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Guest Editorial

Drug Eluting Stent: A Major Advance in Fighting Coronary Artery Restenosis

YUK-KONG LAU

From Department of Medicine, Ruttonjee and Tang Shiu Kin Hospitals, Hong Kong

Since the first use of coronary angioplasty in 1977, there have been major growth and development in percutaneous coronary intervention (PCI). Due to the advances in techniques, experiences, devices, and newer potent antiplatelet and antithrombotic medications, PCI is increasingly performed in highly complex and high-risk patients with a reasonably low complication rate. Coupled with reduced discomfort, shorter hospital stay and recovery time, it has far outnumbered the volume of coronary artery bypass surgery. Currently, 1.7 million PCI procedures are performed annually worldwide with increases by 15-20% per year the last decade.

Problems in the early years of balloon angioplasty included dissection, abrupt closure and restenosis, the first two of which are largely controlled by coronary stenting since early 1990's. Moreover, stents significantly reduce coronary artery restenosis from an average of 30-50% post balloon angioplasty to 20-30% after stenting. Thus, stents improve the short-term success rate and the safety of PCI. In longer term, they decrease the restenosis and the need for repeat revascularization. As a major breakthrough in PCI, stents are currently widely used in about 80% of such procedures.

Address for reprints: Dr. Yuk-Kong Lau
Division of Cardiology, Department of Medicine, Ruttonjee Hospital, 266 Queen's Road East, Wanchai, Hong Kong

Tel: (852) 2291 1338, Fax: (852) 2291 1335

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However, stenting does not eliminate restenosis. The three major pathogenic factors in restenosis are elastic recoil, negative arterial remodeling and neointimal hyperplasia. Stents virtually eliminate elastic recoil and counteract the arterial remodeling. But neointimal hyperplasia after stenting can still cause significant and refractory restenosis. Depending on the pattern of in-stent restenosis, treatment with balloon angioplasty alone is still followed by a further restenosis in 45-55% of cases. Intravascular brachytherapy has been used in recent years and found to be effective in managing in-stent restenosis, but the recurrence after brachytherapy is still in the order of 26-32%.[1-3] Moreover, the procedure itself adds extra cost, and technical difficulty and consumes extra procedure time. The long-term safety with the extra radiation is still uncertain and meritorious of concern. Thus, to prevent the development of restenosis right after PCI is a critical issue. Enormous amount of research is being conducted to achieve this ideal goal.

The process of neointimal hyperplasia is initiated from the arterial injury sustained during PCI. The arterial injury and intimal denudation trigger off inflammatory responses. Growth factors and cytokines produced would activate smooth muscle cell (SMC) proliferation and migration and elicit production of extracellular matrix. Together these processes significantly limit intra-arterial lumen leading to restenosis. Stent-based drug delivery to intervene this process has been developed in an attempt to counteract this phenomenon. A number of drugs have been studied and additional ones are being pursued at present: anticoagulants (heparin, hirudin), antiplatelet agents (abciximab), anti-inflammatory drugs (dexamethasone), and antiproliferative agents

(sirolimus, paclitaxel, actinomycin D and batimastat). To date, the sirolimus-eluting stents appear to demonstrate a remarkable efficacy and safety in preventing restenosis.

Sirolimus is the generic name of Rapamycin, a drug used in preventing renal transplant rejection. Food and Drug Administration (FDA) in the USA had approved this clinical use in 1999 and CE Mark in Europe was obtained in 2000. Sirolimus is a cytostatic agent, by virtue of cell cycle inhibition which suppresses SMC proliferation and inflammatory cell activity. A small fractional amount of systemtic dose of sirolimus is incorporated into a polymer matrix surrounding a balloon-expandable metallic stent (Bx Velocity, Cordis, Johnson & Johnson). In vivo, the drug is released slowly and gradually over 30 to 45 days after deployment in the coronary artery.

The First-In-Man (FIM) study[4] was a small pilot trial involving 45 patients with de novo coronary lesions of length <18 mm and vessel diameter 3.0-3.5 mm. All patients were treated with an 18 mm long sirolimus-eluting stent. Follow-up to 24 months revealed 0% in-stent restenosis and minimal neointimal hyperplasia. There was no subacute or late stent thrombosis. Only one patient required another PTCA at 14th month due to new progression at a site outside the previously stented segment.

A RAndomized double-blind study with the sirolimus-eluting Bx VElocity balloon expandable stent in the treatment of patients with de novo native coronary artery Leision (RAVEL)[5] involved 238 patients from 19 centers. One hundred and twenty patients received the sirolimus-eluting stents while 118 patients received the bare stents as control. At 6 months, there was 0% restenosis rate in the sirolimus arm as opposed to 26% in the control arm ($p<0.0001$). At 12 months, target lesion revascularization (TLR) rate was 0% in the sirolimus group. There was no difference in death rate and myocardial infarction (MI) but the major adverse cardiac event (MACE) rate was 5.8% in the sirolimus group versus 28.8% in the control arm ($p<0.0001$), mainly due to the 27% TLR rate in the latter.

Subsequently, the results of a multicenter, randomized double blind study of the SIRolImUS-coated Bx Velocity balloon expandable stent in the treatment of patients with de novo coronary artery leisions (SIRIUS-400),[6] were presented in May 2002. SIRIUS involved over 1,100 patients from 53 sites in the U.S. with half of whom received sirolimus stents. All received 3 months of dual antiplatelet therapy (aspirin and clopidrogrel). The patient cohort was more complex than in RAVEL: 28% diabetes, 72% hyperlipidemia, 42% multivessel disease, 24% Type C lesions and 100% with a longer lesion length of 15 mm-30 mm. The primary endpoint was Target Vessel Failure (TVF: cardiac death, MI or TVR) at 9 months. Preliminary findings of the first 400 patients showed that the 8-months in-stent restenosis rate as assessed by protocol-based reangiogram was reduced from 31% in the control arm to 2% in the treated arm ($p<0.001$). Independently, intravascular ultrasound confirmed a 94% reduction in neointimal hyperplasia in the sirolimus group, as compared with control. The in-lesion (defined as in-stent plus 5 mm proximal and distal to the stent margin) restenosis decreased from 32.3% in the control group to 9.2% in the sirolimus group ($p<0.001$). Target lesion revascularization was reduced from 16.7% in the control to 4.7% in the sirolimus group (a 72% reduction). At 9-months follow-up, the event-free (from death, MI, CABG and Re-PTCA) survival was 90.8% in the sirolimus group versus 80.6% in the control ($p=0.001$). There was no acute, subacute or late stent thrombosis in the treatment group.

Though long-term safety beyond 2 years is still pending, the data obtained in the last few years are encouraging enough by the demonstrated superiority of the sirolimus-eluting stents in significantly reducing coronary artery restenosis and TLR. Such stent has been approved by CE Mark in April and is available for use in Hong Kong since May 2002.

There are other ongoing trials using sirolimus-eluting stents. The E-SIRIUS trial involves 350 patients in Europe. The C-SIRIUS trial involves 100 patients in Canada. Another coronary bifurcation trial on 75 patients will be completed later this year.

However, the cost of the sirolimus-eluting stent is substantially higher than its bare stent counterpart by more than ten thousand Hong Kong dollars (~US$1,300). Despite the higher initial cost, such stents can markedly reduce the need of repeated revascularization procedure (and potential complications). Cost-effectiveness analysis based on more clinical data and local patient demographics is needed before any definite recommendation can be made. It is likely that two groups of patients will benefit most from using the drug eluting stents: patients with high risk of coronary artery restenosis like diabetes, small coronary vessel and long diffuse lesion; and patients with high clinical risk due to restenosis such as those with poor ventricular function and artery supplying a large proportion of remaining viable myocardium. Meanwhile, cardiologists should exercise clinical judgement in individual situation and should refrain from routine widespread use of sirolimus-eluting stents until further health economic data of such stent are available.

In summary, sirolimus-eluting stents represent a major advance in our battle against coronary artery restenosis. They will likely alter the use and approach of PCI in managing a major cause of death in developed countries including Hong Kong. Nevertheless, primary and secondary prevention with healthy life style, exercise and low cholesterol diet and control of smoking, hyperlipidemia, diabetes, as well as hypertension should be the fundamental strategy in fighting against coronary artery disease.

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Carotid Stent-Supported Angioplasty Using Different Distal Protection Devices

STEVEN SIU-LUNG LI, YUI-CHI SO, CHIU-LAI FU, CHEUK-HON WONG, CHIU-WAH LAM, SIU-FUNG YIU, CHUNG-SEUNG CHIANG, KAU-CHUNG HO

From Division of Cardiology, Department of Medicine, Queen Elizabeth Hospital, Kowloon, Hong Kong

LI ET AL.: ***Carotid Stent-Supported Angioplasty Using Different Distal Protection Devices.*** *Stroke is an important cause of morbidity and mortality in Hong Kong. Extra-cranial carotid stenosis is a common cause of thrombotic stroke, although its incidence is less in Chinese compared with Caucasians. Carotid endarterectomy is the conventional revascularization procedure for carotid stenosis. In the past decade, carotid angioplasty has been emerging as a treatment option for patients with significant carotid stenosis. Due to the intrinsic mechanism of angioplasty, distal embolization causing thromboembolic stroke has been one of the most important complications of carotid stenosis. Distal protection has been shown to be safe and effective in preventing distal embolization during the procedure. According to their mechanism, distal protection devices can be categorized into two major types, namely distal occlusion balloon and filters. Distal occlusion balloon system is of lower crossing profile but it causes temporary cessation of blood flow during the procedure, which may not be well tolerated in all patients. Filters, on the other hand, allow continuous blood flow during the procedure but are of much higher crossing profile, which may make their passage through tight and angulated lesions difficult and traumatic. The choice of the different distal protection devices depends on the characteristics of the lesions and the status of contralateral carotid artery and collateral supply. Local experience reported similar feasibility and efficacy as in the literature. Although the ideal distal protection device is yet to be developed, the use of distal protection devices would become, wherever feasible, a standard during carotid stent-supported angioplasty. (J HK Coll Cardiol 2002;10:179-183)*

Carotid angioplasty, carotid stenosis, distal cerebral protection

摘要

在香港，中風是致死和致殘的重要原因。頸外動脈狹窄是血栓形成性中風中最常見的病因。頸動脈內膜剝脫術是頸動脈狹窄傳統的血運重建方法。在過去的十年，頸動脈成型術已經成為嚴重頸動脈狹窄的一種治療選擇。由於血管成型術的一些內在機制，遠端血栓栓塞導致的血栓栓塞性中風已經成為頸動脈狹窄最嚴重的併發症。在操作期間應用遠端保護裝置已經顯示在防止遠端栓塞方面是安全有效的。根據它們的作用機制，遠端保護性裝置可以分為兩種類型，分別稱為遠端阻塞球囊和篩檢程式。遠端阻塞球囊裝置系統有著較小的橫截面積，可在操作過程中使血流一過性中斷，但並不是所有患者均可耐受。相反，篩檢程式在操作過程中允許血流持續通過，但它們有著較大的橫截面積，有可能使它們在通過窄的或成角的病變時困難和造成損傷。不同遠端保護裝置的選擇依賴病變的特點和對側頸動脈和側枝迴圈的供血狀態。本市的經驗和文獻報道一樣，是可行和有效的。儘管理想的遠端保護裝置仍需要發展完善，但遠端保護性裝置的應用將成為行頸動脈支撐性支架成型術的常規。

關鍵詞：頸動脈血管成型術　頸動脈狹窄　遠端腦動脈保護

Address for reprints: Dr. Steven Siu-Lung Li
Division of Cardiology, Department of Medicine, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon, Hong Kong

Tel: (852) 2958 8888, Fax: (852) 2384 4698

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Stroke is an important cause of morbidity and mortality in Hong Kong. Extra-cranial carotid stenosis is a common cause of thrombotic stroke. The therapy of carotid stenosis may be either medical or revascularizational. Carotid endarterectomy is the gold standard of surgical revascularization of carotid stenosis and has been shown to be superior to medical therapy by several large randomized trials.[1-3] However, in the recent few years, with more and more published data regarding its efficacy and safety, carotid stenosis has been emerging as a treatment option for the treatment of carotid stenosis.[4-7]

Due to the intrinsic mechanism of angioplasty, distal embolization is an inevitable phenomenon. Plaque disruption may occur during engagement of guiding catheter, wire and balloon passage, balloon expansion and stent deployment at the site of atherosclerotic lesion. The clinical significance of the generation of embolic particles depends on the number released and the size of the particles. Ohki demonstrated in his ex-vivo model that echolucent plaques and plaques with a degree of stenosis greater than 90% produced a higher number of embolic particles.[8]

There may be a number of ways to minimize the cerebral embolization during carotid angioplasty. Premedication with aspirin and Clopidogrel is important. Selection of patients is also important. Advanced age, lesion severity, long or multiple stenoses are independent predictors of procedural stroke and are associated with increased risk of stroke.[9] Proper technique during the angioplasty procedure with the least traumatic way to engage the guiding catheter and to cross the lesion with low profile wires and balloons should minimize the risks of distal embolization. Finally, cerebral distal protection devices should mechanically catch the maximal number of embolic particles released.

The ideal protection device should be simple and easy to use, and yet low profile and atraumatic. It should effectively eliminate embolic particles and be well tolerated without any cerebral ischemic phenomenon. The current commonly available distal protection systems may be divided into two main categories, namely the occlusion balloon system and filters. The distal occlusion balloon system occludes the internal carotid artery above the lesion with the balloon inflated at 1-2 atmosphere. The debris released by the dilatation and stent placement is then eliminated by aspiration. Filters, on the other hand, trap dislodged particles without interrupting the blood flow to the distal vascular bed.

Currently, the occlusion balloon systems include the PercuSurge Guardwire system (Medtronic, USA) and the PARODI system (ArteriA Medical Science, Inc) whereas the filters include the Angioguard (Cordis, USA), NeuroShield (Mednova, UK) and EPI (Boston Scientific Cooperation, USA) filter systems (Table 1).

The PercuSurge GuardWire distal protection system (Figures 1a and 1b) composed of three major components: the GuardWire temporary occlusion balloon, the inflation/deflation kit (consisting of the Microseal Adaptor and EZ Flator) and the Export Aspiration Catheter. The GuardWire has a dual role by acting as a primary angioplasty wire and the temporary occlusion balloon. It has a crossing profile of 0.014" at its tip and 0.036" at the site of un-inflated occlusion balloon. The wire itself has a 2.5 cm shapeable tip and a working length of 200 and 300 cm. The distal occlusion balloon has a working length of 4.5 mm and an inflatable diameter range of 3.0 to 6.0 mm. The Export Aspiration catheter has a working length of 145 cm with a rapid exchange design and an aspiration lumen of 1 mm.

During the intervention procedure, the Guardwire

Table 1. Comparison of different distal protection devices

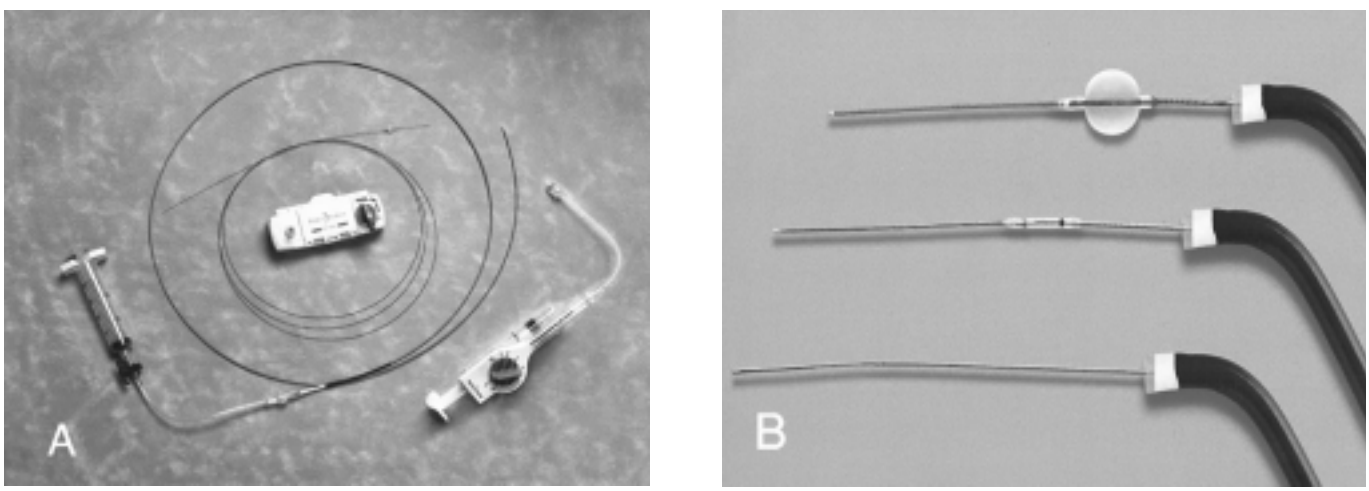
	GuardWire Plus	Angioguard XP	NeuroShield	EPI Filter Wire
Wire	0.014"	0.014"	0.014" with a 0.018" tip	0.014"
Shapeable tip length (cm)	2.5	3.5	3	3
Length of wire(cm)	300	300	300	300
Crossing profile	0.036" at balloon site	3.2-3.9 F	3.5 F	3.9 F
Sizes of devices (mm)	3.0-6.0 mm inflatable range	4-8	4-6	3.5-5.5

is first advanced carefully beyond the lesion. The distal occlusion balloon is then inflated to a size about 0.5 mm larger than the reference vessel diameter. When the balloon is optimally inflated, it becomes square shaped and complete occlusion is confirmed by a test of contrast injection. With the occlusion balloon inflated, the lesion is pre-dilated, stented and post-dilated as usual. Due to the presence of vertebrae as bony landmarks, positioning of the balloon and stent without contrast injection is rarely a problem. Aspiration is then performed with the Export catheter. The occlusion balloon is then deflated and flow is restored.

The PARODI system is a 'flow reversal' system. It consists of two units: one is a small balloon catheter that is used to occlude the external carotid artery; the other is a large sheath that is used to occlude the common carotid artery. Reverse flow is established by connecting the arterial sheath with a venous sheath placed into the femoral vein. Any debris generated during the angioplasty procedure would be directed away from the cerebral circulation. A filter located in the arteriovenous shunt prevents embolic particles to enter the venous system.

The filters in general consist of a basket or net-shaped device mounted or delivered on a steerable 0.014" wire. The filters have a porous membrane that can block the passage of particles greater than 80 microns or above, while allowing blood to pass through. The device is delivered across the lesion within a delivery sheath. For tight lesions, they may be first pre-dilated with a 2.5 mm balloon. When positioned at the desired distal site, the delivery sheath is withdrawn and the filter is released in a self-expanding manner. The angioplasty procedure is then proceeded as usual with the filter protection. After the angioplasty procedure, the filter is then withdrawn with a capture sheath with all the debris retrieved within the device. Angioguard XP (Figure 1c) has a crossing profile from 3.2 to 3.9 F (depending on the size of the filter which ranges from 4-8 mm) and can be used to treat vessels of diameters ranging from 3-7 mm. The filter basket with 100-micron pores is mounted on a 0.014" wire, which has a 3.5 cm shapeable tip. The Mednova III NeuroShield (Figure 1d) device uses a floating filter on a bare wire design that has a 3 cm long 0.018" shapeable wire tip and a 0.014" wire shaft. The delivery catheter has a catheter profile of 3 F and a crossing profile of 3.5 F. The filter diameters range from 4.0 to 6.0 mm and are compatible for vessel sizes of 3.5 to 6.2 mm diameters. The EPI Filter Wire (Figure 1e) has a crossing profile of 3.9 F and has a one-size-fits-all and monorail design that can treat vessels from 3.5 to 5.5 mm. The filter consists of a 1.5 cm long polyurethane membrane basket with 80-100 micron pores, which is mounted on a 0.014" wire with a 3 cm long shapeable tip.

Due to the different mechanism of protection, the choice of the distal protection devices depends very



Figures 1a and 1b. *GuardWire Plus system.*

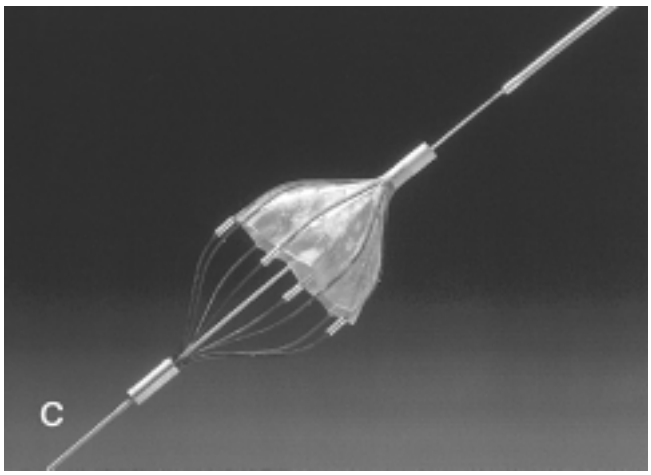


Figure 1c. *Angioguard XP.*

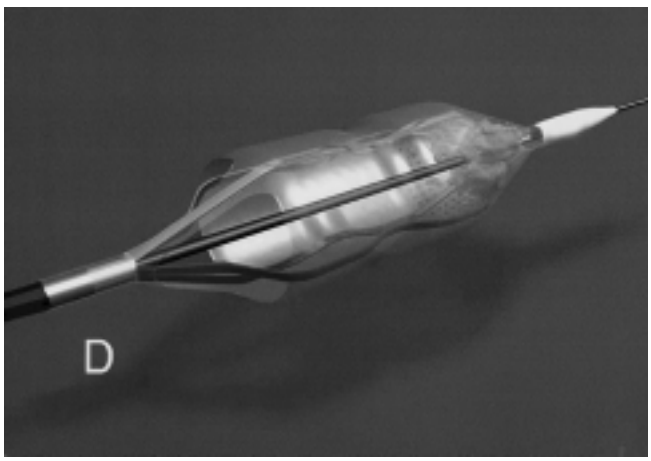


Figure 1d. *NeuroShield.*

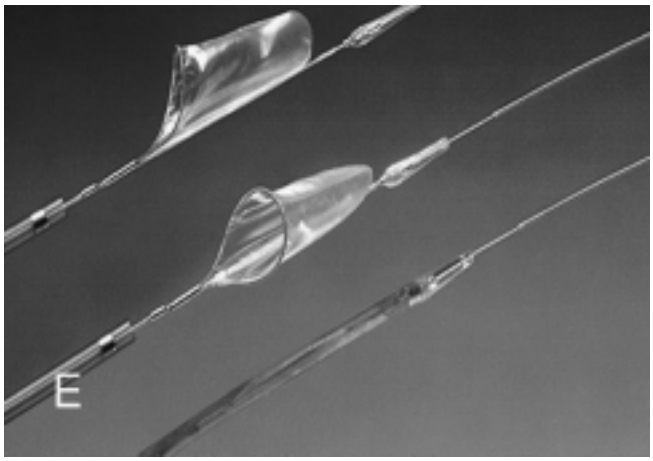


Figure 1e. *EPI Filter Wire.*

much on the lesion characteristics, status of collateral circulation and the experience of the operator. Due to its smaller crossing profile, the PercuSurge Guardwire system is useful in crossing tight, tortuous, long or angulated lesions. However, since the mechanism of protection involves temporary cessation of blood flow during the procedure, it should be avoided in patients with contralateral carotid artery stenosis or occlusion, or when the collateral blood supply through the circle of Willis is deemed inadequate. On the other hand, the filters allow antegrade blood flow during the procedure; they are not contraindicated even in patients with contralateral carotid artery occlusion. Nevertheless, due to their higher crossing profile (>3 F), the filters may not be indicated in those tight or angulated lesions or tortuous blood vessels because forceful passage of the device itself through the stenosis may cause significant local disruption to the plaque, which may in turn, induce dissection or distal embolization.

With the favorable results of distal protection,[10-14] the use of distal protection devices has become a routine, wherever feasible, during carotid angioplasty at the author's institution. From August 2000 to January 2002, 13 patients underwent carotid angioplasty at our institution with distal protection. The age of the patients ranged from 52-79 years (mean 69.3±8.8 years). The reference internal carotid artery diameters, lesion length, pre-procedural stenosis and residual stenosis were 3.15-6.0 mm (mean 4.07±0.87 mm), 10-35mm (mean 20.3±7.5 mm), 70-99% (mean 88.7 ± 9.9%) and 0-30% (mean 11.2 ±12.5%) respectively. PercuSurge GuardWire Plus system was used in 8 patients, Angioguard filter was used in 2 patients, NeuroShield filter was used in 2 patients and EPI filter wire was used in 1 patient. All procedures were successful with no peri-operative neurological event. No pre-dilatation was needed in all cases with the GuardWire system and the GuardWire was able to cross the lesion at the first attempt in all cases. In the case using the EPI filter wire, in view of the kinking morphology of the lesion, pre-dilatation of lesion was done before it was crossed with the filter. In other cases using the filters, no pre-dilatation was done. The mean balloon occlusion time in the cases using the GuardWire system was 10.2 minutes. In those patients undergoing the distal protection of the GuardWire Plus system, one patient could not tolerate the distal protection balloon occlusion

and early deflation of the occlusion balloon was needed. Another patient suffered from acute stent thrombosis, which was successfully treated with abciximab. No peri-operative neurological event was observed. At 30 days after the procedures, no neurological event or procedure related death was observed. No local injury to the distal vessel was observed apart from some reversible local spasm in three cases (one with Angioguard, one with NeuroShield and one with GuardWire Plus system). In all cases, macroscopically visible debris was retrieved from the protective devices, but the amount was only mild in all cases.

Although the distal protection devices have undergone repeated improvement and miniaturization, the ideal device is yet to be developed. We are still waiting for a device that has the best characteristics of the currently available systems, i.e. having the low profile of the distal occlusion balloon while allowing continuous blood flow as in the filters. While proper selection of patients and matching of the devices to different lesions would minimize the distal embolization phenomenon, no current distal protection device may safely protect, for example, a long, irregular and angulated 99% stenosis with contralateral carotid occlusion. Though effective in preventing distal embolization, distal protective devices are costly and are marketed at the price of the stents. Although further studies on the health-economics of these devices are needed before we can draw any conclusion on their cost-effectiveness, the decrease in the incidence of major stroke during carotid angioplasty as shown in many published series might already make their cost justified.

In conclusion, distal embolization is the most important complication of carotid angioplasty. Distal protection devices have been shown to reduce the distal embolization phenomenon. Although the ideal protection device is yet to be developed, the currently available protective devices appear to be useful adjunct in carotid angioplasty.

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Left Cardiac Sympathetic Denervation via Thoracoscope to Treat Long QT Syndrome

DAYI HU[1], CUILAN LI[1], JUN WANG[2], LEXIN WANG[3], CHIEN-CHIH LIN[4], WENLING LIU[1], JIANFENG LI[2], ZHIMING LI[1], LEI LI[1]

From [1]Department of Cardiology, [2]Department of Thoracic Surgery, the People's Hospital of Peking University, Beijing 100044, China; [3]School of Biomedical Sciences, Charles Sturt University, Australia; [4]The Surgical Department of Tainan Municipal Hospital, Tainan, Taiwan

HU ET AL.: ***Left Cardiac Sympathetic Denervation via Thoracoscope to Treat Long QT Syndrome. Purpose:*** *Long QT syndrome (LQTS) is a cardiovascular disorder characterized by prolongation of the QT interval on ECG and presence of syncope, seizures, and sudden cardiac death. The therapy for LQTS is mainly dependent on medicines. The aim of the present study was to investigate the feasibility and efficacy of a new surgical method of cardiac sympathectomy for LQTS patients.* ***Methods:*** *Left cardiac sympathetic denervation (LCSD) were conducted on 4 LQTS patients who were resistant to β-blockers. Patients' ECG and clinical symptoms were assessed before and after the surgery.* ***Results:*** *LCSD was successful in all patients. QTc decreased from 0.54±0.08 to 0.51±0.06s immediately after the procedure. However the shortened QTc returned to prior surgery level in one patient within 24 hours of the surgery. Before LCSD, horizontal bike exercise induced a significant change in T wave amplitude and prolongation in QTc. These changes diminished following LCSD. After 5-month follow-up, one patient who had frequent syncopal attacks before LCSD experienced 2 episodes of transient syncope. No syncope was reported by other patients.* ***Conclusions:*** *LCSD is a safe and effective therapy for LQTS resistant to β-blockers. These results may have significant implications in patients of developing countries like China, where expensive therapies such as implantable cardioverter defibrillator are unlikely to be widely applied due to financial constraints of the patients. (J HK Coll Cardiol 2002;10:184-190)*

Corrected QT interval, Holter monitoring ECG, horizontal bike exercise test, left cardiac sympathetic denervation, long QT syndrome(LQTS)

摘要

長 QT 綜合征(LQTS)指具有心電圖上 Q T間期延長，T 波異常，易產生室性心律失常，尤其是尖端扭轉性室速，暈厥和猝死的一組綜合征。為探討β-阻斷劑治療無效的 LQTS 經胸腔鏡行左側心交感神經切除術(LCSD)的療效，選擇4例確診為 LQTS，服用β-阻斷劑效果不佳的患者進行 LCSD。結果 4 例手術均成功，其中只有 1 例發生短暫的左眼充血和Horner's綜合征，但症狀隨後逐漸減輕，出院時幾乎完全消失。術中切除神經節後即有 QTc 縮短，平均由 0.54±0.08s 降低到 0.51±0.06s。24小時動態心電圖上測得的平均 QTc 術後與術前相比也有不同程度的縮短。臥式踏車運動試驗顯示，術前病人在運動後 T 波形態較之運動前有很大變化；而手術後再做運動試驗，運動後T 波形態較之運動前則很少發生變化；另外，術前運動引起 QTc 升高較多，而術後運動對 QTc 改變很小，提示術前 LQTS 病人受交感神經影響較大，而術後 LQTS 病人較少受交感神經的影響，說明切除交感神經的效果。術後隨訪 5 個月，4 例中有 1 例術前經常發作長時間暈厥的患者（每年7-8次以上）在術後發生過 2 次時間短暫的暈厥，初步顯示出 LCSD 手術對服用β-阻斷劑無效的 LQTS 患者有效。結論：本研究在小樣本 LQTS 病人中發現經胸腔鏡行 LCSD 手術對傳統藥物治療無效的 LQTS 病人是安全有效的。LCSD 對多數病人可縮短 QTc，預防暈厥發作，無嚴重併發症。LCSD 能否作為LQTS 的一線治療尚需進一步研究。

關鍵詞：校正的 QT 間期　24小時動態心電圖　　臥式踏車運動試驗　　左側心交感神經切除術(LCSD)　長 QT 綜合征

Address for reprints: Dr. Dayi Hu
Department of Cardiology, The People's Hospital of Peking University, Beijing 100044, China

Tel: (86) 10-68314422-5940, Fax: (86) 10-68792845

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Introduction

The long QT syndrome (LQTS) is a cardiovascular disorder characterized by prolongation of the QT interval on ECG and presence of syncope, seizures, and sudden cardiac death.[1] According to the latest epidemiological data, the incidence for LQTS is around 1 of 5000-7000[2] and the mortality in untreated symptomatic patients is about 70%.[1,3] The young age of most patients and the high mortality in untreated symptomatic patients stress the importance of development of effective therapies.

LQTS is a genetic disease with 5 genes being identified to be responsible for its occurrence.[4] The major mode of treatment is still medications in most patients. β-blockers have been proven effective in preventing syncope in 75-80% of LQTS patients,[3,5] but more than 20% of patients continue to have syncopal episodes and remain at high risk for sudden cardiac death despite full-dose β-blockers. Experimental and clinical studies have suggested that left cardiac sympathetic denervation (LCSD) may be useful for preventing cardiac events associated with LQTS.[3] However, despite its relative simplicity, LCSD is still not widely performed in many high-risk patients partially because the physicians, or the thoracic surgeons in their hospitals, are not familiar with the procedure. The consequence is that too often, the choice goes to what appears to be the easiest approach, such as a pacemaker or an implantable cardioverter defibrillator, even when this choice may not be the best choice for many patients.[1] The present work summarized the immediate and follow up results of LCSD via thoracoscopy in 4 Chinese patients who were resistant to β-blockers.

Methods

Patient Selection

We currently have a total of 93 LQTS patients from 38 families under our care for more than 2 years. Among these patients 4 were selected for LCSD due to frequent syncope refractory to large dose of β-blockers. Patients' clinical presentation is listed in Table 1.

Surgical Procedures

Under single-lumen tracheal incubation anaesthesia, multiple port approach was used to enter the pleural cavity.[6] The sympathetic chain was identified under the parietal pleura, running vertically over the necks of the ribs in the upper costovertebral region. The left sympathetic chain between T2 and T5 was isolated and then clamped in one patient by titanium clamps (Auto Suture Company, USA) to block the sympathetic nervous truck. In other three patients the sympathetic chain was cut after clamping. In these patients the lower

Table 1. Patients' clinical history before surgery

	Case 1	Case 2	Case 3	Case 4
Sex	F	F	F	M
Age at surgery	42	36	44	6
Age at first syncope (yr)	32	7	25	0.5
Syncope	+	+	+	+
Cardiac arrest	–	–	–	–
Pharmacological therapy				
β-blockers	+	+	+	+
β-blockers+others	+	+	+	+
Cardiac events				
Rate (events/yr)	7-8	2-3	1-3	5-6
ECG parameters				
Heart rate (beats/min)	50	52	56	60
QTc(s)	0.50	0.48	0.63	0.61

+: yes; –: no

part of the left stellate ganglion was carefully removed. Care was taken to resect all the anterior branches coming off the lower part of the ganglion.

Non-invasive Tests

24 hour Holter monitoring electrocardiogram (MS8000, Marqutte Company, USA) was conducted 2 days before surgery and second day after surgery. The horizontal bike exercise test was conducted using ergometer (EGM-II, jointly made by Yueyang Instrument and Meter Plant of Hunan Province and First Hospital of Peking University, China) 2 days before and 7 days after surgery.

Measurement of QT Intervals

A 12-lead ECG was obtained before general anaesthesia. ECG was also recorded immediately before and after LCSD. Three limb lead ECGs were continuously monitored during the procedure.

QT interval of the body surface ECG was always measured on lead in which the end of T wave was clear, in most cases, on lead II or V5, sometimes on V2-V3. The corrected QT interval (QTc) was calculated according to the formula of Bazett ($QTc = QT/RR^{1/2}$), and reported in seconds. The RR interval was measured during sinus rhythm, taken the mean for at least 5 beats.

Statistical Analysis

Data were expressed as means±SD. Because patient numbers were small, no statistical analysis was attempted.

Results

LCSD was successful in all patients. There was no mortality or serious complications. After the operation, one patient developed mild Horner's syndrome, which fully resolved in 7 days without any specific intervention.

Alterations in QTc During the Surgery

The heart rate in the 4 patients remained unchanged during or after the surgery. QTc was shortened following the LCSD (Table 2).

The 6-year-old male patient experienced an episode of ventricular tachycardia (TdP) and frequent ventricular ectopics during the isolation of the sympathetic chain. However, these arrhythmias were terminated spontaneously (Figure 1).

QTc and Arrhythmias After the Surgery

The 24 hour Holter monitoring electrocardiogram

Table 2. The QTc alteration during surgery

Case	Before removal of ganglion	5 min after removal of ganglion	ΔQTc
1	0.50	0.48	0.02
2	0.46	0.46	0
3	0.55	0.52	0.03
4	0.64	0.59	0.05

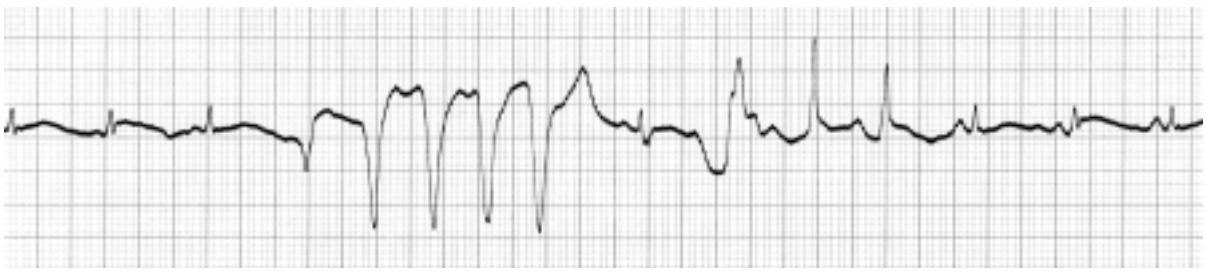

Figure 1. *An episode of TdP during surgery on patient 4, a 6-year-old boy.*

showed that the mean value of QTc within 24 hours was decreased in 3 patients to various degrees, except that the QTc increased in one patient (Table 3). Among the 4 patients, there was one patient (case 1) who had frequent ventricular ectopics before surgery. After LCSD the ventricular ectopics was decreased from 1,959 to 107 beats/24 hr, and bigeminy decreased from 1,356/24 hr to 0.

Table 3. The mean QTc comparison measured by 24 hour Holter ECG

Case	1	2	3	4
Before surgery	0.46	0.48	0.53	0.61
After surgery	0.45	0.45	0.49	0.64
QTc alteration	0.01	0.03	0.04	-0.03

Exercise Tests

The horizontal bike exercise was completed in two patients. A 36-year-old female patient was house bound for 6 years due to extreme anxiety caused by syncopal attacks. She declined the exercise test before the surgery. An after-surgery exercise test was conducted but the protocol was not completed due to her poor coordination. Bike exercise test was not attempted in the 6-year-old male patient.

In the two patients who completed the exercise test, there was a significant change in the T wave morphology immediately after the test, and these changes were abolished by LCSD (Figure 2).

Before LCSD, exercise induced a greater increase in QTc. However, there was little exercise-induced increase in QTc after LCSD (Table 4).

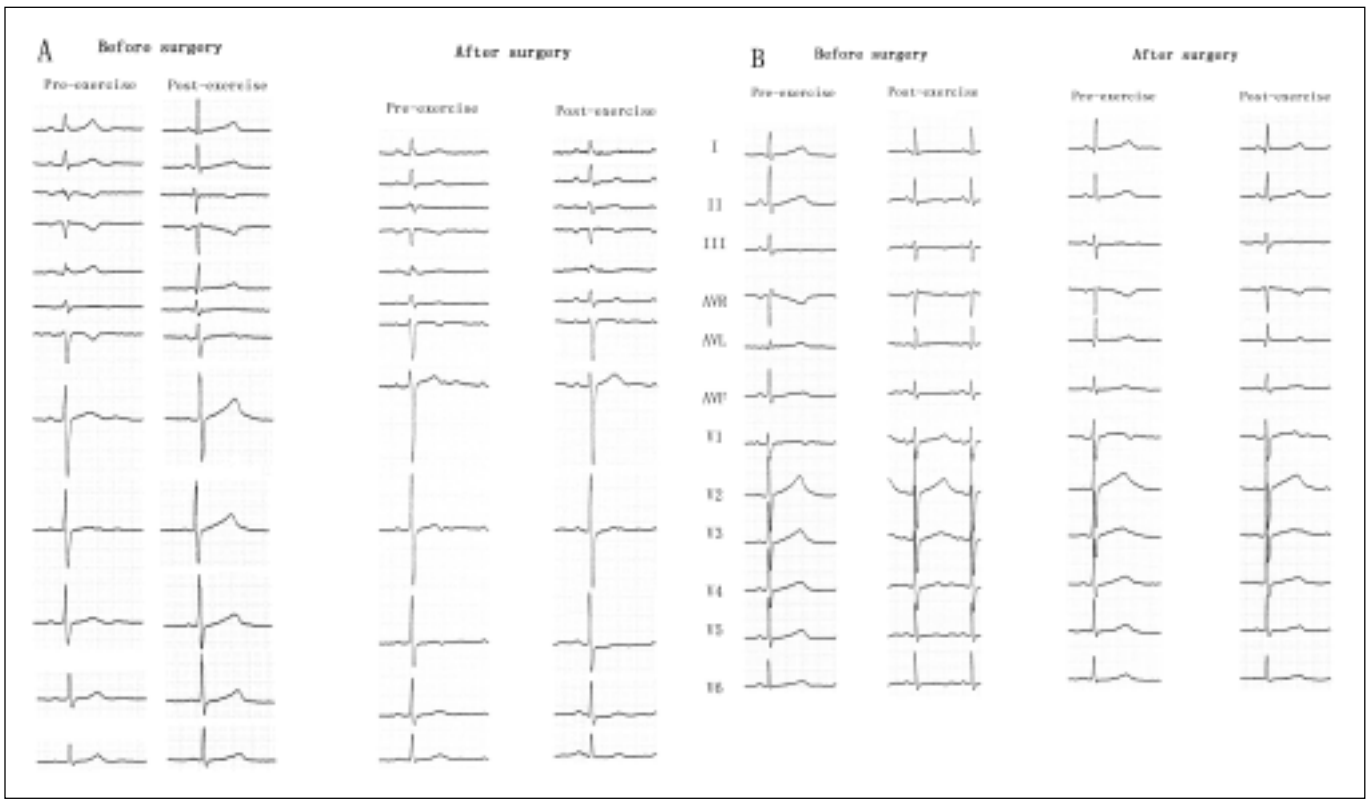

Figure 2. *The alteration of 12 lead ECG during horizontal bike exercise test before and after surgery. (A) shows that in case 1 exercise resulted in more T wave morphology change before surgery, the amplitude of T wave increased almost on all leads and that after surgery the exercise nearly resulted in no change of T wave morphology. (B) shows that in case 3 exercise resulted in more T wave morphology change before surgery, and it is manifested decrease of the amplitude of T wave and step-up of heart rate. After surgery the amplitude of T wave and heart rate were less influenced by exercise.*

Table 4. Pre- and post-exercise QTc comparison before and after surgery

	Case 1 (s)			Case 2 (s)		
	Pre	Post	ΔQTc	Pre	Post	ΔQTc
Before surgery	0.48	0.54	0.06	0.62	0.67	0.05
After surgery	0.45	0.46	0.01	0.63	0.64	0.01

Pre: data from pre-exercise; Post: data at 8 min after exercise termination; The data during exercise were not counted due to the indefinability of T wave measurement during exercise because of noises.

Follow-up

The 4 patients were followed-up for 5 months. Three patients remained symptom free. One patient who had frequent (7-8 times/yr) syncopal attacks experienced 2 episodes of brief syncope 3 months after the surgery.

Discussion

This study is the first systematic assessment of the role of LCSD in LQTS management in China. It shows that LCSD is able to shorten QTc and reduce syncopal attacks in most patients who have failed full-dose β-blocker therapy.

Rationale of LCSD for LQTS

Although the cause of long QT syndrome remains unclear, abnormal cardiac sympathetic innervation and myocardial repolarisation are believed to be responsible.[7-9] T wave alternans, one of the characteristics of long QT syndrome, can be reproduced by stimulation of the left stellate ganglion in animals[10] and in humans.[11] Animal experiments found that left stellectomy increases ventricular fibrillation threshold whereas right stellectomy decreases it.[12,13] In humans, left sympathectomy normalizes the prolonged QT interval, thereby reducing the probability of malignant arrhythmia.[3]

In 1991, Schwartz et al.[3] summarized the results of 85 LQTS patients who underwent LCSD. These patients, whose mean age at the time of surgery was 20 years, were followed for an average of 5.9 years. LCSD significantly reduced the number of patients with cardiac events, from 99% to 45% after the surgery.[3] It also diminished the number of cardiac events from 22 to 1 per patient, and shortened QTc by an average of 41 ms.[3] The 5-year survival rate in these patients was 94%.[3]

The results of our 4 patients who successfully underwent LCSD are consistent with the report by Schwartz.[3] The non-invasive tools, such as 24 hour Holter monitoring ECG and horizontal bike exercise test used before and after surgery are very useful in assessing the effect of LCSD. Continuous monitoring of a 3-lead ECG during surgery showed that following the removal or clamping of stellate ganglion and thoracic ganglia, QTc was decreased immediately in most patients. The QTc measured from Holter monitoring ECG was also decreased after surgery in most patients, indicating that this is a useful tool to assess the effect of LCSD. The analysis of ECG during exercise test demonstrated that LCSD attenuated the exercise-induced changes in T wave morphology, indicating cardiac sympathetic denervation.[14]

Techniques of LCSD

Left stellectomy involves ablation of the left stellate ganglion and often produces Horner's syndrome.[1] It provides only limited cardiac denervation in humans.[1,3] Left cervicothoracic sympathectomy involves total left stellectomy and removal of the first 4 or 5 thoracic ganglia. This procedure produces an adequate cardiac sympathetic denervation but with an associated Horner's syndrome, resulting from interruption of the nerve fibers directed to the ocular region that cross the upper portion of the stellate ganglion.[1] High thoracic left sympathectomy (HTLS) involves removal of the lower part of the left stellate ganglion and the first 4 or 5 thoracic ganglia. This procedure produces an adequate cardiac sympathetic denervation and extremely low incidence of Horner's syndrome because the ocular fibers are spared.[1,3] For these reasons, HTLS was used in our study for the surgical cardiac sympathetic denervation. There

is one patient in whom sympathetic nerve was clamped only using titanium clamps without cutting sympathetic nervous truck in our study. According to the QTc alteration measured during surgery and during exercise test before and after surgery there was no difference between the effects of clamping and cutting. Of course, there is a need to accumulate more data to draw the final conclusion.

In the earlier report by Schwartz et al[3] where left stellectomy or left cervicothoracic sympathectomy was used, there were two patients experienced chronic hyperemia of left eye, which responded to topical vasoconstrictor therapy. Horner's syndrome was present in most patients early after surgery, but almost always decreased or disappeared after surgery. In the present study where LCSD was used, there was one patient developed Horner's syndrome, which resolved after a week. These results indicate that complications like Horner's syndrome can be largely avoided via the thoracoscopic technique.

Effects of LCSD

Although LCSD may largely reduce the sympathetic innervation to the heart, it is unlikely to completely abolish the influence of catecholamines to the heart because the circulating adrenaline or noradrenaline is not affected to a significant extent by the procedure. Therefore the pathophysiology of myocyte membrane ionic channels responsible for LQTS may not be corrected completely through LCSD. As a result, QTc is decreased, but may not return to the normal level after LCSD. Therefore patients who underwent successful LCSD are still advised to take β-blockers for a period of time after surgery.

The study by Conrath et al[15] demonstrated that gender differences exist in response to β-adrenoceptor blockade in patients with types 1 and 2 of LQTS. During treatment males with LQT1 have shorter QTc interval than females and adult patients with LQT2. Also treated females with LQT1 exhibited less dispersion than those with LQT2. In our study, the gender difference of QTc shortening in response to LCSD was not seen due to the small number of patients and lack of genotyping data (genotyping work is in progress in our lab).

All our patients had frequent syncopal attacks refractory to β-blockers. During a 5-month follow-up, only one patient had a minor recurrence of symptoms whereas other patients remained symptom free. These results indicate that LCSD is effective in refractory patients in the short and media term.

Summary

This study in a small number of patients has found that LCSD via thoracoscope is a safe and effective method for the management of LQTS patients refractory to conventional pharmacological therapy. LCSD reduces QTc and prevents syncopal attacks in most patients with no serious complications. Whether LCSD can be used as a first choice of therapy in LQTS patients remains to be seen.

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Use of Distal Protection Device for Percutaneous Intervention in Native Coronary Arteries

KENNETH KA-HING LAM, SHU-KIN LI

From Cardiology Team, Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong

LAM and LI: ***Use of Distal Protection Device for Percutaneous Intervention in Native Coronary Arteries.*** *Microembolization of particulate debris during percutaneous coronary intervention (PCI) will lead to various degree of microvascular obstruction, terminating in no-reflow phenomenon observed angiographically. Different methods, including angiography, non-invasive imaging, and assays of myocardial injury markers, have been used for detection of occurrence of microvascular obstruction. The prevalence of, and the adverse prognosis associated with microvascular obstruction have led to the concept and application of distal protection for coronary interventions. While its value has been confirmed in saphenous vein grafts intervention, data is now growing to support use of distal protection devices in native coronaries. Findings from a local registry that reveals the initial experience on use of GuardWire Plus System, a kind of occlusive distal protection device, for elective PCI are discussed herein. (J HK Coll Cardiol 2002;10:191-197)*

Distal protection, microembolization, microvascular obstruction, percutaneous coronary intervention

摘要

在經皮冠脈介入干預（PCI）中破碎的斑塊引起的微栓塞將導致不同程度的微血管阻塞，冠脈造影上出現無複流現象。有不同的方法，如冠脈造影、無創性顯像技術、心肌損傷標誌物用以檢查微血管阻塞的發生。微血管阻塞現象的頻繁發生及其不良預後帶來了冠脈介入遠端保護的概念與技術應用。這種技術的價值在大隱靜脈移植血管介入干預中得到證實後，現在有越來越多的資料支援其在冠脈介入干預中使用血管遠端保護裝置。從一個地區的註冊登記中顯示了 GuardWire Plus 系統 －一種遠端閉塞性保護裝置使用的初步經驗，本文就擇期 PCI 中使用這一裝置進行討論。

關鍵詞：遠端保護　微栓塞　微血管阻塞　經皮冠脈介入干預

Introduction

Microembolization, Microvascular Obstruction and No-Reflow: Pathophysiology

With the advances seen in various devices used for percutaneous coronary intervention (PCI) and the widespread use of stents, acute complications are uncommon during the procedure. However, slow distal flow or no-reflow phenomena remain one of the frustrations facing interventional cardiologists. The pathophysiology underlying such phenomena seen during PCI is likely to be complex, but probably starts off with microembolization of particulate debris dislodged from atherosclerotic/thrombotic lesions down to distal capillary bed, causing microvascular obstruction.[1] This in turn results in microvascular plugging, microvascular spasm or edema, and/or platelet aggregation. Experiments in canine models had shown that embolization of a coronary artery with minute particles/microspheres measuring less than 100 μm resulted in regional contractile dysfunction and perfusion-contraction mismatch.[2] Following microvascular obstruction, epicardial flow is initially

Address for reprints: Dr. Kenneth Ka-Hing Lam
Cardiology Team, Department of Medicine, Pamela Youde Nethersole Eastern Hospital, 3 Lok Man Road, Chaiwan, Hong Kong

Tel: (852) 2595 6111, Fax: (852) 2515 3182

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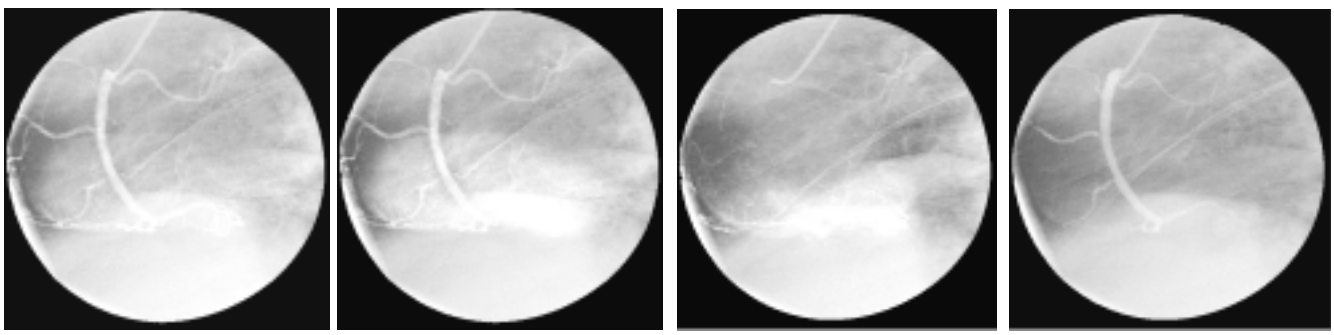
maintained or even enhanced due to an adenosine-related hyperaemia of the myocardium surrounding the embolized microregions, with blood shunting around the areas of microvascular obstruction.[1] However, as the total embolized burdens increase, the epicardial flow will eventually become reduced, corresponding to the angiographic manifestation of slow distal flow or no-reflow. In other words, no-reflow represents an advanced stage of significant degree of microvascular obstruction.

Detection of Microembolization and Microvascular Obstruction

The presence and extent of microvascular obstruction can be assessed by examining the degree of impairment of myocardial perfusion. Several methods have been used for this purpose. The angiographic method is perhaps the simplest way in the catheterization laboratory. Two different approaches have been derived: first, to record the Corrected TIMI Frame Count (CTFC) which is defined as the number of cine frames required for contrast to first reach distal coronary landmarks in that artery;[3] and second, to report on the TIMI Myocardial Perfusion (TMP) Grades (0-3) by noting the appearance of blush, and the rate at which the blush disappears (Figure 1).[4] Myocardial contrast echocardiography constitutes another method for assessing myocardial perfusion by intravenous or intracoronary injection of sonicated bubbles. Ito et al[5] showed that myocardial perfusion defects was detectable in up to 26% of patients who had TIMI 3 flow in the infarct-related artery after reperfusion therapy (either thrombolysis or primary angioplasty). Nuclear imaging using Sestamibi Single-Photon Emission Computerized Tomography (SPECT) has also been used for detection of myocardial perfusion defects. Koch et al[6] demonstrated that up to 87% of patients undergoing rotational atherectomy had detectable perfusion defects on SPECT, but the figure dropped to 33% with infusion of abciximab, thereby providing evidence that platelet emboli were at least partly involved. Magnetic Resonance Imaging (MRI), on the other hand, is able to demonstrate subendocardial microvascular obstruction by showing regions of hypoenhancement after contrast injection.[7] Finally, reduction in relative coronary flow velocity reserve (as measured by intracoronary Doppler flow analysis) after successful coronary intervention has been observed, and has been related to microvascular obstruction.[8,9]

Abnormal levels of myocardial injury markers represent the sequelae (when other confounding factors like acute closure during the procedure or jailing of side-branch are absent), and also serve as circumstantial evidence for occurrence of microvascular obstruction during PCI. In a study by Hong et al[10] recording successful,



TMP Grade 3
Normal ground-glass appearance of blush. Contrast mildly persistent at end of washout

TMP Grade 2
Contrast strongly persistent at end of washout. Disappears by next injection

TMP Grade 1
Stain present. Blush persists on next injection

TMP Grade 0
No or minimal blush

Figure 1. *TIMI Myocardial Perfusion (TMP) Grades (Graphics supplied by Medtronic Inc.).*

angiographically and clinically uncomplicated PCI in over 700 patients with saphenous vein graft (SVG) lesions, raised creatine kinase-MB fraction (CK-MB) levels, defined as levels above upper normal limit, were detected in 38.5% of patients. In a recent study which measured serum troponin T and I levels after successful uncomplicated elective PCI in native coronary arteries, up to 14% of patients had raised troponin T or I levels in absence of side-branch occlusion.[11] More evidence to suggest microembolization during PCI comes from the observation of a higher incidence of microvascular obstruction associated with more aggressive coronary intervention. Directional atherectomy, for instance, was the strongest correlate of post-procedure CK-MB elevation in a series of patients who underwent successful PCI (odds ratio 4.1 when compared to balloon angioplasty).[12] The paradoxical finding of a decrease in TIMI 3 flow in patients after stenting as compared to balloon angioplasty in the Primary Angioplasty in Myocardial Infarction (PAMI) trial lends more support to the occurrence of microembolization.[13]

Impact of Microvascular Obstruction on Outcomes Post-PCI

It is well known that occurrence of no-reflow during PCI is associated with higher incidence of major adverse cardiac events (MACE). In a study addressing this issue, the incidences of non-Q myocardial infarction and in-hospital mortality were reported as 31% and 15% respectively.[14] Even when epicardial flow is preserved, the occurrence of microvascular obstruction will lead to a worse outcome. In a study which recruited patients with normal or mildly raised (<2 times upper limit of normal) creatine kinase after successful PCI, Abdelmeguid et al[12] showed that the subgroups with elevated CK-MB carried a higher incidence of MACE over a median follow-up period of 3 years. Hong et al[10] in the study on SVG interventions showed that the 1-year mortality rate in patients with post-procedure CK-MB 1-5 times upper limit of normal and those with CK-MB more than 5 times normal were, respectively, at least 2 times and 4 times higher than patients with normal CK-MB levels. In another study, Stone et al[15] discovered that only 29.4% of patients who had TIMI 3 flow in the infarct-related artery after primary angioplasty achieved a TMP Grade of 3. More importantly, the 1-year mortality rates in this group of patients were closely correlated to the TMP Grades: 6.8% for TMP Grade 3; 13.2% for TMP Grade 2; and up to 18.3% for TMP Grade 0/1.

Distal Protection for PCI

Distal Protection Devices

It is therefore reasonable to hypothesize that protecting distal vessels from particulate embolization can improve immediate and long-term outcome after PCI. Different distal protection devices have been designed. As of today, they fall into one of two categories: a) distal occlusion balloon on a wire; any particulate debris within the column of occluded blood will be aspirated after intervention on target lesion; and b) filter that can be deployed distal to target lesion, trapping any particulate debris; the filter with the entrapped debris are then retrieved with a capture sheath. The former, as exemplified by the GuardWire Plus System (Medtronic®) (Figure 2), has the advantages of having a low crossing profile and completeness of debris retrieval, but vessel occlusion is inevitable during the procedure. The latter, as exemplified by the AngioGuard Emboli Capture Guidewire (Cordis®) (Figure 3) and the EPI FilterWire (Boston Scientific®) (Figure 4) have the advantages of allowing continued blood flow during the procedure, but suffer from having a larger crossing profile (4.0F or more) and uncertainties in offering complete protection or retrieval of entrapped particulates.

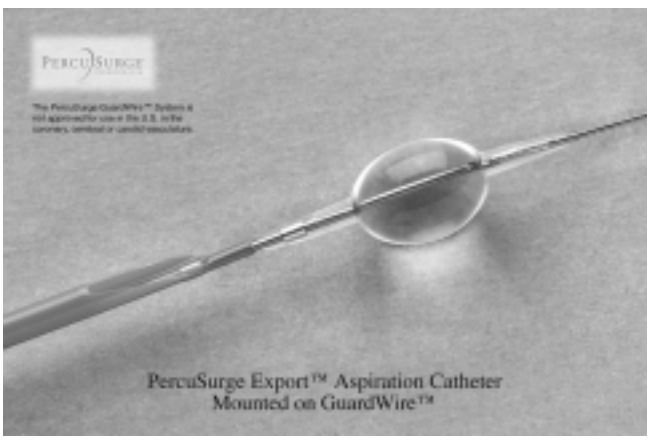


Figure 2. *The GuardWire Plus System (Medtronic®).*

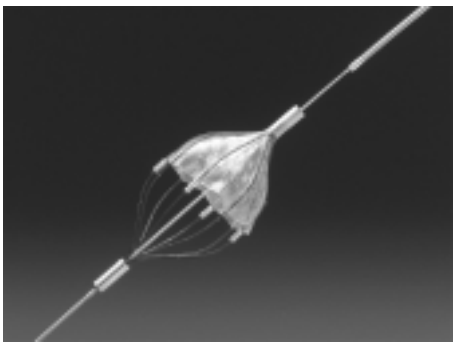


Figure 3. *The AngioGuard Emboli Capture Guidewire (Cordis®).*

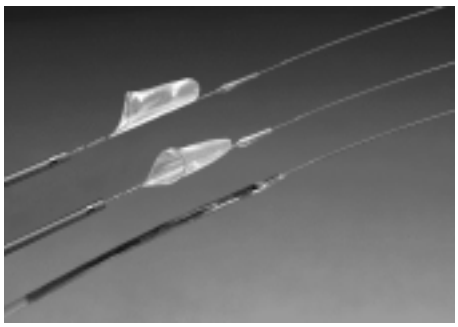


Figure 4. *The EPI FilterWire (Boston Scientific®).*

Clinical Data on Use of Distal Protection for PCI

The value of distal protection has been/is being tested in two high-risk areas for microembolization: interventions in saphenous vein grafts and on culprit lesions of acute coronary syndromes. The SAFER trial[16] is the first randomized clinical trial examining the benefit of distal protection using GuardWire System (Medtronic®) during interventions in SVG. Over 800 patients were enrolled in the trial. The incidence of no-reflow was 3.4% using distal protection versus 8.8% without distal protection. Incidences of in-hospital MACE and 30-day MACE were decreased by 38% and 42% respectively with the use of distal protection. In the setting of intervention for acute ST elevation myocardial infarction (STEMI), a multicentre registry in Europe recorded in 37 patients an improvement in TIMI 3 flow from 24.3% to 86.1% and improvement in TMP Grade 3 from 2.7% to 58.8% of patients post-intervention with the use of GuardWire System.[17] Similarly, in a single-centre cohort of 51 STEMI patients, an improvement in TIMI 3 flow from 0% to 96% of patients was noted post-intervention using the same GuardWire System,[18] with 54.5% of patients who had TIMI 3 flow achieving TMP Grade 3. Though randomized comparison was not available, this 54.5% of TMP Grade 3 was a significant improvement over the 18.8% figure obtained from historical trial data. In 96% of this cohort, either thrombus or atherosclerotic materials were successfully aspirated.

Use of Distal Protection for Elective PCI in Native Coronary Arteries

Slow distal flow or no-reflow does occur occasionally in the setting of elective PCI (excluding interventions during acute phase of acute coronary syndromes). In a review on all elective PCI in native coronary arteries conducted in the authors' catheterization laboratory in year 2001, the incidence of slow distal flow/no-reflow was up to 3% when vessels ≥3.5 mm in diameter were counted, and up to 13% in vessels ≥4.0 mm in diameter. As from deduction and also from observation, larger plaque burden and more friable plaque predispose to occurrence of such adverse phenomena. However, there is as yet little controlled data on the use of distal protection for elective PCI in native coronary arteries. A recent report from Grube et al[19] included the experience of using the AngioGuard Emboli Capture Guidewire (Cordis®) for distal protection in 15 native coronary lesions. Particles retrieved from the filters were sent for histochemical staining, and the study constitutes "the first direct evidence that embolization of arterial plaque components occurs routinely during native coronary artery interventions".

Local Registry on Use of Distal Protection for Elective PCI in Native Coronaries

In view of the potential value of distal protection for elective PCI in native coronaries, a registry on the use of GuardWire Plus System (an improved version of the original GuardWire System) has been set up in the authors' hospital. Lesions included are those within large native coronary arteries (≥3.5 mm), or lesions with heavy plaque load/complex morphology/overlying thrombus in coronary arteries ≥3.0 mm. Exclusion criteria are: a) the presence of significant (≥1.5 mm)

side-branch between the target lesion and potential location of distal protection balloon on the GuardWire (as otherwise most of the dislodged particulates may embolize down the side-branch); b) diameter of distal vessel segment where protection balloon would be inflated is <3.0 mm; c) planned use of adjunctive devices other than coronary stents, which would lengthen the procedure and also the occlusion time; and d) anticipated difficult stenting procedure (e.g. proximal calcified segment or excessive proximal tortuosity), as the protection balloon is usually only positioned 20-40 mm distal to the lesion, and support from the GuardWire is not as good as ordinary coronary wires. The first three exclusion criteria are specific to the GuardWire Plus System, and serve to illustrate that each protection system available in market bears its own characteristics and limitations. Two or three operators co-operated in using the system. Basically the procedure can be divided into 4 parts (Figure 5): a) passing the GuardWire across the lesion and inflating the distal protection balloon; b) performing intervention on the lesion as is required; c) aspirating any particulate debris which may be present in the column of occluded blood; and d) deflating the distal protection balloon. In cases of tight lesions or in totally occluded vessels, an ordinary coronary guidewire may be used to cross the lesion first (as "buddy" wire), with or without gentle predilatation with a small diameter balloon to allow subsequent passage of the GuardWire. Three different strategies could be employed for target lesion intervention, depending on coronary anatomy and expected patient's tolerance on vessel occlusion during distal protection: a) direct stenting; b) balloon angioplasty followed by an interim period of rest before stenting (referred here as balloon-rest-stent); c) combined balloon angioplasty and stenting (balloon+stent) without interruption.

So far, distal protection for elective PCI in native coronaries has been performed for 20 lesions in 17 patients (Table 1). Majority of the lesions were in RCA, as expected because of the large size of this vessel often encountered (Table 2).

Predilatation for initial passage of the GuardWire was required only in 3 lesions. In fact, with more experience in manipulating the GuardWire and in the presence of good guiding catheter support, it is possible to pass it through critical lesions without the need for predilatation. Direct stenting was performed on 11 lesions; balloon-rest-stent on 7 lesions; and

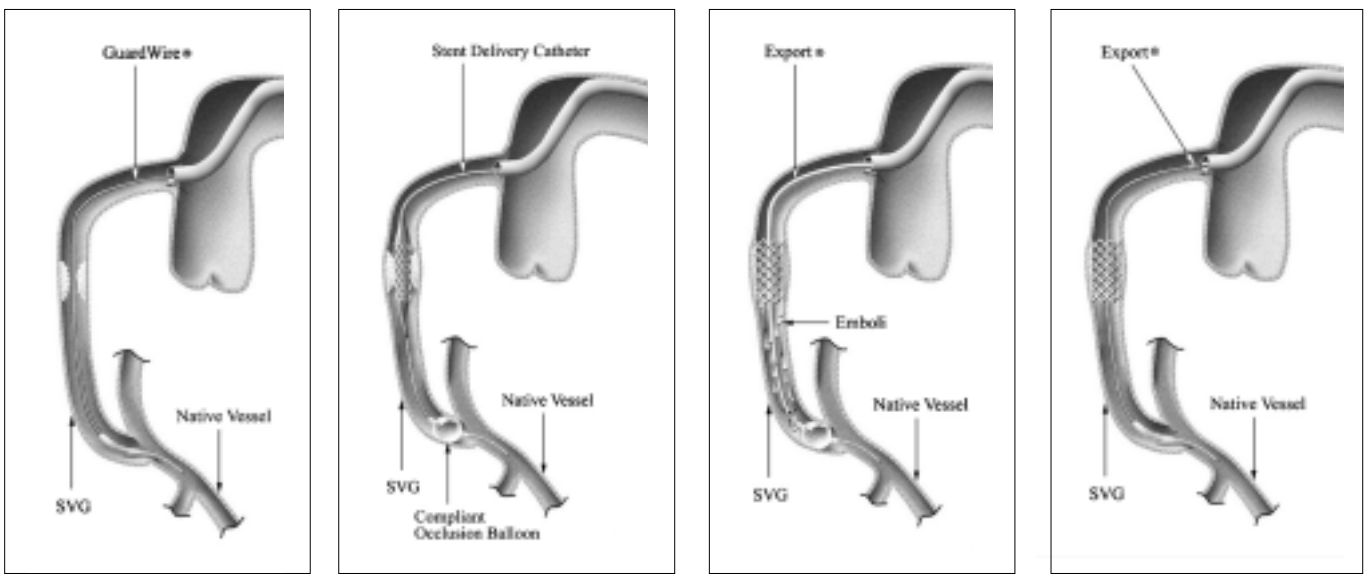


Figure 5. *Use of the GuardWire Plus System in a SVG is illustrated. (A) Crossing the lesion with the GuardWire. (B) Performing intervention on target lesion while distal protection balloon is inflated. (C) Aspirating particulate debris through the aspiration catheter. (D) Deflating the distal protection balloon.*

Table 1. Patients undergoing distal protection for elective PCI

Total no.	17
M:F ratio	14:3
Mean age (yrs)	65.9±11.7
Indication for PCI	
Stable angina	10
Stabilized after recent ACS	7

Table 2. Lesion characteristics

Vessel	
RCA	15
LCx	3
LAD	2
Mean vessel size (mm)	3.56±0.36
Lesion type	
A	3
B1	11
B2	11
C	6
Mean % stenosis	87.4±9.6

balloon+stent on 2 lesions. Mean vessel occlusion time was 181 seconds for stenting in direct stenting and balloon-rest-stent; 182 seconds for balloon angioplasty during balloon-rest-stent; and 354 seconds for balloon+stent. There is definitely a learning curve in using the system. The mean occlusion time for stenting in the last 5 lesions, for instance, has dropped to 146 seconds. The incidence of chest pain during distal protection occurred in about half of patients, bradycardia and BP drop (>20 mmHg from baseline) in around 60% and 50% respectively; and ST segment changes in about 90%. All these symptom and changes disappeared on relief of the vessel occlusion. Distal protection was successfully performed for all lesions. TIMI 3 flow and TMP Grade 3 were noted in every case. Amount of plaque debris retrieved was recorded in a semi-quantitative manner: small, moderate, and large. In around two-thirds of instances, the amount retrieved was either moderate or large (Figure 6). In none of the cases was the yield negative. Problems encountered were: one dissection at site of distal protection balloon caused by over-sizing, handled by stenting; one incident of initial difficulty in retracting the GuardWire due to the protection balloon impinging on stent struts; and one incident of non-deflating protection balloon, handled by cutting the GuardWire. The first two problems could have been avoided by more careful use, while the last problem is reportedly rare according to manufacturer. There was no in-hospital MACE related to the use of distal protection. It thus appears that distal protection using GuardWire Plus System for elective PCI in native coronaries is a feasible option. The successful retrieval in virtually all cases of particulate debris which would otherwise have embolized down the distal (micro) vasculature reflected the system's efficacy in providing myocardial protection. Indeed, the system has probably avoided several incidents of adverse slow flow/no-reflow phenomenon, judging

Figure 6. *Plaque debris retrieved.*

from the large size of the debris retrieved in some cases. Whether these benefits would transcribe into better clinical outcome would require confirmation by randomized studies. On the other hand, there is definitely a learning curve in the use of the device. Operators are expected to encounter problems in their early experience, and should be prepared to overcome them if they do occur. In fact, with careful use and as experience grows, most problems can be avoided. It should be emphasized, however, that as the benefit-risk ratio is comparatively lower in the setting of elective PCI than in PCI for acute coronary syndromes, proper case selection, as well as acquaintance with and proper use of the system are important issues.

Conclusion

Evidences are now growing in support for distal protection during PCI in native coronary arteries. Well-controlled randomized studies may eventually confirm its clinical value, just as in the case of intervention in saphenous vein grafts, especially in the area of primary angioplasty for STEMI. In the setting of elective PCI in native coronaries, further studies are required to identify lesions that are prone to distal microembolization in order to justify its use. With distal protection devices becoming user-friendlier, they may one day turn into a frequently used gadget that will help prevent adverse consequences secondary to particulate embolization that cannot be effectively prevented or handled by pharmacological means.

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Is Dynamic Atrial Overdrive Pacing Antiarrhythmic or Proarrhythmic: A Case Report

NGAI-YIN CHAN, MIU-FONG KWOK, CHI-CHUNG CHOY

From Cardiology Team, Department of Medicine and Geriatrics, Princess Margaret Hospital, Hong Kong

CHAN ET AL.: ***Is Dynamic Atrial Overdrive Pacing Antiarrhythmic or Proarrhythmic: A Case Report.*** *Dynamic atrial overdrive (DAO) pacing algorithm is designed for prevention of atrial arrhythmias, specifically atrial fibrillation (AF). We describe a patient who underwent implantation of a dual chamber pacemaker with DAO function, for sinus node dysfunction, paroxysmal AF and supraventricular tachycardia. The patient developed persistent high rate pacing alternating with a long RP tachycardia, which was maintained by the DAO pacing algorithm. Sinus rhythm resumed on turning off the DAO pacing. (J HK Coll Cardiol 2002;10:198-202)*

Dynamic atrial overdrive, proarrhythmia

摘要

動態心房超速起搏（ＤＡＯ）技術用於房性心律失常，尤其是心房纖顫（ＡＦ）的治療。1 例患者因竇房結功能失常，陣發性心房纖顫和室上性心動過速行帶有 DAO 功能的雙腔起搏器置入術。患者出現由 DAO 起搏機制所致的具有長 RP特徵的持續性高頻率起搏心律。竇性節律的恢復終止了 DAO 起搏。

關鍵詞：動態心房超速起搏　　致心律失常

Introduction

Dynamic atrial overdrive (DAO) is a recently described pacing algorithm for prevention of atrial arrhythmias, specifically atrial fibrillation (AF).[1-3] Stabile[2] found that DAO pacing markedly reduced AF recurrences in a group of 47 patients who had both paroxysmal AF and indications for permanent cardiac pacing. DAO pacing algorithm is designed to maintain continuous atrial pacing. This is accomplished by continual monitoring of the atrial rate and promptly increasing the pacing rate when intrinsic rhythm emerges. The pacing rate is reduced periodically to search for atrial activity and inappropriately rapid pacing is avoided. Possible mechanisms of its effectiveness include prevention of bradycardia, reduction of intraatrial conduction times and reduction of intraatrial dispersion of refractoriness.[4]

DAO pacing is therefore supposed to be antiarrhythmic. A case of supraventricular tachycardia (SVT) maintained by DAO pacing is reported here. To the best of the author's knowledge, this is the first case report describing a possible proarrhythmic effect of DAO pacing.

Address for reprints: Dr. Ngai-Yin Chan
Cardiology Team, Department of Medicine and Geriatrics, Princess Margaret Hospital, Princess Margaret Hospital Road, Kowloon, Hong Kong

Tel: (852) 2990 1111, Fax: (852) 2990 3329

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Case Report

A 90-year-old woman was referred to our unit for consideration of permanent cardiac pacing. She has history of hypertension and had one episode of syncope

6 years ago. She also complained of on and off fast palpitation and dizziness. 24 hours Holter monitoring revealed evidence of sinus node dysfunction with pauses of 2 seconds and frequent episodes of supraventricular tachycardia and atrial fibrillation. After obtaining consent from the patient, permanent pacemaker implantation was arranged.

A dual chamber pacemaker with DAO pacing algorithm was chosen. SVT occurred during the procedure both spontaneously and during pacing leads manipulation. It was a long RP tachycardia with rate of 136/min (Figure 1). The P waves were negative in inferior leads. The arrhythmia could only be terminated transiently with intravenous adenosine (Figure 1), atrial or ventricular overdrive pacing. The patient was haemodynamically stable during SVT and the procedure was successful with atrial and ventricular leads placed at right atrial appendage and right ventricular apex respectively. Echocardiogram performed after the procedure revealed satisfactory left ventricular systolic function. In view of the advanced age, electrophysiology study and radiofrequency ablation of the arrhythmia is not preferred. Verapamil 80 mg thrice daily was started for prevention of SVT. DAO pacing was turned on for paroxysmal AF. The maximum pacing rate was set at 150/min and the search interval was set at 8 cycles. This setting will allow the V-A interval to be lengthened by 8 ms (DAO rate recovery for all rates) when there are 8 consecutive atrial paced beats. This new V-A interval is used until either an intrinsic atrial sensed event occurs and the algorithm shortens the V-A interval by 8 ms (overdrive rate for all rates), or the end of the next search interval of 8 cycles and the V-A interval is again increased by 8 ms.

However, the patient developed persistent high rate sequential atrioventricular pacing 120-130/min after pacemaker implantation. A recurring pattern of sequential atrioventricular pacing followed by several beats of long RP tachycardia and then sequential atrioventricular pacing again was observed (Figure 2).

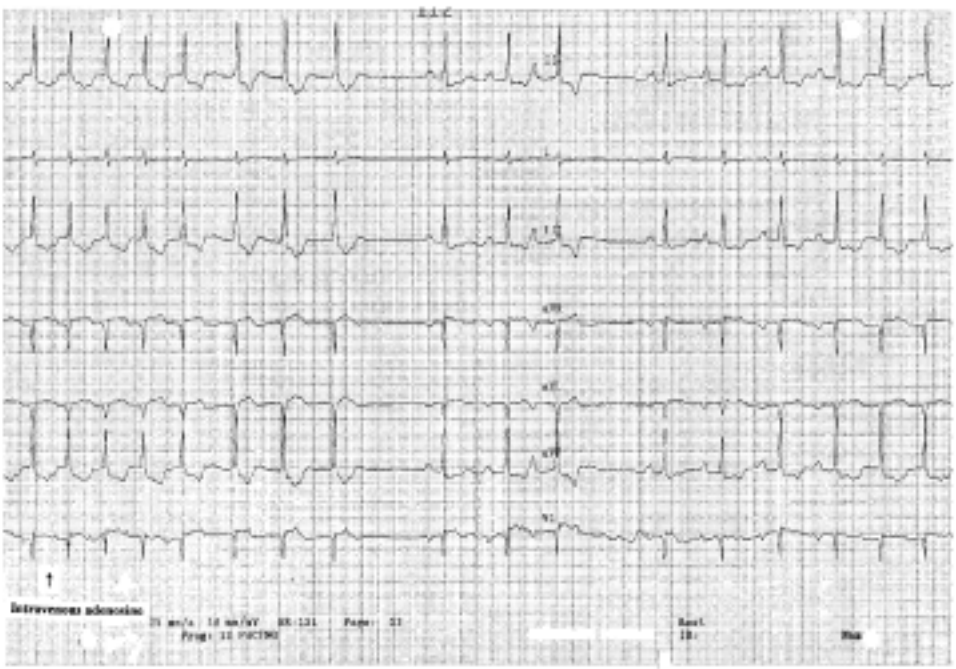

Figure 1. *Long RP tachycardia during pacemaker implantation. Negative P waves are well seen in inferior leads. The tachycardia was terminated by intravenous adenosine and recurred spontaneously. There is prolongation of tachycardia cycle length with increasing PR interval just before termination. The tachycardia ends with a P wave. Atrial tachycardia is unlikely with these features.*

Intravenous adenosine or verapamil failed to terminate this recurring pattern. Verapamil was then stopped and Amiodarone was given. An intravenous loading dose of 200 mg was given, followed by maintenance dose of 600 mg per day for two days and 720 mg per day for another two days. However, same pattern of arrhythmia persisted. On reviewing the recurring and alternating pattern of high rate pacing and long RP tachycardia, the following mechanism was postulated. As shown in Figure 2, the unusual behaviour of DAO mechanism that allows high rate sequential atrioventricular pacing, in this case of rate around 110/min, served to induce the long RP tachycardia. The rate of the tachycardia induced was around 125/min. With the sensed atrial activity during SVT, the V-A interval was gradually shortened according to the DAO pacing algorithm. Sequential atrioventricular pacing at a rate faster than the SVT was then resumed and the SVT was terminated. The V-A interval was then gradually lengthened according to the DAO pacing algorithm and SVT was then induced with a slower pacing rate. This pattern was actually maintained by the DAO pacing algorithm and the easily inducible SVT.

The DAO pacing function was turned off. The arrhythmia subsided immediately and sinus rhythm was resumed (Figure 3). Amiodarone 200 mg once per day was continued for prevention of both paroxysmal AF and SVT. The patient has been followed up for seven months and there has been no clinical recurrence of SVT or AF. 24 hour Holter monitoring did not reveal AF, SVT or persistent high rate pacing.

Discussion

This patient has a long RP tachycardia. Differential diagnoses include atrial tachycardia, permanent form of junctional reciprocating tachycardia (PJRT) and atypical atrioventricular nodal reentrant tachycardia (AVNRT). The SVT was terminated transiently with intravenous adenosine and the cycle length also varied with the PR interval just before termination (Figure 1). The SVT ended with a P wave. Atrial tachycardia is unlikely with these features. And

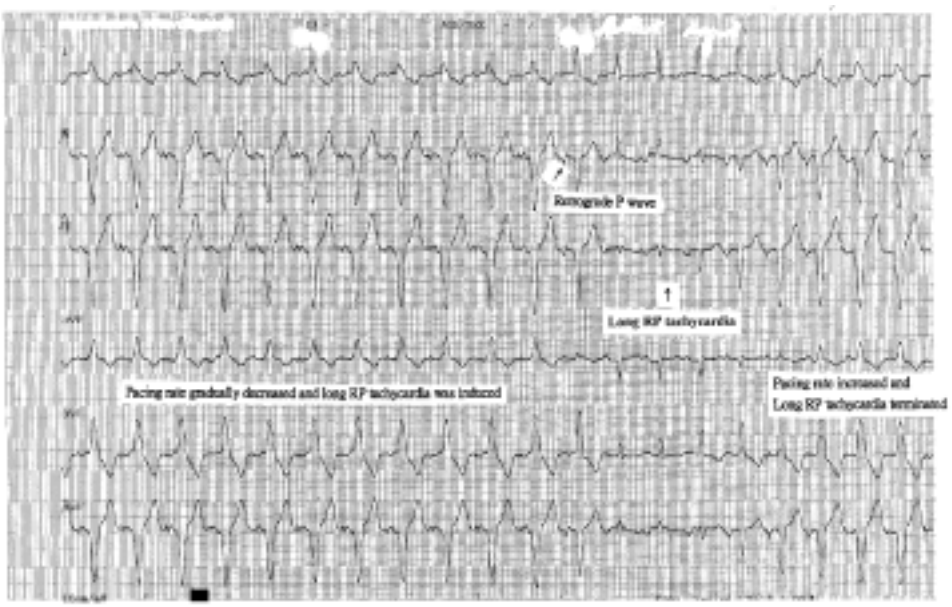

Figure 2. *Incessant high rate sequential atrioventricular pacing alternating with long RP tachycardia. Pacing rate was increased gradually by the dynamic atrial overdrive (DAO) pacing algorithm in response to the long RP tachycardia. The tachycardia was then terminated and high rate sequential atrioventricular pacing remained. The DAO pacing algorithm allows the pacing rate to decrease gradually and at the point indicated by the arrow, a retrograde P wave followed by the same long RP tachycardia was induced. This pattern of arrhythmia has been recurring for days since pacemaker implantation.*

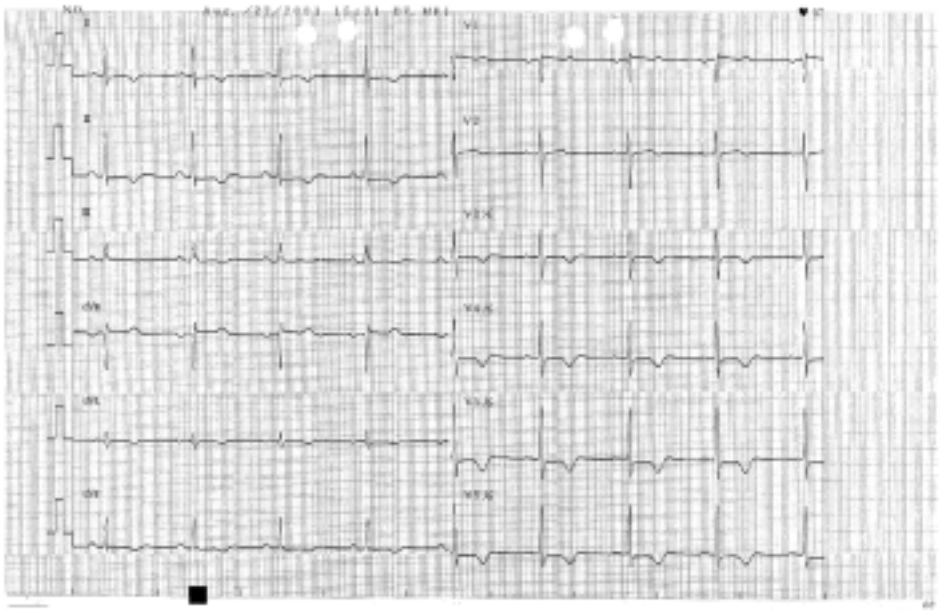

Figure 3. *Sinus rhythm immediately resumed after turning off of the dynamic atrial overdrive pacing.*

possibilities therefore include PJRT and atypical AVNRT. Because of the advanced age of this patient, electrophysiology study was not performed and the definitive diagnosis cannot be made.

Spontaneous PJRT initiation and induction during electrophysiology study usually occur after only trivial increases in sinus rate or atrial overdrive pacing.[5] The exact mechanism is not known. One likely mechanism is a concealed Wenckebach-type block at the atrial-bypass tract junction. The block relieves any antegrade concealed conduction that may have prevented retrograde conduction up the bypass tract.[6] An orthodromic atrioventricular reentrant tachycardia is then facilitated. In this case, the fact that the SVT, which is a long RP tachycardia, is readily initiated spontaneously or by atrial overdrive pacing above the sinus rate, favours the diagnosis of PJRT. With the active DAO pacing algorithm, the pacing rate is gradually increased until it is faster than the SVT which is then terminated. The same pacing algorithm allows the pacing rate to drop gradually and at some point, the SVT will be induced again. This pattern becomes persistent and is maintained by the DAO pacing algorithm and the easily inducible SVT. The remote possibility of persistent SVT even during high rate pacing is highly unlikely. It will require some form of "entrainment" during sequential atrioventricular pacing. This is difficult, if not impossible, to achieve. On the other hand, the fact that sinus rhythm immediately resumed after turning off DAO pacing argues against the mechanism of persistent SVT even during high rate pacing. Effect of Amiodarone also cannot explain the immediate response to the turning off of DAO pacing.

Although DAO pacing is designed to be antiarrhythmic in atrial arrhythmias, specifically atrial fibrillation, it can be proarrhythmic. Persistent high rate pacing may result especially in patients with SVT which is easily initiated spontaneously or induced by atrial overdrive pacing just above the sinus rate. Definitive treatment with electrophysiology study and radiofrequency ablation can confirm the diagnosis and eliminate the substrate for arrhythmia. However, when invasive procedure is not preferred as in this patient, the DAO pacing algorithm may have to be turned off.

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ECG Quiz

TSE-FUN LAM

From Department of Medicine, Kwong Wah Hospital, Kowloon, Hong Kong

A 76-year-old shopkeeper presented to Emergency Department (ED) with a minor forehead laceration sustained at work. He was sitting at the cashier when he experienced a faint and landed on left side of his body. He denied any chest symptom before the event and regained full consciousness upon reaching the floor. He did experience on and off giddiness in the past few days. He was not taking any medication, either recently or in the long term. Family history was negative of any significant medical illness.

He had a prior admission to another hospital one year ago for fever and cough, and was incidentally found to have bradycardia. He defaulted follow-up since then, as he was not symptomatic from it.

Figure 1 showed the ECG performed at ED. What was the cause of his syncope?

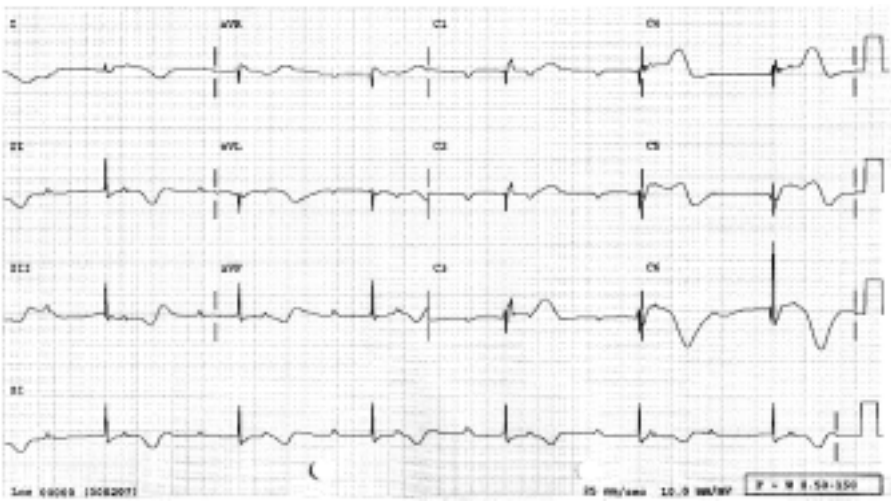

Figure 1.

Answer

The presenting ECG showed a sinus rate of 65/min and a ventricular rate of 38/min. There was complete atrio-ventricular dissociation. The QT interval was markedly prolonged, most prominent in lead V6. The corrected QTc interval was definitely excessive.

The presence of bradycardia and profoundly long QT raised the suspicion of Torsade de Pointes (TdP) as the underlying mechanism of syncope. TdP is a type of polymorphic ventricular tachycardia with continuous phasic alteration of the QRS morphology. It was first described by Desertenne in 1966.

Figure 2 was an ECG captured after the patient arrived at the ward. It illustrated the onset of polymorphic ventricular tachycardias initiated by a timed premature ventricular coupling (PVC) on the terminal end of a QT after a long cycle. This "long-short" phenomenon together with the underlying bradycardia and QT prolongation are the three key points to TdP.

QT prolongation-TdP couple can be congenital or acquired. Common acquired causes include anti-arrhythmic agents, phenothiazines, tricyclic anti-depressants and various anti-microbial agents. Profound bradycardia and electrolyte disturbance such as hypokaelemia and hypomagnesemia can also result in QT prolongation and precipitate TdP.

Management of this gentleman depends on the accurate diagnosis and correction of the underlying cause for the QT prolongation. Together with the correction of the reversible elements such as electrolyte disturbance, temporary overdrive pacing should be contemplated to prevent inappropriately firing PVC and thus achieving rate regularization.

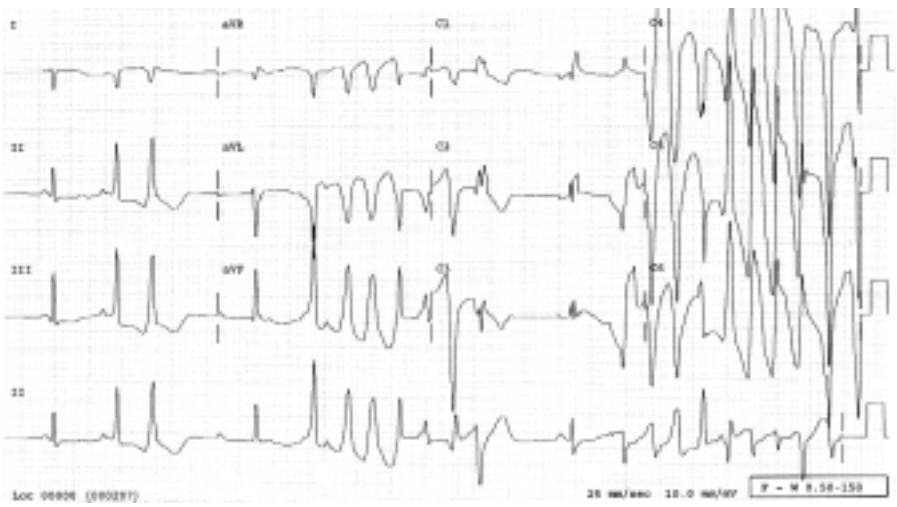

Figure 2.