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Mediterranean Diet adherence, physical activity level, and quality of life in patients affected by thyroid diseases: Comparison between pre- and post-lockdown assessment

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Abstract

Background: SARS-CoV-2 pandemic resulted in lifestyle change of world's population because of the measures adopted by governments to contain the virus spread.

Design and Methods: This study examined whether lockdown impacted anthropometric indices, Mediterranean Diet (MD) adherence, Physical Activity Level (PAL), and Quality of Life (SF-12) in a cohort of 116 patients (96 F, aged 57.2 ± 13.1 years) affected by thyroid disorders. Before lockdown, data were collected during the endocrinological examination; after lockdown they were collected through a tele-phone interview (via video call).

Results: Data revealed an overweight condition in 59% of patients, with no significant differences between the two observations (BMI values: 26.5 ± 4.9 vs 26.6 ± 4.9 kg/m^2), whereas waist circumference values significantly increased over time (93.3 ± 12.6 vs 94.4 ± 12.5 cm; $p = 0.003$). Moreover, a lower adherence to the MD (PREDIMED score: 7.3 ± 1.8 vs 7.0 ± 1.8; $p = 0.003$) and a significant increase of sitting time (6.4 ± 3.2 h/die vs 9.0 ± 4.2; $p < 0.001$) were observed. A not significant decrease in PAL, which revealed a sedentary condition in pre- and post-lockdown (648 and 562 METs/week respectively), was found. The SF-12 score did not show relevant changes between the two observations.

Conclusion: Our study highlights that patients with thyroid diseases are often sedentary and exhibit a high prevalence of over-weight, underscoring the need for a systematic anthropometric evaluation and, at times, lifestyle interventions.

Keywords

Lifestyle, quality of life, COVID-19 pandemic, lockdown, obesity, thyroid disease

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Introduction

Recently, the world has been affected by the SARS-CoV-2 pandemic, an acronym for Severe Acute Respiratory Syndrome Coronavirus 2, which started in Wuhan, China, in late 2019, and was renamed COVID-19 by the WHO in February 2020.[1] In order to contain and counteract the spread of SARS-CoV-2, and reduce the impact on the National Health System, restrictive containment measures were applied, and Italy, like many nations, entered

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emergency quarantine with the issuance of the "DECRETO PRESIDENZA CONSIGLIO MINISTRI (DPCM)" (translated as "Decree of the Presidency of the Council of Ministers") from 9 March 2020.[2] The so-called lockdown (decree #iorestoacasa, translated as #stayathome decree) has led to a profound and unexpected change in the habits and life-style of the Italian population with a significant increase in smart-working, a reduction in socializing and a consequent self-isolation.[3] Due to the changed routine and the restriction on daily spending, a deterioration in eating habits has been observed, with a greater consumption of unhealthy and processed foods[4] and a lower consumption of fresh foods such as fruit and vegetables.[3] The lockdown has also led to a reduction in the daily physical activity due to both the restrictions caused by the "I'm staying at home" decree and an increase in work-related and hedonistic web use, with a noticeable increase in the daily sitting-time[5] which plays an important role in the development of the non-communicable diseases (NCDs).[6] Among the multiple consequences, overall, the COVID-19 pandemic has induced in the general population an increase of body weight,[7] of the rate of type 2 diabetes,[8] and psychological disturbances such as anxiety disorders, depressive symptoms, and post-traumatic stress disorder.[9] In addition, an increase of poor sleep quality[3] and smoking habit has been reported, the latter due to the perception of cigarettes as a relief from stress.[10] Recent studies have also shown that chronic environmental stress is associated with an increased preference for energy-dense foods.[11] Moreover, anxiety, depression, and in general a poor mental health, which have a bidirectional relationship with obesity and metabolic syndrome,[12,13] are associated with an unhealthier lifestyle.[14] Referring to the rapid weight gain associated with the lockdown, the term "Covibesity" has been coined, a worldwide phenomenon of major importance and in need of both recognition and intervention.[15] On this issue, it has been reported that the increase of body weight was higher in people with overweight or obesity, who tended to be eating more and less healthy.[3,16] Beyond weight gain, it is established that unhealthy dietary changes and a reduced physical activity level have the potential to favor or accelerate sarcopenia, and such a worsening in body composition is also associated with the development of NCDs.[17] Furthermore, the presence of cardio-vascular or metabolic diseases, particularly in case of visceral adiposity, is associated with an increased risk of COVID-19 infection and more severe symptoms, emphasizing the importance of avoiding the development of these morbidities.[18] In addition, the unhealthy lifestyle linked to the lockdown may further increase the risk of developing severe COVID-19 disease in individuals with such pathologies.[16] Nevertheless, although the majority of the international studies indicated that lockdown measures led to unhealthy nutritional choices, in a Spanish adult population, an improvement of dietary habits, and more specifically a higher adherence to the Mediterranean Diet (MD), has been reported.[19] As regards the thyroid, a well-functioning gland requires, among other factors, a balanced and healthy diet, with foods rich in micronutrients, mainly iodine and selenium, such as sea fish, shellfish, nuts, fresh fruit and vegetables.[20] In addition, a moderate physical activity is necessary to reduce cardiovascular risk,[21] which is present also in subclinical thyroid disease.[22] Furthermore, a positive correlation was found between Body Mass Index (BMI) values and Thyroid Stimulating Hormone (TSH) levels even in the normal range, although the data on this issue are quite conflicting.[23] Thyroid autoimmunity could play a role, and in particular, the female sex and positivity of thyroid autoantibodies appear to be fundamental in determining this correlation.[24] Moreover, unhealthy nutritional habits, specifically a high consumption of animal foods and a low intake of foods with antioxidant properties, may lead to an increased risk of developing inflammatory and immune-mediated thyroid disorders.[25] For these reasons, in January 2020, we started a study aimed at evaluating lifestyle, particularly adherence to the MD and Physical Activity Level (PAL), quality of life, and anthropometric indices in outpatients affected by thyroid diseases attending the Endocrinology and the Obesity Unit of the University Hospital of Cagliari (Sardinia, Italy), as a part of a larger survey focused on the lifestyle and eating habits in the Sardinian population. Indeed, in a previous epidemiological study, we have observed that the prevalence of overweight and obesity has increased in the male Sardinian population.[26] Due to the arrival of the Covid-19 pandemic, and especially the lockdown, we re-assessed at the end of the quarantine period the cohort of thyroid patients who had been examined before the pandemic, in order to investigate the impact of the lockdown measures, on lifestyle, anthropometric indices, and quality of life. However, the suspension of outpatient activities following the outbreak of the pandemic, made it impossible to collect the aforementioned data directly, thus the re-assessment was carried out via telephone by means of a video call.[27,28]

Design and methods

The study sample included 116 adult patients, aged between 18 and 89 years ($M \pm SD = 57.2 \pm 13.1$), with a diagnosis of thyroid disease, attending the Endocrinology Unit of the University Hospital of Cagliari (Sardinia, Italy). Among them, 96 (82.8%) were females, a difference that correlates with the higher incidence of thyroid disease in the female sex. There was a clear prevalence (70%) of Autoimmune Thyroid Diseases (AITD), particularly Hashimoto's thyroiditis (HT, 48%). All patients had serum TSH levels within the reference range (0.55–4.78 μUI/ml) and were therefore functionally euthyroid. Pregnant or nursing women, patients with

serious heart diseases, severe and/or uncontrolled hypertension, severe or uncompensated diabetes mellitus, kidney or liver disease, painful pathologies with severe functional limitations, tumors in chemo/radiotherapy, severe psychopathology, or major dietary restrictions related to particular conditions were excluded. All patients underwent a clinical evaluation, including a full medical history and a physical examination, carried out by the endocrinologist. Both the familiar and individual medical history was mainly focused on lifestyle related diseases such as cardiovascular, metabolic, and endocrinological diseases. Anthropometric and lifestyle data were collected at baseline between January and February 2020, while the follow-up evaluation was performed at the end of the lockdown period, between May and June 2020. However, due to the restrictive measures that prevented people from leaving their homes, the methodology of the two evaluations differed. In the pre-Covid-19 lockdown assessment, data on anthropometric measures and lifestyle were collected by the endocrinologist and nutritionist of the Endocrinology and Obesity Unit during routine outpatients visit, and only demographic data (name, sex, age) and perceived health status were self-reported via questionnaires. Furthermore, to establish the prevalence of weight excess in the study group, baseline anthropometric and lifestyle data were compared with those of 248 healthy adults (65% females, aged 18–78 years, $M \pm SD = 53.1 \pm 12.1$), from the general population of the same geographical area (Sardinia, Italy), previously evaluated. In the post-lockdown assessment, all data from the study group were collected via video call interviews with the same researchers who carried out the pre-lockdown assessment. These researchers provided patients with accurate explanations, especially regarding the self-measurement of anthropometric data.[27,28] Personal information was anonymized to ensure privacy protection.

Height, weight, and waist circumference (WC) were measured in the morning, after an overnight fast, as previously reported.[29] Height, expressed in cm, was measured on barefoot patients with an altimeter (SECA, Hamburg Germany), and weight, expressed in kg, was measured under wearing light clothes (round to 0.5 kg) with a digital scale (SECA, Hamburg Germany). BMI, calculated as the ratio between weight and the square of height (kg/m^2), was used to classify the weight status: normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obesity ($\geq$30 kg/m^2). The WC was measured using an ergonomic tape measure on the patient in an upright position, with the abdomen uncovered and the abdominal muscles relaxed. The measurement, expressed in cm, was taken just above the upper margin of the iliac crests with the tape measure parallel to the floor, considering as reference values the cut-off indicated by the International Diabetes Federation for the European population: 94 cm for the male sex and 80 cm for the female sex.[30] In the post-lockdown evaluation, patients were asked to self-measure their body weight (with a home weighing scale) and waist circumference (with the support of a family member or friend) during the video call interview, guided by the same researchers who carried out the pre-lockdown assessment, following the same procedure.[27,28]

The health-related Quality of Life was assessed with the 12-Item scale of the Short Form Survey (SF-12), namely the shortened version of the original SF-36 questionnaire.[31] The scale measures both physical and mental aspects of the health, and the answers are used to calculate two indices, the physical component summary (PCS) and mental component summary (MCS), by means of the OrthoToolKit ©2020 calculator. For both the SF-12 components, the scores range between 0 and 100, with a higher score indicating better health. As recommended, a score of 50 on the PCS-12 and 42 on the MCS-12 have been considered as a cut-off for indicating a good physical and mental health respectively.[32]

The adherence to the MD was evaluated by means of two validated questionnaires: the Mediterranean Diet Score (MDS), and the PREvention with MEDiterranean Diet (PREDIMED), which were administered to the patients by the same nutritionist through a face-to-face interview in the pre-lockdown evaluation, and a telephonic interview in the post-lockdown. Briefly, the MDS questionnaire assesses the monthly or weekly frequency of consumption of 11 food categories, and assigns an increasing score (0–5), for the categories considered typical of the Mediterranean model, and a decreasing score (5–0), for those considered far from the same model. The MDS is calculated from the sum of the scores obtained for the 11 food groups and ranges from 0 to 55. The higher is the score obtained, the greater will be the adherence to the MD.[33] Due to the lack of a specific cutoff for defining a good or poor adherence to the MD with MDS, we considered the average value obtained in the healthy subjects from the general population as reference value for ascertaining the level of adherence to the MD of the study sample.[34] The PREvention with MEDiterranean Diet (PREDIMED) questionnaire consists of 14 items investigating about the consumption of different groups of foods or drinks. Each item is assigned a score zero or one, and the total PREDIMED score, coming from the sum of the scores of the individual items, indicates the grade of adherence to the MD: high adherence (score $\geq$10), average adherence (score 6–9), and low adherence (score 0–5).[35]

The PAL was measured through the shortened version of the International Physical Activity Questionnaire (IPAQ),[36] consisting in seven items which assess the patient's weekly energy expenditure expressed in METs (Metabolic Equivalent of Task) and the sedentary behavior, expressed in h/day spent in a sitting/laying position (excluding sleeping time) in any day of the same week. As with the MD questionnaires, the IPAQ was administered by the same endocrinologist via face-to-face interview before the lockdown or through a telephone interview

Table 1. Anthropometric and lifestyle comparison between patients with thyroid disease and healthy subjects (Chi-square test and Student's *t*-test between groups).

Parameters	Patients	Healthy subjects	Student's *t*-test	χ^2	*p*-value
	(*n* = 116)	(*n* = 248)			
BMI (M ± SD)	26.5 ± 4.9	23.6 ± 4.1	*t* = 5.95; df 362; mean difference 2.92; 95% CI 1.95–3.88	—	<**0.05**
BMI <25 kg/m^2 (%)	48 (41.4%)	172 (69.5%)	—	29.16	<**0.001**
BMI ≥25 kg/m^2 (%)	68 (58.6%)	76 (30.5%)			
MDS (M ± SD)	30.04 ± 5.2	32.5 ± 6.5	*t* = −3.54; df 362; mean difference −2.43; 95% CI −3.78 to −1.08	—	<**0.001**
Score <32.57 (%)	80 (69.0%)	122 (49.2%)	—	15.21	<**0.001**
Score ≥32.57 (%)	36 (31.0%)	126 (50.8%)			
PAL <700 METs/week (%)	77 (66.4%)	77[a] (34.5%)	—	33.24	<**0.001**
PAL ≥700 METs/week (%)	39(33.6%)	146[a] (65.5%)			

BMI: body mass index (kg/m^2); M: mean; SD: standard deviation; MDS: Mediterranean Diet Score (0-55): cut-off: 32.57 based on the mean value of the healthy subjects; PAL: physical activity level (METs/week).
[a]Missing data for 25 healthy subjects.

during the post-lockdown evaluation. The PAL calculation takes into account the METs consumed. If the sum of the expenditure corresponding to the individual activities (vigorous, moderate, and walking), which represents the estimated weekly energy expenditure, is ≤700 METs/week the patient is considered sedentary, if the value falls between 700 and 2519 METs/week the patient is sufficiently active, if the value is ≥2520 METs/week the patient is considered active.

Descriptive analysis, including frequency and percentage, and mean ± standard deviation (M ± SD), was performed for the studied variables. The cut-off values for the study variables were defined based on the sample distribution in percentiles (e.g. 25° = low values; 75° = high values). An independent-samples Student's *t*-test analysis was performed to analyze differences in the mean values of the continuous variables between patient and healthy groups in the pre-lockdown assessment.

Chi-square analysis was carried out to compare categorical variables expressed as percentage values. Wilcoxon test for paired samples was performed to compare pre and post-lockdown evaluations. The analyses were performed by using SPSS software, version 23 (SPSS Inc., Chicago, IL, USA)

The study was conducted according to the Helsinki Declaration and approved on the September 30th, 2020 by the AOUCA Independent Ethics Committee of Southern Sardinia, Italy (Prot. NP/2020/3883).

Results

As shown in Table 1, the pre-lockdown assessment revealed a mean BMI value in the study group corresponding to overweight (26.5 ± 4.9) and a high prevalence of overweight or obesity (58.6%). These values were significantly higher than those previously observed in a healthy group from the general Sardinian population. Moreover, the study group exhibited lower adherence to the MD and a higher level of sedentariness compared to the healthy subjects. Considering the mean MDS value obtained in the latter (32.5 ± 6.5), as the reference value for indicating adherence to the MD in the general Sardinian population, the MDS mean value was significantly lower in the study group. Additionally, the majority of patients with thyroid diseases had a significantly lower MDS than that reported by the healthy subjects ($p < 0.001$). A similar result was obtained for PAL, with the percentage of thyroid patients considered sedentary, significantly higher than that observed among the healthy subjects ($p < 0.001$).

Table 2 shows the frequency distribution for the study variables, comparing the two evaluations in the study group. Regarding the anthropometric variables, during the lockdown, there was no significant change in the prevalence of overweight or obesity, and only a slight increase of the percentage of patients with WC values above the sex-specific upper reference limit. Regarding the adherence to the MD, the results of the MDS reveal that the distribution of the sample remained unchanged. Similarly, the results of the PREDIMED did not show a significant change between the two periods, although a slight increase in the percentage of patients with poor adherence and a decrease in the percentage of patients with medium and good adherence was observed. Regarding physical activity, our data show an increase of the percentage of sedentary patients in the post-lockdown period and a decrease in the physical activity level. However, the statistical analysis reveals a change just above the limit of significance. Regarding the quality of life, both the indices, PCS and MCS, did not significantly differ between the pre- and post- lockdown periods.

Table 3 shows the results of the comparison of the analyzed variables, expressed as M ± SD, in the pre- and

Table 2. Frequency distribution and Chi-square test for the study variables in pre- and post- lockdown.

Parameters	Groups	Pre-lockdown	Post-lockdown	χ^2	*p*-value
		N (%)	*N* (%)		
BMI	$<25\,kg/m^2$	48 (41.4)	47 (40.5)	0.018	0.894
	$\geq 25\,kg/m^2$	68 (58.6)	69 (59.5)		
WC	Normal values	24 (20.7)	22 (19.0)	0.108	0.742
	High values	92 (79.3)	94 (81.0)		
MDS	Low adherence	80 (69.0)	80 (69.0)	0.000	1.000
	Good adherence	36 (31.0)	36 (31.0)		
PREDIMED	Low adherence	18 (15.5)	24(20.7)	1.120	0.571
	Medium adherence	85 (73.3)	81 (69.8)		
	Good adherence	13 (11.2)	11 (9.5)		
PAL	Sedentary	77 (66.4)	90 (77.6)	3.612	0.057
	Active	39 (33.6)	26 (22.4)		
PCS	<50	73 (62.9)	73 (62.9)	0.000	1.000
	≥ 50	43 (37.1)	43 (37.1)		
MCS	<42	43 (37.1)	44 (37.9)	0.018	0.892
	≥ 42	73 (62.9)	72 (62.1)		

Cut-off: MDS (based on the mean value of the healthy subjects = 32.57): <32.57 = low adherence; ≥ 32.57 = good adherence. PREDIMED: 0-5 = low adherence; 6-9 = medium adherence; 10-14 = good adherence. PAL: <700 METs/week = sedentary; ≥ 700 METs/week = active. PCS: <50 = low physical health; ≥ 50 high physical health. MCS: <42 = low mental health; ≥ 42 = high mental health.
BMI: body mass index (kg/m^2); MCS: mental component summary; MDS: Mediterranean Diet Score; PCS: physical component summary; WC: waist circumference (cm).

Table 3. Mean values comparison between the pre- and post-lockdown evaluations (Wilcoxon test for two-related samples).

Parameters	Pre-lockdown	Post-lockdown	*Z*	**p* H_0	Improved in POST	Worsened in POST	Unchanged
	(M ± SD)	(M ± SD)			*N* (%)	*N* (%)	*N* (%)
BMI	26.5±4.92	26.6±4.96	–1.568	0.117	50 (43.1)	66 (56.9)	0 (0.0)
WC	93.3±12.60	94.4±12.53	–2.931	**0.003**	25 (21.5)	49 (42.2)	42 (36.2)
MDS	30.04±5.24	30.19±5.42	–0.027	0.979	20 (17.2)	27 (23.3)	69 (59.5)
PREDIMED	7.30±1.78	7.04±1.80	–2.978	**0.003**	8 (7.0)	29 (25.2)	78 (67.8)
PAL	647.70± 779.97	562.0± 604.87	–1.479	0.139	31 (27.0)	41 (35.6)	43 (37.4)
hour seated/day	6.41±3.17	9.03±4.25	–6.718	**<0.001**	7 (6.4)	67 (60.9)	36 (32.7)
PCS	43.50±10.62	43.00±11.37	–0.810	0.418	23 (19.8)	25 (21.5)	68 (58.6)
MCS	44.10±11.52	43.05±12.46	–1.533	0.125	23 (19.8)	32 (27.6)	61 (52.6)

BMI: body mass index (kg/m^2); M: mean; MCS: SF-12 mental component summary; MDS: Mediterranean Diet Score; PAL: physical activity level (METs/week); PCS: SF-12 physical component summary; SD: standard deviation; WC: waist circumference (cm).
*Probability that health parameters in PRE-lockdown and POST-lockdown periods are not different for each variable (H0), $p < 0.05$.

post- lockdown periods. Regarding the anthropometric variables, no significant change in BMI was observed, and the mean value remained constant over time, indicating a status of overweight in both the evaluations. On the other hand, the WC mean value increased significantly over time, and WC values worsened in 42.2% of patients. As for lifestyle and quality of life, the results show a significant increase of the mean value of daily sitting time (from 6.41 to 9.03 h/day; $p < 0.001$), and overall, a significant worsening of sedentariness was reported by 61% of patients. Concerning the physical activity level (PAL), it showed an average score referred to a sedentary behavior in both pre and post-lockdown periods, with a further decrease, although not significant, in post-lockdown. Non-significant results also emerged for the MDS variable, with mean values below the limit we have considered as a reference value for adherence to the MD in both pre and post-lockdown evaluations. Nevertheless, considering the PREDIMED, a significant decrease in the mean adherence score was observed in the post- lockdown period ($p = 0.003$), and 25% of patients showed a worsening of adherence. As for the PCS and MCS indices of quality of life, non-particularly evident changes of their mean values were found in post-lockdown.

Discussion

This study started in January 2020, as a part of a larger survey focused on the lifestyle and adherence to the MD in the Sardinian population with the aim to evaluate the anthropometric variables (BMI and WC), lifestyle (adherence to the MD and physical activity level), and quality of life in patients with thyroid diseases in euthyroid state, attending the Endocrinology and the Obesity Unit of the University Hospital of Cagliari (Sardinia, Italy). Indeed, a link between obesity and thyroid diseases,[23] particularly autoimmune thyroid diseases, has been reported,[24,37] and our previous observations showed an increase of the prevalence of overweight and obesity in the Sardinian male population.[26] Concerning thyroid diseases, the majority of patients were affected by AITD, particularly HT, according to the high prevalence of autoimmune diseases in the Sardinian population.[38] The arrival of the COVID-19 pandemic, and especially the lockdown, interrupted this investigation, when only 116 patients had been evaluated, thus we re-assessed the cohort already examined to elucidate the impact of the lockdown on the same variables. All patients were recalled, via telephone (more specifically a video-call),[27,28] in the immediate post-lockdown period and both the anthropometric and lifestyle assessment, updated to the post- quarantine, were performed to establish the effect of lockdown on nutritional habits, physical activity level, quality of life, and anthropometric indices. All questionnaires were administered during the telephonic interview,[27,28] by the same researchers (endocrinologist and nutritionist) who carried out the pre-lockdown evaluation, while the anthropometric assessment in this case, was performed autonomously by the patients, under the guidance of the researchers (by means of a video call).[27,28] The different methodology of the anthropometric evaluation, although a complete and accurate explanation was provided by the researchers during the video call,[27,28] certainly constitutes a limitation. However, this limitation was insuperable due to the blockade of the normal outpatient activity during the lockdown period. The first evaluation, carried out during the pre-lockdown period, showed that patients affected by thyroid diseases, had a BMI mean value corresponding to an overweight, significantly higher than that of a healthy group from the Sardinian general population previously evaluated. Furthermore, over 50% of patients showed a weight excess, against less 30% of the healthy subjects, and the comparison of the two groups gave a significant result. This finding is supported by several studies that report a relationship between thyroid diseases, particularly AITD, and overweight or obesity.[37] Moreover, a potential role of obesity, as well as dietary habits in the development of thyroid cancer has been recently hypothesized.[39] As for the lifestyle analysis in the pre-lockdown period, overall, the study group showed a significantly lower adherence to the MD, and a significantly lower physical activity level compared with the healthy general population. These findings are in line with those already reported by other authors. Regarding eating habits, the role of good nutrition on health is well known. Particularly, a greater adherence to plant-based diets, such as the MD, is associated to a successful aging and in general a good health due to their antioxidant and anti-inflammatory properties.[40,41] As regards the role of good and healthy nutrition in patients with thyroid disease, it has been described in some studies.[20,25] Ruggeri et al. observed both a greater consumption of animal foods and higher levels of stress-oxidative markers in a cohort of 81 patients with euthyroid HT than in control subjects. Moreover, these authors found that meat consumption was associated with an increased odds ratio of developing thyroid autoimmunity, while Mediterranean Diet traits were protective against thyroid autoimmunity, suggesting a positive influence of the Mediterranean dietary pattern on redox balance and possibly on oxidative stress-related diseases.[25] These results are in agreement with those of Kaliˇcanin et al. who analyzed the frequency of food consumption, by means of a 51-items questionnaire, in a large cohort of patients with HT compared with a healthy control group, finding a higher consumption of processed meat and saturated fats in HT patients, and a more frequent consumption of plant-based foods in controls.[42] Furthermore, in a recent review, Bellastella et al. concluded that, although there are still few studies, especially on large samples, MD seems to be beneficial on autoimmune and non-autoimmune thyroid diseases including cancer.[43] In our study, patients with thyroid diseases, mostly affected by HT, were found to have not only a lower adherence to the MD, as we previously observed in patients with obesity or inflammatory diseases[34,44] but also a predominantly sedentary lifestyle compared to the general healthy population of the same geographical area. As regards physical activity, our findings partially support those of Tanriverdi et al., who compared the physical activity level, measured by means of an accelerometer, of 32 women with newly diagnosed subclinical hypothyroidism (SCH), not undergoing replacement therapy, with that of 28 healthy women, finding a significantly lower duration and number of steps in the SCH group. The same group showed a significant difference in neuromuscular symptoms, handgrip and quadriceps muscle strength, and distance at 6 min Walking Test, as well as a significantly higher pulse wave velocity as an index of arterial stiffness than the control group.[45] Moreover, a limitation in the moderate physical activity performance has been observed in female patients with hypothyroidism on hormone replacement therapy, particularly AITD, compared to control subjects.[46] Finally, we examined the perceived state of health and the quality of life using the SF-12 questionnaire, revealing that half of patients had a low score of both the physical and mental indices. An impaired quality of life has been described in patients with hypothyroidism undergoing thyroid hormone therapy despite having a normal biochemical status.[47] The

follow-up evaluation was carried out in the immediate post-lockdown period, but in this case, data were collected via a video-call interview with the same researcher of the pre-lockdown evaluation who provided appropriate explanations for patients, especially regarding the measurement of the anthropometric variables.[27,28] The post- lockdown evaluation, highlighted that the adherence to the MD, assessed by means of the MDS, remained substantially unchanged, as shown by the similar score in the two evaluations. In this regard, it should be emphasized that the dietary changes most frequently reported during the quarantine period, concern an increased consumption of refined carbohydrates, such as bread, pizza or sweets,[3] that, unlike whole grain cereals, are not typical of the Mediterranean model and thus are not included in the Mediterranean Diet Score. In our patients we can hypothesize a similar change in eating habits, that is, an increased frequency of consumption of refined carbohydrates. Instead, we suppose that the consumption of the food groups included in the MDS, has not changed during the quarantine, explaining the unchanged result of the score, which revealed a moderate adherence to the MD, although lower than that of the healthy subjects, in both the evaluations. This result is in line with that obtained by Di Renzo et al., who, in a web-survey including over three thousand people from all the Italian regions, reported an adequate intake of foods typical of the Mediterranean pattern, especially olive oil, but also vegetables and legumes, and overall, a moderate adherence to the MD during the Covid-19 lockdown.[3] Nevertheless, the analysis of the PREDIMED questionnaire, showed in our patients a significant reduction of the total score in the post- lockdown assessment, probably attributable to the more frequent consumption of refined carbohydrates and sweets, which is investigated by a specific item of the PREDIMED, but not by the MDS questionnaire. Besides the already observed increased interest in cooking and the more time spent in preparing homemade recipes, particularly bread and cakes,[4] a possible explanation of this dietary choice is represented by the rewarding effect induced by the increased consumption of sweets as partial compensation for the high stress load due to the health emergency as well as the reduced social and working life, associated with lockdown. In line with this hypothesis, an increase of the consumption of comfort foods and after-dinner snacks, has been reported during the quarantine period.[3] The comparison of data regarding physical activity shows, in the post- lockdown evaluation, an increased rate of sedentary patients and a decreased rate of active patients. This result, that is just above the limit of statistical significance, can be mainly attributed to the significant increase in the daily sitting time during the lockdown period. Indeed, the mean score of the physical activity level, expressed in METs/week, revealed a sedentary behavior in both the pre- and post-lockdown evaluations, and only a slight but not significant decrease, in the post-lockdown. The beneficial effect of a moderate physical activity on general health and cardiometabolic diseases is well known.[6,48] As regards thyroid diseases, an inverse correlation between physical activity level and thyroid cancer incidence has been reported in the USA,[49] while a Korean prospective study, found a significant association between physical activity level and thyroid cancer risk, stronger in overweight females, suggesting a protective effect of physical activity on the development of thyroid cancer.[50] As for sedentary behaviors, a systematic review highlighted the important role of the prolonged and uninterrupted sitting time both in reducing the non-exercise activity thermogenesis and insulin sensitivity, and in increasing postprandial hyperglycemia, dyslipidemia or hypertension. Furthermore, the increase in inflammatory indices, particularly in the presence of visceral adiposity, could worsen the risk of cardiometabolic diseases and cancer.[6] An increased sitting time has also been associated with an increased risk of anxiety and depression, an effect which could be improved by a moderate physical activity.[51,52] This is a crucial issue, due to the strong impact of the Covid-19 pandemic and the restrictive measures to limit its spread on both mental and physical health.[9] In our study the comparison of data obtained with the SF-12 questionnaire did not show any statistically significant difference between the two evaluations, but only a downward trend of both the PCS and MCS, suggesting a weak influence of the lockdown on the two areas, physical and mental, of the perceived health. Nevertheless, an Italian study revealed a significant worsening of the mental component of the SF-12 questionnaire during the Covid-19 pandemic, especially in the youngest cohort, while the reduction of the mental health score was less marked in older people, and individuals aged 70 or more did not show any significant change.[53] Moreover, the aforementioned survey evaluated a much larger number of individuals than our study, thus the discrepancies in the sample size, as well as the older age of our patients, could justify the different result. Regarding the anthropometric variables, our patients showed a significant increase in the mean waist circumference value, which is a highly accurate index of central adiposity and has been shown to have a stronger positive association with cardiometabolic risk than BMI.[54] It should be underlined that in the post-lockdown assessment, the anthropometric measures were taken autonomously by the patients, although according to the instructions provided by the researchers via video call, and this different methodology represents a limitation of the study. However, we can hypothesize that the changes in lifestyle, observed in our study, could have negatively influenced the level of adiposity, favoring, even in the short term, the deposition of abdominal and visceral fat. Our patients, showed a significant reduction in adherence to the MD as indicated by the PREDIMED score, and especially a significant increase in sedentary behavior during the lockdown period.

Sedentary behaviors have been demonstrated to exert a more important effect on visceral fat and waist circumference compared with caloric intake.[55] Therefore, the significant increase in the sitting time during the lockdown, could *per se* justify the increase in waist circumference at the follow-up assessment. Our sample is represented by patients with thyroid disease, most affected by AITD, in whom weight excess, especially visceral adiposity, could worsen the clinical outcomes of thyroid disease.[37] Therefore, the change in lifestyle observed in these patients, especially the increased sitting time, and the subsequent increase in visceral fat, could have pathological consequences over time. Moreover, a reciprocal interaction between endocrine disorders, including thyroid diseases, and Covid-19 infection has recently been reported, although we do not have information regarding the development of the infection among our patients.[56] On the other hand, our results did not show any variation in BMI values, nor in the frequency of obesity compared to the pre-lockdown evaluation. This finding is in contrast with that found by other authors in the general population[7] probably due to the small cohort included in our study. However, despite the limitations represented by the small sample size and the different methodology used in the two evaluations, we hypothesize that the increased sedentary behavior, even independent from the caloric intake, could have determined a change in body composition with a reduction in muscle mass,[17] justifying the unchanged BMI despite the increased WC. Further studies with larger sample sizes and direct anthropometric measurements, including body composition assessment will be necessary for a better understanding of the effects of lifestyle on body weight.

Additional limitations of this study include the lack of stratification by sex, BMI categories, and type of thyroid disease which was not possible due to the small sample size, as well as the lack of information regarding possible changes in hormonal status or therapy during the follow-up period. However, it is reasonable to assume that patients neither assessed their hormonal status nor modified their therapy during the lockdown period, when they were unable to leave their homes and clinical activities were suspended.

Conclusions

This study is, to our knowledge, the first to assess adherence to the Mediterranean diet, the level of physical activity, quality of life, and anthropometric indices, in a cohort of patients affected by thyroid disease, both before and after the lockdown period. Our results indicate that these patients have a lower adherence to the MD compared to that of a healthy group from the general population of the same geographical region, but, notably, they are inherently sedentary. The sedentary behaviors could explain the high frequency of weight excess observed in the pre-lockdown evaluation. Particularly, the significant increase in daily sitting time during the lockdown period, coupled with a slight reduction in the physical activity level and a minor worsening in eating behavior, could justify the higher waist circumference value observed in the post-lockdown evaluation compared to the pre-lockdown assessment. Given the connections between unhealthy lifestyle, visceral obesity, and thyroid diseases, we suggest the importance of assessing anthropometric indices, eating patterns, and physical activity level in patients with thyroid diseases. Moreover, if deemed necessary, integrating lifestyle interventions into the therapeutical management of these patients is recommended.

Author contributions

Conceptualization, S.C., A.L., F.V.; methodology, M.G., A.D.; validation, M.G.; formal analysis, M.G.; investigation, S.C., M.F., G.B., A.O., F.P., M.M., R.R., A.P., C.P., A.D., L.P.; writing—original draft preparation, A.L.; S.C.; M.F.; writing—review and editing, A.L. and F.V.; visualization, S.C., M.F.; supervision, F.V.; project administration, A.L., A.O., F.P., G.B., F.B.; All authors have read and agreed to the published version of the manuscript.

Data availability statement

The datasets used and/or analyzed during the current study will be made available by the authors on reasonable request.

Declaration of conflicting interests

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Institutional review board statement

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of AOU Cagliari of Southern Sardinia, Italy (Prot. NP/2020/3883).

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

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