant of diastolic blood pressure.[22]

Obesity and sodium intake are modifiable risk factors. In patients with mild hypertension, lifestyle measures may be sufficient to control blood pressure or at least ameliorate it. For the whole population, universal screening for hypertension and a healthier lifestyle are likely to bring about the largest amount of benefit to the greatest number of people with the minimum of risks.

Acknowledgement

BMY Cheung is a member of the Institute of Cardiovascular Science and Medicine of the University of Hong Kong.

References

1. The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Arch Intern Med 1997;157:2413-46.
2. Janus ED. Epidemiology of cardiovascular risk factors in Hong Kong. Clin Exp Pharmacol Physiol 1997;24:987-8.
3. Hansson L, Zanchetti A, Carruthers SG, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet 1998;51:1755-62.
4. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ 1998;317: 703-13.
5. 1999 World Health Organization - International Society of Hypertension Guidelines for the management of hypertension. J Hypertens 1999;17:151-83.
6. Yusuf S, Sleight P, Pogue J, et al. for the Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. N Engl J Med 2000; 342:145-53.
7. Ramsay L, Williams B, Johnston G, et al. Guidelines for management of hypertension: report of the third working party of the British Hypertension Society. J Hum Hypertens 1999; 13:569-92.
8. Cheung BMY, Kumana CR. Should decisions on treatment be based on absolute benefit rather than absolute risk? NZ Med J 2001;114:214-5.
9. Furberg CD, Psaty BM, Meyer JV. Dose-related increase in mortality in patients with coronary heart disease. Circulation 1995;92:1326-31.
10. Staessen JA, Fagard R, Thijs L, et al. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. Lancet 1997;350:757-64.
11. Liu L, Wang JG, Gong L, et al. Comparison of active treatment and placebo in older Chinese patients with isolated systolic hypertension. Systolic Hypertension in China (Syst-China) Collaborative Group. J Hypertens 1998;16:1823-9.
12. Hansson L, Lindholm LH, Ekbom T, et al. for the STOP-Hypertension-2 study group. Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity in the Swedish Trial in Old Patients with Hypertension-2 study. Lancet 1999;354:1751-56.
13. Brown MJ, Palmer CR, Castaigne A, et al. Morbidity and mortality in patients randomised to double-blind treatment with a long-acting calcium-channel blocker or diuretic in the International Nifedipine GITS study: Intervention as a Goal in Hypertension Treatment (INSIGHT). Lancet 2000;356:366-72.
14. Hansson L, Hedner T, Lund-Johansen P, et al. Randomised trial of effects of calcium antagonists compared with diuretics and beta-blockers on cardiovascular morbidity and mortality in hypertension: the Nordic Diltiazem (NORDIL) study. Lancet 2000;356:359-65.
15. Pahor M, Psaty BM, Alderman MH, et al. Health outcomes associated with calcium antagonists compared with other first-line antihypertensive therapies: a meta-analysis of randomised controlled trials. Lancet 2000;356:1949-54.
16. Neal B, MacMahon S, Chapman N. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. Blood Pressure Lowering Treatment Trialists' Collaboration. Lancet 2000;356:1955-64.
17. ALLHAT Collaborative Research Group. Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). JAMA 2000; 283:1967-75.
18. Perinodopril pROtection aGainst Recurrent Stroke Study (PROGRESS). Presented at the European Society of Hypertension Congress in Milan, 2001.
19. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N Engl J Med 1997;336:1117-24.
20. Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. N Engl J Med 2001;344:3-10.
21. Whelton PK, Appel LJ, Espeland MA, et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. JAMA 1998;279:839-46.
22. Cheung BMY, Ho SPC, Lau CP. Diastolic blood pressure is related to sodium intake in hypertensive Chinese. Q J Med 2000; 93:163-8.

ECG Quiz

CHIU-SUN YUE, WAI-KWONG CHAN

From Division of Cardiology, Department of Medicine & Geriatrics, United Christian Hospital, Kowloon, Hong Kong

A 90-year-old gentleman was referred to Accident and Emergency Department (AED) by community nurse because he complained of dizziness. He has history of atrial fibrillation, congestive heart failure and Parkinsonism on regular medical treatment. At AED, a 12-lead ECG was done. What was the diagnosis ? (see ECG attached)

1) a) Fast atrial fibrillation with aberrant conduction
   b) Atrial flutter with 1:1 conduction
   c) Non-sustained ventricular tachycardia
   d) Tremor-induced ECG artifact

What would be your initial management for this patient ? (His blood pressure was 119/89mmHg and he was conscious)

2) a) Intravenous lignocaine
   b) Intravenous ATP
   c) Intravenous verapamil
   d) Observe and repeat ECG later

Cardiologist was consulted for further management because of suspected ventricular tachycardia and dizziness. Physical examination revealed the features of Parkinsonism. A 12-lead ECG was repeated which showed atrial fibrillation and right bundle branch block with tremulous isoelectric line. Blood biochemistry was unremarkable. Echocardiogram revealed satisfactory left ventricular function with mild mitral, aortic and tricuspid regurgitation. He remained stable after admission and was discharged home shortly afterwards. The diagnosis in this patient was tremor-

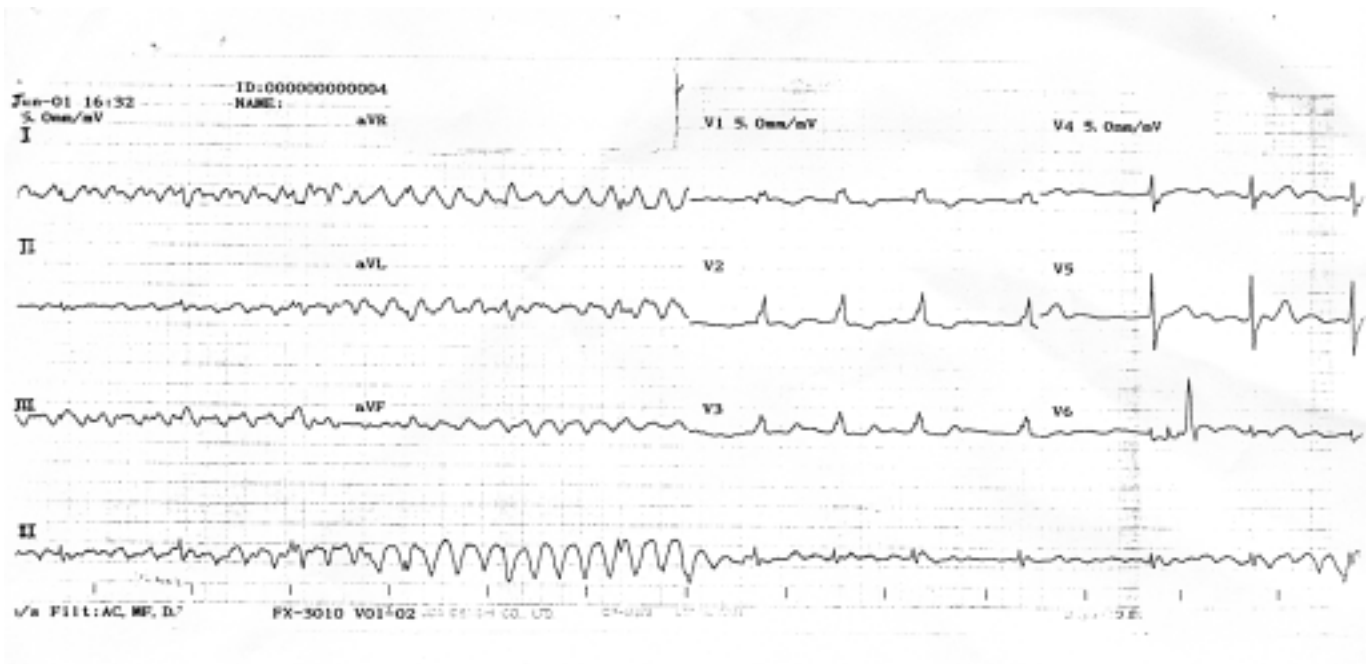

Figure 1. *12-lead ECG done at Accident and Emergency Department*

induced ECG artifact mimicking ventricular tachycardia due to underlying Parkinsonism with marked resting tremor.

Answers

1) d) Tremor-induced ECG artifact
2) d) Observe and repeat ECG later

Discussion

This patient suffers from Parkinsonism for years with history of frequent fall and marked resting tremor. Tremor-induced ECG artifact was suspected at first glance after admission because of the following reasons. First, he was relatively asymptomatic and hemodynamically stable apart from some non-specific dizziness prior to admission. Second, distinct QRS complexes were shown to be buried in the wide amplitude repetitive electrical activity mimicking ventricular tachycardia on careful inspection.[1] Third, judging from the cycle length of the wide amplitude electrical activity, the frequency of the resting tremor was estimated to be 3 to 4 Hz which correlated with that seen in Parkinsonism. Fourth, the wide amplitude electrical activity was more pronounced in the limb leads. Fifth, the ECG was interpreted in the context of the patient with history mentioned above. His previous ECGs already revealed tremulous isoelectric line with background atrial fibrillation and right bundle branch block. Fortunately, no treatment was prescribed for the ECG artifact in this patient.

In daily clinical practice, electrocardiogram is a common and useful investigation, especially for patients presenting with cardiac problems. Physician should be aware of common ECG artifacts, which can be caused by skeletal muscle tremor, electrical interference from the network or appliance and electrode movements. ECG artifacts may make ECG interpretation difficult or may cause incorrect ECG interpretation with inappropriate subsequent management.

Knight et al. reported 12 artifacts simulating monomorphic or polymorphic ventricular tachycardia.[2] All those twelve patients underwent unnecessary diagnostic or therapeutic interventions as a result of ECG misdiagnosis, for example, cardiac catheterization, electrophysiologic testing, intravenous lignocaine, implantation of permanent pacemaker and implantable cardioverter defibrillator. Moreover, the use of health care resources was increased and inappropriate in those cases.

In conclusion, when one interprets a wide QRS complex ECG, tremor-induced ECG artifact should be included in the differential diagnosis, especially if the patient has relevant medical illness.

References

1. Srikureja W, Darbar D, Reeder GS. Tremor-induced ECG artifact mimicking ventricular tachycardia. Circulation 2000; 102:1337-8.
2. Knight BP, Pelosi F, Michaud GF, et al. Clinical consequences of electrocardiographic artifact mimicking ventricular tachycardia. N Engl J Med 1999;341:1270-4.