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Asian Medical Journal and Alternative Medicine
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Instruction for Authors

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Office Address Research Administration Office, Faculty of Medicine, Thammasat University (Rangsit Campus)
Klongluang, Pathum Thani 12120, Thailand
Tel. +66 2564 4444 ext.7530-39
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Editor's Note

Our editorial team would like to congratulate the Faculty of Medicine, Thammasat University to hold the annual meeting for 2023. The meeting theme this year is "Transformative medicine in the post-pandemic era", which is suitable for the current situation where medical knowledge changes rapidly. This supplementary issue includes several interesting abstracts, original articles and review articles from the annual meeting. Advancement of science will drive the future practice of medicine and the faculty is continuously working hard to publish new information for scientists to help improve the patient care. We wish the Faculty of Medicine, Thammasat University well for all future successes that may arise.

Sincerely,

Opas Traitanon , M.D.
Associate Professor in Medicine-Nephrology
Deputy Editor
Asian Medical Journal and Alternative Medicine (AMJAM)

Original Article

Association of Vision-Related Quality of Life with Happiness in Vision Impairment Patients

Nattapon Wongcumchang, Onnicha Srivanich*,
Irada Sirikridsada

Abstract

Introduction: Vision impairment affects both physical and mental problems in occupational performance and daily life. However, the improvement in the quality of life of the patient may not be enough to confirm that the patient is truly able to be happy in himself or herself.

Objectives: To study relationship between vision-related quality of life and happiness in vision impairment patients in aspect of distance vision, mobility, adjustment, reading and activities of daily living.

Methods: This pilot study enrolled 101 impairment patients at the ophthalmology department, Thammasat University Hospital in 2021. Oxford happiness questionnaire was assessed by impairment patients. In details, distance vision, mobility and lighting, adjustment, reading and fine work and activities of daily living were evaluated using Low Vision Quality of Life (LVQOL) questionnaire and statistical method using multiple regression analysis.

Results: There is a significant relationship between LVQOL score and happiness ($p = 0.006$) in the low vision group. In details, distance vision, mobility and lighting ($p = 0.038$), adjustment ($p = 0.003$) and activities of daily living ($p = 0.004$) are significantly and positively related to Low vision's happiness but LVQOL is not an important factor for happiness among blindness.

Conclusions: LVQOL was significantly associated happiness in low vision patients.

Keywords: Low vision, Blindness, Visual impairment, Vision-related quality of life, Happiness

Department of Ophthalmology, Faculty of Medicine, Thammasat University, Thailand
*Corresponding author: Onnicha Srivanich, M.D., Department of Ophthalmology, Faculty of Medicine, Thammasat University, Thailand. Email: onnichasrivanich@gmail.com, Tel: +66850563635

Introduction

Vision impairment is an important issue in occupational health because it greatly affects occupational performance and daily life. Visual impairment refers to loss of vision, low vision and blindness. Blindness can be congenital or acquired. It can be caused by glaucoma, retinal disease, corneal disease, optic neuropathy and trauma. As a result, low vision and blindness can affect both physical and mental problems. Education and socioeconomic differences according to age group and gender for visual impairment in children affects both physical, fine motor skills and perception. While disabilities in other age groups tend to affect both the body, mind and quality of life. As a result, vision loss or impairment can be considered a major issue in the ophthalmology community as well as on a national scale.[1,2]

In 2012, the World Health Organization (WHO) estimated that 285 million individuals around the world were visually impaired. It is separated into two groups: blind people, who account for about 39 million people and have a prevalence of about 5%, and people with visual impairment, who account for roughly 124 million people and have a prevalence of about 4%. More than 90% of people who are blind or have visual impairment reside in developing countries. However, investigations have revealed that there is a lack of data on the prevalence, incidence, and causes of visual impairment in children in Europe and many other countries.[1,3,4]

Visual impairment, whether low vision or blindness, affects daily living, mental, social and economic conditions. As a result, rehabilitation is critical for visual impairment patients. Visual and psychological medical rehabilitation, educational rehabilitation, social rehabilitation and vocational rehabilitation are all recommended for visual impairment patients. These suggestions will motivate patients to improve their physical, emotional, social and professional well-being. As a result, patients quality of life has improved.

However, the improvement in the quality of life of a patient may not be enough to confirm that the patient is truly able to be happy with himself or herself. Therefore, the authors would like to study the quality of life associated with vision in vision impared patients as being related to happiness. In addition, the various dimensions of quality of life-related to vision also need to be studied. For example, distance vision, mobility and lighting plus adjustment, reading, fine work and activities of daily living need to be included.

Methods

This Pilot study was conducted in March 2021 to March 2022 at the Department of Ophthalmology, Thammasat University, Thailand. All individuals with low vision and blindness were recruited from outpatients clinics. Written informed consent was obtained from all participants following an explanation of all questionnaires involved in both English and Thai version. The protocol followed the tenets of the Declaration of Helsinki. *Ethic committee approved* : MTU-EC-OP-0-060/64. Oxford happiness questionnaire (Figure 1) was assessed by impairment patients. The Low Vision Quality of Life (LVQOL) questionnaire (Figure 2) had 25 questions regarding the following aspects of life: distance vision, mobility and lighting (12 questions), adjustment (4 questions), reading and fine work (5 questions) and activities of daily living (4 questions). Questionaire questions were read by a relative to patients. Demographic data were collected using a data sheet. Data analysis was performed using SPSS. Validity and reliability were assessed using the multiple regression methods. All *p-value* less than 0.05 were considered significant.

Inclusion criteria

1. Visual impairment patients cover low vision and blindness as following by WHO :

1.1 Low vision means the patient has the best side vision. When the patient is wearing eyeglasses, their vision ranges from 3 parts 60 meters (3/60) or 20 parts 400 feet (20/400) to worse than 6 parts 18 meters (6/18) or 20 parts 70 feet (20/70) or the field of vision narrower than 30 degrees down to 10 degrees.

1.2 Blindness means the patient has the best side vision. When the patient is wearing eyeglasses, their vision is worse than 3 parts 60 meters (3/60) or 20 parts 400 feet (20/400) until the light is not even visible or the field of vision is narrower than 10 degrees.

2. Patients who have received or terminated routine medical care but the defect persists and cannot be corrected with conventional eyeglasses is subject to the following conditions:

2.1 When inflammation has been treated for at least 3 months.

2.2 After surgery for at least 6 months

2.3 Patients with abnormalities of extraocular muscle, traumatic cataract, traumatic vitreous hemorrhage after at least 12 months of eye damage.

3. Patients were over 18 years old.

Exclusion criteria

1. Patients who are unable to speak in Thai.

2. Patients with co-existing illnesses such as HIV, cancer or psychiatric disorders.

	Strongly Disagree	Moderately Disagree	Slightly Disagree	Slightly Agree	Moderately Agree	Strongly Agree
I don't feel particularly pleased with the way I am	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I am intensely interested in other people	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I feel that life is very rewarding	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I have very warm feelings towards almost everyone	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I rarely wake up feeling rested	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I am not particularly optimistic about the future	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I find most things amusing	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I am always committed and involved	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
Life is good	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I don't think that the world is a good place	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I laugh a lot	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I am well satisfied about everything in my life	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I don't think I look attractive	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
There is a gap between what I would like to do and what I have done	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I am very happy	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I find beauty in some things	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I always have a cheerful effect on others	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I can fit in everything I want to	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I feel that I am not especially in control of my life	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I feel able to take anything on	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I feel fully mentally alert	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I often experience joy and elation	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I do not find it easy to make decisions	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I do not have a particular sense of meaning and purpose in my life	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I feel I have a great deal of energy	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I usually have a good influence on events	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I do not have fun with other people	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I don't feel particularly healthy	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6
I do not have particularly happy memories of the past	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6

Figure 1 Oxford Happiness Questionnaire Interpreting the score, by Stephen Wright: 1-2: Not happy, 2-3: Somewhat unhappy, 3-4: Not particularly happy or unhappy, 4: Somewhat happy or moderately happy. Satisfied. This is what the average person scores, 4-5: Rather happy; pretty happy, 5-6: Very happy, 6: Too happy.

Distance Vision, Mobility and Lighting

How much of a problem do you have:	GRADING None		Moderate		Great		
With your vision in general	5	4	3	2	1	x	n/a
With your eyes getting tired (e.g only being able to do a task for a short period of time)	5	4	3	2	1	x	n/a
With your vision at night inside the house	5	4	3	2	1	x	n/a
Getting the right amount of light to be able to see	5	4	3	2	1	x	n/a
With glare (e.g dazzled by car lights or the sun)	5	4	3	2	1	x	n/a
Seeing street signs	5	4	3	2	1	x	n/a
Seeing the television (appreciating the pictures)	5	4	3	2	1	x	n/a
Seeing moving objects (e.g. cars on the road)	5	4	3	2	1	x	n/a
With judging the depth or distance of items (e.g. reaching for a glass)	5	4	3	2	1	x	n/a
Seeing steps or curbs	5	4	3	2	1	x	n/a
Getting around outdoors (e.g. on uneven pavements) because of your vision	5	4	3	2	1	x	n/a
Crossing a road with traffic because of your vision	5	4	3	2	1	x	n/a

Adjustment

Because of your vision, are you:	No		Moderately		Greatly		
Unhappy at your situation in life	5	4	3	2	1	x	n/a
Frustrated at not being able to do certain tasks	5	4	3	2	1	x	n/a
Restricted in visiting friends or family	5	4	3	2	1	x	n/a

	Well				Poorly	Not explained
How well has your eye condition been explained to you	5	4	3	2	1	x

Reading and Fine Work

With your reading aids / glasses, if used, how much of a problem do you have:	None		Moderate		Great		
Reading large print (e.g. newspaper headlines)	5	4	3	2	1	x	n/a
Reading newspaper text and books	5	4	3	2	1	x	n/a
Reading labels (e.g. on medicine bottles)	5	4	3	2	1	x	n/a
Reading your letters and mail	5	4	3	2	1	x	n/a
Having problems using tools (e.g. threading a needle or cutting)	5	4	3	2	1	x	n/a

Activities of Daily Living

With your reading aids / glasses, if used, how much of a problem do you have:	None		Moderate		Great		
Finding out the time for yourself	5	4	3	2	1	x	n/a
Writing (e.g. cheques or cards)	5	4	3	2	1	x	n/a
Reading your own hand writing	5	4	3	2	1	x	n/a
With your every day activities (e.g. house-hold chores)	5	4	3	2	1	x	n/a

Figure 2 Low Vision Quality of Life (LVQOL) questionnaire. Patients are asked to complete the questions by circling the number most appropriate to how they feel. If they can no longer perform the task because of their vision, they are to circle "x" and if they do not perform the task for nonvisual reasons, to circle "n/a".

Results

One-hundred one were eligible for enrollment in this study. Patients with low vision and blindness differed significantly in gender, education and work status. Fifty-eight participants were low vision and 43 participants had blindness. Of these individuals, 60% were men and 40% were women. In terms of education, most of the low vision patients had a high school education (38%) or a bachelor's degree (40%), while 40% of the Blindness group had less than high school education. In terms of working status, 36% of the Low vision group was employed compared to 12% of the Blindness group, up to 65% of Blindness patients were unemployed. Studies have shown that low vision and blindness are more common among retinal diseases, up to 47%. Other information is shown in Table 1.

Table 1 Baseline characteristics

	Low Vision (n = 58)	Blindness (n = 43)	*P*-value
Sex, n(%)			
Male	72	47	0.008
Female	28	53	
Age (years), n(%)			
<40	5	9	0.223
40-49	10	16	
50-59	21	7	
60-69	29	28	
70-79	24	30	
80 or higher	10	9	
Education, n(%)			
Primary school	22	40	0.047
High school	38	42	
Bachelor degrees	40	19	
Master degrees	0	0	
Doctoral degrees	0	0	
Marital status, n(%)			
Married	83	70	0.208
Single	10	23	
Divorce	7	7	
Work status, n(%)			
Employed	36	12	0.029
Unemployed	40	65	
Retired	22	21	
Student	2	2	
Eye conditions, n(%)			
Glaucoma	31	19	0.547
Retina	47	47	
Cornea	3	5	
Neuropathy	3	5	
Trauma	0	2	
Uveitis	0	2	
Multiple conditions	16	21	

Table 1 Baseline characteristics (Cout.)

	Low Vision (n = 58)	Blindness (n = 43)	*P*-value
Non Ocular Comorbidities, n(%)			
Absent	26	28	0.546
Hypertension	5	12	
Cardiovascular disease	0	2	
Diabetes mellitus	9	7	
Pulmonary disease	0	2	
Central nervous system disease	3	0	
Dyslipidemia	3	2	
Multiple systemic diseases	53	47	
Duration, n(%)			
Congenital	0	5	0.097
Acquired	100	95	
Low visual aids, n(%)			
None	72	81	0.079
Magnifiers	0	5	
Glasses	28	14	

Patients in the low vision group had significantly higher scores in both happiness and quality of vision than in the blindness group in all respects (Table 2). Activities of daily living score (Figure 3) also found that the proportion of Low vision differed significantly from blindness. The majority of low vision (59%) was non-dependence, while the majority of blindness (49%) was total dependence.

Table 2 Comparing happiness scores and LVQOL scores between low vision and blindness

	Low Vision (n = 58)	Blindness (n = 43)	*P*-value
Happiness Scores*	138.10 ± 20.12	127.12 ± 23.17	0.013
LVQOL[#] scores (Total 125 points)	65.03 ± 23.50	41.88 ± 25.44	0.000
- Distance vision, mobility and lighting (60 points)	30.22 ± 12.54	21.12 ± 11.86	0.000
- Adjustment (20 points)	12.97 ± 4.21	9.93 ± 5.64	0.003
- Reading and fine work (25 points)	10.52 ± 6.00	4.67 ± 5.29	0.000
- Activities of daily living (20 points)	11.33 ± 5.21	5.98 ± 5.60	0.000

* Oxford happiness questionnaire

[#] Low vision quality of life (LVQOL) questionnaire

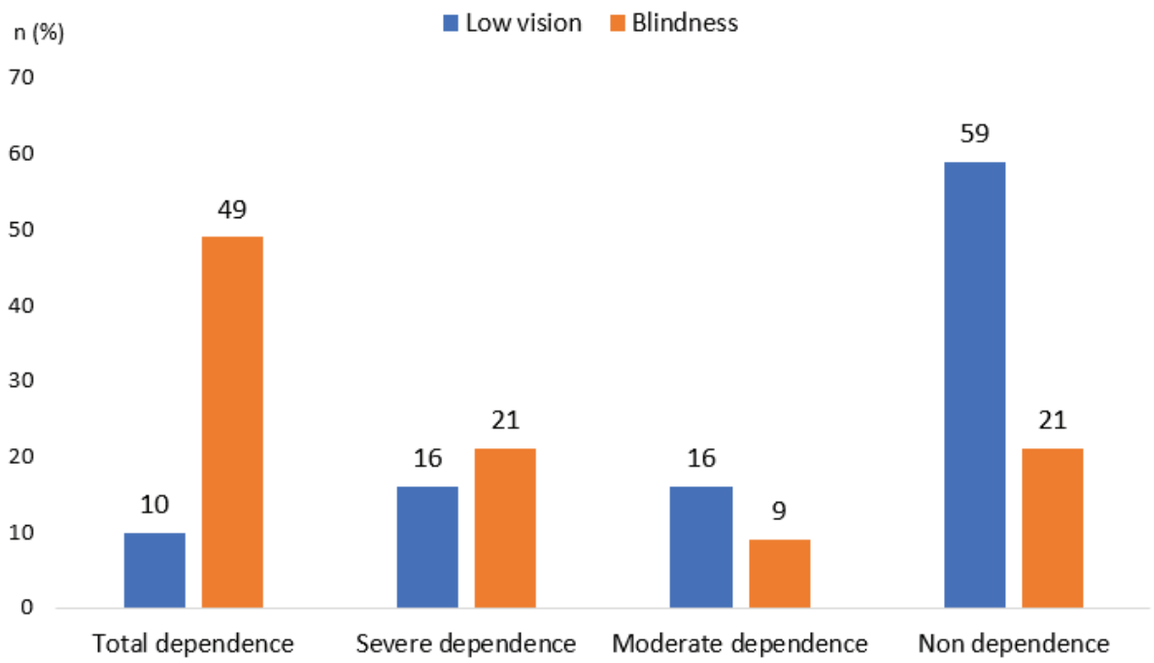

Figure 3 Activities of daily living scores

Among low visions, results of multiple regression analysis show that there is a significant and positive relationship between LVQOL score and happiness (β = .356, t-value = 2.853, *p-value* = .006). In details, distance vision, mobility and lighting (β = .273, t-value = 2.122, *p-value* = .038), adjustment (β = .380, t-value = 3.070, *p-value* = .003) and activities of daily living (β = .368, t-value = 2.964, *p-value* = .004) are significantly and positively related to Low vision's happiness. In other words, these three variables are significant determinants of happiness for low vision. While reading and fine work were not significantly associated with patient happiness (*p-value* > 0.05) (Table 3).

Table 3 LVQOL score in low vision

	Standardized Coefficient (β)	t-value	*p-value*
LVQOL[#] scores	.356	2.853	.006
- Distance vision, mobility and lighting	.273	2.122	.038
- Adjustment	.380	3.070	.003
- Reading and fine work	.240	1.847	.070
- Activities of daily living	.368	2.964	.004

[#] Low vision quality of life (LVQOL) questionnaire
[#] Regression analysis

Among blindness, results of multiple regression analysis show that LVQOL is not significantly related to happiness. (β = .130, t-value = .838, *p-value* = .407)

Table 4 LVQOL score in blindness

	Standardized Coefficient (β)	t-value	*p-value*
LVQOL[#] scores	.130	.838	.407
- Distance vision, mobility and lighting	.096	.615	.542
- Adjustment	.091	.586	.561
- Reading and fine work	.132	.852	.399
- Activities of daily living	.174	1.133	.264

[#] Low vision quality of life (LVQOL) questionnaire

Discussion

We study the relationship between vision-related quality of life and happiness in vision impairment patients in aspect of distance vision, mobility, adjustment, reading and activities of daily living. Different causes of sight loss were reported including congenital, for example, blindness due to measles, neurological causes such as stroke, retinal disease such as diabetic retinopathy and maculopathy. Genetic causes such as macular dystrophies and retinitis pigmentosa were also reported as well as corneal degenerations and optic nerve disease such as glaucoma as well as loss due to trauma.

The study of Susanne et al. assessed central retinal function using low luminance, including best corrected visual acuity (BCVA), low luminance visual acuty (LLVA), moorfields acuity chart-visual acuity (MAC-VA) and contrast sensitivity. These methods affect quality of life in low vision patients with macular degeneration.[10] The study of Masoud Khorrami-Nejad et al. showed the group without stereopsis had lower quality of life scores in terms of social and leisure time. The tunnel vision group had low scores on mobility and self-care.[3]

For the study of the influence of visual impairment on quality of life in Ghana, it was found that people with visual impairment had poor quality of life scores on physical, mental, environmental and social relationships.[2] The study of Nabila Jones and Hannah Elizabeth Bartlett towards the impact of people with visual impairment on daily living and visual quality of life (VR-QoL) among people with visual impairment living in the UK found that visual impairment affecting the purchase and preparation of food may contribute to malnutrition in people with visual impairment.[4] The study of Gertrudis IJM Kenpen and et al. towards the impact of low vision on daily living, depression, anxiety and social support with low vision showed that older adults with low vision had worse levels of daily activity, depression and anxiety, while the level of social support was better than the older group with chronic disease.[8]

The study of James et al. studied the quality of life of low-vision patients and assessed the effects of visual rehabilitation. Data was collected in the form of a questionnaire. The sample consisted of 278 patients. It divided inquiries into 4 main groups: 1. Distance vision, mobility and lighting, 2. The patient's adjustment to vision, 3. Reading and fine working and 4. Daily routine. Studies have shown that visual rehabilitation can improve a patient's quality of vision.[9] Barthel Activities of Daily Living: ADL is an assessment of a person's ability to perform daily activities. Issues include eating when having the deck ready in front of you, washing your face, combing your hair, brushing your teeth and shaving in the last 24-28 hours. It included getting up from bed or from bed to chair, using the bathroom, moving inside a room or house, wearing clothes, going up and down stairs, taking a shower, holding back defecation with urinary incontinence during the past 1 week.[7]

Over the past decade, it has been found that Thailand and other countries have increased the quality of life of people with visual impairments, low vision and blindness. For example: Physiological needs, Patients needed to be able to spend their daily lives on their own at 66.67, Psychological needs, Patients required public acceptance at 46.67% and Socioeconomic needs, Patients needed to be able to take care of themselves without the burden of society and their families at 50%.[5]

According to the results of this study, relationship between LVQOL score and happiness

are significantly and positively related to low vision's happiness. In other words, low vision patients with high vision-related quality of life tended to be happy. Mostly they were in the non-dependence. They can help themselves in daily living. In contrast, the blindness LVQOL is not significantly related to happiness, meaning that LVQOL is not an important factor for happiness among blindness. There were some patients in the research who have good quality of life but are not happy because some have mental or socioeconomic problems. Although the quality of life of blind patients was not good, they were happy because most of them are taken care of from their families and have good mental supporters. There are often limitations in daily living in chronic disease patients. Blindness is the cause of not only morbidity, but also mortality. If there were some problems in morbidity, bladder control, bowel and bathing, there would be major difficulties in activities daily living. Blind patients have increased the risk of death.[8] It was observed that mostly there were no visual aids in impairment vision patients. In Thailand, there has been no studies on happiness in low-vision patients.

From the above studies, it can be seen that visual impairment, whether low vision or blindness, affects daily life, mental, social and economic conditions. For the care of visual impairment patients, Thailand has a guideline for low vision patients through medical rehabilitation, both visual and mental health, educational rehabilitation, social rehabilitation and vocational rehabilitation.[9] It is a physical, mental, social and professional rehabilitation that results in a better quality of life for patients. Although rehabilitation service can be effective and helpful in current situations. Nowadays we find that we still lack rehabilitation programs aimed to improve functional status. Even though, the effectiveness of rehabilitation in people with blindness is less than those with normal visual acuity, it greatly and deeply changes their level of independency and they will have more independency especially in daily living. However, the limitation of this study is the number of patients. A larger or multicenter study may confirm this result.

In conclusion, among low visions, there is a significant relationship between LVQOL score and happiness but not significantly related to happiness among blindness.

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Original Article

Usage of Shanghai Scoring System for Predicting Ventricular Arrhythmic Events in Brugada Syndrome (BrS) Patients in Thailand

Kumpol Chintanavilas[1*], Nilubon Methachittiphan[2], Sirin Apiyasawat[2]

Abstract

Background: Many risk factors are associated with ventricular arrhythmic events in Brugada syndrome (BrS) patients. The Shanghai scoring system for diagnosis of BrS was initially published in 2015.[1] A single study also validated using this scoring system for risk stratification of arrhythmic events in BrS patients.[2] There has been no study to demonstrate the role of this scoring system in the risk stratification of BrS patients in the Thai population. This study aimed to evaluate the role of the Shanghai scoring system in predicting ventricular arrhythmic events in Thai BrS patients.

Methods: We studied a retrospective cohort of BrS patients who were diagnosed from 1999 to 2019 at Ramathibodi Hospital. The patients were classified according to the Shanghai scoring system. All patients were followed for arrhythmic events and clinical outcomes.

Results: 54 eligible Patients were found with BrS (14 with cardiac arrest, 30 with syncope, 3 agonal respirations and 7 asymptomatic) and were classified by the Shanghai score into group A (very high risk); score ≥ 5.5 (n = 34), group B (high risk); score 4-5 (n = 14) and group C (non-high risk); score ≤ 3.5 (n = 6). During the mean follow-up period of 114 months, 11 arrhythmic events occurred (1 sudden cardiac arrest, 9 appropriate ICD therapy, 1 documented VT/VF from surface ECG). Incidence of ventricular arrhythmic events was highest in Group A (26.5%), followed by Group B (14.3%) and no event in Group C. Shanghai scores of more than 3.5 tend to be associated with increased ventricular arrhythmic events (HR 4.85, CI 0.037-630.2, $p = 0.525$), compared to the lower risk group (Shanghai score ≤ 3.5). Five inappropriate ICD shocks occurred. Device-related complications occurred in 8 patients, with lead fracture being the most frequent complication (9.3%).

Conclusions: Risk stratification by the Shanghai scoring system may be useful in predicting ventricular arrhythmic events in Thai BrS patients. However, a larger cohort is needed for statistically significant results.

Keywords: Brugada syndrome, Shanghai scoring system, Risk stratification, Arrhythmic events

[1] Chulabhorn International Collage of Medicine, Thammasat University, Cooperative learning center, Piyachart 2, 99 Moo 18, Klongluang, Rangsit, Pathum Thani 12120 Thailand
[2] Ramathibodhi Hospital, 270 Rama VI Road, Rajataewe, Bangkok 10400 Thailand
[*] **Corresponding author:** Kumpol Chintanavilas, M.D., Chulabhorn International Collage of Medicine, Thammasat University, Cooperative learning center, Piyachart 2, 99 Moo 18, Klongluang, Rangsit, Pathum Thani 12120 Thailand
Email: kumpol07@staff.tu.ac.th

Introduction

Since 1992, Brugada syndrome (BrS) has been described and defined as a genetically determined channelopathy leading to ventricular arrhythmia, syncope and sudden death in young males.[3] Incidence of this syndrome in adults is approximately 0.05-0.6% with an average age of diagnosis around 41 years old.[4] Many studies have shown that clinical presentation is the strongest predictor of recurrent major arrhythmic events while other predictors such as spontaneous type 1 ECG, and family history of sudden cardiac death at age 45 years, also show considerable risks.[4-9] In 2015, the Shanghai scoring system for the diagnosis of Brugada syndrome was published (Table 1).[1] This scoring system includes clinical presentation, electrocardiography, family history of BrS or sudden cardiac arrest and pathogenic mutations in BrS susceptibility genes. Only one study demonstrated the role of diagnosis and risk stratification in this scoring system.[2] At present, validation of this scoring system for risk stratification in Thailand has not been carried out. This study aimed to validate this score for risk stratification of arrhythmic events in Thai Brugada syndrome patients.

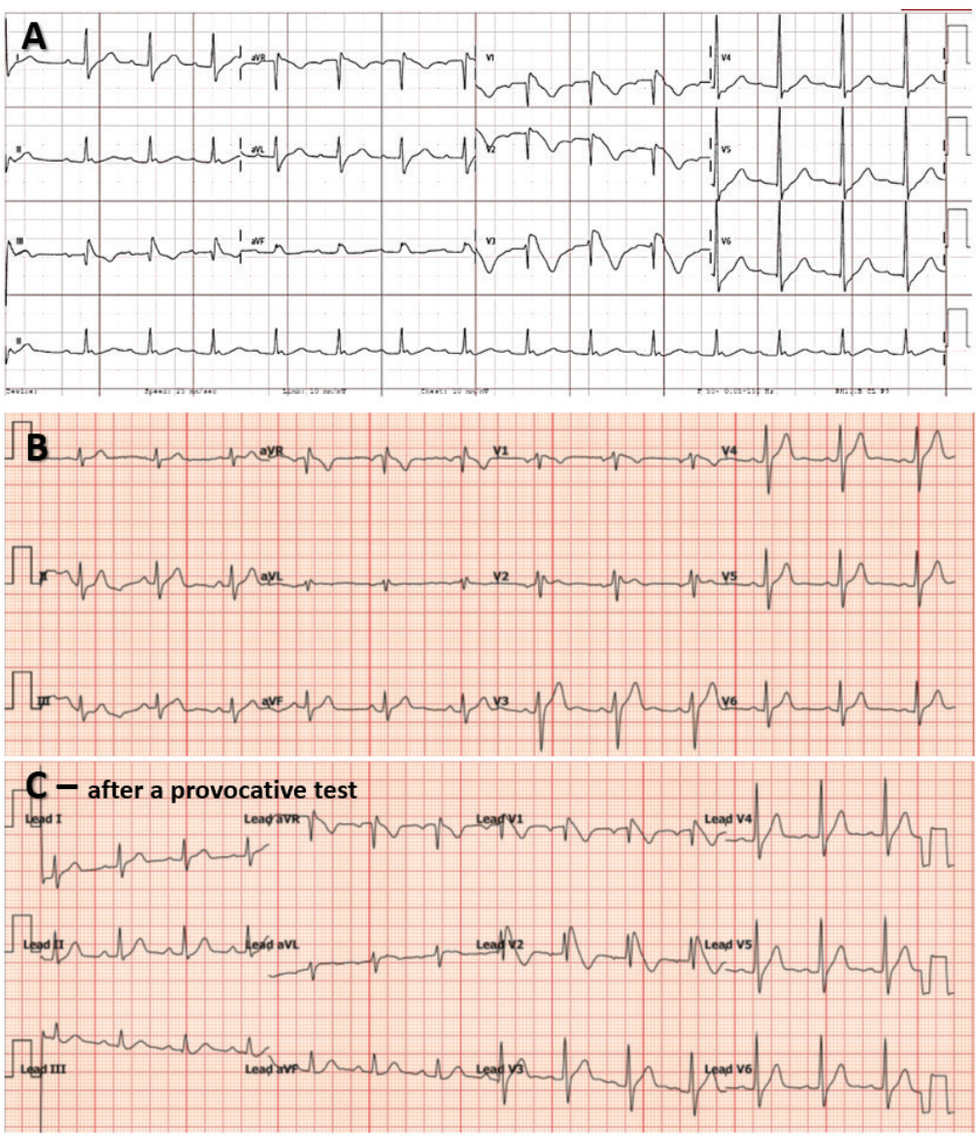

Figure 1 Type 1 Brugada pattern electrocardiogram, (A) Electrocardiogram of a 32-year-old man who survived ventricular fibrillation, (B) Baseline electrocardiogram of a 41-year-old man with a history of arrhythmic syncope and (C) electrocardiogram after provocative by flecainide and high intercostal lead

Table 1 Proposed Shanghai score system for diagnosis of Brugada syndrome[1*]

	Points
I. ECG (12-Lead/Ambulatory) *	
A. Spontaneous type 1 Brugada ECG pattern at nominal or high leads	3.5
B. Fever-induced type1Brugada ECG pattern at nominal or high leads	3
C. Type 2 or 3 Brugada ECG pattern that converts with provocative drug challenge	2
**Only award points once for the highest score within this category. One item from this category must apply.*	
II. Clinical History*	
A. Unexplained cardiac arrest or documented VF/polymorphic VT	3
B. Nocturnal agonal respirations	2
C. Suspected arrhythmic syncope	2
D. Syncope of unclear mechanism/unclear etiology	1
E. Atrial flutter/fibrillation in patients ≤ 30 years without alternative etiology	0.5
**Only award points once for the highest score within this category*	
III. Family History	
A. First- or second-degree relative with definite BrS	2
B. Suspicious SCD (fever, nocturnal, Brugada aggravating drugs) in a first- or second-degree relative	1
C. Unexplained SCD < 45years in first- or second-degree relatives with negative autopsy	0.5
**Only award points once for the highest score within this category.*	
IV. Genetic Test Result	
A. Probable pathogenic mutation in BrS susceptibility gene	0.5
Score (requires at least 1 ECG finding) ≥3.5 points: Probable/definite BrS 2-3 points: Possible BrS < 2 points: Nondiagnostic	

BrS = Brugada syndrome; SCD = sudden cardiac death; VF = ventricular fibrillation; VT = ventricular tachycardia

[*]C. Antzelevitch et al. / Journal of Arrhythmia 32 (2016) 315-339

Methodology

This is a retrospective cohort study of patients who were diagnosed with BrS between 1999 and 2019 at Ramathibodhi Hospital. After an electronic record review from 701 patients who were diagnosed with ICD10 code I49.0 (Ventricular fibrillation and flutter), I49.8 (Other specified cardiac arrhythmia e.g., Brugada syndrome, Long QT syndrome), and I49.9 (Cardiac arrhythmia, unspecified). Based on the presence of type 1 BrS pattern ECG with no other heart diseases, sixty-two BrS patients were identified 3 patients who had incomplete data for Shanghai score calculation at diagnosis and 5 patients who followed up less than 1 year were excluded. According to risk stratification from the study of Kawada (2018), 54 eligible patients (sudden cardiac arrest: n = 14, syncope: n = 30, nocturnal agonal respiration: n = 3, asymptomatic: n = 7) were classified into three groups based on their Shanghai score at diagnosis; Group A or very high risk (Score ≥5.5), Group B or high risk (Score 4-5) and group C or non-high-risk (Score ≤3.5). Arrhythmic events were defined as sudden cardiac death, appropriate shock or ATP delivery by an ICD, and/or documented VT/VF by conventional ECG. Device-related complications were defined as an inappropriate shock, device infection, leads and pocket-related complications. The study protocol was approved by the institutional Ethics committee of the Office of The Committee for Research Faculty of Medicine, Ramathibodi Hospital, Mahidol University.

Continuous variables are expressed as mean ± SD. Categorical variables are expressed as numbers and percentages. An unpaired *t*-test was used to test for significant differences between continuous variables, while chi-square or Fisher's exact tests were used for categorical variables. Survival and cumulative hazards were calculated using the Kaplan-Meier method. Differences between survival curves were compared using the log-rank test. All statistical analyses were performed using SPSS 23 for Windows. A *p-value* of less than 0.05 was considered statistically significant.

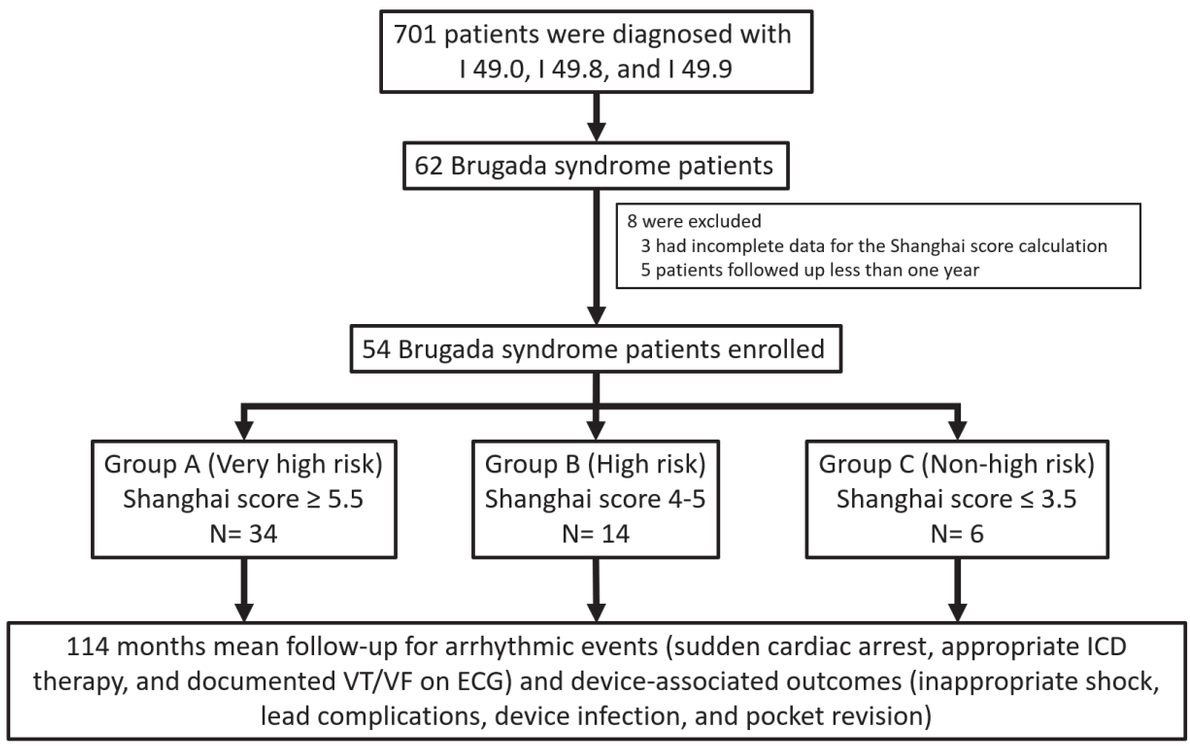

Figure 2 Flow chart of the patient population

Results

After an electronic record review of 701 patients with diagnosed ICD10 codes I49.0, I49.8, and I49.9, 62 BrS patients were identified. Three patients were excluded due to incomplete data for Shanghai score calculation at diagnosis and 5 patients were followed for less than 1 year. A total of 54 Patients (group A-score ≥ 5.5; n = 34, group B-score 4-5; n = 14, group C-score ≤ 3.5; n = 6) were followed up for 114.1 ± 63.2 months. Two Brugada patients with automated implantable cardioverter defibrillator (AICD) and Shanghai scores less than 3.5 were also included in group C. The mean age of diagnosis was 45.8 years and 98.1% of patients were male. Of all the patients who displayed type 1 ECGs that appeared spontaneously (n = 44), two were caused by febrile illness (n = 2) and seven were induced by sodium channel blockers (n = 7). Syncope and sudden cardiac arrest were common presenting symptoms and 31.5% of patients had a family history of sudden cardiac arrest or Brugada syndrome. Inducible ventricular fibrillation was demonstrated in 3 out of 8 asymptomatic patients in group A.

Table 2 Clinical characteristics of the study patients, according to Shanghai score group

Characteristics	All patients (N = 54)	Group A Very high risk (N = 34)	Group B High risk (N = 14)	Group C Non-high risk (N = 6)	P-value
Age, years	45.8 ± 13.2	45.35 ± 12.7	45.3 ± 16	49.3 ± 10.2	
Male	53 (98.1)	34 (100)	14 (100)	5 (83.3)	0.017
Shanghai score	5.4 ± 1.45	6.29 ± 0.91	4.42 ± 0.4	3.16 ± 0.6	
ECG 12 lead Spontaneous type 1 ECG	44 (81.5)	33 (97)	7 (50)	4 (66.7)	0.01
Fever-induced type 1 ECG	2 (3.7)	1 (2.9)	1 (7.1)	0 (0)	NS
Drug-induced type 1 ECG	8 (14.8)	0 (0)	6 (42.6)	2 (33.3)	0.001
Clinical history Cardiac arrest or VT/VF	14 (25.9)	14 (41.2)	0 (0)	0 (0)	0.004
Nocturnal agonal respiration	3 (5.6)	2 (5.9)	1 (7.1)	0 (0)	NS
Suspected arrhythmic syncope	22 (40.7)	18 (52.9)	4 (28.6)	0 (0)	0.029
Syncope of unclear mechanism	8 (14.8)	0 (0)	8 (57.1)	0 (0)	0
AF/AFL in patients < 30 yrs of age	1 (1.9)	0 (0)	1 (7.1)	0 (0)	NS
Family history in first- or second-degree relatives Definite Brs	4 (7.4)	4 (11.8)	0 (0)	0 (0)	NS
Suspicious SCD related to Brs	8 (14.8)	4 (11.8)	3 (21.4)	1 (16.7)	NS
Unexplained SCD at < 45 yrs of age	5 (9.3)	3 (8.8)	2 (14.2)	0 (0)	NS
Probable pathogenic mutation (SCN5A)	0 (0)	0 (0)	0 (0)	0 (0)	NS
LVEF (%)	64.7 ± 5.5	64.3 ± 5.2	63.4 ± 6.7	69 ± 3.67	NS
EPS	8 (14.8)	4 (11.8)	3 (21.4)	1 (16.7)	NS
Inducible VF	3 (5.6)	3 (8.8)	0 (0)	0 (0)	NS
AICD implantation	47 (87)	30 (88.2)	14 (100)	3 (50)	0.023
Follow-up, months	114.1 ± 63.2	124.18 ± 70.4	105.6 ± 42.3	77 ± 49	NS

Values are n (%) or mean ± SD

ECG = electrocardiogram; AF = atrial fibrillation; AFL = atrial flutter; BrS = Brugada syndrome; SCD = sudden cardiac death; VF = ventricular fibrillation; VT = ventricular tachycardia; LVEF = left ventricular ejection fraction; EPS = electrophysiologic study; AICD = automated implantable cardioverter defibrillator; NS = not significant

Overall, the mean Shanghai score was 5.4 ± 1.45. 63% of the patients were classified to group A or Shanghai score ≥ 5.5. AICD implantation was performed on 87% of patients, with higher prevalence in group A and group B (88.2% in group A, 100% in group B, and 50% in group C based on the patient's insistence to have the AICD implantation after discussion, $p = 0.023$).

Table 3 Outcomes of study patients, according to Shanghai score groups

Outcomes	All patients (N = 54)	Group A Very high risk (N = 34)	Group B High risk (N = 14)	Group C Non-high risk (N = 6)	P-value
Arrhythmic event	11 (20.4)	9 (26.5)	2 (14.3)	0 (0)	0.27
Sudden cardiac arrest	0 (0)	0 (0)	0 (0)	0 (0)	
Appropriate AICD therapy	10 (18.5)	9 (26.5)	1 (7.1)	0 (0)	0.13
Documented VT/VF	1 (1.9)	0 (0)	1 (7.1)	0 (0)	0.23
Inappropriate shock	5 (9.3)	2 (5.9)	3 (21.4)	0 (0)	0.17
Device-related complications	13 (24.1)	8 (23.5)	5 (35.7)	0 (0)	0.20
Lead fracture	5 (9.3)	3 (8.8)	2 (14.2)	0 (0)	0.59
CIED Infection	1 (1.9)	1 (2.9)	0 (0)	0 (0)	0.74
Pocket revision	2 (3.7)	2 (5.9)	0 (0)	0 (0)	0.53

Values are n (%)
AICD = automated implantable cardioverter defibrillator; VF = ventricular fibrillation; VT = ventricular tachycardia; CIED = cardiac implantable electronic device; NS = not significant

During the mean 114-month follow-up period, a total of 11 arrhythmic events occurred with one case of documented ventricular fibrillation by surface electrocardiogram. 10 patients had appropriate ICD therapy that led to radiofrequency ablations in three patients. Arrhythmic events were highest in group A (26.5%) followed by group B (14.3%) and none in group C. When comparing the very high-risk group (Shanghai score ≥5.5) to the cohort, the incidence of arrhythmic events was higher but did not reach statistical significance (26.5% vs 11.8%, $p = 0.147$, HR 2.44, CI 0.52-11.4, $p = 0.26$).

Non-high-risk patients with a Shanghai score ≤3.5 had no incidence of ventricular arrhythmic events, while those with a score >3.5 showed a trend towards an increase in arrhythmic events (22.2% vs 0%, HR = 4.85, CI 0.037-630.2, $p = 0.525$).

Device-related complications occurred in 13 patients, including 5 cases of lead fracture, 2 cases of pocket-related complications and one case of CIED infection. In addition, 5 patients experienced inappropriate shocks, with one associated with lead fracture, one resulting from electrocautery interference and one triggered by a supraventricular episode (1 case of atrial fibrillation, 1 case of supraventricular tachycardia and 1 case of sinus tachycardia).

Table 4 The annual incidence of ventricular arrhythmia stratified by Shanghai score and compared with another study[2]

Group	Shanghai score	Annual incidence of ventricular arrhythmia	
		Current study	S. Kawada (2018)[2]
Very high risk	≥5.5	2.8%	2.5%
High risk	4-5	1.5%	1.76%
Moderate risk	3.5	0%	0.68%
Low risk	<3.5		0%

Discussion

The present study demonstrated a difference in the frequency of ventricular arrhythmic events between different Shanghai score risk-predicting groups without genetic testing results. Compared to a previous study by S. Kawada in 2018, this study showed a comparable incidence of ventricular arrhythmia in the very high-risk group with a Shanghai score of ≥ 5.5 (26.5% vs 25%) and the high-risk group with a Shanghai score of 4-5 (14.3% vs 17.6%). Both studies confirm the usefulness of the Shanghai scoring system as a prognostic tool for managing BrS patients. Non-high-risk patients especially score less than 3.5 have very low incidence of ventricular arrhythmias.

Ventricular arrhythmia in our very high-risk group was lower compared to symptomatic BrS patients who presented with sudden cardiac arrest or syncope (26.5% vs 32.9%) in another study.[10] This may be due to the inclusion of asymptomatic patients with risk factors such as family history.

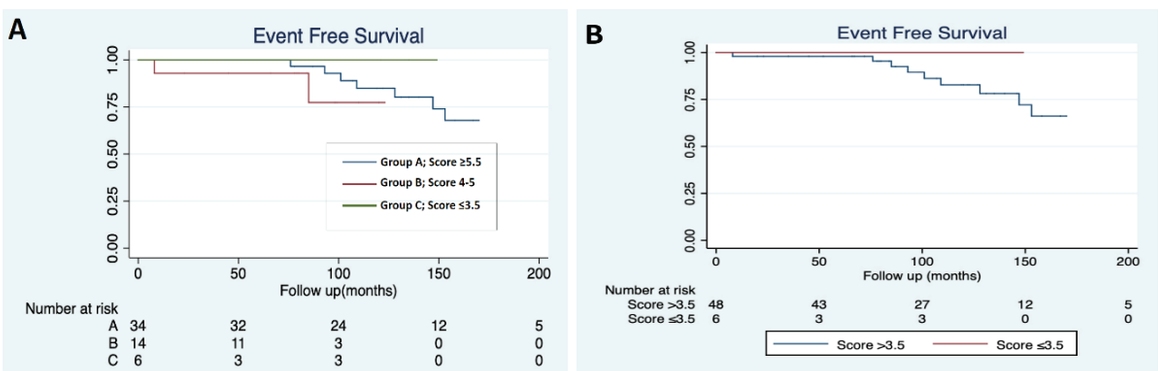

Figure 3 Cumulative event-free survival as a function of score, (A) Event-free survival of the entire cohort classified by the group, (B) Event-free survival is classified by intermediate-low risk (Shanghai score ≤ 3.5) compared to the higher risk group (Shanghai score > 3.5)

There were no ventricular arrhythmic events observed in non-high-risk patients. However, survival analysis demonstrated a trend towards an increased ventricular arrhythmic event in patients with a Shanghai score of more than 3.5 or higher risk (22.2% vs 0%, HR= 4.85, CI 0.037-630.2, $p = 0.525$). The validation of this cutoff could not be proved by this study due to the very small number of lower risk population, resulting in no ventricular arrhythmic events and a wide range of hazard ratios. Therefore, the generalization of these results is limited and requires further studies with larger populations in the intermediate and low-risk groups.

Moreover, this study rarely performed genetic tests (only 2 cases, with negative results). This may have made Shanghai scores in our cohort lower than in other studies. However, our study results may reflect the feasibility of using clinical-based, non-genetic testing Shanghai score for risk stratification, which may be applicable to countries with limited resources like Thailand. A further study with a larger cohort is needed to confirm the true accuracy of this method.

This study has certain limitations. Firstly, BrS had no specific diagnosis based on the ICD-10 code, which may have led to missed cases during enrollment. The majority of the patients in this study were very high risk with a very high Shanghai score, which limits the generalizability of this study to the true populations of BrS. Further studies with a larger number of intermediate and low-risk patients may provide more helpful data for using the Shanghai scoring system to identify patients who will benefit from ICD, and to reassure asymptomatic low-risk BrS patients.

Conclusion

Risk stratification by the Shanghai scoring system, without genetic testing, may be useful in predicting ventricular arrhythmic events in BrS patients in Thailand.

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Review Article

Health Risks and Concerns Associated with E-cigarettes (ECs) and Heated Tobacco Products (HTPs): A Comprehensive Review

Sombat Muengtaweepongsa

Introduction

E-cigarettes (ECs) and heated tobacco products (HTPs) are alternatives to traditional combustible cigarettes and operate on different principles. ECs, also known as electronic cigarettes or vapes, heat a liquid, often called e-liquid or vape juice, to produce an aerosol that users inhale. The e-liquid typically contains a base chemical such as propylene glycol (PG) or vegetable glycerin (VG), a carrier for nicotine, flavorings and other additives. When the liquid is heated, it vaporizes, creating an aerosol that users inhale into their lungs. ECs come in various forms and designs. Initially, cigar-like devices resembled traditional cigarettes in size and shape. These early models were often low-power and disposable. Additionally, small devices using high-concentration nicotine salt pods gained popularity, as did disposable ECs discarded after use.[1] On the other hand, HTPs heat specially designed sticks or cartridges of processed tobacco, usually at lower temperatures than traditional combustion. This process, called pyrolysis, releases the active compounds in the tobacco, which are then inhaled as an aerosol by the user.[2]

While ECs and HTPs are considered alternatives to smoking, they still carry potential health risks. The long-term effects of using these products are still being studied, and their use among certain populations worldwide, including Thailand, such as youth and non-smokers, is a concern.[3-5] According to the National Health and Nutrition Examination Survey (NHANES) data from 2013 to 2014, the prevalence of ECs/HTPs use among adolescents in the United States was reported to be 1.21%. It was estimated that this percentage represented around 236,000 U.S. adolescents.[6]

The typical ECs/HTPs liquid composition, consisting of various substances, are found in vaping aerosols. ECs/HTPs liquid, used to create the aerosol vapor in ECs/HTPs, consists of several components. The solvent carriers comprise the most liquid, usually propylene glycol (PG) and/or vegetable glycerin (VG). These solvents help create the aerosol when heated. In ECs/HTPs liquid, water is also found in smaller proportions (around 20%).[7] Flavoring substances are added to enhance the taste of the aerosol vapor and generally account for approximately 10% of the ECs/HTPs liquid composition. Nicotine, the addictive component of tobacco products, is typically included in ECs/HTPs liquid, albeit at varying concentrations. It's important to note that nicotine levels in ECs/HTPs liquid can vary widely depending on the product and user preferences. When ECs/HTPs liquid is heated and vaporized, it forms vaping-derived aerosols, which the user inhales. The aerosols contain the constituents of the ECs/HTPs liquid that may be concerning from a health perspective. These include

Faculty of Medicine, Thammasat University, Pathum Thani, 12121, Thailand

formaldehyde and acrolein, produced as byproducts of the heating process and can harm health.[8] Additionally, vaping-derived aerosols may contain trace amounts of potentially harmful substances, such as heavy metals (e.g., lead, cadmium), phenolic compounds and polycyclic aromatic hydrocarbons (PAHs). These substances can be present due to various factors, including the materials used in the ECs/HTPs device and the heating process.[9, 10]

Of the reported health risks, several cross-sectional studies of teenagers have found associations between ECs/HTPs use, increased risks of bronchospasm symptoms and asthma-related school absenteeism.[11, 12] These studies suggest that there may be a link between ECs/HTPs use and negative respiratory health outcomes in young people. Furthermore, similar associations between ECs/HTPs use and self-reported chronic respirational disorders have been described in adults.[13] This indicates that the potential respiratory risks associated with ECs/HTPs may extend beyond the adolescent population. When it comes to clinical trials specifically focusing on the respiratory changes resulting from ECs/HTPs exposure, the results have been mixed. Some early studies have not found impaired pulmonary outcomes.[14,15] However, latter studies reported significant lung damage following ECs/HTPs use.[16, 17]

Significant concern has arisen due to the increased incidence of a condition known as ECs or vaping product use-associated lung injury (EVALI). EVALI is a severe lung injury recognized as a nationwide outbreak in the United States. This outbreak has raised significant alarm about the potential acute respiratory risks of ECs/HTPs use. [18]

Increasing evidence suggests a potential link between using ECs/HTPs and adverse effects on cardiovascular health. Several studies have indicated an association between ECs use and an increased risk of cardiovascular diseases, including myocardial infarction.[19] Numerous studies have focused on investigating the acute effects of ECs/HTPs on vascular function using different biomarkers. These biomarkers include flow-mediated dilation, circulating endothelial progenitor cells, pulse wave velocity and others. The findings from these studies have provided evidence indicating that ECs/HTPs use can cause vascular harm. The observed transient abnormalities in these biomarkers may be attributed to the pharmacological effects of nicotine. Nicotine is a vasoactive substance found in ECs/HTPs aerosols and it can constrict blood vessels and affect endothelial function, thereby impairing vascular health. The presence of nicotine in ECs/HTPs aerosols has been associated with hemodynamic instabilities following acute exposure, such as increased pulse rate, elevated blood pressure and cardiac sympathetic activation. These findings suggest that the adverse cardiovascular effects associated with its use, such as changes in vascular function and hemodynamics, may be influenced by the presence of nicotine. Nicotine, an addictive substance, is known to have various physiological effects on the cardiovascular system. Its stimulant properties can lead to increased pulse rate and blood pressure and activation of the sympathetic nervous system, which controls the body's "fight or flight" response.[20, 21]

ECs/HTPs in traditional smoking cessation

Many ECs/HTPs advertising campaigns claim that they can help individuals quit smoking. However, the effectiveness of ECs/HTPs as a smoking cessation tool is a topic of ongoing debate and research. While some studies have found that ECs/HTPs with nicotine can help manage withdrawal symptoms during quit attempts, it is important to note that this does not automatically translate into long-term smoking cessation success.[22] Quitting smoking is a complex process involving more than managing withdrawal symptoms. It often requires a structured plan, behavioral support and a comprehensive approach to address addiction's psychological and social aspects.[23]

Moreover, research has shown a tendency toward dual use of ECs/HTPs and conventional cigarettes rather than complete substitution or cessation of smoking. This means many individuals who start using ECs/HTPs continue to smoke traditional cigarettes alongside ECs use. A cross-sectional study using The National Health and Nutrition Examination Survey (NHANES) database of the US population from 2015 to 2018 showed that dual smoking was the highest among the smoking population at 61%, while the ECs and traditional were 10 and 30%, respectively.[24]

It is crucial to consider that scientific understanding of ECs/HTPs and their efficacy as smoking cessation tools is evolving. While some studies suggest potential benefits in certain contexts, others have raised concerns about the long-term health effects and the impact of ECs/HTPs on overall smoking behaviors.

ECs/HTPs as a risk of stroke

The Behavioral Risk Factor Surveillance System (BRFSS), an annual survey conducted by the Centers for Disease Control and Prevention (CDC) to collect data on various health-related behaviors and chronic conditions among adults in the United States, reported that ECs/HTPs use leads to increased risk of not only myocardial infarction but also stroke.[25]

The experimental animal study showed that acrolein in ECs/HTPs products could trigger NOX-2 -driven oxidative stress in the cerebrovascular system, leading to inflammation. This implies a potential mechanism through which ECs/HTPs use, specifically the presence of acrolein, may contribute to cerebrovascular diseases.[26]

The NHANES cross-sectional study from 2015 to 2018 showed that individuals who use ECs/HTPs have 1.15 times higher odds of having a stroke history than traditional smokers. Similarly, individuals who use both ECs/HTPs and traditional cigarettes (dual smokers) have 1.14 times higher odds of having a stroke history than traditional smokers.[24] Another cross-sectional study using the NHANES database during a similar period showed that current ECs/HTPs use is associated with elevated triglycerides and reduced HDL-cholesterol. Moreover, former ECs/HTPs use is associated with elevated fasting glucose, reduced HDL-cholesterol and elevated blood pressure. Also, dual users have higher odds of having metabolic syndrome than never-smokers. They also have elevated triglycerides and reduced HDL-cholesterol compared to never-smokers. Furthermore, dual users are likelier to have metabolic syndrome and reduced HDL-cholesterol than exclusive traditional cigarette users.[27]

Another retrospective cross-sectional study based on the NHANES database from 2013 to 2018 showed that ECs/HTPs use is associated with higher odds of cerebrovascular disease or stroke when compared to other substance use disorders. According to the study, ECs/HTPs use is associated with an odds ratio of 2.03, suggesting that individuals who use ECs/HTPs have more than twice the odds of experiencing cerebrovascular disease or stroke compared to individuals with other substance use disorders.[28]

ECs/HTPs as brain toxicity

ECs and HTPs use remain a relatively recent phenomenon and scientific research often requires time to catch up with emerging trends and technologies. While awareness of the potential hazards associated with ECs and HTPs usage is growing, understanding its brain-toxic effects remains limited.[29] However, a few studies have specifically addressed the brain toxicity of ECs/HTPs, particularly in brain development. An animal study demonstrated that dams (mother mice) were exposed to ambient air and ECs/HTPs aerosols, with some aerosols containing nicotine and others without nicotine. The exposure occurred during and after pregnancy. Offspring from dams exposed to ECs/HTPs aerosols showed deficits in short-term memory compared to offspring exposed to ambient air. This suggests that maternal ECs/HTPs exposure negatively impacted the offspring's cognitive abilities. The study suggests that the observed memory deficits in the offspring were likely caused by nicotine, as the effect was stronger when compared to the group exposed to ECs/HTPs aerosols without nicotine. Interestingly, both groups exposed to ECs/HTPs aerosols, with and without nicotine, showed reduced anxiety levels, as observed in elevated plus maze tests. This implies that other constituents in ECs/HTPs aerosols might have brain-toxic effects related to anxiety regulation.[30]

Exposure to nicotine-free ECs/HTPs aerosols was found to increase global DNA methylation soon after birth significantly. This suggests that the aerosols, even without nicotine, impacted epigenetic modifications (chemical modifications to DNA) that can influence gene expression and cellular function. The study also indicates that the exposure affected histone acetyltransferases, enzymes involved in gene regulation. Additionally, changes were

observed within genes linked to neurological activity, suggesting potential effects on brain function and development.[31]

Numerous studies highlight the potential toxicity of solvent carriers, such as propylene glycol (PG) and vegetable glycerin (VG), in ECs/HTPs liquids. As mentioned earlier, solvent carriers, specifically PG and VG, make up a significant proportion (> 3/4) of the e-liquid used in e-cigarettes. These solvents are responsible for creating the aerosol when heated. When heated in an ECs device at temperatures ranging from 150 to 350 °C, both PG and VG undergo pyrolysis, producing mist or aerosol. This aerosol contains various toxic carbonyl compounds, including acrolein, acetaldehyde and formaldehyde.[32] The carbonyl compounds generated during vaping, particularly formaldehyde, are associated with neurotoxic effects. Formaldehyde is a known environmental neurotoxicant linked to neurodegeneration. At high voltages (e.g., 5V), formaldehyde can react with ECs/HTPs solvents to form potentially toxic formaldehyde hemiacetal.[33] Acrolein, another carbonyl compound found in ECs aerosols, is a common environmental pollutant known for its pro-inflammatory and pro-oxidative properties. It has been linked to neurodegeneration.[34] Acetaldehyde, also present in EC aerosols, has been shown to exhibit neurotoxic effects through mechanisms such as oxidative stress, calcium dyshomeostasis and activation of NMDA receptors.[35] Pyrolysis of solvent carriers in ECs/HTPs vapor can produce other hazardous compounds. For example, glycidol is considered a developmental neurotoxicant. Compounds like glyoxal and methylglyoxal also act as potent glycating agents that contribute to developing advanced glycation end-products (AGEs) linked to neurodegeneration.[36]

Vitamin E acetate has been detected in most tetrahydrocannabinol (THC)-containing products and lung fluid samples from patients with EVALI.[37] This suggests a possible link between vitamin E acetate and the occurrence of this vaping-related illness. According to the U.S. Food and Drug Administration (FDA) reports, outbreak-associated THC products have been found to contain vitamin E acetate at an average concentration of 50%, ranging from 23% to 88%.[38] It is used as a solvent for THC due to its similar viscosity. Vitamin E acetate is commonly used in dietary supplements and cosmetics and when ingested, it has not been associated with adverse health outcomes. It is generally recognized as safe (GRAS) for ingestion. However, the safety profile of vitamin E acetate inhalation, particularly in aerosolized forms like those found in ECs/HTPs, is poorly understood. There is a lack of studies investigating the effects of inhaling aerosolized vitamin E acetate specifically. In animal studies conducted with rats, it has been observed that inhalation of vitamin E acetate did not have the same protective effect as vitamin E in attenuating the inflammatory response to bacterial lipopolysaccharide toxicity in the lungs. This suggests that there may be differences in the effects of vitamin E acetate when inhaled compared to other forms of vitamin E.[39] Additional research is necessary to examine the potential health effects of inhaling aerosolized vitamin E acetate and its lung and other organs toxicity. The safety and risks associated with its inhalation are still not well understood.

Flavorings are crucial in attracting ECs/HTPs users, including youth and individuals with little or no smoking experience. Flavored products are more likely to initiate vaping among these populations. A recent study suggests that popular flavor substances in ECs/HTPs may trigger a reward mechanism in mice, indicating their potential role in enhancing the pleasurable experience of vaping.[40] Flavorings in ECs/HTPs have become a major focus for regulatory authorities due to concerns raised by the outbreak of EVALI and fatal cases, particularly among young ECs/HTPs users. [41] This has prompted increased attention to regulating the availability and use of flavored products. Hundreds of flavor substances have been detected in e-liquids, with some in most commercial ECs/HTPs products. While flavorants used in food products are GRAS, their aerosolized and inhaled safety is often poorly understood. Most flavor substances have only been tested for safety through ingestion and chronic exposure and their potential risks when inhaled as aerosols are often unrecognized.[42] Multiple studies have suggested that the high number and concentration of flavor substances in e-liquids are critical for their cellular and brain toxicity[42, 43] However, no differences in neurobehavioral outcomes have been observed among various flavors in mice.[30] Currently,

research is lacking in addressing the brain toxicity of ECs/HTPs -derived flavoring substances.

Various organic compounds, including toluene, p,m-xylene, ethyl acetate, benzene, ethanol and methanol, have been found in e-liquids. Some of these compounds have been detected in e-liquids at levels exceeding established safety limits, indicating potential health risks associated with inhalation.[44] It's important to note that these organic compounds in e-liquids raise concerns about potential health risks, including brain toxic effects. Further research is needed to understand better the extent of exposure and the specific health implications of these compounds when inhaled through ECs/HTPs. Regulatory authorities and scientific communities continue to investigate and assess the safety of these substances in relation to ECs/HTPs use.

Several brain-toxic heavy metals, including arsenic (As), cadmium (Cd), lead (Pb), manganese (Mn), zinc (Zn), nickel (Ni), aluminum (Al), tin (Sn), chromium (Cr) and copper (Cu), have been found in ECs/HTPs vapors.[45] These metals primarily originate from components of the ECs/HTPs atomizer, such as the metallic coil, but may also be present in e-liquids. ECs-derived metals can contribute to an overall increase in the body's internal dose of these metals. Studies have demonstrated increased internal doses of chromium (Cr), nickel (Ni), cadmium (Cd) and lead (Pb) among its users.[46] ECs users have been found to have higher serum levels of selenium (Se), silver (Ag), vanadium (V), lanthanides and other rare earth elements.[47] Many metals detected in ECs/HTPs vapors exhibit brain-toxic properties when inhaled, indicating potential risks to the nervous system.[29]

All potential brain toxicity caused by e-cigarettes (ECs) and heated tobacco products (HTPs) is shown in Figure 1.

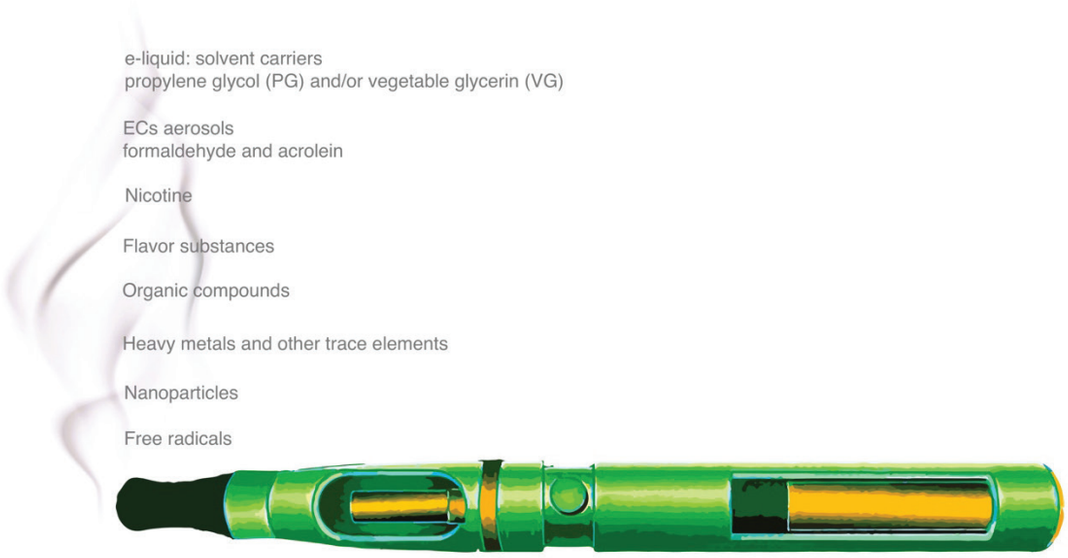

Figure 1 Potential brain toxicity caused by e-cigarettes (ECs) and heated tobacco products (HTPs)

Conclusions

E-cigarettes (ECs) and heated tobacco products (HTPs) are alternative products to traditional combustible cigarettes that operate on different principles. ECs heat a liquid to produce an aerosol, while HTPs heat specially designed sticks or cartridges of processed tobacco. Both ECs and HTPs carry potential health risks and the long-term effects of their use are still being studied. Concerns exist about their use among certain populations, including youth and non-smokers. ECs/HTPs liquid composition typically includes solvents (propylene

glycol and vegetable glycerin), flavorings, nicotine and other additives. Heating the liquid can produce aerosols containing potentially harmful substances such as formaldehyde, acrolein, heavy metals, phenolic compounds and polycyclic aromatic hydrocarbons (PAHs). Studies have found associations between ECs/HTPs use and increased risks of respiratory symptoms, asthma-related school absenteeism and chronic respiratory disorders in both adolescents and adults. However, results from clinical trials focusing on respiratory changes resulting from ECs exposure have been mixed. The e-cigarette or vaping product use-associated lung injury (EVALI) outbreak raised significant concerns about the acute respiratory risks of ECs/HTPs use. Evidence suggests a potential link between ECs/HTPs use and adverse effects on cardiovascular health, including an increased risk of cardiovascular diseases such as myocardial infarction. The presence of nicotine in ECs/HTPs aerosols can contribute to vascular harm and adverse cardiovascular effects. The effectiveness of ECs/HTPs as a smoking cessation tool is still debated and many individuals tend to engage in dual use, using both ECs/HTPs and traditional cigarettes. ECs/HTPs use has been associated with an increased risk of stroke and cerebrovascular diseases. Acrolein, a compound found in ECs/HTPs products, may trigger oxidative stress and inflammation in the cerebrovascular system. Research suggests that ECs and HTPs use may have brain-toxic effects, including cognitive deficits, epigenetic modifications and potential neurotoxicity related to solvent carriers, such as propylene glycol and vegetable glycerin. The safety and risks of inhaling aerosolized vitamin E acetate, a substance found in some ECs/HTPs products, are poorly understood. Flavorings significantly attract ECs/HTPs users, particularly youth, but their safety when inhaled as aerosols is often poorly understood. The high number and concentration of flavor substances in e-liquids may contribute to cellular and brain toxicity.

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Review Article

Mindfulness-Based Cognitive Therapy in Psychiatric Disorders : Basic Knowledge with a 2023 Update

Lampu Kosulwit*

Abstract

Introduction: Mindfulness meditation, rooted in Buddhism, has become Mindfulness-Based Cognitive Therapy (MBCT), an evidence-based depression treatment, but its efficacy in other psychiatric conditions remains uncertain.

Methods: The assessment of MBCT's effectiveness in psychiatric disorders was carried out through the examination of Clinical Practice Guidelines (CPGs) and relevant research articles. A search restricted to meta-analyses and systematic reviews was conducted in the PubMed database, covering the period from January 2015 to May 2023.

Results: This search uncovered one network meta-analysis, 13 meta-analyses and 2 systematic reviews regarding the effectiveness of MBCT. MBCT demonstrates additional effectiveness in preventing long-term depression relapse, addressing sleep issues in patients with depression and anxiety and providing a short-term anxiolytic effect.

Conclusions: There is insufficient evidence for the effectiveness of MBCT in treating other psychiatric disorders. Future studies should concentrate on assessing the effectiveness of each mindfulness technique to discern their active ingredients.

Keywords: Mindfulness, Cognitive Behavioral Therapy, Mindfulness-based intervention, Psychotherapy, Mental disorders, Psychiatric illnesses

Department of Psychiatry, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand

* **Corresponding author:** Lampu Kosulwit, M.D., Department of Psychiatry, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand, Tel. +668 14893558, +6629269204-5 Email: klampu@tu.ac.th

Introduction

A form of Evidence-based psychotherapy, Mindfulness-Based Cognitive Therapy (MBCT), has gained recognition and support from mental health professionals and researchers worldwide. MBCT is considered an effective therapeutic approach for individuals with depression[1-2] and has been recommended as a treatment option for various clinical conditions such as anxiety disorder, post-traumatic stress disorder, suicidal ideation, post-stroke depression, insomnia and pain in patients with cancer.[3-7]

Background and Basic Knowledge about MBCT [8]

MBCT is a form of scientific-based psychotherapy developed by Zindel Segal, Mark Williams and John Teasdale in the 1990s. It is based on Mindfulness-based Stress Reduction (MBSR) combined with Cognitive Behavioral Therapy (CBT) for depression.

Cognitive Behavioral Therapy (CBT) for depression was first developed by Aaron T. Beck using clinical research principles at the University of Pennsylvania in the 1960s. In 1979, Mindfulness-based Stress Reduction (MBSR) was applied for stress management by Jon Kabat-Zinn at the University of Massachusetts Medical School. It was the first scientific Western mindfulness intervention and its benefits are widely recognized in the clinical psychology discipline. Subsequently, Vipassana Meditation, rooted in Theravada Buddhism as an integral part of the MBSR, was scientifically developed in the name of MBCT. The general goal of mindfulness is to improve self-introspection through self-awareness, self-integrity, self-knowledge and equanimity. The goal of mindfulness in MBCT is to improve one's metacognition.

With MBCT a person becomes more aware of their thoughts, emotions and bodily sensations with non-judgmental acceptance, without evaluating or reacting. MBCT started to prevent relapses in depressed patients, who were prone to ruminating negative thoughts leading to relapse depression. It helps depressed patients recognize their depressogenic thinking and negative ruminations, which helps break the cycle as they understand how distressed automatic thoughts lead to unhealthy moods and responses. They perceive and accept the inner experience of emotional and mental processes which naturally arise and disappear. This essential component of MBCT can also be applied to other mental illnesses.

Therapeutic modality of MBCT

The MBCT process usually consists of 8 sessions per course. Each session lasts approximately 2-2.5 hours and daily practice at home is 30-45 minutes between sessions. The process of MBCT includes the following:

Psychoeducation: The first session of MBCT involves studying mindfulness and its relationship to cognitive and emotional processes, as well as introducing the rationale for using mindfulness in mental health treatment.

Formal Mindfulness Training: The core of MBCT involves learning and practicing mindfulness, including sitting meditation, mindfulness of breath, body scanning, loving-kindness meditation and mindful movement for focused awareness of routine daily activities. These involve focusing on the present moment, non-judgmental observation of thoughts and emotions, and developing a perception that is not responsive to inner experience.

Cognitive restructuring: This involves identifying and challenging negative thought patterns that lead to distress and developing more adaptive ways of thinking. "By identifying and modifying negative thought patterns, individuals can prevent or reduce mental disorder relapse"

Group Discussion: In each session, participants have opportunities to discuss their experiences with both formal and home mindfulness practices, and any challenges or ideas they had during the week.

Home Practice: Participants are encouraged to practice daily mindfulness for 30-45 minutes per session. This reinforces the skills learned in group sessions and fosters continued growth and change.

Group and Individual MBCT Studies show no significantly different primary or secondary outcomes between group MBCT (gMBCT) and individual MBCT (iMBCT).[9] Therefore, MBCT treatment can be performed either as a group or individually. In both forms, the patient must attend the formal form, with a session 2-2.5 hours/time/week for 8 weeks.

Group therapy (gMBCT): The therapist leads a client group (8-12 participants) to practice diverse mindfulness techniques and discussions. Clients learn from others' experiences and create a sense of connection with the group.

Individual therapy (iMBCT): Treatment sessions are of the same format and duration as group sessions, but therapy is tailored to that individual. This iMBCT was first applied particularly for patients who were unable to participate in group sessions due to disabilities, severe illness, pain, or fatigue. It allows more focus on specific issues and more flexible scheduling.

An important limitation to the success of MBCT

As we know, exercise is not something everyone seeks out. Likewise, mindfulness is like an exercise for the mind. The same is true for mindfulness in which everyone has a different motivation to practice continuously particular psychiatric patients. The true obstacle to success in MBCT is a lack of motivation, particularly the practice of sitting still. [10,11] Studies reported a rate of engagement at the first MBCT session around only 50% in depressive patients. The drop-out rate of participants was nearly 20% before they reached an adequate dose of treatment (defined as four sessions).[10]

Update of trial evidence in MBCT

Many preliminary MBCT studies found positive outcomes in various physical conditions, e.g., post-stroke depression, vascular disease, cancer, systemic lupus erythematosus, diabetes, dementia and mental disorders. However, repeatable higher-quality randomized controlled trials are required to confirm these findings. MBCT is definitely an effective treatment for depression, but further study is underway, particularly of long-term effects. New research is also investigating positive effects in other psychiatric illnesses e.g. different anxiety disorders, psychosis, post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), somatic symptom and related disorders and substance use disorders.[7] This study is a narrative review of mindfulness-based cognitive therapy to treat psychiatric conditions. The question is: What current evidence suggests MBCT can treat psychiatric patients?

Method of review: This review focused on recent publications regarding MBCT effectiveness, such as Clinical Practice Guideline (CPG), meta-analytic and systematic review studies. The search used time limits and psychiatric diagnoses with no limiting the age of patients. ***The inclusion criteria*** were 1. mindfulness-based cognitive therapy or MBCT 2. PubMed 3. human 4. the English language with the full version available. ***The exclusion criteria*** were 1. non-psychiatric subjects such as psychologically vulnerable or healthy subjects and people with physical illnesses, 2. preprint

The steps of the review

Step 1 CPG related to MBCT is searched on Google and found 4 CPGs of NICE (The National Institute for Health and Care Excellence), CANMAT (Canadian Network for Mood and Anxiety Treatments), RANZCP (The Royal Australian and New Zealand College of Psychiatrists) and APA (American Psychiatric Association).

Step 2 PubMed database was searched with the filter of meta-analysis, systematic review with a period of 1/1/2022-26/5/2023. The first result articles were 110 and manually excluded 98 papers by not meeting the inclusion criteria. The included papers were 12 (10 meta-analyses, 2 systematic reviews).

Step 3 PubMed database was searched with the filter of Meta-analysis with a period of 1/1/2015-31/12/2021. The first results were 43 and manually excluded 39 papers by inclusion/exclusion criteria. The studies with the same psychiatric conditions or research aim for any depressive conditions as in Step 2 were not included to review. The final included articles were 3 meta-analyses and one network meta-analysis.

The results of the most updated studies and details about MBCT are shown in ***Table 1***.

Evidence of CPGs and Meta-analyses:

Mood and related conditions: A network meta-analysis showed MBCT is equally effective as in TAU [Treatment as Usual = Antidepressants and/or CBT)] for patients with acute mild-moderate depression, including a 12-month maintenance period for recurrence depressive patients. There was no current good evidence to support that MBCT use helps depressed patients with suicidal ideation. Meta-analysis showed that MBCT might improve depression and anxiety symptoms in bipolar disorders and not alleviate manic symptoms in bipolar disorder.

Other psychiatric conditions: MBCT has a role of adjunctive treatment in generalized anxiety disorder and panic disorder. MBCT was also recommended in children and adolescents with social anxiety disorder. The effectiveness of MBCT in specific phobia, adult social anxiety disorder, agoraphobia, OCD, PTSD, somatic symptom disorders, substance use disorders and psychosis, was limited by included studies of each meta-analysis.

Evidence of 2 systematic reviews:

The first Cochrane systematic review of 29 RTCs of psychological interventions (N = 2599) on MCI and dementia, which included 2 RCTs of MBCT (n = 90) showed inadequate data to conclude the effectiveness of MBCT on reducing depressive and anxiety symptoms in patients with mild-moderate dementia. The second review showed the undetermined positive effect of MBCT on PTSD due to different combined treatments in the included 4 studies (only one RCT).

Table 1 Summarized results of MBCT effectiveness in Psychiatric conditions [1/1/2015 - 26/5/2023 of PubMed database]

Conditions	Authors (Year), Origin	Studies	Year of included meta-analyses	N meta-analyses	N Partici-pants	Summary results	Limitation of studies	Evidence of MBCT in psychiatric disorders
Major depressive disorder **- Relapse prevention** **- Recurrent depression** **- Residual depressive symptom**	RANZCP (2015) Australia[12]	CPG				Role as a relapse prevention intervention, particularly amongst patients with recurrent ≥3 depressive episodes.		Recommended
	CANMAT (2016) Canada[2]	CPG				1st line: Maintenance treatment (Level 1 Evidence) for recurrent MDD (relapse prevention). 2nd line: Alternative to long-term maintenance antidepressant treatment (Level 2 Evidence). 2nd line: Adjunctive treatment (Level 2 Evidence) for acute depression.		Recommended
	NICE (2022) UK[1]	CPG				Relapse prevention therapy for remitted depression with a two-year high-risk of relapse (effective and cost-effective compared to TAU) Can be used as an adjunct to TAU or as an alternative treatment in cases of a ntidepressant discontinuation		Recommended
	APA (2019)[13], (2021) USA	CPG				1. Initial treatment: Unable to recommend MBCT as monotherapy for initial treatment, despite having at least one strong piece of evidence. The patient should share decision-making with therapeutic options. BUT MBCT was recommended as 1st line psychotherapy treatment for mild to moderate major depressive disorder. 2. Relapse prevention: There was insufficient evidence to be able to recommend MBCT rather than TAU.		Recommended (combined with TAU in the initial treatment) Insufficient evidence (In relapse prevention)

Table 1 Summarized results of MBCT effectiveness in Psychiatric conditions [1/1/2015 - 26/5/2023 of PubMed database] (Cont.)

Conditions	Authors (Year), Origin	Studies	Year of included meta-analyses	N meta-analyses	N Partici-pants	Summary results	Limitation of studies	Evidence of MBCT in psychiatric disorders
Prevention and time to depressive relapse	McCartney M. (2021) UK[14]	NMA	Up to June 2019	17RCTs from 23 included papers	2077 of 14RCTs (relapse depression) 2017 of 13RCTs (time to relapse)	Depression-related outcomes and follow-up at ≥12 months. Statistically significant long-term effectiveness of MBCT over TAU for relapse of depression (RR = 0.73, 95% CI 0.54 to 0.98) and for time to relapse of depression (MBCT vs TAU: HR = 0.57, 95% CI 0.37 to 0.88; MBCT vs placebo: HR = 0.23, 95% CI 0.08 to 0.67).	Some heterogeneity in some of the analyses.	Strong
MDD with multiple episodes, Sui-cidal ideation	Hui-Wen Tseng (2023) USA[15]	S&M of RCTs	2008-2019	9 RCTs	1327	Based on this meta-analysis, MBCT sessions lasting 1.5-2.5 h, five times per week for 8 weeks can effectively relieve depression and suicidal ideation indicators of MDD patients. MBCT is an effective way of preventing and improving block rumination for MDD patients.	High Heterogeneity. Constrained statistical power. (Q =29.654, p =0.000, I^2 = 83.139)	n/a
Suicidal ideation in patients with depression	Zhang B (2022), China[5]	S&M of RCTs (compared between MBCT and TAU groups using a random-effects model)	2000-Aug.2021	7 RCTs	479	A significant benefit of MBCT is to improve suicidal ideation in a specific patient group. Block rumination.	High hetero-geneity of 7 RCTs. Unknown long-term effect.	n/a

Table 1 Summarized results of MBCT effectiveness in Psychiatric conditions [1/1/2015 - 26/5/2023 of PubMed database] (Cont.)

Conditions	Authors (Year), Origin	Studies	Year of included meta-analyses	N meta-analyses	N Partici-pants	Summary results	Limitation of studies	Evidence of MBCT in psychiatric disorders
Bipolar disorders de-pression	RANZCP (2020), Australia[16]	CPG				Lack of adequately powered randomized trials means MBCT cannot as yet be recommended for improving cognitive function, emotional regulation, and symptoms of anxiety, depression, and mania in bipolar disorder.		Insufficient evidence
	CANMAT (2018), Canada[4]	CPG	2018	1 RCT (2013)[6] reference in CPG(n = 95) 2 small studies: 1 systematic review (2016) (n = 62 of MBCT)[17] 1 controlled fMRI study (2013)[18]		1 RCT - less anxiety and depressive symptoms in the MBCT arm. - but no difference in relapse prevention compared to a TAU group.[6] 2 small MBCT studies: have a role in reducing anxiety.[17,18]	Only one RCT	Insufficient evidence
	Xuan R (2020), China[19]	S&M	2020	7 uncontrolled trial studies 3 controlled trial studies		Do not alleviate mania. Subgroup analysis: depression and anxiety significantly improved at 3 months post-intervention but not at 12 months. In between-groups analysis: significantly reduced depression but not anxiety.	Limitation of meta-analysis power.	Moderate evidence of positive effect on depressive and anxiety symptoms in bipolar disorder

Table 1 Summarized results of MBCT effectiveness in Psychiatric conditions [1/1/2015 - 26/5/2023 of PubMed database] (Cont.)

Conditions	Authors (Year), Origin	Studies	Year of included meta-analyses	N meta-analyses	N Partici-pants	Summary results	Limitation of studies	Evidence of MBCT in psychiatric disorders
Generalized anxiety disorder (GAD)	CANMAT (2014), Canada[20]	CPG	2014			MBCT has demonstrated efficacy for the treatment of GAD as adjunctive treatment		Recom-mended
	Ghahari (2020), Iran[21]	S&M	up to November 2018	6 (various clinical trials: mean revised Jadad score of 4.3)	403	Effective intervention for GAD. The overall risk ratio for MBCT vs controls was 0.65. No evidence of publication bias.	Small number of included studies. Neglected evidence of heterogeneity between individual studies with the reason of vast cultural differences between countries of studies.	Strong
Panic disorder	CANMAT (2014), Canada[20]	CPG	2014			Adjunctive therapy with medication to reduce depression and anxiety.		Recom-mended
Social anxiety disorder in child and adolescents	CANMAT (2014), Canada[20]	CPG	2014			CANMAT indicated that MBCT has demonstrated efficacy in treating social anxiety disorder (SAD) in children and adolescents.[22]		Recom-mended

Table 1 Summarized results of MBCT effectiveness in Psychiatric conditions [1/1/2015 - 26/5/2023 of PubMed database] (Cont.)

Conditions	Authors (Year), Origin	Studies	Year of included meta-analyses	N meta-analyses	N Partici-pants	Summary results	Limitation of studies	Evidence of MBCT in psychiatric disorders
Social anxiety disorder, Agoraphobia, Specific phobia, OCD, PTSD	CANMAT (2014), Canada[20]	CPG	2014			No strong suggestion of MBCT for Social anxiety disorder, Specific phobia, OCD and PTSD in CANMAT. CANMAT referred S&M of MBT (= MBSR+MBCT) which studied MBT for reducing anxiety symptoms and depressive symptoms.[23]	Individual patients should be evaluated for particular anxiety or related disorders first before MBCT selection.	n/a
Posttraumatic stress disorder	Wagner (2022), UK.[24]	Systema-tic review	2018-2022	4 papers (1RCT)	253	The positive effect is undetermined.	Different combined treatments in included studies	n/a
DSM-5 anxiety disorders	Haller H (2021), Germany[25]	S&M	2007-June 2021	23RCTs (3 of MBCT vs TAU)	1815(ABT+ ABBT+ MBSR+ MBCT) MBCT N = 248	MBCT showed short-term anxiolytic effects compared with TAU. MBCT at 2, 6 and 12 months no significantly differ from psychoedu-cation.	Unable to sub-group analyses for each anxi-ety disorder, so the results should not be applied to spe-cific diagnoses of anxiety disorders	Strong (in short-term anxiety effect)
Sleep problems in depression and anxiety disorders	Chan SH (2022), HongKong [26]	S&M	2010-2019	10RTCs (2RTCs of MBCT in the year 2010 and 2012	541 (all mindfulness interventions) MBCT N = 39	MBCT, with its large effect sizes and various forms of MBI programs, such as MBTT, IMMI and MBSR (except MM), are effective options for improving sleep problems among individuals with depression or anxiety disorders.		Strong
Depression and anxiety (in dementia, and mild cognitive impairment)	Orgeta V. (2022) UK[27]	Systema-tic review	1997-2020	29RTCs (3 RCTS of different MBIs combined with/without-MBCT)[28-30]	2599 (all psychological interventions) MBIs N = 93	There was very little data and very low-certainty evidence to draw conclusions about the MBIs and MBSR effectiveness.	Low validity of 3 included studies.	n/a

Table 1 Summarized results of MBCT effectiveness in Psychiatric conditions [1/1/2015 - 26/5/2023 of PubMed database] (Cont.)

Conditions	Authors (Year), Origin	Studies	Year of included meta-analyses	N meta-analyses	N Partici-pants	Summary results	Limitation of studies	Evidence of MBCT in psychiatric disorders
Adult Bodily distress **(defined as symptoms of Somatoform symptom disorders)**	Maas Genannt Bermpohl F (2023), Germany. [31]	Meta-analysis	Jan 2016 - April 2020	16RCTs (2MBCT)	1288	Very little data and very low-certainty evidence to draw conclusions about the effectiveness of MBIs and MBSR. MBCT showed greater clinical benefit than control conditions, with a small to moderate effect.	Various control conditions. Treatment evaluation in only group settings which study could not eliminate the potential confounding effect of social support.	n/a
Substance use disorder	Korecki JR (2020), USA[32]	Systema-tic review	2016 - April 2020	30	749	MBIs reduced the frequency and quantity of alcohol and drug use, substance-related problems, craving for substance use and increased the rate of abstinence	Mindfulness-based programs, not MBCT	n/a
Psychosis	Lazzari (2022) UK.[33]	S&M	2015-2020	9 studies (8 quantitative + 1qualitative studies) 5 MBCT (with 2 MBCT RCT) and 4 MBIs]	170 intervention 165 comparison	MBIp had a moderate effect size ($r = 0.34$; $p<0.001$) on psychosis (95% CI 0.26-0.42 (small to high)). MBIp increased acceptance of psy-chotic symptoms, self-awareness and empowerment with reduced anxiety and depression.	1. Limitation of population validity. The result cannot be claimed to other psychotic groups. 2. Mixed in-cluded studies.	n/a

Note: ABT Acceptance and Commitment therapy, **ABBT** Acceptance-Based Behavioral Therapy, **IMMI** Internet mindfulness meditation intervention, **MBI** Mindfulness-Based Intervention or Meditation-Based Intervention, **MBCT** Mindfulness-Based Cognitive Therapy, **MBIs** Mindfulness-Based Interventions, **MBIp** Mindfulness-Based Intervention for psychosis, **MBSR** Mindfulness-Based Stress Reduction, **MBTT** Mindfulness-Based Touch Therapy, **MBSR** Mindfulness-Based Stress Reduction, **MCI** Mild Cognitive Impairment, **MM** Mindfulness Meditation, **n/a** no answer, **NMA** Network Meta-Analysis, **OCD** Obsessive Compulsive Disorder, **PTSD** Posttraumatic Stress Disorder, **RCTs** Randomized Controlled Trial studies, **SAD** Social Anxiety Disorder, **S&M** Systematic review and Meta-analysis, **RANZCP** The Royal Australian and New Zealand College of Psychiatrists, **TAU** Treatment As Usual = Antidepressants (SSRIs, SNRIs, TCAs and CBT)

Discussion

This review affirms the effectiveness of MBCT in managing depressive symptoms, encompassing the treatment of mild to moderate acute depressive episodes, prevention of depression relapse during long-term follow-ups extending beyond 12 months[14] and the mitigation of sleep problems.[26] However, its role as an adjunctive treatment for depression and anxiety in individuals with bipolar disorders needs further clarification.[4, 19]

In 2014, CANMAT approved MBCT as an adjunctive treatment for GAD and panic disorder and it was also approved for use in social anxiety disorder in children and adolescents.[20] The meta-analysis in 2020 also found evidence supporting the effectiveness of MBCT as an intervention for GAD.[21] A meta-analysis conducted in 2021[25] revealed moderate evidence of the short-term anxiolytic effect of MBCT when compared to TAU for anxiety disorders. However, it did not significantly differ from psychoeducation in the longer term, specifically at 2, 6 and 12 months. Additionally, MBCT is an effective option to improve sleep problems among patients with depression and anxiety disorders.[26]

There are many systematic reviews and meta-analyses on the effectiveness of MBCT in various psychiatric disorders. Nevertheless, recently published meta-analyses are limited by the heterogeneity of included studies, variability in control conditions across studies, effect size estimation, small sample size, various outcome measurements, limited follow-up periods, potential confounding factors (such as demographic data, dropout rate, therapist competence)[34] and negative/nonsignificant publication bias. Furthermore, analyzing the studies included in meta-analyses to determine the effectiveness of MBCT on each specific psychiatric disorder is challenging compared to assessing common clinical symptoms associated with these disorders, such as depression, anxiety, insomnia and ruminative thoughts. Hence, it can be concluded that our review corroborates the effectiveness of MBCT in alleviating symptoms of depression and anxiety, consistent with prior research findings.

This review identified limitations in the evidence from meta-analyses regarding the positive effects of MBCT as an alternative treatment for psychiatric illnesses. These include suicidal ideation in depressive patients, adult social anxiety disorder, agoraphobia, specific phobia, OCD, PTSD, somatic symptom disorders, depression and anxiety in dementia and Mild Cognitive Impairment (MCI), psychosis and substance use disorders.

The key element of MBCT is mindfulness. While MBCT has a clear therapeutic structure that makes it difficult to flexibly compare to other forms of treatment as usual, it may result in the emergence of various forms of mindfulness-based interventions in RCTs instead of using the complete MBCT model. Research studies utilizing RCTs, which are included in meta-analyses, often explore the outcomes of various forms of mindfulness-based interventions (MBIs) to a greater extent when compared to RCTs specifically focused on MBCT. Consequently, the results of MBCT for the treatment of psychiatric disorders have been analyzed alongside other mindfulness-based interventions, leading to less robust findings in meta-analysis studies.

The basic idea is that meditation operates in a dose-dependent manner. This indicates that the effects of mindfulness training depend on the frequency, duration and intensity of the practice. While the development and utilization of various MBIs are significant endeavors, it is equally crucial to understand the unique inner transformations associated with each mindfulness technique.

The dynamic nature of the mind, which experiences ongoing fluctuations, presents unique challenges, particularly in individuals with diverse psychiatric disorders. Conducting large RCTs with rigorous experimental controls may help provide a clearer picture of the effectiveness of each mindfulness technique. Analyzing the physiological and psychological changes that manifest within the body and mind during the utilization of various mindfulness techniques integrated into different MBIs, such as mindfulness of breathing, body scanning, progressive muscle relaxation, mindfulness meditation with mantras, visualized meditation, guided imagery, middle-way meditation and others, can potentially illuminate the essential active elements inherent to each method. This could assist in the identification of the most efficacious techniques for expeditious patient outcomes. Consequently, this might pave the way for research endeavors focused on evaluating the effectiveness of individual mindfulness techniques

and their respective neurological impacts, including neurotransmitter modulation and inflammation regulation, among psychiatric patients.

Fortunately, neuroscience has progressed over the past two decades and studies are now underway to identify macro-micromolecular, genetic and epigenetic connections between brain-mind and body. Further studies on the mechanism of action of mindfulness at the molecular level may help to show similarities and differences between mindfulness and medication treatment in psychiatric patients.

Conclusion

MBCT plays a significant role in the treatment of mild to moderate depressive episodes, relapse prevention in depression and as an adjunctive treatment for depression in bipolar disorders, generalized anxiety disorder, panic disorder, and social anxiety disorder in children and adolescents, as well as for managing sleep problems in individuals with depression and anxiety disorders.

To assess the effectiveness of MBCT in diverse psychiatric conditions, it is crucial to conduct rigorous randomized controlled trials. These trials should investigate its potential for addressing suicidal ideation in individuals with depression and bipolar disorder, as well as its applicability in adult social anxiety disorder, PTSD, OCD, depression occurring in cases of MCI and dementia, substance use disorder, and psychosis.

Limitation

The neuroscience of MBCT and its applications for physical illnesses are beyond the scope of this article.

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Conflict of Interest: The author is a mindfulness meditator who is interested in the application of mindfulness.

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Review Article

Transitional Care of Older Adults from Hospital to Home

Mallika Chuansangeam*

Abstract

Older adults often have reduced body reserve, multiple illnesses of many organ systems, and receive polypharmacy thus requiring complex medical care. Older adults have the opportunity to be cared for in different settings leading to changes in all dimensions of care. This creates a chance for medical mistakes and affects the safety of older adults that come with each transition of care. Transitional care is especially important in older adults. Fast and important information transfer between care teams who provide information to patients and caregivers in a language that is easy to understand is vital. Involving patients in the decision-making review of medication use and follow-up after the patient leaves the hospital contributes to reducing the chance of hospital re-admission of the patient. This requires cooperation from a multidisciplinary team. Effective transitional care improves the quality of life and reduces the cost of treating older adults.

Objectives: This review aimed to indicate the importance of effective transitional care. The review consisted of examples of transitional care models and components of each model. Also, specialized care in disease specific patients were mentioned.

Keywords: transitional care, hospital discharge, discharge planning, older adults

Department of Medicine, Thammasat University, Pathum Thani, Thailand
* **Corresponding author:** Mallika Chuansangeam, MD, Department of Medicine, Thammasat University, Pathum Thani, Thailand, Email: mallikaanne@gmail.com, Tel: +6629429554

Introduction

Older adults are different from other ages because they have complex health conditions. There are multiple illnesses of many organ systems and many chronic diseases thus requiring complex medical care. During hospitalization, older adults tend to limit their activities, leading to functional decline. Older adults often develop complications such as infection, immobilization syndromes (e.g., pressure ulcers, joint stiffness and orthostatic hypotension), or confusion. After hospitalization, older adults may require various forms of medical support (e.g., feeding, monitoring symptoms and preparing medication) including social support to meet their needs.[1], Nevertheless, older adults have the opportunity to be cared for in different settings, such as hospitals, homes, or long-term care facilities. Thus, each change of location presents a challenge. It is not just a physical change but also changes in all dimensions of care for the elderly - new caregivers, medicines and goals of care. This creates a chance for medical mistakes and affects the safety of older adults that comes with each transition.

Unplanned transitions are a common problem leading to rehospitalization and increased cost of elderly care.[2] Adverse events may occur after discharge of the patient caused by the transmission of incomplete or erroneous information, such as treatment or diagnosis data. However, the most common and severe problems are medication-related problems. In addition, cognitive impairment among the elderly may affect communication or memory of self-care information. This may also relate to a lack of available caregivers to care for the elderly who are functionally or cognitively impaired. After discharge from a hospital, approximately 20 percent of older adults will be rehospitalized within 30 days and one-third of patients are rehospitalized within 90 days.[3] In one study, those with early rehospitalization had 3 times higher one-year mortality than those without early rehospitalization.[4] Most patient adverse events during transition of care relate to problems with medication. With each admission and discharge from the hospital, the risk of medical error increases. One study found that more than half of the patients experienced at least one accidental medication error after hospital discharge[5] and approximately 20% of patients experienced an adverse event within 1 month after discharge from the hospital.[6] Also, more than two-thirds of these events were medication-related, which could be prevented. Importantly, those who did not come for laboratory tests after discharge from the hospital as scheduled were 6 times more likely to be hospitalized again compared to the group without the aforementioned mistakes.[7] Overall, there are six categories of issues which can result in negative outcomes in patients while in hospital and post-discharge at home. The issues can be grouped as follows: limited patient involvement regarding their own care, inadequate communication, little cooperation between the medical team, difficulties associated with follow-up and patient monitoring, insufficient continuity of care and a disparity in the services provided to patients after being discharged.[8]

The following review aimed to describe the importance of transitional care. The review consisted of examples of transitional care models and components of each model. This will show the significance of the multidisciplinary team in taking care of high-risk patients. Poor transitional care may lead to increased healthcare problems, including seeing a doctor at an outpatient clinic or visiting the emergency department and hospitalization.[9]

Benefits of effective transitional care

A systematic review[10] consisting of 23 studies with a total of 20,997 participants, median age 76 years, found that transitional care significantly reduced hospital readmission rates at 30 days (odds ratio [OR] 0.75, 95% confidence interval 0.62 to 0.91, $p < 0.01$). In addition, transitional care may increase the use of primary care services, which has a good effect on preventive care.

Effective transitional care has many benefits.[11] It can reduce the length of hospital stay (mean difference length of stay -0.91, 95% confidence interval -1.55 to -0.27),[12] reduce the risk of readmission to hospital (relative risk 0.82, 95% confidence interval 0.73 to 0.92),[12] reduce long-term visits to aged care facilities (odds ratio of effective number of subjects living at home at 6-12 months was 1.44, 95% confidence interval 1.07 to 1.95),[13] improve health and enhanced quality of life,[14] and improve the care experience for patients and caregivers.[15]

Transitional care model

There are many transitional care models that have been shown to be effective as demonstrated in Table 1. Although the target population was different, most of the models showed similarity

in core components. The core components consist of screening high risk patients (e.g., older adult, multiple comorbidities, heart failure and cerebrovascular disease), assessment (e.g., function, cognition, home environment and social support), multidisciplinary plan of care (including goals of care), medication management, discharge planning, personal health records and discharge summary, patient or caregiver education and close follow-up.

1. Care Transitions Intervention (CTI)[16-17] is a model of care developed in 2003 and is in use at numerous hospitals. This model was initially studied in older adults undergoing treatment for cerebrovascular disease and chronic disease, however it more widely used nowadays. The aim of CTI is to involve patients and caregivers in self-care and self-management after hospitalization. This model is based on 4 fundamental principles: (1) medication self-management; (2) utilizing updated and dynamic personal health records to ensure ease of communication and continuity of care plan across providers and settings; (3) primary care and specialist follow-up (4) awareness of red flags and how to respond when symptoms worsen. An advanced practice nurse, who doubles as a transition coach, makes home visits and phone calls to check patient involvement and self-management in chronic disease care. This model of care has undergone studies in several clinical settings and uncovered a statistically significant reduction in re-admission to the hospital at 30 days, along with an increased quality of life and the ability of the patient to take care of themselves more.

2. The Transitional Care Model (TCM)[18] is a widely recognized model of transitional care developed at the University of Pennsylvania, which screens people who are at high risk of poor outcomes during the transition from hospital to home. It has also been effective in managing older adults with congestive heart failure and myocardial infarction.[2] The transitional care nurse will develop a discharge plan based on needs, considering specific goals and preferences. Emphasis is placed on information sharing with the patient being followed up from the hospital to home. This will then prepare both patients and families to manage health conditions of the patient at home. Communication is an integral part of this process, including with physicians at outpatient clinics, home visits and follow-up telephone calls after hospital discharge. TCM emphasizes a multidisciplinary approach to patients led by transitional care nurses who remain in contact with a variety of service providers.

3. Coordinated-Transitional Care (C-TraC)[19] is an emerging model of transitional care using similar procedures to CTI and TCM done among veterans but has also targeted high-risk patients, especially those who are cognitively impaired, patients who refuse home visits or are too far away for a home visit. The telephone method was used by the nurse case manager to coordinate the patient's transitional care by follow-up phone calls after leaving the hospital and working with patient care teams both in-hospital and post-hospital. The goals of care are (1) educating and reassuring veterans and their caregivers on medication management, (2) ensuring follow-up appointments are available and will be available for check-ups, (3) educating them about symptoms, (4) providing monitoring and contact information upon leaving the hospital. The results of the care were found to reduce readmission to hospital by one-third of patients.

4. Reengineered Discharge (RED)[20] was studied in general internal medicine patients and focuses on a multidisciplinary approach to patient care. The nurse engages patients during their hospitalization, arranges individualized clinical information and post-hospital treatment plan after leaving the hospital. The pharmacist will conduct follow-up calls 2 to 4 days after discharge from the hospital, reviewing medications and communicating directly with the physician at the outpatient clinic. This project reduced hospital visits by about 30 percent, including emergency room visits and re-hospitalization within 30 days.

5. The Better Outcomes for Older Adults Through Safe Transitions (BOOST)[21] program is a collaborative model of transitional care to improve quality across healthcare facilities around the United States. This program focused on internal medicine and general surgery patients. Specialists will improve the quality of transitional care based on the context of each hospital. The project involves several methods: risk assessment, review of drug use, discharge checklist and a multidisciplinary approach to the distribution process. The study found that the rate of rehospitalization decreased.

6. The Transsectoral Intervention Program for Improvement of Geriatric Care in Regensburg (TIGER)[22] was a study of the transitional care model from hospital to home for people aged 75 years

and older. This program consists of individualized care plans based on patient symptoms, risks, needs and values. There are home visits and phone calls. Necessary care is included such as adjusting housing or nutrition. Outpatient services, patients and caregivers will be involved in the care plan. The study's outcome was the rate of readmission to the hospital within 12 months. The results of the study are pending.

Table 1 Review of transitional care models

Model	Population	Contents	Health care providers	Methods
Care Transitions Intervention (CTI)	Older adults with cerebrovascular disease and chronic disease	- Medication management - Personal health records - Close follow-up with physician - Knowledge of red-flag signs	Transition coach who is advanced practice nurse	Personal health record home visits and phone call
Transitional Care Model (TCM)	High risk patients (aged ≥80, low self-care, depression, cognitive impairment, ≥4 underlying diseases, ≥6 medications, re-admission	- Provide care focused on discharge planning and home follow-up - Discharge plan based on needs, goals and preferences - To ensure information is shared and to prepare patients and families to manage their health conditions	Transitional care nurses who contact with doctors, nurses, social workers, discharge planners and pharmacists	Communicating with physicians at outpatient clinics, home visits and follow-up phone calls
Coordinated-Transitional Care (C-TraC)	Veterans with targeted high-risk patients, who are cognitively impaired, refuse home visits or are too far away for a home visit	- Educating and reassuring patients and caregivers on medication - Ensuring follow-up appointments - Educating about symptoms - Providing monitoring information and contact information	Nurse case manager	Follow-up phone calls
Reengineered Discharge (RED)	General internal medicine patients	- Engaging with patients during hospitalization, clinical information and discharge plan - Medication review - Communicating with physician at outpatient clinic	Nurses, pharmacist	Follow-up phone calls
Better Outcomes for Older Adults Through Safe Transitions (BOOST)	Internal medicine and general surgery patients	Based on the context of each hospital	Specialists	- Risk assessment - Medication review - Discharge checklist - Multidisciplinary approach
Transsectoral Intervention Program for Improvement of Geriatric Care in Regensburg (TIGER)	People aged 75 years and older	- Individualized care plans - Necessary care (adjust housing and nutrition) - Outpatient services		Home visits and phone calls

Core components of effective transitional care

Transitional care is care that begins before discharge and continues until the patient leaves the hospital. The goal is to ensure a safe and efficient patient transition e.g., from hospital to home. Transitional care is divided into: pre-discharge and post-discharge care. Pre-discharge care includes: assessing the risk of adverse events or re-hospitalization, patient involvement, such as patient or caregiver knowledge, creating individual patient records (a document that records clinical information at a level that the patient can understand and use after leaving the hospital), involving the multidisciplinary discharge planning team and dedicated transition service specialists (who had contact with patients both before and after discharge) when patients were ready to be discharged. The post-discharge care includes patient access (including follow-up by phone hotline accessible to patients and home visits), the convenience of clinical follow-up (including follow-up at outpatient clinics), and review of discharge medications.

Effective transitional care depends on many factors such as:[17,18,20] (1) the communication process between the discharge team and the continuing care team (e.g., identifying and arranging post-hospital needs, summary discharge form of information to physicians who continue to care for patients, physician appointments and access to public health services), (2) providing education to patients and caregivers about diagnosis and treatment plans since being in the hospital and upon leaving the hospital, as well as how to notice worsening symptoms and what to do, (3) participation of patients and caregivers in decisions about expectations of care at different stages, make comments and decisions about treatment goals, (4) effective medication reviews are used to identify and correct medication errors, such as medication changes, repetition, frequency, or method of administration to prevent adverse drug events and later endangering the patient. The medication review should begin with the patient's medication history. This must include all medications the patient is currently taking both prescription medications, over-the-counter medications, herbs and supplements. History of drug allergies and side effects, including adherence to medication use should be reviewed. A medication review should consist of five steps: a current list of medications, a list of newly prescribed medications, comparison between both lists, comparison and decision on medication, and notifying caregivers and patients about the new medication list, and (5) contacts with the patient at home, such as a home visit by a nurse, a follow-up phone call, or a medication inquiry by a pharmacist.

The discharge summary should be brief short and to the point, especially for patients with complex care, so that continuing care personnel can easily draw out key points and recommendations. The most important points to be included are the principal diagnosis, physical examination, laboratory results, medication received at the time of discharge and the follow-up appointment.[23] Accurate discharge summaries improve the follow -up of results of tests pending at discharge.[24] Continuing care personnel should identify changes made and audit the results. Advice is also received by patients and caregivers. As a consequence, poor quality discharge summaries increase the risk of medical errors, including medication errors and delays in outpatient reviews.[25-26]

The follow up time is important. All older adult patients should make a follow-up appointment within 2 weeks of discharge.[27] Follow-up appointments should be planned before the patient leaves the hospital and the follow-up time should depend on the severity of the patient's medical problems and the risk of their condition worsening. High-risk patients should make an appointment within a few days of leaving the hospital and low-risk patients can make a follow-up appointment within 2 weeks

Discussion

Improving the transitional care process is aimed at reducing rehospitalization and adverse events. There are many transitional care programs that have shown benefit. Most of the models mainly consist of a transitional care nurse and multidisciplinary team. The components consist of screening, collaborating, promoting continuity, staffing, engaging patients and caregivers, assessing and managing risks and symptoms, and educating self-management.

Although many transitional care models have shown clinical benefits, this intervention requires resources such as multidisciplinary teams and added time. Models based on the context of

hospitals might be used for selected high-risk patients to garner more attention to meet their needs.

For specific conditions, such as people with cognitive impairment or heart failure, specialized transitional care may be needed. Cognitively impaired people are at increased risk of having poor outcomes during the transition. Studies suggest that dementia may increase the risk of hospitalization by 40%.[28] People with dementia have limited abilities to learn, remember and communicate, which are components of effective caring. This can result in inability to communicate well and affect rehospitalization. Those with dementia may have greater transition within the last three months of life than those without dementia.[29] People with dementia may be excluded from participating in decisions about transitional care. This is due to the misconception that people with dementia are unable to make decisions. People with dementia benefit the most from empowerment-focused care, preparing caregivers and adjusting patient care methods to meet individual needs. The C-TraC model of care is one method that engages caregivers and uses a way to monitor patients with dementia. Elderly people with dementia who live in the community are often cared for by family caregivers. Caregivers of people with dementia are burdened, which can have a negative impact on patient health outcomes. Transitional care should therefore be responsive to the needs of families and carers. Supporting and mentoring caregivers can be helpful both in the short and long term.

In patients with heart failure, this condition impairs the patient's ability to support themselves. There are times of periodic exacerbations of the disease, resulting in re-admission to the hospital including visits to the emergency department. Most of the patients with heart failure were discharged from the hospital without adequate self-care instructions, risk assessment, education and advice, food and water intake, medication management, activities and daily body weight monitoring. Telephone follow-up home visit and rehabilitation can assist with this.[30]

Thailand has a health service system that covers home care at the community level. This home care is coordinated by health volunteers and primary care medical personnel, who can assist patients with daily activities, medication management and rehabilitation. Also, they provide home visits to people who need ongoing care. However, one of the problems of caring for patients after leaving the hospital is the lack of systematic transfer of patient information from the hospital to the community. Most of the information during hospital stays is limited to use in the hospital. There is no systematic data transfer to primary care medical personnel, resulting in inadequate continuity of care and insufficient rehabilitation. Solving this issue might need a change in policy as it involves multiple ministries and needs cooperation. The transmission of information of a personal health record must be able to be accessed by all relevant personnel. Otherwise, establishing a central coordination center for transitional care between organizations could be a practical solution, especially in the context of developing countries.

Conclusion

Transitional care is an intervention that has been shown to decrease hospital re-admission rates and adverse events post hospital discharge. It is managed by a multidisciplinary team. The model aims to transfer important information between care teams to patients and caregivers in a language that is easy to understand. Involving patients in decision-making, review of medication uses and follow-up after discharge, all contribute to reducing the chance of re-admission to the hospital. Effective transitional care improves the quality of life and reduces the cost of treating the elderly. Patient-centered approach should be emphasized in all high-risk patients.

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Case report

Quinolone Induced Torsades De Pointes: A Life Threatening Complication of Conventional Medication

Lanlalin Sojikul, Kunchanit Chongtanapipat, Kumpol Chintanavilas*

Abstract

The use of antibiotic drugs, particularly the quinolone group, can cause acquired QT prolongation and blockage of the potassium channel (Ik). We report a case of torsade de pointes (TdP) triggered by the use of ciprofloxacin to treat arteriovenous fistulas infection.

Keywords: Fluoroquinolone, Ciprofloxacin, Torsades De Pointes, Long QT interval, Polymorphic ventricular tachycardia

Chulabhorn International College of Medicine, Thammasat University, Pathum Thani, Thailand

* **Corresponding author:** Kumpol Chintanavilas, M.D., Chulabhorn International College of Medicine, Thammasat University, Pathum Thani, Thailand. Email : Kumpol07@staff.tu.ac.th, Tel. : +6662926599

Case information

A 59-year-old man with an end-stage renal disease requiring hemodialysis via arteriovenous fistula was admitted due to an infected left radiocephalic arteriovenous graft. His current medications at the time were atorvastatin, warfarin, losartan and doxazocin. Intravenous ciprofloxacin was administered for three days before radiocephalic vein ligation under general anesthesia was performed. At midnight after the operation, the patient experienced pulseless cardiac arrest, which was successfully treated with defibrillation and two cycles of CPR. A twelve-lead electrocardiogram taken just before cardiac arrest showed polymorphic ventricular tachycardia with waxing and waning patterns. After the restoration of spontaneous circulation, the electrocardiogram showed atrial fibrillation with QT prolongation (QTC increased from a baseline of 470 to 591 ms). Laboratory results revealed low magnesium levels and normal potassium levels (Mg 1.8 mg/dL and K 4.5 mmol/L). A coronary angiogram was performed, which showed a diffuse 20% lesion in the proximal left anterior descending artery with no significant obstruction. After intravenous administration of 1 gram of magnesium sulfate, correction of hypomagnesemia, and discontinuation of ciprofloxacin, the patient's atrial fibrillation returned to sinus rhythm the next day. The patient's QT interval returned to the baseline of 470 ms two weeks later, with no other cardiac arrhythmias reported.

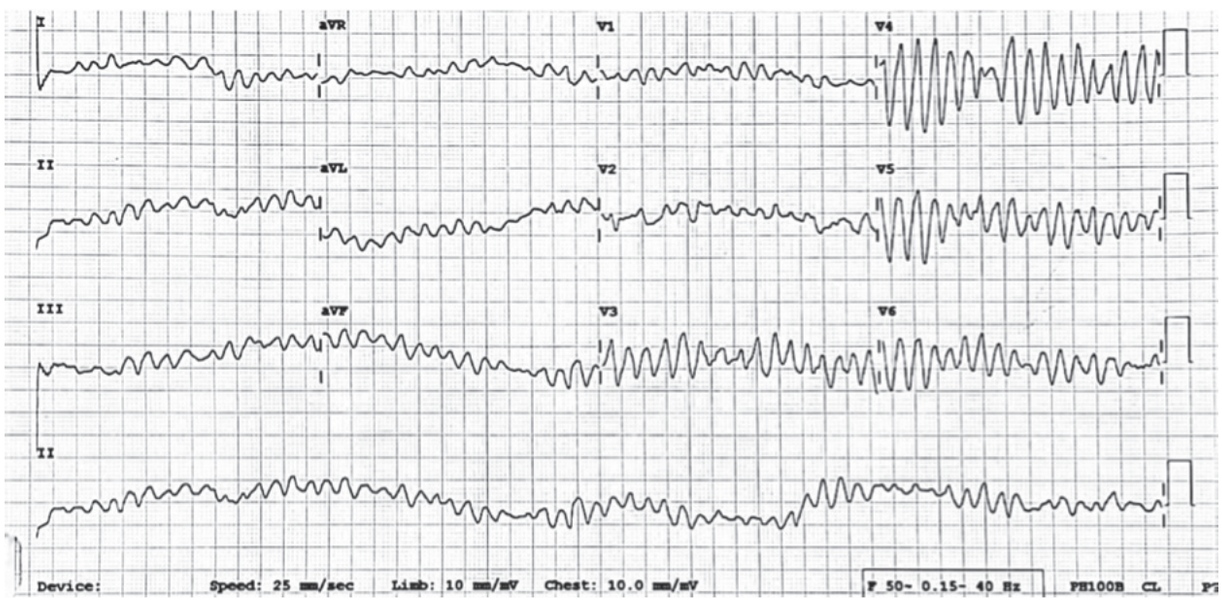

Figure 1 The patient's ECG of the polymorphic ventricular tachycardia with waxing and waning patterns coincides with Torsade de Pointes.

Discussion

Ciprofloxacin, a broad-spectrum fluoroquinolone antibacterial drug, is commonly prescribed for the treatment of bacterial infections in various organ systems. The main mechanism of fluoroquinolone is inhibiting bacterial DNA gyrase, which can lead to an acquired QT prolongation and blockage of the potassium channel (IK), resulting in early afterdepolarization and ventricular arrhythmias such as Torsade de Pointes [1]. Although ciprofloxacin appeared to be the lowest risk for QT prolongation and TdP rate[2], our case demonstrated an example of a ventricular arrhythmia from ciprofloxacin usage in a borderline QT prolonged patient.

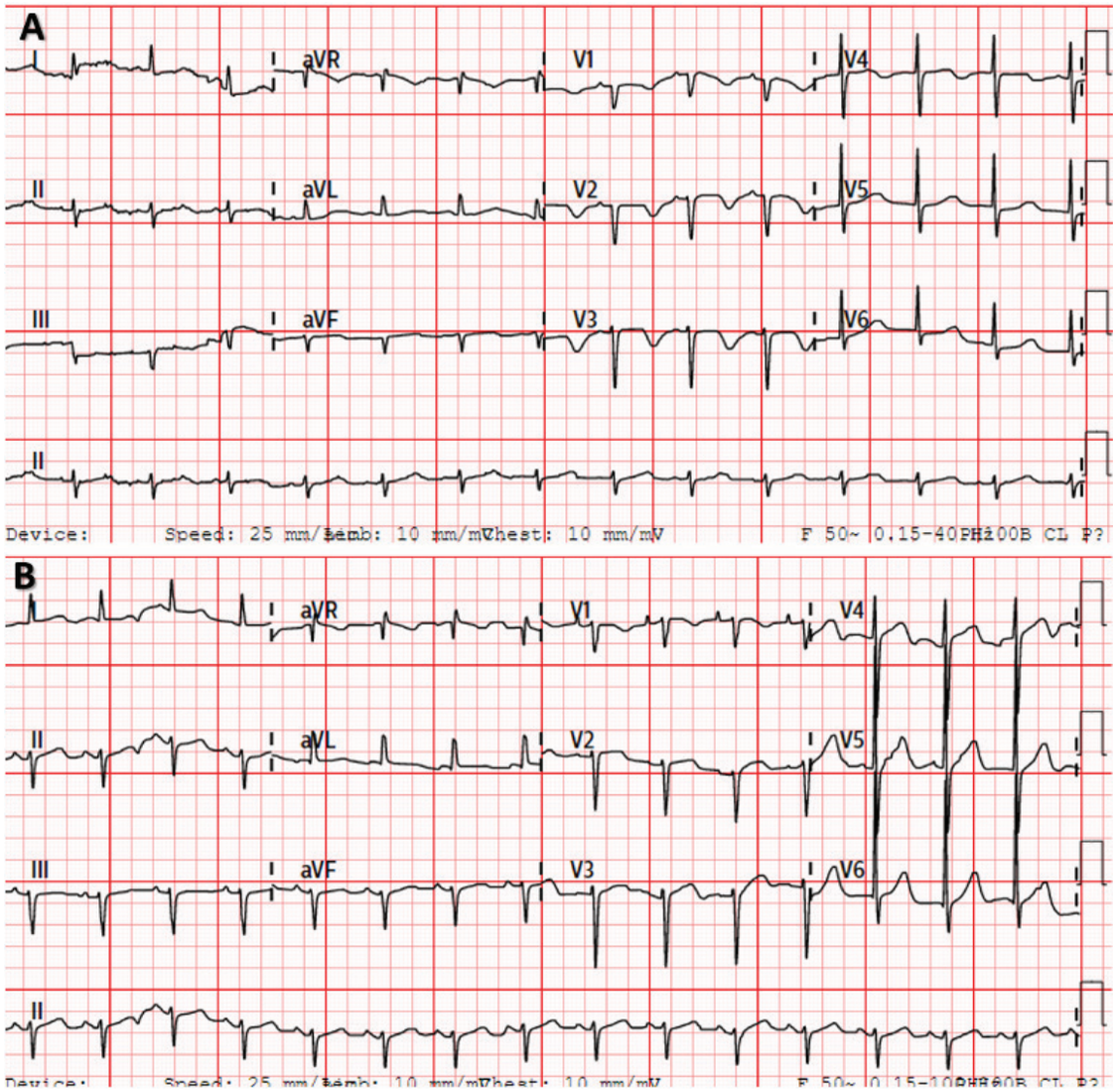

Figure 2 The patient's electrocardiogram, with (A) indicating the prolonged QT interval of 591 ms observed after the polymorphic ventricular tachycardia event, (B) indicating the baseline QT interval of 470 ms observed two weeks later

This patient suffers from Torsades de Pointes (TdP), a type of polymorphic ventricular tachycardia. The key characteristic findings on an electrocardiogram (ECG) include a waxing and waning pattern due to the twisting of QRS complexes around an isoelectric line. The onset of ventricular arrhythmias begins with premature ventricular contractions (PVCs) showing R waves superimposed on T waves as the 'R-on-T' phenomenon. Additionally, a "long-short" initiating sequence on the ECG may also be present[3]. The impact of this arrhythmia can lead to an in-hospital mortality of 10.7% and 1-year mortality of 25.0%[4].

One of the main mechanisms underlying TdP is the abnormal prolongation of the repolarization phase. This is caused by blockage of the delayed rectifier potassium current (Ikr), which results in decreased potassium efflux and an excess of positive ions inside the cellular membrane, ultimately leading to a prolonged repolarization phase. This prolonged repolarization is manifested as a prolonged QT interval on the surface electrocardiogram (ECG). In addition, conditions that cause small inward currents, such as Na window current and Na/Ca exchange current, create suitable conditions for a large prolonged membrane

depolarization, which is prone to late calcium channel reactivation and results in ectopic beats. This phenomenon creates the pathognomonic R-on-T phenomenon in TdP[5].

Drug-induced QT prolongation is defined as a QTc of 500 ms or greater or an increase of 60 ms or greater in QT interval. Our patient has end-stage renal disease as the main risk factor, other patient factors that can increase the risk of developing drug-induced long QT syndrome, include female sex, age over 65 years, structural heart disease, hepatic insufficiency, and electrolyte abnormalities such as hypokalemia, hypomagnesemia, or hypocalcemia. Certain medications, such as diuretics and multiple QT-prolonging drugs, can also increase the risk[6]. To assess the risk of drug-induced QT prolongation, there are various risk assessment tools available such as the Tisdale risk score, the MedSafety Scan (MSS) QT prolongation risk score and the Risk of QT drug-drug interactions assessment tool. A baseline prolonged QT interval without a diagnosis of long QT syndrome (2 points from modified long QT diagnosis score) in this patient was also included in these risk scores. High-risk patients should undergo regular ECG monitoring until the steady state of the torsadogenic agent is reached[7].

Emergency treatment of torsade de pointes consists of removing any torsadogenic stimulus and suppressing early afterdepolarizations (EADs), which may include accelerating the heart rate to reduce the QT interval. In this patient, discontinuation of ciprofloxacin was implemented. Initial treatment should include correcting hypokalemia and hypomagnesemia and administering intravenous magnesium sulfate. Magnesium sulfate suppresses torsade de pointes by decreasing the influx of calcium ions, inhibiting calcium influx via L-type calcium channels and reducing the amplitude of EADs. However, care should be taken due to the high risk of magnesium toxicity especially in renal insufficiency patients[8]. Apart from the treatment plan approached in our case, there is a wide range of treatments available for these circumstances. The administration of isoproterenol can increase the heart rate due to its properties as a non-selective b1/b2-adrenoceptor, which shortens the QT interval. Moreover, transvenous pacing has been proven to increase the heart rate and suppress or abolish episodes of TdP. In the case that the patient has a hemodynamic compromise, it can be treated with unsynchronized cardioversion, beginning with 100 joules. Nevertheless, for patients who failed to respond to the regimen described above, IV lidocaine, a class 1B antiarrhythmic drug, can be selected as an alternative. It has been shown to shorten the QT interval due to its property of blocking voltage-gated Na^+ channels (VGSC/NaVs)[9]. Automatic implantable cardioverter defibrillator (AICD) consideration in reversible TdP, such as drug induced TdP, should be avoided[10].

In conclusion, quinolone antibiotics have been associated with QT prolongation, which can increase the risk of life-threatening ventricular arrhythmias. It is important to monitor and manage any underlying abnormalities that may predispose patients to QT prolongation, such as electrolyte imbalances, heart disease and genetic factors. Prompt and appropriate acute management is essential for improving clinical outcomes in these cases.

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Conflict of interest: The authors declare that they have no conflict of interest.

Author contributions: The author's indicated in parentheses made substantial contributions to the following task of the case report : Initial conception (K.Chi.); Management of case in the report (K.Chi.); Supervised the project (K.Chi.); Analyzed the data (K.Cho., L.S.); Contribute to the interpretation of the case (K.Chi., K.Cho., L.S.). All authors discussed the result and contributed to the final manuscript.

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ABSTRACTS
(ORAL PRESENTATION)

Abstracts *(Oral Presentation)*

Diagnostic Accuracy of Three Screening Questionnaires for Predicting Moderate to Severe Obstructive Sleep Apnea in Patients with Morbid Obesity

Narongkorn Saiphoklang[1,2], Natapan Chinnalai[2], Ailada Chinnalai[2]

Abstract

Background: Obstructive sleep apnea (OSA) is a common disease among subjects with morbid obesity. Sleep questionnaires are practical tools to screen OSA prior to undergoing a diagnostic polysomnography (PSG).

Objectives: To evaluate the accuracy of Epworth sleepiness scale (ESS), STOP-BANG, and Berlin Questionnaire (BQ) for detecting moderate to severe OSA in patients with morbid obesity.

Methods: A cross-sectional study was conducted between October 2020 and December 2021 in Thammasat University Hospital, Thailand. Adult subjects with morbid obesity suspected of OSA were included. Morbid obesity was defined as body mass index (BMI) ≥ 40 kg/m^2 or BMI ≥ 35 kg/m^2 and obesity-related health conditions. ESS, STOP-BANG and BQ were performed in each patient before undertaking PSG. OSA severity was classified by apnea-hypopnea index (AHI): mild (AHI 5.0-14.9), moderate (AHI 15.0-30.0), and severe (AHI>30.0).

Results: A total of 205 subjects (40.5% male) were included. Mean age was 43.2 ± 14.3 years. BMI was 40.9 ± 5.3 kg/m^2. Comorbidities included hypertension (68.3%), dyslipidemia (39.0%) and diabetes (27.8%). AHI was 59.4 ± 39.2 per hour. No OSA was 2.4%. Mild, moderate and severe OSA were 9.8%, 14.6% and 73.2, respectively. The best cutoff values of ESS, STOP-BANG and BQ for detecting moderate to severe OSA were 6.5, 4.5 and 1.5, with sensitivity levels of 61.7%, 67.2% and 88.9%, respectively, and specificity levels of 52.0%, 36.0% and 36.0%, respectively. Area under the ROC curve values of ESS, STOP-BANG and BQ were 0.595, 0.696 and 0.669, respectively with all statistical significances.

Conclusion: BQ has the highest sensitivity whereas ESS has the highest specificity for predicting moderate to severe OSA in patients with morbid obesity. These questionnaires might be applied as predictive tools with optimal cut-point levels for screening OSA in morbid obesity.

Keywords: Berlin Questionnaire, Epworth Sleepiness Scale, obesity, obstructive sleep apnea, STOP-BANG

[1] Department of Internal Medicine, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[2] Medical Diagnostics Unit, Thammasat University Hospital, Pathum Thani, Thailand

Abstracts *(Oral Presentation)*

Prevalence and Associating Factors of Long COVID in Pediatric Patients During the Delta and The Omicron Variants

Tananya Lokanuwatsatien[1], Araya Satdhabudha[2], Auchara Tangsathapornpong[2], Pornumpa Bunjoungmanee[2], Phakatip Sinlapamongkolkul[2], Chanapai Chaiyakulsil[1], Paskorn Sritipsukho[2,3], Pichaya Tantiyavarong[4*]

Abstract

Introduction: The number of pediatric COVID-19 infections is increasing; however, the data on long COVID conditions in children is still limited.

Objective: Our study aimed to find the prevalence of long COVID in children during the Delta and Omicron waves, as well as associated factors.

Methods: A single-center prospective cohort study was conducted. We included 802 RT-PCR-confirmed COVID-19 pediatric patients in the Delta and Omicron periods. Long COVID was defined as having symptoms for ≥3 months after infection. Parents and/or patients were interviewed by phone. Multivariable logistic regression was performed to find associated factors with long COVID.

Results: The overall prevalence of long COVID was 30.2%. The Delta period had more prevalence than the Omicron (36.3% vs. 23.9%). Common symptoms for patients 0-3 years old were loss of appetite, rhinorrhea and nasal congestion. Conversely, patients 3-18 years old had hair loss, dyspnea on exertion, rhinorrhea and nasal congestion. However, there was no significant negative impact on daily life. Most symptoms improved after a 6-month follow-up. Factors associated with long COVID-19 conditions were infection during the Omicron period (adjusted OR 0.54; 95% CI 0.39-0.74, $P < 0.001$), fever (adjusted OR 1.49, 95% CI 1.01-2.20, $P = 0.04$) and rhinorrhea (adjusted OR 1.47, 95% CI 1.06-2.02, $P = 0.02$).

Conclusions: Infection during the Omicron wave has a lower prevalence of long COVID. The prognosis is often favorable and most symptoms gradually become less. However, pediatricians may schedule appointments to surveil long COVID in children with fever or rhinorrhea as an initial symptom.

Keywords: long COVID, SARS-CoV-2, COVID-19, Delta variant, Omicron variant

[1] Department of Pediatrics, Thammasat University Hospital, 12120, Thailand
[2] Department of Pediatrics, Faculty of Medicine, Thammasat University, 12120, Thailand
[3] Center of Excellence in Applied Epidemiology, Thammasat University, 12120, Thailand
[4] Department of Clinical Epidemiology, Faculty of Medicine, Thammasat University, 12120, Thailand
[*] **Corresponding author:** Pichaya Tantiyavarong, Assist. Professor, Department of Clinical Epidemiology, Faculty of Medicine, Thammasat University, 12120, Thailand, Email: pichaya_t@tu.ac.th

Abstracts *(Oral Presentation)*

Safety Profiles of Three Major Types of COVID-19 Vaccine Among Two Cohorts of People Living with HIV

Thana Khawcharoenporn[1], Sirashat Hanvivattanakul[2]

Abstract

Background: Data on adverse effects (AEs) of COVID-19 vaccines among people living with human immunodeficiency virus (PLHIV) are currently limited.

Objectives: To determine safety profiles of three major types of COVID-19 vaccine among PLHIV.

Methods: A cohort study was conducted among PLHIV receiving care at two clinics during COVID-19 epidemics in Thailand (2021-2022). Data were collected using the online survey system.

Results: Of the 398 vaccinated PLHIV, 153 received two doses and 245 received three doses of COVID-19 vaccines. Inactivated and viral vector were the common vaccine types received by the PLHIV as the first and second doses while mRNA vaccine was commonly used as a booster dose. For the first and second vaccine doses, the most common AEs were fever (15% and 11%) and injection site pain (11% and 11%). For a booster dose, viral vector vaccine significantly caused more injection site pain and headache than the other two types. The majority of all AEs of the first, second and booster doses spontaneously recovered without treatment (55%, 59% and 59%). By multivariable analysis, receipt of viral vector or mRNA vaccine and age less than 40 years were independently associated with any AEs of the primary series vaccines, while having AEs from the previous dose and female sex were factors associated with any AEs of a booster vaccine.

Conclusions: The three types of COVID-19 vaccines were generally safe among PLHIV. PLHIV who were elderly, female or had AEs from the previous vaccine dose should be closely monitored for AE development.

Keywords: Adverse effects; COVID-19; Vaccine; People living with HIV

[1] Infectious Diseases Unit, Department of Internal Medicine, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand, 12120
[2] Faculty of Medicine, Thammasat University, Pathum Thani, Thailand, 12120

Abstracts *(Oral Presentation)*

The Accuracy of An Upright Chest X-ray as A Diagnostic Screening Tool for The Acromioclavicular Joint Dislocation

Adinun Apivatgaroon, Warunyoo Puntu

Abstract

Background: A chest radiograph (CXR), either supine or upright, is the standard investigation tool in primary assessment of blunt thoracic and abdominal trauma. Patients with thoracic injury frequently have associated shoulder girdle injuries such as scapular fracture, clavicular fracture, or acromioclavicular joint (ACJ) injury. The Zanca view of both shoulders is the standard radiograph for ACJ dislocation to assess the vertical displacement of the distal clavicle by measuring the coracoclavicular distance (CCD), compared to the unaffected contralateral side.

Hypothesis/Purpose: To determine accuracy of CCD measurement of upright CXR, comparison to the standard Zanca view in the diagnosis ACJ dislocation.

Study design: Matched case-control study; Level of evidence, 3.

Methods: CXRs from 70 patients with history of ACJ dislocation at Thammasat University Hospital from 2010-2021 were collected, and were 1:1 age-and gender-matched with the 70 CXRs of control group. Totally 140 cases were randomized and measured regarding CCD difference by two independent doctors (musculoskeletal radiologist and orthopaedic sports medicine). Accuracy was defined, comparing to the standard Zanca radiograph. Inter-and intra-observer agreement were measured.

Results: There were 55 male and 15 female patients with an average age of 46 in both cases and controls. In the disease group, the percentage of CCD difference, compared to the unaffected side (ΔCCD) was 130.25 ± 88.42 and 152.6 ± 106.56 (mean difference 22.44 with 95% CI [2.4, 42.48], *p-value* = 0.029) in upright CXR and Zanca view, respectively. Totally 140 CXRs, Zanca as the gold standard, the upright CXRs with definition of abnormal CCD difference of >25%, revealed 95.71% sensitivity, 85.71% specificity, 6.7 of the positive likelihood ratio (+LLR), 0.05 of the negative likelihood ratio (-LLR). The accuracy was 90.71%. The intra-observer reliability was 94.29% agreement and 0.94 of weighted kappa coefficient (95%CI = 0.89-0.98). The inter-observer reliability was 95.7% agreement and 0.95 with weighted kappa coefficient (95%CI = 0.92-0.99).

Conclusions: Upright CXR can be used as a diagnostic screening tool for ACJ dislocation in patients with more than 25% superior displacement as compared to the Zanca radiographs. The CCD measurement in upright CXR has almost perfect agreement of inter- and intra-observer reliability.

Keywords: acromioclavicular dislocation; coracoclavicular distance; upright chest X-rays; Zanca view; accuracy

Faculty of Medicine, Thammasat University, Pathum Thani, Thailand

Abstracts *(Oral Presentation)*

A Flight-testing Study for Drone Delivery of Automated External Defibrillators in Simulating Out-of-Hospital Cardiac Arrest in Suburban Areas of Thailand

Winchana Srivilaithon[1], Nalinas Khunkhlai[2]

Abstract

Background: Immediate access to an automated external defibrillator (AED) and early defibrillation are vital to survival from out-of-hospital cardiac arrests (OHCAs). The use of drones for delivering AEDs in the event of OHCAs have been proposed as a feasible alternative to traditional EMS. However, there is limited data on flight testing of such drone deliveries in suburban areas.

Objectives: This study aims to evaluate the flight capabilities and accuracy of drones delivering AEDs to OHCAs.

Methods: The study took place at the Thammasat University, Pattaya campus, Thailand. Ninety test flights were performed on DJI M-600 with three different payloads: no load, 2 kg AED and 4 kg AED. The testing evaluated the speed and accuracy of difference points of landing by using drone and mobile phone GPS location. Flight distance, drone response time, drone overall speed, wind speed, battery usage and landing distance error to target location were recorded. Multivariable regression analysis was used to determine the association of different factors with drone overall speed.

Results: This study completed 90 flights totalling 487.52 km, 14 hours of flight time and 88 successful deliveries. The median flight distance was 4.04 km (IQR 2.28-7.98). The drone's overall speed was negatively affected by payload weight, with a mean absolute difference of 0.83 m/s for 2 kg AED and 1.29 m/s for 4 kg AED compared to no load. The maximum distance coverage was around 4.35 km for the drone could fly to reach target within 8 minutes. Landing distance errors were mostly within one-meter range, successful delivery rates ranging from 96.67% to 100%.

Conclusions: Drone delivery of AEDs can be an effective alternative means of responding to OHCAs in suburban areas. The heavier payload weight resulted in slower speed, while mobile phone GPS location is accurate for landing purposes. Future studies should continue exploring the viability and safety of drone emergency response systems.

Keywords: drone delivery, AED, out-of-hospital cardiac arrest, early defibrillation, suburban area

[1] Department of Emergency Medicine, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[2] Thai Resuscitation Council, Bangkok, Thailand

Abstracts *(Oral Presentation)*

Analgesic and Anti-inflammatory Effects of 1% Cannabidiol Gel

Sitthiphon Bunman[1,2], Sombat Muengtaweepongsa [1*], Dilok Piyayotai[1], Ratthaphol Charlermroj[3], Korawit Kanjana[4], Sudtida Phuengwas[3], Manlika Makornwattana[3], Sanghyun Kim[5,6]

Abstract

Background: Cannabidiol (CBD) is an active ingredient in cannabis plants. Moreover, CBD is widely used for analgesic and anti-inflammatory effects. However, CBD's pharmacological efficacy may decrease when used via the oral route, regarding the high first-pass metabolism with cytochrome P450. Consequently, this study evaluated the analgesic and anti-inflammatory effects of 1% CBD gel in animal models.

Objectives: The study aimed to investigate the analgesic and anti-inflammatory effects of 1% CBD use in animal models.

Methods: The formalin and writhing test were evaluated for analgesic effect. Carrageenan-induced edema was used for the anti-inflammatory effect of CBD in rats. Paw volume was measured at baseline and after injection at 1, 2, 3 and 4 h. At the end of the experiment, rats were sacrificed with isoflurane and confirmed with cardiac puncture. All tissues and blood samples were collected after being sacrificed with isoflurane by the veterinarian staff.

Results: The 1% of tropical CBD gel had significantly decreased times of paw licking, decreased writhing response, and degree of paw edema when compared to Placebo and Diclofenac (p<0.01 or less). Moreover, the 1% CBD gel reduced the degree of inflammation and inflammatory cell infiltration displayed by histopathological analysis (p<0.05).

Conclusions: The study demonstrated that the 1% CBD gel had the potential for analgesic and anti-inflammatory effects in an animal model. Further safety and efficacy investigations of 1% CBD gel use in large populations and clinical settings are required.

Keywords: Cannabidiol, Cannabidiol gel, Analgesic, Anti-inflammatory

[1] Center of Excellence in Stroke, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[2] Department of Community and Family Medicine, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[3] National Center for Genetic Engineering and Biotechnology (BIOTEC), National Science and Technology Development Agency (NSTDA), Pathum Thani, Thailand
[4] Center for Immunology and Inflammatory Diseases, Division of Rheumatology, Allergy and Immunology, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA
[5] Group of Research in Ecology-MRC Abitibi (GREMA), Forest Research Institute, University of Québec in Abitibi-Témiscamingue, Amos Campus, Amos, QC J9T 2L8, Canada
[6] Center for Forest Research, University of Quebec in Montreal, Montréal, QC H3C 3P8, Canada
[*] **Corresponding author:** Sombat Muengtaweepongsa, Center of Excellence in Stroke, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand, E-mail: musombat@tu.ac.th

Abstracts *(Oral Presentation)*

Antinociceptive and Anti-inflammatory Activity of 1% Cannabidiol Cream

Sombat Muengtaweepongsa[1], Sitthiphon Bunman[1,2*], Dilok Piyayotai[1], Ratthaphol Charlermroj[3], Sudtida Phuengwas[3], Manlika Makornwattana[3], Korawit Kanjana[4], Sanghyun Kim[5,6]

Abstract

Background: Cannabidiol (CBD) is a non-psychoactive compound of products derived from the plant *Cannabis sativa.* CBD has therapeutic potential for analgesic and anti-inflammatory. The bioavailability of oral administration CBD has been reported to be poor because of the high first-pass metabolism with cytochrome P450. Transdermal delivery systems of CBD may decrease via cytochrome P450 and increase bioavailability. This study aimed to evaluate the antinociceptive and anti-inflammatory activities of 1% CBD cream in a rodent model.

Objectives: The study aimed to evaluate the antinociceptive and anti-inflammatory activities of 1% CBD cream in a rodent model.

Methods: We evaluated the antinociceptive and anti-inflammatory of 1% CBD cream. Antinociceptive activity was used for the formalin and writhing tests. The anti-inflammatory activity was used for carrageenan-induced edema.

Results: Formalin test, Area under the curve (AUC) values in all treatments were significantly decreased when compared with placebo cream ($P<0.0001$ and $P<0.0001$, respectively), which were the same results in both phases. The results of the acetic-induced writhing response test have demonstrated that diclofenac and CBD cream showed significantly reduced writhes, comparing with a placebo group. Carrageenan-induced edema showed that 1% CBD cream has significantly decrease paw volume from 1 to 4 h when compared to the placebo group.

Conclusions: The study demonstrated that 1% CBD cream has a benefit for analgesia and anti-inflammation. Even though the mechanism of the actions has not been completely understood but also, the topical of 1% CBD cream may also be a good candidate for analgesic and anti-inflammatory conditions.

Keywords: Cannabidiol, Cannabidiol cream, Antinociceptive, Anti-inflammation

[1] Center of Excellence in Stroke, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[2] Department of Community and Family Medicine, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[3] National Center for Genetic Engineering and Biotechnology (BIOTEC), National Science and Technology Development Agency (NSTDA), Pathum Thani, Thailand
[4] Center for Immunology and Inflammatory Diseases, Division of Rheumatology, Allergy and Immunology, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA
[5] Group of Research in Ecology-MRC Abitibi (GREMA), Forest Research Institute, University of Québec in Abitibi-Témiscamingue, Amos Campus, Amos, QC J9T 2L8, Canada
[6] Center for Forest Research, University of Quebec in Montreal, Montréal, QC H3C 3P8, Canada
[*] **Correspondence to:** Sitthiphon Bunman, Department of Community and Family Medicine, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand, E-mail: Bunman@tu.ac.th

Abstracts *(Oral Presentation)*

The Impact of Metformin on The Osteogenic Differentiation of Mesenchymal Stromal Cells from Placenta.

Sirikul Manochantr[1,2*], Nungruethai Chadee[1], Chairat Tantrawatpan[1,2], Pakpoom Kheolamai[1,2], Duangrat Tantikanlayaporn[1,2], Jintamai Suwanprateeb[3]

Abstract

Background: Metformin has been shown to influence bone regeneration. However, its impact on human placenta-derived mesenchymal stem cells (PL-MSCs) remains unknown.

Objectives: This study aimed to investigate the effects of metformin on the viability and osteogenic differentiation of PL-MSCs.

Methods: After characterization, PL-MSCs were treated with metformin. The cell viability was examined using an MTT assay. The osteogenic differentiation potential after metformin treatment was investigated using alkaline phosphatase (ALP) activity assay and Alizarin red staining. The phosphorylated and unphosphorylated adenosine 5'-monophosphate-activated protein kinase (AMPK) were quantified by Western blot analysis in response to metformin.

Results: The results showed that PL-MSCs exhibited the characteristics of mesenchymal stem cells. Metformin at a concentration of less than 320 μM did not affect the viability of PL-MSCs. Metformin stimulated alkaline phosphatase activity and enhanced mineralized nodule formation. Metformin activated the AMPK pathway in a dose-dependent manner.

Conclusions: This study demonstrated that metformin enhanced the osteogenic differentiation and mineralization of PL-MSCs. This essential information could increase the possibility of using metformin for bone repair.

Keywords: Mesenchymal stem cells, Metformin, Osteogenic differentiation, Placenta

[1] Division of Cell Biology, Faculty of Medicine, Thammasat University, Pathum Thani, 12120, Thailand
[2] Center of Excellence in Stem Cell Research and Innovation, Thammasat University, Pathum Thani, 12120, Thailand
[3] Biomedical Engineering Research Unit, National Metal and Materials Technology Center (MTEC), Ministry of Science and Technology, Pathum Thani 12120, Thailand
[*] **Corresponding author:** Sirikul Manochantr, Division of Cell Biology, Faculty of Medicine, Thammasat University, 12120, Thailand
Email: bsirikul@tu.ac.th

Abstracts *(Oral Presentation)*

A Phytoestrogen from *Curcuma comosa* Roxb Enhances *in vitro* Osteogenesis of Mesenchymal Stem Cells

Moe Moe Paing[2], Pakpoom Kheolamai[1,2], Sirikul Manochantr[1,2], Chairat Tantrawatpan[1,2], Duangrat Tantikanlayaporn[1,2]

Abstract

Backgroud: Human umbilical cord-derived mesenchymal stem cells (UC-MSCs) are one of attractive candidates for cell-based therapy and regenerative medicine. However, the diferentiation ability is inefficient when compared to MSCs derived from bone marrow (BM-MSCs). Therefore, efforts to increase the osteogenic potential of UC-MScs would be a significant step forward in regenerative medicine.

Objectives: We aimed to investigate the potential of A phytoestrogen (AS-DT01) from *Curcuma comosa* Roxb on *in vitro* osteogenesis of UC-MSCs

Methods: Mesenchymal stem cells were isolated from full-term normal human umbilical cords and were characterized before using. Cell cytotoxicity effect of AS-DT01 were examined by MTT. The non-toxicity concentrations of AS-DT01 were further examined for osteogenic effect determined by alkaline phosphatase (ALP) expression and activity, alizarin red staining and osteoblast-specific gene expressions.

Results: The results demonstrated that AS-DT01 at 1-10 μM had no cytotoxic effect on the UC-MSCs. AS-DT01 also accelerated the osteogenic differentiation of UC-MSCs as indicated by the increased of ALP staining, ALP activity, calcium deposition by Alizarin Red S stain and osteogenic markers genes such as RUNX2, OSX, ALP, OCN, COL1A1. Furthermore, DPHD increased the OPG/RANKL ratio to improved bone formation.

Conclusions: AS-DT01 has the potential in promoting osteogenesis of UC-MSCs which appears to be a promising new agent for improving osteogenic differentiation capability of hUC-MSCs and for use in stem cell-based bone regeneration therapy.

Keywords: Phytoestrogen, osteogenesis, mesenchymal stem cells, regenerative medicine

[1] Division of Cell Biology, Faculty of Medicine, Thammasat University, Pathum Thani, 12120, Thailand
[2] Center of Excellence in Stem Cell Research, Thammasat University, Pathum Thani, 12120, Thailand

Abstracts *(Oral Presentation)*

Development of A Chemical Analysis Method for Thatbunjob Remedy

Jaiboonya Jaicharoensub[1], Intouch Sakpakdeecharoen[2], Sumalee Panthong[2]

Abstract

Introduction: The formulation of medicinal products often involves combining different active and inactive substances. To accurately assess these formulations, it is necessary to use reliable analytical methods. Relying only on a single herb-based validation method using high-performance liquid chromatography (HPLC) may not provide a complete understanding and can potentially change the chemical composition. This study focuses on Thatbunjob, a traditional herbal remedy from Thailand. It used to treat non-infectious diarrhea and flatulence. However, there is limited research on the active compounds present in commercially available Thatbunjob products, making it challenging to control their quality standards.

Objectives: To develop a validated HPLC method for determining active compounds in Thatbunjob. The main compounds, gallic acid, chebulagic acid, rutin and eugenol, were estimated following the International Conference on Harmonization (ICH) guideline.

Methods: The HPLC samples were prepared using a methanolic extract of Thatbunjob powder. The extract was injected into a C18 reverse-phase column, and the separation was achieved using a mobile phase consisting of water with 0.1% phosphoric acid and acetonitrile. The concentration ratios of the mobile phases were adjusted during the analysis. The analytical method was validated according to the ICH guidelines.

Results: The developed analytical method exhibited excellent linearity, with correlation coefficients (R^2) ranging from 0.9992 to 0.9998. The LOD and LOQ values were determined based on the calibration curve and were found to be in the ranges of 7.29-14.99 µg/ml and 22.09-45.42 µg/ml, respectively. The method demonstrated precision, with relative standard deviation values below 2%. Accuracy assessment using recovery percentage within the acceptable range of 90.12% to 105.39%. Furthermore, the validated method was applied to analyze the concentrations of an active compounds in eight different commercially available Thatbunjob products in Thailand.

Conclusions: The developed and validated analytical method has demonstrated its suitability for the accurate quantification of an active compound in Thatbunjob. This validated method can serve as a valuable tool for quality control of Thatbunjob formulations.

Keywords: Gallic acid, Chebulagic acid, Rutin, Eugenol, Validation

[1] Faculty of Medicine, Thammasat University, Klongluang, Pathum Thani 12120, Thailand
[2] Department of Applied Thai Traditional Medicine, Faculty of Medicine, Thammasat University, Klongluang, Pathum Thani 12120, Thailand

Abstracts *(Oral Presentation)*

Inhibition of Colorectal Cancer Cell Proliferation by A Molecular Hybrid of miR-143 and AS1411 Aptamer Used as Carrier for Doxorubicin

Khanittha Laowichuwakonnukul[1], Boonchoy Soontornworajit[2], Pichayanoot Rotkrua[1]

Abstract

Background: Colorectal cancer (CRC) is the third most common cancer worldwide and the second leading cause of death in 2020. However, there are many limitations of current therapy, including undesired side effects. Therefore, smart drug delivery systems (SDDSs) are promising methods to improve treatment efficiency.

Objectives: This research aims to investigate the effectiveness of a molecular hybrid (MAH) composed of tumor-suppressor miR-143 and AS1411 aptamer as an anticancer drug carrier.

Methods: The MAH was constructed by combining miR-143 and AS1411 aptamer via a hybridization strand, and subsequently loading doxorubicin (Dox), a chemotherapeutic drug, into the molecule. The uptake capability of MAH into the SW480 cells was explored by a fluorescence microscope. The expression levels of miR-143 before and after treatment of MAH were detected using RT-qPCR. Changes in miR-143 target genes, *KRAS*, were measured at both mRNA and protein levels using RT-qPCR and western blotting. MTS assay was used to determine cell proliferation, and flow cytometry was performed to assess cell apoptosis following Dox-MAH treatment.

Results: AS1411 aptamer can specifically bind to the nucleolin receptors on SW480 cells, leading to the endocytosis of MAH. MiR-143 level was significantly increased, while KRAS mRNA and protein levels were subsequently decreased in MAH-treated SW480 cells. Treating cells with Dox-MAH resulted in the inhibition of cell proliferation and induction of apoptosis.

Conclusions: The success of this research proposed a new strategy to use MAH as a Dox carrier with multiple functions. Therapeutic efficacy could be increased due to SDDSs' ability.

Keywords: MicroRNA-143, AS1411 aptamer, Colorectal cancer, SDDSs

[1] Division of Biochemistry, Department of Preclinical Science, Faculty of Medicine, Thammasat University, Pathum Thani 12120, Thailand
[2] Department of Chemistry, Faculty of Science and Technology, Thammasat University, Pathum Thani, 12120, Thailand

Abstracts *(Oral Presentation)*

Efficacy and Safety of 0.13% CBD Acne Cream with 2.5% Benzoyl Peroxide vs. 1% Standardized Clindamycin Gel with 2.5% Benzoyl Peroxide in Acne Vulgaris Treatment.

Sirashat Hanvivattanakul, Isaree Laonipon, Virunpat Vilaichone, Panlop Chakkavittumrong, Benjaporn Srisantithum

Abstract

Background: Acne vulgaris is a common dermatological condition affecting populations worldwide. In vitro studies have indicated that cannabidiol (CBD), derived from cannabis, has anti-inflammatory, antibiotic, and lipostatic properties, which may be used for acne treatment.

Objectives: This study aimed to compare the efficacy and adverse effects of a 0.13% CBD-containing acne cream and 1% clindamycin gel.

Methods: Twenty-nine patients were randomly assigned to receive either the 0.13% CBD acne cream or the clindamycin gel, both with applied 2.5% benzoyl peroxide, applied on the different sides of the face twice daily for four consecutive weeks. The study outcomes were assessed at four weeks.

Results: Of the participants, about 62% were female with average age of 23.45 years old. At 4 weeks, both groups demonstrated significant reductions in acne lesions compared to baseline ($p<0.001$) and the mean reductions were comparable between CBD and clindamycin groups (-8.48 vs – 8.97, $p = 0.88$). Acne severity of patients who had mild to moderate acne decreased from 27 to 20 cases in the CBD group and from 26 to 22 cases in the Clindamycin group, respectively. The reported adverse effects occurred in less than 20% of the patients and were mild, and not significant different between the two groups.

Conclusions: Both the 0.13% CBD acne cream and the clindamycin gel used with 2.5% benzoyl peroxide demonstrated comparable efficacy in reducing acne lesions and mild adverse effects.

Faculty of Medicine, Thammasat University, Pathum Thani, Thailand

Abstracts *(Oral Presentation)*

Prevalence and Factors Associated with Burnout and Depression of Thai medical Students During The COVID-19 pandemic

Rinradee Lenavat[1], Sirashat Hanvivattanakul[1], Veevarin Charoenporn[1], Kanathip Jongmekwamsuk[2], Korravit Hanvivattanakul[3]

Abstract

Background: Burnout and depression have always been the subject of concern in medical students. COVID-19 effects are uncertain.

Objectives: To investigate the prevalence of burnout and depression, associated factors, and the correlation between these conditions in medical students of COVID-19 era.

Methods: 1st-6th year medical students attending Thammasat university took part in this cross-sectional study. The online survey consisted of a demographic and health behavior questionnaire, the Maslach Burnout Inventory-student survey (MBI-SS), and the Patient Health Questionnaire-9 (PHQ-9). Students' social network platforms were used as distribution.

Results: Of the 386 participants, 57% were female. The mean age was 20.6 ± 2 years. The prevalence of burnout was 9.3%. Within this group, 79.3% had high emotional exhaustion, 70% had high depersonalization and 49% had low personal efficacy. Compared to before COVID-19, 64.8% of participants felt their burnout worsened. Lack of sleep was the associated factor with burnout ($p = 0.042$). The prevalence of mild, moderate and major depressive disorder were 35%, 23.8% and 10.9% respectively. 52.6% reported their depression has worsened after COVID-19. For moderate and major depressive groups, associated factors were interpersonal factors, lack of people to give advice, failing exams and thoughts of resignation ($p = 0.02$, 0.016, 0.022 and <0.001, respectively). Significant correlation was found ($p < 0.001$) between three dimensions of burnout (emotional exhaustion, depersonalization and personal efficacy) with depression.

Conclusions: Burnout and depression are common problems medical students face, and the COVID-19 pandemic makes them even more prominent.

Keywords: Burnout, depression, Covid-19

[1] Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[2] Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[3] Faculty of Dentistry, Rangsit University, Pathum Thani, Thailand

Abstracts *(Oral Presentation)*

Survey of The Knowledge of And Attitude Toward Antibiotic Use and Resistance Among Thammasat University Medical Students

Porntita Sae-li[1], Sirashat Hanvivattanakul[1], Ruj Nana[1], Thana Khawcharoenporn[2]

Abstract

Background: Antibiotic resistance is a global threat, highlighting the importance of medical professionals' knowledge of appropriate antibiotic use and fostering a positive attitude towards antibiotic usage and resistance management.

Objectives: To evaluate knowledge of and attitude toward antibiotic use and resistance among medical students.

Methods: An online survey study was conducted from January to April 2023 among Thammasat University medical students in preclinical and clinical years. Knowledge levels were assessed based on responses to the 15 statements, and attitudes were evaluated using a 5-point Likert scale.

Results: Of the 313 participating students, 65% and 35% were preclinical-year and clinical-year students, respectively. The male population accounted for 44%, and the median grade point average was 3.5. Furthermore, 71% reported having searched for antibiotics online. Clinical-year students had a higher median knowledge score compared to preclinical-year students (12 vs. 9; $p<0.001$). Less than 50% of preclinical-year students answered specific statements correctly, such as those related to antibiotic resistance in gonorrhea and the transmission of antibiotic resistance. Similarly, less than 50% of both preclinical- and clinical-year students responded correctly to the statement linking antibiotic use in animals to antibiotic resistance in humans. Attitudinal differences were observed, with preclinical-year students more likely to support early antibiotic resistance education in high schools and the belief that we can always discover and develop new antibiotics. Clinical-year students were less likely to agree that the Faculty of Medicine provided sufficient knowledge about antibiotic use and resistance ($p<0.05$). Multivariable regression analysis indicated that higher academic year, monthly household income of $USD 3,000 or more, and high English proficiency were associated with higher knowledge scores.

Conclusions: Tailored interventions should be developed, considering the specific academic years of medical students, to enhance knowledge and improve attitudes regarding antibiotic use and resistance. Additionally, the identified factors associated with knowledge scores should be considered when implementing interventions, aiming to improve understanding and attitudes towards antibiotic use and resistance among the students.

Keywords: Knowledge, Attitude, Medical students, Antibiotic use, Antibiotic resistance

[1] Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[2] Infectious Diseases Unit, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand

ABSTRACTS
(POSTER PRESENTATION)

Abstracts *(Poster Presentation)*

Comparative study on Efficacy of the Court-Type Traditional Thai Massage, Taping and Plantar Fascia Stretching in Plantar fasciitis patients: A Randomized, controlled trial

Jurairat Boonruab[1], Sunyarn Niempoog[2], Phiyaphon Poonsuk[1]

Abstract

Background: Plantar Fasciitis is caused by chronic inflammation in the medial calcaneal tuberosity.

Objectives: This study investigated the efficacies of Court-Type Traditional Thai Massage (CTTM), Taping (KT) and Plantar Fascia Stretching (PFS) in plantar fasciitis patients.

Methods: Ninety patients were randomly assigned for 4 weeks to receive either: 1) CTTM twice a week, 2) KT once a week, or 3) PFS of the Achilles tendon and plantar fascia every day. Pain Intensity (VAS), Pressure Pain Threshold (PPT), Ankle Range of Motion (A-ROM), Foot Function Index (FFI), Foot and Ankle Ability Measure (FAAM), and Quality of Life (QOL) were assessed at week 0, week 4 and week 8.

Results: After treatment, VAS-M, VAS-24h, Ankle Dorsiflexion, PPT, FFI and FAAM were significantly improved. In addition, CTTM, KT, and PFS showed significant increases in all age groups with QOL at week 4 and week 8. Furthermore, Ankle Plantar Flexion significantly increased in CTTM but did not significantly increase in KT and PFS. Comparative efficacy, CTTM showed significant improvements in VAS-24h, Ankle Plantar Flexion, and FFI at week 4 and week 8. Nevertheless, VAS-M and PPT only showed improvement during the follow-up period. In contrast, Ankle Dorsiflexion was significantly increased in all three groups. Additionally, all three groups did not significantly enhance FAAM. The QOL, when comparing Physical Health domain scores among the three groups found that only the Bodily Pain in middle age patients showed significant differences at week 4 after treatment. Meanwhile, when comparing Mental Health domain scores among the three groups showed no significant differences at week 4 and week 8 in all ages.

Conclusions: CTTM is an effective treatment that can be used as an optional treatment technique for plantar fasciitis patients.

Keywords: Plantar Fasciitis, Court-Type Traditional Thai Massage, Heel pain

[1] Department of Applied Thai Traditional Medicine, Faculty of Medicine, Thammasat University
[2] Department of Orthopedic Faculty of Medicine, Thammasat University

Abstracts *(Poster Presentation)*

Longcovid Condition at 3 and 6 Months During Delta Epidemic Wave

Paskorn Sritipsukho[1], Sasinuch Rutjanawech[2], Narongkorn Saiphoklang[2], Adisai Buakhamsri[2], Ratchaya Lertnawapan[2], Bubpha Pornthisan[2], Thana Khawcharoenporn[2], Thonvarin Aphichotwasit[3], Chonlawat Chaichan[4]

Abstract

Background: Longcovid condition has been introduced as a diverse set of symptoms after a minimum of 4 weeks from the onset of a diagnosed COVID-19 infection.

Objectives: This study aimed to determine the 3 & 6 month-prevalence of longcovid condition and its clinical characteristics after Covid-19 infection during Delta-variant epidemic wave.

Material & Methods: All Covid-19 individuals, aged >18 years, at Thammasat University Hospital during October to December 2021 were recruited and followed for symptoms of longcovid condition at 3 and 6 months by telephone interview using the structured questionnaire.

Results: Of 1,400 eligible Covid-19 cases enrolled in the study, there were 1,129 and 932 cases completed the interview at 3 and 6 months after the infection respectively. There were 431 cases and 314 cases having at least one persist symptom defined as longcovid condition. The point prevalence of longcovid condition at 3 months and 6 months a fter the infection were 38.2% (95% confidence interval: 35.3% to 41.1%) and 33.7% (95% confidence interval: 30.7% to 36.7%) respectively. By multivariable logistic regression model, independent risk factors of the longcovid condition included female, diseases severity, and symptomatic acute infection.

Conclusions: Longcovid is common among covid-19 during delta epidemic wave in Thailand.

[1] Department of Pediatrics, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[2] Department of Internal Medicine, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[3] Thammasat University Hospital, Pathum Thani, Thailand
[4] Postgraduate studies, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand

Abstracts *(Poster Presentation)*

The Diagnostic Accuracy of Harris Imprint Index, Chippaux-Smirak Index and Staheli Index Compared with Talar-First Metatarsal Angle for Screening Arch of The Foot

Siranya Paecharoen[1], Marut Arunakul[2], Nuttharat Tantivangphaisal[1]

Abstract

Objectives: To determine the diagnostic accuracy and reliability of the Harris imprint index (HII), Chippaux-Smirak index (CSI), and Staheli index (SI) compared with the talar-first metatarsal angle

Methods: Data was collected at the orthotic and prosthetic clinic, Thammasat university hospital from 1 January 2016 to 31 August 2020. The three footprints were measured by the rehabilitation physician and the orthotist. The talar-first metatarsal angle was measured by the foot and ankle orthopaedist.

Results: The data from one hundred and ninety-eight patients with 274 feet was analyzed. The diagnostic accuracy of the footprint triad showed that CSI was the most accurate in pes planus prediction, followed by HII and SI (AUROC = 0.73, 0.68, 0.68, respectively). In pes cavus, HII was the most accurate, followed by SI and CSI (AUROC = 0.71, 0.61, 0.60, respectively). For pes planus, the intra-observer reliability by Cohen's Kappa was 0.92 for HII, 0.97 for CSI, and 0.93 for SI, the inter-observer reliability 0.82, 0.85, and 0.70 respectively. For pes cavus, the intra-observer reliability was 0.89 for HII, 0.95 for CSI, and 0.79 for SI, inter-observer reliability of 0.76, 0.77 and 0.66 respectively.

Conclusions: The accuracy of HII, CSI, and SI was fair in screening of pes planus and pes cavus. The intra- and inter-observer reliability were in the moderate to almost perfect range by Cohen's Kappa.

Keywords: pes planus, flatfoot, pes cavus, high-arched foot, reliability and validity

[1] Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[2] Department of Orthopaedics, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand

Abstracts *(Poster Presentation)*

Case Fatality Rate and Characteristics of COVID-19 death cases in Thailand

Surasak Buranatrevedh

Abstract

This research aimed to find case fatality rate and characteristics of COVID-19 death cases in Thailand between January 1, 2020 and December 31, 2021 by searching data from Facebook page of Thai Covid-19 data center. There were 2,223,435 cases and 21,698 deaths of Covid-19 in Thailand during that period. Case fatality rate was 0.98%. Death cases were males (53.91%) more than females (45.51%). Mean and standard deviation of age of death cases were 54.98 and 21.91 years. Common races of death cases were Thai (96.41%) and Myanmar (1.77%). Most death cases lived in Bangkok (31.21%), Samut Prakarn (6.73%), Samut Sakorn (3.96%), Pathum Thani (3.71%) and Chonburi (3.63%). Common underlying diseases among death cases were hypertension (1.37%), chronic kidney disease (1.24%), hyperlipidemia (1.23%), and obesity (1.17%). Common risk factors of death cases were contact with Covid-19 patients (48.59%), living in risk areas (40.83%), going to crowded areas (2.22%), risk career (1.65%) including health care workers (0.06%). Further study from more complete data will have benefit to prevent deaths from Covid-19.

Faculty of Medicine, Thammasat University, Klongluang, Pathum Thani 12120
Email: sburana@tu.ac.th

Abstracts *(Poster Presentation)*

Comparison of Cytotoxic Activity Against Gastrointestinal Cancers and Anti-inflammatory Activity of *Basella alba* L. and *Basella rubra* L.

Srisopa Ruangnoo[1,2], Yanisa Ruaysup[1], Arunporn Itharat[1,2]

Abstract

Background: Gastrointestinal (GI) cancer is one of the most common cancers around the world. The incidence and death rate of GI cancers are very high. *Basella* (Indian spinach or Ceylon spinach) is an importance leafy vegetable grown for its nutritive value and has been shown to have biological activities i.e. wound healing, anti-microbial, anti-inflammatory and anti-ulcer activities.

Objectives: To compare the in vitro cytotoxic activity against GI cancers and anti-inflammatory activity of fresh and dry *B. alba* and *B. rubra*.

Methods: The ethanolic and aqueous extracts of fresh and dry *B. alba* and *B. rubra* were test cytotoxic activity against five types of GI cancer and one type of normal cell by using SRB assay and the anti-inflammatory activity through inhibition of nitric oxide (NO) production.

Results: The ethanolic extract of fresh *B. alba* showed the highest cytotoxicity against colon cancer cells (SW480), gastric cancer cells (KATOIII), bile duct cancer cells (KKU-M156), oral cavity cancer cells (KB) and liver cancer cells (HepG2) with IC_{50} values of 31.54, 33.82, 33.79, 39.31 and 59.63 µg/mL, respectively, but this extract showed less cytotoxic activity against normal cells (HaCaT). Interestingly, the aqueous extract of fresh *B. alba* possessed potent NO inhibitory activity against lipopolysaccharide (LPS) induced nitric oxide production with an IC_{50} value of 4.27 µg/mL.

Conclusions: The ethanolic and aqueous extracts of *B. alba* exhibited potent and selective cytotoxic and anti-inflammatory activities. These two extracts have potential for further development as anticancer and anti-inflammatory drugs.

Keywords: *Basella alba* L., *Basella rubra* L., Cytotoxic activity, Anti-inflammatory activity, Gastrointestinal cancers

[1] Department of Applied Thai Traditional Medicine, Faculty of Medicine, Thammasat University, Pathum Thani, 12120, Thailand
[2] Center of Excellence on Applied Thai Traditional Medicine Research (CEATMR), Faculty of Medicine, Thammasat University, Pathum Thani, 12120, Thailand

Abstracts *(Poster Presentation)*

Effect of Curcumin on The Expression of *Helicobacter pylori* virulence genes

Sasichai Kangsadalampai, Nantapong Ritdet

Abstract

An increased antibiotic resistance of *H. pylori,* a major cause of dyspepsia and a carcinogenic agent of gastric cancer, leads to a number of searches for new antibacterial compounds. Curcumin, a major bioactive ingredient of turmeric (*Curcuma longa* L.), shows the capability to inhibit *H. pylori* growth and a therapeutic potential against the bacterial infection. Several effects of curcumin were demonstrated on patient gastric tissues while those on *H. pylori* have not been clear. To gain a better understanding of the effects on *H. pylori,* the bacteria were grown in the presence of curcumin at subinhibitory concentration and expression of their major virulence genes (*cagA*, *vacA*, *ureA*, *ureB*, *rocF*, *ggt*, *babA*, *sabA*, *napA* and *oipA* genes) were analyzed by the qPCR method. After curcumin exposure, the spiral-shape bacteria transformed into the coccoid form in dose dependent manner. It was noted that the curcumin-induced coccoid bacteria continuously expressed the virulence mRNAs with the topmost up-regulation of the *ureA*, *ureB* and *babA* genes. Data obtained in this study not only suggested other possible bacterial targets of curcumin but also revealed the infectious ability of the *H. pylori* after exposure to antibacterial compounds such as curcumin at subinhibitory concentration.

Division of Biochemistry, Faculty of Medicine, Thammasat University, Rangsit Centre, Khlong Nueng, Khlong Luang, Pathum Thani 12120

Abstracts *(Poster Presentation)*

Ethanolic Extract of *Dioscorea membranacea* in vitro Inhibition of The Endometrial Cancer Cell Line and Inflammation

Sumalee Panthong, Duangpacharaporn Kwanchian, Srisopa Ruangnoo, Intouch Sakpakdeejaroen

Abstract

Background: Endometrial cancer is the most common genital cancer in women and uterine cancer constitutes about 5.1% of the female cancer burden in Thailand. Currently, alternative medicine and natural products are preferred cancer treatment choices. *D. membranacea* is used by Thai traditional doctors as an ingredient in the herbal preparation for treating lymphography, inflammation, cancer, venereal disease and leprosy. However, anticancer properties of *D. membranacea* against endometrial cancer cells has yet to be explored.

Objectives: To investigate anticancer activity of *D. membranacea* ethanolic extract against the endometrial HEC-1A cell line and determine its anti-inflammatory activity.

Methods: The *D. membranacea* rhizome extract was obtained by maceration, using 95% ethanol. Anticancer activity was tested by sulforhodamine B assay and anti-inflammatory activity was investigated in LPS-stimulated RAW264.7 cells.

Results: *D. membranacea* ethanolic extract showed significantly inhibited growth of HEC-1-A with IC_{50} values of 48.26 μg/mL. It also demonstrated low toxicity to HaCaT cell lines with IC^{50} values of 90.57 ± 0.13 μg/mL. The extract selective index was 1.88 compared with HaCaT. In addition, the extract inhibited nitric oxide production and IL-6 with IC_{50} values of 15.75 and 39.57 ± 2.34 μg/mL, respectively; it showed no toxicity on RAW264.7 cells.

Conclusions: Results were that *D. membranacea* ethanolic extract had a potent *in-vitro* anticancer effect inhibiting pro-inflammatory cytokines. These findings offer a useful basis for further studying *D. membranacea* as part of an anti-endometrial cancer mechanism.

Keywords: *Dioscorea membranacea*, Endometrial cancer, Anti-inflammation

Department of Applied Thai Traditional Medicine, Faculty of Medicine, Thammasat University, Pathum Thani 12120, Thailand

Abstracts *(Poster Presentation)*

Genetic Variation of The Lymnaeid and Physid Snails (Mollusca, Gastropoda) in Thailand examined by Mitochondrial CO1 sequence

Chairat Tantrawatpan[1], Weerachai Saijuntha[2]

Abstract

Background: The freshwater lymnaeid and physid snails serve as the sole intermediate hosts of several medically and veterinary important trematodes, such as fascioliasis, schistosomiasis and echinostomiasis that can infect and cause diseases in livestock and human. In Thailand, there is little information on the genetic variation of lymnaeid and physid snails.

Objectives: This study aims to explore the mitochondrial cytochrome c oxidase subunit 1 (CO1) sequence variation of lymnaeid and physid snails from different localities in Thailand.

Methods: The lymnaeid and physid snails were collected from 36 different geographical areas in Thailand, including 161 *R. rubiginosa*, 7 *Orientogalba* sp., 9 *Racesina* sp., and 75 *Physa acuta*. These snails were subjected to CO1 sequence analysis.

Results: A high level of genetic variation in *R. rubiginosa* was detected, with 40 haplotypes (H1 - H40) being recorded. Phylogenetic analyses revealed two clades in the material identified as *R. rubiginosa*. One clade contained all samples examined in this study with a sequence from Indonesia, while the second clade comprised specimens found in Singapore, Malaysia and Vietnam.

Conclusions: Our finding suggests that a lymnaeid snail *R. rubiginosa* in Southeast Asia is a species complex, comprises at least two species.

Keywords: Pulmonated snail; radicine snail; intermediate host; species complex; mitochondrial DNA

[1] Division of Cell Biology, Department of Preclinical Sciences, Faculty of Medicine and Center of Excellence in Stem Cell Research and Innovations, Thammasat University, Pathum Thani, Thailand

[2] Walai Rukhavej Botanical Research Institute (WRBRI), Biodiversity and Conservation Research Unit, Mahasarakham University, Maha Sarakham, Thailand

Abstracts *(Poster Presentation)*

Large-scale Production of 4^G-α-D-maltotriopyranosyl-hesperidin by Intermolecular Transglucosylation of Recombinant Cyclodextrin Glycosyltransferase

Jarunee Kaulpiboon[1,2]

Abstract

Background: Diabetes mellitus (DM) is one of the major health problems in several countries, including in Thailand. The natural compounds such as phenolic substances from plants have been studied as alternative treatments for DM. One of those, hesperidin, shows α-glucosidase inhibitory activity which decreases blood glucose levels. This benefit can be applied for clinical application in DM treatment.

Objectives: This study focused on the production of hesperidin glucoside, 4^G-α-D-maltotriopyranosyl-hesperidin (HG_3), in large-scale level to obtain the higher yield for its structural identification and evaluation of the α-glucosidase inhibitory activity.

Methods: The recombinant CGTase, prepared from the p19bBC *E. coli* cells, was used to synthesize HG_3 under optimum conditions. The synthesized HG_3 was identified its structure by mass spectrometry and NMR. The α-glucosidase inhibitory activity of HG_3 and other hesperidin derivatives was also comparatively studied.

Results: Preliminary-structural investigation, HG_3 was treated with glucoamylase and analyzed on thin layer chromatography (TLC). The result revealed that after glucoamylase treatment, the spots of HG_3 disappeared and only the intensities of hesperidin (H) and glucose (G_1) increased. This result implied the presence of α-1,4 glycosidic bond in the HG_3 molecule. In addition, the LC-MS profile of HG_3 showed the peak at *m/z* ratio of 1,119.34; this value was in accordance with calculated HG_3. The combined ^{1}H- and ^{13}C-NMR analysis confirmed that the structure of HG_3 was 4^G-α-D-maltotriopyranosyl-hesperidin. For the α-glucosidase inhibitory activity, the IC_{50} values of hesperidin, HG_3, diosmin and acarbose (commercial α-glucosidase inhibitor) were 2.75 ± 1.57, 2.23 ± 1.45, 2.99 ± 1.23 and 1.64 ± 1.04 mg/mL, respectively. The most effective α-glucosidase inhibitor among the hesperidin derivatives, HG_3, was continuously studied on enzyme inhibition kinetics. Its Lineweaver-Burk plot revealed to be a competitive inhibition towards α-glucosidase with a K_i of 2.09 ± 0.13 mM.

Conclusions: Thereby influencing its bioavailability and bioactivity, HG_3 is an interesting compound to be developed as a new drug for treatment of type 2 diabetes patients.

Keywords: Chemical structure, Cyclodextrin glycosyltransferase, Diabetes mellitus, α-Glucosidase inhibitor, 4^G-α-D-maltotriopyranosyl-hesperidin

[1] Department of Pre-Clinical Science (Biochemistry), Faculty of Medicine, Thammasat University, Pathum Thani 12120, Thailand
[2] Department of Biochemistry, Phramongkutklao College of Medicine, Phramongkutklao Hospital, Bangkok 10400, Thailand

Abstracts *(Poster Presentation)*

The Effects of Human Mesenchymal Stem Cells on The Proliferative, Migratory, and Invasive Properties of Glioblastoma Multiforme

Tanawat Uthanaphun[1], Sirikul Manochantr[2,3], Chairat Tantrawatpan[2,3], Duangrat Tantikanlayaporn[2,3], Pakpoom Kheolamai[2,3]

Abstract

Glioblastoma Multiforme (GBM) is considered the most common and most aggressive brain tumor. GBM rapidly invades the surrounding brain tissue and resists most chemotherapeutic agents resulting in a high mortality rate even after receiving treatment. Previous studies suggest that several cancer stromal cells, especially the human mesenchymal stem cells (hMSCs) that are parts of the tumor, play essential roles in the growth, metastasis and drug responses of GBM cells. However, distinct sources of hMSCs might release different combinations of soluble factors that affect GBM cells differently. Therefore, in the present study, we established hMSCs from the placenta (PL-hMSCs) and chorion (CH-hMSCs) to study the effects of their released soluble factors on the proliferation, migration and invasion of human GBM cell, U251. The results showed that the soluble factors derived from PL-hMSCs and CH-hMSCs suppressed the proliferation of U251 cells in a dose-dependent manner. The soluble factors derived from PL-hMSCs have a higher suppressive effect on U251 proliferation than those of CH-hMSCs. On the contrary, the soluble factors derived from both hMSC sources increased the migration of U251 cells but did not affect the invasive property of those cells. The gene expression analysis showed that the soluble factors derived from PL-hMSCs and CH-hMSCs down-regulated the expression levels of *E2F1*, *E2F2*, *NFKB1*, *NFKB2*, *NOTCH1*, *NOTCH2*, *PROM1*, *MYC*, and *ITGA1* which promote GBM proliferation. These results suggest that the soluble factors derived from both hMSC sources might suppress the proliferation of GBM cells by inhibiting the expression of genes that promote GBM proliferation. Our study will provide a better understanding of the interaction between the GBM cells and hMSCs, which are the critical parts of the GBM stroma. This knowledge could be used to develop a more effective treatment that improves the survival and quality of life of GBM patients.

Keywords: Mesenchymal stem cell, Glioblastoma, Cytokine

[1] Master of Science Program in Stem Cell and Molecular Biology Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[2] Center of Excellence in Stem Cell Research and Innovation, Faculty of Medicine, Thammasat University, Pathum Thani 12120, Thailand
[3] Division of Cell Biology, Faculty of Medicine, Thammasat University, Pathum Thani 12120, Thailand

Abstracts *(Poster Presentation)*

High Glucose Stimulates The Expression of The Senescence Genes in Human Mesenchymal Stem Cells.

Supawadee Duangprom[1], Chairat Tantrawatpan[2, 3], Pakpoom Kheolamai[2, 3], Duangrat Tantikanlayaporn[2, 3], Sirikul Manochantr[2, 3*]

Abstract

Background: Glucose is an essential senescence regulator. High glucose prevents cell division and induces permanent growth arrest. A previous study has demonstrated that high glucose causes cells to enter a premature senescence state. However, high glucose-induced senescence's effects and molecular mechanisms in mesenchymal stem cells remain unknown.

Objectives: This study aimed to determine whether exposure to high glucose could result in mesenchymal stem cell senescence.

Methods: Under high glucose conditions, the cellular senescence and stemness of human mesenchymal stem cells (MSCs) were investigated. The expression of the senescence markers *(p53*, *p21, p16)* and stemness marker *(Oct-4*, *Nanog*, *Sox-2)* were determined by quantitative real-time reverse transcription polymerase chain reaction (qRT-PCR). The normal glucose concentration-treated MSCs served as a control.

Results: The results demonstrated that MSCs had significantly increased the expression of *p53*, *p21* and *p16* under high glucose conditions compared with those of the control. Moreover, MSCs also showed significantly decreased expressions of stemness genes, *Oct-4*, *Nanog* and *Sox-2.*

Conclusions: The results indicate that high glucose induces senescence of MSC as evidenced by increased expression of the senescence markers and decreased expression of the stemness markers.

Keywords: Mesenchymal stem cells, High glucose, Senescence

[1] Stem Cell and Molecular Biology Program, Faculty of Medicine, Thammasat University, Pathum Thani 12120, Thailand
[2] Division of Cell Biology, Faculty of Medicine, Thammasat University, Pathum Thani 12120, Thailand
[3] Center of Excellence in Stem Cell Research and Innovation, Thammasat University, Pathum Thani 12120, Thailand
* **Corresponding author:** Sirikul Manochantr, Division of Cell Biology, Faculty of Medicine, Thammasat University, Pathum Thani 12120, Thailand
Email: bsirikul@gmail.com

Abstracts *(Poster Presentation)*

Molecular Identification of *Fasciola gigantica* Retinoid X Receptor (FgRXR)

Nattaya Torungkitmangmi[1], Pathanin Chantree[2], Phornphan Sornchuer[2], Amornrat Geadkaew-krenc[3], Poom Adisakwattana[4], Pongsakorn Martviset[2]

Abstract

Background: Fasciolosis is a parasitic infection caused by the liver fluke genus *Fasciola* that has spread throughout the world. The disease has a huge economic impact on domestic livestock industry. Due to the drug resistance has been increasingly reported, the discovery of new drug targets is required. Nuclear receptor (NR) is the huge protein family accumulating in the nucleus of the metazoans which regulates several cell metabolisms; therefore, NR would be potential drug target.

Objectives: This study aims to identify a novel Retinoid X Receptor (FgRXR) from the liver fluke *Fasciola gigantica* for further development as a drug target.

Methods: In this present study, nucleotide and amino acid sequences of retinoid X receptor of *F. gigantica* (FgRxR), a heterodimeric forming NR, were isolated from the transcriptome of the adult parasite. It has been analyzed by bioinformatics, cloned and expressed as a recombinant protein in *E. coli* expression system. The recombinant protein was used as an immunogen for raising of polyclonal antibodies. The native protein in parasite extracts and tissue was investigated using Western analysis and immunohistochemistry.

Results: The bioinformatics revealed the conservation of FgRXR to family 2 of NR with predicted properties and functions along with this NR family. The 2D and 3D structures demonstrated that FgRXR contained conserved functional domains both DNA binding domain (DBD) and ligand binding domain (LBD). The full-length cDNA encoding FgRXR was cloned and expressed as a recombinant protein in the bacterial expression system by using pET32a(+) together with thioredoxin then used for immunization. Western analysis confirmed that FgRxR could be detected in the parasite crude worm antigen but not excretory/secretory products.

Conclusions: Our findings indicated that FgRXR will probably be a novel drug target for developing of effective anthelmintic drugs combating drug resistance *Fasciola* spp. in the future.

Keywords: Fasciolosis; *Fasciola gigantica*; Retinoid X receptor; drug target

[1] Graduate Program in Biochemistry and Molecular Biology, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[2] Department of Preclinical Science, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[3] Graduate Study in Biomedical Sciences, Faculty of Allied Health Sciences, Thammasat University, Pathum Thani, Thailand
[4] Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Abstracts *(Poster Presentation)*

Antibiotic self-Medicating and Associated Factors Among Medical Students in Thailand: Identifying Predictors and Evaluating Potential Consequences.

Porntita Sae-li, Sirashat Hanvivattanakul, Ruj Nana, Thana Khawcharoenporn

Abstract

Background: Self-medication with antibiotics is common in Thailand due to their easy availability without a prescription, but can lead to antibiotic resistance.

Objectives: To assess antibiotic self-medicating, adverse outcomes, associated factors among Thai medical students.

Methods: An online survey was conducted among preclinical and clinical-year students at a Thai public university from January to April 2023 among Thammasat University medical students. Antibiotic self-medicating and associations with knowledge about antibiotic use and resistance and other factors were determined. The knowledge score was calculated based on the correct response to the 15 provided statements about antibiotic use and resistance.

Results: A total of 313 participants were included, 65% were in preclinical years and 56% were female. Most students (>85%) did not self-initiate antibiotics for conditions which antibiotics were not indicated. However, 13% reported adverse effects from self-initiated antibiotics and 26% were not given appropriate advice on antibiotic use from a pharmacy. Clinical-year students had significantly higher median knowledge scores than preclinical-year students (12 vs. 9; $p < 0.001$). Students who demonstrated proper antibiotic utilization, such as adhering to recommended treatment duration and indications had higher median knowledge score than those who did not ($p<0.05$). In multivariable analysis, higher academic year was protective against not completing a full course of antibiotic treatment ($p = 0.01$) while being female was associated with initiating antibiotics with any upper respiratory tract symptoms ($p = 0.03$).

Conclusions: This study highlights antibiotic self-medicating practices, their adverse outcomes and associated factors among medical students. Efforts should focus on enhancing preclinical-year and female students' knowledge to establish a strong foundation in appropriate antibiotic use and combat the increasing antibiotic resistance.

Keywords: Antibiotics, Self-medication, Antibiotic resistance, Infectious control

Faculty of Medicine, Thammasat University, Pathum Thani, Thailand 12120

Abstracts *(Poster Presentation)*

Examining The Incidence and Factors Influencing Zoom Fatigue in Thai Medical Students during the COVID-19 Pandemic

Rinradee Lenavat[1], Sirashat Hanvivattanakul[1], Veevarin Charoenporn[1], Kanathip Jongmekwamsuk[2], Korravit Hanvivattanakul[3]

Abstract

Background: The COVID-19 pandemic necessitated a shift from onsite to online learning for medical students, introducing the concept of "Zoom fatigue" due to the excessive use of video conferencing platforms.

Objectives: The objective is to assess the prevalence of Zoom fatigue among medical students during the COVID-19 pandemic and identify the possible associated factors.

Methods: This cross-sectional study involved Thai medical students from a large public university in Thailand. An online survey was administered to 1st - 6th-year students, collecting data on demographics, health behaviors, and the validated Thai version of the Zoom Exhaustion & Fatigue Scale (ZEF-T). Zoom fatigue and depression were defined as ZEF-T scores >1 standard deviation and PHQ-9 scores >9, respectively.

Results: A total of 386 students participated, with 57% being female and a mean age of 20.6 years. On average, students attended about 2 Zoom sessions per day, with 83.7% of the participants spending more than 1 hour per session. The prevalence of Zoom fatigue was 14.3% (N = 55). Multivariable regression analysis revealed that a lower academic year ($p < 0.001$) and a higher number of Zoom sessions ($p < 0.001$) were significant predictors of Zoom fatigue. Regular exercise ($p < 0.001$) and sufficient sleep ($p = 0.05$) were identified as protective factors.

Conclusions: Online learning during the COVID-19 pandemic resulted in a substantial prevalence of Zoom fatigue among medical students. Strategies such as reducing online learning sessions, promoting regular exercise and ensuring adequate sleep may help alleviate Zoom fatigue.

Keywords: Zoom fatigue, ZEF-T scores, medical students, student's mental health

[1] Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
[2] Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[3] Faculty of Dentistry, Rangsit University, Pathum Thani, Thailand

Abstracts *(Poster Presentation)*

Investigating The Knowledge, Attitudes and Their Correlation with Vaccine Acceptance Regarding COVID-19 and Its Vaccines among Individuals Living with HIV: A multicenter study.

Sirashat Hanvivattanakul, Thana Khawcharoenporn

Abstract

Background: Data existing on knowledge and attitudes toward COVID-19 and vaccine acceptance are limited among people living with HIV (PLHIV).

Methods: An online survey study was conducted among PLHIV receiving care at two medical centers in Pathum Thani, Thailand between July and December 2022.

Results: There were 513 participating PLHIV (57.9% male and median age 50 years). Most of the PLHIV (95%) were knowledgeable about transmission, prevention, symptoms, causative agent and cause of death of COVID-19, but more than a quarter were less knowledgeable about adverse effects (AEs) of COVID-19 vaccines and populations at-risk for severe COVID-19. Most PLHIV agreed that "COVID-19 is a major public heath and socioeconomic problem" and "everyone should have an equal right and access to the vaccines". Of the 513 PLHIV, 46 (9%) did not accept the vaccine. No confidence in vaccine safety was the main reason for no acceptance (82.6%). In multivariable analysis, unknown HIV viral load within one year, advanced age, national health plan coverage, being a merchant and living outside Bangkok and its vicinity were factors associated with no vaccine acceptance.

Conclusions: Educational interventions regarding AEs of COVID-19 vaccines and at-risk populations for severe COVID-19 are needed among PLHIV. While those with factors associated with no vaccine acceptance should be explored for their underlying reasons and provided appropriate measures to improve vaccine acceptance.

Faculty of Medicine, Thammasat University, Pathum Thani, Thailand 12120

INSTRUCTION FOR AUTHORS

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Case Reports/Brief Research should include a title page, a narrative abstract of no more than 50 words, a text of no more than 1,200 words, no more than 2 tables or figures, and no more than 10 references.

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Letters to the Editor should not exceed 900 words and should include no more than 1 table or figure and no more than 10 references.

Commentaries are by invitation only. Please contact the journal office if you are interested in writing a Commentary.

MANUSCRIPT PREPARATION

Authors who are not fluent in English should have their manuscript checked by a native speaker of English and/or an editing service that provides such assistance. Please concept editorial office if author would like suggestion on editing service. Manuscripts that do not follow the required format or are poorly prepared may be asked to revised for resubmission.

All submitted manuscript most include institutional ethical approval certificate. Single space the entire manuscript, including title page, abstract, body, references, tables, and figure legends. Use left justification only, so that the right margin is ragged. Number pages consecutively, beginning with the title page. Use a standard font Times New Roman and set the font size to 12 points (for tables as well as text). All numbers published in AMJAM will be in Arabic numbers. Each component of the article should begin on a separate page, as follows: title page, abstract, body text, acknowledgments, references, appendices, figure legends, and tables. All these components must be in a single file.

Title Page

The title page should include the following information: (1) the title of the manuscript; (2) the names of the author(s), including each author's highest academic degree or professional certification; (3) the departmental and institutional affiliation of each author, including city, state, and country; (4) the name, address, telephone number, fax number, and email address of the author responsible for correspondence, and (if different) the name and address to be used for reprint requests; (5) if relevant, a statement about any previous presentation of the data or findings in a preliminary report or abstract; (6) an abbreviated title of not more than 45 characters (including spaces), to be used as a running head in print and for search results online; and (7) a word count for the body of the text (ie, excluding the abstract and the references). Acknowledgment of financial support and potential conflicts of interest must be included and should be placed in the Acknowledgments section (see below).

Abstract
Original Articles should include a structured abstract of no more than 250 words. The following headings are suggested: Introduction/Objective, Design, Methods (or Interventions), Results, Conclusions, and Key words (3-5 words or phrases). If this list of headings is inappropriate, variations are permitted: for example, a study that involved no intervention would use the heading "Methods" rather than "Intervention"; or an analysis of an existing data set might use the heading "Methods" in place of both "Intervention". For brevity, parts of the abstract can be written in phrases rather than complete sentences (eg, "Design: Retrospective cohort study" or "Design: Before-after trial").

The contents of each section should conform to the guidelines below.

Body Text
The main sections and subdivisions of the body text should be indicated by side heads flush with the left margin and two lines above the text. Keep Methods, Results, and Discussion distinct and separate. The Methods section should provide detail sufficient to allow others to re-create your experiment. Methods may not be described or restated in figure legends or table notes, but must be all together in the Methods section. The Results section contains the previously unpublished data derived by this application of your methods, without commentary (beyond the minimum that might be necessary to ensure intelligibility to the reader). The Discussion section contains your interpretation of the reported data and comments on its meaning. There should be no separate section labeled "Conclusion." Avoid duplicating in the text data that have been provided in tables or figures (minimal duplication, for emphasis or clarity, is acceptable). Also avoid duplication within the text; for example, the Discussion section should not restate all the findings that have been presented in Results and/or in tables and figures

Acknowledgments
Financial support. The Acknowledgments section should list all sources of financial support for the work, including any financial arrangement with a company whose product is related to the study. If there was no financial support, that too should be stated. Acknowledgments, including grant support, should be placed at the end of the text.

Example:
Financial support. The XXX Project is supported by the Thai Ministry of Health. Additional support for this study was provided by Becton-Dickinson.

Financial support. None reported.

Conflict of interest. The Acknowledgments section must contain a statement of potential conflicts of interest. If the manuscript is accepted for publication, the disclosures will be published. The Acknowledgments section of the manuscript must list the name of each contributing author and any potential conflicts of interest for each author for the previous three years; if no potential conflict exists, that too should be stated.

Example:
Potential conflicts of interest. K.L.H. reports having consulted for and having received grant support from Astellas and reports having received an honorarium from Cubist before starting employment with the New York Department of Public Health in 2009.

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

References

Use the Style Guide of the American Medical Association (AMA) as a reference. References should be cited consecutively in the text, with superscript numbers placed outside periods and commas and inside colons and semicolons. References cited only in tables or figure legends should be numbered as though all were cited at the point at which the table or figure was first mentioned.

A paper that is "in press" may be included in the reference list if it has been accepted for publication. Citations such as "in preparation," "submitted for publication," "unpublished data," and "personal communication" should be given in parentheses in the text only, including the names of all individuals to whom the information should be attributed, as well as each person's highest academic degree and the month and year of the information's origin. For personal communications, specify whether the communication was written or oral.

At the end of each manuscript, list the references in numerical order, single spaced, according to the order they are cited in the text. If there are 7 or more authors, list the first 3 authors' names, followed by "et al"; otherwise, list all authors. Abbreviations of journal names should conform to Index Medicus or MEDLINE. Unlisted journals should not be abbreviated. Authors are responsible for bibliographic accuracy. Journal titles should be cited as they existed at the time of publication. Format references according to the style given in the AMA Manual of Style, 10th Edition.

Example:

Journal article (examples)

1. Pittet D, Simon A, Hugonnet S, Pessoa-Silva CL, Sauvan V, Perneger TV. Hand hygiene among physicians: performance, beliefs, and perceptions. *Ann Intern Med.* 2004;141:1-8.
2. Camins BC, Richmond AM, Dyer KL, et al. A crossover intervention trial evaluating the efficacy of a chlorhexidine-impregnated sponge in reducing catheter-related bloodstream infections among patients undergoing hemodialysis. *Infect Control Hosp Epidemiol.* 2010;31:1118-1123.

Journal article in press (example)

3. Figueroa P, Johanssen KL, Price FG, et al. Outbreak of Acinetobacter infection in a neonatal intensive care unit. *Pediatr Infect Dis J* (in press).

Paper presented at a professional meeting (example)

4. Chen LF, Freeman JT, Sexton DJ, Choi YI, Anderson DJ. NHSN definition of laboratory-detected BSI is overly sensitive for Enterococcus. In: Program and abstracts of the 19th Annual Scientific Meeting of the Society for Healthcare Epidemiology of America (SHEA); March 18-22, 2009; San Diego, CA. Abstract 359.

Book (example)

5. Heoprich PD. Infectious Diseases. *2nd ed.* New York, NY: Harper & Row; 1977.

Chapter in a book (example)

6. Schaffner W. Psittacosis: ornithosis, parrot fever. In: Beeson PB, McDermott W, Wyngaarden JB, eds. *Cecil Textbook of Medicine.* 15th ed. Philadelphia, PA: W. B. Saunders; 1979:336-338.

Web page (example)

7. Clinical laboratory fee schedule. Centers for Medicare and Medicaid Services website. https://www.cms.gov/ClinicalLabFeeSched/02_clinlab.asp#TopOfPage. Published 2010. Accessed April 2, 2010.

Tables and Figures

Prepare tables with the MS Word table editor; text formatted to look like a table by use of tabs and hard returns is not acceptable and will be rejected. Include tables in the same file, not in separate files. Tables should be single spaced. Number tables in the order in which they are cited in the text, and provide a descriptive title for each table.

Every column in a table requires a head that describes the contents of the cells below. The units of measure for all data must be clearly stated in the heads, in the stub (leftmost) column, or in data cells, as appropriate. Do not use vertical lines, and do not use ditto marks for repeated information.

List and define any abbreviations in a note below the table, above the table footnotes (no footnote designator is required for this line), even if the abbreviations have been defined in the text. Use superscript letters for footnote designators.

That are too large to be reproduced in print, if accepted for publication, will appear only in the online version of the article, and information about the online-only table (including a full or partial title) will be included in the print version of the article.

Example of Tables:

Example 1

Table 2. Anemia and Red Blood Cell Transfusions: Intervention and Cointerventions[a]

	Red Blood Cell Group, No. (%)		
	Fresh (n = 728)	Standard-issue (n = 733)[b]	*P* Value
Transfusions after randomization			
No. of transfusions	1630	1533	
Duration of storage, median (IQR), d	5 (4-6)	18 (12-25)	<.001
Volume of units transfused per patient, median (IQR), mL/kg	17.5 (12.9-32.8)	16.6 (12.3-30.6)	.19
No. of patients	723	731	
Time from randomization to first transfusion, median (IQR), h	2.0 (1.0-3.0)	2.0 (1.0-3.0)	
No. of patients	726	733	
Donor exposure to red blood cell units in patients transfused, No. of exposures per patient, median (IQR)	1 (1-2)	1 (1-2)	.24
No. of patients	727	733	
Adherence, No./Total (%)			
Adherence to study protocol[c]	679/727 (93.4)	733/733 (100)	<.001
Adherence to transfusion protocol instructions[d]	1520/1630 (93.3)	1533/1533 (100)	<.001
Cointerventions after randomization			
Received other blood products	323 (44.4)	303 (41.3)	.24
Frozen or fresh frozen plasma	160 (22.0)	149 (20.3)	.44
Apheresis platelets	109 (15.0)	113 (15.4)	.81
Random donor platelets	63 (8.6)	53 (7.2)	.31
Cryoprecipitate	87 (11.9)	75 (10.2)	.30
Albumin 5%	116 (15.9)	95 (13.0)	.11
Albumin 25%	204 (28.0)	187 (25.5)	.28
Systemic corticosteroids	268 (36.8)	251 (34.2)	.30

Abbreviation: IQR, interquartile range.

[a] In all comparisons, the fresh group was used as the reference. Postrandomization characteristics of interventions and cointerventions are presented using frequency distributions with measures of central tendency and dispersion, and analyzed using relative risks and 95% CIs for dichotomous data and either independent *t* tests or Wilcoxon rank-sum tests for continuous data depending on their distribution.

[b] Total number of participants was 1461. One patient who was randomized to the standard-issue group died in the operating room during cardiac surgery and had no data available for the primary outcome, some secondary outcomes, and some cointerventions. This patient was not included in the primary outcome but was included in mortality analyses.

[c] For the purpose of this study, patients in the fresh group were considered adherent to protocol if 80% of the units were stored for for 7 days or less and if no units were stored for more than 14 days during the 28-day follow-up period.

[d] Adherence to transfusion protocol instructions was defined as (number of transfusions with units stored for ≤7 days)/(total number of transfusions) for fresh group and as (number of standard-issue transfusions)/(total number of transfusions) for the standard-issue group.

Example 2

Table 3. Hazard Ratios for Incident Cardiovascular Disease Diagnoses Associated With Natural and Surgical Premature Menopause (ie, Menopause Before Age 40 Years)

	Sparsely Adjusted Models[a]					Fully Adjusted Models[b]				
	Surgical Premature Menopause		Natural Premature Menopause			Surgical Premature Menopause		Natural Premature Menopause		
	Hazard Ratio (95% CI)	*P* Value[c]	Hazard Ratio (95% CI)	*P* Value[c]	*P* Value for Heterogeneity[d]	Hazard Ratio (95% CI)	*P* Value[c]	Hazard Ratio (95% CI)	*P* Value[c]	*P* Value for Heterogeneity[d]
First cardiovascular disease diagnosis[e]	2.21 (1.66-2.92)	<.001	1.60 (1.42-1.80)	<.001	.04	1.87 (1.36-2.58)	<.001	1.36 (1.19-1.56)	<.001	.08
Coronary artery disease	3.76 (2.42-5.86)	<.001	1.81 (1.44-2.28)	<.001	.004	2.52 (1.48-4.29)	<.001	1.39 (1.06-1.82)	.02	.05
Heart failure	2.74 (1.42-5.29)	.003	1.56 (1.14-2.16)	.006	.14	2.57 (1.21-5.47)	.01	1.21 (0.81-1.82)	.35	.08
Aortic stenosis	3.41 (1.27-9.16)	.02	2.48 (1.62-3.80)	<.001	.56	2.91 (0.92-9.15)	.06	2.37 (1.47-3.82)	<.001	.75
Mitral regurgitation	3.40 (1.41-8.27)	.007	0.95 (0.52-1.74)	.87	.02	4.13 (1.69-10.11)	.002	0.73 (0.34-1.55)	.41	.004
Atrial fibrillation	1.87 (1.14-3.06)	.01	1.44 (1.18-1.77)	<.001	.34	1.60 (0.91-2.83)	.11	1.25 (1.00-1.58)	.05	.44
Ischemic stroke	1.18 (0.38-3.66)	.78	1.59 (1.12-2.28)	.01	.62	0.43 (0.06-3.12)	.41	1.50 (1.01-2.25)	.04	.23
Peripheral artery disease	2.19 (0.70-6.83)	.18	1.96 (1.27-3.03)	.002	.86	1.34 (0.33-5.41)	.68	1.34 (0.79 -2.26)	.27	.99
Venous thromboembolism	2.57 (1.41-4.67)	.002	1.68 (1.29-2.20)	<.001	.20	2.73 (1.46-5.14)	.002	1.70 (1.27-2.29)	<.001	.18

[a] Sparsely adjusted models are adjusted for age at enrollment and race/ethnicity.

[b] Fully adjusted models are adjusted for age, race/ethnicity, prevalent type 2 diabetes, ever having smoked, systolic blood pressure, use of antihypertensive medication, non–high-density lipoprotein cholesterol, use of cholesterol-lowering medication, body mass index, C-reactive protein, and history of menopausal hormone therapy use.

[c] *P* values derived from Cox proportional hazards models.

[d] Reflects comparison between hazards associated with natural vs surgical premature menopause using the statistical test of heterogeneity.

[e] Comprised of coronary artery disease, heart failure, aortic stenosis, mitral regurgitation, atrial fibrillation, ischemic stroke, peripheral artery disease, and venous thromboembolism.

Example of Figure:

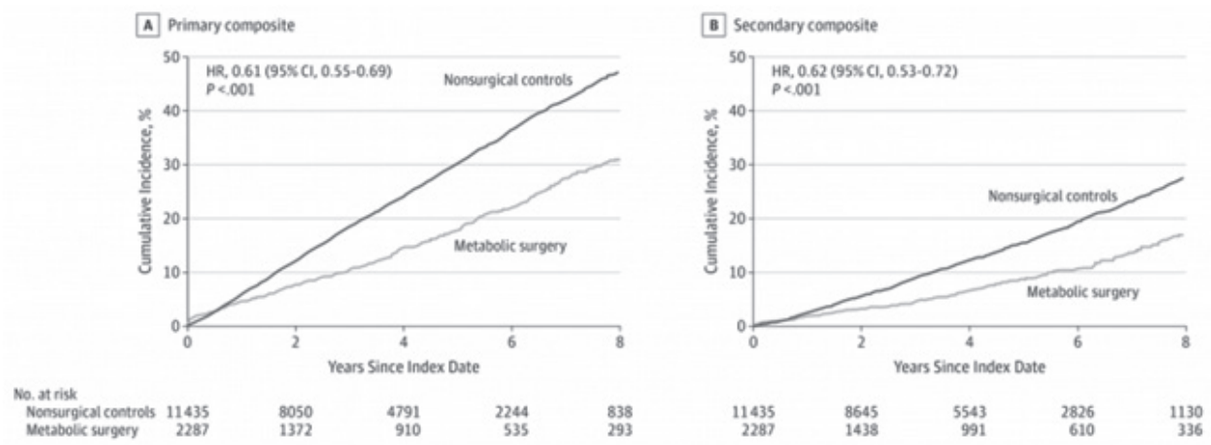

Figure 1 Eight-year Cumulative incidence Estimates (Kaplan-Meier) for 2 Composite End Points.