Mediterranean Journal of Clinical Psychology MJCP

ISSN: 2282-1619 VOL 6 N.2 (2018)

Quality of life in postmenopausal women: which role for vitamin D?

Gabriella Martino[1], Antonino Catalano[2], Federica Bellone[2], Viviana Langher[3], Carmen Lasco[4], Assunta Penna[5], Giacomo Nicocia[2], Nunziata Morabito[2]

[1] Department of Cognitive Science, Psychological, Educational and Cultural Studies, University of Messina

[2] Department of Clinical and Experimental Medicine, University Hospital of Messina, Messina, Italy

[3] Department of Dynamic and Clinical Psychology , University of Rome "Sapienza", Rome, Italy

[4] University of Messina

[5] Department of Cognitive Sciences, Psychology, Education and Cultural Studies, University of Messina, Italy

Email Corresponding author: martinog@unime.it

Abstract

Quality of life (QoL) represents a dramatic issue in an aging population. Vitamin D has been consistently associated with several diseases. Thus, vitamin D may be considered a hallmark of health status. Our aim was to investigate whether vitamin D could be a determinant of self-perceived quality of life.

The 36-Item Short Form Health Survey (SF-36) for quality of life, the Hamilton Anxiety Rating Scale (HAM-A), the Beck Depression Inventory II edition (BDI-

II), in addition with multiple clinical risk factors for fractures and FRAX score, BMD at lumbar spine and femoral neck, were evaluated in a group of 177 postmenopausal women referring to an outpatients clinic for the prevention of osteoporosis.

Serum levels of vitamin D [25(OH)D], indicative of vitamin D status, were detected by high-performance liquid chromatography.

Scores of each dimension of the SF-36 were significantly related with the measurements of anxiety and depression by HAM-A and BDI-II respectively. Moreover role emotional, vitality, general health and bodily pain were significantly associated with vitamin D status. However, at a stepwise multiple regression analysis the physical component summary, obtained from SF-36, was not independently predicted from vitamin D.

In conclusion we found an association between vitamin D status and QoL, thus we suggest physicians to consider vitamin D levels as a marker of QoL.

Further studies testing the impact of vitamin D administration in improving QoL over time are needed.

Key words: Quality of life , Vitamin D, Anxiety, Depression, Osteoporosis, Vitality.

Introduction

The concept of quality of life is thought as a multidimensional construct which includes several different dimensions. It can be defined as the degree to which people perceive themselves physically, emotionally and socially. Quality of life is what precious makes life worth living (Rafiq et al., 2014).

On the other hand, it is known that vitamin D has been traditionally considered as a main regulator of bone and mineral metabolism (Catalano et al., 2015, Holick, 2007) and that its deficiency causes rickets in children and osteomalacia and osteoporosis in adults (Holick, 2007).

Several scientific evidences, from in vivo and in vitro studies, suggest that vitamin D represents a crucial determinant for the development of major clinical conditions and health-related events (Holick, 2004). A large number of extraskeletal disorders as immune, metabolic, cardiovascular, neurological and oncological, have been previously associated with vitamin D (Brighenti et al. 2018, Wu et al., 2016; Smolders et al., 2011; Goodwill & Szoeke, 2017; Atteritano et al., 2016; Chu et al., 2017; Catalano et al. 2017; Fedotova et al., 2017; Catalano et al., 2015b). Especially in the elderly, a poor vitamin D status has been accompanied by cognitive and mood disorders (Merendino et al., 2004; Nguyen, T.T.T. et al., 2017; Pu, D. et al., 2018), muscle weakness, poor physical performance, balance problems and falls (Gerdhem et al., 2005). Recently vitamin D has been also associated with psychological features as depressive and anxiety symptoms (Atteritano et al., 2013; de Koning et al. 2017; Martino et al., 2018; Catalano et al., 2018).

Consequently, vitamin D deficiency may not only influence the onset of chronic conditions, which are frequent causes of disability, but may also affect psychological and physical functional status.

Since vitamin D is fundamentally involved in mental and physical function potentially influencing quality of life, the aim of this study was to investigate the associations between the perceived quality of life and the vitamin D status in outpatients postmenopausal women evaluated for osteoporosis.

Methods

The recruitment of postmenopausal women occurred at the Outpatients Clinic for the Prevention and Treatment of Osteoporosis at the Department of Clinical and Experimental Medicine, University Hospital of Messina. Women were excluded from the study if affected by a known psychiatric condition, including cognitive decline or addiction, by chronic diseases as from moderate to severe kidney or liver or respiratory failure, hearth failure with NYHA (New York Heart Association) class ≥2, history of cancer, malabsorption, endocrine disorders and if under treatment with bone or brain active agents (Catalano et al., 2013). Assumption of vitamin D and calcium supplements was not an exclusion criteria

if in accordance with the dietary reference intakes from the Institute of Medicine (Ross et al. 2015).

The Italian version of the Short Form-36 (SF-36) questionnaire was used to measure the perception of the patient's health. SF- 36 consists of 36 items organized in eight dimensions known as physical functioning, social functioning, role limitations because of physical problems, role limitations because of emotional problems, mental health, vitality, pain, and general health perception. For each dimension administered, a score ranged from 0 to 100 points was obtained, with higher scores indicating a better perception of quality of life, with less roles limitations too (Ware et al.,1992)

The Hamilton Anxiety Rating Scale (HAM-A) was performed to evaluate the entity of anxiety symptoms; it consists of 14 symptom-defined elements, including psychological and somatic symptoms. Tension (e.g. fatigability, restlessness); fears (e.g. dark/strangers/crowds); insomnia (initial/intermediate/late); intellectual (e.g. poor memory); depressed mood; somatic symptoms (e.g. aches and pain); sensory (e.g. tinnitus, blurred vision); cardiovascular (including tachycardia and palpitations); respiratory (chest tightness, choking); gastrointestinal (e.g. irritable bowel syndrome-type symptoms); genitourinary (e.g. urinary frequency, loss of libido); autonomic (e.g. dry mouth, tension headache) and observed behaviour at interview (as restless or fidgety). Each item results in a numeric score from 0 to 4 directly proportional to the entity of perceived symptom (Hamilton et al. 1959). The Beck Depression Inventory-second edition (BDI-II), consisting of 21 items, each scored from 0 to 4, was implemented to detect depressive symptoms (Beck et al. 1996).

A computer-based algorithm (http://www.shef.ac.uk/FRAX) was applied to evaluate the 10-year probability of a major fracture and femoral fracture on the basis of clinical risk factors as prior fragility fracture, parental history of hip fracture, current tobacco smoking, ever use of long-term oral glucocorticoids, rheumatoid arthritis and secondary causes of osteoporosis.

Bone mineral density (BMD) was detected through dual-energy X-ray absorptiometry (DXA) densitometer at the femoral neck and lumbar spine (L1-L4).

A blood sample was collected for each woman to evaluate vitamin D status measuring 25(OH)D plasmatic levels through high-performance liquid chromatography (Ju, S.Y. et al., 2013; de Koning, E.J. et al., 2017). Our study was carried out in accordance with the 1964 Declaration of Helsinki and its later amendments, and written informed consent was obtained from all the participants. Statistical analyses were achieved by MedCalc software (version 10.2.0.0; Mariakerke, 173 Belgium). Differences were evaluated using the Student's t-test for unpaired observations or Mann-Whitney test as appropriate. The degree of association between two selected variables was calculated by Pearson correlation coefficient. A multiple regression analysis was conducted in order to investigate the relationship between a dependent variable and one or more predictive variables. Values of $P < 0.05$ were considered to indicate statistical significance.

Results

We recruited a total of 177 postmenopausal women, aged 67 ± 9.57 yr., whose main clinical characteristics are shown in Table 1.

Table 1 - Main clinical features of postmenopausal women.

	Results (n=177)
Age (yr)	67 ± 9.57
Age at menopause (yr)	47.5 ± 5.94
Time since menopause (yr)	20.63 ± 9.08
Weight (kg)	62.78 ± 13.18
Height (cm)	158.29 ± 5.94
BMI (Kg/m2)	24.97 ± 5.11
Current smoking [n(%)]	19 (10)
Lumbar spine T-Score [SD]	-2.29 ± 1.35
Femoral neck T-Score [SD]	-1.98 ± 0.81
10-year probability of a major fracture (%)	20.1 ± 9.7
25(OH)D (ng/ml)	39.11 ± 14.69

Data are expressed as mean ± SD

On the overage, patients were considered “osteopenic” in accordance with the WHO criteria (World Health Organization 1994) and showed sufficient plasmatic concentration of vitamin D. They were slight overweight and a smoking habit was encountered in 10% of them.
Table 2 shows the results for the eight dimensions of the SF-36 questionnaire and the mean values of mental and physical health. HAM-A mean score was 27.72 ± 6.84 and BDI-II mean score was 7.26 ± 3.34.

Table 2 - Measurement of quality of life through SF-36 questionnaire.

	Results *(n=177)*
Mental health	34.12 ± 19.97
Role emotional	20.17 ± 29.77
Social functioning	43.34 ± 20.63
Vitality	35.07 ± 15.91
General health	38.04 ± 18.69
Bodily pain	37.45 ± 23.93
Role physical	19.53 ± 30.21
Physical functioning	54.45 ± 26.32
Physical component summary	36.04 ± 8.80
Mental component summary	30.187 ± 8.49

Data are expressed as mean ± SD

It was interesting the finding that the scores of each dimension of the SF-36 were significantly related with the measurement of anxiety and depression by HAM-A and BDI-II respectively. Moreover the dimensions role emotional, vitality, general health and bodily pain were significantly associated with vitamin D status (Table 3).

	Age	***Age at menopause***	***BMI***	***HAM-A score***	***BDI-II score***	***25(OH)D***
Mental health	**0.34**	-0.14	0.05	**-0.47**	**-0.52**	0.05
Role emotional	**0.29**	-0.06	-0.06	**-0.51**	**-0.32**	**0.20**
Social functioning	**0.33**	-0.07	0.02	**-0.44**	**-0.46**	0.11
Vitality	**0.28**	**-0.24**	-0.04	**-0.47**	**-0.47**	**0.15**
General health	**0.29**	0.06	0.03	**-0.52**	**-0.53**	**0.14**
Bodily pain	**0.44**	**-0.15**	-0.11	**-0.45**	**-0.43**	**0.16**
Role physical	**0.15**	-0.09	-0.07	**-0.43**	**-0.30**	0.02
Physical functioning	**0.48**	-0.06	-0.04	**-0.54**	**-0.39**	0.06

Table 3 - Correlation coefficients (r) between studied variables

Statistically significant values of "r" ($p<0.05$) are shown in bold.

At a stepwise multiple regression analysis it turned out that age, BMI, HAM-A score, BDI-II score and femoral neck BMD were independently associated with the physical component summary (PCS) after correcting for mental component summary (MCI), age at menopause, lumbar spine BMD and vitamin D status ($p<0.05$).

Discussion

The findings from this cross-sectional study suggest that quality of life is associated with vitamin D status in postmenopausal women referred for osteoporosis. However this association was lost after adjusting for confounders.

Vitamin D receptor (VDR) is widespread to make plausible pleiotropic action of vitamin D on a large spectrum of systems, apparatuses and tissues (Timpini et al.

2011; Windelinckx et al., 2007). Thus, vitamin D has growingly been involved as a primary determinant of biological modifications and specific clinical conditions. As known, the role of vitamin D extends beyond calcium homeostasis and includes modulation of skeletal and cardiac muscle function, immune cell function, and anticancer activity (Holick, 2004, Catalano et al 2013). Vitamin D is mainly involved also in the developing brain and in adult brain function (Hayes, 2010). VDRs are expressed in areas of the brain important to behavioral regulation, including the cortex, cerebellum, and limbic system. In animal models, mice with genetically impaired VDRs had abnormal brain shapes, decreased levels of neural growth factors, and exhibited behavioral aberrations including high anxiety, poor grooming, and poor social interaction (Kalueff et al., 2007).

VDR gene polymorphisms able to determine different phenotypes and biological responses to vitamin D have been described, not only able to affect bone mineral density, but also body composition, muscle strength and other clinical outcomes suggesting a role for vitamin D in determining age-related physical decline, and disabling process (Cesari et al. 2011).

Low vitamin D levels is frequently encountered in the elderly, since the aging process itself predisposes to a progressive decline in the cutaneous capacity to synthesize vitamin D from ultraviolet B radiations and an increased resistance of target organs to the vitamin D action due to reduced concentrations of VDRs or post-receptorial modifications (Hayes, 2010; Armstrong, D.J., 2007).

Whether vitamin D may be an elisir able to improve quality of life remain an unsolved question, since available evidence are inconsistent (Callegari et al., 2017). Data from a cross-sectional analysis of the Iowa Women's Health Study showed that women who consumed at least 400 IU/day of vitamin D showed slightly higher mental health related QoL scores compared to women who consumed less than 400 UI/day (Motsinger et al., 2012; Michelle et al., 2015; Lerchbaum, 2014). However in a 2-year, double-blind, placebo-controlled vitamin D and open exercise intervention trial, neither vitamin D (800 UI/day) nor exercise contributes to better QoL, or mental wellbeing in community-dwelling healthy older women with sufficient vitamin D levels (Patil et al., 2016).

Although the key role of vitamin D in human biology and pathophysiology, whether quality of life may depend directly from vitamin D status was not supported from our study and we hypotized that a poorer quality of life observed in subjects with lower vitamin D levels may merely be the indirect manifestation of a poorer health status.

We must recognize some limitations of our study. First, the exclusion of patients with more severe diseases, decided to exclude a deterioration in the quality of life due to serious medical or psychological-clinical pathology. Second, the cross-sectional design not able to investigate the causality of association. Third the absence of corrections for common non complicated diseases. The strength of our research consists in a large sample size involving only postmenopausal women, so that gender differences are excluded.

Since the high prevalence of hypovitaminosis D, searching for at risk patients for hypovitaminosis D may also offer an opportunity to find people with a poor quality of life. Thus QoL could be improved with several strategies, proportionally to the psychological and physical needs highlighted (Langher et al., 2017).

In conclusion we found an association between vitamin D status and QoL, thus we suggest physicians to consider vitamin D levels as a marker of QoL.

Further prospective research studies calibrated with adequate doses of vitamin D may be useful to establish the possible impact of vitamin D administration in improving QoL over time (Merlo, E.M., 2016).

References

1. Armstrong, D. J., Meenagh, G. K., Bickle, I., Lee, A. S. H., Curran, E. S., & Finch, M. B. (2007). Vitamin D deficiency is associated with anxiety and depression in fibromyalgia. *Clinical rheumatology*, *26*(4), 551-554.
2. Atteritano, M., Lasco, A., Mazzaferro, S., Macrì, I., Catalano, A., Santangelo, A., ... & Frisina, N. (2013). Bone mineral density, quantitative ultrasound parameters and bone metabolism in postmenopausal women with depression. *Internal and emergency medicine*, *8*(6), 485-491.
3. Atteritano, M., Santoro, D., Corallo, G., Visalli, E., Buemi, M., Catalano, A., ... & Squadrito, F. (2016). Skin involvement and pulmonary hypertension are associated with vitamin D insufficiency in scleroderma. *International journal of molecular sciences*, *17*(12), 2103.
4. Beck AT, Steer RA, Brown GK. Manual for the Beck Depression Inventory–II. San Antonio, TX: Psychological Corporation 1996.
5. Brighenti, S., Bergman, P., & Martineau, A. R. (2018). Vitamin D and tuberculosis: where next?. *Journal of internal medicine*.
6. Callegari, E. T., Reavley, N., Gorelik, A., Garland, S. M., Wark, J. D., & Safe-D Study Team. (2017). Serum 25-hydroxyvitamin D and mental health in young Australian women: Results from the Safe-D study. *Journal of affective disorders*, *224*, 48-55.
7. Catalano, A., Martino, G., Bellone, F., Gaudio, A., Lasco, C., Langher, V., ... & Morabito, N. (2018). Anxiety levels predict fracture risk in postmenopausal women assessed for osteoporosis. *Menopause* (New York, NY).
8. Catalano, A., Martino, G., Morabito, N., Scarcella, C., Gaudio, A., Basile, G., Lasco, A. (2017). Pain in osteoporosis: from pathophysiology to therapeutic approach. *Drugs Aging*; 34:755-765.
9. Catalano, A., Morabito, N., Atteritano, M., Basile, G., Cucinotta, D., & Lasco, A. (2012). Vitamin D reduces musculoskeletal pain after infusion of zoledronic acid for postmenopausal osteoporosis. *Calcified tissue international*, *90*(4), 279-285.
10. Catalano, A., Morabito, N., Basile, G., Cucinotta, D., & Lasco, A. (2015). Calcifediol improves lipid profile in osteopenicatorvastatin-treated postmenopausal women. *European journal of clinical investigation*, *45*(2), 144-149.

11. Catalano, A., Morabito, N., Basile, G., Fusco, S., Castagna, G., Reitano, F., ... & Lasco, A. (2013). Fracture risk assessment in postmenopausal women referred to an Italian center for osteoporosis: a single day experience in Messina. *Clinical Cases in Mineral and Bone Metabolism*, *10*(3), 191.
12. Catalano, A., Morabito, N., Di Stefano, A., Morini, E., Basile, G., Faraci, B., ... & Lasco, A. (2015). Vitamin D and bone mineral density changes in postmenopausal women treated with strontium ranelate. *Journal of endocrinological investigation*, *38*(8), 859-863.
13. Cesari, M., Incalzi, R. A., Zamboni, V., & Pahor, M. (2011). Vitamin D hormone: a multitude of actions potentially influencing the physical function decline in older persons. *Geriatrics & gerontology international*, *11*(2), 133-142.
14. Chu, F., Ohinmaa, A., Klarenbach, S., Wong, Z. W., & Veugelers, P. (2017). Serum 25-hydroxyvitamin D concentrations and indicators of mental health: an analysis of the Canadian Health Measures Survey. *Nutrients*, *9*(10), 1116.
15. De Koning, E. J., Verweij, L., Lips, P., Beekman, A. T., Comijs, H. C., & Van Schoor, N. M. (2017). The relationship between serum 25 (OH) D levels and anxiety symptoms in older persons: Results from the Longitudinal Aging Study Amsterdam. *Journal of psychosomatic research*, *97*, 90-95.
16. Fedotova, J., Pivina, S., & Sushko, A. (2017). Effects of Chronic Vitamin D3 Hormone Administration on Anxiety-Like Behavior in Adult Female Rats after Long-Term Ovariectomy. *Nutrients*, *9*(1), 28.
17. Gerdhem, P., Ringsberg, K. A. M., Obrant, K. J., & Akesson, K. (2005). Association between 25-hydroxy vitamin D levels, physical activity, muscle strength and fractures in the prospective population-based OPRA Study of Elderly Women. *Osteoporosis International*, *16*(11), 1425-1431.
18. Goodwill, A. M., & Szoeke, C. (2017). A systematic review and meta-analysis of the effect of low vitamin D on cognition. *Journal of the American Geriatrics Society*, *65*(10), 2161-2168.Hamilton M. The assessment of anxiety states by rating. Br J Med Psychol 1959;32:50-55
19. Hayes DP. Vitamin D and ageing. *Biogerontology*. 2010;11:1–16
20. Holick, M. F. (2004). Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. *The American journal of clinical nutrition*, *80*(6), 1678S-1688S.

21. Holick, M. F. (2007). Vitamin D deficiency. *New England Journal of Medicine*, *357*(3), 266-281.
22. Ju, S. Y., Lee, Y. J., & Jeong, S. N. (2013). Serum 25-hydroxyvitamin D levels and the risk of depression: a systematic review and meta-analysis. *The journal of nutrition, health & aging*, *17*(5), 447-455.
23. Kalueff, A. V., & Tuohimaa, P. (2007). Neurosteroid hormone vitamin D and its utility in clinical nutrition. *Current Opinion in Clinical Nutrition & Metabolic Care*, *10*(1), 12-19.
24. Langher, V., Caputo, A., & Martino, G. (2017). What happened to the clinical approach to case study in psychological research? A clinical psychological analysis of scientific articles in high impact-factor journals. *Mediterranean Journal of Clinical Psychology*, *5*(3).
25. Lerchbaum, E. (2014). Vitamin D and menopause—A narrative review. *Maturitas*, *79*(1), 3-7.
26. Martino, G., Catalano, A., Bellone, F., Sardella, A., Lasco, C., Caprì, T., ... & Morabito, N. (2018). Vitamin D status is associated with anxiety levels in postmenopausal women evaluated for osteoporosis. *Mediterranean Journal of Clinical Psychology*, *6*(1).
27. Merendino, R. A., Di Pasquale, G., De Luca, F., Di Pasquale, L., Ferlazzo, E., Martino, G., ... & Gangemi, S. (2004). Involvement of fractalkine and macrophage inflammatory protein-1 alpha in moderate-severe depression. *Mediators of inflammation*, *13*(3), 205-207.
28. Merlo, E.M., (2016). Responsibility and Hope. *Mediterranean Journal of Clinical Psychology*, 4(2).
29. Hoffmann, M. R., Senior, P. A., & Mager, D. R. (2015). Vitamin D supplementation and health-related quality of life: a systematic review of the literature. *Journal of the Academy of Nutrition and Dietetics*, *115*(3), 406-418.
30. Motsinger, S., Lazovich, D., MacLehose, R. F., Torkelson, C. J., & Robien, K. (2012). Vitamin D intake and mental health-related quality of life in older women: the Iowa Women's Health Study. *Maturitas*, *71*(3), 267-273.
31. Nguyen, T. T. T., Tsujiguchi, H., Kambayashi, Y., Hara, A., Miyagi, S., Yamada, Y., ... & Hayashi, K. (2017). Relationship between Vitamin Intake and Depressive Symptoms in Elderly Japanese Individuals: Differences with Gender and Body Mass Index. *Nutrients*, *9*(12), 1319.

32. Patil, R., Karinkanta, S., Tokola, K., Kannus, P., Sievänen, H., & Uusi-Rasi, K. (2016). Effects of vitamin D and exercise on the wellbeing of older community-dwelling women: a randomized controlled trial. *Gerontology*, *62*(4), 401-408.
33. Pu, D., Luo, J., Wang, Y., Ju, B., Lv, X., Fan, P., & He, L. (2018). Prevalence of depression and anxiety in rheumatoid arthritis patients and their associations with serum vitamin D level. *Clinical rheumatology*, *37*(1), 179-184.
34. Rafiq, R., Swart, K. M. A., van Schoor, N. M., Deeg, D. J., Lips, P. T. A. M., & de Jongh, R. T. (2014). Associations of serum 25-hydroxyvitamin D concentrations with quality of life and self-rated health in an older population. *The Journal of Clinical Endocrinology & Metabolism*, *99*(9), 3136-3143.
35. Ross, A. C., Manson, J. E., Abrams, S. A., Aloia, J. F., Brannon, P. M., Clinton, S. K., ... & Kovacs, C. S. (2011). The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. *The Journal of Clinical Endocrinology & Metabolism*, *96*(1), 53-58.
36. Smolders, J., Moen, S. M., Damoiseaux, J., Huitinga, I., & Holmøy, T. (2011). Vitamin D in the healthy and inflamed central nervous system: access and function. *Journal of the neurological sciences*, *311*(1-2), 37-43.
37. Timpini, A., Pini, L., Tantucci, C., Cossi, S., & Grassi, V. (2011). Vitamin D and health status in elderly. *Internal and emergency medicine*, *6*(1), 11-21.
38. Ware JE Jr, Sherbourne CD The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical care*,1992;30:473-483.
39. Windelinckx, A., De Mars, G., Beunen, G., Aerssens, J., Delecluse, C., Lefevre, J., & Thomis, M. A. I. (2007). Polymorphisms in the vitamin D receptor gene are associated with muscle strength in men and women. *Osteoporosis International*, *18*(9), 1235-1242.
40. World Health Organization. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Technical Report Series. WHO, Geneva 1994.

41. Wu, C., Ren, W., Cheng, J., Zhu, B., Jin, Q., Wang, L., ... & Zhao, J. (2016). Association between serum levels of vitamin D and the risk of post-stroke anxiety. *Medicine*, *95*(18).

Doi: 10.6092/2282-1619/2018.6.1875