

TITLE:

Hydra, a Computer-Based Platform for Aiding Clinicians in Cardiovascular Analysis and Diagnosis

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SUMMARY:

This article presents a protocol based on Hydra — a web-based system for clinical decision support that integrates a full and detailed set of functionalities and services required by physicians for complete cardiovascular analysis, risk assessment, early diagnosis, treatment, and monitoring over time.

ABSTRACT:

Cardiovascular diseases (CVDs) are the leading cause of death throughout the world. The total risk of developing CVD is determined by the combined effect of different cardiovascular risk factors (e.g., diabetes, raised blood pressure, unhealthy diet, tobacco use, stress, etc.) that commonly coexist and act multiplicatively. Most CVDs can be prevented by an early identification of the highest risk factors and an appropriate treatment. The stratification of cardiovascular risk factors involves a wide range of parameters and tests that specialists use in their clinical practice. In addition to cardiovascular (CV) risk stratification, ambulatory blood pressure monitoring (ABPM) also provides relevant information for diagnostic and treatment purposes. This work presents a list of protocols based on the Hydra platform, a web-based system for clinical decision support which incorporates a set of functionalities and services that are required for complete cardiovascular analysis, risk assessment, early diagnosis, treatment and monitoring of patients

over time. The program includes tools for inputting and managing comprehensive patient data, organized into different checkups to track the evolution over time. It also has a risk stratification tool to compute a CV risk factor based upon several risk stratification tables of reference. Additionally, the program includes a tool that incorporates ABPM analysis and allows the extraction of valuable information by monitoring blood pressure over a specific period of time. Finally, the reporting service summarizes the most relevant information in a set of reports that aid clinicians in their clinical decision-making process.

INTRODUCTION:

Cardiovascular diseases (CVDs) are a group of disorders of the circulatory system that constitute the leading cause of disability and premature death throughout the world^{1,2}. According to the World Health Organization (WHO), an estimated 17.7 million people died from CVDs in 2015, representing 31% of all global deaths^{1,2}. There are many risk factors for CVDs, including behavioral factors such as tobacco use, an unhealthy diet, harmful use of alcohol and inadequate physical activity as well as physiological factors, including raised blood pressure (hypertension), high cholesterol or elevated blood glucose, among others^{2,3}. Hypertension represents a major risk factor for premature cardiovascular disease, being responsible for a high level of cardiovascular morbidity and mortality^{4,5}. Furthermore, it is estimated that the incidence of hypertension among adults in developed countries is almost 40%^{6,7,8}. However, it remains widely undetected, undertreated and poorly controlled^{3,4}.

CVD is a major public health problem which imposes a significant economic burden on any given health-care system⁶. Early identification of the highest cardiovascular risks and appropriate treatment can prevent clinical events and premature deaths^{4,5}. Hence, there are noticeable health and economic gains attached to comprehensively and thoroughly tracking all these factors. The total risk of developing a CVD is determined by the combined effect of cardiovascular risk factors^{2,4,5}, which commonly coexist and act multiplicatively. Therefore, a total-risk approach is advisable for early detection, as well as for clinical decision-making on the intensity of preventive interventions. Thus, morbidity, early mortality and disability could be reduced and the quality of life could be improved in individuals with an elevated total CVD risk².

The diagnosis of CVDs is determined by the analysis of a wide range of parameters that are gathered by different procedures used by physicians in their clinical practice. The assessment of these parameters allows the computation of a total CV risk factor which is useful for diagnostic and treatment purposes^{2,4,5}. In addition to the stratification of CV risks, ambulatory blood pressure monitoring (ABPM)⁹ also provides valuable information. The ABPM test allows the tracking of the patient's blood pressure (BP) during their daily routine, avoiding the influence of the clinical setting (white coat syndrome). Thus, a reliable set of measurements is obtained, allowing the extraction of additional information that supports the clinical decision-making process.

Therefore, the analysis of the cardiovascular system involves a large amount of data, entailing a tedious and time-consuming task that complicates diagnosis and treatment prescription. In this regard, the availability of a patient's full profile that gathers all the required data together with a

set of automated services to extract the necessary information would be a significant improvement to guide clinicians in their decision-making process. Apart from this, the availability of an accessible platform that centralizes all patient information not only enables collaboration among different specialists from different locations but also allows discussion of debatable cases and provides reliable diagnoses.

In recent years, the use of computer-based applications and telemedicine has increased considerably, playing an important role in improving public health and welfare in all sectors of the population. This is due to their ability to extract relevant and useful information for the early diagnosis and treatment of several diseases¹⁰. The use of these tools improves the quality of health-care services, thus conveniently and reliably satisfying patient demand as well as reducing costs¹¹. As a reference, the number of global imaging-based procedures has risen considerably, given the increasing availability of medical equipment and more sophisticated capture devices. Therefore, Lundberg et al.¹² proposed a telemedicine tool to assess digital image quality and agreement between examiners in the field of the otorhinolaryngology. Ortega et al.¹³ developed SIRIUS, a computer-aided diagnosis framework for the analysis of retinal images. Novo et al.¹⁴ also presented their platform for the analysis of retinal microcirculation in combination with carotid macrocirculation.

With regard to CV assessment, there has been a steady increase in the number of tools available throughout the years. Some of the utilities are designed to predict cardiovascular disease risk — such as the tool proposed by Paredes et al.¹⁵ — or to calculate risk online by implementing the algorithm proposed by Goff et al.¹⁶ according to a guideline on the assessment of cardiovascular risk to calculate the 10-year risk of heart disease. Other systems are designed to be used with mobile phones, such as the proposal of Sufi et al.¹⁷ that identifies diseases from body sensors, the device designed by Lin et al.¹⁸ for tracking the electrocardiogram in order to detect the presence of abnormal rhythms and send an alarm, the app from Lee et al.¹⁹ for monitoring breathing and heart rate values while a person exercising or the application implemented by Kang and Park²⁰ to manage raised blood pressure on the basis of clinical guidelines.

The available utilities are mainly designed to satisfy patient demand in specific scenarios. On the other hand, this article describes a protocol based on Hydra²¹, a platform focused on the analysis of the cardiovascular system, that is designed entirely to support specialists in their clinical decision-making process. This tool incorporates a set of functionalities and services that physicians require for reliable cardiovascular analysis including risk assessment, early diagnosis, treatment prescription and the monitoring of patients over time. Therefore, there is a tool for the input and management of patient data recorded in different checkups. Then, a risk stratification tool automatically provides a CV risk factor based on different risk stratification tables of reference. In addition to this, the ABPM analysis tool allows the extraction of valuable information from the analysis of blood pressure recordings over a specific period of time. Finally, the most relevant information is summarized in a set of reports that guide clinicians in diagnosis and proper treatment prescription. In this way, the described protocol leads to an improvement in complete cardiovascular analysis supporting a reliable diagnosis and proper treatment.

Furthermore, the presented platform allows collaboration among experts, thereby promoting clinical research.

PROTOCOL:

All procedures were conducted under institutionally approved protocols with patient consent.

1. Patient and checkup registration

NOTE: See **Figure 1**.

1.1 Go to <http://www.varpa.org/Hipertension/> using any modern web browser.

1.2. Use an existing account associated with a doctor to **Log In** to the Hydra web tool.

1.3. Fill in the patient registration form including patient code, date of birth, gender and ethnicity to register a new patient. Click on the **include** button to fill in the family background of premature CVDs. Click on the **Next** button to move forward to introduce the first checkup.

NOTE: These global parameters are included in patient enrollment and the information added from here relates to a specific checkup.

1.4. Add a new checkup.

NOTE: The input data is organized in thematic blocks. Each block includes the option to be hidden or visible. If all the information of a block is unknown, use the hidden option. Keep the option **NR/DK** (no response/do not know) in the fields that do not match any case. See **Figure 2**.

1.4.1. Fill in the checkup date; the current date used by default.

1.4.2. Fill in the block corresponding to patient habits such as smoking, exercise, diet, etc.

1.4.3. Fill in the block corresponding to precedents of cardiovascular illness such as cardiopathy, acute aortic dissection, strokes, etc.

1.4.4. Fill in the block corresponding to concomitant illnesses such as diabetes, obesity, nephropathy, etc.

1.4.5. Fill in the block corresponding to urological records with the information related to erectile malfunction, prostatic hyperplasia, etc.

NOTE: This block is enabled in the checkup form when the gender of the patient is male.

1.4.6. Fill in the block corresponding to gynecological records with the information related to hypertension in pregnancy, menopause, the age of menopause, surgical menopause, etc.

NOTE: This block is enabled in the checkup form when the gender of the patient is female.

1.4.7. Fill in the block corresponding to anti-hypertensive treatment taken before the checkup date including the treatment type, the schedule, and the dose.

1.4.8. Fill in the block corresponding to treatments that can alter blood pressure such as vasoconstrictors, oral contraceptives, corticosteroids, etc.

1.4.9. Fill in the block corresponding to any other treatments such as fibrates, statins, insulin, etc.

NOTE: The options to input the timetable, dose or type are only enabled when each specific treatment is selected.

1.4.10. Click on the **Next** button to move forward to the second checkup form relating to the physical examination and clinical analysis.

NOTE: See **Figure 3**.

1.4.11. Fill in the block corresponding to the physical examination with the information related to height, weight, circumference of the dominant arm, etc.

NOTE: The body mass index and the waist height index are automatically computed from the previous data.

1.4.12. Fill in the block corresponding to blood pressure recordings such as systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse, including 1 measurement standing and 3 measurements sitting. Check the boxes related to abdominal murmurs, carotid murmur, etc.

NOTE: The mean of the 3 repetitions of sitting blood pressure measurements is automatically computed.

1.4.13. Fill in the block corresponding to the ABPM recording. Upload the ABPM file and complete the information related to the time during which the patient wore the monitor such as the hours and quality of sleep, the time of going to bed and waking up, etc.

NOTE: The ABPM upload is mandatory for the block related to ABPM information to be included. If there is no ABPM file available, click on the hide button.

1.4.14. Fill in the block corresponding to biological/analytical recordings with the information related to blood analysis such as glycemia, creatinine, ferritin, microalbuminuria, etc.

NOTE: The standard units for the parameters are indicated on the checkup form, as reference.

1.4.15. Fill in the block corresponding to the electrocardiogram recording with the information related to the different wave intensities, arrhythmia, ischemic cardiopathy, etc.

1.4.16. Fill in the block corresponding to the echocardiogram recording with the information related to the interventricular septum, left ventricle diameter in systole, posterior wall of the left ventricle, etc.

1.4.17. Fill in the block corresponding to other measurements such as pulse wave velocity, carotid stenosis, ankle-arm index, etc.

1.4.18. Click on the **End** button to record the checkup associated with the corresponding patient on the platform.

NOTE: The platform moves forward to the checkup page that includes all the introduced data. See **Figure 4**.

1.4.19. Click on the **Edit** button to add new information or update the introduced data throughout the checkup forms. Click on the **End** button to go back to the checkup page.

1.4.20. Click on the **Implemented treatment** button to move forward to the form and prescribe any specific treatment.

1.4.21. Fill in the block corresponding to anti-hypertensive treatment including the dose, the schedule and the type of the prescribed treatment.

1.4.22. Fill in the block corresponding to treatments that can affect blood pressure such as vasoconstrictors, oral contraceptives, corticosteroids, etc.

1.4.23. Fill in the block corresponding to other treatments such as fibrates, statins, insulin, etc.

1.4.24. Click on the **Definitive report** button to generate the final report. It proceeds to the checkup report including all the introduced data and the prescribed treatment.

1.5. Update patient profile and perform checkup management.

1.5.1. Click on the **Find patient** link on the main menu bar and insert the patient code, or press the **List patients** link and select the patient code to proceed to the profile of a registered patient.

1.5.2. Click on the **Update** button to revise and update any patient information (except the patient code, which is fixed) in the patient profile.

1.5.3. Click on the **Revise checkup** link to access the checkup report (see step 4.2).

1.5.4. Click on the **Smart report** link to access a brief checkup overview (see step 4.3).

1.5.5. Click on the **ABPM report** link to access an overview of the ABPM results (see step 4.4).

1.5.6. Click on the **Edit** link to add new information or modify the information introduced in the
checkup.

NOTE: This option is available only before the generation of the definitive report.

1.5.7. Click on the **New checkup** button to add a new checkup for the patient.

NOTE: Consecutive checkups are automatically prefilled with the information details that were
included in the previous revision. See **Figure 5**.

2. Risk stratification tables

NOTE: The risk stratification service provides an automatic computation of the CV risk factor
based upon various risk stratification tables that are recommended in the guidelines of the
European Society of Hypertension/European Society of Cardiology (ESH/ESC)²². For each of the
tables, the CV risk factor is computed and recorded based upon various parameters that are
uploaded in the patient profile throughout the steps of the checkup data input. The higher or
lower importance of each of the tables in the analysis is provided by the specialist while ensuring
that each designed stratification table pays special attention to the specific conditions of the
patient.

2.1. Click on the **Find patient** link and insert the patient code or click on the **List patients** link and
select the patient code for a patient with existing registered checkups.

2.2. From the list of checkups, click on the **Revise checkup** link to access the checkup report and
go to the block of risk stratification tables.

2.3. Click on the **ESH/ESC table** link to access the table page. Check the highlighted cell to get the
qualitative level of cardiovascular risk. Check the recommendations and possible
antihypertensive treatment related to the resulting risk. Click on the **Go back** link to access the
general checkup report.

NOTE: This decision table uses the SBP and DBP measurements together with several risk factors
and diseases (age, abdominal obesity, dyslipidemia, metabolic syndrome, etc.) to provide the CV
risk factor as well as recommendations or treatment²³.

2.4. Click on the **MS table** link to access the Metabolic Syndrome (MS) table page. Check the
presence of MS on the basis of the Adult Treatment Panel (ATP) III criterion. Check the presence
of MS on the basis of the International Diabetes Fund (IDF) 2005 criterion. Click on the **Go back**
link to access the general checkup report.

NOTE: This table uses the information related to abdominal obesity, triglyceridemia, c-HDL, BP and fasting glucose²⁴. ATP III criterion indicates the presence of MS if 3 of the above measures are outside the tolerance levels. According to IDF 2005 criterion, MS is determined by the presence of abdominal obesity together with 2 of the other measures outside the tolerance levels.

2.5. Click on the **Score table** link to access the Systematic Coronary Risk Evaluation (SCORE) table page. Check the highlighted cell to obtain the 10-year risk of fatal cardiovascular events. Check the color of the highlighted cell in the legend to obtain the qualitative level related to the risk. Click on the **Go back** link to access the general checkout report.

NOTE: This table uses information related to age, gender, SBP, smoking, and cholesterol²⁵.

2.6. Click on the **Framingham table** link to access the table page. Check the highlighted cell in the last table to obtain the 10-year risk of suffering a coronary event (angina, heart attack, with or without symptoms, fatal or not). Click on the **Go back** link to access the general checkout report.

NOTE: This table uses information related to the parameters of age, gender, smoking, diabetes, cholesterol, cholesterol HDL, and BP²⁶. The highlighted cells indicate the contribution of each category to the final risk.

3. ABPM analysis

NOTE: ABPM is a common test that allows the monitoring of the patient's blood pressure throughout their daytime/nocturnal routine⁹. The device selected for recording ABPM measurements (see the **Table of Materials**) is among the few BP monitors that are officially validated by international organizations such as the British Hypertension Society (BHS) or the ESH.

3.1. Put the BP monitor on the patient and check that it is operating properly by taking an initial manual measurement. Instruct the patient on how to obtain the measurements manually before going to sleep and on waking up in order to delimit the day and night recordings.

3.2. After the recording period, remove the BP monitor from the patient and retrieve the ABPM file. Upload the ABMP file to the block of ABPM measurements of an existing or a new checkout related to the patient (step 1.4.13).

NOTE: The monitor remains connected throughout a period of time (usually 24h or 48h) and the measurements are regularly recorded at predefined intervals (typically 15 or 30 minutes).

3.2. Perform ABPM analysis.

3.2.1. Click on the **Find patient** link and insert the patient code, or click on the **List patients** link and select the patient code of a patient with any registered checkout containing ABPM data.

3.2.2. Click on the **Revise checkup** link to access the checkup report and go to the block of ABPM analysis.

3.2.3. Click on the **ABPM** link to access the ABPM information display.

3.2.4. Check the rate of valid records in the general information section to ensure that the results extracted from the ABPM file are reliable.

3.2.5. Check the information regarding the period of time during which the patient wore the monitor such as the number of hours and quality of sleep, the time of going to sleep and waking up, etc.

3.2.6. Check the ABPM map including the graphical representation of all the recordings, such as the SBP, DBP and pulse as well as the areas under or over the maximum normal levels for each measurement.

3.2.7. Click on the buttons for **48h**, **24h (i)** or **24h (ii)** to change the visualization mode for the 48h ABPM files.

3.2.8. Click on the **means** button to switch the visualization mode to an even representation of the measurements.

NOTE: This visualization mode computes each point from the average among consecutive measurements in the raw data.

3.2.9. Check the additional information extracted from the original data such as the means and standard deviations of SBP, DBP, pulse rate and pulse pressure (the difference between SBP and DBP).

3.2.10. Check the parameters regarding BP evolution that were automatically computed by the tool: nocturnal BP drop, sleep thought, pre-waking morning surge and day/night quotient for SBP and DBP measures.

3.2.11. Check the summary table that contains the automatically computed areas under or over the maximum clinically defined thresholds for the nocturnal and diurnal measurements of SBP, DBP, and pulse pressure.

NOTE: Furthermore, the ABPM service also calculates the circadian profile from the relation between the daytime and nocturnal BP²³. This profile allows cardiovascular risks to be determined by analyzing the presence of BP deviations. The smart report (step 4.4) and the ABPM report (step 4.5) contain the information related to the circadian profile.

4. Clinical reports

NOTE: The report service provides a set of reports that gather all the relevant information to support the clinical decision-making process, helping physicians in their clinical practice and promoting collaboration among experts.

4.1. Click on the **Find patient** link and insert the patient code, or click on the **List patients** link and select the code of a patient with any registered checkup.

4.2. Click on the **Revise checkup** link to access the full checkup report which contains all the data recorded during the checkup registration process grouped into the various categories.

4.3. Click on the **ABPM** link to access the data extracted from the ABPM analysis. Click on the specific link of each risk stratification table to review all the information regarding the computation of the risk value. Click on the **Go back** link to return to the patient page.

NOTE: The parameters that are outside their normal levels are shown in red in order to facilitate their identification. In the same way, the **Yes/No** fields are also marked with green or red icons for an intuitive visualization of the normal and pathological cases, respectively.

4.4. Click on the **Smart report** link to access a brief overview of the checkup which only contains essential information.

4.4.1. Check the summary of the risk stratification tables, containing the results that were extracted from each table. Check the ABPM graph included in the final report and click on the **ABPM map** link for further information. Click on the **Go back** link to return to the patient page.

4.5. Click on the **ABPM report** link to access an additional smart report, in this case focused on the ABPM information and results. Check the information corresponding to the ABPM recording such as the statistical measurements extracted from the SBP, DBP, and pulse, the areas over and under the normal values, the circadian profile, etc. Click on the **Go back** link to return to the patient page.

NOTE: The report service provides the option to print the reports or export to standard formats, such as PDF, making it easier to present the report to the patient or use it for discussions with other clinicians.

REPRESENTATIVE RESULTS:

The patient registration described in step 1 is carried out by filling in the form presented in **Figure 1**. Once the user registers a new patient, the application moves forward to introduce the first checkup, which allows the input of comprehensive patient data. **Figure 2** shows a screenshot of the first form of the checkup information. Once the **Next** button is clicked, the application moves forward to the second checkup form presented in **Figure 3**. After clicking on the **End** button, the checkup is recorded by the system (assigned to the patient). Hydra (referred to as the 'platform') moves forward to the register checkup page, including all the introduced data. From this page,

the user can edit the introduced data or access the implemented treatment form shown in **Figure 4**, in order to prescribe the patient a specific treatment. Once the checkup registration process is complete, the platform moves forward to the patient page shown in **Figure 5**, including general data and a list of the submitted checkups.

Besides the centralized management of all the patient data, the platform also provides an automatic computation of the total cardiovascular risk factor based on different risk stratification tables recommended in the standard guidelines of the ESC/ESH. **Figure 6** shows an example of CV risk calculation on the basis of the antihypertensive treatment decision table. In this case, the computed risk appears highlighted in the table, and below, the recommendations and treatment related to this risk are shown. Moreover, the different factors that have contributed to the computation of the risk are listed below. An example of the metabolic syndrome (MS) table is shown in **Figure 7** including the risk that is obtained using two different criteria of reference and the factors involved in these computations. **Figure 8** shows an example of the systematic coronary risk evaluation (SCORE) table indicating the 10-year risk of suffering a coronary event and the list of relevant parameters. Finally, **Figure 9** shows an example of the Framingham table that calculates the risk of severe CVD or a hard event and the contribution of each category to the final risk. This way, the service of risk stratification allows an automatic computation of the CV risk on the basis of different tables of reference as well as the involvement of the different parameters that have contributed to reaching the related risk, for a more detailed analysis by the expert clinician.

In addition to risk stratification, the ABPM also provides valuable information to support the clinical decision-making process. Therefore, given an ABPM file containing recordings over a period of time, the tool can provide automatic computation of additional relevant parameters such as the mean and standard deviation of the different measurements (SBP, DBP and pulse), the area of the records over and under the thresholds that represent the maximum normal values, the circadian profile, etc. **Figure 10** shows a graphical representation of the ABPM map and a table containing the information automatically computed by the ABPM tool.

Finally, the reporting service provides summarized reports that gather all the relevant, available information to help clinicians in their decision-making process and promotes collaboration among experts. An example of some representative parts of a full report is shown in **Figure 11**. Similarly, **Figure 12** and **Figure 13** show examples of a smart report and an ABPM report respectively. All the services the platform has to offer result in improved quality of health-care, while helping physicians perform complete cardiovascular analysis.

FIGURE AND TABLE LEGENDS:

Figure 1. Patient registration form. The form is used to register a new patient and includes various global parameters related to patient enrolment. The block of family precedents of premature cardiovascular illness can be hidden.

Figure 2. First form for checkup registration. This includes information about habits, pathologies and previous treatments grouped into different blocks. All the different blocks have the option to keep them hidden or visible. If all the information of a block is unknown, the user should use the hide the block.

Figure 3. Second form for checkup registration. This covers the physical and clinical analyses, grouped in different blocks. All the different blocks include the option to be hidden or visible. If all the information of a block is unknown, the user should use the hidden option.

Figure 4. Implemented treatment form to prescribe the patient any specific treatment. This includes blocks for anti-hypertensive treatment, treatments that can affect blood pressure and other treatments.

Figure 5. The patient profile page. This includes general data and a list of submitted checkups. From this list, it is possible to access the different reports of each checkup.

Figure 6. Example of an antihypertensive treatment decision table. The highlighted cell represents the computed CV risk and the “Risk/treatment” field details the recommendations related to this risk. Moreover, the contribution of the different factors to the final result is listed below.

Figure 7. Example of an MS risk stratification table on the basis of two different criteria. The conditions that are true for each criterion are highlighted in red. The results for each criterion and the factors involved in these computations are shown on the right-hand side.

Figure 8. Example of a SCORE risk stratification table. The highlighted cell corresponds to the 10-year risk of CVD and the list of risk factors summarizing the parameters that lead to this result.

Figure 9. Example of a Framingham risk stratification table. In each table, the contribution of each category is highlighted in red. The computed risk of severe CV or hard events is shown below the tables as well as the risk factors involved in the calculation.

Figure 10. Example of an ABPM map. This includes the graphical representation and complementary measurements of a 48 h monitor register. Green dots represent manual measurements. The red and blue lines are related to the maximum levels for systolic and diastolic blood pressure, respectively. The filled areas correspond to the intervals that exceed these maximum levels during the day and night.

Figure 11. Example of a full report. This report lists all the introduced data for a specific checkup. Some representative portions are included.

Figure 12. Example of a smart report. This report includes essential information to support the clinical decision-making process. It includes the results of the risk stratification tables, the ABPM map and a list of relevant parameters for diagnosis and treatment.

Figure 13. Example of an ABPM report. It includes the ABPM map and all the information extracted from the ABPM service.

DISCUSSION:

The early identification and monitoring of various cardiovascular risk factors together with an appropriate treatment are critical for the prevention of cardiovascular diseases and premature deaths. In the daily clinical routine, clinicians have to handle large amounts of diverse information to check all the different variables and parameters that affect the circulatory system. Hence, it is a tedious and time-consuming task that complicates diagnosis and treatment prescription.

The proposed protocols allow a complete analysis of the cardiovascular system. These protocols include the input of all data related to cardiovascular analysis which are recorded in a full patient profile and organized into different checkups throughout time. The centralized management of these data together with the various services provided by the platform facilitates the clinical decision-making process as well as information interchange between experts. The various services included on the platform were designed and implemented considering the needs and preferences of expert clinicians in order to incorporate all the necessary tools in the best possible way for a comfortable professional use. This way, the checkup service allows the recording of comprehensive patient data, organized into different checkups to track the evolution over time. From the raw data, the platform automatically analyzes and extracts all the properties that are needed for diagnostic and treatment purposes resulting in considerable reduction in time and effort. Here, various risk stratification tables of reference are incorporated into the platform for automatic CV risk computation. Furthermore, the ABPM service allows the tracking of blood pressure over a period of time, allowing the extraction of additional, valuable information. Finally, the report services allow an efficient review of the summarized relevant data.

Therefore, the proposed platform collects a large quantity of diverse, relevant parameters and gathers them using different standard protocols according to ESH/ESC guidelines²² in order to support the decision-making process. The limitation of this protocol is the availability of the large amount of data involved since it comprises an exhaustive anamnesis, a physical examination, recordings of several measurements, biological data extracted from the blood test, knowledge about family precedents, etc. Each of the tools/services combines multiple medical parameters to compute the cardiovascular risk factors in such a way that these calculations cannot be performed when no data are available. However, even if the patient profile is not complete, the availability of partial data allows the computation of some of the risk factors providing relevant results to support the clinical decision-making process. Each service details the data involved in its computation and the results are incremental on the basis of the available data.

There are a number of tools available for CV assessment which are mainly focused on satisfying patient demand in specific scenarios. However, the proposed protocol is fully oriented to medical specialists, covering all the services to support the decision-making process in their daily routine. Regarding BP monitoring, there are several commercial systems that are mostly focused on the performance of the measurements, the compatibility with other operative systems, the ease of use, etc. These devices do not analyze recorded data whereas the ABPM service, given a

recording file, will analyze all the information from the measurements and automatically extract valuable parameters relevant for clinical practice. Moreover, it provides a graphical representation incorporating additional data that facilitates visualization and analysis. Finally, the reporting service allows an efficient review of the summarized data containing all the relevant information with the aim of helping clinicians in their clinical practice. Therefore, the proposed protocol allows a complete and reliable analysis of the cardiovascular system to support the clinical decision-making process via a set of functionalities and services that are required by physicians for risk evaluation, early diagnosis, treatment prescription, and tracking over time. This leads to a qualitative improvement in health-care services and a reduction in time and effort, facilitating the work of clinicians in their daily practice.

The large amount of medical data involved together with the possibility of discussions among experts provides an adequate environment for clinical research. Future work in this field will include the analysis of the impact of the different CV risk factors and the correlation between various medical parameters in order to extract additional information relevant to clinical practice. The gathering and storage of significant volumes of clinical data can also serve as a basis for computational analysis of big data with the objective of data dimensionality reduction; this can also serve as a complementary source of information for the clinical users of the platform. Furthermore, future work will involve the inclusion of specific questionnaires — for a more exhaustive analysis of some factors (e.g., stress, diet or exercise) — and internalization in the form of support for more languages and reference units. Graphical improvements are also planned, e.g., the integration of cosinor analysis for blood pressure times series which can facilitate the inspection of blood pressure characteristics and tendencies.

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DISCLOSURES:

The authors have nothing to disclose.

REFERENCES:

1. World Health Organization, Cardiovascular Diseases (CVDs). *World Health Organization* www.who.int/cardiovascular_diseases/en/ Accessed 8 May 2018.
2. World Health Organization. Hearts: technical package for cardiovascular disease management in primary health care. *World Health Organization, Technical Documents*. isbn: 9789241511377, <http://www.who.int/iris/handle/10665/252661> (2016).
3. World Health Organization. A global brief on hypertension : silent killer, global public health crisis: World Health Day 2013. *World Health Organization, Technical Documents*. <http://www.who.int/iris/handle/10665/79059> (2013).

4. Stamler, J., Stamler, R., Neaton, J.D. Blood pressure, systolic and diastolic, and cardiovascular risks: US population data. *Archives of Internal Medicine*. **153** (5), 598 - 615, doi: 10.1001/archinte.1993.00410050036006 (1993).
5. Kannel, W., Wilson, P. An update on coronary risk factors. *Medical Clinics of North America*. **79** (5), 951 – 971, doi:10.1016/S0025-7125(16)30016-5 (1995).
6. Tarride, J. E., et al. A review of the cost of cardiovascular disease. *The Canadian Journal of Cardiology*. **25** (6) 195 – 202, doi: 10.1016/S0828-282X(09)70098-4 (2009).
7. Wolf-Maier, K., et al. Hypertension prevalence and blood pressure levels in 6 European countries, Canada, and the United States. *The Journal of American Medical Association*. **289** (18), 2363 – 2369, doi:10.1001/jama.289.18.2363 (2003).
8. Kearney, P., Whelton, M., Reynolds, K., Muntner, P., Whelton, P., He, J. Global burden of hypertension: analysis of worldwide data. *The Lancet*. **365** (9455), 217 – 223, doi: 10.1016/S0140-6736(05)17741-1 (2005).
9. Hermida, R., Smolensky, H., Ayala, E., Portaluppi, F. Ambulatory Blood Pressure Monitoring (ABPM) as the reference standard for diagnosis of hypertension and assessment of vascular risk in adults. *Chronobiology International*. **32** (10) 1329 – 1342, doi: 10.3109/07420528.2015.1113804 (2015).
10. Field, M. (Ed.). Telemedicine: A Guide to Assessing Telecommunications in Health Care. *National Academy Press*. Doi: 10.17226/5296 (1996).
11. Charles, B. Telemedicine can lower costs and improve access. *Healthcare Financial Management*. **54** (4), 66 – 69 (2000).
12. Lundberg, T., Westman, G., Hellstrom, S., Sandstrom, H. Digital imaging and telemedicine as a tool for studying inflammatory conditions in the middle ear – evaluation of image quality and agreement between examiners. *International Journal of Pediatric Otorhinolaryngology*. **72** (1), 73–79, doi: 10.1016/j.ijporl.2007.09.015 (2008).
13. Ortega, M., Barreira, N., Novo, J., Penedo, M., Pose-Reino, A., Gómez-Ulla, F. Sirius: a web-based system for retinal image analysis. *International Journal of Medical Informatics*. **79** (10), 722–732, doi: 10.1016/j.ijmedinf.2010.07.005 (2010).
14. Novo, J., Rouco, J., Barreira, N., Ortega, M., Penedo, M.G., Campilho, A. Wivern: a Web-Based System Enabling Computer-Aided Diagnosis and Interdisciplinary Expert Collaboration for Vascular Research. *Journal of Medical and Biological Engineering*. **37** (6), 920 – 325, doi: 10.1007/s40846-017-0256-y (2017).
15. Paredes, S., Rocha, T., de Carvalho, P., Henriques, J., Morais, J. Matlab tool for cardiovascular disease risk prediction. *Experiment@ International Conference (exp.at' 13)*. 190 – 191, doi: 10.1109/ExpAt.2013.6703067 (2013).
16. Goff, D., et al. 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk. *Circulation*. **137** (11) doi: 10.1161/01.cir.0000437741.48606.98 (2013).
17. Sufi, F., Khalil, I., Tari, Z. A cardioid based technique to identify cardiovascular diseases using mobile phones and body sensors. *Conference Proceedings IEEE Engineering in Medicine and Biology Society*. **2010**, 5500 – 5503, doi: 10.1109/IEMBS.2010.5626578 (2010).
18. Lin, C.T., et al. An intelligent telecardiology system using a wearable and wireless ECG to detect atrial fibrillation. *IEEE Transactions on Information Technology in Biomedicine*. **14** (3), 726 – 733, doi: http://10.0.4.85/TITB.2010.2047401 (2010).

- 657 19. Lee, H., Wang, W., Lu, S., Wu, B., Ko, L. Home-based mobile cardio-pulmonary rehabilitation
658 consultant system. *Conference Proceedings IEEE Engineering in Medicine and Biology Society*
659 **2011**, 989 – 992, doi: 10.1109/IEMBS.2011.6090229 (2011).
- 660 20. Kang, H., Park, H. Development of hypertension management mobile application based on
661 clinical practice guidelines. *Studies in Health Technology and Informatics*. **210**, 602–606 (2015).
- 662 21. Novo, J., Hermida, A., Ortega, M., Barreira, N., Penedo, M.G., López, J.E., Calvo, C. Hydra: A
663 web-based system for cardiovascular analysis, diagnosis and treatment. *Computer methods and*
664 *programs in biomedicina*. **139**, 61 – 81, doi: 10.1016/j.cmpb.2016.10.019 (2017).
- 665 22. Janes, H., Pepe, M., Gu, W. Assessing the value of risk predictions by using risk stratification
666 tables, *Annals of Internal Medicine*. **149** (10), 751 - 760 (2008).
- 667 23. Mancia, G., et al. 2007 Guidelines for the management of arterial hypertension: the Task
668 Force for the Management of Arterial Hypertension of the European Society of Hypertension
669 (ESH) and of the European Society of Cardiology (ESC), *Journal of Hypertension*. **25** (6), 1105 –
670 1187, doi: 10.1097/HJH.0b013e3281fc975a (2007).
- 671 24. Grundy, S., Brewer, H., Cleeman, J., Smith, S., Lenfant, C. Definition of metabolic syndrome:
672 report of the National Heart, Lung, and Blood Institute/American Heart Association Conference
673 on scientific issues related to definition. *Circulation*. **109** (3), 433 – 438, doi:
674 10.1161/01.CIR.0000111245.75752.C6 (2004).
- 675 25. Conroy, R., et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the
676 SCORE project. *European Heart Journal*. **24** (11), 987–1003 (2003).
- 677 26. Kannel, W., McGee, D., Gordon, T. A general cardiovascular risk profile: the Framingham
678 study. *American Journal of Cardiology*. **38** (1), 46 – 51 (1976). **23.** O'Brien, E., et al. European
679 Society of Hypertension position paper on ambulatory blood pressure monitoring. *Journal of*
680 *Hypertension*. **31** (9), 1731 – 1768, doi: 10.1097/HJH.0b013e328363e964 (2013).