Use of the online Framingham platform for the evaluation of the cardiovascular risk in diabetes mellitus and systemic arterial hypertension patients in primary health care

Leonardo Hesley Ferraz Durans¹ · Lisa Steffany Pinheiro Pereira¹ · Thamyres da Cruz Miranda¹ · Fabrício Silva Sousa¹ · Geylene Albuquerque Ribeiro² · Adriana Sousa Rêgo² · Tatiana Cristina Fonseca Soares de Santana¹ · Patrícia Rodrigues Ferreira¹ · Maria Cláudia Gonçalves³ · Ilana Mirian Almeida Felipe da Silva² · Fabrício Brito Silva³ · Daniela Bassi-Dibai¹,²

Received: 1 July 2020 / Accepted: 26 November 2020 / Published online: 7 January 2021
© Research Society for Study of Diabetes in India 2021

Abstract
Background Cardiovascular disease (CVD) is influenced by several factors. In this context, identifying cardiovascular risk (CVR) may contribute to taking action on modifiable risk factors especially in the population with diabetes mellitus (DM) and systemic arterial hypertension (SAH) in primary health care, where laboratory tests are often difficult to access.
Objective The objective of this study was to evaluate the risk of developing cardiovascular disease in the next 10 years in diabetic and hypertensive primary healthcare patients using the online Framingham platform.
Material and methods This is a cross-sectional study. Were evaluated 246 individuals by medical records, from the Center for Specialized Medicine in Diabetes and Hypertension. The Framingham Heart Study online table was used to assess CVR. The variables collected were blood pressure and body circumferences.
Results Sixty-five (26.42%) were diabetic, 67 (27.23%) were hypertensive, and 114 (46.34%) had DM and SAH. Significant values of CVR were observed in the SAH (19.76%) and DM + SAH (33.79%) groups when compared with the DM group (10.68%).
Conclusion In conclusion, the online Framingham platform tool was able to identify the CVR. Additionally, SAH seems to be a more powerful factor to increase CVR, and the coexistence of DM and SAH increases this risk even more.

Keywords Diabetes mellitus · Systemic arterial hypertension · Cardiovascular risk · Risk score calculator

Introduction
Diabetes mellitus (DM) is now considered a worldwide endemic, especially in poorer countries [1]. The literature is robust in showing the link between DM and cardiovascular disease (CVD). Thus, DM is expected to be a major driver of CVD worldwide [2]. Systemic arterial hypertension (SAH) is a clinical condition characterized by increased pressure levels and affects the world population significantly [3]. Its prevalence has steadily increased even with the expanded use of antihypertensive drugs. It is already well established in the literature that hypertension is associated with increased all-cause mortality, independent of other risk factors [4].

SAH, DM, and dyslipidemia are important collective health problems in Brazil, due to their high prevalence, the acute and chronic complications that they give rise to, and because they represent risk factors associated with CVD, conditioning high morbidity and mortality rates [5], social and economic costs arising from the use of health services. Together, DM and SAH are the major contributors to the global burden of disease [6].
In an attempt to assess and predict long-term cardiac risk, vascular age has been shown to be a valuable indicator/predictor [7]. In this context, as the vascular age increases, so does the progression of arterial stiffness [7]. Some well-known factors such as age [8], DM [9], and SAH [10] are associated with vascular aging, sometimes prematurely.

Thus, the aim of this study was to establish the risk of developing cardiovascular disease in the next 10 years in diabetic and hypertensive patients, especially in primary health care, as access to laboratory tests is often extremely difficult. Additionally, we further assessed the impact of coexistence of DM and SAH over 10 years, as we hypothesized that this coexistence would increase this cardiovascular risk when compared with the population with the disease alone. Finally, as secondary objectives, we evaluated the vascular age in these conditions in isolation (DM or SAH) and in their coexistence (DM + SAH), as well as making correlations between the waist, wrist, neck and calf circumferences, and CVR and vascular age.

Methods

Study design and ethical aspects

This is a retrospective, descriptive, quantitative study aiming to analyze the profile of patients enrolled at the Center for Specialized Medicine in Diabetes and Hypertension in São Luís (Maranhão, Brazil). The inclusion criteria adopted for the medical records were individuals of both genders, aged between 30 and 74 years, with a medical diagnosis of DM and SAH, undergoing treatment for both, diagnosed within a maximum of 5 years. Medical records with missing, unreadable, or erased data were excluded.

Analysis of medical records

The data contained in the medical records were recorded in an identification form containing the following items: name, gender, age, medical diagnosis, and time since diagnosis, medications in use, systolic blood pressure (SBP), diastolic blood pressure (DBP), height, weight, body mass index (BMI), perimeter (abdominal, right wrist, right ankle, right calf), and capillary blood glucose.

Cardiovascular risk assessment

To assess cardiovascular risk, we used the online platform Gencardio based on the study conducted by D’Agostino et al. [11], available on The Framingham Heart Study website: https://www.framinghamheartstudy.org/fhs-risk-functions/cardiovascular-disease-10-year-risk. In this platform is calculated, through multivariate regression using some predictors, the risk of the individual developing cardiovascular disease within the next ten years. It is noteworthy that the use of this tool is encouraged in the strategy for modifying risk factors, as well as for calculating the estimate of vascular or cardiometabolic age by the Brazilian Society of Cardiology [12].

The Gencardio platform was fed with the following data: gender (male or female); age (between 30 and 74 years), SBP, if being treated for hypertension (yes or no), if you were a smoker (yes or no), if you had diabetes (yes or no), and BMI (15 to 50 kg/m²). After the data entry, through the calculations performed by the software, it was possible to obtain the percentage of CVR and the vascular age in years.

Statistical analysis

Histograms were created to test data normality, and all outcomes had normal distributions. The data were expressed as mean and standard deviation (SD) values. Multivariate analysis of variance (MANOVA) analysis was used, and groups that differed significantly were compared at a pair level using the Tukey test. Pearson’s correlation coefficient was used to correlate waist, wrist, ankle, and calf circumferences with CVR and vascular age. The SPSS program, version 17.0 (Chicago, IL, USA), was used for all analyses, with a 5% significance level established for comparisons.

Results

A total of 2113 medical records were reviewed. After applying the eligibility criteria, the medical records of 246 patients were included, 145 (58.94%) women and 101 (41.05%) men, with a medical diagnosis of DM and hypertension. Data were obtained by reviewing the medical records of patients treated at the service between 2017 and 2018.

Differences in the sample diagnoses showed that 65 (26.42%) of the patients were diabetic, 67 (27.23%) were hypertensive, and 114 (46.34%) were associated with diabetes and hypertension.

Table 1 presents the sample characterization data, according to the division by group. It was observed that age, weight, BMI, SBP, DBP, waist, and wrist circumferences were significantly higher (p < 0.05) in the SAH and DM + SA groups when compared with the DM group. In addition, as expected, blood glucose was significantly (p < 0.05) elevated in the DM and DM + SAH groups when compared with the SAH group.
Data regarding CVR and vascular age are presented in Table 2. For CVR, significantly ($p < 0.05$) higher values were observed in the SAH and DM + SA groups when compared with the DM group. However, the DM + SAH group also presented significantly higher ($p < 0.05$) CVR values than the SAH group. Regarding vascular age, the DM + SAH group presented values significantly ($p < 0.05$) higher than the SAH and DM group.

The correlations of waist, wrist, ankle, and calf circumferences with CVR and vascular age are shown in Table 3. Significant ($p < 0.05$), positive, and weak magnitude ($0.140 \leq r \leq 0.367$) correlations were observed between the abdominal and wrist circumferences and the CVR and vascular age.

The drugs used by the patients are described in Table 4, showing the greater use of biguanides (70.76%) and sulfonylureas (44.66%) in the DM group; angiotensin antagonists (76.62%), and diuretics (31.34%) in the SAH group; and biguanides (81.57%), sulfonylureas (58.77%), angiotensin antagonists (55.26%), and diuretics (28.94%) in the DM + SAH group.

| Table 1 | Sample characterization according to the groups |
|---------|------------------------------------------------|
| Variables | All ($n = 246$) | DM ($n = 65$) | SAH ($n = 67$) | DM + SAH ($n = 114$) |
| Age (years) | 54.10 (11.84) | 48.69 (11.80) | 54.61 (11.53)$^a$ | 56.88 (11.08)$^a$ |
| Gender (female) | 145 (58.94%) | 41 (63.07%) | 34 (50.74%) | 70 (61.40%) |
| Height (m) | 1.56 (0.09) | 1.55 (0.08) | 1.57 (0.09) | 1.55 (0.08) |
| Weight (kg) | 69.57 (15.88) | 62.41 (11.64) | 73.27 (17.39)$^a$ | 71.47 (15.89)$^a$ |
| BMI (kg/m²) | 28.42 (5.84) | 25.80 (3.59) | 29.47 (7.36)$^a$ | 29.29 (5.44)$^a$ |
| Glycemia (mg/dL) | 187.06 (92.14) | 223.66 (107.85) | 111.40 (23.46)$^a, b$ | 210.66 (82.28) |
| SBP (mmHg) | 133.25 (26.40) | 112.15 (7.80) | 140.74 (27.54)$^a$ | 140.87 (26.19)$^a$ |
| DBP (mmHg) | 81.74 (13.29) | 74.61 (13.47) | 87.16 (13.55)$^a$ | 86.22 (12.36)$^a$ |

| Body composition |
|-------------------|
| Underweight | 8 (3.3%) | 2 (3.08%) | 2 (2.99%) | 4 (3.51%) |
| Eutrophic | 58 (23.6%) | 26 (40%) | 13 (19.40%) | 19 (16.66%) |
| Overweight | 100 (40.7%) | 29 (44.61%) | 28 (41.79%) | 43 (37.72%) |
| Obese I | 53 (21.5%) | 8 (12.31) | 12 (17.91%) | 33 (28.95%) |
| Obese II | 19 (7.7%) | 0 | 8 (11.94%) | 11 (9.65%) |
| Obese III | 8 (3.3%) | 0 | 4 (5.97%) | 4 (3.51%) |

| Circumferences (cm) |
|---------------------|
| Abdominal | 95.36 (12.29) | 88.93 (10.06) | 96.15 (13.47)$^a$ | 98.57 (11.38)$^a$ |
| Wrist | 16.91 (1.58) | 16.30 (1.15) | 17.11 (1.41)$^a$ | 17.14 (1.79)$^a$ |
| Ankle | 21.59 (3.16) | 20.91 (1.76) | 22.53 (3.79)$^a$ | 21.43 (3.27) |
| Calf | 34.61 (4.58) | 33.43 (3.52) | 35.49 (5.64)$^a$ | 34.76 (4.31) |

Table 2 | Prediction of cardiovascular risk and vascular age according to group division |
|------------------|-------------------------------|----------------|-------------|----------------|
| Cardiovascular risk prediction | All ($n = 246$) | DM ($n = 65$) | SAH ($n = 67$) | DM + SAH ($n = 114$) |
| Cardiovascular risk (%) | 23.86 (19.11) | 10.68 (8.88) | 19.76 (15.93)$^b$ | 33.79 (19.75)$^a$ |
| Vascular age (years) | 72.13 (13.80) | 66.69 (14.75) | 67.79 (13.41)$^b$ | 80.00 (8.33)$^a$ |

DM: diabetes mellitus; SAH: systemic arterial hypertension; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure

BMI according to Word Health Organization: <18.5 underweight; 18.5–24.9 Normal or eutrophic; 25–29.9 Overweight or pre-obesity; 30–34.9 Obesity class I, 30–39.9 Obesity class II and, ≥40.0 Obesity class III

$^a$ Differs from DM group ($p < 0.05$, MANOVA post hoc Tukey);

$^b$ Differs from DM + HAS group ($p < 0.05$, MANOVA post hoc Tukey)
Discussion

The main findings of this study showed (i) SAH, even if controlled, seems to be a major risk factor for the onset of cardiovascular disease when compared to DM alone; ii) the coexistence of DM and SAH significantly increases the CVR; iii) vascular age is higher when DM and SAH coexist; iv) the higher the abdominal and wrist circumference, the greater the CVR and vascular age.

SAH and CVR

Recently, a systematic review was conducted by Petrie et al. [13] in order to clarify the pathophysiological mechanisms of vascular complications and concluded that DM is associated with a higher CVR, which is increased when there is a coexistence of SAH. Our findings showed that being hypertensive results in a higher CVR (7.05% increase) than DM itself. However, our study agrees to show that the coexistence of both diseases significantly increases CVR when compared with the isolated presence of DM or SAH.

In addition, results from the Trial Evaluating Cardiovascular Outcomes with Sitagliptin—TECOS trial—show that, although SAH is one of the leading modifiable causes of cardiovascular events in adults with diabetes, it remains with suboptimal values worldwide. In addition, around 40% of individuals with high CVR have SBP values of ≥140 mmHg, which corroborates our study [14].

Table 3  Correlation of abdominal, wrist, ankle and calf circumferences with cardiovascular risk and vascular age

| Circumferences (cm) | Cardiovascular risk | Vascular age |
|---------------------|---------------------|--------------|
| Abdominal           | $r = 0.367, p < 0.001^a$ | $r = 0.314, p < 0.001^a$ |
| Wrist               | $r = 0.323, p < 0.001^a$ | $r = 0.140, p = 0.015^a$ |
| Ankle               | $r = 0.102, p = 0.112$ | $r = 0.012, p = 0.844$ |
| Calf                | $r = 0.037, p = 0.563$ | $r = 0.047, p = 0.438$ |

$^a$ Significant correlation ($p < 0.05$, Pearson correlation coefficient)

Table 4  Medicines used according to groups

| Medicines                  | DM ($n = 65$) | SAH ($n = 67$) | DM + SAH ($n = 114$) |
|----------------------------|---------------|----------------|----------------------|
| **Oral antidiabetics**     |               |                |                       |
| Sulfonylureas              | 29 (44.66%)   | 0              | 67 (58.77%)          |
| Biguanides                 | 46 (70.76%)   | 0              | 93 (81.57%)          |
| Antidislipidemic           | 11 (16.92%)   | 18 (29.84%)    | 35 (30.7%)           |
| Insuline                   | 16 (24.61%)   | 0              | 12 (10.52%)          |
| Thiazolidinediones         | 0             | 0              | 2 (1.75%)            |
| Combination                | 9 (13.84%)    | 0              | 5 (4.38%)            |
| **Antihypertensives**      |               |                |                       |
| Diuretics                  | 0             | 21 (31.34%)    | 33 (28.94%)          |
| Beta blockers              | 0             | 14 (20.89%)    | 14 (12.28%)          |
| Angiotensin antagonist     | 0             | 50 (74.62%)    | 63 (55.26%)          |
| Calcium blocker            | 0             | 10 (14.92%)    | 16 (14.03%)          |
| ACE inhibitor              | 0             | 4 (5.97%)      | 15 (13.15%)          |
| Antiplatelet/Anticoagulant| 0             | 17 (25.37%)    | 13 (11.4%)           |
| Cardioglycosides           | 0             | 1 (1.49%)      | 1 (0.87%)            |
| Combination                | 0             | 1 (1.49%)      | 4 (3.5%)             |

**DM** diabetes mellitus, **SAH** systemic arterial hypertension, **ACE** angiotensin-converting-enzyme

Data presented in absolute values (%). Combination: Patients taking more than one drug for the same purpose
events in patients with DM [19]. However, the findings of Bergmark et al. partially corroborate the findings of this study, as the authors found a persistent association between subclinical myocardial injury and risk of myocardial infarction in diabetic patients with elevated CVR [19].

A study conducted by Böhm et al. aimed to evaluate the relationship of blood pressure in the CVR of individuals with and without DM and found that in patients without DM, high blood pressure, i.e., systolic > 160 or diastolic > 90 mmHg, was associated with higher CVR and death, and levels considered low/normal (< 120 or < 70 mmHg) had the same cardiovascular outcome, except for stroke and death, whereas patients with DM have higher risks across the full range of blood pressure consistently [20]. This fact was not identified in our study since patients with only DM had blood pressure within the normal limits.

**Vascular age and CVR**

Arterial aging is characterized by increased arterial stiffness, which can be assessed by pulse wave velocity [21], which is considered the gold standard for such diagnostic purposes [22]. On the other hand, it is understood that performing this exam in an accessible manner is still a distant reality due to its high cost [23]. From this perspective, other tools for calculating vascular age have been investigated and indicated in an attempt to fill this gap, such as the tool used in this study [12].

**Body circumferences and CVR**

The literature is robust with regard to abdominal circumference showing a positive correlation with negative cardiovascular outcomes [24, 25]. According to a study conducted by Rezende et al., which corroborates our findings, overweight, especially above-expected abdominal circumference, has a major impact on increased CVR, as shown by the positive correlation between the abdominal circumference and CVR.

Currently, another anthropometric measure, wrist circumference, has been suggested to be associated with insulin resistance in both obese children and adolescents, as reported by a study conducted by Capizzi et al. [26].

In this context, an interesting cohort study conducted by Noudeh et al. aiming to analyze whether wrist circumference was associated with the incidence of DM, independently of other adiposity measures such as BMI or waist circumference of an Iranian adult population, found that in a 20-year-old population, wrist circumference was significantly associated with DM and its risk factors in both sexes [27]. The results observed in the present study reinforce the findings of Noudeh et al. since a positive correlation was found between wrist circumference and CVR; however, it should be remembered that the individuals in this study already had a clinical diagnosis of DM. Thus, wrist measurement could also be considered an additional predictor for the development of CVD in individuals with a definite diagnosis of DM and SAH, especially in the primary care as is the case in our study.

This study has some limitations that should be cited, such as the lack of complementary laboratory tests (e.g., glycated hemoglobin). The lack of correct completion of medical records was another limiting factor, which we tried to remedy by excluding incomplete medical records. The DM group had a BMI statistically lower than the others, which is an important limitation. However, all groups had mean BMI within the same category, i.e. overweight (25 to 29.9 kg/cm²).

**Conclusion**

In view of the above, we can conclude that SAH seems to be a more powerful factor for increased CVR, and the coexistence of DM + SAH further increases this risk. Online CVR prediction tools should be encouraged especially in the primary healthcare. Thus, secondary prevention measures could be adopted to prevent the coexistence of a more severe cardiovascular disease in these patients. However, the groups have heterogeneity and differences in some clinical aspects.

**Acknowledgments** This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior—Brasil (CAPES)—Finance Code 001.

**Compliance with ethical standards**

**Conflict of interest** The authors declare they have no conflicts of interest.

**Ethical consideration** This study was submitted to the research ethics committee of the Ceuma University (São Luís, Brazil) in accordance with the Declaration of Helsinki and approved under protocol number 2.524.515.

**References**

1. Bukhman G, Bavuma C, Gishoma C, Gupta N, Kwan GF, Laing R, et al. Endemic diabetes in the world’s poorest people. Lancet Diabetes Endocrinol. 2015;3:402–3.
2. Kengne AP, Turnbull F, MacMahon S. The Framingham study, diabetes mellitus and Cardiovascular disease: turning Back the clock. Prog Cardiovasc Dis. 2010;53:45–51.
3. Corrigendum to: 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J [Internet]. Narnia; 2019 [cited 2019 May 23];40:475–475. Available from: https://academic.oup.com/eurheartj/article/40/5/475/5137110
4. Wermelt JA, Schunkert H. Management der arterial Hypertension. Herz [Internet]. 2017 [cited 2019 may 23];42:515–526. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28555286.
5. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Prospective studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet (London, England)
5. Viera AJ. Screening for hypertension and lowering blood pressure for prevention of cardiovascular disease events. Med Clin North Am [Internet]. Elsevier; 2017 [cited 2019 May 21];101:701–712. Available from: https://www.sciencedirect.com/science/article/pii/S002512517300263?via%3Dihub
6. Thijssen DHJ, Carter SE, Green DJ. Arterial structure and function in vascular ageing: are you as old as your arteries? J Physiol [Internet]. Wiley-Blackwell; 2016 [cited 2019 May 27];594:2275–2284. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26140618.
7. Kucharska-Newton AM, Stoner L, Meyer ML. Determinants of Vascular Age: An Epidemiological Perspective. Clin Chem [Internet]. 2019 [cited 2019 May 27];54:108–118. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29359170.
8. Denison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension [Internet]. 2018 [cited 2019 Jul 12];71:1269–1324. Available from: https://doi.org/10.1161/HYP.0000000000000666
9. Bergmark BA, Scirica BM, Gabriel Steg P, Fanola CL, Guzmí, Y, Mosenzon O, et al. Blood pressure and cardiovascular outcomes in patients with diabetes and high cardiovascular risk. [cited 2019 Jul 4]; Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6012971/pdf/ehx809.pdf
10. Scuteri A, Morrell CH, Ortu M, Sattró PK, Ferreli LAP, et al. Longitudinal Perspective on the Conundrum of Central Arterial Stiffness, Blood Pressure, and Aging. Hypertension [Internet]. 2014 [cited 2019 Jul 13];64:1219–1227. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25223210.
11. Kim H-L, Kim S-H. Pulse Wave Velocity in Atherosclerosis. Front Cardiovasc Med [Internet]. Frontiers; 2019 [cited 2019 Jul 13];6:41. Available from: https://doi.org/10.3389/fcmv.2019.00041/full
12. Huxley R, Mendis S, Zheleznyakov E, Reddy S, Chan J. Body mass index, waist circumference, and waist:hip ratio as predictors of cardiovascular risk—a review of the literature. Eur J Clin Nutr [Internet]. Nature Publishing Group; 2010 [cited 2019 Jun 18];64:16–22. Available from: http://www.nature.com/articles/jcn200968
13. Cameron AJ, Magliano DJ, Söderberg S. A systematic review of the impact of including both waist and hip circumference in risk models for cardiovascular diseases, diabetes and mortality. Obes Rev [Internet]; 2013 [cited 2019 Jun 18];14:86–94. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23072327.
14. Capizzi M, Leto G, Petrone A, Zampetti S, Papa RE, Osimani M, et al. Wrist circumference is a clinical marker of insulin resistance in overweight and obese children and adolescents. Circulation [Internet]. Lippincott Williams & WilkinsHagerstown, MD; 2011 [cited 2019 Jul 13];123:1757–1762. Available from: https://doi.org/10.1161/CIRCULATIONAHA.110.1227.
15. Jahangiri Nousheh Y, Sadjadi S, Zaremoradi R, et al. Wrist circumference as a novel predictor of diabetes and prediabetes: results of cross-sectional and 8.8-year follow-up studies. J Clin Endocrinol Metab [Internet]. Narnia; 2013 [cited 2019 Jul 13];98:777–784. Available from: https://doi.org/10.1210/jc.2012-2416