Theses of Doctoral (PhD) Dissertation

They psychological aspects of Raynaud’s disease

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Introduction

In the management of many chronic diseases usually only the level of the somatic changes is treated thoroughly. However, if we seek to provide the best complex care to keep up with the constantly developing medical sciences, it is warranted to investigate those emotional and behavioural responses, which may affect the course of the diseases. Up to this day, the exact course of the development of the autoimmune disorders and the casual factors are still not precisely known. The only widely accepted opinion is that we are facing the complex interaction of several influencing factors. Scientific attention which integrates psychological aspects in research, paid to autoimmune disorders is rather heterogeneous. Specific disorders, such as Raynaud’s syndrome (RS), received very little attention. We can’t really find studies using a notable psychological point of view. Only a few, no more than five published, study applied psychological aspects in the last 20 years. It is even more surprising if we recall the fact that since the first description of the disease from 1862 it is known that psychological factors have an unquestionable role in the symptom development. The role emotional distress in the symptom development makes possible and justifies investigate Raynaud’s syndrome including psychological aspects. Up to this point, not a single comprehensive study has been conducted to examine the detailed psychological adaptation to Raynaud’s syndrome in Hungary. The main goal of our study was to bring the role of psychological aspects in Raynaud’s disease to clinicians’ attention thereby contribute to develop a more detailed understanding and effective treatment models in this often neglected autoimmune disorder.

RESEARCH AIMS

1. Quality of life

Even though the quality of life in patients with Raynaud’s syndrome is affected by the recurrent somatic symptoms, the necessary life adjustments and the treatment side-effects, the disease-specific aspects have not received no serious professional attention yet. The first main goal the investigation of disease-specific aspects of quality of life in Raynaud’s disease.

2. Mental health in primary and secondary RS

On the basis of literature assumptions, the secondary Raynaud’s syndrome (SRS) can be considered more serious than the primary Raynaud’s syndrome (PRS). One of the main characteristics of the disease course of Raynaud’s syndrome is that more serious functional impairments and more severe symptoms may develop over time. PRS might “transform” into SRS. Since with more severe physical complaints usually correlate with more severe mental and emotional difficulties, we can hypothesize that both the physical and mental health condition of patients with SRS might be worse compared to patients with PRS. The comparative psychological analysis of the primary and secondary forms has not been realized yet and what’s more; mental health in PRS received no professional attention at all. Therefore, the second main goal of our study was to explore the disease specific aspects of general health condition, anxiety, depression and quality of life in a comparative analysis among patients with PRS and SRS.

3. Alexithymia and emotion regulation

It is well-known since Raynaud’s first study that besides cold, emotional distress triggers the characteristic symptoms. Therefore, we can hypnotize that personal differences in experiencing emotional distress and in the ability of cognitive regulation of emotions may influence psycho-social adaptation to the somatic symptoms. Therefore, we can also presume that the awareness about internal states, the perception and understanding of emotional states and feelings could be a key influencing factor in Raynaud's syndrome. The third main goal of our research was the investigation of alexithymia and emotional regulation strategies (cognitive reappraisal and suppression) and their association of with depression and quality of life.

METHODS

In our recent study we applied both qualitative (semi-structures interviews to explore the patients subjective experiences) and qualitative (a survey battery which is partially based on the qualitative phase) data collection methods. We carried out our research objectives through two phases and three data collections. In the first phase of the study we applied a qualitative research method: semi-structed interviews. In the second phase we applied a quantitative research approach: administering survey questionnaires in two different samples. Our patients were recruited from the Raynaud's Outpatient Clinic of the Department of Internal Medicine, University of Debrecen, where they receive regular follow-up care.

Measures

In that stage, in order to identify factors reflecting patients' health-related quality of life, the patients were asked to describe the impact of RS and its treatment on their daily life, including physical functioning, emotional well-being, social interactions, and work. Interviews continued until no new issues emerged. Transcripts were analyzed qualitatively to identify participants' expressions of domains. The authors independently proposed domains after reviewing the transcripts. Afterwards, difference in domains were discussed until a final agreement was reached.

During the second and third phase we applied overlapping choice of measures two times in data collection.

The *Beck Depression Inventory* (BDI) is a self-report questionnaire used to measure the presence and severity of depression.

The 7-item *Generalized Anxiety Disorder Scale* (GAD-7) is a one-dimensional scale applied to assess the presence of the symptoms of anxiety.

As an abbreviated version of SF-36, the 12-item Short Form Health Survey (SF-12) is a generic health status evaluation tool. It has two subscales; in the present study only the *Physical Component Summary* (PCS-12) was used to measure general physical health condition.

The *Raynaud Specific Quality of Life Questionnaire* (RQLQ) was used to measure disease-specific quality of life. It includes five dimensions: emotional burden (six items), impaired hand function (eight items), control (four items), social interaction (eight items), and sleep (three items). All 29 items are rated on a five-point Likert scale ranging from “extremely” to “not at all” with higher scores indicating a better quality of life. The measure has been developed and validated recently by our research group.

The *Toronto Alexithymia Scale* (TAS) was used to measure alexithymia. It is composed of 3 subscales which were not interpreted separately during analysis.

Participants in this study completed the 10-item *Emotion Regulation Questionnaire*, which measures individual differences in the habitual use of the emotion regulation strategies of cognitive reappraisal (ERQ-R) and suppression (ERQ-S).

Demographic data and treatment history were assessed by a questionnaire created by the authors.

Statistical analysis

Statistical analyses were performed using SPSS v. 22 (SPSS Inc., IBM, Chicago, IL, USA). The normality of the data was checked by the Kolmogorov-Smirnov test. Continuous variables between groups were compared by using Student’s t-test or the Mann-Whitney U test, while comparisons between discrete variables were made by the chi-square test or Fisher's exact test, where appropriate. For continuous data one-way analysis of variance (ANOVA) with Bonferroni post hoc tests were used. Pearson correlations were calculated to explore the association between quantitative variables. A two tailed p value of < .05 was considered statistically significant. The rate of missing data was below 0.5% for each variable. Missing data were replaced by the respective sample mean.

RESULTS

In the first, qualitative phase semi-structured interviews were conducted with 28 patients with RS. 64.39 % of the participants were women. Mean age was 53.5, with a range of 19–70. 53.57% of participants were diagnosed with primary RS.

In the second, quantitative phase a total of 101 patients (60 PRS, 41 SRS) with a diagnosis of RS were enrolled in the study. The overall mean (SD) age of the participants was 50.5 (15.3) years. While there were no statistically significant differences between both groups in terms of gender, family status, employment status or smoking, there were significant differences between the groups in the duration of education (for

PRS patients: 13.16±2.69 years; for SRS: 11.68±2.1 years, p = .02).

In the third, quantitative phase study sample included 110 patients diagnosed with RD. The sample consisted of predominantly female participants (87.3%). The mean age was 53.65 (SD = 13.41). Regarding demographic data, there were no statistically significant differences between the groups in terms of gender and family status; there were significant differences between the groups in employment status (χ 2 (1) = 4.58, p = .032), duration of education (U = 275.0, p = .042), and age (t = -2.41, p = .02). There was no significant difference between the groups in disease duration.

1. Quality of life

After analyzing the transcripts of the interviews, the resulting eight main domains were the following: experiences of the symptoms, decreased functionality, treatment and prevention, relationships, emotional and cognitive difficulties, work, travel, and sleep.

2. Mental health in primary and secondary RS

Anxiety was more common than depression. Using a score greater than 10 as the cut-off, anxiety was present in 23.3% and 43.9% of patients with primary and secondary RS, while when using 18 as the cut-off score, depression was present in 11.7% and 31.7% of patients, respectively. Both the mean±SD GAD-7and BDI scores were significantly higher in the SRS group than in the PRS group (for anxiety: 9.5 ± 6.1 vs 6 ± 5.9, p < .001; for depression: 15.2 ± 13.2 vs 6.6 ± 8.9, p < .001). The proportions of patients with anxiety and depression were not similar in the two groups. Significantly more patients with SRS had anxiety (43.3% vs 23.3%, p = .05) and depression (31.7% vs 11.7%, p = .21) than patients with PRS when the cut-off scores of 10 and 18 were used to define clinical anxiety and depression, respectively.

The mean±SD PCS-12 score was significantly lower in the SRS group than in the PRS group (39.8 ± 27.4 vs 62.6 ± 26.4, p < .001). The same was true for the four subscales of the PCS-12 scale.

The summary score for RQLQ was significantly lower in the SRS group than in the PRS group (82.4 ± 27.2 vs 107.9 ± 24.3, p < .001). There were significant differences between the two groups for four of the five RQLQ dimensions (p < .001), but not for the RQLQ Control dimension (11.1 ± 4.8 vs 10.1 ± 4.7, p = .22).

3. Alexithymia and emotion regulation

Non-alexithymic patients had significantly higher scores on ERQ-R ($t = 3.39$, $p < .001$) and RQLQ ($U = 221.5$, $p = .001$), and significantly lower scores on ERQ-S ($t = -5.16$, $p < .001$), TAS ($U = .0$, $p < .001$) and BDI ($U = 126.0$, $p < .001$) than patients with alexithymia (see Table 1). The borderline alexithymic group was excluded from subgroup comparisons and subgroup correlation analysis because those results were not important or relevant in the light of the final conclusions.

In the whole sample, age significantly positively correlated with TAS ($r = .29$), ERQ-S ($r = .23$), BDI ($r = .22$) and RQLQ ($r = -.32$). Statistically significant negative correlations were observed between education level and TAS ($r = -.29$), BDI ($r = -.24$) and RQLQ ($r = -.32$), while disease duration negatively correlated only with RQLQ ($r = -.37$). TAS was positively associated with ERQ-S ($r = .54$) and BDI ($r = .51$), but negatively associated with ERQ-R ($r = -.26$) and RQLQ ($r = -.40$). Significant positive correlations were observed between ERQ-R and RQLQ ($r = .21$). In addition, RQLQ was associated with BDI ($r = -.59$). Interestingly, there were significant positive correlations between the two subscales of ERQ ($r = .24$).

To explore the background of this unexpected association between ERQ-R and ERQ-S, we conducted the same correlational analyses, but now only in the Alexithymic and Non-Alexithymic subsamples. We found significant differences between the Alexithymic and Non-Alexithymic subsamples. There was a strong positive association between ERQ-S an ERQ-R ($r = .59$, $p < .01$.) in the Alexithymic subsample, while there was no significant association between these scales ($r = .13$, $p = .46$) in the Non-Alexithymic subsample. In the Alexithymic subsample TAS was strongly related to BDI ($r = .53$) and RQLQ ($r = -.46$), while ERQ-S was only related to ERQ-R, as mentioned above. However, in the Non-Alexithymic subsample TAS was only related to ERQ-S ($r = .56$), and ERQ-S was associated with BDI ($r = .38$) and RQLQ ($r = -.35$). Education was only related to RQLQ ($r = .63$) in the Alexithymic subsample, while age was associated with ERQ-S ($r = .37$) in the Non-Alexithymic subsample.

We compared mean ERQ subscale scores in the three study subgroups to assess the differences in the tendency to use cognitive reappraisal and expressive suppression. A series of one-way ANOVA with Bonferroni post hoc tests showed significant differences between subgroups in ERQ-S, and a significant difference between the Non-Alexithymic and Alexithymic subgroup in ERQ-R.

In addition, we compared ERQ subscales by standardizing ERQ-R and ERQ-S scores to 0 from 100 in the three study subgroups. In the Non-Alexithymic ($t = -10.37$, $p <$

.001) and Borderline (t = -10.37, p < .001) subsamples there were significant differences in the tendency to use cognitive reappraisal and expressive suppression. However, in the Alexithymic subsample there was only a small, non-significant difference (t = .99, p = .33) in the tendency to use these emotional regulation strategies.

DISCUSSION

1. Quality of life

The first main goal of our study was to investigate quality of life in Raynaud's syndrome. According to our results, almost every domain of quality of life is negatively affected. The somatic symptoms cause significant suffering, they are accompanied by loss of functionality; frequent preventive actions are needed; furthermore they affect job performance, commuting and sleep quality. Similarly to other chronic disorders, disease burden was experienced on physical, psychological (behavioural, emotional and cognitive) and social levels. The findings of this study show that the disease is present as significant hardship in every aspect of daily life. Based on the data collected through semi-structed interviews we developed a Raynaud-specific quality of life scale, which was applied in the following phases of our research to examine the changes in quality of life in greater detail. The items were organized into five main factors after psychometric testing and screening: emotional burden, impaired hand function, social interaction, control and sleep. At same time of our first phase, an other study was conducted by Pauling and his collegues with SRS patients with systemic sclerosis arriving mostly to the same conclusions.

According to previous sources, emotional distress has a significant influence in Raynaud's syndrome. Even though we can conclude that the described quality of life affecting factors may serves as further stressors. Such drugs are not available which may decrease symptom severity without serious side-effects. Raynaud's syndrome can be considered as a tangible burden in the patient's everyday life, which statement is supported by our own study as well. These factors may contribute negatively to the patient's long-term quality of life and disease course.

2. Mental health in primary and secondary RD

In this phase, we compared anxiety, depression, physical health and quality of life in patients who had been referred to a specialized center for RD. We used self-administered questionnaires in the present study. Our results highlighted a significant difference between the two groups in all the measures.

In particular, the findings reported the presence of higher levels of anxiety and depression in patients with SRS compared to patients with PRS, indicating poorer emotional distress in patients with SRS. Our study population reported rates of anxiety and depression that were similar to those described in previous studies conducted on patients diagnosed with diseases where RD can be also diagnosed as a secondary syndrome. Clinically relevant anxiety and depression were more common in patients with SRS than patients with PRS. However, it is not only the prevalence values of depression and anxiety found in patients with SRS - which is considered more severe than PRS – which are in line with previous studies, the prevailing values of depression and anxiety found in patients with PRS are similar to most of the results of investigations of patients with various rheumatological and autoimmune diseases.

The results of this study contribute to the assumptions outlined previously, i.e. that a diagnosis of SRS indicates a worse health condition than a diagnosis of PRS. As expected, based on the literature, patients with SRS had worse physical health than patients with PRS. In the course of the disease, after the first symptoms of RD, greater physical disability and more serious symptoms can develop which explains the decreased physical health in patients with SRS. Since, it has been reported that PRS may evolve into SRS in a few years. Therefore annual clinical follow-up is necessary with the use of noninvasive tests such as Doppler flux, duplex ultrasonography, and nail-fold capillary microscopy and serologic testing to evaluate for the possible development of a connective tissue disorder. However, just as the present study showed, it is not only the physical aspect of health, but emotional well-being should be regularly checked.

3. Alexithymia and emotion regulation

The main goal of the present study was to shed light on the relationship between alexithymia, emotion regulation strategies (in particular cognitive reappraisal and suppression), depression and quality of life in patients with RD.

As expected on the basis of previous evidence, alexithymia was associated with impaired quality of life and depression. These findings are consistent with findings indicating the significant association of alexithymia with quality of life and depression. Naturally, alexithymic patients reported lower levels of quality of life and greater levels of depression compared to non-alexithymic participants.

As hypothesized, the results demonstrated that higher levels of alexithymia were significantly related to higher levels of suppression and lower levels of reappraisal in the whole sample. This finding is consistent with previous research reporting that alexithymic individuals have a tendency to use more suppression-like emotion regulation strategies and fewer reappraisal ones. In addition, we found a significant correlation between age, education and alexithymia, which is in accordance with previous studies.

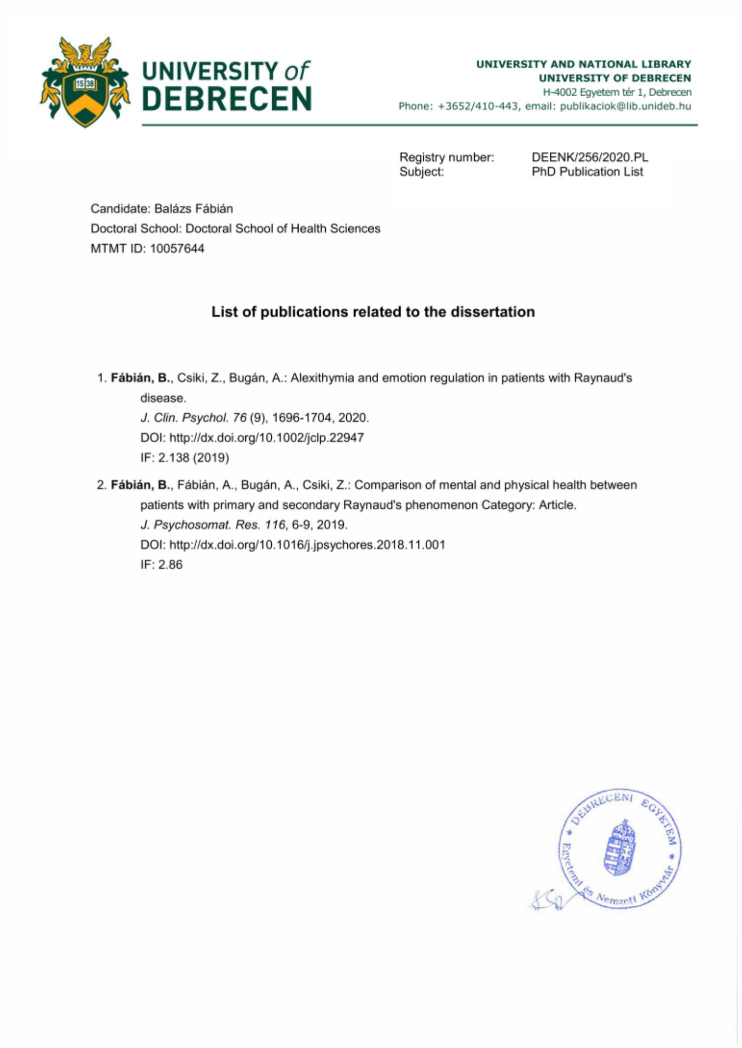
The present study revealed that the use of a suppression strategy was positively related to depression and negatively to quality of life, while the use of a reappraisal strategy was shown to have only a weak but significant association with quality of life scores. This result is supported by studies that show that suppression was associated with lower mental health, more intense symptoms of depression and lower quality of life. Similarly, it has been shown that cognitive reappraisal was related to better quality of life. Moreover, the tendency to use suppression was related to age, which is in line with previous findings. Based on our results we can conclude that the use of suppression as a regulation method can be considered an important risk factor; however, the use of cognitive reappraisal may be a less important protective factor in patients with RS. Therefore, in therapeutic interventions it may be more useful to focus on teaching RS patients to use suppression strategies less frequently, rather than just teaching cognitive reappraisal.

Unexpectedly, we found a strong and positive correlation between the scores on the suppression and cognitive reappraisal subscales of ERQ among alexithymic patients. By definition alexithymia means having impaired emotional awareness, introspection and ability to identify subjective feelings and emotions. Therefore, it seems plausible that, besides emotions, alexithymic individuals also find it hard to distinguish different emotion-related regulation strategies. This may raise the question of the reliability of responses to any affectivity or emotion regulation related tool, since these self-report measures require the respondents to be aware of their reduced ability to identify and describe feelings.

SUMMARY

In our research we confirmed that we have gained valuable experiences in the understanding of the clinical aspects of Raynaud's syndrome by using a psychological point of view, therefore further psychological studies are warranted. Autoimmune disorders are considered as major public health issues, generating a serious challenge for medical care providers and causing severe financial burdens. Autoimmune disorders affect several aspects of everyday life and they have a great impact on one's life. Even though, healthcare mostly focusing on the reduction of physical symptoms, psychological aspects should not be ignored. Currently we know hardly anything about the psychological background of Raynaud's syndrome, related research is still in its infancy. The aim of our research was the investigation of those emotion regulation related factors which may have a significant impact on the daily life of patients diagnosed with Raynaud's syndrome. 239 patients with Raynaud's syndrome (115 primary and 114 secondary) participated in our study. During the first phase of our study interviews have been conducted to identify those aspects of everyday life which may have affected by the disease. During the next two phases of our study we have used a disease specific quality of life tool developed on the basis of the first phase. We

have applied different measures of depression, anxiety, alexithymia and emotion regulation as well. By group comparisons we have found that patients with secondary Raynaud's syndrome have lower levels of quality of life, worse physical health and more symptoms of depression and anxiety. Having alexithymia and tendencies of cognitive suppression might be significant risk factors during the course of disease This study will, hopefully, generate professional interest in the role of the psychological aspects in Raynaud's syndrome and encourage researchers to conduct further multidisciplinary studies, which may help healthcare professionals to solve the complex challenge lying in the medical care of Raynaud's syndrome.



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Candidate: Balázs Fábián
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List of publications related to the dissertation

1. **Fábián, B.**, Csiki, Z., Bugán, A.: Alexithymia and emotion regulation in patients with Raynaud's disease.
   J. Clin. Psychol. 76 (9), 1696-1704, 2020.
   DOI: http://dx.doi.org/10.1002/jclp.22947
   IF: 2.138 (2019)
2. **Fábián, B.**, Fábián, A., Bugán, A., Csiki, Z.: Comparison of mental and physical health between patients with primary and secondary Raynaud's phenomenon Category: Article.
   J. Psychosomat. Res. 116, 6-9, 2019.
   DOI: http://dx.doi.org/10.1016/j.jpsychores.2018.11.001
   IF: 2.86

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List of other publications

3. Mile, M., Tatai, C., **Fábián, B.**, Csiki, Z.: A fizikai aktivitás hatásai az időskori kognitív működésre.
   Orv. hetil. 161 (5), 163-168, 2020.
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4. Szabó, J., **Fábián, B.**: Can Psychological Questionnaires Predict the Academic Talent during Higher Education Studies?
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5. Bollmann, A. K., **Fábián, B.**, Molnár, J.: Az alvás és a kimerültség vizsgálata daganatos betegek körében = Investigation of sleep and fatigue in patients with cancer.
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   Theol. Szle. 59 (3), 149-158, 2016.

Total IF of journals (all publications): 6,623
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