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Review Article

Oxidative Stress and Hemodialysis

Paik-Seong Lim

Division of Nephrology, Tungs' Taichung MetroHartor Hospital

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Abstract

It is well documented that cardiovascular morbidity as well as mortality are increased in patients along with the development of chronic kidney disease (CKD)[1-5]. Traditional risk factors per se are not able to give a satisfactory explanation for this burden in these patients[6-9]. Recently, other non-traditional risk factors, including oxidative stress, have been proposed to participate in the cardiovascular mortality in uremia [10, 11].There is a body of evidence indicating that oxidative stress occurs in patient with CKD. Oxidative stress is defined as the imbalance between prooxidant and antioxidant mechanisms in favor of the former that ultimately leads to oxidation of all basic cell components, i.e. proteins, lipids, DNA, and carbohydrates. This article (1) reviews the evidence and causes for oxidative stress in CKD, (2) briefly discuss the current strategies for ameliorating oxidative stress in these patients

Key words: Chronic kidney disease, oxidative stress, cardiovascular mortality

Introduction

Cardiovascular disease remains the most frequent complications in end-stage renal disease (ESRD) patients undergoing dialysis, accounting for approximately half of the deaths in this population[1-4]. While it is well documented patients on hemodialysis have an age-adjusted mortality rate 3.5-4 times that of the general population[5], the cardiovascular mortality rate is estimated to be 5-20 times that of the general population[6]. Accelerated atherosclerosis may play an important role in the pathophysiology of cardiovascular dysfunction in ESRD patients.

Besides traditional cardiovascular risk factors, patients with ESRD are also exposed to a number of conditions that are specific to uremic state and that may have contribute to the development of cardiovascular disease. Presumably, these uremic specific factors may explain why these patients have higher mortality rates than counterparts with normal renal function. Among them, oxidative stress is a major mediator of various putative complications of ERSD[7-8].

Free radicals are highly unstable molecules containing one or more unpaired electrons in atomic or molecular orbitals[9]. These molecules, more generally known as reactive oxygen species (ROS), along with reactive nitrogen species (RNS), are constantly produced in physiological conditions and represent part of the defense mechanisms against invading microorganisms and malignant cells. ROS play an important role in numerous biologic functions as signal molecules and is important in tissue healing and remodeling. Under normal conditions, ROS produced in the course of metabolism are contained by the antioxidant defense system consisting of antioxidant enzymes and endogenous and dietary antioxidants. Oxidative stress resulted if a serious imbalance between production of reactive oxygen species (ROS)/reactive nitrogen

*Correspondence to: Dr. Lim Paik-Seong, Division of Nephrology, Tungs' Taichung MetroHartor Hospital, No.699, Sec. 1, Chungchi Rd., Wuchi Dist., Taichung City 43503, Taiwan (R.O.C.).

species (RNS) and antioxidant defenses[10]. It can result from the following:

1) Depletion of endogenous antioxidants or of diet-derived antioxidants, caused by malnutrition.

2) Excess production of ROS/RNS e.g. by exposure to elevated O2 concentrations, the presence of toxins that are metabolized to produce free radicals or excessive activation of "natural" radical-producing systems e.g.inappropriate activation of phagocytic cells in chronic inflammatory diseases[11].

Cells can tolerate mild oxidative stress, which often results in upregulation of the synthesis of antioxidant defence systems in an attempt to restore the balance. However, severe oxidative stress can produce major interdependent derangements of cell metabolism, including DNA strand breakage, rises in intracellular "free Ca 2+", damage to membrane ion transporter and/or other specific proteins and peroxidation of lipids[12-13]. Mechanisms of cell injury by oxidative stress are complex and overlapping. Moreover, oxidative stress can also lead to cell death and may involved in cell apoptosis [14].

ROS/RNS can attack, modify, and denature functional and structural molecules causing cytotoxicity, tissue damage, and dysfunction. Apparently, ROS/RNS play an important role in tissue injury [Fig 1] and has thus been implicated to play a pathogenic role in a bewildering array of chronic diseases such as cardiovascular and rheumatologic diseases, infection, cancer, diabetes and neurodegenerative diseases. Tissue damage by disease, trauma, toxic agents and other causes usually leads to formation of increased amounts of putative "injury mediators" such as prostaglandins, NO, leukotrienes, interleukins, interferons and cytokines such as tumour necrosis factors (TNFs)[15]. All of these at various times have been suggested as playing important roles in different human diseases. In human disease, oxidative stress may be a secondary phenomenon, a consequence of the disease activity [Fig 2] and there is growing evidence that oxidative stress is a major contributor to chronic inflammatory, neuro- degenerative and even cardiovascular diseases.

In recent years several lines of evidence suggested that subjects with chronic kidney disease, with or without dialysis, appears to be in a state of increased oxidative stress. Indeed, increased oxidative stress in patients with renal failure was first reported as the decreased antioxidation activity of uremic serum [16] and increased synthesis of methylguanidine, a uremic toxin[17] at the workshop on uremic toxin at the Japanese Society of Nephrology in 1984. Since then, many lines of evidence have revealed that increased oxidant stress is increased in renal failure. Many investigators believed that oxidative stress may play an important role in some of pathologies associated with uremia

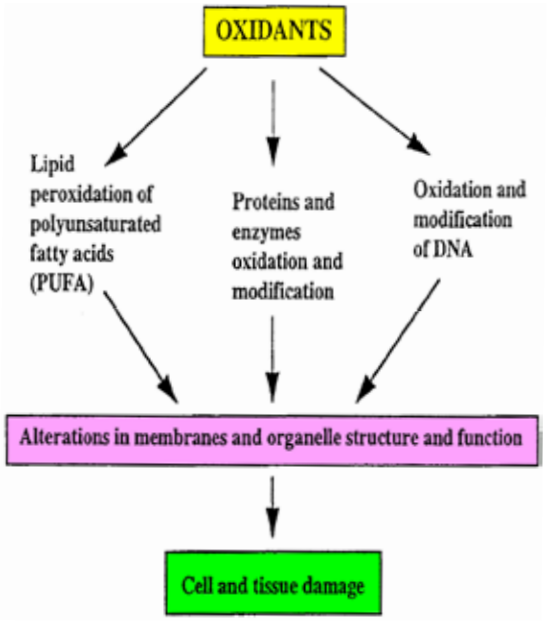

Fig. 1 Influence of oxidants on the major biomolecules of biological systems.

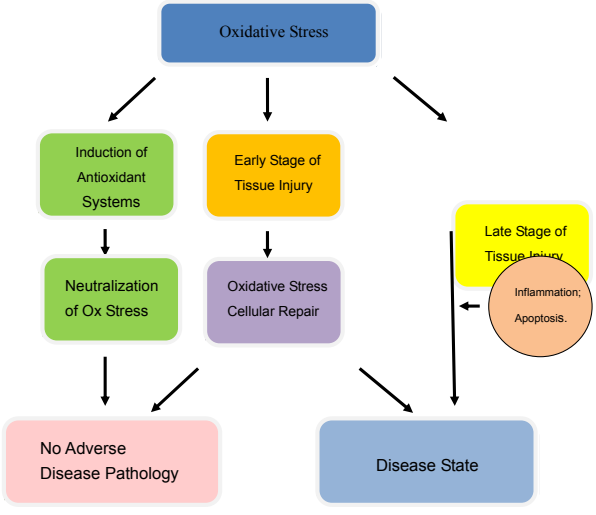

Fig. 2 Conditions for occurrence of oxidative stress

and hemodialysis such as cardiovascular disease, amyloidosis and immune dysfunction[18] [Fig 3]. In addition, oxidatively modified molecules may behave as a mediator of inflammation and might exert immunomodulating activities causing uremia-associated immune system dysregulation. The propensity of uremic patients to develop oxidative stress appears to be attributed to abnormal production of oxidants and defective antioxidant defense. The factors involved are listed in Table 1. In hemodialysis, the absence of a complete correction of the uremic toxicity together with the untoward effects of the dialysis therapy, malnutrition and metabolic abnormalities associated with uremic milieu probably account for the increased oxidative stress. The oxidants typically generated in uremic milieu such as hypochlorite, hydroxyl radical, peroxy radical and peroxylnitrite are very reactive and short-lived. By contrast, some of the modifications in biological molecules have relatively long half-lives, ranging from hours to weeks[19]. Hence, modified lipids, proteins and nuclei acids can serve as reporter groups for the presence of oxidative stress.

Conditions for the increased generation of oxidative stress are generally present in the uremic patients on hemodialysis in whom intermittent generation of oxidants recurs at each dialysis session. Using chemiluminescence detection[20-21] flow cytomtetry[22], increased generation of intracellular ROS in both monocytes and polymononuclear cells occurred during dialysis sessions and this event is closely related to the membrane bioincompatibility and amount of C_{5a} and C_{3a} generation[23]. Raised levels of the lipid peroxidation marker such as malondialdehyde (MDA-lysine) [Fig 4a] and the accumulation dialyzable oxidants measured by electron spin resonance spectroscopy have been demonstrated in uremic plasma[24]. Free-radical attack on arachidonic acid in vivo initiates a series of modifications that can terminate in a stable end-product with 3-OH groups, with structural similarity to prostaglandin F2-alpha[25], named collectively as F2-isoprostanes". We and several other groups have observed isoprostanes levels were significantly increased in patients on long-term dialysis[26-28]. [Fig 4b]

Proteins constitute more than 50% of the dry weight of cells, and as such can be considered

Table 1. Factors causing increased oxidative stress in ESRD patients.

Retention of oxidants or pro-oxidants Substances to be excreted in urine or oxidants: Phenol, indoxyl, carbonyl, methyguanidine, metals, oxidized lipids
Decreased renal reduction activity GSSG to GSH, cystine to cysteine, arginine synthesis.
Malnutrition Decrease ROS scavengers
Increased ROS generation Protein kinase C activation in non-inflammatory cells Activation of inflammatory cells by hemodialysis (mechanical, endotoxin, chemical)

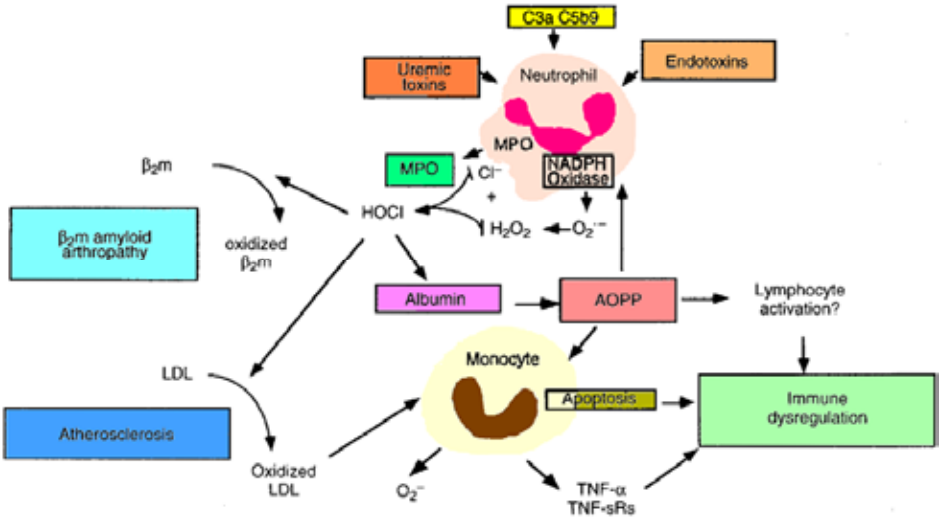

Fig 3. Possible pathophysiological role of oxidized protein products. Adapted from Descamps-Latscha B (2001)

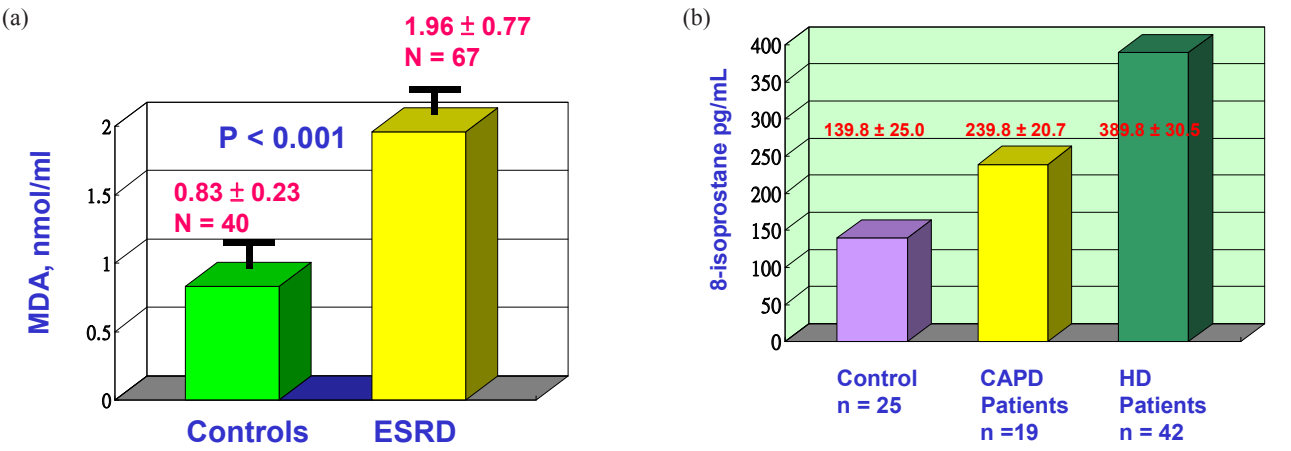

Fig. 4 (a) Levels of malondiadehyde (MDA) (nmol/ml) in end-stage renal disease patients (ESRD) and controls. The difference is significant (p <0.001). b. Levels of F2-isopprostanes (pg/mL) in end-stage renal disease patients on hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD)and controls. The difference is significant between both patients groups and controls (p <0.001)

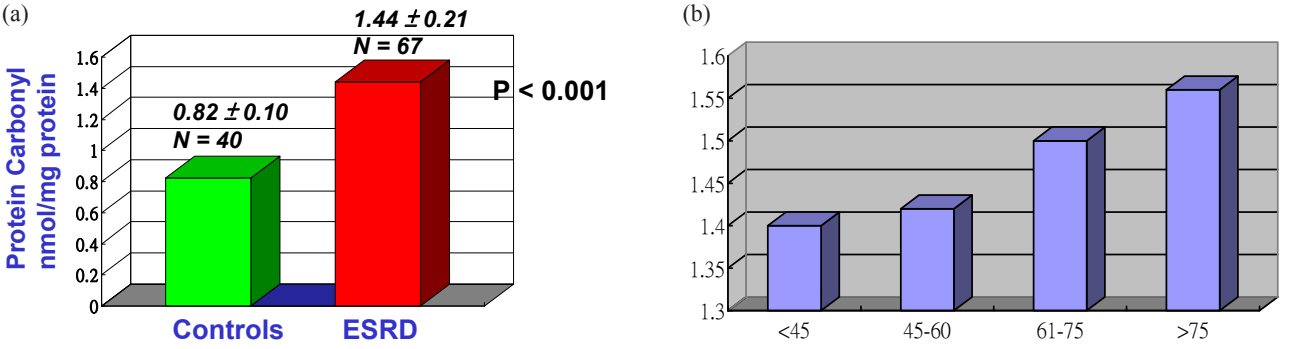

Fig. 5 a. Levels of protein carbonyl (nmol/mg protein) in end-stage renal disease patients (ESRD)and controls. The difference is significant (p <0.001). b. Mean plasma values of protein carbonyls of different age subgroups.(a, < 40 y, n=, b, 41-60, n y, c, 61-75 y, n= d, > 75y, n=) of hemodialysis (HD) patients expressed as nmol DNPH/mg of protein. The levels of protein carbonyls in individual HD groups did not differ significantly except an increase in the amount was observed between the youngest and oldest groups (> 75y) [p <0.001].

important targets of oxidants-mediated injury. Biochemical and structural modifications of protein-injured by oxidative attack may lead to functional alterations and the progressive loss of their metabolic, enzymatic or immunologic properties. For a given oxidant, depending on the intensity of the oxidative attack, these modifications may go from the oxidation of a single amino acid residue, to the fragmentation or complete denaturation of the protein across intermediary steps of increased hydrophobicity, augmented susceptibility or resistant to proteolysis. The most general indicator and by far the most commonly used early marker of protein oxidation is protein carbonyl content. It involves cations of the redox cycle such as Fe^{2+} and Cu^{2+}, which have binding sites on proteins and may transform amino acid residues in carbonyls in the presence of hydrogen peroxide and superoxide anion. The most likely amino acids residues to form carbonyl derivatives are lysine, arginine, proline and histidine. Metal-catalyzed protein oxidation leading to increased in carbonyl formation has been detected in various tissues in uremic patients on hemodialysis[18,29-30] [Fig 5a and b]. Tyrosine dimerisation has been proposed to contribute to the aggregation of proteins frequently observed on oxidation. The nucleophilic non-radical oxidant, HOCl, is particularly

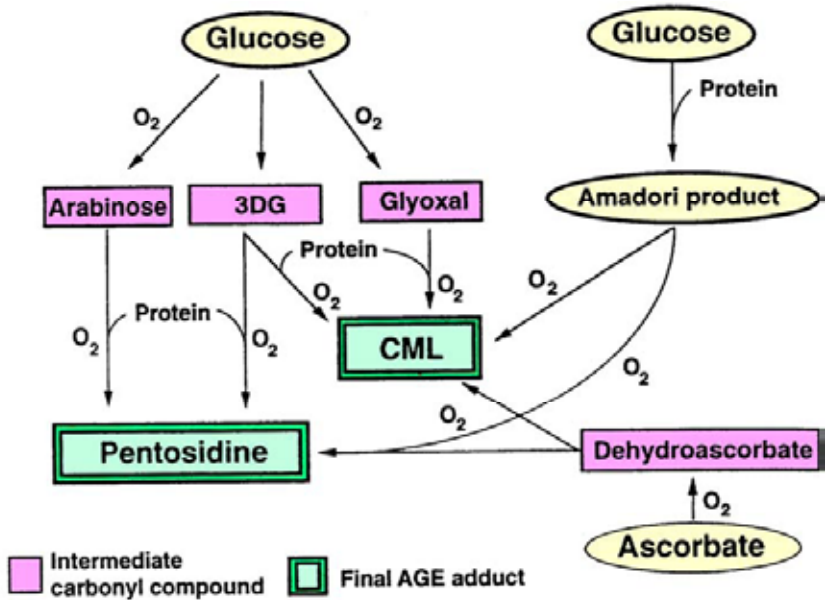

Fig. 6 Maillard reaction pathway for formation of Ne-[carboxymethyl] lysine (CML) and pentosidine. Fructoselysine is the Amadori compound, the first intermediate in the Maillard reaction occurring between glucose and protein. CML and pentosidine are formed by sequential glycation and oxidation (glycoxidation).Adapted from Miyata (1999)

reactive with tyrosine, inducing the characteristic chlorotyrosine. On the other hand, nitrotyrosine, is formed from attack by nitrating species including peroxynitrite and reactions between hypochlorite and nitrogen containing species[31]. The importance of amino-acid-derived aldehydes generated by myeloperoxidase in the formation of atherosclerosis has been reported recently. Hypochlorite- modified proteins have been shown to be present in human atherosclerotic lesions[32]. Both markers had been shown to be elevated in dialysis patients[33-34]. Moreover, the presence of elevated circulating levels of oxidatively-modified proteins such as "advanced oxidation protein products (AOPPs) is a good reflection of the state of oxidative stress[33]. AOPPs appear to act as true inflammatory mediators since they are able to trigger the oxidative burst in neutrophils as well as monocytes[35]. In addition, under oxidative stress, carbohydrate, lipid and ascorbate may be converted into noxious carbonyl groups that, in turn, react with proteins and eventually form advanced glycation end-products (AGEs) and related protein adducts[36-37]. Carbonyl stress with increased AGEs/ALEs has been associated with many dialysis -related pathologies such as dialysis related amyloidosis and atherosclerosis[36-37] [Fig 6].

More interestingly, oxidative stress can also induce DNA damage such as base modification[38] and strand break[39]. Among the base modifications, 8-hydroxy-2'-deoxyguanosine (8-OHdG) is one of the most abundant oxidative DNA products. Numerous studies have established that 8-OhdG is a novel marker for the assessment of oxidative DNA damage in ROS-mediated diseases[40-41]. Recent works from our laboratory showed that the nuclei acid oxidation marker represented by 8-OHdG of leukocyte[42] [Fig 7a] and hair follicles[43] [Fig 7b] DNA are also elevated in hemodialysis patients.

Apart from the overproduction of oxidants, oxidative stress has been attributed to several other causes as reduced antioxidant capacity[44], uremic toxins[45], and the oxidizing effects of the hemodialysis membranes and intravenous iron infusions[46]. Although this review focus on a broad range of issues related to oxidative stress in dialysis patients, the discussion of this topics is beyond the scope of the present review.

Because of their numerous deleterious effects of oxidative stress on the various organ systems in dialysis patients, amelioration of oxidative stress could be an important target in therapeutic interventions for reducing morbidity and mortality in CKD patients. For

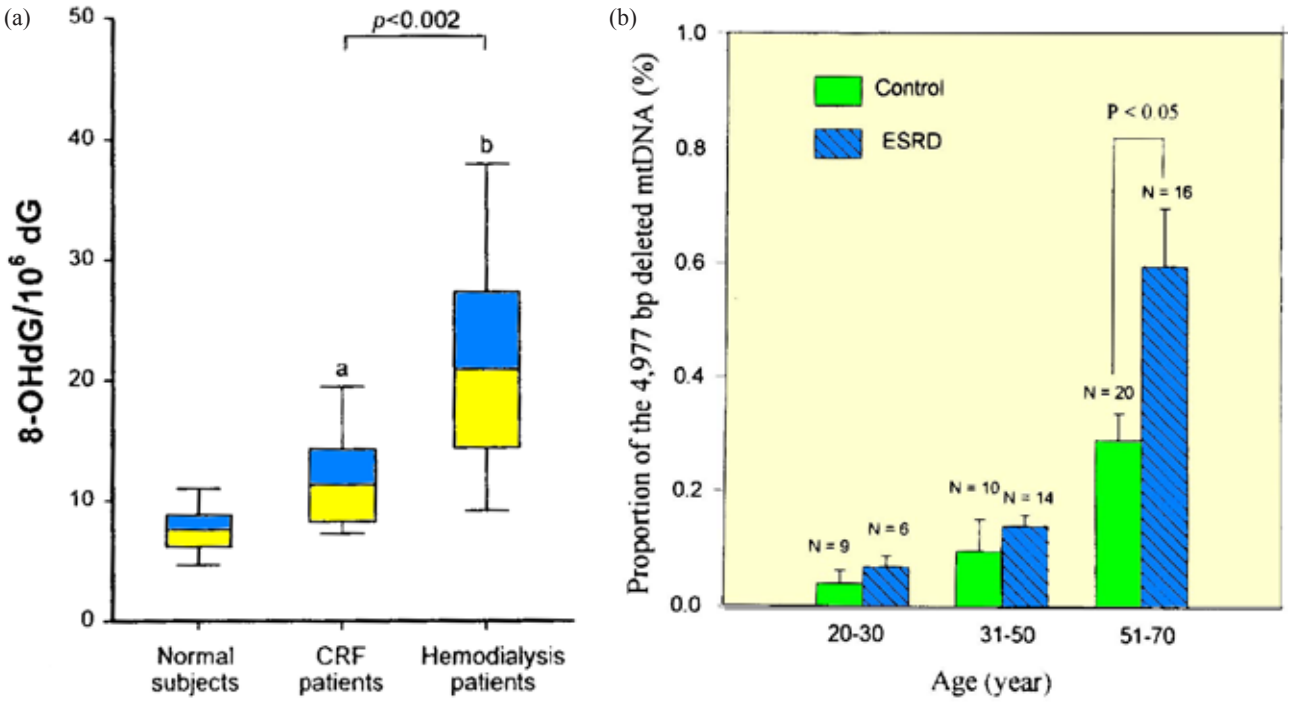

Fig. 7 a. Whisker plots showing differences of 8-OHdG levels among healthy subjects, undialyzed patients with advance renal failure and hemodialysis patients. Adapted from Tarng DC (2000). b. Comparison of the proportion of mtDNA with the 4977 bp deletion in hair follicles of the subjects in three age groups. The column in each age group represents the average proportion (mean ±SEM) of mtDNA with the 4977 bp deletion in hair follicles. Adapted from Liu CS(2001)

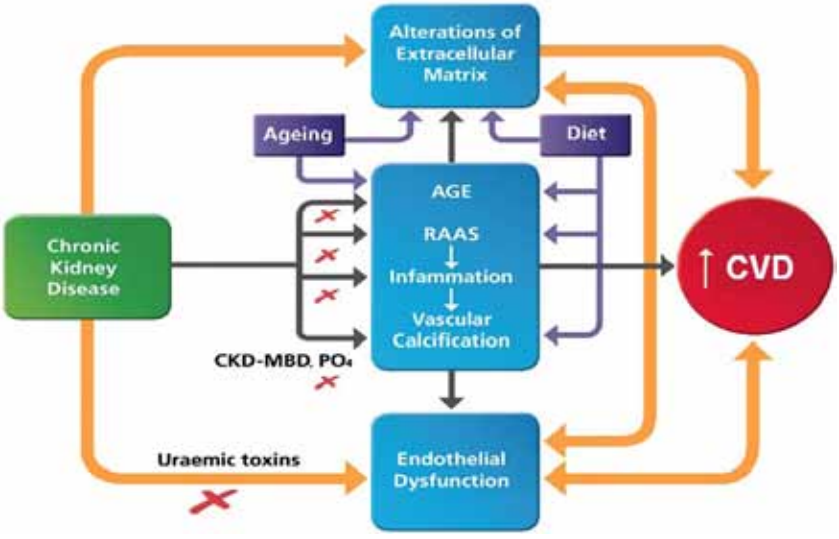

Fig 8. Therapeutic Approaches to reduce oxidative stress. Pathway of interventions ✗

this, there are two possible approaches (Fig. 8). The first therapeutic option is to lower the uremic toxin concentrations with vascular toxicity such ADMA, homocysteine and various protein-bounds toxins. Because of their protein binding, these toxins are poorly removed by conventional HD. Other means have been proposed to reduce their concentrations, such as other dialysis techniques or different drugs.

The second therapeutic approach is to counterbalance the deleterious effects of uremic toxins. Indeed, uremic toxins induce endothelial injury by mechanisms mainly involving increased oxidative stress, impaired NO metabolism or availability, and reduced EPC survival and functions. Anti-oxidants, statins, renninangiotensin-aldosterone system (RAAS) blockers, or EPO could be used to counter the action of uremic toxins with variable success. There are a few published studies that demonstrate the promise of antioxidant therapy in reducing cardiovascular patients and ESRD patients. However, much further research is needed before the optimal antioxidant regimen for dialysis patients is determined.

In conclusion, oxidative stress is a pathogenic element of great importance in dialysis patients. A better understanding of this issue is not only imperative for elucidating the pathogenic mechanism of CKD, but may also provide novel insights into developing new therapeutic strategies. Undoubtedly, in recent years, our understanding of the patho-mechanism of oxidative stress in CKD patients has greatly expanded. Many therapeutic interventions appear effective in animal models; however, translation of these results into humans in the clinical setting remains a daunting task and more studies are clearly needed.

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氧化壓力與血液透析

林柏松

童綜合醫療社團法人童綜合醫院　腎臟內科

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摘要

心血管疾病造成慢性腎臟病患者極高的死亡率公已是重要的公共健康議題。一般引導心血管疾病的因素，有傳統的與非傳統的因子。但是只用傳統性危險因子無法充份解釋慢性腎臟病病人在心血管疾病的高危險性，甚至會低估心血管疾病在慢性腎臟病病人發生的機率和嚴重度。許多研究陸續發現，在慢性腎臟病患，統性危險因子如氧化壓力會增加心血管疾病，相較於一般健康人群，慢性腎臟病患有明顯偏高的氧化壓力。氧化壓力是活性氧化物生成和抗氧化防禦兩者失衡的結果。對慢性腎臟病患而言，氧化壓力的增加，主要來自於抗氧化物質的缺乏，及氧化物質清除系統的缺陷。此篇文章主要在探考慢血液透析患者氧化壓力增加的各種原因及證據，也會簡述有效改善氧化壓力的策略及方法。

關鍵詞：慢性腎臟病、氧化壓力、心血管死亡率

* 通訊作者：林柏松醫師　童綜合醫療社團法人童綜合醫院　腎臟內科　43503 台中市梧棲區中棲路一段 699 號

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Original Article

Age-related changes in left ventricular torsion assessed by 3-dimensional ultrasound speckle tracking imaging

Chin-Hung Tsai, Ying-Tsung Chen*, Hung-Yi Hsu

Department of Internal Medicine, Tungs' Taichung MetroHarbor Hospital Taichung, Taiwan

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Abstract

Background: It is increasingly accepted that aging results in changes in left ventricular (LV) structure and function, which may play an important role in the development and progression of cardiovascular diseases. The application of 3-dimensional speckle tracking echocardiography (3D-STE) for evaluation of LV function has not been widely studied, and few data on its use for assessment of cardiac strain and torsional change with aging exist. The purpose of this study was to establish the normal values of LV torsion in healthy persons and to examine the effects of aging on these values using 3D-STE.

Methods: Echocardiographic examinations were performed on 87 healthy volunteers who were divided into 3 age groups: young (20–40 years, 30 patients), middle-aged (41–59 years, 31 patients), and elderly (≥60 years, 26 patients). For the apical 3D volumetric images, torsion was analyzed in 16 myocardial segments. Using commercially available 3-dimensional torsion analysis software, time–domain speckle tracking was performed and mean values of torsion were assessed.

Results: There were no statistically significant differences in body height, weight, heart rate, blood pressure, or ejection fractions between the 3 groups. A comparison of the global values of rotation, twist, and torsion revealed no differences between the 3 groups. However, regional differences were found among basal, middle, and apical segments; moreover, apical twist and apical torsion increased with age ($p < 0.05$).

Conclusions: The newly developed 3D-STE technique appears to be a reliable tool for assessment of LV regional and global function. This methodology could be applied clinically to assess alterations of myocardial function by accurately measuring regional and global LV torsion and the changes in regional heterogeneity in systolic function seen with increasing age. Our findings imply that regional function parameters may be more sensitive than global function parameters for evaluating systolic function. These results may be of value as reference data for healthy adults in further clinical studies.

Key words: 3-dimensional ultrasound speckle tracking imaging, 3D-STE, LV torsion

Introduction

Assessment of left ventricular (LV) torsion is useful for gaining better understanding and quantification of LV function.[1-3] Two-dimensional speckle tracking imaging (2D-STE) has provided clinicians with a noninvasive method of evaluating regional and global functions of LV. [4-9] However, 2D-STE is only capable of detecting 2-dimensional planes. Recently, 3-dimensional speckle tracking echocardiography (3D-STE) was developed and this technique can evaluate LV motion in all directions and can overcome the problem of out-of-plane motion encountered in 2D-STE. It is increasingly accepted that aging results in changes in LV structure and function, which may play

*Correspondence to: Dr. Chen Ying-Tsung, *Department of Internal Medicine, Tungs' Taichung MetroHarbor Hospital,* No. 699, Sec. 1, Chungchi Rd, Wuchi Township, Taichung County 43503, Taiwan (R.O.C.)

an important role in the development and progression of cardiovascular diseases. However, only few studies have analyzed the application of 3D-STE in the evaluation of LV function,[10-14] and few data exist regarding the effects of aging on cardiac torsional change. The purpose of this study was to establish the normal values of LV torsion in healthy adults and to examine the effects of aging on these values using 3D-STE.

Methods

Study groups

This study was approved by the local ethics committee, and all subjects gave written informed consent. One hundred consecutive healthy volunteers were enrolled and divided into 3 age groups. Thirteen subjects were excluded from this study because of poor image quality for analysis. In total, there were 30 subjects (20–40 years) in the young group, 31 subjects (41–59 years) in the middle-aged group, and 26 subjects in the elderly group (≥60 years). All studied subjects were normotensive,[2] in normal sinus rhythm, and without valvular lesion or hypertrophy,[3] according to conventional echocardiography.

Speckle tracking analysis by 3D echocardiography

Real-time 3D echocardiographic imaging was performed from the apical position using the fully sampled matrix array transducer (PST-25SX) (Artida 4D, Toshiba Medical Systems, Tokyo, Japan). A wide-angled acquisition "full-volume" mode was used to optimize the frame rate of acquisition, and depth was minimized to include only LV. A frame rate of 20–30 Hz was used in this study. In the apical 2-chamber and apical 4-chamber views, 3 short-axis views at different levels of LV from the base to the apex were automatically selected from the real-time 3D echocardiographic pyramidal data set obtained at end diastole. The 3D images of the LV wall were automatically divided into 16 segments (6 basal, 6 mid, and 4 apical segments) using standard segmentation. The software automatically tracked the contour on the subsequent frame in different vectors simultaneously (Figures 1 and 2). Rotation is the rotary motion of the myocardium during contraction, during which the apex moves counter-clockwise and the base moves clockwise. Counter-clockwise is defined as the plus direction (Figure 2, left upper). Twist is the difference in myocardial rotation at any given short-axis level relative to the corresponding point at the left ventricular base (Figure 2, left lower).

Basal torsion is the rotation gradient with respect to the basal plane (Figure 2, right upper). Regional torsion is the difference in rotation angle between two nearby planes. (Figure 2, right lower). All torsion data were obtained from the data from

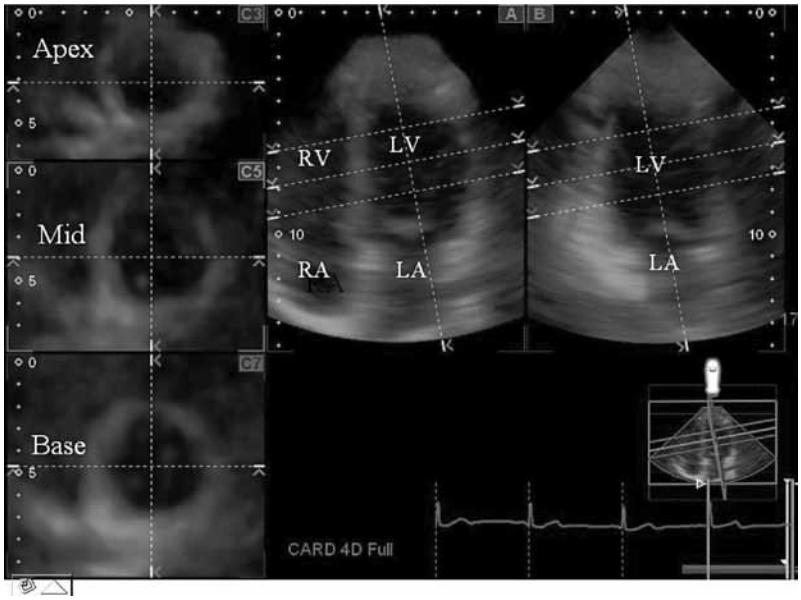

Fig. 1 Example of images generated from a 3-dimensional data set. The multiplanar reconstruction images correspond to the apical 2-chamber (right panel: B) and 4-chamber views (central panel: A) and 3 short-axis views at different levels (left panel: C3, C5, and C7).

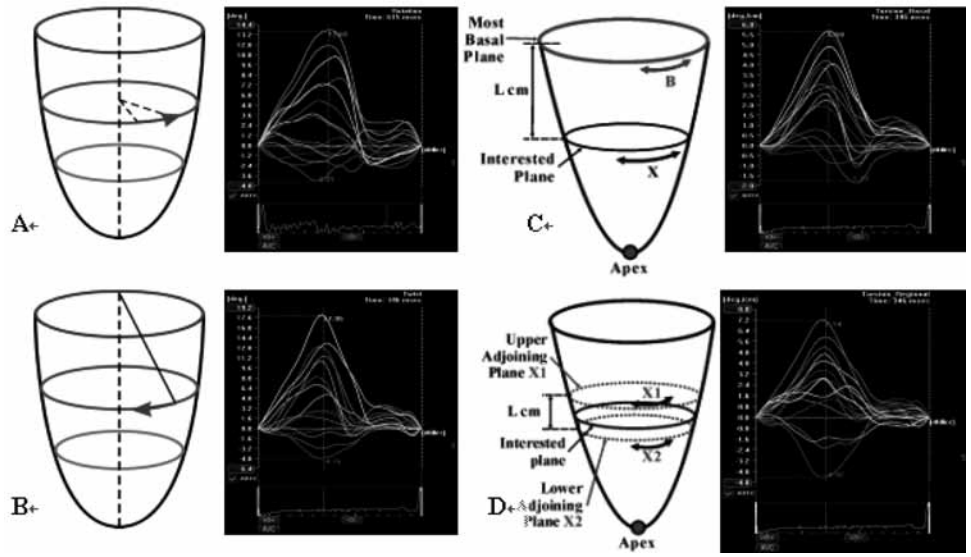

Fig. 2 Calculation of rotation, twist, and torsion A. Rotation: In each plane, rotations [deg.] are calculated. Counter-clockwise is defined as the plus direction. B. Twists [deg.] calculation: rotation value of each plane minus rotation value of basal short axis C. Torsion-basal calculation : (Rotation of interested plane X deg.)–(Rotation of the most basal plane B deg.)/ (Distance between interested plane and most basal plane L cm) D. Torsion-regional calculation: (Rotation of adjoining plane X2 deg.)–(Rotation of adjoining Plane X1 deg.)/ (Distance between two adjoining plane L cm)

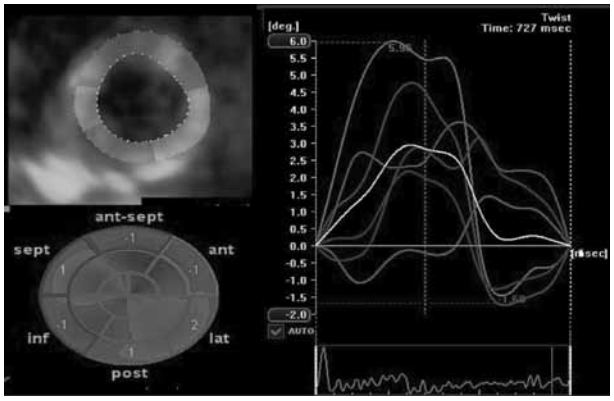

Fig. 3 Basal twist values detected by color coded 3-dimensional speckle tracking echocardiography from basal short-axis level of LV (top left) and bullseye plot image (bottom left) and corresponding time-to-strain curves from basal segment sites (right)

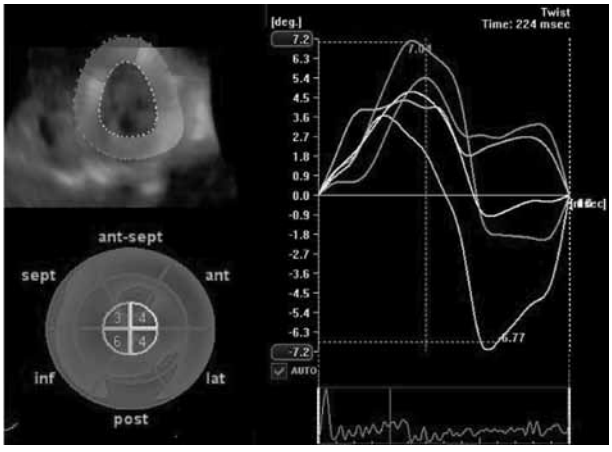

Fig. 4 Apical twist values detected by color coded 3-dimensional speckle tracking echocardiography from apical l short-axis level of LV (top left) and bullseye plot image (bottom left) and corresponding time-to-strain curves from apical segment sites (right)

one heart beat with good tracing and were automatically calculated for each segment (Figures 3 and 4).

Intraobserver and Interobserver Variability

Intraobserver variability was determined by having an experienced sonographer repeat the measurement of LV torsion in 10 randomly selected subjects. For interobserver variability, offline measurement was made by another sonographer who was unaware of the results of previous studies. Intraobserver and interobserver variabilities were calculated as the absolute difference between the corresponding repeated measurements as a percent of their mean.

Statistical methods

Data were expressed as mean ± SD for continuous variables. Values of different groups of patients were compared using an analysis of variance test. A p value of <0.05 was considered statistically significant.

Results

Among the 100 healthy subjects who had been initially considered eligible for the present study, 87 subjects (40 males and 47 females) were found to have good quality images for assessment of LV function. Thus, approximately 87% of images obtained using 3D-STI were of good quality. Body weight, heart rate, blood pressure, and ejection fractions were not statistically different between the 3 groups.

The effects of age on global values of rotation, twist, and torsion were not statistically different between the young and middle-aged groups; there was a trend of an increase with age but it was not significant (1.09 ± 0.81, 1.01 ± 0.70, 1.31 ± 1.76, $p > 0.05$). A further comparison of the basal, middle, and apical segments revealed that the average apical twist (7.27 ± 3.94, 7.16 ± 0.97, 10.59 ± 7.43, $p < 0.05$), apical torsional regional (2.11 ± 0.98, 2.37 ± 0.97, 3.17 ± 1.64, $p < 0.05$), and apical torsional basal (1.47 ± 0.79, 1.45 ± 0.67, 2.23 ± 1.62, $p < 0.05$) values significantly increased with age, chiefly at the apical anterior, apical septal, apical inferior, and apical portions (Tables 1 and 2).

Reproducibility

The intraobserver variabilities for LV torsion measurements were 10% ± 4%, and the corresponding interclass correlation coefficient (CICC) was 0.96. The interobserver variabilities were 13% ± 10%, and CICC was 0.93.

Table 1. Left ventricular parameters in the three age groups

		20–40 yr (n=30)	41–59 yr (n=31)	≧ 60 yr (n=26)	p value
	Age (years)	29.1 ± 6.2	4.9 ± 6.3	61 ± 9.9	<0.01
	Males	16 (30)	14 (31)	12 (26)	NS
	Weight (kg)	64.8 ± 1.2	65.8 ± 1.8	65.7 ± 1.5	NS
	SBP (mmHg)	117 ± 11.4	119 ± 10.2	120.3 ± 18.7	NS
	DBP (mmHg)	70.2 ± 10.6	70.6 ± 10.4	73.4 ± 19.8	NS
	HR (beats/min)	72.31 ± 14.0	71.20 ± 11.0	70.11 ± 13.23	NS
	EF%	61.4 ± 6.6	60.4 ± 7.8	59.2 ± 5.5	NS
Twist	Basal (avg)	1.76 ± 0.78	1.90 ± 1.23	1.80 ± 1.02	0.873
	Middle (avg)	4.95 ± 2.06	5.12 ± 2.89	5.85 ± 3.35	0.448
	Apical (avg)	7.27 ± 3.94	7.16 ± 3.27	10.59 ± 7.43	0.021
	Global	3.33 ± 2.18	3.37 ± 2.44	4.72 ± 3.84	0.130
Torsion Regional	Basal (avg)	1.94 ± 0.77	2.11 ± 1.31	2.18 ± 1.28	0.724
	Mid (avg)	2.78 ± 2.37	2.08 ± 1.85	3.13 ± 3.26	0.278
	Apical (avg)	2.11 ± 0.98	2.37 ± 0.97	3.17 ± 1.64	0.005
	Global	1.09 ± 0.81	1.01 ± 0.70	1.31 ± 1.76	0.130
Rotation	Basal (avg)	−3.7 ± 2.1	−3.6 ± 1.8	−5.0 ± 3.7	0.074
	Mid (avg)	3.83 ± 1.81	4.02 ± 2.14	3.79 ± 2.41	0.908
	Apical (avg)	5.84 ± 3.53	5.81 ± 2.76	7.53 ± 5.09	0.170
	Global	2.62 ± 2.03	2.87 ± 2.08	2.99 ± 2.81	0.829
Torsion Basal	Basal (avg)	1.66 ± 0.74	1.82 ± 1.15	1.73 ± 1.03	0.834
	Mid (avg)	1.79 ± 0.73	1.88 ± 1.08	2.17 ± 1.29	0.385
	Apical (avg)	1.47 ± 0.79	1.45 ± 0.67	2.23 ± 1.62	0.012
	Global	1.11 ± 0.73	1.16 ± 1.00	1.51 ± 1.31	0.291

Table 2. Comparison of significant differences in LV wall segments among three age groups in $P < 0.05$

		20–40 yr (n=30)	41–59 yr (n=31)	≧ 60 yr (n=26)	p value
Twist	AA	5.4 ± 3.7	7.4 ± 5.3	9.7 ± 8.0	0.027
	AS	9.8 ± 6.2	7.2 ± 4.6	12.0 ± 7.3	0.013
	AI	5.0 ± 4.1	5.6 ± 4.3	9.4 ± 6.9	0.004
	AL	7.8 ± 6.1	8.3 ± 5.4	8.8 ± 7.4	0.837
	A	8.4 ± 6.3	7.3 ± 5.0	13.1 ± 13.2	0.034
	Apical (avg)	7.27 ± 3.94	7.16 ± 3.27	10.59 ± 7.43	0.021
Torsion Basal	AA	1.2 ± 0.9	1.5 ± 1.2	2.1 ± 1.8	0.042
	AS	2.1 ± 1.3	1.5 ± 1.0	2.8 ± 1.8	0.004
	AI	1.1 ± 0.9	1.2 ± 0.9	2.2 ± 1.7	0.002
	AL	1.7 ± 1.3	1.8 ± 1.2	1.9 ± 1.6	0.832
	A	1.4 ± 1.1	1.2 ± 0.9	2.3 ± 2.5	0.024
	Apical (avg)	1.47 ± 0.79	1.45 ± 0.67	2.23 ± 1.62	0.012
Torsion Regional	AA	1.6 ± 1.3	2.7 ± 1.7	3.4 ± 2.4	0.002
	AS	3.2 ± 1.9	2.7 ± 1.9	4.2 ± 2.3	0.021
	AI	1.7 ± 1.5	1.6 ± 1.4	2.9 ± 2.2	0.011
	AL	2.3 ± 2.4	2.5 ± 1.9	3.3 ± 2.7	0.364
	A	1.1 ± 1.0	1.6 ± 1.4	2.3 ± 1.7	0.006
	Apical (avg)	2.11 ± 0.98	2.37 ± 0.97	3.17 ± 1.64	0.005

Discussion

The investigation described herein was a pilot study, and to the best of our knowledge, this is the first study to establish the normal values of cardiac torsion measured by 3D-STE in healthy Chinese adults, ranging in age from 20 years to well over 60 years of age. Our results showed good feasibility for the 3D-STE technique (87% good images). The 13 subjects who were excluded from the study were chiefly in the elderly group and the reason for their elimination was poor cardiac image definition. Previous studies that have used 3D-STE have reported feasibility rates ranging from 78%–95%.[14, 16-17] By calculating and reconstructing the motion and deformation of the myocardial tissue, 3D-STE achieves accurate qualitative and quantitative estimations of twist and torsion.[13-17] Changes in LV torsional function with age have been studied by 2D Doppler and 2D-STE,[6, 18-24] although conflicting results were obtained. Our findings showed that global values of rotation, twist, and torsion in the elderly group were similar to values observed in the two younger groups; however, there were discrepancies in apical, middle, and basal segments, with increasing values in the apical region in the older groups, chiefly in the apical anterior, apical septal, and apical inferior segments. The regional heterogeneity in systolic function observed is consistent with previous findings.[25-26] Thus, regional function parameters may be more sensitive than global parameters for evaluating systolic function. LV twist deformation is because of the complex helical myocardial fiber architecture. The orientation of the fibers in the different portions of the myocardial wall are as follows: the subepicardial fibers in a left-handed helix pattern, the fibers of the middle portion of the wall in a circumferential orientation, and the subendocardial fibers in a right-handed helix pattern. Despite being partially counteracted by the subendocardial fibers, the subepicardial fibers mainly generate the LV torsion in the normal heart. This wringing motion of the heart is the result of the clockwise rotation of the base and the counter-clockwise rotation of the apex, and it plays an important role in

ventricular performance.

Greater regional nonuniformity of twist and torsion with age was found in this study. These findings are consistent with those of previous studies[6,19,21,27] and indicate the possible contribution of twist and torsion in preserving ejection fraction in the elderly. Of note, it is the helical fiber architecture of the heart that doubles the LV ejection fraction.[28] In others words, even when LV diastolic function has been decreased, optimization of torsion and twist still allows for preservation of LV systole.

The mechanism of augmented LV rotation and LV torsion with aging is still not precisely understood. One possible mechanism is related to subendocardial underperfusion, which occurs as a result of an increased LV end diastolic pressure or subendocardial fibrosis, and this in turn diminishes the counteractive motion of the subendocardial fibers against that of the subepicardial fibers.[19-20] Dalen et al. have postulated that the increased twist and torsion with advancing age can be explained by an increase in apical rotation, but the decrease in rotational deformation delay with advancing age may also play an important role.[21] In the present study, our LV rotation data were not completely concordant with those obtained by 2D-STE. Discordant results between 3D-STE and 2D-STE in previous reports may be explained by the fact that 3D-STE assesses the real motion of the myocardium, showing changes in volume and space in 3 dimensions, whereas in 2D-STE out-of-plane motion may confound the analyses.[13-14,16]

Conclusions

The newly developed 3D-STE technique appears to be a reliable tool for assessment of the regional and global function of LV. This methodology could be applied clinically to assess alterations in myocardial function by accurately measuring torsion in basal, mid, and apical LV segments and global torsion. In addition, these data can be acquired within an acceptable amount of acquisition and analysis time. Regional heterogeneity in systolic function was observed. Thus, regional function parameters may be more sensitive than global parameters for evaluating systolic function. LV torsion during systole showed statistically significant augmentation with advancing age, and this may be mainly due to the increased apical LV rotation. Our results on age-related changes in LV function of healthy adults may be of value as reference data for further clinical study. 3D-STE was found to be a powerful tool for assessment of the regional and global function of LV in a clinical setting.

Limitations

The limitations of the present study are similar to those reported in previous studies. There is still no gold standard for measuring LV torsion. Although cardiac magnetic resonance is widely used as a reference technique for LV function, it is not a true 3D imaging technique. Essentially, it is a two-dimensional imaging modality that has an ability to take multiple slices. The reliability of 3D-STE for assessment of regional myocardial function needs to be confirmed by further clinical studies.

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三維超聲斑點追踪影像評估左室扭轉與年齡有關的變化

蔡慶宏　陳穎從*　許弘毅

童綜合醫療社團法人童綜合醫院　內科部

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摘要

背景：老齡增長左心室結構和功能產生變化，影响心血管疾病的進展和預後。三維超聲斑點追踪影像(three-dimensional speckle tracking echocardiography (3D-STE)評價左心室功能的應用並沒有被廣泛研究，只有少數研究評估心臟的扭轉改變與老化。這項研究的目的是要建立在健康人左心室扭轉（torsion）的正常價值，評估左心室扭轉與年齡有關的變化。

方法：在87名健康志願者分成三個年齡組，30位年輕（20-40歲），31位中年（41-59歲）和26位年長組（≧60歲）。根據三維立體圖像，使用3維扭轉分析軟體,分析16個心肌節段，評估局部（regional）及整體（global）心肌扭轉。

結果：身高，體重，心率，血壓，射血分率顯示，3組間無統計學差異。整體旋轉（rotation），扭曲（twist），並扭轉（torsion）平均值的比較，3組之間亦無差異。但在心底，中間和心尖段之間有局部性差異，以及心尖扭曲和心尖扭轉隨著年齡增加而增加（P<0.05）。

結論：新開發的3D- STE技術，可用於臨床評估左心性室整體性及局部性功能改變，並精確測量心底，中間，心尖段局部的差異變化，區域功能參數可能比整體性參數評估心室收縮功能更為敏感。這些結果可作為進一步研究健康成人參考的數據。

關鍵詞：三維超聲、扭轉

* 通訊作者：陳穎從醫師　童綜合醫療社團法人童綜合醫院　內科部　43503台中市梧棲區中棲路一段699號

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Original Article

Minimally invasive plate osteosynthesis in the treatment of complicated fractures of the tibia

Shu-Ang Wang*

**Department of Orthopaedic, Tungs' Taichung MetroHarbor Hospital*

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Abstract

A study of minimally invasive plate osteosynthesis (MIPO) in the treatment of 11 patients with comminuted fractures of the tibia compares to the conventional open plating in other studies. All were not allowed to have intramedullary nailing because of intra- or peri- articular fracture or smaller caliber of tibia. The MIPO techniques are by way of closed reduction before the operation and limited operative exposure without opening the fracture site. All cases went to union after one year of the operation. The evaluations of subjective feeling and joint motion both showed excellent recoveries. Three patients complained of skin tension because the plate was placed on the medial side of the tibia shaft. However, these patients were satisfied with their physical conditions. One case didn't submit the initial non-weight bearing and had implant failure. Furthermore, she acted against medical advice to receive informal management and got infection as a result. Through one time of debridement, the fracture union was attained after later open reduction and plating.

In conclusion, MIPO for these complicated tibia fractures has good bone union result, less operation time, less blood loss, shorter hospital stay, and no infection occurrence, compared with conventional open plating.

Key words: minimally invasive, tibia, osteosynthesis

Introduction

Complicated tibia fracture is usually caused by high energy impaction. The damage does not only involve the bone but soft tissue. Therefore, initial neurovascular examination and soft tissue condition should be meticulously scrutinized.[1]

The early stabilization of the bone and soft tissue will prevent advanced soft tissue injury if possible. [2] As a result, the best techniques, either closed or open reduction, and, the appropriate osteosynthesis, either plating or intra-medullary nailing, are important to provide the stability and less advanced soft tissue injury. That the conventional closed nailing will make less soft tissue injury is no doubt and has the satisfactory results.[3] However, the closed nailing is inappropriate in some special cases, such as intra- or peri- artricular fractures (Figure1) or smaller caliber of bone marrow which was not indicated for intramedullary nailing (Figure2). In such conditions, closed plating is also able to provide the alternative stabilization and less soft tissue trauma, rather than the open method which leads to a variety of complications like delayed union or non-union and higher infection rate. This is due to achieve anatomic reduction, wide surgical exposure is necessary and the fracture fragments are stripped off the soft tissue attachments. [4-6] In this study, I am looking forward to evaluating the outcome of the complicated tibia fractures treated with closed plating instead of open plating.

*Correspondence to: Dr. Wang Shu-Ang, Department of Orthopaedic, Tungs' Taichung MetroHarbor Hospital. No.699, Sec. 1, Chungchi Rd., Wuchi Dist., Taichung City 43503, Taiwan (R.O.C.)

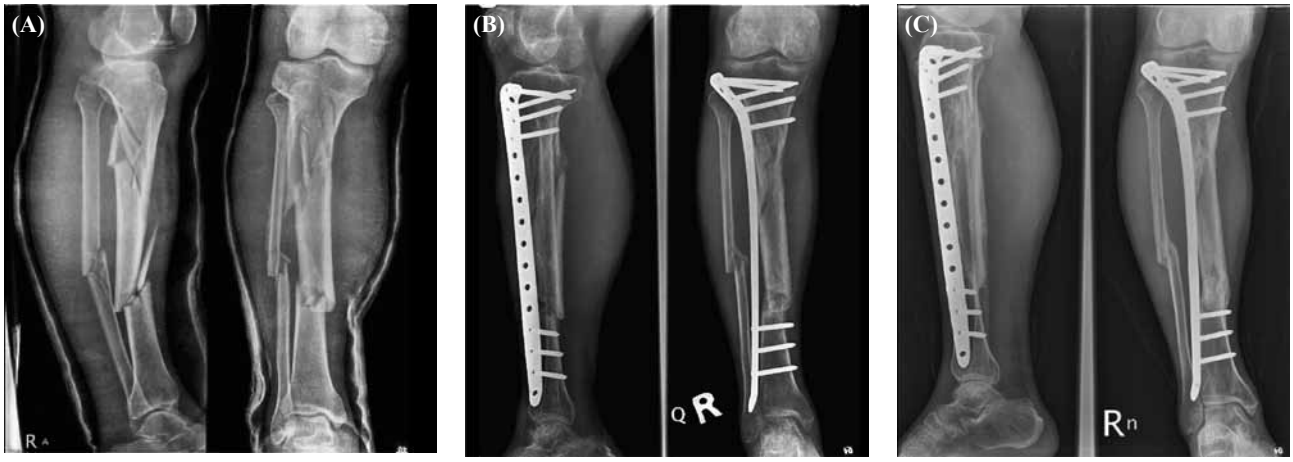

Fig. 1 A 48 years old male, suffered from a road traffic accident, had intra-articular and multi-fragmentary fractures of his right tibia. Initially, closed reduction with long leg cast was managed but loss of alignment at follow-up x-rays film (A). In 8 days after the injury, closed plating was done (B). Eight months after the operation, there was bony union (C).

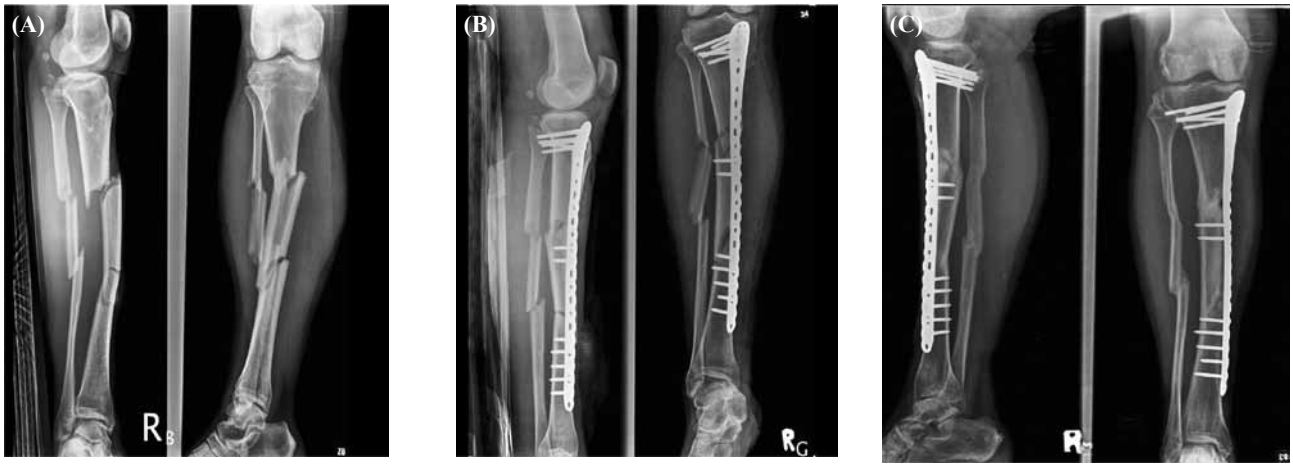

Fig. 2 A 42 years-old female, suffered from a motorcycle accident, has multi-fragmentary fractures of right tibia (A). The tibia canal was too small to use intra-medullary nail, thus closed plating was instead. (B). Eight months after the operation, there was bony union (C).

Materials and Methods

Eleven cases of multi-fragmentary fractures of the tibia admitted to Tung's Taichung MetroHarbor Hospital between March 2008 and February 2010 were studied/recruited. Duration of follow-up ranged from 12 months to 24 months. Only closed or grade I open fractures were included.

All cases received first aid in casualty with thorough/full examination to detect associated injuries. Patients were subjected to routine pre-anesthetic investigations and additional investigations when indicated. Standard anterior-posterior (A-P) and lateral radiographs were taken.

Calcaneal pin traction or ankle traction was given on the fracture table. The A-P and lateral X-rays were evaluated for the whole alignment and the likely length of the plate after closed reduction by the fluoroscope before the operation.

NB past tense? Surgery was performed under the regional anesthesia. A small incision is taken on one end of the fractured area without disturbing the soft tissue envelope of the fractured fragments. The incision is deepen down to the bone, where is far from the fracture site, with raising the intact periosteum. A sub-periosteal tract is made along with the

surface of the bone where the plate is going to be applied and extended across the fracture site to the other side. The tract is done with the plate itself, used as the periosteal elevator. The plate used depended on the anatomy and location of the fracture. An anatomic locking plate is used for proximal metaphyseal and diaphyseo-metaphyseal junctional fractures. A Locking Compression Plate (LCP) is used for diaphyseal fractures. Once the tract is made, an appropriate length plate is selected so that at least 4 to 5 holes are able to be fixed on either side. The plate is first fixed by a compression screw rather than locking screw to make the plate closer the bone over the one end of the fractured site. Then, the second hole is fixed in the locking hole, thus leading to have two holes fixation in the one end of the fractured site. The same procedure is done over the other side as the above under fluoroscope with A-P and lateral view. Confirming the acceptable alignment of the reduction after there are two screws fixation on each end of the fracture site, the rest of the screws are fixed with percutaneous. Use of tourniquet is indispensible for less operative bleeding and clear surgical field.

Contouring of the fixation plate is sometime necessary when the plating involving the proximal or distal end of the tibia fracture. The plate can be placed on either the medial or the lateral aspects of the tibia in the proximal or distal end depending on the fracture geometry.

Postoperatively, the limb is elevated with free range of motion of knee and ankle joint started as early as possible. Non-weight bearing with aids is mandatory in the initial healing time. Full weight bearing is permitted only with good clinical and radiological evidence of progressive fracture healing, usually about 4 months later. In multiply injured patients the protocol was adapted to treat the associated injuries. Long term results were evaluated by pain score, subjective feeling, joint motion and radiograph.[7]

Results

A total number of 11 patients were operated upon. Mean age of patients was 42 years (Table 1). The youngest case was a 28 years old male and the oldest was a 58 years old male. All cases were caused by high velocity impact. There were 7 closed fractures while remaining four were grade I open (Gustilo Anderson classification). Three cases have both tibia plateau and diaphyseal fractures. Two cases have proximal associated with diaphyseal fractures. Eleven cases have diaphyseal fractures (Table 2). Four cases had associated with other injury resulting from the same trauma. The injuries noted were fracture of femur, ribs and forearm. There were two cases with head injury.

The average surgical interval was 2 days in the period of 1- 10 days after the occurrence of injury (Table 3). The average operative time was 72 minutes. Routinely, negative pressured drainage was used after the operation/post-operatively. The average blood loss was 30 c.c. All fractures went to union in/during/towards the end of one year follow-up. Most of them showed union between 14 and 18 weeks (Table 4). Average time taken for full weight bearing was 16 weeks. Average hospitalization/hospital stay was 5 days. There was one complication occurred

Table 1. Age and sex distribution.

Age and sex distribution of cases		
Age	Male	Female
21-30	1	0
31-40	3	1
41-50	3	1
51-60	2	0

Table 2. The distribution of the fractured site and pattern by Muller AO classification.

(1) Proximal tibia (41)

Group and subgroup	A3	B1
number	2	3

(2) Diaphysis (42) ; There were two cases whose tibia canal was too small to use intra-meduallary nailing.

Group and subgroup	A2	A3	B3	C2	C3
Number	2	2	2	3	2

Table 3. The surgical intervals.

The interval between injury and surgery	Number of cases
1 day	8 patients
2 days	2 patients
10 days	1 patient

in about 8 weeks after the operation. The patient didn't obey the order to initial non-weight bearing, thus resulted in implant failure. Furthermore, she asked for bone setter with herb drug application which made an infection (Figure 3). However, through thorough debridement and later open reduction with plating were done. Lastly, fracture healing was seen in 24 weeks.

Table 4. The average bone union after the operation.

Period in weeks	Number of cases
14 - 18	9
19 - 24	2

The results were evaluated by the assessments of pain, subjective feeling, joint movement of the knee. The scales of pain are/showed excellent results for pain free, good results for local tenderness, fair results for motion pain and poor results for intractable pain. The assessments of joint motion are/were excellent for full range of motion, good for above 90 degrees of range of motion, 30 to 90 degrees of range of motion for fair results and poor results for below

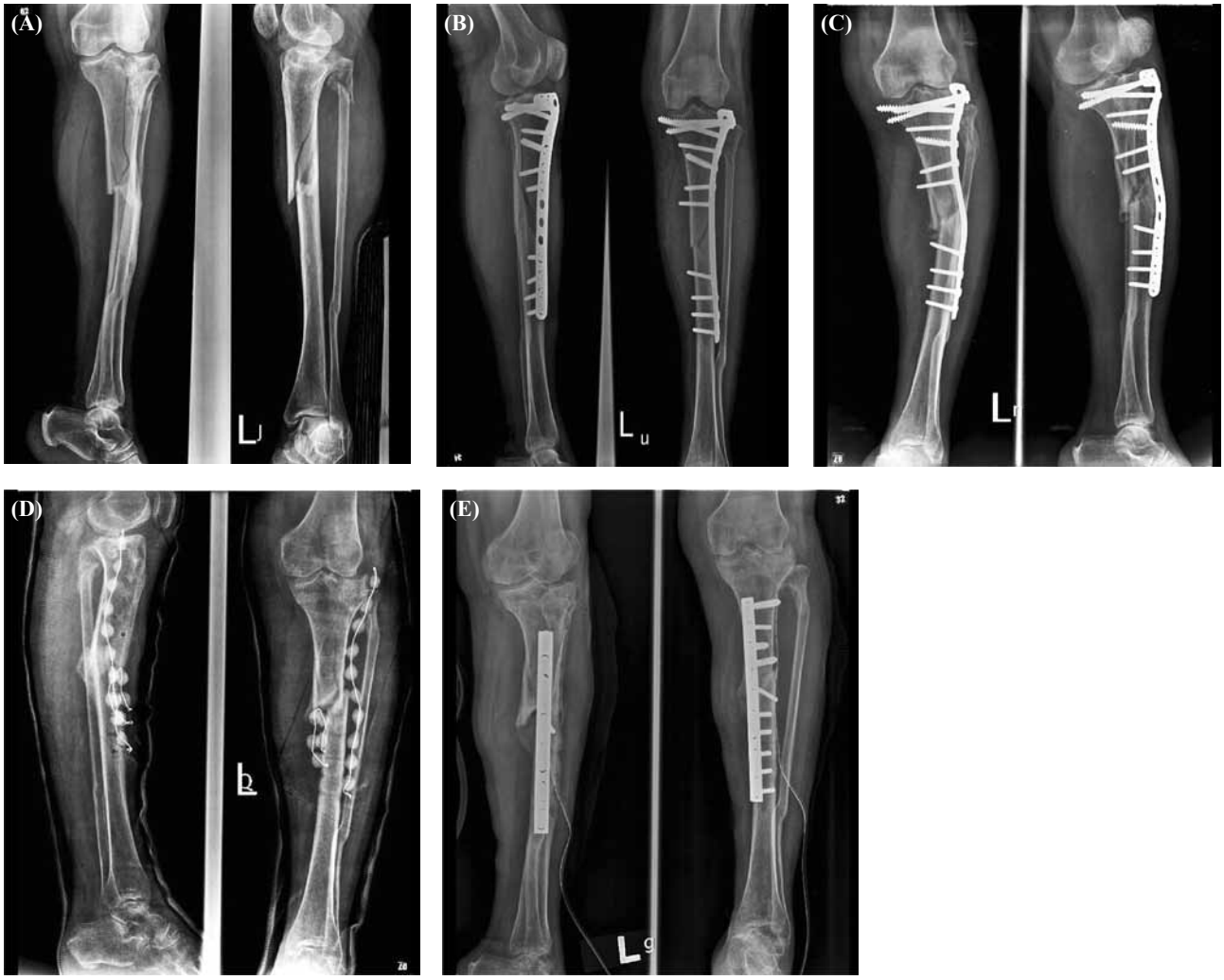

Fig. 3 A 38-years-old female with motor vehicle accident had intra-articular and multi-fragmentary fractures of her left tibia (A). MIPO was done at the same day of the injury (B). However, the patient didn't obey the order of non-weight bearing. The plate at the proximal tibia fracture site was deformed but the inter-condylar fracture showed healed, at 2 months after the operation (C). Initially, she called for bone setter and had herb drug management which contributed to the subsequent infection. Then, she was re-admitted with the treatment of debridement and antibiotic-impregnated bead implantation (D). Lastly, open reduction with plate was done after the wound became stable and she was satisfied with her physical conditions (E).

30 degrees of range of motion. All had excellent to good outcome (Table 5). Most patients complained of pain because the implant placed over the medial side of the tibia where the shin skin tension would be increased.

Table 5. The evaluation of pain scale, subjective feeling, knee and ankle joint movement

	Pain scale	Subjective feeling	Range of motioin
Excellent	8	11	11
Good	3	0	0
Fair	0	0	0
Poor	0	0	0

Discussion

The management of complicated tibia fractures has been treated by conservative methods earlier in the form of casting or traction but poor results with regards to joint function and prolonged hospitalization.[8-9] Modern orthopedic technology, internal fixation with osteosynthesis is able to provide the good result.[10] However, conventional plating will make an irrespective of the soft tissue attachments also led to a lot of problems like non union, delayed union, increasing the infection risk, etc. As a result, closed interlocking nailing is an established method in the treatment of comminuted diaphyseal fractures with less soft tissue injury. Extended indications also cover the proximal and distal metaphyseal fragments. As to minimally invasive plate osteosyntheses is an alternative treatment in some inappropriate indications for intra-medullary nailing.

In my study, all fractures went to union. The patient's subjective feeling and range of motion of their knee or ankle joints both showed excellent recoveries. Three patients complained of skin tension which was caused by implantation over the medial side of tibia shaft. Although one patient disobeyed the order and had early weight bearing which made implant failure, she still had excellent scale over pain, subjective feeling and range of motion after further treatment.

Helfet et al in their study of distal tibial fractures and Radziejowski et al in their 22 cases of proximal tibial fractures treated with MIPO both have also shown good results with union.[11-12] On the contrary, Johner and Wruhs in their study reported a significant increase in complications with the treatment by ways of open reduction and conventional internal fixation. [13] Jensen et al in the treatment of tibia fracture by open AO compression plate, they had 8% of non-union rate.[14]

The successful MIPO procedure was indispensible to have an acceptable alignment of the fracture site which was obtained on the fracture table before the operation. Closed plating (MIPO) was the idea of bridging the fracture sites. Locking plate was the preferable implant to be chosen for diaphyseal fracture. Because locking plate won't distract the curved bone contour after a good closed reduction. The anatomic locking plate was the best choice for the intra-articular, or proximal tibia fractures.

In conclusion, the advantages of the treatment with MIPO are less soft tissue dissection, less infection risk, less blood loss, shorter hospital stay and good fracture healing. The disadvantage of MIPO is easier to have implant failure. Because there will be probable several holes which couldn't be screwed on the comminuted fracture site, thus leading to increase the possibility of implant failure from these weak points. Therefore, absolute non-weight bearing after the operation is mandatory until callus formation occurs. Or we can design a new hole-less solid plate in the middle part of the plate.

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微創鋼板固定手術治療複雜性脛骨骨折

王叔昂*

童綜合醫療社團法人童綜合醫院　骨科部

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摘要

比較利用微創鋼板固定手術與其他傳統開放式鋼板固定手術治療複雜性脛骨骨折的差異。本報告病人因為骨折處接近關節處或因為骨髓腔較小並不適用骨髓內釘固定，而採用不破壞到骨折處軟體組織的小傷口鋼板固定。這種手術方法，需在手術前先做好可接受的骨折處復位。本報告中所有病人的骨折處，在一年後均癒合。評估項目中所有病人的主觀感覺及膝關節活動都達到滿意程度。在疼痛的評估項目中，有三個病人因鋼板置放在脛骨內側造成該處皮膚緊繃而不舒適外，其他影響並不大。在本報告中，一個病人術後因不遵從使用輔助器的指示，造成鋼板變型，爾後又接受傳統民俗療法，而致感染。不過經過一次清創手術，待傷口穩定後重做鋼板固定手術，最後骨折處癒合。

微創鋼板固定手術針對複雜性脛骨骨折有手術時間短、手術中出血少、感染機會少、住院時間短及良好的骨折癒合率的優點。

關鍵詞：微創鋼板固定手術、骨髓內釘、複雜性脛骨骨折

* 通訊作者：王叔昂醫師　童綜合醫療社團法人童綜合醫院　骨科部　43503 台中市梧棲區中棲路一段 699 號

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Case Report

Takotsubo Cardiomyopathy Syndrome or Neurogenic Stunned Myocardium Induced by Acute Subarachnoid Hemorrhage: A Case Report and Discussion

Yin-Yee Chu[1,*], Chun-Yi Li[2]

[1]*Depratment of Internal Medicine, Critical Care Division, Tungs' Taichung Metroharbor Hospital*
[2]*Department of Internal Medicine, Cardiology Division, Chief of Corornary Care Unit, Tungs' Taichung Metroharbor Hospital*

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Abstract

A case of a 59-year-old female was admitted to our hospital due to suspected acute myocardial infarction with cardiogenic shock. Her serum levels of cardiac enzymes were slightly elevated and electrocardiography revealed inferior wall ST-segment elevations. Significant coronary artery stenosis was excluded by coronary angiography. A left ventriculogram revealed apical ballooning syndrome or Takotsubo cardiomyopathy. Brain Computed Tomography [CT] scan then disclosed subarachnoid hemorrhage. This rare cardiomyopathy syndrome associated with intracranial hemorrhage was addressed.

Key words: Takotsubo cardiomyopathy, subarachnoid hemorrhage, Acute myocardial infarction, intracranial hemorrhage.

Introduction

The relationship between the heart and the brain is complex and integral in the maintenance of normal cardiovascular function [1]. Certain pathological conditions can interfere with the normal brain-heart regulatory mechanisms and result in impaired cardiovascular function [1].

Cardiac abnormalities may be associated with subarachnoid hemorrhage [SAH]. ECG changes are seen in 50 to 100% of patients. Troponin elevation is seen in 20% to 40%, and regional wall motion abnormalities (RWMA) in 10% of patients [4]. Ampulla {takotsubo} cardiomyopathy was named because the typical findings of left ventriculography, characterized by hypokinesia around the apical area and hyperkinesia at the basal area [5], resemble a "fishing pot with a narrow neck and wide base that is used to trap octopus" [3]. We present a case of Takotsubo cardiomyopathy in a patient with subarachnoid hemorrhage.

Case History

A 59 year old woman with no cardiac related history presented to our Emergency Department with collapse in a public place. Prior to this event she had no complain of severe headache, nausea, vomiting, neck pain, photophobia nor localizing neurologic signs. On arrival, her consciousness was in comatose state with Glasgow Coma Scale of 3 [E1M1V1]. On examination, blood pressure was immeasurable, heart rate was 75 beats per minute, respiratory rate was 6 per minute. Bilateral pupils size were 5/5mm with no light reflexes detected. She was intubated tracheally. An initial electrocardiogram revealed ST segment elevation of inferior leads (II, III, aVF) (Figure

*Correspondence to: Dr. Yin-Yee Chu, Depratment of Internal Medicine, Critical Care Division, Tungs' Taichung Metroharbor Hospital,

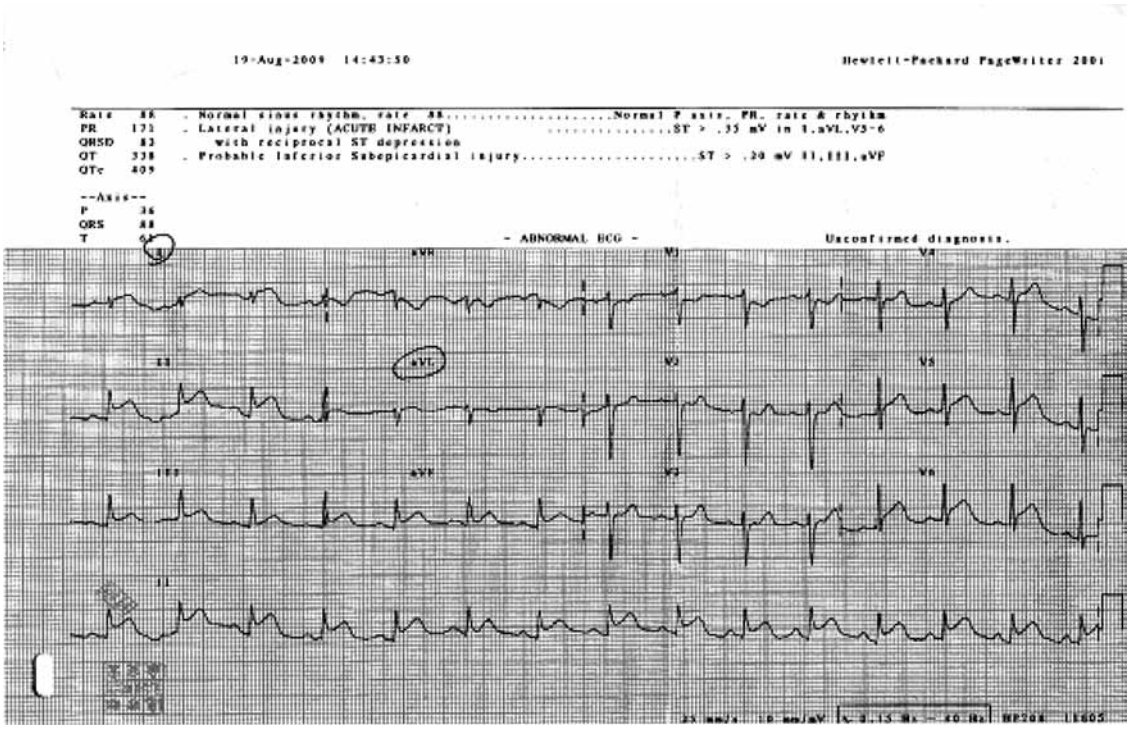

Fig. 1 EKG showed ST segment elevation on leads II, III and aVF.

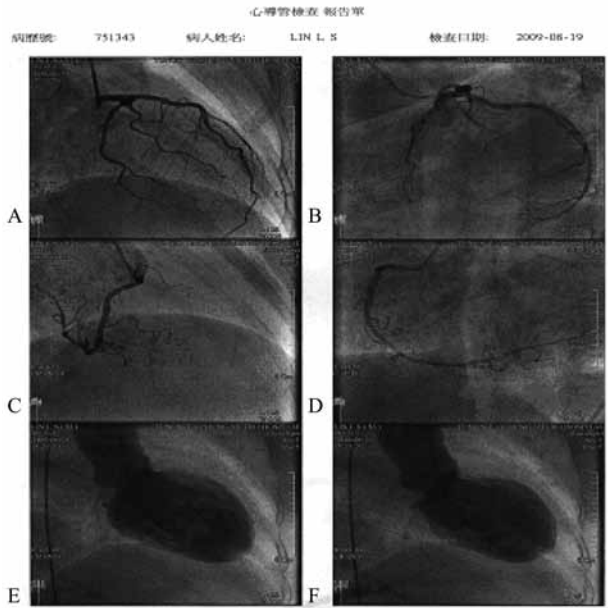

Fig. 2 Coronary angiogram[A,B,C,D] showed insignificant coronary artery disease. Left ventriculogram [E,F]. On "F" picture showed akinesia over mid to apical anterior, lateral, posterior and inferior wall with severe left ventricular systolic dysfunction, compatible with Takotsubo cardiomyopathy or apical ballooning syndrome.

1). Initial cardiac enzymes were within normal limits (CPK:128 u/L [20-134 u/L; CK-MB: 1.1 ng/ml [<18 ng/ml] and Troponin-I 0.09 ng/ml [<0.8 ng/ml]]. Transthoracic echocardiogram at bedside showed severe left ventricular dysfunction with an estimated left ventricular ejection fraction of 20%-30%. She was diagnosed initially as acute myocardial infarction with cardiogenic shock. She received coronary artery angiogram but showed insignificant coronary artery disease (Figure 2). However, left ventriculography showed akinesia over middle to apical anterior, lateral, posterior and inferior wall with severe left ventricular systolic dysfunction, compatible with Takotsubo cardiomyopathy or apical ballooning syndrome (Figure 2). Intra-Aortic Balloon Pumping was inserted for cardiac support. Glascow Coma scale improved to E3M4VE post catheterization and she was transferred to coronary care unit for further management. On day 2 post-admission, alteration of conscious level was noted again (decreased GCS from E3M4VE to E1M1VE). Brain Computed Tomography scan was performed and revealed diffuse subarachnoid hemorrhage with rupture to ventricles (Figure 3,

4). The patient then deteriorates rapidly and unfortunately died on the 4th day since admission.

Discussion

Takotsubo cardiomyopathy [TC] has been recently been acknowledged by the American College of Cardiology and American Heart Association as a unique form of reversible cardiomyopathy[1]. The presentation of TC is usually similar to that of an acute coronary syndrome [ACS] with symptoms primarily consisting of ischemia-like chest pain and ischemia-like ECG changes in most patients[1]. However cardiogenic shock, syncope , collapse and cardiac arrest were also reported in the literature[4-10].

Formal diagnostic criteria have not yet been established but researchers at the Mayo Clinic proposed diagnostic criteria in 2004 which have been modified recently and has been put forth requiring the following: (A) transient LV wall motion abnormalities involving the apical and/or midventricular myocardial segments with wall motion abnormalities extending beyond a single epicardial coronary distribution; (B) absence of obstructive epicardial CAD [coronary artery disease] or angiographic evidence of acute plaque rupture that could be responsible for the observed wall motion abnormality; and (C) new ECG abnormalities such as transient ST-segment elevation and/or diffuse T-wave inversions or troponin elevation[1-2] and (D) the absence of pheochromocytoma and myocarditis[2].

The precise pathophysiology of TC is unknown. It has been suggested that transient multivessel epicardial spasm may be responsible [1-3]. Other have suggested that a dynamic intraventricular pressure gradient due to midseptal hypertrophy[1] and enhanced catecholamine mediated cardiotoxicity or "cardiac stunning" may be the inciting event for TC[1-2]. Another hypothesis is that of microvascular ischemia in the absence of obstructive epicardial coronary artery disease [1-3].

Catecholamine mediated cardiotoxicity is likely to be an important component of the pathophysiology of TC because the syndrome commonly occurs proximate to an acute emotional and/or physical stress [1]. [See Figure 5]

Another common feature of TC is female predisposition [1], especially postmenopausal and elderly

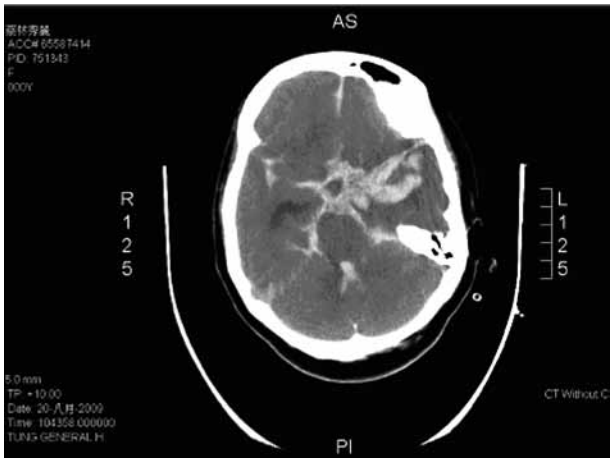

Fig. 3. CT scan showed massive subarachnoid hemorrhage on left sylvian fissure.

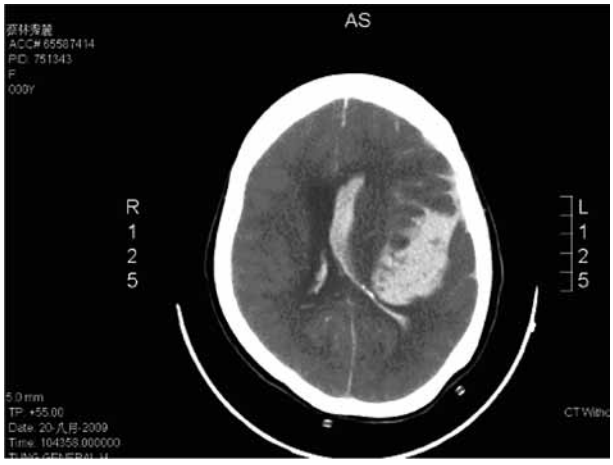

Fig. 4. Rupture of intracranial aneurysm(probable left Middle Cerebral Artery) into ventricle is depicted.

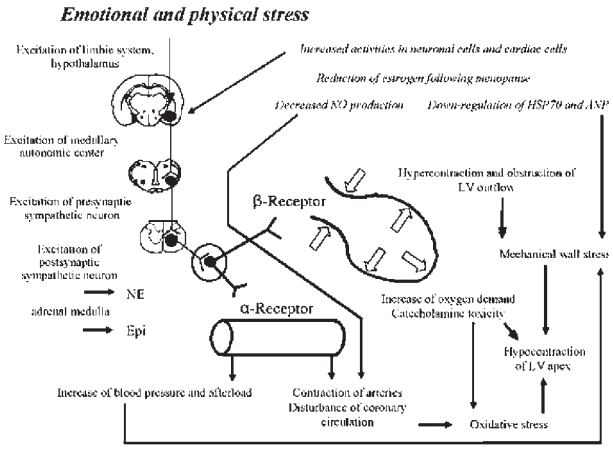

Fig. 5 Possible underlying mechanisms of classic takotsubo cardiomyopathy.

women. Although the cause is still unknown, but it may be related to gender difference in myocardial sensitivity to catecholamine toxicity and subsequent intramyocyte calcium overload [1].

The other reason for the unique, non-coronary distribution of wall motion abnormalities in TC is also unknown but may be related to regional differences in myocardial autonomic innervation and myocardial adrenergic stimulation [1].

In our case, brain CT scan or angiography was not done at emergency room because the patient did not manifest the typical presentations of Subarachnoid Hemorrhage [SAH] like severe "thunderclap headache with a rapid onset of nausea, vomiting, neck pain, photophobia nor localizing neurologic signs. The only presentation was lowered level of consciousness. In addition, the EKG showed acute inferior wall myocardial infarction. In concordance to the guideline set by the American Heart Association [AHA] and American College of Cardiology [ACC], the treatment for this is emergency percutaneous coronary intervention which is critically time dependent. We believed this patient's SAH was due to rupture of an intracranial aneurysm as seen in her brain CT scan and not directly due to anticoagulants nor antiplatelet agents. However the use of these drugs could aggravate the condition of SAH.

Our case, as well as the others reported previously, supports the diagnosis of TC in patients with SAH who fulfilled the clinical and imaging description of this syndrome. This condition is typically associated with sudden emotional or physical stress accompanied by catecholamine surge. This hypersympathetic state can be seen in other entities including SAH.

This case highlights the importance of cardiac insults that can be induced by neurological injury. Treatment for TC is essentially supportive as changes are usually reversible. Prognosis is generally favorable provided with the patients survive the initial severe insult without complications.

As awareness and recognition of this complex cardiomyopathy syndrome increases, a deeper understanding of this underlying disease and its pathogenesis will develop a treatment guidance and prevention strategies.

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急性蜘蛛膜下腔出血導致章魚壺心肌症或神經性心肌冬眠狀態：個案報告與討論

朱賢義[1] 李俊毅[2]

童綜合醫療社團法人童綜合醫院 重症內科[1] 心臟內科[2]

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摘要

一名59歲女性被收住院因懷疑急性心肌梗塞併心因性休克。她的血清心肌酵素檢驗呈現輕度的升高，心電圖顯示下壁ST段抬高。冠狀動脈狹窄被排除。左心室造影發現壺腹形心肌病變或章魚壺心肌症。頭部電腦斷層檢查顯示蜘蛛膜下腔出血。強調這種罕見的心肌病症候群跟顱內出血有相關性。

關鍵詞：章魚壺心肌症、蜘蛛膜下腔出血、急性心肌梗塞、顱內出血

*通訊作者：朱賢義醫師 童綜合醫療社團法人童綜合醫院 重症內科 43503台中市梧棲區中棲路一段699號

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Case Report

鼻腔鼻竇黏膜惡性黑色素瘤之病例報告

甯中柱[1]　李佳茹[2]　蔡青劭[2,3]*

童綜合醫療社團法人童綜合醫院　皮膚科[1]　醫研部[2]　耳鼻喉科[3]

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摘要

惡性黑色素瘤根據發生的位置可分為皮膚性及黏膜性，雖然鼻腔黏膜惡性黑色素瘤是最常發生的頭頸部黏膜黑色素瘤，但仍是罕見，只佔全部惡性黑色素瘤 0.3-2%，佔頭頸部黑色素瘤 4%。本院 2008 年 10 月經歷一名 69 歲男性，主訴鼻流血持續 1 個月、鼻涕倒流及右眼瞼腫脹，經病理報告及免疫組織化學報告診斷為鼻腔鼻竇惡性黑色素瘤，電腦斷層掃描、核磁共振影像及正子斷層造影顯示腫瘤已侵犯至顱底，且有骨轉移，病人接受廣泛手術切除病灶，術後採免疫治療，治療 1 次後病人因高燒未再持續治療，於隔年 2 月過世。鼻腔黏膜惡性黑色素瘤因無特殊症狀且腫瘤位置隱密，容易延誤診斷，以致預後不佳，所以當發現鼻流血、鼻塞及鼻內有黑色病變時，應接受鼻內視鏡、病理及電腦斷層掃描檢查，以期早期發現，予以治療，減少局部復發或遠端轉移，以提高存活率。

關鍵字：惡性黑色素瘤、鼻腔鼻竇黏膜惡性黑色素瘤、黑色素瘤

前　言

黑色素細胞（melanocytes）是一種源自神經脊的樹狀細胞，當惡化時即形成惡性黑色素瘤（malignant melanoma），根據發生的位置可分爲皮膚性（cutaneous）及黏膜性（mucosal），約有 15-20% 發生在頭頸部 [1]。頭頸部惡性黑色素瘤有超過 80% 是發生在皮膚，其次是眼睛及黏膜。最常引起頭頸部黏膜黑色素瘤是在上呼吸消化道約有 0.5-3%，其中又以鼻腔與口腔最常見 [1-2]。雖然鼻腔黏膜惡性黑色素瘤（nasal cavity mucosal malignant melanoma）是最常發生的頭頸部黏膜黑色素瘤，但仍是罕見只佔全部惡性黑色素瘤 0.3-2%[3]，佔頭頸部黑色素瘤 4%[4]。黏膜黑色素瘤的預後及治療結果都比皮膚性黑色素瘤（cutaneous melanoma）差 [2]。根據 Patel 等人 [5] 以多變量分析（multivariate analysis）發現不利於存活率的原因包括臨床分期晚期、原發腫瘤厚度超過 5 公分、出現血管侵犯、局部復發及遠端轉移（distant metastases）。在國內有關鼻腔鼻竇黏膜黑色素瘤的相關文獻並不多，特提出報告，並加以討論。

* 通訊作者：蔡青劭醫師　童綜合醫療社團法人童綜合醫院　耳鼻喉科　43503 臺中市梧棲區中棲路一段 699 號

病例報告

患者爲一名 69 歲的男性，於 2008 年 10 月至本院門診，主訴鼻子流鼻血持續 1 個月、鼻涕倒流及右眼瞼腫脹。他曾至診所接受治療，但流鼻血現象依舊沒有改善，診所醫師建議他至大醫院接受進一步檢查，於是到本院耳鼻喉科就診。鼻咽鏡檢查（圖 1）發現右側鼻腔及篩竇有一腫瘤組織，有接觸出血現象（touch bleeding）。核磁共振影像顯示（圖 2），腫瘤穿過篩骨進入右眼窩，並侵犯至顱底。電腦斷層掃描報告（圖 3）腫瘤已侵犯至顱底，且穿過中線至左側鼻腔鼻竇，術中也確切於左側鼻腔鼻竇發現腫瘤。正子斷層造影則顯示（圖 4）腫瘤已從右鼻腔延伸至顱內，並且轉移至胸椎、右薦骨及左側股骨骨髓腔。X 光片未發現侵犯至肺部。病理切片檢查發現，組織爲小結瘤、小泡狀之腫瘤細胞，有圓形至橢圓形的核與大而突出的核仁，及大量的黑色素；免疫組織化學染色報告，HMB-45（圖

5）、S-100 protein 及 vimentin（圖 6）爲陽性反應，CK（cytokeratin）爲陰性，經診斷爲鼻腔鼻竇惡性黑色素瘤。根據臨床分期爲 T4bN0M1，stage IV B。經會診神經外科醫師，因侵犯範圍大，故建議安排病人接受保守手術切除病灶，採用 Weber-Ferguson 方式開放性切至病灶，施行鼻腔及鼻竇的腫瘤切除。唯顱底及右眼窩的腫瘤因侵犯範圍不易清除，且併發症多，故僅施行 tumor debulking，術後無腦脊髓液滲漏、失明或出血等症狀。術前有解釋術後尚需接受放射線治療，但病人選擇接受免疫療法。根據 NCCN 臨床治療指引以 interleukin-2 治療，治療 1 次後病人因高燒未再持續治療，於隔年 2 月過世。

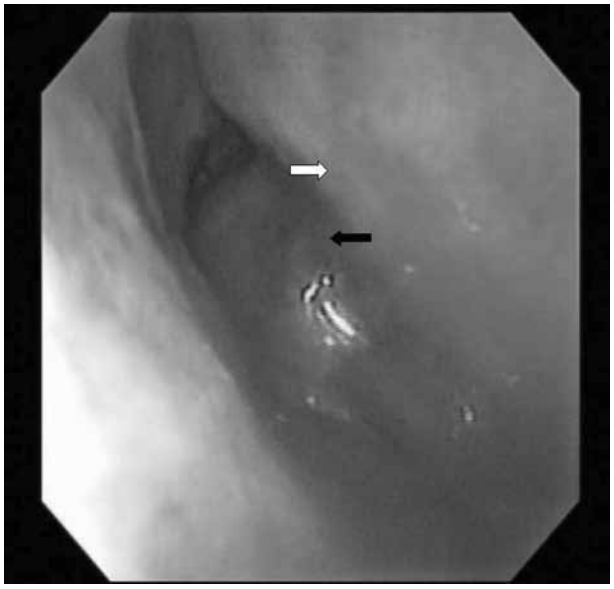

圖 1　軟式內視鏡檢查顯示，右側鼻腔有一黑色腫瘤組織（黑色箭頭），白色箭頭爲鼻中隔。

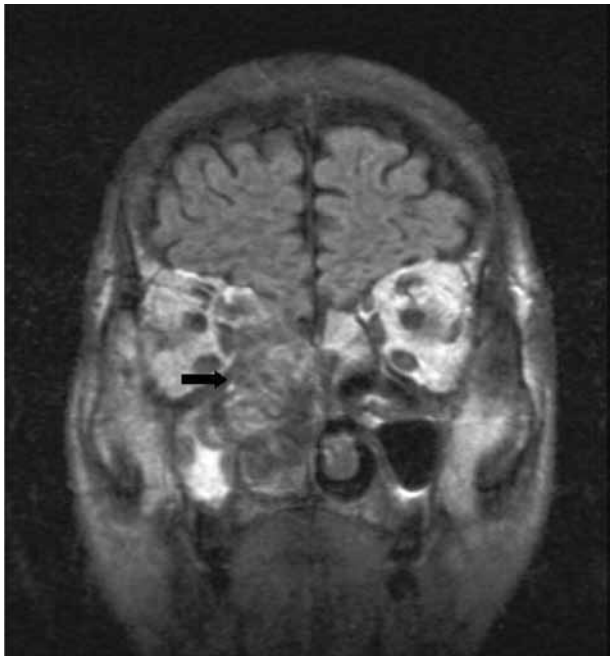

圖 2　核磁共振影像顯示，腫瘤（箭頭所指處）穿過篩骨進入右眼窩，並侵犯至顱底。

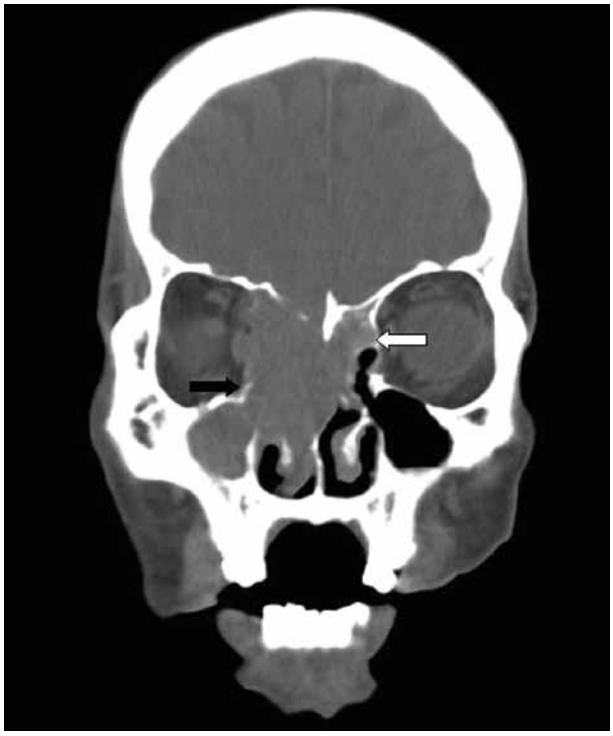

圖 3　電腦斷層掃描顯示，在 T1-weighted 影像可觀察到腫瘤（黑色箭頭所指處）已侵犯至顱底，且穿過中線至左側鼻腔鼻竇（白色箭頭所指處）。

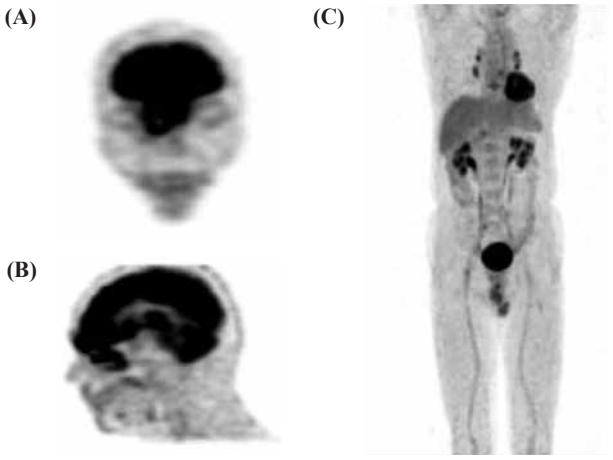

圖 4　正子斷層造影顯示，腫瘤已從右鼻腔延伸至顱內，並且轉移至胸椎、右薦骨及左側股骨骨髓腔。A、B 圖爲頭部影像，C 圖爲全身影像。

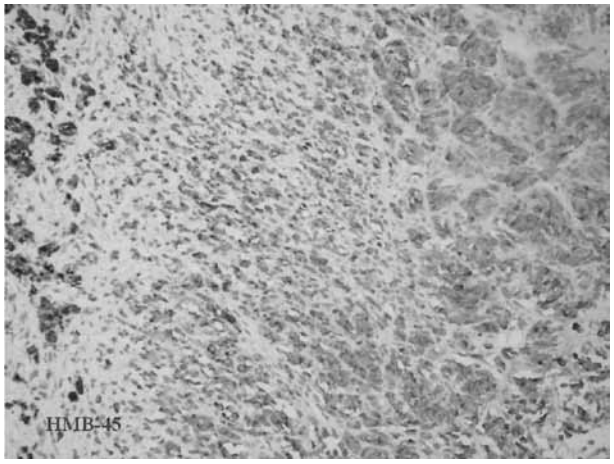

圖 5　免疫組織化學染色，HMB-45 呈陽性反應，（IHC 染色，200×）。

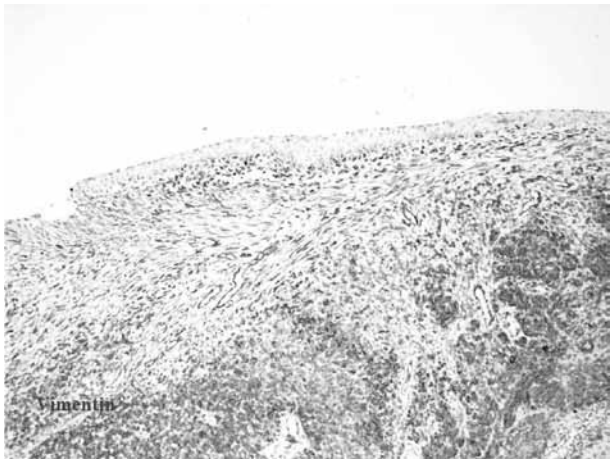

圖 6　免疫組織化學染色，Vimentin 呈陽性反應，（IHC 染色，100×）。

討　論

黏膜黑色素瘤通常好發於老年人，年齡約在 50-80 歲，而皮膚性黑色素瘤好發年齡較輕，約在 50-65 歲 [6]。黏膜黑色素瘤男女性的發生率相當，然而也有報告指出男性的發生率稍高 [2]；皮膚性黑色素瘤則以男性發生率較高 [3]。鼻腔黏膜黑色素瘤最常見的位置於鼻中隔（41%），中鼻甲（29%），下鼻甲（23%），外側鼻腔壁（7%），及鼻底（1%），這與黑色素細胞的分佈密度有關 [7]；而臨床症狀以鼻流血（76%）與鼻塞（47%）最常見，因無特殊症狀且腫瘤位置隱密，所以容易延誤診斷 [2,7-8]；常見轉移的位置是肺臟（33%）及腦部（14%）[5]。

黏膜黑色素瘤的診斷主要是利用免疫組織化學染色，因在光學顯微鏡下的特徵很容易誤診爲淋巴瘤，橫紋肌肉瘤，漿細胞瘤，嗅神經母細胞瘤，與低分化癌 [7]。鼻腔黏膜惡性黑色素瘤的免疫組織染色標記與皮膚性黑色素瘤是相同，如 S-100、HMB-45、vimentin、cytokeratin、Melan-A 等 [4]。S-100 雖然並非黑色素瘤的特定標記，但是一般不表現在非神經源的上皮細胞，因此可用來區別上皮癌與黑色素瘤，陽性表示爲黑色素瘤。HMB-45 蛋白是一種黑色素的特殊蛋白，幾乎在所有原發及轉移黑色素瘤都是陽性，包括無黑色素黑色素瘤（amelanotic melanoma）、梭形細胞黑色素瘤（spindle cell melanoma）及肢端雀斑黑色素瘤（acral lentiginous melanoma）[9]。根據文獻指出，S-100 在黏膜黑色素瘤敏感度較低，而 HMB-45 則有較高特異性 [2,9-10]。

典型黏膜黑色素瘤的電腦斷層掃描可顯示軟骨組織是否侵犯到周圍骨頭，而核磁共振影像則有幫助於評估鼻腔腫瘤的範圍，尤其是顱底的轉移 [4,11]。多數的專家建議可利用正子斷層造影評估局部和遠端轉移，但對於診斷其他常見的鼻部非黑色素瘤與轉移性皮膚黑色素瘤則需仰賴更多的檢查 [2,10]。廣泛的外科手術切除是主要的治療，可提供頭頸部惡性黑色素瘤最好的治療與局部控制 [11-12]。放射性治療是最常見的輔助治療，但因黑色素瘤細胞具有自行修復的能力，所以治療效果不佳 [8,10]；然而，事實上術後放射性治療或化學性治療，因在不同研究有不相同的結果，故在頭頸部黏膜黑色素瘤的角色未能明確定義 [4,8]。而在皮膚性黑色素瘤的治療有潛力的免疫治療，如 interferon-2α，也有報告運用於黏膜黑色素瘤，但只對部份病人有效 [4,7,13]。因此，如何提升治療成效將是未來的研究重點。

黏膜黑色素瘤是個預後不好的疾病，局部復發是治療失敗的主要原因，約有 29-79.4%[2,4]，5 年存活率只有 17.1-44%，其中鼻腔（nasal cavity）預後較佳，5 年存活率爲 15-30%，而口腔黑色素瘤 5 年存活率爲 12.3%，鼻竇黏膜黑色素瘤（sinonasal mucosal melanoma）5 年存活率爲 0-5%[2,4]；若有遠端轉移平均存活時間約 6-12 個月 [2]。相較之下，皮膚性黑素瘤 5 年存活率較高約有 88%[3]。本病例爲臨床分期第四期且已侵犯至顱底，並有骨轉移，雖接受手術治療及免疫治療，但對免疫治療產生排斥，故短短 5 個月內即死亡。因此，當發現鼻流血、鼻塞及鼻內有黑色病變時，應接受鼻內視鏡、病理及電腦斷層掃描檢查，以期早期發現，予以治療，減少局部復發或遠端轉移，以提高存活率 [4,9,11]。

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Sinonasal Mucosal Malignant Melanoma- A Case Report

Chung-Chu Ning[1], Chia-Ru Li[2], Stella Chin-Shaw Tsai[2,3]*

[1]*Department of Dermatology,* [2]*Department of Medical Research,*
[3]*Department of Otolaryngology, Tungs' Taichung MetroHarbor Hospital*

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Abstract

Malignant melanoma can be classified according to the site of the lesion into cutaneous and mucosa. Although nasal cavity mucosal malignant melanoma is the most common head and neck mucosal melanoma, it is still rare and accounting for only 0.3- 2.0% of all malignant melanoma, and 4% of all head and neck melanoma. We report a case of a 69 year-old man presented to our hospital in October, 2008 with complaints of epistaxis for 1 month, nasal obstruction and swelling of the right eyelid. Biopsy was taken/performed and the subsequent pathology reports and immunohistochemistry studies confirmed the diagnosis of sinonasal malignant melanoma. Computer tomography, magnetic resonance imaging and PET computer tomography were performed and the tumor was shown to have extended to skull base and metastasized to the bone marrow cavity (with bone metastasis). The patient received wide excision of the tumor followed by postoperative immunotherapy. However after 1 course of immunotherapy, the patient did not continue with the treatment due to high fever. He died in February the following year. Diagnosis of nasal cavity malignant melanoma is often delayed due to its non-specific presentations and its insidious tumor location, resulting in poor prognosis. Hence, physicians should raise their awareness when encountering patients presented with epistaxis, nasal obstruction and black nasal lesions, nasal endoscopy, pathology examination and computed tomography scan can be arranged to avoid delayed diagnosis. Early detection and appropriate treatment would reduce the local recurrence or distant metastases and ultimately improve the overall prognosis.

Key words: malignant melanoma, sinonasal mucosal malignant melanoma, melanoma

*Correspondence to: Stella Chin-Shaw Tsai, MD, Department of Otolaryngology, Tungs' Taichung MetroHarbor Hospital, No. 699, Chungchi Road., Sec. 1, Wuchi, Taichung, 43503, Taiwan, R.O.C.
E-mail addresses: t5722@ms.sltung.com.tw

Case Report

陰蝨感染於老婦女之報告

阮正雄

童綜合醫療社團法人童綜合醫院　婦產部

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摘要

陰蝨（Phthirus Pubis）是一種寄生於人體，有毛部位的不完全變態的昆蟲。以吸食人血為生。其全部生活史，都在人體上完成。故為人類真正的外寄生蟲（Ectoparasite）。好發於男性及青年成人，因親密性行為肉體的接觸，或同睡一張床而感染。已往所常遇見的案例都在較年青族群，而老人婦女甚為少見，故提供出為參考。

關鍵詞：陰蝨、蝨、蟹蝨、外寄生蟲

前　言

陰蝨是一種很古老的疾病，在數千年前就有記載。蝨蟲有超過 4000 種，其中僅 560 種以吸食哺乳類的血維生。因爲蝨蟲具有宿主專一性，所以專門吸食人血的人蝨不會傳染到寵物，也不會由寵物傳染給人。感染於人體的蝨蟲（Lice）有二種，即人蝨及陰蝨。人蝨有二種亞種即頭蝨（Pediculus humanus capitis）及體蝨（Pediculus humanus humanus）形態很相似，祇能依寄生部位而分，頭蝨寄生於頭髮，偶而可在鬍鬚、胸毛找到，體蝨則寄生於衣服皺縫內，僅於吸血時離開衣服，人蝨呈長形約 2-4.5 mm 背部扁平、灰色、無翅、觸角短、三對足很發達、其體節頂端有一指狀剛毛、而附節上有一曲爪、適於握持毛髮、稱爲攀緣足（Climping leg）。陰蝨個體更小（僅 1-3 mm）身體長寬約略相等，狀如蟹，故又名蟹蝨（Crab lice）、其腹部兩側有瘤狀突起、前足較小、中、後足強壯、有力，不輸螃蟹的大螯。一個卡鉗夾住陰毛，足以支撐全身的穩定 [1]。

陰蝨之感染與親密性行爲有關 [2]。已往所常遇見的案例，都在較年青族群 [3] 而老人婦女甚爲少見，故提供出爲參考。

*通訊作者：阮正雄醫師　童綜合醫療社團法人童綜合醫院　婦產部　43503 臺中市梧棲區中棲路一段699號

病　例

病人爲 82 歲經產婦，最近半年來主訴下體搔癢，看過許多位皮膚科及婦產科醫師，情況一直未見得改善，因陪 83 歲的丈夫到醫院內科看病（平時經常喜歡出入風月場所），順便道婦產科看診，醫師詳細觀察發現陰唇及恥骨聯合附近，有長毛處之皮膚，有輕微的水腫與出血點，陰部皮膚有出現紅疹、丘疹、血痂，緊接著皮膚的毛根多處有覆蓋有如皮屑的灰白色的東西，有些中央還有紅點，有些還會移動，用鑷子挾拾放置於玻璃片上，用顯微鏡 40 倍率即可觀察到節肢蟲體，成蟲蟲卵與幼蟲（圖 1-3）。當有吸食人血時，更可見到其心臟搏動之情況，蟲卵呈橢圓形，一端有如栓著瓶蓋似的的樣子，另一端會連在毛髮上。其他檢查發現子宮已萎縮變小，兩側附屬器也無異常，治療則建議病人將毛髮徹底剃乾淨，並以毛刷將皮膚刷洗乾淨，再塗抹抗炎藥膏即可，一星期後回診，所有症狀都已消失痊癒。感染期間所使用之衣物、棉被、床單要隔離清洗或高溫煮沸消毒，以防重複感染。此老婦人之感染陰蝨俗稱八菊八腳蟲（實爲六腳），可能是來自其丈夫。臨床上以陰部有毛處搔癢來表現，陰毛間抓到陰蝨爲其診斷、剃毛刷洗陰部有毛區後塗抹抗炎藥膏處理皮膚之炎症反應爲其治療方式。

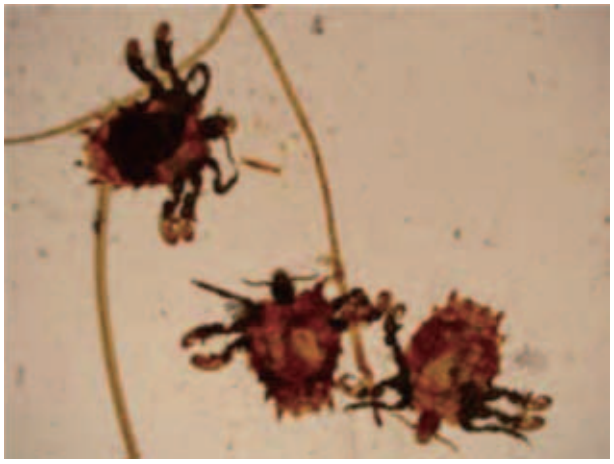

圖 1　陰蝨成蟲腳緊勾毛髮 40x

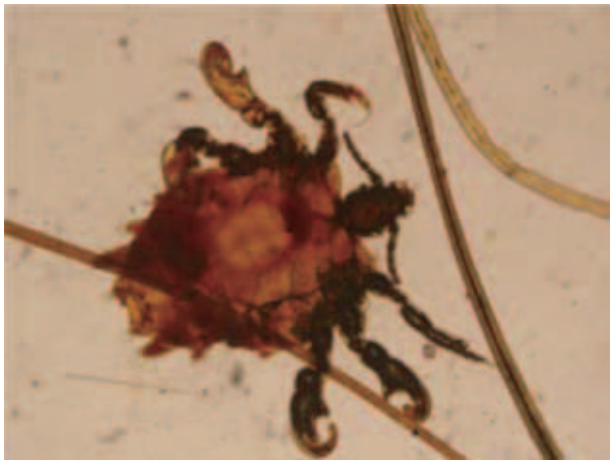

圖 2　40x 公成蟲

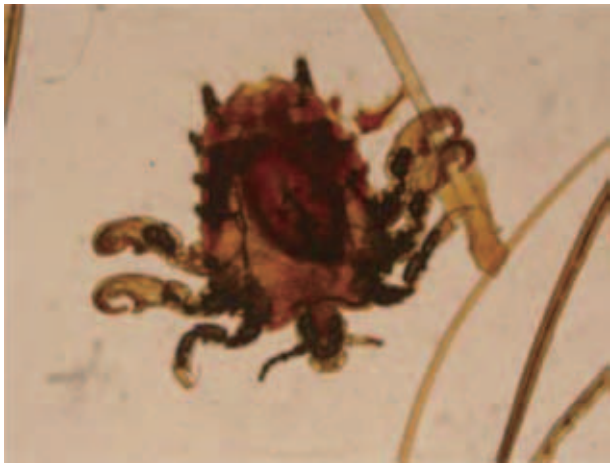

圖 3　母成蟲 體內有蟲卵

討　論

在過去 13.5 年間（民國 85 年元月至民國 98 年 6 月底）在童綜合醫院共有 8 例陰蝨感染例（ICD-9 爲 132.9），其中男女各 4 位，以本案例爲最大年紀（表 1）平均年齡，男女均爲 66 歲。與往昔所見的案例，感染於較年青族群情況不一樣 [2-4]。

陰蝨蟲通常俗稱八菊八腳蟲（實爲六腳）侵犯陰部毛髮處，對於較多毛的患者，更可能傳染到腹部、胸部、大腿小腿、腋下、鬍鬚等部位，甚至可傳染到頭髮及小孩的眼睫毛。以往陰蝨蟲感染例都見與年輕人，也有寄生於睫毛、腋毛、眉毛、頭髮及其他濃密體毛處的報導。 1976 年張永昌、劉顯榮、鍾文政即曾在中華民國眼科學會雜誌報告睫毛部陰蝨蟲（phthirus pubis）寄生之一例報告 [4]。多見於不重視性衛生者，而今感染的對象似乎無年齡與性別的限制。只要有機會接觸，就有感染的機會。

人蝨感染於人體者有三種，即頭蝨、體蝨及陰蝨 [1-4]。

1. 頭蝨（Head Louse, Pediculus Humanus Capitis）：寄生於人類頭髮中，體長約 3 mm，雌虱略大於雄虱，身體狹長，呈灰白色或白色。

2. 體蝨（Body Louse, Pediculus Humanus）：人體蝨又稱衣蝨，寄生於人類軀幹和四肢，不吸血時隱藏於衣物縫隙褶皺內，體蝨外表與頭蝨相似，體型略大。

3. 陰蝨（Pubic Louse, Phthirus Pubis）：主要寄生於人體陰毛處，但在絕大部份人類毛髮上均可寄生生存，身體扁平，遠看如同皮屑，細看則如同小螃蟹，故在英語中又稱蟹蝨（Crab Louse）。其特徵陰蝨體型較體蝨、頭蝨爲小，約 1-3 mm，身體扁平，陰蝨蟲卵產于陰毛根部，橢圓形，紅褐色或鐵鏽色。蟲卵孵化後的幼蟲比成蟲小，也以血液爲食。陰蝨的傳播途徑主要是來自於親密的接觸（例如性交），或睡同一張床（床單或被子傳染），共用毛巾、共穿內褲等，其中以性交傳染最常見。因此陰蝨感染被認爲是性傳播疾病的一種。衣物和床鋪也是陰蝨的重要傳播途徑之一。據估計，陰蝨是傳染性最高的性病 [2]，如果性伴侶有陰蝨，一次性交傳染

表 1　童綜合醫院（民國 85 年元月至民國 98 年 6 月底）陰蝨的感染

案例（n = 8）	男（n = 4）	女（n = 4）
1	49　歲	64 歲
2	76	55
3	63	63
4	76	82 本例
平均年齡	66　歲	66 歲

率可達 90% 以上，而梅毒或淋病一次性交的傳染率約 30%。

陰蝨以人類的血液爲食物，牠以口器插入皮膚吸取血液，並釋放出一種唾液，所以陰部常會搔癢，內褲也會有點狀的出血。因此陰蝨棲息的患處會不時感到搔癢。另外，陰蝨亦可能帶有其他病菌，和其他蝨子一樣使患者產生感染，陰蝨患者 30% 會合併其他性病[6]，所以同時篩檢愛滋病、梅毒、淋病、單純疱疹、病毒疣、披衣菌等性病是很必要的。

圖 4　幼蟲 100x 體胖圓短

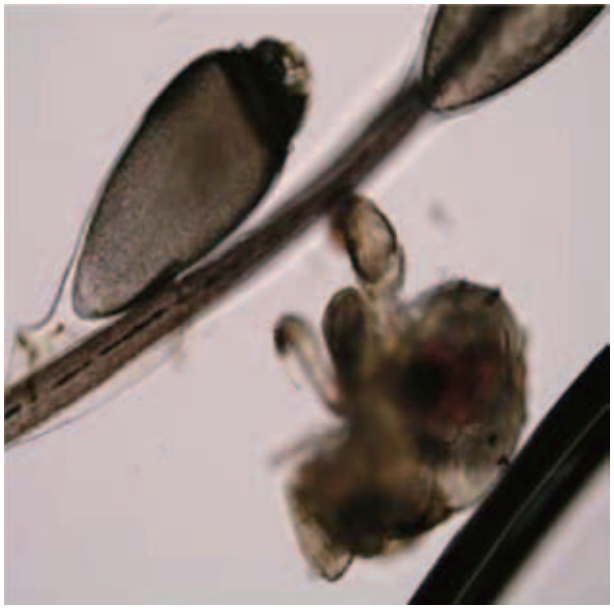

圖 5　蟲卵 幼蟲 100x

一、陰蝨生活週期史分為：蟲卵、幼蟲和成蟲三個階段。[3,7]

1. 卵：陰蝨的蟲卵一般都緊附在陰毛的毛幹根部上（圖 5-9），呈淡紅色或鐵鏽色的橢圓形，類似於點狀血痂。蝨卵（圖 5-9）利用人的體溫孵化，孵化期約爲一星期。大約五到十天大功告成，破繭而出，就在陰毛間游走生活，陰蝨走走停停、自由自在，在「發育」期間，猛吸「主人」的血液，尤其是在晚上時段，更爲活躍，叮咬後，令人奇癢無比，有時候皮膚就發炎紅腫，甚至出血，如果它們活躍在陰囊表皮，第二天早上的內褲

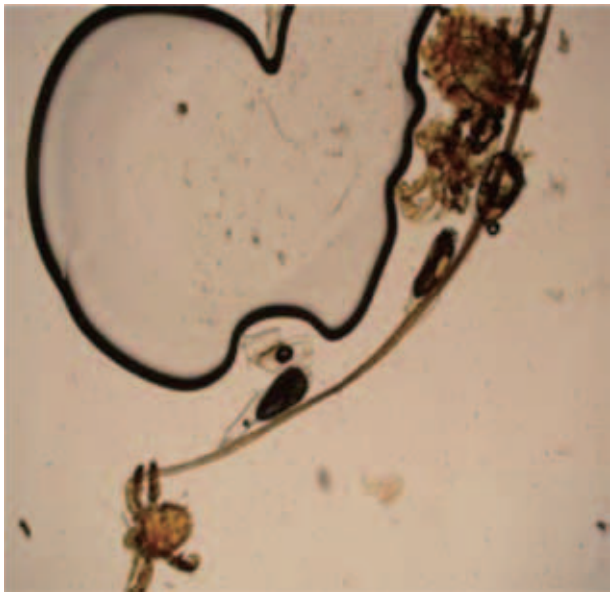

圖 6　蟲卵 幼蟲及成蟲 20x

圖 7　100x 蟲卵以幾丁質附毛根

圖 8　40x 蟲卵 幼蟲 及成蟲

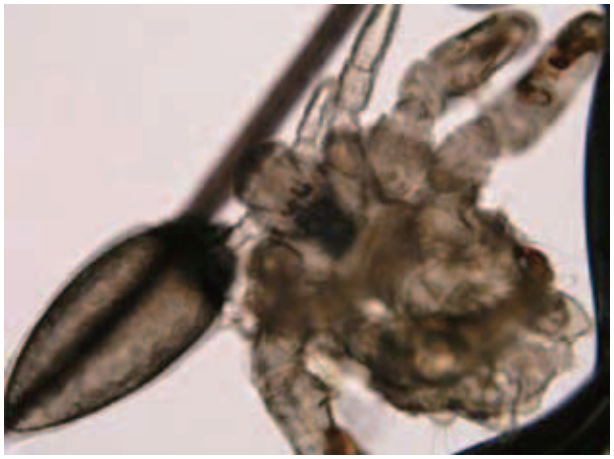

圖 9　100x 蟲卵 及成蟲

上，就滿佈密密麻麻的出血點，通常一個點就代表一隻蟲。

2. 幼蟲：幼蟲是陰蝨自卵孵化後，成長爲成蟲之前的形態。幼蟲（圖 4-6，圖 8）的樣子與成蟲相似，但是要小很多。幼蟲的成長期亦爲一星期左右。通常一個點就代表一隻蟲。大概十到十二天，經過三次脫殼，小蟲變「成蟲」，成蟲找尋異性伴侶交配後，就在陰毛間繁殖。

3. 成蟲：陰蝨的成蟲呈灰白色或褐色，雌蟲（圖 3）一般比雄蟲（圖 2）爲大。呈現體長和寬大約相同的圓或方形，不同於體蝨及頭蝨的橢圓形。成蟲長約 0.1-0.2 公分，成蟲每分鐘可以移動 10 至 20 公分之遠，主要寄生在人體的陰毛根部。陰蝨因有較寬的身體及較長的腳，使其可左右兩邊分別抓住分得很開的陰毛。陰蝨成蟲通常可以活兩週，母陰蝨（圖 6，圖 8-9）會在陰毛上產卵，呈白色或黃色的橢圓形。陰蝨產卵時，會分泌一種強力的黏膠－－幾丁質（Chitin），把卵黏在陰毛近表皮處，一根毛「綁」一個卵（圖 7），我們用水、酒精、甚至工業用的有機溶劑甲苯，都「擦不掉」，用鑷子去夾也夾不起來，唯一的方法，就是把毛刮除，才能把蟲卵清理掉 [8]。

二、陰蝨的臨床症狀：

身體陰毛及肛門周圍，或睫毛、眉毛、頭髮、鬚、腋下等若受到陰蝨感染，在臨床表現方面，大多數患者都會感覺非常癢。陰蝨叮咬的部位會產生刺激作用，並因抓癢的結果，產生局部性濕疹且在叮咬後會引起約 0.2 至 0.3 mm 直徑的藍色反應，此反應多在叮咬後數小時出現，此反應可持續幾日。

很多患者知道有東西在腹股溝爬動，但大部分的患者沒有看見到陰蝨，也不了解這個疾病。約 50% 的患者有發炎反應，大多是很輕微的，以致於臨床上沒有明顯的皮膚疹子。太晚求醫的患者，可能出現廣泛的發炎，甚至腹股溝的淋巴腫大。偶爾可以在腹股溝及小腹，發現特異性的 1~2 公分大的灰藍色的斑點，這是因爲陰蝨叮咬後，造成眞皮深層血鐵質堆積所導致。

1. 陰部搔癢，特別是夜間搔癢更甚；
2. 陰部出現紅疹、丘疹、血痂或青斑；
3. 內褲上有鐵鏽色粉末狀或顆粒狀蝨糞；
4. 陰毛根部可發現鐵鏽色或紅褐色橢圓形蟲卵；

三、陰蝨的臨床檢驗：

可由觀察其寄生部位的形態後，直接鑷取其蟲體於顯微鏡觀察確認。

四、在治療方面：

有 2 種基本概念，即除蟲與殺蟲，除蟲者將陰毛剃淨並用塑膠袋密封丟棄；殺蟲者使用局部殺蟲劑，有數種可殺死陰蝨的外用藥物，（其中 10% DDT 粉噴灑對肝臟毒性較強今已不用），使用的方法是塗抹在乾燥的陰毛上，停留 5~10 分鐘後洗掉。因爲在濕的毛髮上，藥物的濃度會遭到稀釋而影響藥效，所以必須擦乾後再塗藥。因爲許多藥物，無法百分之百殺死蟲蛋，所以一週後須再次塗藥，以殺死後來孵化的蟲卵。如果藥物治療失敗，首先必須考慮是否塗抹時間太短，藥物是否遭到稀釋，以至於無法達到有效的殺蟲濃度，藥物劑型的不同也影響藥效，以及患者再度被未治療的人所感染等因素。其次才考慮到抗藥性的問題，如果多次治療失敗，可以考慮剃掉所有毛髮。

1. 剃淨陰毛及肛門周圍毛髮並將其焚燒；
2. 將被污染的衣物、床單、被罩蒸煮或開水燙燙消毒，殺滅蟲卵及成蟲；

3. 使用熱水及肥皂（硫磺皂）清洗陰部；

4. 使用林旦（Lindane）乳膏（1% r-benzene hexachloride, BHC, 六氯環己烷）、1% 氯菊酯（Permethrin）、50% 百部酊（中藥百部的酒精浸泡液）或其他殺蟲劑塗於陰部。

由於殺蝨劑林旦（Lindane）乳膏具有神經毒性，且可在體內積聚，因此對孕婦、哺乳期婦女及兒童應避免使用。治療方法是剃除陰毛以除去可能的蟲卵，合併使用含 BHC 的藥膏。爲預防蟲卵無法被殺死，一週後會孵化，所以一週後再施予同樣藥劑的治療即可。另外內衣褲以熱水清洗消毒及性伴侶的治療都應同步進行，以免再繼續彼此感染。

五、陰蝨的預防：

預防之道，除了避免不正常接觸外，平常即應注意個人衛生，保持身體清潔，維持局部的乾燥通風，勤換床單衣物。當陰部搔癢或內褲有血跡時，千萬不要覺得不好意思就醫，務必儘早接受治療，以根絕陰蝨的繁殖。

若已發現有陰蝨的存在，應徹底治療，此時應加強環境衛生，貼身衣物及棉被套，先用開水燙過再洗濯，地毯暫時移除包括其周圍有接觸的人、物都應檢查、治療或消毒完全。

結　論

陰蝨（Phthirus Pubis）又稱爲八足蟲（實際上是二鬚六足，肉眼觀看有如八足）是一種不完全性變態，寄生於人體，有毛部位的昆蟲。以吸食人血爲生。其全部生活史，都在人體上完成。故爲人類眞正的外寄生蟲（Ectoparasite）。感染於 82 歲老婦女誠屬少見。本案例中，病患 83 歲的丈夫，性情風流又不注重性衛生，因此其感染途徑可能來自親密行爲的接觸或睡同一床，共用床單棉被而來。以往所見之陰蝨感染多在年青族群，而今在本院所見則在年齡較大者，故感染似乎與年齡無關。臨床上，陰部毛髮區域搔癢症時，陰蝨感染應列爲重要鑑別項目。治療上，以將毛髮剃除，並將該區皮膚徹底刷洗乾淨，再塗抹抗皮膚炎症藥膏，爲其最簡易、方便、有效之方式。

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Phthirus Pubis Infestation in an Elderly Woman: a case report

Cheng-Hsiung Roan

Department of Obstetrics & Gynecology, Tungs' Taichung MetroHarbor Hospital

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Abstract

Phthirus pubis is a parasite to the human body, which lives off human blood and most commonly found in the pubic area. All of its life cycle are completed on the human body surface. Phthirus pubis, also known as crab louse, is an ectoparasite. Crab lice are often found in sexually active young adults, in which its infescation is associated with sexual activity or close body contact or sleeping in the same bed. We report a case of crab lice infestation in an elderly woman.

Key word: Phthirus Pubis, Lice, Crab Louse, Ectoparasite

*Correspondence to: Dr. Cheng-Hsiung Roan, Department of Obstetrics & Gynecology, Tungs' Taichung MetroHarbor Hospital, No.699, Sec. 1, Chungchi Rd., Wuchi Dist., Taichung City 43503, Taiwan (R.O.C.).

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3. Monographs with multiple authors:
   Levinsky NG: Fluid and electrolytes. In: Thorn GW, Adams RD, Braunwald E, Isselbacher K, Petersdprf RG eds. Harrison's Principles of Internal Medicine, 8th ed. New York: Mcgraw-Hill, 1977:364-75.

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例：Bhasin S, Storer TW, Berman N, Callegari C, Clecenger B, Phillips J, et al. The effects of supraphysiologic doses of testosterone on muscle size and strength in normal men. N Engl J Med 1996; 335:1-7.

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例：One of the first well documented reports of ECH poisoning with fatality in young children was reported by Miller et al. in 1970[2].

例：Boulet 等人 [3] 報告氣喘患者接受衛教後的知識改變量不受個人因素影響。

三、參考範例

A. 期刊：[作者姓名：題目。雜誌簡稱 年代；卷數（期數）：起迄頁數]

1. 許吟姿、楊光道、張恆鴻：結締組織疾病併發間質性肺病變患者 99mTc-DTPA 肺廓清率之臨床研究。內科學誌 1992;3:79-83.
2. Yang KTA, Chen HD: A semi-automated method for edge detection in the evaluation of left ventricular function using ECG-gated single-photon emission tomography. Eur J Nucl Med 1994;21:1206-11.

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1. 楊志良：生物統計學新論，一版。台北；巨流圖書公司，1984：33-8.
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C. 多重作者之單行本：[有關文章作者姓名：書名，版數（卷數）。發行地；出版公司，年代：引用部份頁數]。

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