

## Original article

# Quality of life and related factors of patients with Brugada syndrome type 1 at King Chulalongkorn Memorial Hospital

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**Background:** Brugada syndrome (BrS) is a rare cardiac arrhythmic syndrome which can increase the risk of sudden cardiac death in patients without structural heart disease. BrS may affect patients' quality of life due to long-term follow-up.

**Objective:** To identify the quality of life and related factors in patients with BrS.

**Methods:** Twenty-nine patients with BrS from King Chulalongkorn Memorial Hospital were recruited between August 2019 to April 2020. We collected demographic data, evaluated depression/anxiety with Thai-HADS test, and administered cognitive tests and the quality of life questionnaires (MacNew and SF-36). Descriptive and multiple linear regression were used to analyze the data.

**Results:** There were 28 male and 1 female subjects. The average age was  $45.2 \pm 13.8$  years old. The result of MacNew questionnaire score was  $5.6 \pm 0.8$ . For SF-36, the physical component score was  $49.8 \pm 6.4$  and mental component score was  $52.9 \pm 6.3$ . The score of anxiety and depression from HADS was  $4.4 \pm 2.9$  and  $3.3 \pm 3.3$ , respectively. For the cognitive test, the following results were observed; the Grooved Pegboard on dominant ( $78.4 \pm 27.9$  seconds) and non-dominant ( $84.5 \pm 26.0$  seconds), Trail A ( $53.7 \pm 20.7$  seconds) and B ( $181.0 \pm 80.9$  seconds), and memory tests (Word List Memory  $21.0 \pm 4.4$  words; recall  $7.2 \pm 2.6$  words; and recognition  $9.6 \pm 1.0$  words). From multiple regression analysis, only the anxiety score from HADS had a statistically significant impact on the quality of life.

**Conclusion:** Most BrS patients had a moderate quality of life and anxiety was an essential predictor for quality of life in BrS patients.

**Keywords:** Brugada syndrome, quality of life, anxiety, depression, cognition.

Brugada syndrome (BrS) is a rare inherited arrhythmic syndrome which can increase the risk of sudden cardiac arrest/death (SCA/ SCD) in young Southeast Asian male without structural heart disease. Clinical manifestations of BrS included asymptomatic, unexplained syncope, agonal nocturnal breathing, ventricular tachycardia/ fibrillation (VT/ VF) and sudden cardiac arrest/ death. BrS is diagnosed by coved-type ST elevation in the right precordial leads

of electrocardiogram (EKG) based on HRS/ EHRSA/ APHRS consensus report.<sup>(1)</sup> Patients with BrS should have long-term monitoring for life-threatening ventricular arrhythmia, especially in patients who had implantable cardioverter-defibrillator (ICD). Patients with BrS may develop psychological trauma after VT/ VF or ICD shock. Moreover, some patients had morbidity from post-cardiac arrest and require life-style change to prevent future cardiac events. The prevalence of patients with BrS was estimated to range from 1 in 5,000 to 1 in 2,000. The incidence of BrS in men is approximately 8 - 10 times more frequent than in women.<sup>(2-4)</sup>

After SCA, patients with BrS had cognitive impairment from hypoxia, which can lead to a mood disorder.<sup>(5-7)</sup> Thus, patients with BrS may lose some

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income and time for work for every follow-up visit at the hospital. Accordingly, the quality of life in BrS patients needs to be further explored.

There is very limited investigation on the quality of life in patients with BrS. The research on the impact of ICD implantation on patients with BrS by *Probst V, et al.*<sup>(8)</sup> found that score of SF-36 for three groups of patients with BrS (Group 1: symptomatic patients with BrS implanted ICD; Group 2: asymptomatic patients with BrS implanted ICD; and Group 3: asymptomatic patients with BrS without ICD implantation) were similar. Moreover, the score of SF-36 in the patients with BrS was similar to the overall French population. However, specific questions about ICD suggest that ICD implantation had a significant negative impact on the quality of life.

*Lundgren-Nilsson A, et al.*<sup>(5)</sup> found that the cognitive function, activity, participation, and quality of life over a one-year period in patients who previously had cardiac resuscitation improved slightly after patients were discharged from hospital. In addition, work capacity was 13.0 % after one year of successful cardiac resuscitation. Health-related quality of life including emotion, physical mobility and sleep was improved greatly over a year.

The research on health-related quality of life and the related factors in elderly patients with permanent pacemaker by *Duangsakul W, and Choowattanapakorn T.*<sup>(9)</sup> found that depression, co-morbidity, and limited activity had a negatively significant impact on the quality of life. Social support had a positively significant impact on the quality of life.

BrS in Thailand is an under-recognized condition affecting men of working age. Individuals with this condition often do not have any symptoms prior to suffering from sudden cardiac arrest. Due to the lack of knowledge regarding this disease and how it affects the quality of life in those who have been diagnosed, the objective of this research was to identify the quality of life, anxiety, depression, cognitive test, and related factors in Thai patients with BrS at King Chulalongkorn Memorial Hospital in Bangkok.

## Materials and methods

This study was a cross-sectional descriptive study. This study enrolled all patients who were diagnosed with BrS type 1 by physicians, came for a follow-up treatment, and consented to participate. Twenty-nine

participants were recruited between August 2019 to April 2020 from Pacemaker Clinic, King Chulalongkorn Memorial Hospital and agreed to participate in this study, which has been approved by the Institutional Review Board (IRB) of the Faculty of Medicine of Chulalongkorn University (IRB no. 311/62). Informed consent was obtained from all subjects. Inclusion criteria were patients diagnosed with BrS type 1, had at least one of the electrocardiography results presenting Brugada pattern type 1 with or without high chest lead or drug challenge, and were over 18 years old. Patients with other cardiac diseases such as myocardial infarction, congenital heart disease, had severe infectious disease or were unable to understand Thai language were excluded from this study.

This study included four parts. The first was demographic data. The second involved the quality of life questionnaire using MacNew<sup>(10)</sup> and The Short-Form 36 Health Survey (SF-36). The third was anxiety and depression questionnaire using Hospital Anxiety and Depression Scale in the Thai language version (Thai-HADS). The last part was cognitive test using Pegboard, Trail A and B and Consortium to Establish a Registry for Alzheimer's Disease–Neuropsychological battery (CERAD), including Word List Memory, Word List Recall and Word List Recognition tests. Quality of life measurements, namely MacNew and the Short-Form 36 Health Survey (SF-36) questionnaires, were selected for this study for their psychometric properties and widespread use. Furthermore, there was no specialized quality of life questionnaires specifically for patients with BrS. We used these two questionnaires to measure heart disease health and general health in order to evaluate consistencies in results and to compare the outcomes.

### *MacNew Heart Disease Health-related Quality of Life questionnaire*<sup>(10 - 12)</sup>

MacNew questionnaire was developed from the original Quality of Life after Myocardial Infarction (QLMI) questionnaire, a self-reporting questionnaire about how ischemic heart disease (IHD) affects daily functioning for the past two weeks. This questionnaire had 27 questions with a global score to describe physical, emotional and social function in subscales. The Cronbach's alpha coefficient in the Thai version of the MacNew range was 0.936 from previous research by *Lortajakul C, et al.*<sup>(13)</sup>

### **Short form Health Survey 36 (SF-36)<sup>(14, 15)</sup>**

SF-36 was a generic health survey with 36 questions including two summary scales: physical component scale (PCS) and mental component scale (MCS). These were subdivided into eight factors including physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotion and mental health. The Cronbach's alpha coefficient of eight scales in the Thai version of the SF-36 ranging was 0.72 - 0.94 from research by *Jirarattanaphochai K, et al.*<sup>(16)</sup>

### **Hospital Anxiety and Depression Scale version Thai (Thai HADS)<sup>(17, 18)</sup>**

HADS was designed for screening for anxiety and depression in the patients in hospital and for self-reporting with one-week timeframe. HADS had 14 items with 4 choices for each item. At the best cut-off point > 11, the sensitivity of anxiety and depression sub-scales of Thai HADS were 100.0% and 85.7%, respectively. The specificity of anxiety and depression of Thai HADS were 86.0% and 91.3%, respectively. Both sub-scales showed Cronbach's alpha coefficient of anxiety at 0.8551, and depression sub-scale at 0.8259 from research by *Nilchaikovit T, et al.*<sup>(18)</sup>

### **Trail A and B test<sup>(19, 20)</sup>**

These tests assessed attention and executive function. Part A was designed for assessing a simple cognitive processing speed and was  $\leq 40$  seconds in cut-off point. Part B was designed for assessing a complex cognitive processing speed and was  $\leq 90$  second in cut-off point.

### **Grooved Pegboard<sup>(21)</sup>**

This test assessed manipulative dexterity and visual-motor coordination. The Grooved Pegboard included 25 holes with randomly positioned slots. There were many pegs which must be rotated to match the hole before inserting.

### **Consortium to Establish a Registry for Alzheimer's Disease-Neuropsychological battery (CERAD)<sup>(22, 23)</sup>**

The subtests selected for the current study assessed memory and was established for an evaluation and a diagnosis in Alzheimer patients. This

study used CERAD Thai version developed by *Tangwongchai S, et al.*<sup>(22)</sup> which had a sensitivity at 1.0 and specificity at 0.82 when the cut-off point was < 62. This study used CERAD in the part of Word List Memory, Word List Recall and Word List Recognition.

### **Statistical analysis**

The analyses were performed by using the SPSS program version 22. All descriptive statistics were presented as mean, standard deviation (SD) and percent for demographic data, quality of life questionnaires, anxiety and depression questionnaires and cognitive test. Relative factors for quality of life were analyzed by multivariate linear regression. A *P* - value of < 0.05 was considered statistically significant.

### **Results**

There were 29 patients with BrS from Pacemaker Clinic, King Chulalongkorn Memorial Hospital, Bangkok, Thailand participating in this study. There were 28 males (96.6%); the mean age was  $45.2 \pm 13.8$  years old. The median age was 46.0 years (range from 19 - 72 years old). Most of them were employee (44.8%), graduated from the primary school level (34.5%) and were the fat level II on BMI level (37.9%). The mean income was  $28,810.3 \pm 33,302.0$  baht. The median income was 15,000.0 baht (range from 2,000 - 150,000 baht). Most of them were born in the Northeastern Region of Thailand (48.3%) and then moved to live in the Central Region, Thailand (51.7%). Twenty patients lived in a nuclear family (69.0%). Most of them determined the treatment decision related to BrS by themselves (48.3%) (Table 1).

There were 17 patients (58.6%) whose family history of sudden cardiac arrest or BrS was absented, 22 patients (75.9%) were healthy. Most of them were presented unexplained syncope in the first cardiac event (34.5%). There were 18 patients (62.1%) who had cardiac arrest history; 25 patients were implanted ICD; 13 patients (52.0%) had a least of appropriate shock by ICD since implanting ICD; 23 patients (92.0%) had no ICD shock at the last follow-up and 22 patients (75.9%) were treated without radiofrequency ablation (RFA) (Table 1).

**Table 1.** Participants' demographic data and clinical characteristics.

Characteristics	Number (%) (n = 29)
<b>Gender</b>	Male 28 (96.6)
<b>Occupation (n = 29)</b>	Employee 13 (44.8) Freelance 8 (27.6) Owner 5 (17.2) State enterprise 2 (6.9) Student 1 (3.4)
<b>Education (n = 29)</b>	Primary school 10 (34.5) Secondary school 9 (31.0) High vocational certificate 2 (6.90) Bachelor degree 6 (20.7) Master degree 2 (6.9)
<b>BMI (kg/m<sup>2</sup>) (n = 29)</b>	Underweight 4 (13.8) Normal 9 (31.0) Obese class I 5 (17.2) Obese class II 11 (37.9)
<b>Place of birth (n = 29)</b>	Northeastern 14 (48.3) Central 13 (44.8) East 2 (6.9)
<b>Place of living (n = 29)</b>	Northeastern 6 (20.7) Central 15 (51.7) East 8 (27.6)
<b>Family formation (n = 29)</b>	Single 6 (20.7) Nuclear family 20 (69.0) Extended family 3 (10.3)
<b>Main decision of treatment (n = 29)</b>	Him/herself 14 (48.3) Him/herself, spouse and/or child 8 (27.6) Him/herself and/or parent 4 (13.8) Other 3 (10.3)
<b>Family history of sudden cardiac arrest or BrS in family</b>	Yes 12 (41.4)
<b>Underlying (n = 29)</b>	Yes 7 (24.1)
<b>Nature of the first cardiac event (n = 29)</b>	Document with VT/VF with or without SCA 6 (20.7) Abort sudden cardiac arrest (SCA) 4 (13.8) Unexplained syncope 10 (34.5) Agonal nocturnal breathing 3 (10.3) Asymptomatic case 6 (20.60)
<b>History of cardiac arrest (n = 29)</b>	Yes 18 (62.1)
<b>Implanting ICD (n = 29)</b>	Yes 25 (86.2)
<b>RFA (n = 29)</b>	Yes 7 (24.1)
<b>ICD shock since implanting ICD (n = 25)</b>	No shock 11 (44.0) Appropriate shock 13 (52.0) Inappropriate shock 1 (4.0)
<b>ICD shock at last follow-up date (n = 25)</b>	No shock 23 (92.0) Appropriate shock 1 (4.0) Inappropriate shock 1 (4.0)

Mean of global MacNew questionnaire was  $5.6 \pm 0.8$  points (range from 4.0 - 6.8), the mean of PCS of SF-36 questionnaire was  $49.8 \pm 6.4$  points (range from 34.3 - 58.6), and the mean of MCS of SF-36 questionnaire was  $52.9 \pm 6.3$  (range from 40.9 - 65.2). The anxiety of Thai HADS was  $4.4 \pm 2.9$  points which separated into two groups including 24 patients (82.8%) who were in a normal range and five patients (17.2%) who were in a doubtful range. The depression of Thai HADS was  $3.3 \pm 3.3$  points which separated into three groups includes 25 patients (86.2%) who were in a normal range, three patients (10.3%) who were in a doubtful range

and one patient (3.4%) who were in a case range (Table 2). As for the cognitive part, the results are presented in Table 2.

In this study, the variable factors studied in Probst *V, et al.*<sup>(8)</sup> were chosen for analysis by multiples linear regression, including age, nature of BrS, ICD implantation, anxiety, and depression. The related factor associated global score of MacNew questionnaire, PCS of SF-36 and MCS of SF-36 were analyzed by multivariate linear regression. The result found that anxiety was significant impact on the quality of life (Table 3 - 5).

**Table 2.** The findings from the quality of life questionnaires; (MacNew and SF-36), HADS, and the cognitive tests.

Questionnaire	Subscale	Mean $\pm$ SD
MacNew	Physical	5.8 $\pm$ 0.8
	Emotional	5.4 $\pm$ 0.8
	Social	5.9 $\pm$ 0.9
	Global	5.6 $\pm$ 0.8
SF-36	Physical function	77.1 $\pm$ 18.8
	Role physical	82.8 $\pm$ 18.8
	Bodily pain	88.1 $\pm$ 13.9
	General health	71.4 $\pm$ 19.7
	PCS*	49.8 $\pm$ 6.4
	Vitality	65.5 $\pm$ 14.4
	Social function	91.4 $\pm$ 13.0
	Role emotion	86.5 $\pm$ 19.7
	Mental health	77.1 $\pm$ 15.0
	MCS*	52.9 $\pm$ 6.3
	HADS	Anxiety
Depression		3.3 $\pm$ 3.3
Grooved Pegboard	Dominant hand (seconds)	78.4 $\pm$ 27.9
	Non-dominant hand (seconds)	84.5 $\pm$ 26.0
Trial A-B	Trial A (seconds)	53.7 $\pm$ 20.7
	Trial B (seconds)	181.0 $\pm$ 80.9
CERAD	Word List Memory (words)	21.0 $\pm$ 4.4
	Word List Recall (words)	7.2 $\pm$ 2.6
	Word List Recognition (words)	9.6 $\pm$ 1.0

Note \*PCS and MCS were from the calculation.

**Table 3.** The associated factors of the global score of MacNew questionnaire.

Variables	Coefficient (SE)	95 % CI	t	P - value
Age	0.003 (0.007)	-0.012, 0.017	0.36	0.722
Nature Group 2*	-0.317 (0.402)	-1.150, 0.516	-0.79	0.438
Nature Group 3*	-0.057 (0.419)	-0.925, 0.811	-0.14	0.893
ICD implantation	-0.114 (0.479)	-1.107, 0.878	-0.24	0.813
Anxiety	-0.157 (0.040)	-0.241, -0.074	-3.90	0.001
Depression	-0.059 (0.036)	-0.133, 0.015	-1.67	0.110

Constant = 6.661, R<sup>2</sup> = 0.575, F = 7.32, P < 0.001

**Table 4.** The associated factors of the PCS (SF-36).

Variables	Coefficient (SE)	95 % CI	t	P-value
Age	-0.135 (0.069)	-0.278, 0.008	-1.96	0.062
Nature Group 2*	-6.558 (3.845)	-14.532, 1.415	-1.71	0.102
Nature Group 3*	-5.527 (4.008)	-13.839, 2.785	-1.38	0.182
ICD implantation	5.120 (4.582)	-4.383, 14.623	1.12	0.276
Anxiety	-1.191 (0.386)	-1.991, -0.391	-3.09	0.005
Depression	-0.203 (0.341)	-0.911, 0.505	-0.59	0.558

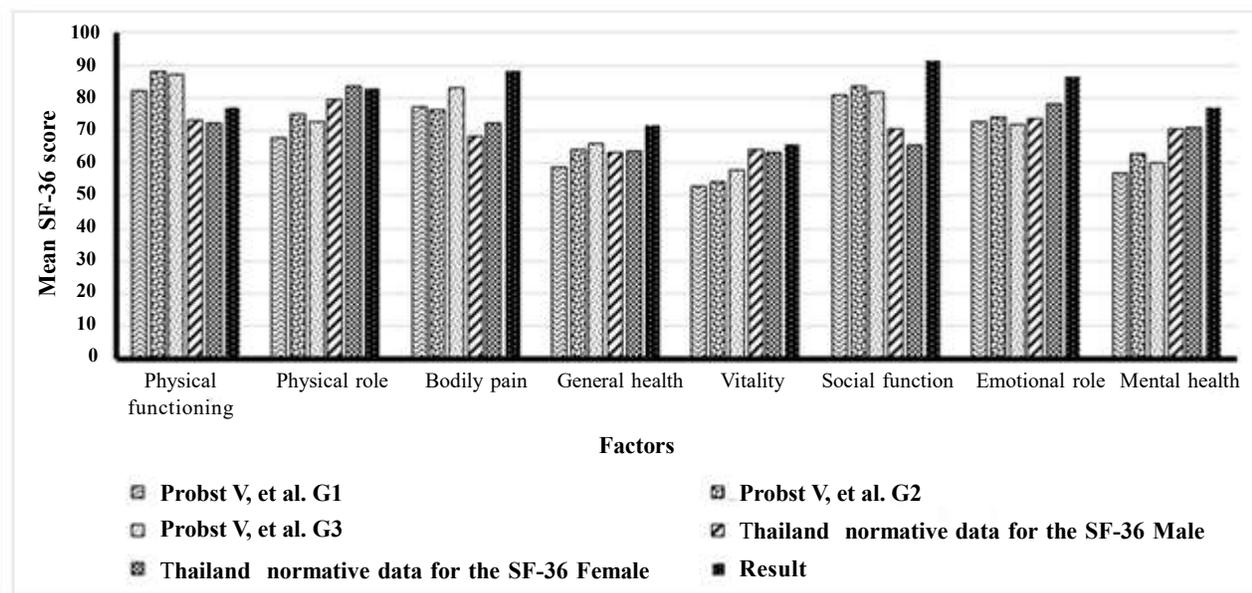
Constant = 62.320, R<sup>2</sup> = 0.464, F = 5.04, P < 0.05

**Table 5.** The associated factors of the MCS (SF-36).

Variables	Coefficient (SE)	95 % CI	t	P-value
Age	0.059 (0.067)	-0.080, 0.198	0.88	0.389
Nature Group 2*	2.774 (3.748)	-4.999, 10.546	0.74	0.467
Nature Group 3*	2.424 (3.907)	-5.679, 10.527	0.62	0.541
ICD implantation	-1.040 (4.467)	-10.304, 8.223	-0.23	0.818
Anxiety	-1.491 (0.376)	-2.271, -0.711	-3.96	0.001
Depression	-0.240 (0.333)	-0.930, 0.451	-0.72	0.479

Constant = 56.433, R<sup>2</sup> = 0.472, F = 5.17, P < 0.05

\*Nature Group divides by nature of first cardiac event include Group 1; Asymptomatic<sup>(24)</sup>, Group 2; unexplained syncope and agonal breathing, Group 3; document with VT/VF with or without SCA and abort SCA.

**Figure 1.** Comparing of the mean score of SF-36 between the result of this research, the result of the research of Probst V, et al.<sup>(8)</sup> and Thai norm.<sup>(25)</sup>

## Discussion

Comparing to previous studies on the quality of life of patients with BrS, the current study found that the mean score of the physical functioning from SF-36 questionnaires was lower. In contrast, the mean score of physical role, bodily pain, general health, vitality, social functioning, emotional role and mental factor were higher than the study by *Probst V, et al.*<sup>(8)</sup> The age difference of participants between our and previous studies may have resulted in different scores observed. When comparing the current study to the Thai norm (Bangkok)<sup>(25)</sup> by using SF-36, the mean scores of physical functioning, bodily pain, general health, social functioning, emotional role and mental health were higher, and physical role and vitality were similar (Figure 1).

The mean score of anxiety and depression of HADS in this research was similar to the previous studies in patients with the heart disease<sup>(26,27)</sup> which was in a normal range.

Anxiety score from HADS was statistically significantly associated with the quality of life in patients with BrS, which was concordant with that of *Probst V, et al.*<sup>(8)</sup> The previous study found that symptomatic patients were more anxious (68.0%) than asymptomatic patients (41.0%) in regards to their health status. In addition, *Uchmanowicz I and Gobbens RJ.*<sup>(28)</sup> reported that PCS and MCS scores were inversely associated with HADS-anxiety and HADS-depression scores.

Anxiety score from HADS was statistically significantly associated with the quality of life in patients with BrS. However, *Hwang SL, et al.*<sup>(29)</sup> reported that the essential predictors of quality of life in patients with heart failure were age, physical symptoms, duration of heart failure, and depression. In addition, *Suetrong A and Choowattanapakorn T*<sup>(30)</sup> reported that the major factors associated to the quality of life in elderly patients with heart failure were sex, comorbidity, severity of disease, depression, and social support. The population of previous studies were older than in this current study so that the related factors of quality of life may be different.

Our result showed that anxiety was associated with the quality of life in Thai patients with BrS. Therefore, the healthcare teams should consider assessing anxiety before and after patient treatment and refer severe BrS patients for consultation with psychiatrist for psychotherapy, such as group therapy or cognitive behavioral therapy. Although cognitive factor did not significantly affect the quality of life in

patients with BrS, our results showed that there were obviously multiple impairments in cognitive functions among Thai BrS patients. Therefore, healthcare teams should recognize this deficit in patients in order to help improve their cognitive function.

The strength of this research was that this was the first study in Thailand and the second of the world to examine the quality of life in clinically diagnosed BrS patients. This study collected extensive data on patients who were diagnosed with BrS type 1 such as quality of life, anxiety, depression, and impairment cognitive data.

However, the main limitation of this study was the relatively low number of subjects because BrS is a rare disease and not all patients agreed to participate. The subjects in this research were only a part of all patients with BrS in Thailand and these results may not represent all BrS patients. The study period for this cross-sectional study was also limited, and only patients from one hospital was included.

## Conclusion

This research presented that BrS patients had an inadvertent-quality of life, and anxiety might play an important role in the quality of life in patients with BrS. Thus, clinicians should routinely assess the anxiety level of patients with BrS; for example, before and after treatment. This study recruited only patients with BrS at King Chulalongkorn Memorial Hospital so that limitation in the generalization should be recognized on the different culture, age, and symptom reported by the patients.

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## Conflict of interest

The authors, hereby, declare no conflict of interest.

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