Cardiology in the Young

cambridge.org/cty

Health-related quality of life in adults with Marfan syndrome

Anna Stanek Sörner[1], Maja Enelund[1], Åsa Cider[1,2,3] and Linda Ashman Kröönström[1,2,3]

[1]Institute of Neuroscience and Physiology/Physiotherapy, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [2]Occupational and Physical Therapy Department, Sahlgrenska University Hospital, Östra Hospital, Gothenburg, Sweden and [3]Adult Congenital Heart Unit, Sahlgrenska University Hospital, Östra Hospital, Gothenburg, Sweden

Original Article

Cite this article: Stanek Sörner A, Enelund M, Cider Å, and Ashman Kröönström L (2024). Health-related quality of life in adults with Marfan syndrome. *Cardiology in the Young*, page 1 of 7. doi: 10.1017/S1047951124025770

Received: 16 April 2024
Accepted: 3 June 2024

Keywords:
Marfan syndrome; 36-item Short-Form Health Survey; health-related quality of life

Corresponding author:
Linda Ashman Kröönström;
Email: linda.ashman@vgregion.se

Abstract

Background and aim: Marfan syndrome is a rare genetic connective tissue disorder. Research on health-related quality of life in Swedish patients is lacking. We aimed to examine health-related quality of life in patients with Marfan syndrome with respect to reference values, sex, and age. *Methods:* Using the registry for adult CHD, Sahlgrenska University Hospital/Östra Hospital, between 1 April 2009 and 31 January 2023, we identified 1916 patients. Of these, we included 33 patients aged ≥18 years who were diagnosed with Marfan syndrome and had completed the 36-item Short-Form Health Survey. *Results:* The median age was 32 years (interquartile range 25.5–47.0) and 22 (66.7%) were men. Patients with Marfan syndrome had significantly lower values than reference values for all scales in the Short-Form Health Survey except bodily pain, role-emotional, and the physical component summary score. For both men and women with Marfan syndrome, vitality was the subscale with the greatest percentage difference in comparison with healthy reference values (82% in women and 73% in men). Furthermore, men reported significantly higher vitality levels than women (62.5 points, interquartile range 43.8–75.0 vs. 35 points, interquartile range 10.0–65.0, $p = 0.026$). *Conclusion:* Adults with Marfan syndrome in Sweden showed lower health-related quality of life levels in comparison with reference values for most Short-Form Health Survey scales, and there were differences between patients with Marfan syndrome in terms of sex and age.

Introduction

Marfan syndrome is a rare genetic connective tissue disorder.[1] Marfan syndrome affects multiple organ systems, including the skeletal, ocular, and cardiovascular systems.[2] The cause of Marfan syndrome development is a mutation in the *FBN1* gene located on chromosome 15. The *FBN1* gene encodes the protein fibrillin 1,[3] which is found in various tissues, including the skin, muscles, periosteum, blood vessels, and eyes.[4] Patients with Marfan syndrome often have a deficiency of fibrillin 1, leading to issues indicating need[1] such as an increased risk of aortic aneurysm and aortic dissection.[5] According to these connective tissue problems, patients with Marfan syndrome often experience restrictions in terms of physical activity and exercise.[6] The primary known cause of death in individuals with Marfan syndrome is cardiovascular complications, such as aortic dissection, aortic leakage, and heart failure.[7] Therefore, for patients with Marfan syndrome and aortic involvement, lifelong monitoring and treatment are of utmost importance, including methods such as echocardiography[8], pharmacology, surgery, psychological support, and physiotherapy.[5]

Patients with Marfan syndrome experience a high degree of fatigue[9], which is often associated with pain[10], an extensive and challenging symptom of Marfan syndrome. The pain affects patients with Marfan syndrome both physically and mentally[11] and has also been shown to worsen with increasing age.[12]

Quality of life and health-related quality of life are elusive and difficult-to-define concepts.[13] The World Health Organization defines the quality of life as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns"[14], whilst health is a "state of complete physical, mental and social well-being and not merely the absence of disease or infirmity".[15] Health-related quality of life in patients with Marfan syndrome was assessed in a systematic review from 2019 (of which 17 of 20 studies included adult patients) [16] and in other studies published more recently.[17,18] The systematic review reported on lower quality of life in patients with Marfan syndrome than the general population.[16] However, no studies have been conducted in Sweden. We hypothesised that health-related quality of life would be lower in patients with Marfan syndrome in comparison with reference values for healthy, that women would have lower values than men, and furthermore that higher age could impact health-related quality of

life negatively. The primary aim of this study was therefore to assess health-related quality of life among adult patients with Marfan syndrome in Sweden and to compare it with reference values for healthy individuals. The secondary aim was to investigate whether the outcomes of the Short-Form Health Survey differ among adult patients with Marfan syndrome according to sex and age.

Patients and methods

Study population

This was a descriptive registry study. Patients were informed verbally and in writing regarding the adult CHD registry, and if they accepted, they provided their written informed consent. The inclusion criteria were patients aged ≥18 years who were diagnosed with the International Classification of Diseases Tenth Revision code Q874 (Marfan syndrome), included in the physiotherapy registry for patients with adult CHD, and who had completed the self-assessment questionnaire Short-Form Health Survey between 1 April 2009 and 31 January 2023. In total, 1916 patients were identified in the adult CHD registry, among whom 47 patients had Marfan syndrome; of these, 33 patients met the inclusion criteria (Figure 1).

The 14 patients who were excluded owing to not having completed the Short-Form Health Survey were between 19 and 65 years old (median 26.5 years, interquartile range 22.0–45.0), and 35.7% ($n = 5$) of those patients were men. Furthermore, 13 of the 14 patients had NYHA class I, and one patient had NYHA class II. There was no statistically significant difference between the excluded and included patients regarding sex ($p = 0.050$), age ($p = 0.346$), or NYHA class ($p = 0.613$).

The reference group consisted of healthy Swedish men and women from the general population aged 15–64 years living in different geographical areas ($n = 8930$).[19]

Procedure

The clinic for patients with CHD at Sahlgrenska University Hospital/Östra Hospital treats and continuously monitors adult patients with CHD ≥ 18 years old. Patients are offered assessments of physical capacity (aerobic capacity and muscle function), physical activity level, and health-related quality of life by a physiotherapist, using methods previously described.[20,21] The Short-Form Health Survey is used to assess the patients' health-related quality of life.

Short-Form Health Survey

The Short-Form Health Survey comprises 36 questions and is a generic self-assessment instrument used to measure health-related quality of life.[22] The translated standard Swedish Version 1.0 from the International quality of life assessment group was used. The instrument measures both mental and physical health using eight different subscales: (1) physical functioning, (2) role-physical, (3) bodily pain, (4) social functioning, (5) mental health, (6) role-emotional, (7) vitality, and (8) general health.[22]

The eight subscales are individually scored on a scale of 0–100 points, and higher scores indicate better health-related quality of life.[23] Mental health, social functioning, vitality, and role-emotional are summed to create a mental component summary measure. The remaining four subscales are summed to create a physical component summary measure.[23] Summary measures are rated separately, ranging from 2 to 76 points for the physical component summary and -1–81 points for the mental component summary.[24,25]

The instrument has been tested for conceptual, criterion-based, and content validity, as well as internal consistency reliability, in a general population in Sweden, demonstrating good reliability and validity.[26]

Statistical analysis

Data were analysed using the IBM Statistical Package for Social Sciences version 28.0 (IBM Statistical Package for Social Sciences Inc., Armonk, NY, USA). Variables were described using various measures of central tendency and dispersion based on the scale level and distribution. The distribution of variables was assessed using histograms with a normal distribution curve. Non-normally distributed ratio data are described using the median and interquartile range, and nominal variables are presented as count and percentage. Study participants were divided into groups based on sex and age (≤ median or > median).

Health-related quality of life was assessed as ordinal data and was not normally distributed, and therefore, the median was used as a measure of central tendency, and the interquartile range was used as a measure of dispersion. To identify differences between the medians of two independent groups, the Mann–Whitney *U* test was used. Patient values were compared with healthy reference median values Mann–Whitney *U* test was used. Patient values were compared with healthy reference median values[19] using the one-sample Wilcoxon signed-rank test. For the dropout analysis, the Mann–Whitney *U* test was applied for ratio data, and the chi-squared test was used for nominal and ordinal data. A significance level of $p < 0.05$ was adopted in all analyses.

The minimal clinically important difference for the Short-Form Health Survey has not been assessed in patients with Marfan syndrome, but it has been shown to be between 4 and 6 points for the mental component summary and physical component summary in other patient groups.[27–29] In the current study, a 4-point minimal clinically important difference was applied for the analyses.

Results

The included patients were between 18 and 63 years old, and 66.7% ($n = 22$) of them were men. Among the included patients 81.8% ($n = 27$) were treated with medication (Table 1).

Comparison between values for patients with Marfan syndrome and healthy reference values

A statistically significant difference in values was observed between patients with Marfan syndrome and healthy reference values in all scales, except for bodily pain, role-emotional, and physical component summary in women and bodily pain and physical component summary in men. Patients with Marfan syndrome had statistically significantly lower health-related quality of life levels compared with healthy reference values. A clinically relevant difference existed between values for patients with Marfan syndrome and healthy reference values regarding mental component summary, where patients with Marfan syndrome had a lower value (Figure 2, Supplementary Table S1). For both men and women with Marfan syndrome, vitality was the subscale with the greatest percentage difference in comparison with healthy reference values (Figure 2, Supplementary Figure S1). In the vitality subscale, 82% (9/11) of women and 73% (16/22) of men were below the reference value (Supplementary Figure S2).

https://doi.org/10.1017/S1047951124025770 Published online by Cambridge University Press

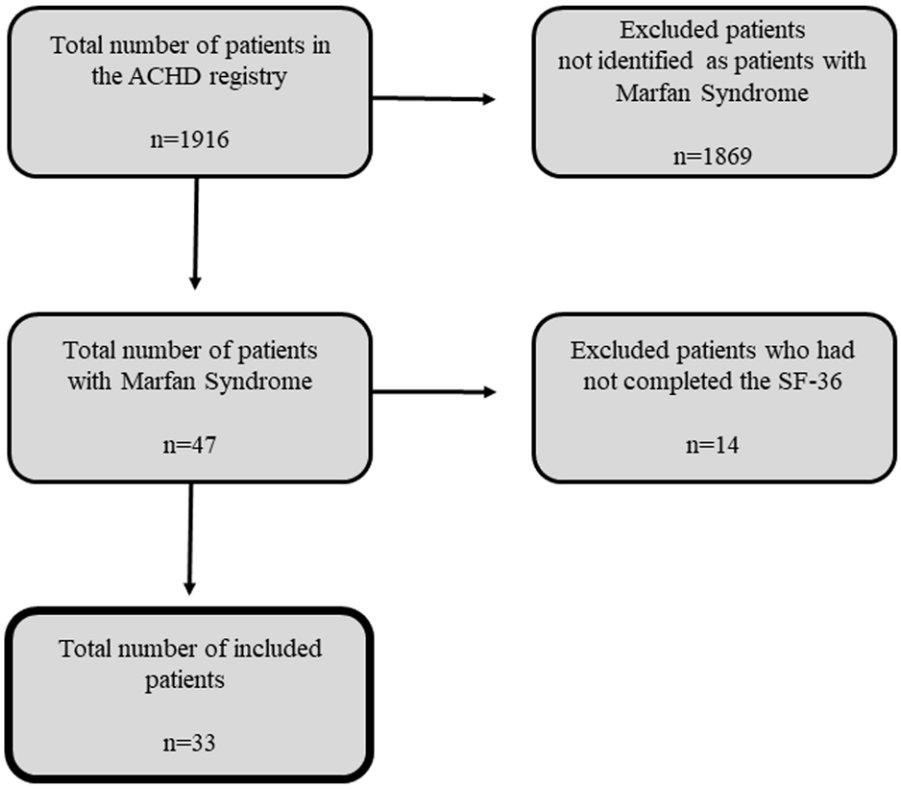

Figure 1. Flowchart illustrating the sampling process. *n* = number; ACHD = adult congenital heart disease; SF-36 = 36-item Short-Form Health Survey.

Comparison between women and men with Marfan syndrome

A statistically significant difference was observed between women and men regarding vitality, where men had a higher value than women ($p = 0.026$). Other variables were not significantly different (Table 2).

Comparison between age groups in patients with Marfan syndrome

A statistically significant difference was found when comparing women in the age groups 18–32 years and 33–63 years regarding physical functioning ($p = 0.030$), where women in the age group 33–63 years had a lower value. Men in the age group 33–63 years had significantly lower values than men in the age group 18–32 years regarding role-physical ($p = 0.040$), general health ($p = 0.002$), and physical component summary ($p = 0.007$). Other variables were not significantly different. A clinically relevant difference existed between age groups for both women and men regarding physical component summary, where patients aged 18–32 years had higher values (Supplementary Table S2).

Discussion

The results of the present study showed that patients with Marfan syndrome had lower health-related quality of life, which is in line with a previous systematic review[16] reporting significantly lower health-related quality of life in patients with Marfan syndrome compared with general populations. The outcome of the Short-Form Health Survey differed in patients with Marfan syndrome aged ≥18 years compared with healthy reference values[19] according to sex. For both men and women with Marfan syndrome, the medians for all scales were less than or equal to the healthy reference values. With the exception of bodily pain, role-emotional, and physical component summary, there was a significant difference between values for patients with Marfan syndrome and healthy reference values, where patients with Marfan syndrome had lower health-related quality of life. There was also a clinically relevant difference with healthy reference values regarding mental component summary, where patients with Marfan syndrome had a lower value. Furthermore, the vitality subscale showed the largest percentage difference compared with healthy reference values for both women and men with Marfan syndrome. Values for most of the study population (82% of women and 73% of men) were below the healthy reference value for the vitality subscale.

The outcome of the Short-Form Health Survey differed significantly among our patients with Marfan syndrome aged ≥18 years based on sex, where men had a higher value than women in the vitality subscale. Otherwise, there were no statistically significant differences between the sexes. Previously published studies have shown divergent results regarding differences in self-assessed health-related quality of life between men and women with Marfan syndrome. Similar to our findings, a Norwegian[12] and a North American study[30] reported no significant difference by sex. These studies included 84 and 389 patients with Marfan syndrome, respectively.[12,30] However, in two other studies,[17,18] there was a statistically significant difference between sexes. In a Dutch study[17] conducted among 123 patients with Marfan syndrome, women had significantly lower scores for physical functioning and physical component summary. A Polish study[18] that included 35 patients with Marfan syndrome also found that women had significantly lower scores for physical functioning and physical component summary as well as for general health, vitality, mental health, and mental component summary. The present study was the first conducted in a Swedish population. Health-related quality of life can vary between different countries depending on several factors.

https://doi.org/10.1017/S1047951124025770 Published online by Cambridge University Press

Table 1. Demographic data of the included patients

	All patients $n = 33$ (100%)	Women $n = 11$ (33.3%)	Men $n = 22$ (66.7%)
Age (years), median (IQR)	32 (25.5–47.0)	32 (27.0–48,0)	32.5 (23.3–46.5)
Age groups, n (%)			
18–32 years	17 (51.5)	6 (54.5)	11 (50.0)
33–63 years	16 (48.5)	5 (45.5)	11 (50.0)
Medication, n (%)	27 (81.8)	10 (90.9)	17 (77.3)
Beta-blockers	19 (57.6)	8 (72.7)	11 (50)
ACE inhibitors	5 (15.2)	3 (27.3)	2 (9.1)
Warfarin	6 (18.2)	2 (18.2)	4 (18.2)
Acetylsalicylic acid	3 (9.1)	1 (9.1)	2 (9.1)
Diuretics	1 (3.0)	0 (0)	1 (4.5)
ARB	6 (18.2)	1 (9.1)	5 (22.7)
Aldosterone inhibitors	0 (0)	0 (0)	0 (0)
Digitalis	2 (6.1)	2 (18.2)	0 (0)
Other	9 (27.3)	5 (45.5)	4 (18.2)
NYHA, n (%)			
NYHA I	29 (87.9)	10 (90.9)	19 (86.4)
NYHA II	4 (12.2)	1 (9.1)	3 (13.6)
NYHA III-IV	0 (0)	0 (0)	0 (0)
Specific heart diagnosis, n (%)	23* (9.7)	8 (72.7)	15 (68.2)
Chronic heart failure	0 (0)	0 (0)	0 (0)
Aortic root dilation/dissected aortic aneurysm regardless of location/aortic dissection	5 (15.2)	2 (18.2)	3 (13.6)
Non-ruptured thoracic aortic aneurysm	5 (15.2)	0 (0)	5 (22.7)
Ruptured thoracic aortic aneurysm	1 (3.0)	0 (0)	1 (4.5)
Aortic insufficiency	3 (9.1)	0 (0)	3 (13.6)
Mitral insufficiency	2 (6.1)	2 (18.2)	0 (0)
Dilation of the ascending aorta	11 (33.3)	4 (36.4)	7 (31.8)
Surgery, n (%)	12** (36.4)	4 (36.4)	8 (36.4)
Catheterisation	2 (6.1)	1 (9.1)	1 (4.5)
Sternotomy	10 (30.3)	3 (27.3)	7 (31.8)
Thoracotomy	2 (6.1)	1 (9.1)	1 (4.5)
Smoking, n (%)			
Smokers	3 (9.1)	1 (9.1)	2 (9.1)
Former smokers	4 (12.1)	3 (27.3)	1 (4.5)
Never smokers	26 (78.8)	7 (63.6)	19 (86.4)

n= number; IQR = interquartile range 25th-75th percentile; ACE = angiotensin converting enzyme; ARB = angiotensin II antagonists; NYHA = New York Heart Association (functional classification).
*The total number of specific heart diagnoses is not equivalent to the sum of all heart diagnoses because four patients had two different diagnoses.
**The total number of surgeries is not equivalent to the sum of catheterisation, sternotomy, and thoracotomy because two patients had undergone multiple surgeries.

Norway is a neighbouring country to Sweden and has a similar healthcare system where care is tax-financed, which speculatively could lead to a more divergent population than in countries where health care is not tax-financed. The results of the Norwegian population of patients with Marfan syndrome[12] generally showed lower scores in all 10 domains of health-related quality of life than results found in the present study; however, commonly both studies found that vitality was the subscale with the lowest values of the eight subscales.

Sullivan et al. (1998)[19] assessed health-related quality of life in the general population of Sweden. The results showed that men had higher health-related quality of life than women for all subscales.[19] In an English study, men in the general population had higher scores for all subscales compared with women, except for

https://doi.org/10.1017/S1047951124025770 Published online by Cambridge University Press

Table 2. Results of SF-36 for the eight subscales and summary measures for patients with MFS. Data are median (interquartile range, 25th-75th percentile)

SF-36	Scores	All patients	Women	Men	p-value Sex difference
PF	0–100	95 (80.0–95.0)	85 (65.0–95.0)	95 (85.0–95.0)	0.317
RP	0–100	100 (75.0–00.0)	75 (50.0–100.0)	100 (75.0–100.0)	0.560
BP	0–100	84 (62.0–92.0)	74 (62.0–84.0)	84 (59.5–100.0)	0.749
GH	0–100	70 (40.0–82.0)	70 (20.0–82.0)	69.5 (41.5–87.0)	0.299
VT	0–100	55 (37.5–72.5)	35 (10.0–65.0)	62.5 (43.8–75.0)	0.026
SF	0–100	87.5 (62.5–100.0)	87.5 (62.5–100.0)	87.5 (62.5–100.0)	0.985
RE	0–100	100 (66.7–100.0)	100 (66.7–100.0)	100 (58.3–100.0)	0.836
MH	0–100	76 (64.0–84.0)	76 (64.0–80.0)	76 (65.0–88.0)	0.585
PCS	2–76	51.9 (40.0–55.3)	50.1 (38.9–53.7)	53.2 (44.7–55.4)	0.317
MCS	−1–81	48.1 (37.9–52.0)	48.1 (31.9–51.1)	48.1 (38.6–53.1)	0.955

MFS = Marfan syndrome; SF-36 = 36-item Short-Form Health Survey; PF = physical functioning; RP = role-physical; BP = bodily pain; GH = general health; VT = vitality; SF = social functioning; RE = role-emotional; *M* = mental health; PCS = physical component summary; MCS = mental component summary.
Bold p-value, statistically significant with Mann–Whitney *U* test.

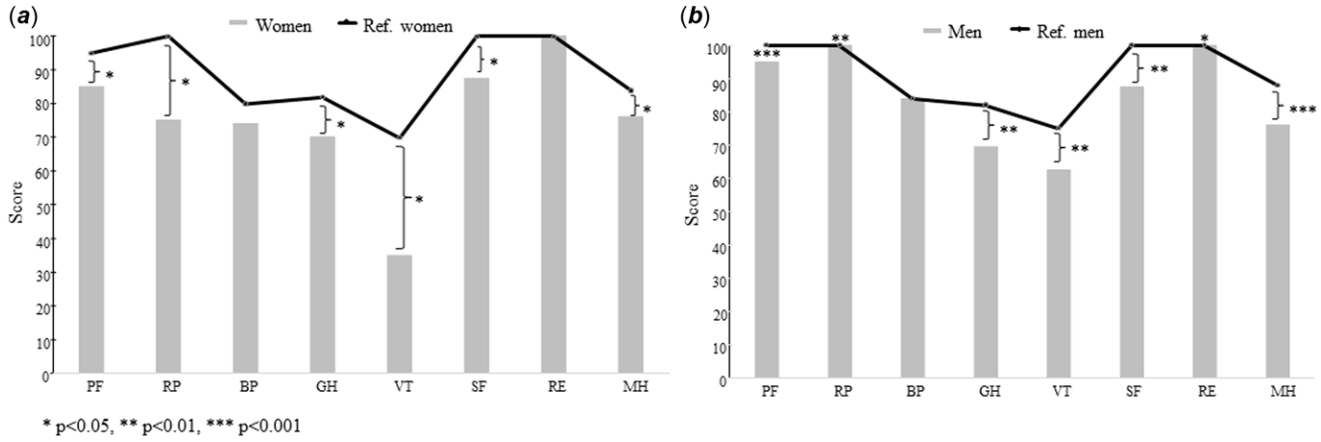

Figure 2. Diagram comparing values for women (A) and men (B) with MFS to healthy reference values. MFS = Marfan syndrome; SF-36 = 36-item Short-Form Health Survey; PF = physical functioning; RP = role-physical; BP = bodily pain; GH = general health; VT = vitality; SF = social functioning; RE = role-emotional; MH = mental health; ref.= reference value.

general health.[31] In the current study, vitality was the only subscale with a statistically significant difference by sexes. However, similarities with the general population can be observed; general health was the only subscale where women had higher scores than men. The absence of differences between sexes in the present study could possibly be explained by the study population's size of 33 participants, with 11 women and 22 men. Furthermore, it could be argued that other factors may influence health-related quality of life more significantly than sex. According to Goldfinger et al. (2017)[30] who assessed the physical subscales and the physical component summary of the Short-Form Health Survey, factors such as educational level, income, health insurance, and employment have the greatest impact on health-related quality of life in patients with Marfan syndrome. Additionally, Sullivan et al. (1998)[19] highlight that lower educational level and unemployment correlate with lower health-related quality of life in the Swedish general population.

Women aged 18–32 years had significantly higher physical functioning than women aged 33–63 years. Men aged 18–32 years had significantly higher role-physical, general health, and physical component summary than men aged 33–63 years. There was also a clinically relevant difference between age groups for both women and men regarding physical component summary, where patients aged 18–32 years had a higher value. This is consistent with the findings of other studies[12,30,32] that discussed how domains related to physical health are most affected by increased age in Marfan syndrome. Sullivan et al. (1998)[19] demonstrated that physical health was most affected by older age in the general population of Sweden. However, the present study population was younger, with a median age of 32 years, and included a small number of participants. Despite this, statistically significant differences were noted in terms of physical health, where the age group >median reported lower scores. Ageing contributes to a reduction in maximal aerobic capacity, decreased muscle mass, and diminished explosive strength, which has significant implications for physical function and activities of daily living.[33]

It can be expected that physical functioning and bodily pain affect patients with Marfan syndrome because pain is commonly

https://doi.org/10.1017/S1047951124025770 Published online by Cambridge University Press

present in this patient population[9] and has been shown to impact physical function.[11] However, in the current study, there was no statistically significant difference by age group or sex, compared with healthy reference values in terms of the bodily pain subscale. Marfan syndrome is a rare disease with both physical[2,5,8] and mental impacts,[5,9] which could partly explain the lower health-related quality of life in patients with Marfan syndrome. Furthermore, Sullivan et al. (1998)[19] showed that the vitality subscale has a strong correlation with fatigue in the Swedish general population. Rand-Hendriksen et al. (2010)[12] have also discussed whether low vitality scores in patients with Marfan syndrome could be attributed to fatigue and reduced physical endurance.[12] Fatigue is a common symptom in patients with Marfan syndrome[9], which could explain the large percentage difference between values for patients with Marfan syndrome and healthy reference values on the vitality subscale. Additionally, women have been shown to experience more fatigue than men[9].

A systematic review assessing physical activity as a future therapy for patients with Marfan syndrome only found one study in humans.[34] Benninghoven et al.[35] have demonstrated the effects of a 3-week rehabilitation programme, including daily exercise, for patients with Marfan syndrome. The results showed statistically significant improvement in the vitality, mental health, bodily pain, and mental component summary scales. The study also showed a statistically significant reduction in fatigue.[35] Therefore, a rehabilitation programme may improve both physical and mental health; thus, it is important for enhancing the health-related quality of life of patients with Marfan syndrome.

The current study indicated that an impact on the health-related quality of life exists in the Swedish population of patients with Marfan syndrome, but more studies with larger study populations in this area are required to draw more reliable conclusions.

Strengths and limitations

The small sample size in the current study can be considered a limitation. However, Marfan syndrome is a rare and understudied condition, which means that even a smaller study population can yield relevant results. Furthermore, the population size is comparable to previous studies on this population.[16,18] Nevertheless, when applying the results to the entire population with Marfan syndrome, the size of the study population must be considered, and the fact that significant results might not have been achieved.

The use of the Short-Form Health Survey as a standardised self-assessment instrument enhances the study. Reliability and validity have not been specifically tested in the patient population with Marfan syndrome, but the Short-Form Health Survey is the most commonly used instrument for assessing health-related quality of life in these patients.[16] Furthermore, the minimal clinically important difference has not been specifically tested on the Marfan syndrome population. However, in a study[32] that assessed health-related quality of life in patients with Marfan syndrome using the Short-Form Health Survey, a 4-point difference was applied as the minimal clinically important difference. Therefore, a 4-point difference was used in the present study.

This study was conducted in the clinical setting and spanned over several years; the possibilities of changing societal conditions during this time period were not possible to analyse. Data regarding sociodemographic factors such as educational level, income, marital status, and employment were unavailable in the current study and therefore could not be evaluated, which is a limitation. Fourteen patients with Marfan syndrome were excluded because they did not complete the Short-Form Health Survey questionnaire, but the reasons for these patients choosing not to participate were not recorded. However, there was no statistically significant difference between excluded and included patients with Marfan syndrome in terms of sex, age, or NYHA classification.

The reference values used in the present study were from the year 2002; more recent values would however have been preferable but do not exist. Finally, in the current study, we could not draw conclusions about whether the outcome of the Short-Form Health Survey differs in terms of values for patients with Marfan syndrome aged ≥18 years compared with healthy reference values[19] concerning age owing to noncomparable age groups and the absence of individual data for healthy.

Conclusion

In the present study, adult patients with Marfan syndrome exhibited significantly lower health-related quality of life levels measured using the Short-Form Health Survey in comparison with healthy reference values across most scales. Within the patient group, differences were also found according to sex and age. Further research can investigate if individualised exercise training can enhance health-related quality of life in patients with Marfan syndrome, with a particular focus on vitality.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S1047951124025770.

Acknowledgements. The authors would like to extend special acknowledgement to Linda Johansson and Anna-Klara Zetterström for their help in the clinical setting, as well as to all the staff at the Physiotherapy Unit at Sahlgrenska University Hospital/Östra. We also thank Analisa Avila, MPH, ELS, of edanz (www.edanz.com/ac) for editing a draft of this manuscript.

Financial support. This work was supported by the Swedish Fund for Congenital Heart Defects (grant number 3/20 FO), the Swedish state under the agreement between the Swedish government and the county council, the ALF agreement (grant number 965264), and the Sahlgrenska University Hospital research funds (grant number SU-984492).

Competing interests. None.

Ethical standard. The authors assert that all procedures contributing to this work comply with the Helsinki Declaration of 1975, as revised in 2008, and have been approved by the Swedish Ethical Review Authority (Dnr: 226-13 and 2021-02149).

References

1. The National Board of Health and Welfare. The National Board of Health and Welfare. Marfan syndrome, 2023. https://www.socialstyrelsen.se/kunskapsstod-och-regler/omraden/sallsynta-halsotillstand/marfans-syndrom/ [Accessed 4 Jan 2023].
2. Ho NCY, Tran JR, Bektas A. Marfan's syndrome. Lancet 2005; 366: 1978–1981.
3. Dietz HC, Cutting GR, Pyeritz RE, et al. Marfan syndrome caused by a recurrent de novo missense mutation in the fibrillin gene. Nature 1991; 352: 337–339.
4. Hollister DW, Godfrey M, Sakai LY, Pyeritz RE. Immunohistologic abnormalities of the microfibrillar-fiber system in the Marfan syndrome. N Engl J Med 1990; 323: 152–159.
5. Kaemmerer H, Oechslin E, Seidel H, et al. Marfan syndrome: what internists and pediatric or adult cardiologists need to know. Expert Rev Cardiovasc Ther 2005; 3: 891–909.

6. Physical Activity Guidelines. The Marfan Foundation. 2017. https://marfan.org/wp-content/uploads/2021/09/FINAL-Physical-Activity-Guidelines-11_17.pdf [Accessed 12 Jan 2023]
7. Pyeritz RE. The Marfan syndrome. Annu Rev Med 2000; 51: 481–510.
8. Judge DP, Dietz HC. Marfan's syndrome. Lancet 2005; 366: 1965–1976.
9. Peters KF, Kong F, Horne R, Francomano CA, Biesecker BB. Living with Marfan syndrome I. Perceptions of the condition. Clin Genet 2001; 60: 273–282.
10. Bathen T, Velvin G, Rand-Hendriksen S, Robinson HS. Fatigue in adults with Marfan syndrome, occurrence and associations to pain and other factors. Am J Med Genet A 2014; 164: 1931–1939.
11. Speed TJ, Mathur VA, Hand M, et al. Characterization of pain, disability, and psychological burden in Marfan syndrome. Am J Med Genet A 2017; 173: 315–323.
12. Rand-Hendriksen S, Johansen H, Semb SO, Geiran O, Stanghelle JK, Finset A. Health-related quality of life in Marfan syndrome: a cross-sectional study of Short Form 36 in 84 adults with a verified diagnosis. Genet Med 2010; 12: 517–524.
13. Karimi M, Brazier J. Health, health-related quality of life, and quality of life: what is the difference? Pharmacoeconomics 2016; 34: 645–649.
14. World Health Organization. WHOQOL : Measuring Quality of Life. 1995. https://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/. Accessed 12 Jan 2023.
15. World Health Organization. Constitution of the World Health Organization. 2006. https://www.who.int/about/accountability/governance/constitution. Accessed 19 Jan 2024.
16. Velvin G, Wilhelmsen JE, Johansen H, Bathen T, Geirdal AØ.Systematic review of quality of life in persons with hereditary thoracic aortic aneurysm and dissection diagnoses. Clin Genet 2019; 95: 661–676.
17. Thijssen CGE, Doze DE,Gökalp AL et al.Male-female differences in quality of life and coping style in patients with Marfan syndrome and hereditary thoracic aortic diseases. J Genet Couns 2020; 29: 1259–1269.
18. Trawicka A, Lewandowska-Walter A, Majkowicz M, Sabiniewicz R, Woźniak-Mielczarek L. Health-related quality of life of patients with Marfan syndrome-Polish study. Int J Environ Res Public Health 2022; 19: 6827.
19. Sullivan M, Karlsson J. The Swedish SF-36 health survey III. Evaluation of criterion-based validity: results from normative population. J Clin Epidemiol. 1998; 51: 1105–1113.
20. Kröönström LA, Johansson L, Zetterström A-K, Dellborg M, Eriksson P, Cider A. Muscle function in adults with congenital heart disease. Int J Cardiol 2014; 170: 358–363.
21. Ashman Kröönström L, Cider Å, Zetterström A-K et al. Exercise capacity, physical activity, and health-related quality of life in adults with CHD. Cardiol Young 2020; 30: 668–673.
22. Ware JE, Snow KK, Kosinski M, Gandek B. SF-36 health survey: manual and interpretation guide. Nimrod Press, Boston, Massachusetts, USA, 1993.
23. Ware JE, Gandek B. Overview of the SF-36 health survey and the International Quality of Life Assessment (IQOLA) project. J Clin Epidemiol 1998; 51: 903–912.
24. Ware JE, Kosinski M, Keller SD. SF-36 physical and mental health summary scales: a user's manual. Health Assessment Lab, Boston, Massachusetts, USA, New England Medical Center, 1994.
25. Taft C, Karlsson J, Sullivan M. Do SF-36 summary component scores accurately summarize subscale scores? Qual Life Res 2001; 10: 395–404.
26. Sullivan M, Karlsson J, Ware JE Jr. The Swedish SF-36 Health Survey-I. Evaluation of data quality, scaling assumptions, reliability and construct validity across general populations in Sweden. Soc Sci Med 1995; 41: 1349–1358.
27. Witt S, Krauss E, Barbero MAN et al. Psychometric properties and minimal important differences of SF-36 in idiopathic pulmonary fibrosis. Respir Res 2019; 20: 47.
28. Badhiwala JH, Witiw CD, Nassiri F et al. Minimum clinically important difference in SF-36 scores for use in degenerative cervical myelopathy. Spine 2018; 43: E1260–1266.
29. Ogura K, Yakoub MA, Christ AB, et al. What are the minimum clinically important differences in SF-36 scores in patients with orthopaedic oncologic conditions? Clin Orthop Relat Res 2020, 478:2148–2158.
30. Goldfinger JZ, Preiss LR, Devereux RB et al. Marfan syndrome and quality of life in the GenTAC registry. J Am Coll Cardiol 2017; 69: 2821–2830.
31. Jenkinson C, Coulter A, Wright L. Short Form 36 (SF36) health survey questionnaire: normative data for adults of working age. BMJ 1993; 306: 1437–1440.
32. Vanem TT, Rand-Hendriksen S, Brunborg C, Geiran OR, Røe C. Health-related quality of life in Marfan syndrome: a 10-year follow-up. Health Qual Life Outcomes 2020; 18: 376.
33. Young A. Ageing and physiological functions. Philos Trans R Soc Lond B Biol Sci, 1997, 352:1837–1843.
34. Jouini S, Milleron O, Eliahou L, Jondeau G, Vitiello D. Is physical activity a future therapy for patients with Marfan syndrome? Orphanet J Rare Dis 2022; 10: 46.
35. Benninghoven D, Hamann D, von Kodolitsch Y et al. Inpatient rehabilitation for adult patients with Marfan syndrome: an observational pilot study. Orphanet J Rare Dis 2017; 12: 127.

https://doi.org/10.1017/S1047951124025770 Published online by Cambridge University Press