Association between Berlin questionnaire index and blood pressure, organ damage and metabolic profile in a general population

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Abstract
We evaluated the relationships between Berlin questionnaire (BQ) scores, hypertension and other metabolic variables in 598 subjects (age: 65.8 ± 10 years, mean ± SD) enrolled in the PAMELA (Pressioni Arteriose Monitorate E Loro Associazioni) study representative of the general population, treated or untreated with antihypertensive drugs. Two hundred and eleven subjects (35%) had a positive BQ with two or more positive categories of the inquiry. Compared to those without sleep disorders these subjects showed a greater male prevalence (55.9%), worse serum cholesterol, triglycerides and glucose profile, greater body mass index (BMI) (28.9 ± 4.9 vs. 24.9 ± 3.4 kg/m²), higher office (and to a lesser extent 24-h) BP and HR values, higher serum creatinine values and greater rate of echocardiographic left ventricular (LV) hypertrophy (25% vs. 13%). These differences were not detected when the data analysis was restricted to treated hypertensive patients. Thus, BQ scores allow to identify among subjects belonging to a general population those with elevated BP, organ damage and altered metabolic. When antihypertensive drug treatment is present, however, the approach fails to detect differences between groups with low or high BQ index.

KEYWORDS
ambulatory blood pressure/home blood pressure monitor, risk assessment, sleep problems and hypertension

1 | INTRODUCTION

Berlin questionnaire (BQ) allows to identify a condition of sleep fragmentation and to detect high risk patients for obstructive sleep apnea (OSA), thereby representing a method useful in the clinical settings with limited capabilities to refer or perform direct overnight polysomnographic evaluation.1–3 OSA is a condition known to be related to the development and progression of the hypertensive state and other cardiovascular disease4 and, recently, also the same condition of sleep fragmentation was associated with a high likelihood of accelerated atherosclerosis.5 Scarce information is available on whether different scores of the BQ might be associated in a general population with differences in the hemodynamic and metabolic profile, as well as in organ damage, thereby allowing to use this evaluation for the assessment of the global cardiovascular risk profile of a given individual.6–8 Aim of the present study was to evaluate in a general population sample the relationships between BQ scores and clinic blood pressure, 24-h blood pressure and blood pressure variability as...
well. Additional aims were to assess in the same cohort the possible association between BQ index, metabolic variables and organ damage, also evaluating the possible influence of antihypertensive drug treatment on the above-mentioned relationships.

2 | MATERIALS AND METHODS

2.1 | Study population

The PAMELA (Pressioni Arteriose Monitorate E Loro Associazioni) study was carried out in a sample of 3200 subjects representative of the population of Monza (a town near Milan, Italy) for sex and age decades (25–74 years). The participation rate was 64%, allowing to collect data in 2051 subjects. Demographic characteristics of nonparticipants and participants were similar, this being also the case for cardiovascular risk factors as assessed by data collected via phone interviews. From the original sample of 2051 subjects who underwent the initial evaluation in the nineties, we examined for the present cross-sectional study a sample of 598 survived subjects who attended the third survey in 2016–2017. All variables reported in the present paper were collected during this third survey.

2.2 | Study variables

Methods employed in the PAMELA study have been previously described in detail elsewhere. Briefly, after being obtained an informed consent, subjects were invited to undergo a comprehensive clinical evaluation at the outpatient clinic of the Saint Gerardo University Hospital of Monza. Collected data included a comprehensive medical history, a thorough physical examination, body weight and height, standard blood tests, three sphygmomanometric systolic (S) and diastolic (D) BP measurements in the sitting position (office BP), a 12-lead EKG and an echocardiogram. Body weight was recorded to the nearest .1 kg using a calibrated electronic scale with patients wearing indoor clothing without shoes and body mass index (BMI) was then calculated. Height was recorded to the nearest .5 cm using a standardized wall-mounted height board. All individuals were then fitted with ambulatory BP monitoring device set to obtain automated oscillometric BP and heart rate (HR) readings every 20 min over the 24 h via a validated ambulatory blood pressure monitoring device (Spacelabs 90207, Issaquah, WA, USA). During the monitoring period, the individuals were asked to pursue their normal activities. In each individual, the 24-h average systolic BP, diastolic BP, and HR average values, standard deviation, cyclic components of variability and individual residual variability were calculated as previously reported. The echocardiographic examination was performed according to standardized procedures, as previously reported. In brief, M-mode and two-dimensional echo examinations were carried out with a commercially available instrument (Acuson 128 CF; computer Sonography). End-diastolic (d) and end-systolic (s) LV internal diameters (LVDD), interventricular septum thickness (IVS), and posterior wall thickness were measured from two-dimensionally guided M-mode tracings recorded at 50–100 cm/s speed, during at least three consecutive cycles. Left ventricular mass (LVM) was estimated by using the corrected American Society of Echocardiography formulae. Echocardiographic tracings were obtained by two skilled operators and read by a third independent observer. Left ventricular (LV) hypertrophy was alternatively defined when LVMIBSA was equal or higher than 114 grams/m2 in men and 99 grams/m2 in women, and when LVMICT was equal or higher than 51 grams/height2.7 in men and 47 grams/height2.7 in women.

2.3 | Measures of end organ damage

For the purposes of the present study assessment of renal function was done via plasma creatinine evaluation (standard assay method) while echocardiography was employed to assess left ventricular mass.

2.4 | Berlin questionnaire

A BQ completed was available in 598 individuals. Subjects with at least two of three positive categories were considered at high risk for OSA (BQ≥2). Category 1 (snoring assessment) was detected with two or more positive responses among five questions, category 2 (daytime sleepiness) was detected with two or more positive responses among three questions, and category 3 was found if the patient was hypertensive or showed BMI > 30 kg/m2.

2.5 | Statistical analysis

Values were expressed as means ± SD or percentages. Comparisons between subjects with positive BQ (BQ≥2) and negative BQ (BQ < 2) scores were made with Student t-test for unpaired samples or Mann-Whitney U-test (continuous variables) and with Chi-Square test (categorical variables). Linear models were used to adjust, by age and sex, the association between BP, HR, metabolic values (dependent variables) and the positive BQ score (independent variable). The same analysis was performed among untreated and treated subjects with antihypertensive drugs. A p-value < .05 was considered to be statistically significant. All analyses were performed using SAS software (version 9.4; SAS Institute Inc., Cary, NC).

3 | RESULTS

Mean age of the whole population sample amounted to 65.8 ± 10 years and 48.5% was males. Two hundred and eleven subjects (35%) had a positive BQ with two or more positive categories of the inquiry (Table 1). These subjects, when compared to those without sleep disorders, showed a greater male prevalence (55.9%), worse serum glucose and triglycerides profile, greater BMI (28.9 ± 4.9 vs. 24.9 ± 3.4 kg/m2), higher office SBP, DBP, and HR values, as reported in Table 1. 24-h BP also showed a tendency, although not significant, to be greater in this group of subjects, which also displayed significantly greater serum creatinine values and a significantly greater rate of echocardiographic
Table 1: Clinical characteristics of the whole study population and of selected subjects with positive (≥2) compared to those with negative (<2) Berlin questionnaire (BQ)

|                      | Whole group | BQ score |  |  | p-value |
|----------------------|-------------|----------|----|---|---------|
|                      |             | <2       | ≥2 |   |         |
| Number               | 598         | 387      | 211|   | .2931   |
| Age, years           | 65.8 ± 10   | 65.4 ± 10.5 | 66.3 ± 9.2 |  | .0002   |
| Male, %              | 48.5%       | 44.4%    | 55.9% |   | .0073   |
| BMI, kg/m²           | 26.3 ± 4.4  | 24.9 ± 3.4 | 28.9 ± 4.9 |  | <.0001  |
| SBP night, mmHg      | 120.1 ± 15.9 | 119.4 ± 16.2 | 121.5 ± 15.4 |  | .1237   |
| DBP night, mmHg      | 68.2 ± 8.6  | 68.1 ± 8.5 | 68.4 ± 8.7 |  | .7606   |
| HR night, b/min      | 63.7 ± 8    | 63.2 ± 8  | 64.5 ± 7.8 |  | .0688   |
| SD 24 h SBP, mmHg    | 21.9 ± 5.9  | 22 ± 6.2 | 21.7 ± 5.3 |  | .5634   |
| SD 24 h DBP, mmHg    | 17.4 ± 5.5  | 17.4 ± 5.8 | 17.3 ± 4.9 |  | .6905   |
| SD 24 h HR, b/min    | 12.6 ± 3.6  | 12.7 ± 3.4 | 12.4 ± 3.9 |  | .4045   |
| Residual variability SBP, mmHg | 14.1 ± 3.9 | 14.1 ± 4.1 | 14 ± 3.4 |  | .6951   |
| Residual variability DBP, mmHg | 11 ± 3.9 | 11.1 ± 4.1 | 11 ± 3.5 |  | .7759   |
| Residual variability HR, b/min | 7.4 ± 2.2 | 7.5 ± 2 | 7.3 ± 2.4 |  | .5016   |
| Antihypertensive therapy, % | 50% | 37.7% | 72.5% |  | <.0001  |
| Total cholesterol, mg/dl | 200.4 ± 36.2 | 203.3 ± 35.1 | 195.1 ± 37.7 |  | .0083   |
| HDL cholesterol, mg/dl | 59.2 ± 17   | 61.9 ± 17.4 | 54.3 ± 15.1 |  | <.0001  |
| LDL cholesterol, mg/dl | 119.9 ± 32.2 | 121.4 ± 31.8 | 117.3 ± 32.7 |  | .1384   |
| Triglycerides, mg/dl | 107.3 ± 58  | 101.9 ± 56.3 | 117.2 ± 59.9 |  | .0003   |
| Glycemia, mg/dl      | 95.1 ± 21.9 | 93 ± 20.8 | 98.9 ± 23.3 |  | <.0001  |
| Creatinine, mg/dl    | .92 ± .23   | .91 ± .21 | .95 ± .26 |  | .0226   |
| LVMI, g/m²           | 85.6 ± 20.6 | 83.4 ± 20.6 | 89.7 ± 20.2 |  | .0004   |
| LVMI > 99/114 g/m², %| 13.6%       | 12.9%    | 15.0% |  | .4644   |
| LVMI > 47/51 g/m², % | 39.6 ± 10.6 | 37.8 ± 10.1 | 43 ± 10.8 |  | <.0001  |
| LVMI > 47/51 g/m², % | 17.3%       | 12.9%    | 25.2% |  | .0002   |

Note: Data are shown as means ± standard deviation of the mean.
Abbreviations: DBP, diastolic blood pressure; HR, heart rate; LVMI, left ventricular mass index; SBP, systolic blood pressure; SD, standard deviation.

LV hypertrophy (25% vs. 13% for LV mass indexed for height²⁻⁷). The percentage of individuals under antihypertensive therapy was also significantly greater in this group of individuals (72.5% vs. 37.7%). No significant difference between subjects with a BQ < 2 and ≥ 2 was found taking into account blood pressure and heart rate variability data analysis.

Table 2 shows the analysis of the data according to subgroups of subjects untreated or treated with antihypertensive drugs (beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, calcium channel blockers, diuretics, alpha blockers in various combinations and daily dosages). While in untreated subjects the differences in the above-mentioned blood pressure, metabolic and organ damage profile between individuals with and without sleep disorders were confirmed, no significant difference was detected in the group of treated patients, except for a higher rate prevalence of males (58.8% vs. 44.5%) and a greater BMI (28.8 ± 5 vs. 26 ± 3.5 kg/m²).

Finally, in the whole population, the positive BQ was associated to worse BP, HR, and metabolic values independently by age and sex.
TABLE 2 Clinical characteristics of selected subjects with positive (BQ ≥ 2) compared to those with negative Berlin questionnaire (BQ < 2) among subjects untreated and treated with antihypertensive drugs

|                          | No anti-hypertensive therapy | Anti-hypertensive therapy | p-Value |
|--------------------------|------------------------------|---------------------------|---------|
|                          | BQ < 2                       | BQ ≥ 2                    |         |
| Number                   | 241                          | 58                        |         |
| Age, years               | 62.5 ± 9.7                   | 63.7 ± 9.5                | .3941   |
| Male, %                  | 44.4%                        | 48.3%                     | .5942   |
| BMI, kg/m²               | 24.3 ± 3.1                   | 29.1 ± 4.9                | <.0001  |
| Office SBP, mmHg         | 131.2 ± 17.2                 | 138.9 ± 18.1              | .0030   |
| Office DBP, mmHg         | 82.4 ± 8.2                   | 86 ± 9.8                  | .0035   |
| Office HR, b/min         | 69.3 ± 8.8                   | 74.1 ± 9.9                | .0003   |
| 24 h SBP, mmHg           | 131.6 ± 13                   | 137 ± 12.8                | .0043   |
| 24 h HR, b/min           | 72.6 ± 7.4                   | 75.7 ± 7.1                | .0045   |
| Day SBP, mmHg            | 137.2 ± 13.8                 | 143.1 ± 13.9              | .0041   |
| Day DBP, mmHg            | 82.4 ± 7.6                   | 83.5 ± 7.9                | .3290   |
| Day HR, b/min            | 76.2 ± 7.7                   | 79.2 ± 7.6                | .0078   |
| SBP night, mmHg          | 117.1 ± 14.6                 | 121.3 ± 13.8              | .0473   |
| DBP night, mmHg          | 68.2 ± 8.1                   | 68.1 ± 7.6                | .9462   |
| HR night, b/min          | 63.5 ± 8.1                   | 66.5 ± 8                  | .0112   |
| 24 h DBP, mmHg           | 22.2 ± 6.5                   | 22.1 ± 4.4                | .9071   |
| 24 h HR, mmHg            | 17.7 ± 6.1                   | 17.7 ± 4.3                | .9737   |
| Residual variability SBP, mmHg | 14.1 ± 4.3 | 14 ± 3.1                  | .9135   |
| Residual variability DBP, mmHg | 11.2 ± 4.3 | 11.2 ± 3.3               | .9759   |
| Residual variability HR, b/min | 7.7 ± 1.9 | 7.6 ± 2.5               | .9010   |
| Total cholesterol, mg/dl | 207.7 ± 33.1                 | 203.2 ± 38.8              | .4354   |
| HDL cholesterol, mg/dl   | 63.9 ± 18.4                  | 56.8 ± 17.7               | .0090   |
| LDL cholesterol, mg/dl   | 124.9 ± 30.1                 | 125.8 ± 36.2              | .8585   |
| Triglycerides, mg/dl     | 97.5 ± 60                    | 105.4 ± 48                | .1320   |
| Glycemia, mg/dl          | 89.5 ± 16.2                  | 94.4 ± 17.5               | .0128   |
| Creatinine, mg/dl        | 89 ± .19                     | .9 ± .23                  | .6970   |
| LVMI, g/m²               | 78.4 ± 16.8                  | 83.6 ± 18.4               | .0433   |
| LVMI > 99/114 g/m²%      | 6.4%                         | 10.5%                     | .2650   |
| LVMI, g/m²²             | 34.9 ± 8                    | 40.6 ± 10.7               | .0004   |
| LVMI > 47/51 g/m²²%      | 6.0%                         | 21.1%                     | .0003   |

Note: Data are shown as means ± standard deviation of the mean. For symbols and abbreviations see Table 1.

In untreated subjects, results were similar except for glycemia and triglycerides (Table 3).

4 | DISCUSSION

BQ allows to identify a condition of sleep fragmentation and to detect high risk patients for OSA, both conditions related to the development of cardiovascular disease, thereby representing a method useful in the settings with limited capabilities to refer or perform direct overnight polysomnographic evaluation made for the OSA’s diagnosis. Scarce information is available on whether different scores of the BQ might be associated in a general population with differences in the hemodynamic and metabolic profile. Only one previous study has described the association between BQ index and lipidic variables in a general population, while the other studies available in the literature were mainly focused on the diagnostic accuracy of BQ in specific population, that is, affected by diabetes or metabolic syndrome.
### TABLE 3
Linear regression models in the whole study population and in subjects untreated with antihypertensive drugs

| Whole study population | Independent variable | Beta    | SE      | p-Value   |
|------------------------|----------------------|---------|---------|-----------|
| Office SBP, mmHg        | BQ > 2               | 3.80405 | 1.4113  | .0072     |
| Office DBP, mmHg        | BQ > 2               | 1.55439 | .76839  | .0435     |
| Office HR, b/min        | BQ > 2               | 3.21212 | .8429   | .0002     |
| Glycemia, mg/dl         | BQ > 2               | 4.42566 | 1.78712 | .0015     |
| Triglycerides, mg/dl    | BQ > 2               | 13.92339| 4.95792 | .0051     |
| Creatinine, mg/dl       | BQ > 2               | .01453  | .01571  | .3554     |
| LVMI, g/m²              | BQ > 2               | 4.10488 | 1.54731 | .0082     |
| LVMI, g/m²             | 2                     | 6.56002 | 2.3085  | .0048     |
| Untreated subjects      |                      |         |         |           |
| Office SBP, mmHg        | BQ > 2               | 6.56002 | 2.3085  | .0048     |
| Office DBP, mmHg        | BQ > 2               | 3.46199 | 1.22183 | .0049     |
| Office HR, b/min        | BQ > 2               | 4.87586 | 1.30612 | .0002     |
| Glycemia, mg/dl         | BQ > 2               | 4.34156 | 2.3126  | .0615     |
| Triglycerides, mg/dl    | BQ > 2               | 6.93661 | 8.40039 | .4096     |
| Creatinine, mg/dl       | BQ > 2               | -.00032 | .02227  | .9885     |
| LVMI, g/m²              | BQ > 2               | 3.58495 | 2.10888 | .0902     |
| LVMI, g/m²             | 2                     | 4.96946 | 1.1144  | <.0001    |

Note: Symbols and abbreviations as in the preceding tables. All models are adjusted for age and sex.

Abbreviations: DBP, diastolic blood pressure; HR, heart rate; LVMI, left ventricular mass index; SBP, systolic blood pressure.

The present study provides two sets of new information on the association between BQ score and hemodynamic, metabolic and organ damage profile in a general population. First, our data, collected in a quite large population sample, show that BQ allows to detect, in a general population, the subjects characterized by a worse hemodynamic and metabolic assessment, as defined on the basis of higher office and 24-h blood pressure and heart rate values, more marked metabolic alterations and more pronounced cardiac and renal organ damage. Second, the sensitivity of the BQ approach to detect high risk patients appears to be reduced in hypertensive patients under antihypertensive drug treatment. Our study does not allow to clarify the reasons responsible for this finding. We can hypothesize, however, that under antihypertensive treatment, particularly if effective as the one employed in treating hypertensive patients of the PAMELA cohort, several hemodynamic, metabolic and organ damage alterations are favorably affected by antihypertensive drugs, which thus decrease blood pressure to normal or near normal values and reverse the metabolic and cardiovascular structural alterations found in the patients. Additional results of the study are worthy to be mentioned. These include the finding that (1) an increased BQ index is capable to detect individuals displaying greater plasma cholesterol, triglycerides and glucose levels, thereby closely mirroring the main metabolic alterations frequently accompanying OSA, (2) blood pressure variability does not appear to be associated with different BQ indices, (3) day/night blood pressure profile also appears to be unrelated to BQ, and (4) BQ indices ≥ 2 are associated with more elevated office and 24-h heart rate values. Given the close association between elevated heart rate and the adrenergic overdrive, this finding may suggest that an increased BQ index is associated with augmented sympathetic neural influences on the heart and the peripheral circulation, as a result of the marked stimulation OSA may exert on the central and peripheral adrenergic neural drive.

5. **STUDY LIMITATIONS**

Our study has some limitations. The first limitation refers to the cross-sectional nature of the study’s findings, which prevented the possibility to assess whether and to what extent the BQ index might be able to detect in a dynamic fashion the changes in the hemodynamic, metabolic, organ damage and risk profile of a given subject occurring throughout months or years. The second limitation concerns the limited sample size of the subgroups of subjects with different BQ indices and untreated or treated hypertension. Another limitation of our study is related to the survival bias: the original sample was representative of the general population of Monza but our study population represents a subgroup of this, that is, survivors at a 25-years of follow-up, and thereby likely presenting a lower CV risk.

6. **CONCLUSIONS**

The results of the present study provide evidence on the clinical utility of the BQ index evaluation for detecting the presence not only of OSA
and OSA-related sleep fragmentation but also for allowing to identify among subjects belonging to a general population those with elevated BP, organ damage and altered metabolic profile. When antihypertensive drug treatment is present, however, the approach fails to detect differences between groups with low or high BQ index.

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CONFLICT OF INTEREST
The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS
Jennifer Vanoli and Michele Bombelli collected the data, Raffaella Dell’Oro blindly analyzed the data, Rita Facchetti made statistical analysis and Guido Grassi and Giuseppe Mancia wrote the first draft and the revised versions of the paper, after comments and criticisms by coauthors.

PATIENT CONSENT STATEMENT
Written informed consent was obtained from all study participants or from their next of kin.

PERMISSION TO REPRODUCE MATERIAL
Not required.

CLINICAL TRAIL REGISTRATION
Not required.

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REFERENCES
1. Lee JJ, Sundar KM. Evaluation and management of adults with obstructive sleep apnea syndrome. Lung. 2021;199:87-101.
2. Senaratna CV, Perret JL, Lodge CJ, et al. Prevalence of obstructive sleep apnea in the general population: a systematic review. Sleep Med Rev. 2017;34:70-81.
3. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea. Am J Respir Crit Care Med. 2002;165:1217-1239.
4. Grassi G, Quartti-Trevano F, Mancia G. Obstructive sleep apnea, CPAP and arterial hypertension: a cardiologist’s view point. Arch Broncopneumol. 2022;58:461-462.
5. Bhagavan SM, Sahota PK. Sleep Fragmentation and atherosclerosis: is there a relationship? Mol Med. 2021;118:272-276.
6. Kikuta TM, Souza R, Mendel MDR, et al. Association between Berlin questionnaire index and lipid profile. Sleep Sci. 2021;14:158-162.
7. Butt AM, Syed U, Arshad A. Predictive value of clinical and questionnaire based screening tools of obstructive sleep apnea in patients with type 2 diabetes mellitus. Cureus. 2021;13(9):e18009.
8. Cepeda FX, Virmondes L, Rodrigues S, et al. Identifying the risk of obstructive sleep apnea in metabolic syndrome patients: diagnostic accuracy of the Berlin questionnaire. PloS One. 2019;14:e0217058.
9. Sega R, Corrao G, Bombelli M, et al. Blood pressure variability and organ damage in a general population. Hypertension. 2002;39:710-714.
10. Cuspidi C, Facchetti R, Sala C, et al. Normal values of left-ventricular mass: echocardiographic findings from the PAMELA study. J Hypertens. 2012;30:997-1003.
11. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28:e14-e39.
12. Netzer N, Stoohs R, Netzer C, Clark K, Strohl K. Using the Berlin questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med. 1999;131:485-491.
13. Williams B, Mancia G, Spiering W, et al. ESC/ESH guidelines for the management of arterial hypertension. Eur Heart J. 2018;39:3021-3104.
14. Mancia G, Masi S, Palatini P, Tsiofis K, Grassi G. Elevated heart rate as cardiovascular risk in hypertension. J Hypertens. 2021;39:1060-1069.
15. Grassi G, Facchini A, Trevano FQ, et al. Obstructive sleep apnea-dependent and -independent adrenergic activation in obesity. Hypertension. 2005;46:321-325.

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