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Characterizing prevalence and severity of depression in coronary artery disease patients in Bangkok, Thailand

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Abstract

CHARACTERIZING PREVALENCE AND SEVERITY OF DEPRESSION IN CORONARY ARTERY DISEASE PATIENTS IN BANGKOK, THAILAND.

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Numerous studies in North America, Europe and Australia have linked depression to increased risk of morbidity and mortality in coronary artery disease (CAD). Although the co-morbidity of depression and CAD is well documented in the western world, little work on the subject has been carried out in Asia. Differing depression presentations in Asia necessitate the use of culture-specific depression rating scales. This study sought to determine whether the correlation between CAD and depression documented in western countries also exists in an Asian nation: Thailand. It was hypothesized that rates of depressive symptoms were higher in Thai inpatients with either unstable angina or recent myocardial infarction than in Thai inpatients with non-cardiac (orthopedic) complications. A 15-question culturally-appropriate self-rating depression inventory was administered to 56 Thai inpatients—33 cardiac and 23 orthopedic—at two public and one private hospital in Bangkok. Subjects were asked to rate each of the fifteen items on a scale from 0-3 based on how they felt during the past week. Higher scores correlated with greater depressive symptoms. Five cardiac and two orthopedic patients were excluded from the final analysis because of past medical history of major depressive disorder. Of the remaining 49 patients, questionnaire scores ranged from 1 to 23, with a mean depression score of 9.00 (S.E.M.=.84). Cardiac patients showed significantly greater depressive symptoms than their orthopedic counterparts at one public and one private hospital: Ramathibodi Hospital (P=.01) and Bangkok General Hospital (P=.005), respectively. For cardiology patients, the three highest scoring items were early insomnia (Mean = 1.39), late insomnia (Mean = 1.25) and loss of appetite (Mean = 1.04). For orthopedic patients, the three highest scoring items were work inhibition (Mean = 1.05), anxiety (Mean = .86), and early insomnia (Mean = .86). On post-hoc analysis, it was shown that patients in hospital units with air-conditioning showed significantly fewer depressive symptoms than patients without air-conditioning (P=.003), where the daily temperature often reached 115^{o}F. Rates of depressive symptoms did not differ in accordance with education level (P=.15), gender (P=.49) or age (P=.29). In conclusion, this study provides some evidence that Thai inpatients hospitalized for severe CAD have greater depressive experience than their orthopedic counterparts. This finding supports our hypothesis that depression and CAD are linked in Thailand as they are in western countries.

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Introduction

Depression in Asia

The World Health Organization estimates that about 20% of the world's population that seeks medical attention suffers from anxiety, depression, or other mental disorders. At some time in their lives, between 4% and 8% of men and 8% to 25% of women will suffer from depression (1). Only half of these cases are recognized and just half of those are treated. The majority of recognized and treated cases of depression occur in Western countries, where depression is largely seen as an organic, biological and therefore treatable illness. In many countries of Asia, depression is largely unrecognized and untreated. Studies of depression in Thailand have found lifetime prevalence to be between 13% - 20% (2,3).

One marker of depression prevalence and treatment in a region is sales of antidepressants in that region. In 2000, antidepressant sales in the U.S. totaled $8.6 billion, or about 70% of the world's total $12.3 billion. During same period, sales in nine Asian countries reached just $100 million, or 0.1% of the world total (4). Lack of depression detection and treatment in Asia is due to a number of factors: inadequate training of physicians to recognize symptoms of depression in their patients, a culture that discourages patients from sharing emotional and mental disturbances with physicians, and lack of culturally-specific definitions of what depression may entail. A large number of Asian nations, like Thailand, are undergoing rapid shifts in economic and social development. The consequences of this shift—poverty, refugees associated with the disintegration of communities, the breakup of whole societies, radical changes in social environments owing to the development of mega-cities, huge shifts in urban/rural populations, exploding population growth and the aging of populations—profoundly

impact psychiatry and the increase the prevalence of symptoms like depression (5,6).

Paradoxically, most Asia nations spend less than 1% of their total health budget on mental health care. Obstacles to improved mental health care in Asia are numerous: stigmatization of mental illness at high levels of government, lack of understanding of the connection between mental health and economic productivity, a culture that aims to hide or ignore rather than treat mental illness, lack of information about the psychosocial basis of organic disease, refusal of insurance companies to cover mental health care, and a dearth of culturally-sensitive instruments for diagnosing mental illness (7). This study seeks to better understand the prevalence and severity of depression in an Asian nation, namely Thailand, focusing particularly on the co-morbidity of depression and coronary artery disease.

Depression and Coronary Artery Disease

Coronary artery disease (CAD), or ischemic heart disease, refers to a set of conditions resulting from coronary atherosclerosis, the accumulation of plaque in coronary arteries. The atherosclerotic process, occurring over the span of many years, involves a series of biochemical, immune-inflammatory, and hemodynamic processes in interaction with various environmental and biological risk factors. The first clinical presentation of artereosclerosis often includes anginal chest pain, myocardial infarction and even sudden death from cardiac arrhythmias. Abundant evidence suggests that the symptomatic manifestations of CAD may be triggered by depression, mental or emotional stress (8,9). Although the mechanism for this interaction has not been fully elucidated, the complex pathophysiology of CAD suggests that both psychosocial and

physiological effects of depression underlie the disease process.

Rates of depression are higher in cardiac patients than in the general population, with studies reporting depression prevalence rates of 16–30% in individuals hospitalized for unstable angina or a myocardial infarction (MI) (10-12). Of patients diagnosed with major depressive disorder (MDD) after an MI, 77% still met criteria for MDD 3-4 months later (10). Depression rates do not appear to change with severity of cardiovascular disease (13). However, risk of cardiovascular disease appears to increase linearly with depression severity (14,15).

The evidence linking depression to increased risk of morbidity and mortality in CAD is robust (16-18). One study found that patients with cardiovascular disease who met the criteria for major depression were 2.5 times more likely to develop a serious cardiac complication over the next 12 months than their non-depressed counterparts (12). After controlling for other independent risk factors, another study showed that depression is associated with a 3.5 fold increased risk of mortality over the course of 18 months in individuals who had recently experienced a myocardial infarction (19). This level of risk is comparable to organic risk factors for cardiac mortality, like congestive heart failure and decreased left ventricular ejection fraction (11).

Behavioral and physiological mechanisms have been proposed to explain the association between cardiovascular illness and depression. MDD may result from the psychological stress of CAD. However, significant evidence exists for the opposite direction of causality as well. Depressed individuals are more likely to smoke and less likely to exercise (20). Even after controlling for behavioral risk factors, depression is still associated with poor cardiac outcomes, suggesting that physiological factors are

involved (21). Several studies have shown that depressed individuals have less available endogenous endothelial nitric oxide, the enzyme responsible for coronary vasodilatation, platelet inhibition, and reduction of smooth muscle proliferation and migration to inflamed endothelium (22,23). Decreased nitric oxide increases the risk of vascular occlusive cardiac events. Other studies have linked depression to increased platelet activation, another risk factor for vascular occlusive cardiac events (18,24). Depression has also been shown to correlate with decreased heart rate variability, a marker for increased sympathetic function, which further increases CAD risk (25). Other studies have shown increased markers of inflammation in depressed individuals (26). Given the central role played by inflammation in the atherosclerotic process, the rise in inflammatory mediators further increases risk of CAD. Psychologically and physiologically, the connection between depression and CAD is robust.

Although substantial evidence exists for the connection between heart disease and depression in the Western world, no studies have examined this interaction in Asia. This study seeks to determine whether the well-characterized relationship between depression and CAD that is seen in the Western world also exists in Thailand.

Statement of purpose

This project will test the hypothesis that rates of depression, as assessed with a 15-question self-rating scale for depression, are higher among Thai inpatients with coronary artery disease than among Thai inpatients being treated for recent non-cardiac (orthopedic) complications.

Research goals

To determine whether the well-characterized relationship between depression and CAD that is seen in the Western world also exists in Thailand

Materials and methods

Measuring Depression in Thailand: The Thai Depression Inventory

Psychological disturbances like depression do not manifest themselves in the same way across different cultures (27). Creating culturally appropriate screening tools for depression is a challenge in the non-Western world because the majority of existing instruments were derived from Western populations and based on Western concepts of depression. The Thai Depression Inventory (TDI) was constructed by Thai psychiatrists to overcome this challenge (28). To construct the TDI, twenty items considered culturally appropriate for Thai patients were selected from the traditional Western instruments used for depression assessment—Beck Depression Inventory (29), Zung Self-Rating Depression Scale (30), Structure Interview Version of the Hamilton Depression Scale (31), Montgomery-Asberg Depression Rating Scale (32), and the Hospital Anxiety and Depression Scale (33). Item selection for the TDI was based on culturally appropriate manifestations of distress and depression among the Thai. When compared against the Thai version of the Hamilton Rating Scale for Depression (the former gold standard), the TDI showed good internal consistency (alpha coefficient = .738) and concurrent validity (Pearson product moment correlation = .7188, $p<.0001$). This indicated that the items on the TDI correlated well with each other and adequately reflected the severity of depression in the tested subjects. Factor analysis validated the construct validity of the TDI, revealing that five distinct factors accounted for 59.8% of the total variance. The anxiety factor—comprised of anxiety, indecisiveness, loss of concentration, agitation, anhedonia, initial insomnia—accounted for the greatest percentage of the variance (29.4%).

When administered to fifty Thai subjects with known depression, all items on the TDI correlated well with the total score except for two: loss of libido and psychomotor retardation. Previous studies reported similar findings about loss of libido among Asian populations (34). Based on these findings, loss of libido and psychomotor retardation were omitted from the questionnaire administered in this study. Since the goal of this study was the measure depression in patients with co-morbid cardiac illness, three additional items were omitted because of their high prevalence in our study population: lethargy, hypochondriasis and somatic anxiety. Individuals having undergone a myocardial infarction are likely to feel lethargy and somatic anxiety even in the absence of depression. Similarly, the presence of hypochondriasis cannot be accurately assessed in patients with documented medical illnesses. The resulting questionnaire used in this study had fifteen items believed to best assess Thai-specific manifestations of depression in patients with co-morbid cardiac and orthopedic illness.

When given the 15-question instrument, the subjects were asked to rate each of the fifteen items on a scale from 0-3 based on how they felt during the past week. The tallied scores were classified in accordance with the guidelines of **Table 1**. Scores of 0-15 signified no depression; 16-19 signified mild depression; 20-25 signified less than major depression; 26-60 signified major depression; and scores greater than 30 signified severe major depression. The Thai and English version of the original 20-question TDI is included in the Appendix.

Table 1: Guidelines for scoring Thai Depression Inventory in Subjects with Co-Morbid Medical Illness

TOTAL SCORE ON THAI DEPRESSION INVENTORY	RANGE
0 – 15	No Depression
16 – 19	Mild Depression
20 – 25	Less Than Major Depression
26 – 30	Major Depression
> 30	Severe Major Depression

Study Population

The study population consisted of two groups of individuals to whom the 15-question modified TDI was administered. The experimental group was composed of Thai inpatients (n=33) over the age of 40 who were hospitalized for unstable angina or an MI within the past four weeks (< 29 days) at one of three hospitals in Bangkok: Ramathibodi Hospital (a public hospital affiliated with Mahidol University), Rajavithi Hopsital (a public community hospital), and Bankok General Hospital (a private hospital). An MI was documented by cardiac enzymes with chest pain compatible with acute MI, and characteristic evolutionary ST-T changes or new Q waves on EKG. Unstable angina was defined as angina or anginal equivalent symptoms at rest, with episodes lasting at least 10 minutes and leading to hospitalization. The majority of unstable angina patients in this study had ECG documentation of transient ST-segment changes. The control group was comprised of Thai inpatients (n=23) over the age of 40 who were hospitalized for an orthopedic complication (such as a broken bone) during the past four weeks (<29 days) at one of the three aforementioned hospitals in Bangkok. Subjects in both groups were gender- and age-matched.

Study Design

Prior to administering the questionnaire to the study population, the alertness of each patient was assessed to ensure that they did not suffer from delirium, a frequent consequence of MI and hospitalization. Alertness was assessed by asking the person their name, the cause of their hospital visit, and whether they felt alert enough to participate in a survey. If the answers to these questions were positive, the subject was asked to respond in writing to the questions on the questionnaire. If the subjects were illiterate or unable to write at the given time (for instance, due to an upper extremity fracture), the questionnaire was administered to the subject by a physician, medical student or hospital staff. All questions on the questionnaire were multiple choice and scale-based ratings, thereby reducing the need for back-translation of the surveys into English at the time of data analysis.

Demographic information, social history and medical history were obtained at the time of questionnaire administration. Demographic information included height, weight, age, race, gender and socioeconomic status (how much money a subject earned per month). Social history included marital status, number of children, profession, highest educational level completed, place of residence, exercise frequency/intensity, dietary habits, vitamin use, history of cigarette smoking and history of drug or alcohol use. Medical history included major physical and psychiatric illness, suicide attempts, hypertension, cholesterol levels, blood pressure, diabetes mellitus, current medications, history of antidepressant use and family history of heart disease. Subjects were excluded from this study if they 1.) exhibited delirium or disorientation at the time of interview 2.) had other life-threatening medical illness, cognitive impairment, severe psychiatric

disorder, alcoholism, or other substance use except tobacco and occasional alcohol use or 3.) were taking antidepressants at the time.

Patient confidentiality was maintained by assigning numbers of each subject in lieu of using subject's names. The questionnaire was approved by the Human Investigations Committee at Yale University and Mahidol University. Subjects were explicitly told that participation in this study was voluntary and that they could cease participation at any time without repercussion. If a subject was found to have moderate or severe depression based on their TDI score, they were provided with counseling support by one of the medical staff.

Data analysis was done using Microsoft Excel. Statistical significance was defined as a two-side t-test $P < 0.05$.

results

The Thai Depression Inventory, adapted from its original version to screen for depression in patients with co-morbid medical illness, contained 15 items that the subjects were asked to rate 0 – 3 based on how they felt over the past week. Higher ratings correlated with greater depressive symptoms. 56 inpatients—33 cardiac and 23 orthopedic—were surveyed in total. Of 45 total points, subjects' scores on the questionnaire ranged from 1 to 27, with a mean depression score of 9.71 (S.E.M.=.83; n=56). From our original sample, 5 cardiac and 2 orthopedic patients were excluded from the analysis because of documented history of psychiatric illness, including major depressive disorder. Of the remaining 49 patients, questionnaire scores ranged from 1 to 23, with a mean depression score of 9.00 (S.E.M.=.84). None of the subjects included in the final analysis met criteria for major depressive disorder (score > 25). However, the presence of depressive symptoms even in the absence of major depression is enough to increase the risk of myocardial infarction (14).

Cardiac subjects included 15 males and 13 females, with a mean age of 69.1 years (S.D.=8.03; range: 53-81). Orthopedic subjects included 10 males and 11 females, with a mean age of 55.5 (S.D.=11.0; range: 40-76). The predominant educational level of both groups was 4^{th} grade (60.7% in cardiac subjects; 57.1% in orthopedic subjects). In the cardiac group, 10.7% of subjects completed university, as compared to 23.8% in the orthopedic group. All subjects were Buddhist.

Table 2 shows the diagnoses for the remaining 28 cardiac patients (**Table 2A**) and 21 orthopedic patients (**Table 2B**) used in our final analysis. For the cardiac patients, 13 were diagnosed with unstable angina, with no prior history of myocardial infarction; 3

were diagnosed with unstable angina, having had one myocardial infarction in the past; 9 were diagnosed with their first myocardial infarction; 3 were diagnosed with their second myocardial infarction. For the orthopedic inpatients, 10 had lower extremity fractures or injuries; 5 had upper extremity fractures or injuries; 4 had spinal stenosis; 1 had spondylolisthesis; 1 had tuberculosis that had disseminated to the spine.

Table 2A: List of Cardiac Diagnoses in Subjects (N = 28)

DIAGNOSIS	N
Unstable angina, with no history of myocardial infarction	13
First myocardial infarction	9
Unstable angina, with history of past myocardial infarction	3
Second myocardial infarction	3

Table 2B: List of Orthopedic Diagnoses in Subjects (N = 21)

DIAGNOSIS	N
Lower extremity fracture or injury	10
Upper extremity fracture or injury	5
Spinal stenosis	4
Spondylolisthesis	1
Tuberculosis of the spine	1

Table 3 lists of the major medical co-morbidities in the cardiac and orthopedic subjects. Cardiac subjects had significantly more medical co-morbidities than their orthopedic counterparts. The primary co-morbid illnesses in both groups were hypercholesterolemia (78.6 % in cardiac subjects; 33.3% in orthopedic subjects), hypertension (75.0% in cardiac subjects; 38.1% in orthopedic subjects) and diabetes (71.4% in cardiac subjects; 14.3% in orthopedic subjects). Tuberculosis was seen in a

small percentage of both groups (3.6% in cardiac subjects; 9.5% in orthopedic subjects). Cardiac subjects also had renal problems (10.7%), chronic heart failure (7.1%), chronic obstructive pulmonary disease (3.6%) and stroke (3.6%). Orthopedic patients had history of organ transplants (9.5%) and cancer (4.8%).

Table 3: List of Medical Co-Morbidities in Cardiac and Orthopedic Subjects

CO-MORBIDITY	% OF CARDIAC PATIENTS (N=28)	% OF ORTHOPEDIC PATIENTS (N=21)
Hypercholesterolemia	78.6%	33.3%
Hypertension	75.0%	38.1%
Diabetes	71.4%	14.3%
Renal Problems	10.7%	0
Chronic Heart Failure	7.1%	0
Tuberculosis	3.6%	9.5%
COPD	3.6%	0
Stroke	3.6%	0
Organ Transplant	0	9.5%
Cancer	0	4.8%

Table 4 lists the marital status and average number of children in the cardiac and orthopedic subjects. The majority of subjects were married in both groups (78.6% of cardiac subjects; 71.4% of orthopedic subjects). Widowed subjects accounted for 10.7% of the cardiac group and 14.3% of the orthopedic group. 3.6% of the cardiac subjects were divorced. 9.5% of the orthopedic subjects were single (never married). The average number of children was 4.4 for cardiac subjects and 3.1 for orthopedic subjects.

Table 4: Marital Status and Children of Cardiac and Orthopedic Subjects

MARITAL STATUS	% OF CARDIAC PATIENTS (N=28)	% OF ORTHOPEDIC PATIENTS (N=21)
Married	78.6%	71.4%
Widowed	10.7%	14.3%
Divorced	3.6%	0
Single	0	9.5%
Not Answered	3.6%	0
Avg # of Children	4.4	3.1

Table 5 lists the employment status of the subjects. 57.1% of the cardiac subjects were employed at the time, as compared to 47.6% of orthopedic subjects.

Table 5: Employment Status of Cardiac and Orthopedic Subjects

EMPLOYMENT STATUS	% OF CARDIAC PATIENTS (N=28)	% OF ORTHOPEDIC PATIENTS (N=21)
Unemployed	42.9%	47.6%
Employed	57.1%	47.6%
Not Answered	0	4.8%

Table 6 lists the health habits of the subjects. More orthopedic subjects smoked than cardiac subjects (14.3% vs. 10.7%), though more cardiac subjects had quit smoking than orthopedic subjects (42.9% vs. 9.5%). More cardiac subjects used alcohol than orthopedic subjects (32.1% vs. 10.0%). Cardiac subjects are more likely to take daily vitamins, exercise three or more times per week and meditate than their orthopedic counterparts (vitamins: 17.9% vs. 9.5%; exercise: 57.1% vs. 28.6%; meditation: 21.4% vs. 4.8%).

Table 6: Health Habits of Cardiac and Orthopedic Subjects

HEALTH HABITS	% OF CARDIAC PATIENTS (N=28)	% OF ORTHOPEDIC PATIENTS (N=21)
Current Smoker	10.7%	14.3%
Quit Smoking	42.9%	9.5%
Alcohol Use	32.1%	10.0%
Daily Vitamins	17.9%	9.5%
Exercises 3X/week	57.1%	28.6%
Meditation	21.4%	4.8%

Table 7A lists the means, standard deviations, and percentage of respondents endorsing response choices 1, 2 or 3 for each question on the modified 15-question TDI for the cardiac subjects (N=28). The highest mean score was seen for Item # 9, Early Insomnia (Mean = 1.39), which was experienced by 71% of the subjects. Item #10, Late Insomnia, had the second highest mean (Mean = 1.25) and was experienced by 68% of the cardiac subjects. The third highest mean was seen for Item #11, Loss of Appetite (Mean = 1.04), experienced by 64% of the subjects.

Table 7B lists the means, standard deviations, and percentage of respondents endorsing response choices 1, 2 or 3 for each question on the modified 15-question TDI for the orthopedic subjects (N=21). The highest mean score was seen for Item #14, Work Inhibition (Mean = 1.05), experienced by 53% o the subjects. Item # 6, Anxiety, and Item #9, Early Insomnia, had the second highest means (Mean = .86 for both items) and were experienced by 57% and 52% of the orthopedic subjects, respectively. Item #1, Hopelessness, was experienced by the greatest percentage of orthopedic patients (67%), with a Mean = .62.

Table 7A: Mean, Standard Deviations and Percentages Symptomatic for the Modified 15-Question Thai Depression Inventory: Cardiac Subjects (N=28)

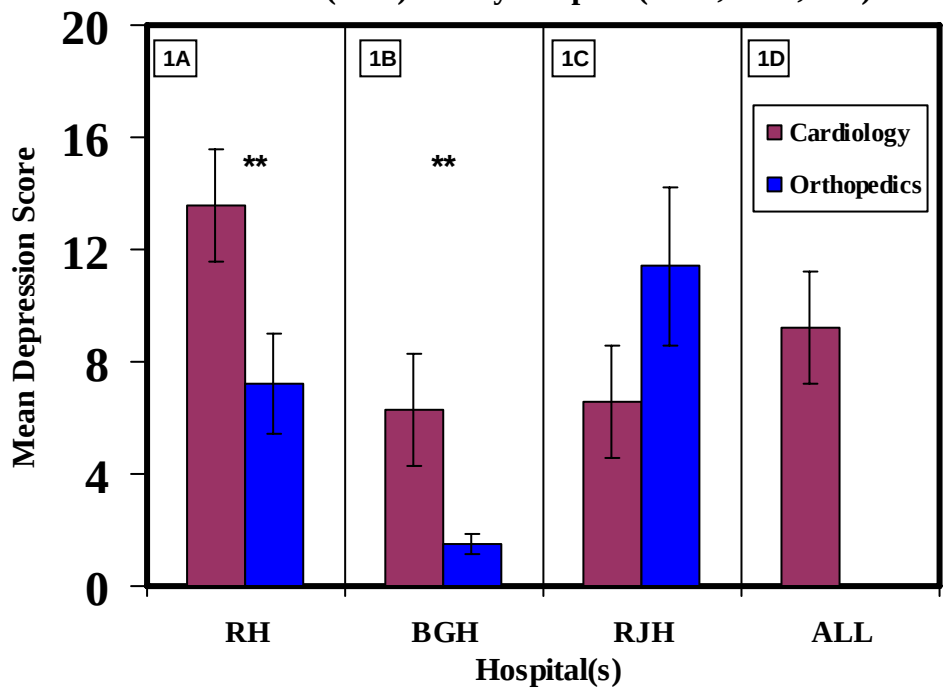
THAI DEPRESSION INVENTORY ITEM	MEAN	S.D.	%
1. Hopelessness	0.68	0.67	61%
2. Suicide	0.04	0.19	4%
3. Guilty Feelings	0.36	0.68	25%
4. Agitation	0.50	0.84	32%
5. Depressed Mood	0.18	0.39	18%
6. Anxiety	0.50	0.79	36%
7. Anhedonia	0.50	0.84	36%
8. Irritability	0.57	0.57	54%
9. Early Insomnia	1.39	1.17	71%
10. Late Insomnia	1.25	1.08	68%
11. Loss of Appetite	1.04	0.96	64%
12. Indecisiveness	0.50	0.64	43%
13. Concentration Loss	0.50	0.64	43%
14. Work Inhibition	0.86	1.18	39%
15. Social Withdrawal	0.43	0.96	21%

Table 7B: Mean, Standard Deviations and Percentages Symptomatic for the Modified 15-Question Thai Depression Inventory: Orthopedic Subjects (N=21)

THAI DEPRESSION INVENTORY ITEM	MEAN	S.D.	%
1. Hopelessness	0.62	0.50	67%
2. Suicide	0.33	0.58	33%
3. Guilty Feelings	0.19	0.51	19%
4. Agitation	0.38	0.80	29%
5. Depressed Mood	0.57	0.81	48%
6. Anxiety	0.86	1.01	57%
7. Anhedonia	0.71	0.72	62%
8. Irritability	0.38	0.59	38%
9. Early Insomnia	0.86	1.06	52%
10. Late Insomnia	0.81	0.93	52%
11. Loss of Appetite	0.29	0.72	19%
12. Indecisiveness	0.43	0.60	43%
13. Concentration Loss	0.62	0.74	57%
14. Work Inhibition	1.05	1.24	52%
15. Social Withdrawal	0.52	0.81	43%

Figure 1 compares the mean depression scores between the cardiology and orthopedic subjects. Data is displayed by hospital: BGH = Bangkok General Hospital (**Figure 1A**); RH = Ramathibodi Hospital (**Figure 1B**); RJH = Rajavithi Hospital (**Figure 1C**)) and ALL = cumulative data from all three hospitals (**Figure 1D**). The mean depression score for each group of patients was calculated by taking the sum total of depression scores for all inpatients in the group and dividing it by the number of patients in that group. At BGH and RH, depression scores in the cardiac units were significantly higher than depression scores in the orthopedic unit (P=.01 and P=.005, respectively). P-values were obtained using a two-tailed t-test comparing two samples of unequal variance. At BGH, the mean depression score was 6.3 (S.E.M.=.48; n=10) for cardiology and 1.5 (S.E.M.=.35; n=2) for orthopedics. For RH, the mean depression score for cardiology was 13.6 (S.E.M.=.45; n=11) and for orthopedics was 7.2 (S.E.M.=.38; n=14). Asterisks above a graph indicate statistical significance (P<.05). No statistically significant differences were noted between cardiac and orthopedic patients at RJH or in the cumulative data (P=.12 and P=.36, respectively). For RJH, the mean depression score for cardiology is 6.6 (S.E.M.=.34; n=7), while for orthopedics it is 11.4 (S.E.M.=1.0; n=5). For the cumulative data (ALL), the mean depression score for cardiology is 9.2 (S.E.M.=.19; n=28), while for orthopedics it is 7.7 (S.E.M.=.27; n=21).

Figure 1: Mean Depression Scores in Cardiology vs. Orthopedic Units in Three Bangkok Hospitals: Cumulative (ALL) and By Hospital (BGH, RJH, RH)



The lack of statistical significance at RJH and in our cumulative data can be explained by examining one additional factor: air conditioning status. Not all hospital units in Thailand are air-conditioned. In the absence of air conditioning, the temperature within the hospital unit can rise to 115°F. **Table 7** lists the air conditioning status of the cardiac and orthopedic units in the three hospitals in which our subjects were inpatients.

Table 7: Air Conditioning Status at Bangkok Hospitals

HOSPITAL	CARDIAC UNIT	ORTHOPEDIC UNIT
Ramathibodi (RH)	NO	NO
Bangkok General (BGH)	YES	YES
Rajavithi (RJH)	YES	NO

Both cardiac and orthopedic units at BGH had air conditioning, while neither unit at RH did. At both of these hospitals, depression rates were significantly higher in cardiac subjects than orthopedic subjects (**Figures 1A and 1B**). Unlike in BGH and RH, RJH does not have consistent air conditioning status between its cardiology and orthopedics departments. At RJH, the cardiology unit is air conditioned while the orthopedics unit is not. No statistically significant difference is observed between orthopedic and cardiac inpatients at RJH and, consequently, in the cumulative data (**Figures 1C and 1D**).

While looking at the cumulative data alone does not appear to confirm our working hypothesis, separating the data by individual hospital reveals that the expected trend—cardiac patients exhibiting higher depression scores than their orthopedic counterparts—does indeed hold true when air conditioning status is consistent between the cardiac and orthopedic units.

Figure 2 shows the effect of air conditioning status on the mean depression score. Inpatients in air-conditioned hospital units showed significantly lower mean depression scores than inpatients at hospital units without air conditioning ($P = .003$). For the air-conditioned hospital units, the mean depression score was 6.0 (S.E.M.=.20; n=20). For units without air conditioning, the mean depression score was 10.3 (S.E.M.=.20; n=30). Data for Figures 2-5 was pooled for both cardiac and orthopedic units.

Figure 2: Mean Depression Scores by Hospital Air Conditioning Status

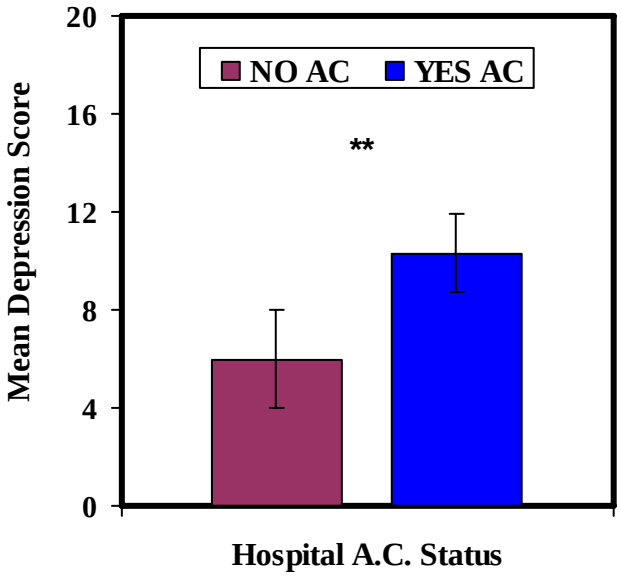


Figure 3 shows that education level does not have a significant effect on mean depression score (P=.15). For individuals having completed between grades 4 and 12 of their education, the mean depression score is 8.9 (S.E.M.=.17; n=35). For individuals having completed a university degree, the mean depression score is 8.2 (S.E.M.=.33; n=15).

Figure 3: Mean Depression Scores by Education Level

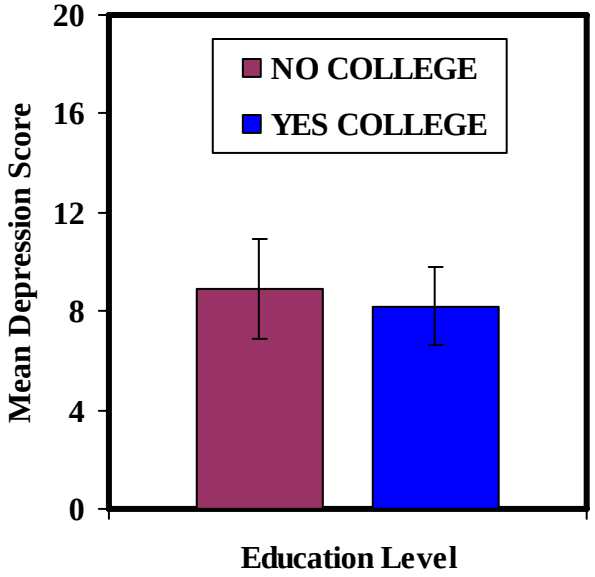


Figure 4 shows that gender does not have a significant effect on mean depression score (p-value = .49). For males, the mean depression score was 8.0 (S.E.M.=.22; n=27). For females, the mean depression score is 9.1 (S.E.M.=.23; n=23).

Figure 4: Mean Depression Scores by Gender

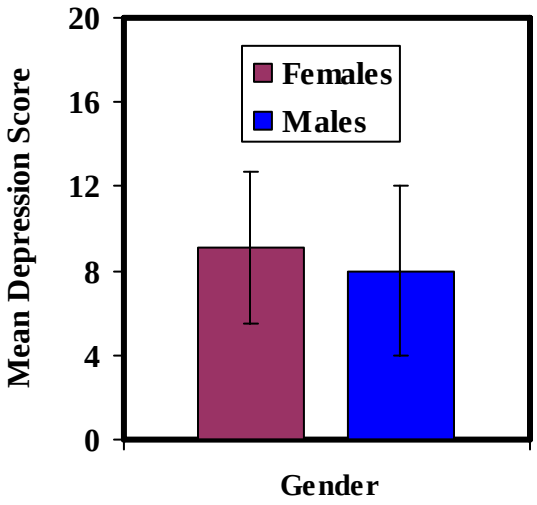
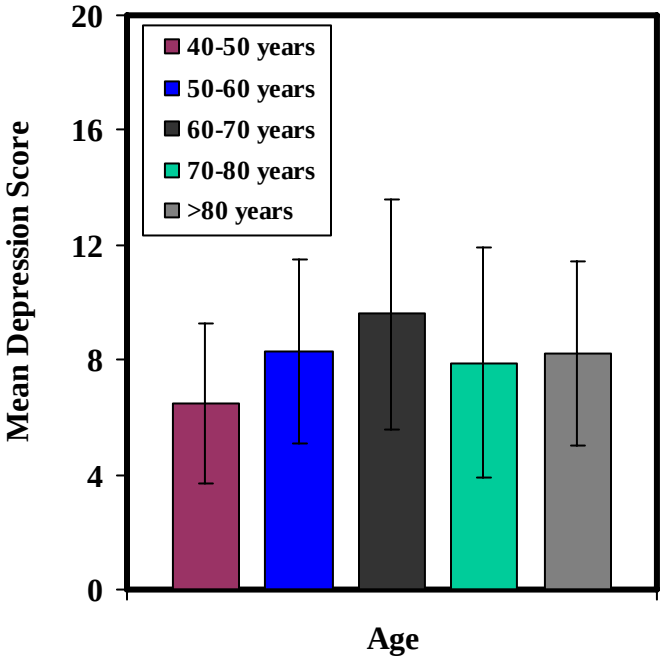


Figure 5 shows that age does not have a significant effect on mean depression score (P=.29). The mean age of patients in this study was 62.0 (S.E.M.=.21; n=50). For patients aged 40-49 years old, the mean depression score was 6.5 (S.E.M.=1.0; n=6). For patients aged 50-59 years old, the mean depression score was 8.3 (S.E.M.=.40; n=13). For patients aged 60-69 years old, the mean depression score was 9.6 (S.E.M.=.40; n=11). For patients aged 70-79 years old, the mean depression score was 7.9 (S.E.M.=.42; n=14). For patients >80 years old, the mean depression score was 8.2 (S.E.M.=1.2; n=5).

Figure 5: Mean Depression Scores by Age



discussion

Although the co-morbidity of depression and cardiovascular disease is well-documented in the western countries, only one study to date has examined the interactions of cardiac health and psychological stress (although not depression per se) in an Asian population, the Japanese (35). One reason for the dearth of Asian studies on

this subject is the lack of culturally sensitive psychiatric instrumentation to assess depression. Differences in language, experience and overall manifestations of distress differ significantly across culture (36,37). Differing depression presentations necessitate the use of culturally-specific depression rating scales.

Through the use of a 15-question modified version of the Thai Depression Inventory, our study has confirmed the existence of a correlation between depressive symptoms and cardiac complications, namely MI and unstable angina, in a Thai population. Thai cardiac inpatients showed greater differences in mean depression scores than their orthopedic counterparts irrespective of gender, age or education level at both private and public hospitals. The majority of subjects in our study showed mild depression or depressive symptoms, previously demonstrated to be risk factors for myocardial infarction (14).

The limitations of this study must be considered in interpreting the results. One limitation is that patients of the experimental group are not representative of all post-MI or unstable angina patients. Inpatients that were delirious were not given questionnaire to complete. Inpatients taking antidepressants or with a previous history of major depression or other psychiatric illness were excluded from this study. The experimental group consisted only of subjects who had undergone non-fatal MI, thereby limiting our ability to assess depression in the most severe cardiovascular cases. This study was further limited by practical considerations of temporal and geographic convenience: the study population was not entirely random. The small samples size (49 patients in total) limits the power of our findings. Furthermore, any self-rating single-administration instrument for measuring depression severity is limited by definition. Such an instrument

takes a single snapshot of a person's mood, or a snapshot of what the person remembers of their mood over the past week. Mood and memory are strongly influenced by environmental factors, such as a presence of air conditioning in the hospital unit. This limitation is inherent in all studies utilizing subjective self-reporting survey methodology, and must be taken into account in understanding these results.

A particularly interesting finding in this study was the differing levels of depression as a function of air conditioning status. Air conditioning appears to decrease depressive symptoms in both cardiac and orthopedic patients. This finding explains the lack of a statistically significant difference between cardiac and orthopedic at RJH, where the cardiac unit was air-conditioned while the orthopedic unit was not. This result begs the question of whether it was actually the air conditioning that accounted for this difference in depression scores, or if air conditioning was simply a proxy for other variables, like lower patient/nurse ratio or the close proximity of family members. Air-conditioning was present at BGH (both orthopedic and cardiac units) and at the RJH cardiac unit. However, patients at BGH also had their own rooms, and therefore often had family members present at the time of TDI administration. BGH also had a lower patient/nurse ratio than the public hospitals. More nurses present ensured that the patients' immediate needs could be more adequately met. All of these factors may have led to decreases in patient's depression scores.

The proximity of family members at the time of TDI administration deserves particular consideration. Having family members nearby may have elevated subjects' moods, thereby decreasing their depression scores. Alternately, it may have influenced the honesty of subjects' disclosure. Since many of the questions on the TDI involved

highly personal disclosure of one's feelings, subjects may have felt less willing or able to fully disclose the extent of their depressive feelings with family members within earshot. This would further reduce their mean depression scores. Therefore, factors such as air conditioning status, room privacy, the proximity of family members and the patient/nurse ratio were confounding variables that must be considered in interpreting our results. Further studies are needed to examine the effects of these variables on cardiac patients' mood and prognosis.

The correlation between of depression and CAD in Thailand underscores the importance of improving diagnosis and treatment of depression among Thai patients with CAD. Appropriate detection and treatment of depression in CAD may significantly improve cardiac prognosis. The antidepressants—selective serotonin reuptake inhibitors (SSRI's)—have been shown to have a protective effect against MI, possibly by inhibiting serotonin-mediated platelet activation (38) and restoring post-MI heart rate variability (39). The SSRI, sertraline, was shown to be a safe and effective treatment of recurrent depression in patients with recent MI or unstable angina (40). An open, baseline controlled study confirmed the efficacy of using sertraline to treat depression in Thai patients (41). SSRI's may offer hope for improving cardiovascular prognosis in Thai patients with co-morbid CAD and depression. Further studies on the interactions of heart disease and depression in Asia are needed to improve cardiac prognosis and quality of life in patients with co-morbid heart disease and depression.

AppendiX

Thai Depression Inventory, English Version

Demographics, Social History, Medical History Questionnaire, English Version

Thai Depression Inventory, Thai Version

Demographics, Social History, Medical History Questionnaire, Thai Version

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INTRATHRYOIDAL PARATHYROIDAL ADENOMA

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Case

A 57 year old woman with a history of childhood radiation therapy to her neck for tonsillar enlargement developed primary hyperparathyroidism (1o HPT). She underwent parathyroid exploration in 2003 and a 190 mg partially intrathyroidal right upper parathyroid gland was excised. The left upper and lower parathyroid glands were found to be eutopic and normal size. The right lower parathyroid gland was not identified. Postoperatively, the patient had persistent 1o HPT with serum calcium levels ranging from 10.9 – 11.0 (normal, 8.4-10.5 mg/dL), an intact parathyroid hormone (PTH) level of 58.1 pg/mL (normal, 6-40 pg/mL) and an alkaline phosphatase level of 151 IU/L (normal, 32-111 IU/L). A bone density scan of the lumbar spine showed a T-score of -2.2. She was referred for remedial parathyroid exploration.

Pre-operative imaging with a technetium Tc 99m sestamibi scan suggested uptake in the right lower thyroid region and an MRI suggested a right inferior lesion. This was corroborated by a thyroid ultrasound that showed a hypervascular hypoechoic mass in the right inferior thyroid pole (Fig. 1). An ultrasound-guided fine needle aspirate of the lesion revealed an intact PTH level of 2330 pg/ml, confirming the presence of parathyroid tissue within the thyroid lobe. Based on this finding, the patient was taken for minimally invasive parathyroid surgery.1 Under cervical block anesthesia the inferior aspect of the right thyroid lobe was resected. Evaluation of frozen section confirmed that the parathyroid adenoma was completely within the thyroid gland. A rapid intraoperative PTH assay indicated a 50% decrease in plasma PTH levels following resection, confirming successful parathyroidectomy (Table 1).2 Pathological examination demonstrated a fully intrathyroidal parathyroid adenoma measuring 1.2 cm (Fig. 2-3, normal size 5-7 x 3-4 x 0.5-2 mm). The patient was discharged home on the day of the surgery. Follow-up serum calcium and PTH levels were within normal limits at 9.8 mg/dL and 9 pg/mL, respectively.

Table 1

Intraoperative Plasma PTH Levels (6 – 40 pg/ml).
The marked decrement in PTH confirms successful parathyroidectomy.

Pre-Operative	93
Time Zero (T_0)	38
T_0 + 5 Minutes	19
T_0 +10 Minutes	9

Table 2

Sites and Respective Percentages of Ectopic Parathyroid Glands at Reoperation (n=384).

Cervical	
Inferior Pole (normal position)	21 %
Superior Pole (normal position)	20 %
Thymic tongue	10 %
Retrotracheal or retroesophageal	6 %
Intrathyroidal	5 %
Tracheoesophageal groove	4 %
Carotid sheath	3 %
Medial to upper pole	2 %
Upper thyroid capsule	1 %
Undescended	1 %
Mediastinal	
Superoposterior	14 %
Anterior	13 %
Middle	1 %

Figure 1

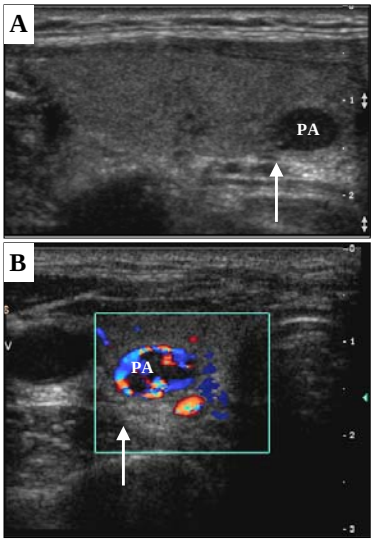


Figure 2

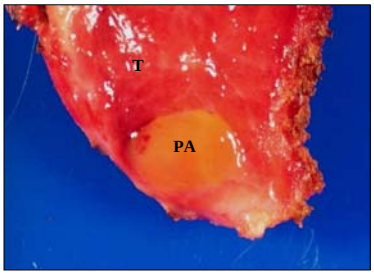
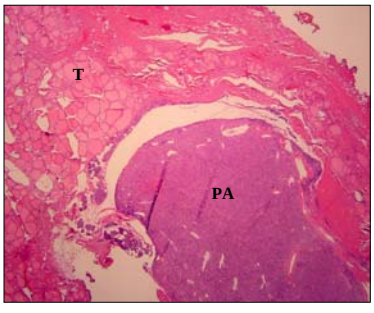


Figure 3



Acknowledgements

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Figure 1. Thyroid ultrasound. **A**, A grey-scale sagittal image of the right lobe of the thyroid demonstrating fully intrathyroidal hypoechoic mass within the lower thyroid lobe. Arrow pointing to posterior margin of thyroid lobe. **B**, A color transverse image of the right lobe of the thyroid with the parathyroid adenoma rimmed in color. Arrow pointing to posterior margin of the thyroid. **PA** = parathyroid adenoma.

Figure 2. Gross specimen demonstrating a parathyroid adenoma embedded within the thyroid parenchyma. **T** = thyroid. **PA** = parathyroid adenoma.

Figure 3. Photomicrograph (10X) under hematoxylin-eosin stained parathyroid adenoma within right thyroid gland. Note rime of thyroid tissue around the parathyroid. **T** = thyroid. **PA** = parathyroid adenoma.

Discussion

Ectopic parathyroid glands located fully within the thyroid parenchyma are very rare. Most individuals have four parathyroid glands located in eutopic positions along the posterior surface of the thyroid gland. However, due to embryologic variance, parathyroid glands can localize anywhere between the angle of the jaw and the pericardium. The most common ectopic site for missed parathyroid glands is within the thymic tongue (Table 2).3 The superior parathyroid glands are derived from the fourth pharyngeal pouch and descend with the lateral lobes of the thyroid. Because of the short descent of these glands, their location is relatively constant. Over 99% of these glands localize dorsal to the superior thyroid lobe, either posterior to the upper pole or within the cricothyroid junction and posterior to the recurrent laryngeal nerve. Retropharyngeal and retroesophageal parathyroid glands account for the upper glands that descend further laterally or posteriorly during embryologic development. The inferior parathyroid glands are derived from the third pharyngeal pouch and descend towards the mediastium with the thymus. With their caudal descent, the inferior parathyroids dissociate from the thymus, localizing mainly in the anterior or lateroposterior aspect of the lower thyroid pole or in the thymic tongue anterior to the recurrent laryngeal nerve. A few glands may remain in the upper neck or descend with the thymus into the mediastinum. Occasionally, a gland will become encased within the thyroid. Of the intrathyroidal parathyroid glands that have been reported, the vast majority span the thyroid capsule and are only partially intrathyroidal.4 Very rarely, the gland will become fully encased within the thyroid parenchyma.

The variability in location of parathyroid glands presents an important challenge in the surgical treatment of hyperparathyroidism. Although missed parathyroid adenomas are most frequently found in eutopic sites, ectopic location of parathyroid glands is the second most common reason for missed parathyroid tumors and re-operation.5 The detection of ectopic parathyroid glands frequently involves several imaging techniques, including radionuclide imaging, high-resolution ultrasonography, computed tomography, magnetic resonance imaging, arteriography, and venous sampling. The diagnostic challenge associated with ectopic parathyroid adenomas underscores the importance of understanding parathyroid embryology and localization.

In summary, we report a case of persistent 1o HPT caused by an ectopic parathyroid adenoma located fully within the parenchyma of the thyroid. The novel use of the rapid PTH assay for an ultrasound-guided tissue fine needle aspiration is described to localize a parathyroid gland in preparation for re-exploration subsequently performed using minimally invasive techniques.

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