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(54) **AORTIC STENOSIS CLASSIFICATION**

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A61B 5/00	(2006.01)

(52) **U.S. Cl.**

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(57) **ABSTRACT**

According to one implementation, a medical device includes a display, a blood pressure sensor for sensing an arterial blood pressure of a patient and for generating a blood pressure signal, an analog-to-digital converter (ADC) for receiving the blood pressure signal and for converting the blood pressure signal to blood pressure data in digital form, and a hardware processor for executing an aortic stenosis diagnostic software code. The hardware processor executes the aortic stenosis diagnostic software code to receive the blood pressure data from the ADC, and to identify parameters indicative of aortic stenosis in the patient, based on the blood pressure data. The hardware processor further executes the aortic stenosis diagnostic software code to classify the severity of aortic stenosis in the patient based on an exponential function of the parameters.

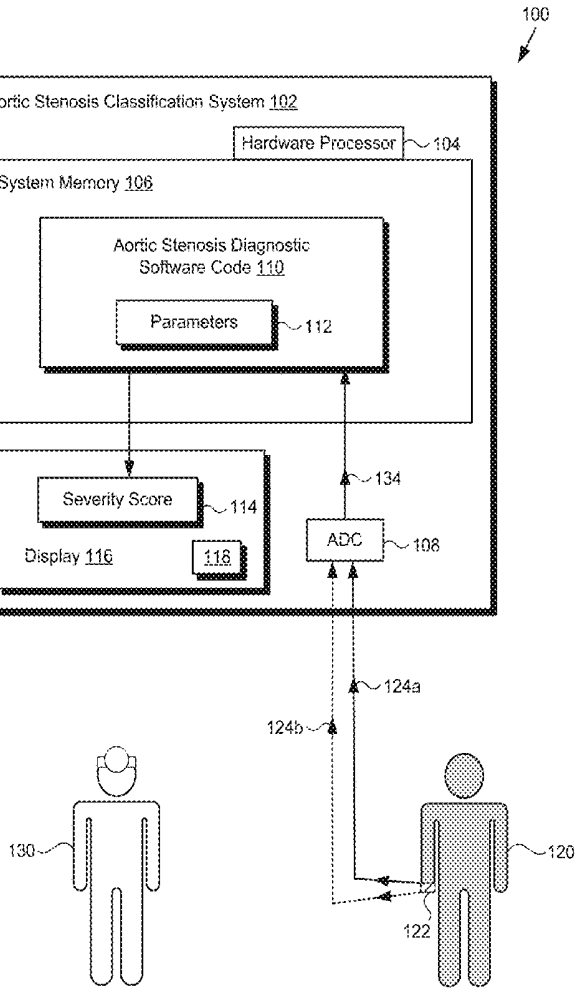


Fig. 1

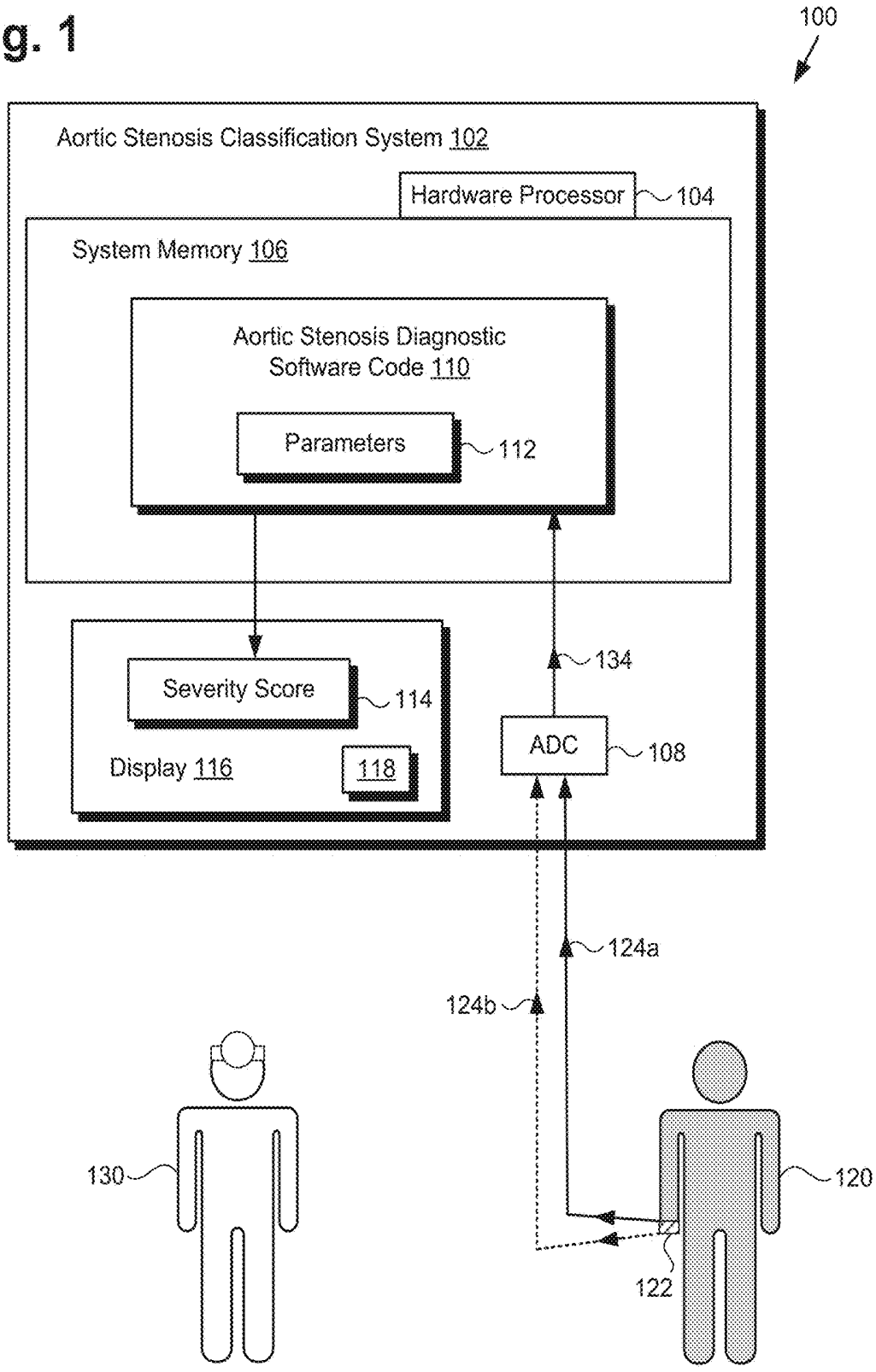

100
Aortic Stenosis Classification System 102
Hardware Processor
104
System Memory 106
Aortic Stenosis Diagnostic Software Code 110
Parameters
112
Severity Score
114
Display 116
118
134
ADC
108
124a
124b
130
120
122

Fig. 2A

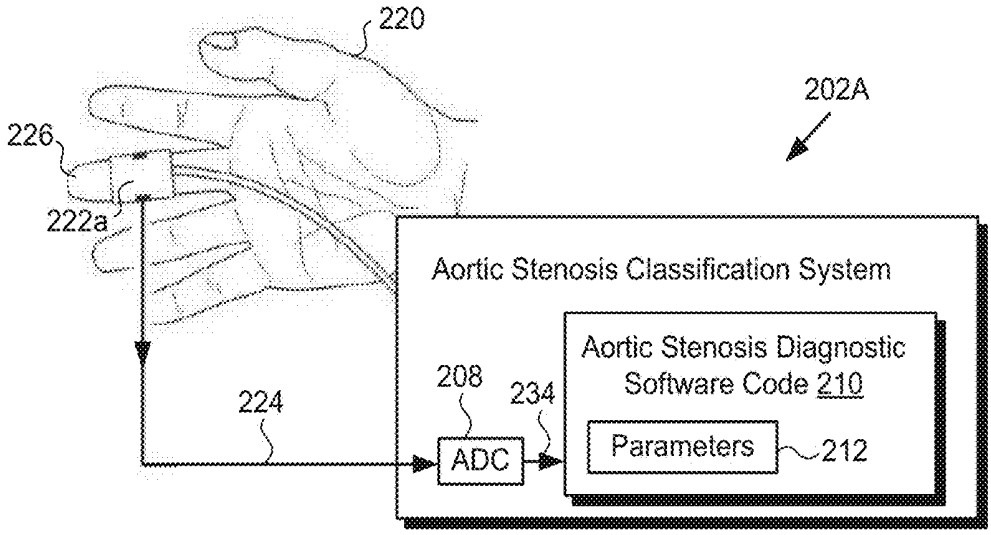

220
202A
226
222a
Aortic Stenosis Classification System
Aortic Stenosis Diagnostic Software Code 210
208
234
224
ADC
Parameters
212

Fig. 2B

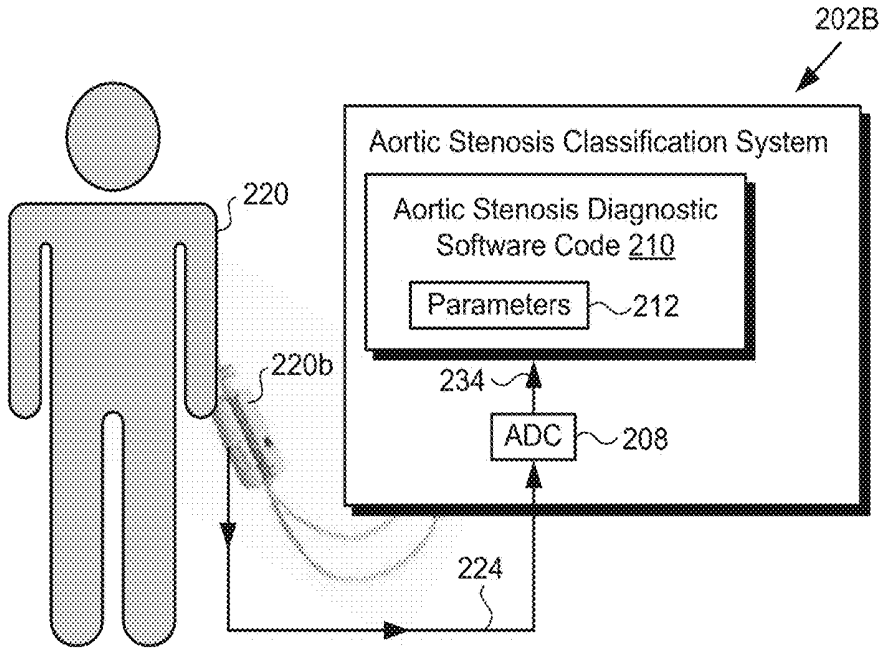

202B
Aortic Stenosis Classification System
Aortic Stenosis Diagnostic Software Code 210
Parameters
212
220
220b
234
ADC
208
224

Fig. 3

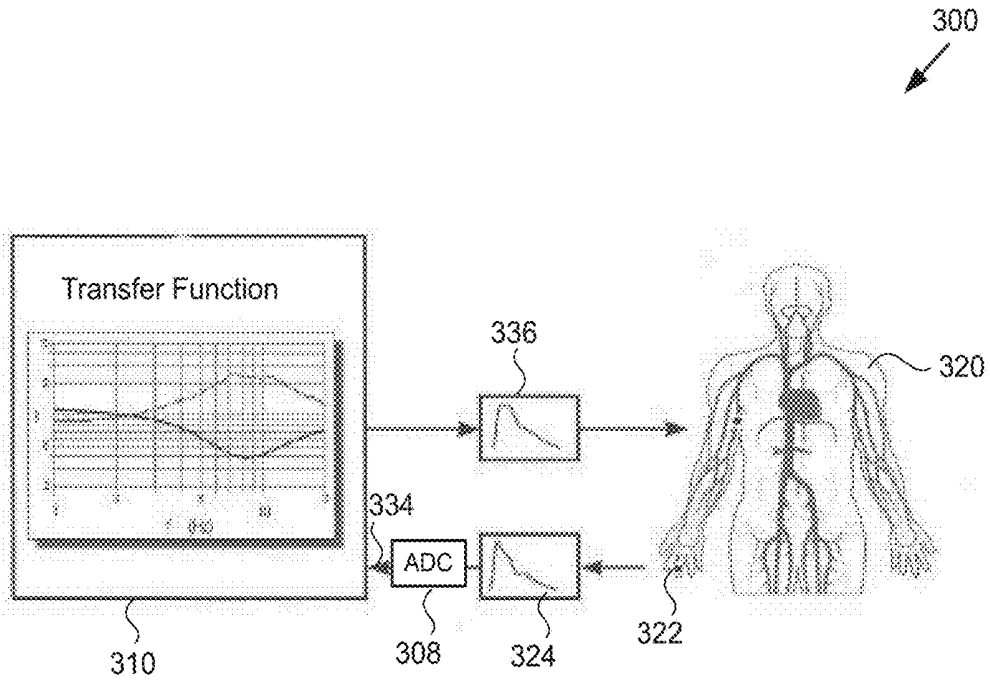


Fig. 4

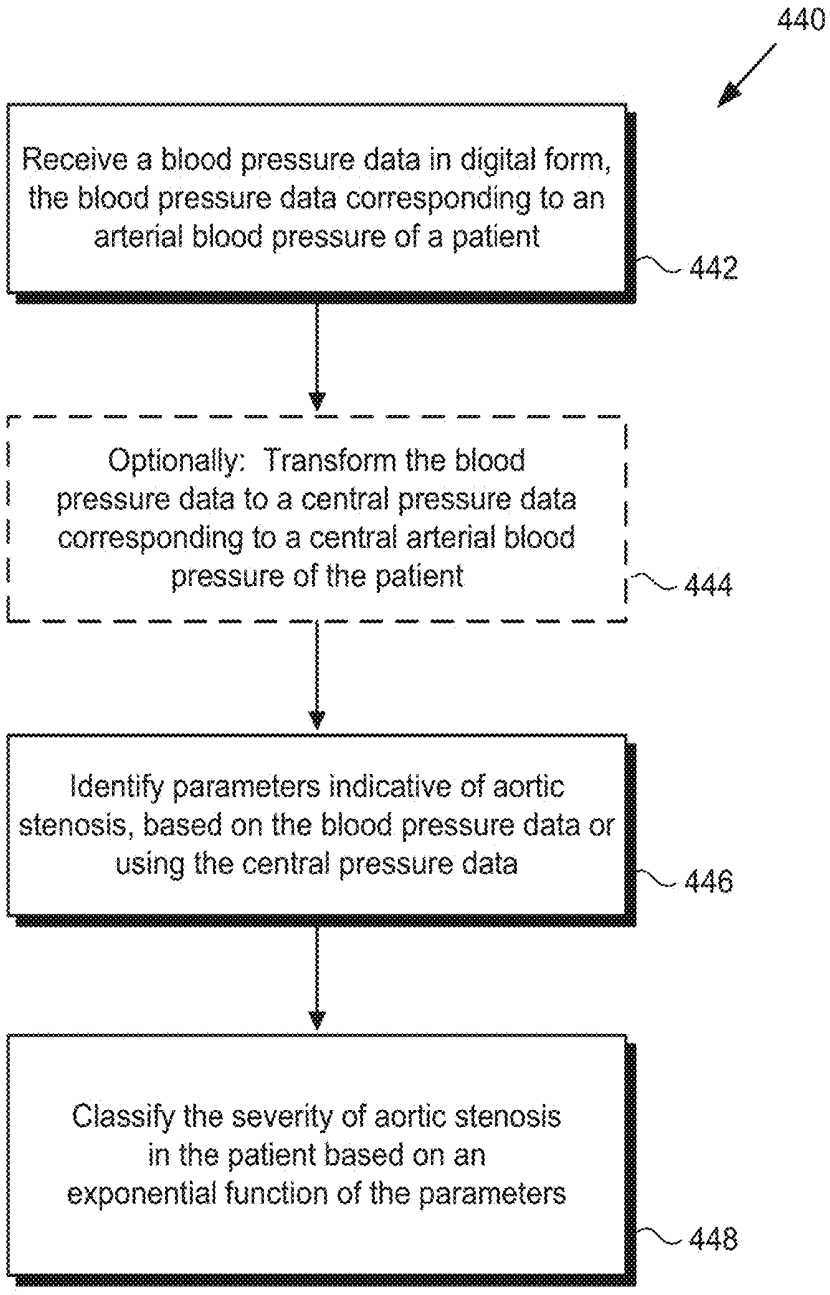

440
Receive a blood pressure data in digital form, the blood pressure data corresponding to an arterial blood pressure of a patient
442
Optionally: Transform the blood pressure data to a central pressure data corresponding to a central arterial blood pressure of the patient
444
Identify parameters indicative of aortic stenosis, based on the blood pressure data or using the central pressure data
446
Classify the severity of aortic stenosis in the patient based on an exponential function of the parameters
448

Fig. 5

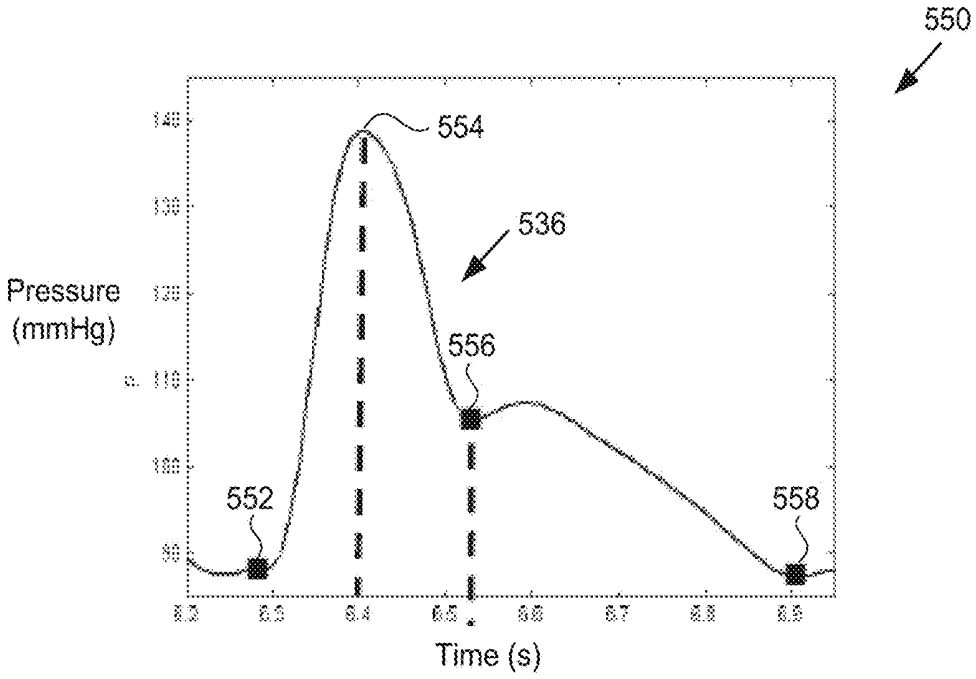


Fig. 6 Cross Validation Results

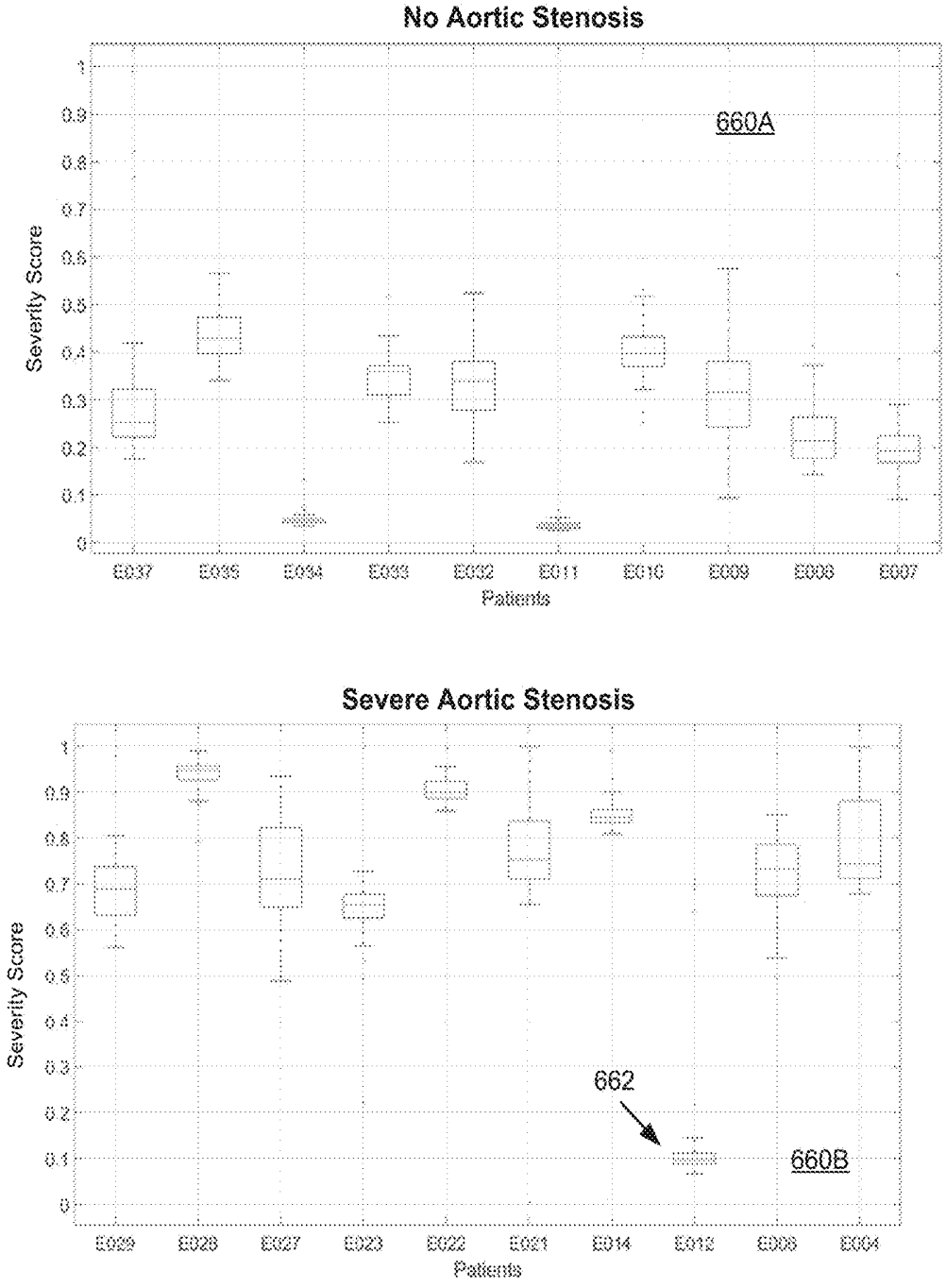
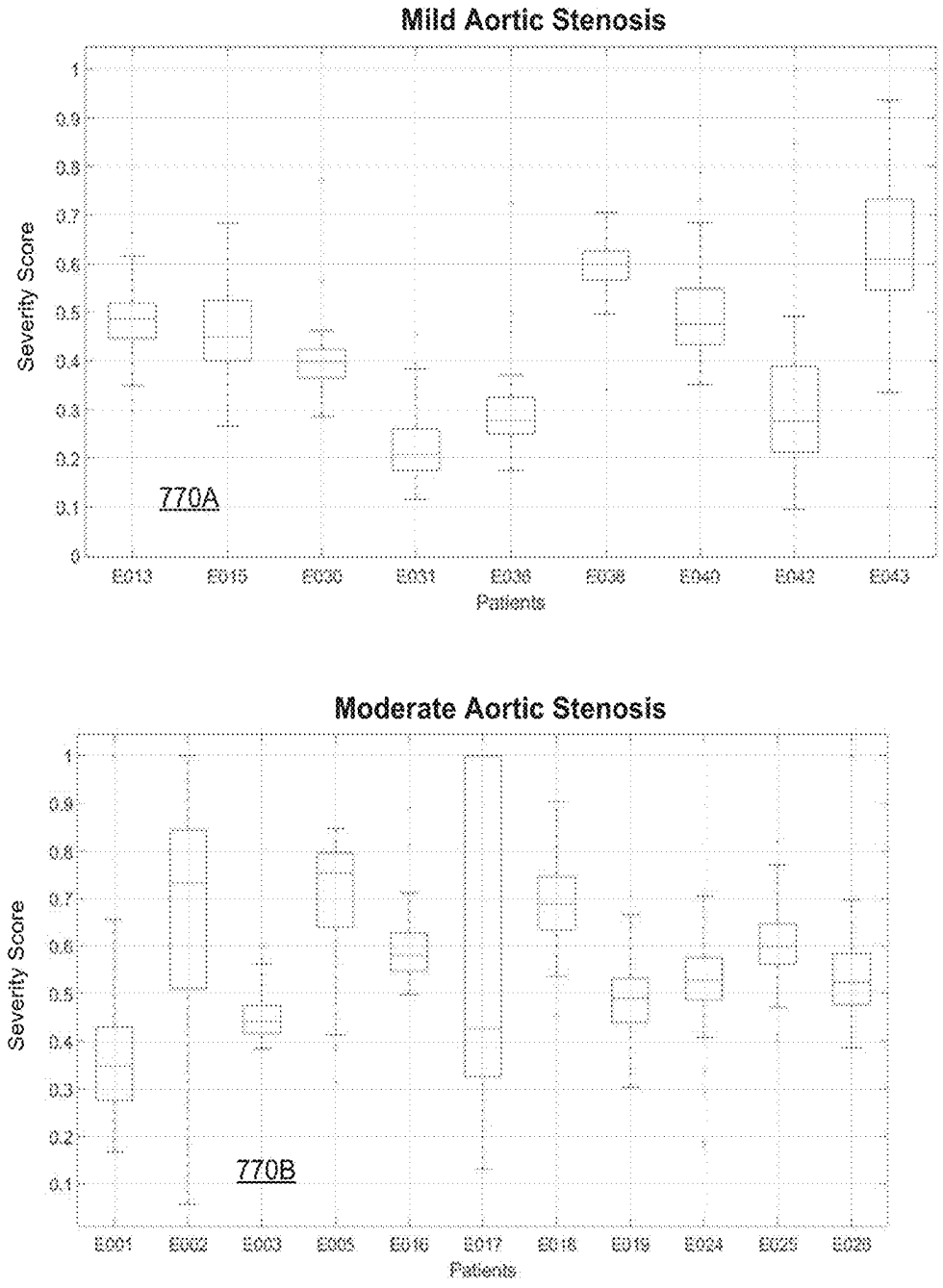


Fig. 7


Mild Aortic Stenosis
Severity Score
Patients
770A
E013
E015
E030
E031
E036
E038
E040
E042
E043
Moderate Aortic Stenosis
Severity Score
Patients
770B
E001
E002
E003
E005
E016
E017
E018
E019
E024
E025
E028

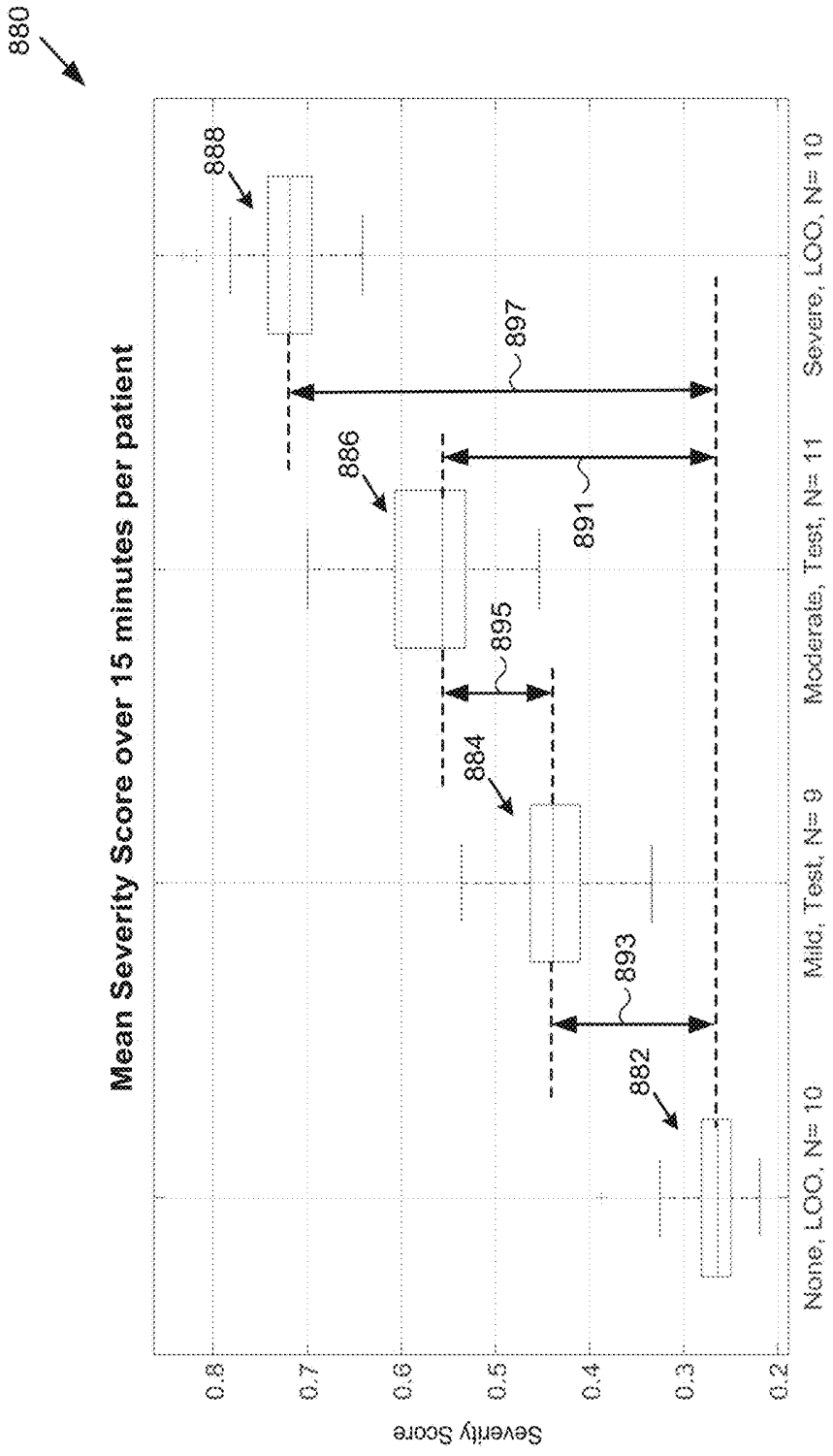

880
Mean Severity Score over 15 minutes per patient
Severity Score
0.8
0.7
0.6
0.5
0.4
0.3
0.2
None, LOO, N= 10
Mild, Test, N= 9
Moderate, Test, N= 11
Severe, LOO, N= 10
882
884
886
888
891
893
895
897

Fig. 8

AORTIC STENOSIS CLASSIFICATION

RELATED APPLICATIONS

[0001] The present application claims the benefit of and priority to a pending Provisional Patent Application Ser. No. 62/429,006, filed Dec. 1, 2016, and titled "Aortic Stenosis Classification," which is hereby incorporated fully by reference into the present application.

BACKGROUND

[0002] Aortic stenosis can be a progressive, debilitating, and life threatening condition if left untreated. Patients in whom aortic stenosis is present are nevertheless typically free from cardiovascular symptoms such as angina, syncope, or heart failure, for example, until late in the course of disease progression. However, once symptoms manifest, patient prognosis is often poor. As a result, early detection of aortic stenosis, prior to the manifestation of symptoms, is important.

[0003] Screening for aortic stenosis has historically been performed by cardiac auscultation, typically through use of a stethoscope to listen to a patient's heart. Although the detection of heart sounds can enable early identification of a subject suffering from aortic stenosis, there are disadvantages to relying on this conventional screening technique. One disadvantage flows from changes in the way clinicians are trained. As high technology diagnostic approaches are increasingly taught, the importance of traditional and relatively low technology diagnostic techniques may receive less emphasis, resulting in fewer diagnosticians being skilled in the use of cardiac auscultation. Another disadvantage results from the general aging of the patient population. Especially in older patients, heart sounds indicative of aortic stenosis may be present but may not reliably indicate significant aortic valvular obstruction requiring medical intervention.

SUMMARY

[0004] There are provided systems and methods for performing aortic stenosis classification, substantially as shown in and/or described in connection with at least one of the figures, and as set forth more completely in the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0005] FIG. **1** shows a diagram of an exemplary aortic stenosis classification system, according to one implementation;

[0006] FIG. **2**A shows an exemplary implementation for non-invasively detecting peripheral arterial blood pressure at an extremity of a patient;

[0007] FIG. **2**B shows an exemplary implementation for performing minimally invasive detection of arterial blood pressure of a patient;

[0008] FIG. **3** shows a diagram depicting transformation of a peripheral arterial blood pressure waveform of a patient to a central arterial blood pressure waveform of the patient, according to one implementation;

[0009] FIG. **4** is a flowchart presenting an exemplary method for use by a system to perform aortic stenosis classification;

[0010] FIG. **5** shows a trace of an arterial blood pressure waveform including exemplary cardiac metrics;

[0011] FIG. **6** shows cross validation results of aortic stenosis classification using the methods and systems disclosed in the present application;

[0012] FIG. **7** shows the results of aortic stenosis classification using the methods and systems disclosed in the present application for subjects having mild or moderate aortic stenosis; and

[0013] FIG. **8** shows a graph of mean severity scores determined using the methods and systems disclosed in the present application for four distinct cohorts of subjects having no aortic stenosis, mild aortic stenosis, moderate aortic stenosis, and severe aortic stenosis, respectively.

DETAILED DESCRIPTION

[0014] The following description contains specific information pertaining to implementations in the present disclosure. One skilled in the art will recognize that the present disclosure may be implemented in a manner different from that specifically discussed herein. The drawings in the present application and their accompanying detailed description are directed to merely exemplary implementations. Unless noted otherwise, like or corresponding elements among the figures may be indicated by like or corresponding reference numerals. Moreover, the drawings and illustrations in the present application are generally not to scale, and are not intended to correspond to actual relative dimensions.

[0015] As stated above, aortic stenosis can be a progressive, debilitating, and life threatening condition if left untreated. Patients in whom aortic stenosis is present are nevertheless typically free from cardiovascular symptoms such as angina, syncope, or heart failure, for example, until late in the course of disease progression. However, once symptoms manifest, patient prognosis is often poor. As a result, early detection of aortic stenosis, prior to the manifestation of symptoms, is important.

[0016] As also stated above, screening for aortic stenosis has historically been performed by cardiac auscultation, typically through use of a stethoscope to listen to a patient's heart. Although the detection of heart sounds can enable early identification of a subject suffering from aortic stenosis, there are disadvantages to relying on this conventional screening technique. One disadvantage flows from changes in the way clinicians are trained. As high technology diagnostic approaches are increasingly taught, the importance of traditional and relatively low technology diagnostic techniques may receive less emphasis, resulting in fewer diagnosticians being skilled in the use of cardiac auscultation. Another disadvantage results from the general aging of the patient population. Especially in older patients, heart sounds indicative of aortic stenosis may be present but may not reliably indicate significant aortic valvular obstruction requiring medical intervention.

[0017] The present application discloses systems and methods for classifying aortic stenosis in a patient that address and overcome the deficiencies associated with the conventional art noted above. The present solution for classifying aortic stenosis includes monitoring an arterial blood pressure of the patient. Such monitoring may be performed invasively, or using non-invasive arterial pressure waveform measurements taken at an extremity of the patient, for example, at a finger or wrist of the patient. In some implementations, the present solution may include applying a transfer function to transform a peripheral arterial

blood pressure data detected at an extremity of the patient to a central pressure data of the patient. The present solution further includes identifying parameters that are indicative of aortic stenosis based on or using the blood pressure data, and classifying the severity of aortic stenosis based on an exponential function of those parameters.

[0018] FIG. **1** shows a diagram of an exemplary aortic stenosis classification system, according to one implementation. As shown in FIG. **1**, aortic stenosis classification system **102** is situated within healthcare environment **100** including patient **120**, and healthcare worker **130**. Aortic stenosis classification system **102** may be a medical device that includes hardware processor **104**, system memory **106**, analog-to-digital converter (ADC) **108** coupled to blood pressure sensor **122**, display **116**, and sensory alarm **118**. As further shown in FIG. **1**, system memory **106** stores aortic stenosis diagnostic software code **110** including parameters **112** indicative of aortic stenosis.

[0019] FIG. **1** also shows signals received by aortic stenosis classification system **102** and corresponding to an arterial blood pressure of patient **120**, in the alternative as wired blood pressure signal **124***a* and wireless blood pressure signal **124***b*. In addition, FIG. **1** shows blood pressure data **134** in digital form, and aortic stenosis severity score **114** generated by aortic stenosis diagnostic software code **110** based on or using blood pressure data **134**.

[0020] Blood pressure sensor **122** is shown in an exemplary implementation in FIG. **1**, and is attached to patient **120**. It is noted that blood pressure sensor **122** may be an invasive or non-invasive sensor attached to patient **120**. In one implementation, as represented in FIG. **1**, blood pressure sensor **122** may be attached non-invasively so as to sense a peripheral arterial blood pressure at an extremity of patient **120**, such as arterial blood pressure measured at a wrist or finger of patient **120**. Although not explicitly shown in FIG. **1**, in other implementations, blood pressure sensor **122** may be attached non-invasively to measure a peripheral arterial blood pressure at another extremity of patient **120**, such as at an ankle or toe of patient **120**. Blood pressure signal **124***a*/**124***b* received by ADC **108** of aortic stenosis classification system **102** may include a central or peripheral arterial blood pressure waveform of patient **120**.

[0021] According to one exemplary implementation, aortic stenosis classification system **102** may correspond to one or more web servers, accessible over a packet-switched network such as the Internet, for example. In another implementation, aortic stenosis classification system **102** may correspond to one or more servers supporting a local area network (LAN), or included in another type of limited distribution network, such as within a hospital setting, for example. In yet other implementations, aortic stenosis classification system **102** may take the form of a computer workstation or personal computer (PC), a dedicated handheld or otherwise portable diagnostic system, or any type of mobile computing device, such as a smartphone or tablet computer, among others.

[0022] According to the exemplary implementation shown in FIG. **1**, hardware processor **104** is configured to utilize ADC **108** to convert blood pressure signal **124***a*/**124***b* to blood pressure data **134** in digital form. Hardware processor **104** is also configured to execute aortic stenosis diagnostic software code **110** to receive blood pressure data **134** from ADC **108**. In addition, in some implementations, hardware processor **104** may be further configured to execute aortic stenosis diagnostic software code **110** to apply a transfer function for transforming blood pressure data **134** to central pressure data corresponding to a central arterial blood pressure of patient **120**. For example, where blood pressure signal **124***a*/**124***b* is provided by non-invasive finger or wrist arterial pressure sensor **122**, aortic stenosis diagnostic software code **110** may be used to apply a transfer function for transforming blood pressure data **134** corresponding to a peripheral arterial pressure of patient **120** to an aortic blood pressure or a brachial blood pressure of patient **120**.

[0023] Hardware processor **104** is also configured to execute aortic stenosis diagnostic software code **110** to extract or otherwise identify parameters **112** indicative of aortic stenosis in patient **120** based on blood pressure data **134** or using blood pressure data **134** when blood pressure data **134** includes the central pressure data of patient **120**. In addition, hardware processor **104** is configured to execute aortic stenosis diagnostic software code **110** to determine severity score **114** for classifying aortic stenosis in patient **120** based on parameters **112**.

[0024] It is noted that severity score **114**, when generated, may be stored in system memory **106**, may be copied to non-volatile storage (not shown in FIG. **1**), or may be displayed to healthcare worker **130** on display **116** of aortic stenosis classification system **102**. Display **116** may take the form of a liquid crystal display (LCD), a light-emitting diode (LED) display, an organic light-emitting diode (OLED) display, or another suitable display screen that performs a physical transformation of signals to light.

[0025] It is further noted that hardware processor **104** may execute aortic stenosis diagnostic software code **110** to activate sensory alarm **118** if severity score **114** meets or exceeds a predetermined threshold value, that is to say, based on the severity of aortic stenosis in patient **120**. In various implementations, sensory alarm **118** may include one or more of a visual alarm, an audible alarm, and a haptic alarm. For example, when implemented to provide a visual alarm, sensory alarm **118** may be activated as flashing and/or colored graphics shown on display **116**. When implemented to provide an audible alarm, sensory alarm **118** may be activated as any suitable warning sound, such as a siren or repeated tone. Moreover, when implemented to provide a haptic alarm, sensory alarm **118** may cause one or more components of aortic stenosis classification system **102** to vibrate or otherwise deliver a physical impulse perceptible to healthcare worker **130**.

[0026] FIG. **2**A shows an exemplary implementation for sensing peripheral arterial blood pressure non-invasively at an extremity of a patient. Aortic stenosis classification system **202**A, in FIG. **2**A, includes ADC **208** and aortic stenosis diagnostic software code **210**. As shown by FIG. **2**A, the arterial blood pressure of patient **220** is sensed non-invasively at finger **226** of patient **220** using blood pressure sensing cuff **222***a*. Also shown in FIG. **2**A are blood pressure signal **224** received by ADC **208** of aortic stenosis classification system **202**A from blood pressure sensing cuff **222***a*, digital blood pressure data **234** converted from blood pressure signal **224** by ADC **208**, and parameters **212** indicative of aortic stenosis in patient **220**, and identified based on blood pressure data **234** by aortic stenosis diagnostic software code **210**.

[0027] Patient **220**, blood pressure signal **224**, and digital blood pressure data **234** correspond respectively in general to patient **120**, blood pressure signal **124***a*/**124***b*, and digital

blood pressure data **134**, in FIG. **1**, and those corresponding features may share the characteristics attributed to any corresponding feature by the present disclosure. Moreover, aortic stenosis classification system **202**A including blood pressure sensing cuff **222***a*, ADC **208**, and aortic stenosis diagnostic software code **210** including parameters **212**, in FIG. **2**A, corresponds in general to aortic stenosis classification system **102** including blood pressure sensor **122**, ADC **108**, and aortic stenosis diagnostic software code **110** including parameters **112**, in FIG. **1**, and those corresponding features may share any of the characteristics attributed to either corresponding feature by the present disclosure. In other words, although not explicitly shown in FIG. **2**A, aortic stenosis classification system **202**A includes features corresponding respectively to hardware processor **104**, display **116**, and sensory alarm **118**.

[0028] According to the implementation shown in FIG. **2**A, blood pressure sensing cuff **222***a* is designed to sense a peripheral arterial blood pressure of patient **120**/**220** non-invasively at finger **226** of patient **120**/**220**. Moreover, as shown in FIG. **2**A, blood pressure sensing cuff **222***a* may take the form of a small, lightweight, and comfortable blood pressure sensor suitable for extended wear by patient **120**/**220**. It is noted that although blood pressure sensing cuff **222***a* is shown as a finger cuff, in FIG. **2**A, in other implementations, blood pressure sensing cuff **222***a* may be suitably adapted as a wrist, ankle, or toe cuff for attachment to patient **120**/**220**.

[0029] It is further noted that the advantageous extended wear capability described above for blood pressure sensing cuff **222***a* when implemented as a finger cuff may also be attributed to wrist, ankle, and toe cuff implementations. As a result, blood pressure sensing cuff **222***a* may be configured to provide substantially continuous beat-to-beat monitoring of the peripheral arterial blood pressure of patient **120**/**220** over an extended period of time, such as minutes or hours, for example.

[0030] FIG. **2**B shows an exemplary implementation for performing minimally invasive detection of arterial blood pressure of a patient. As shown by FIG. **2**B, the radial arterial blood pressure of patient **120**/**220** is detected via minimally invasive blood pressure sensor **222***b*. It is noted that the features shown in FIG. **2**B and identified by reference numbers identical to those shown in FIG. **2**A correspond respectively to those previously described features, and may share any of the characteristics attributed to them above. It is further noted that blood pressure sensor **222***b* corresponds in general to blood pressure sensor **122**, in FIG. **1**, and those corresponding features may share any of the characteristics attributed to either corresponding feature by the present disclosure.

[0031] According to the implementation shown in FIG. **2**B, blood pressure sensor **222***b* is designed to sense an arterial blood pressure of patient **120**/**220** in a minimally invasive manner. For example, blood pressure sensor **222***b* may be attached to patient **120**/**220** via a radial arterial catheter inserted into an arm of patient **120**/**220**. Alternatively, and although not explicitly represented in FIG. **2**B, in another implementation, blood pressure sensor **222***b* may be attached to patient **120**/**220** via a femoral arterial catheter inserted into a leg of patient **120**/**220**. Like non-invasive blood pressure sensing cuff **222***a*, in FIG. **2**A, minimally invasive blood pressure sensor **222***b*, in FIG. **2**B, may be configured to provide substantially continuous beat-to-beat monitoring of the arterial blood pressure of patient **120**/**220** over an extended period of time, such as minutes or hours.

[0032] FIG. **3** shows diagram **300** depicting transformation of digital blood pressure data **334**, converted by ADC **308** from blood pressure signal **324**, to central pressure data **336**, according to one implementation. Also shown in FIG. **3** are patient **320**, blood pressure sensor **322**, and aortic stenosis diagnostic software code **310**. Blood pressure sensor **322**, blood pressure signal **324**, ADC **308**, digital blood pressure data **334**, and aortic stenosis diagnostic software code **310** correspond respectively in general to blood pressure sensor **122**/**222***a*/**222***b*, blood pressure signal **124***a*/**124***b*/**224**, ADC **108**/**208**, digital blood pressure data **134**/**234**, and aortic stenosis diagnostic software code **110**/**210**, in FIGS. **1**, **2**A, and **2**B, and those corresponding features may share the characteristics attributed to any corresponding feature by the present disclosure.

[0033] Thus, blood pressure signal **324** and digital blood pressure data **334** can correspond to a peripheral arterial blood pressure of patient **120**/**220**/**320** detected using blood pressure sensor **122**/**222***a*/**222***b*/**322**. As shown in FIG. **3**, digital blood pressure data **134**/**234**/**334**, converted from blood pressure signal **124***a*/**124***b*/**224**/**324** by ADC **108**/**208**/**308**, may be transformed to central pressure data **336** of patient **120**/**220**/**320**. As further shown by FIG. **3**, such a transformation may be performed by aortic stenosis diagnostic software code **110**/**210**/**310** through application of a transfer function to digital blood pressure data **134**/**234**/**334**. That is to say, application of such a transfer function may be performed by aortic stenosis diagnostic software code **110**/**210**/**310**, executed by hardware processor **104**.

[0034] Example implementations of the present inventive principles will be further described below with reference to FIGS. **4** and **5**. FIG. **4** presents flowchart **440** outlining an exemplary method for use by a system to perform aortic stenosis classification. FIG. **5** shows a trace of a central arterial blood pressure waveform including exemplary cardiac metrics.

[0035] Referring to FIG. **4** in combination with FIGS. **1**, **2**A, **2**B, and **3**, flowchart **440** begins with receiving blood pressure data **134**/**234**/**334** in digital form (action **442**). As noted above, blood pressure sensor **122**/**222***a*/**222***b*/**322** may sense an arterial blood pressure of patient **120**/**220**/**320** and may generate blood pressure signal **124***a*/**124***b*/**224**/**324**. As further noted above, ADC **108**/**208**/**308** of aortic stenosis classification system **102**/**202**A/**202**B may receive blood pressure signal **124***a*/**124***b*/**224**/**324** from blood pressure sensor **122**/**222***a*/**222***b*/**322**, and may convert blood pressure signal **124***a*/**124***b*/**224**/**324** to blood pressure data **134**/**234**/**334** in digital form. Blood pressure data **134**/**234**/**334** may be received by aortic stenosis diagnostic software code **110**/**210**/**310**, executed by hardware processor **104**.

[0036] In some implementations, blood pressure sensor **122**/**222***a*/**222***b*/**322** may be used to sense a central arterial blood pressure of patient **120**/**220**/**320**, and to generate blood pressure signal **124***a*/**124***b*/**224**/**324** as an analog signal corresponding to that central arterial blood pressure. In those implementations, blood pressure data **134**/**234**/**334** may be substantially identical to central pressure data **336** of patient **120**/**220**/**320**, and may be used to identify parameters **112**/**212** indicative of aortic stenosis. However, in other implementations, blood pressure sensor **122**/**222***a*/**222***b*/**322** may be used to sense a peripheral arterial blood pressure of patient **120**/**220**/**320**, and to generate blood pressure signal

124*a*/**124***b*/**224**/**324** as an analog signal corresponding to that peripheral arterial blood pressure.

[0037] In implementations in which blood pressure sensor **122**/**222***a*/**222***b*/**322** is used to sense a peripheral arterial blood pressure of patient **120**/**220**/**320**, flowchart **440** may include transforming blood pressure data **134**/**234**/**334** to central pressure data **336** of patient **120**/**220**/**320** (action **444**). Central pressure data **336** may include a central blood pressure waveform of patient **120**/**220**/**320**, such as an aortic blood pressure waveform of patient **120**/**220**/**320**, for example. The optional transformation of blood pressure data **134**/**234**/**334** to central pressure data **336** may be performed by aortic stenosis diagnostic software code **110**/**210**/**310**, executed by hardware processor **104**, in the manner described above by reference to FIG. **3**.

[0038] Flowchart **440** continues with extracting or otherwise identifying parameters **112**/**212** indicative of aortic stenosis based on blood pressure data **134**/**234**/**334**, or using blood pressure data **134**/**234**/**334** (action **446**). As noted above, in implementations in which blood pressure data **134**/**234**/**334** is converted from blood pressure signal **124***a*/**124***b*/**224**/**324** corresponding to a peripheral arterial blood pressure of patient **120**/**220**/**320**, blood pressure data **134**/**234**/**334** may be converted to central pressure data **336** for use in identifying parameters **112**/**212**. Thus, in those implementations, parameters **112**/**212** are identified based on blood pressure data **134**/**234**/**334** and using central pressure data **336**.

[0039] However, as also noted above, in implementations in which blood pressure data **134**/**234**/**334** is converted from blood pressure signal **124***a*/**124***b*/**224**/**324** corresponding to a central arterial blood pressure of patient **120**/**220**/**320**, blood pressure data **134**/**234**/**334** may be substantially identical to central pressure data **336** of patient **120**/**220**/**320** without transformation. Thus, in those implementations, parameters **112**/**212** may be identified using blood pressure data **134**/**234**/**334** directly. Whether identified based on blood pressure data **134**/**234**/**334**, or using blood pressure data **134**/**234**/**334** directly, parameters **112**/**212** may be identified by aortic stenosis diagnostic software code **110**/**210**/**310**, executed by hardware processor **104**.

[0040] Referring to FIG. **5**, FIG. **5** shows trace **550** of exemplary central arterial blood pressure waveform **536** corresponding to central pressure data **336**, in FIG. **3**. As shown in FIG. **5**, central arterial blood pressure waveform **536** is expressed as a function of time, and includes heartbeat metrics **552**, **554**, **556**, and **558**. Heartbeat metrics **552**, **554**, **556**, and **558** correspond respectively to the start of a heartbeat, the maximum systolic pressure marking the end of systolic rise, the presence of the dicrotic notch marking the end of systolic decay, and the beginning of the next heartbeat of patient **120**/**220**/**320**. Heartbeat metrics **552**, **554**, **556**, and **558** may be included among parameters **112**/**212** indicative of aortic stenosis and identified by aortic stenosis diagnostic software code **110**/**210**/**310**.

[0041] It is noted that although heartbeat metrics **552**, **554**, **556**, and **558** are shown for conceptual clarity, more generally, parameters **112**/**212** indicative of aortic stenosis in patient **120**/**220**/**320** may include a variety of different types of parameters, some of which may include and/or be based on heartbeat metrics **552**, **554**, **556**, and **558**. For instance, parameters **112**/**212** indicative of aortic stenosis may include any or all of mean arterial pressure (MAP), combinatorial parameters, hemodynamic complexity parameters, and frequency domain hemodynamic parameters.

[0042] Hemodynamic complexity parameters quantify the amount of regularity in cardiac measurements over time, as well as the entropy, i.e., the unpredictability of fluctuations in cardiac measurements over time. Frequency domain hemodynamic parameters quantify various measures of cardiac performance as a function of frequency rather than time.

[0043] In some implementations, blood pressure signal **124***a*/**124***b*/**224**/**244** corresponding to an arterial blood pressure of patient **120**/**220**/**320** may be periodically, or substantially continuously monitored by aortic stenosis classification system **102**/**202**A/**202**B during a sampling interval lasting several minutes, such as fifteen minutes, for example. Moreover, during that sampling interval, the parameters **112**/**212** indicative of aortic stenosis may be averaged repeatedly using sampling periods of several seconds, such as twenty seconds, for example. In other words, in an exemplary implementation in which parameters **112**/**212** indicative of aortic stenosis are sampled and averaged repeatedly for twenty seconds over a fifteen minute sampling interval, forty five distinct data points can be collected for each of parameters **112**/**212**.

[0044] Flowchart **440** can conclude with classifying the severity of aortic stenosis in patient **120**/**220**/**320** based on an exponential function of parameters **112**/**212** (action **448**). Classification of the severity of aortic stenosis in patient **120**/**220**/**320** may be performed by aortic stenosis diagnostic software code **110**/**210**/**310**, executed by hardware processor **104**, and may be expressed as severity score **114**.

[0045] In classifying the severity of aortic stenosis in patient **120**/**220**/**320**, it may be advantageous or desirable to place greater emphasis on some parameters **112**/**212** indicative of aortic stenosis than on others when determining severity score **114**. In other words, in some implementations, aortic stenosis diagnostic software code **110**/**210**/**310**, executed by hardware processor **104**, may use a weighted combination of parameters **112**/**212** to determine severity score **114**. Moreover, it is noted that the weighting factors applied respectively to parameters **112**/**212** may by positive or negative.

[0046] In one implementation, for example, the exponential function on which determination of severity score **114**, and thus classification of aortic stenosis in patient **120**/**220**/**320**, is based may be an exponential function of a weighted sum of parameters **112**/**212**. Moreover, in implementations in which parameters **112**/**212** are monitored during a sampling interval lasting several minutes, as described above, classification of the severity of aortic stenosis in patient **120**/**220**/**320** may include identifying an average value for each of parameters **112**/**212** during the sampling interval. In those implementations, the exponential function on which determination of severity score **114** is based may be an exponential function of a weighted sum of the average values of parameters **112**/**212**.

[0047] It is emphasized that severity score **114** for patient **120**/**220**/**320** is determined based on a weighted combination of parameters **112**/**212** identified based on or using blood pressure data **134**/**234**/**334** corresponding to an arterial blood pressure of patient **120**/**220**/**320**. Consequently, according to the inventive concepts disclosed by the present application, hardware processor **104** of aortic stenosis classification system **102**/**202**A/**202**B is configured to execute

aortic stenosis diagnostic software code **110/210/310** to determine severity score **114** for patient **120/220/320** without direct comparison with data corresponding to aortic stenosis in other patients or research subjects.

[0048] Thus, aortic stenosis diagnostic software code **110/210/310** determines severity score **114** for subject **120/220/320** based on parameters **112/212** identified based on or using blood pressure data **134/234/334**, without reference to a database storing information regarding aortic stenosis in patients or research subjects other than patient **120/220/320**. Moreover, execution of aortic stenosis diagnostic software code **110/210/310** by hardware processor **104** can substantially automate determination of severity score **114**, and hence aortic stenosis classification.

[0049] By way merely of example, according to one implementation, severity score **114** may be expressed as:

$$\text{Severity Score}=1/(1+e^{-(bias+\Sigma\beta x)}) \quad \text{(Equation 1)}$$

Where:

$$\Sigma\beta x=w_1\times x_1+w_2\times x_2+w_3\times x_3+w_4\times x_4+w_5\times x_5+w_6\times x_6+w_7\times x_7+w_8\times x_8+w_9\times x_9+w_{10}\times x_{10}+w_{11}\times x_{11}+w_{12}\times x_{12}$$

[0050] In other words, in the present example, $\Sigma\beta x$ is the weighted sum of twelve parameters **112/212**, i.e., "x_i" (i=1, 2, 3, . . . , 12), identified as indicative of aortic stenosis, where the contribution of each parameter to the summation is determined by its respective weighting factor "w_j" (j=1, 2, 3, . . . , 12).

[0051] According to one example implementation:

[0052] bias=0.99

[0053] w_1=1.21

[0054] w_2=0.13

[0055] w_3=0.06

[0056] w_4=0.05

[0057] w_5=0.03

[0058] w_6=−0.01

[0059] w_7=−0.07

[0060] w_8=−0.19

[0061] w_9=−0.28

[0062] w_{10}=−0.54

[0063] w_{11}=−0.58

[0064] w_{12}=−1.17

[0065] And parameters **112/212** include:

[0066] x_1=Cardiac output

[0067] x_2=Entropy of mean arterial blood pressure (MAP)

[0068] x_3=Entropy of the systolic pressure minus dicrotic notch pressure

[0069] x_4=Entropy of duration of the diastolic phase: the time from the dicrotic notch to the start of the next beat

[0070] x_5=The skewness of the pressure waveform within a beat

[0071] x_6=Entropy of stroke volume

[0072] x_7=Time from the first beat sample exceeding the beat mean to the dicrotic notch

[0073] x_8=Vascular tone computed with a balanced multivariate model derived from patients with mild hyperdynamic conditions

[0074] x_9=Cardiac work index

[0075] x_{10}=Cardiac index

[0076] x_{11}=Ratio of heart rate to the systolic blood pressure

[0077] x_{12}=Arterial tone estimate

[0078] In some implementations, severity score **114** may be expressed as a fraction, as represented by Equation 1. However, in other implementations, severity score **114** may be converted to a percentage score between zero percent and one hundred percent. In addition, in some implementations, as shown by FIG. **1**, hardware processor **104** may further execute aortic stenosis diagnostic software code **110/210/310** to output severity score **114** to display **116** of aortic stenosis classification system **102/202A/202B**.

[0079] As noted above, in some implementations, hardware processor **104** may further execute aortic stenosis diagnostic software code **110** to activate sensory alarm **118** based on the severity of aortic stenosis in patient **120/220/320**. For example, hardware processor **104** may further execute aortic stenosis diagnostic software code **110** to activate sensory alarm **118** if severity score **114** meets or exceeds a predetermined threshold value.

[0080] As also noted above, in various implementations, sensory alarm **118** may include one or more of a visual alarm, an audible alarm, and a haptic alarm. For example, when implemented to provide a visual alarm, sensory alarm **118** may be activated as flashing and/or colored graphics shown on display **116**. When implemented to provide an audible alarm, sensory alarm **118** may be activated as any suitable warning sound, such as a siren or repeated tone. Moreover, when implemented to provide a haptic alarm, sensory alarm **118** may cause one or more components of aortic stenosis classification system **102** to vibrate or otherwise deliver a physical impulse perceptible to healthcare worker **130**.

[0081] FIG. **6** shows cross validation results of aortic stenosis classification using the methods and systems disclosed in the present application. Graph **660A** presents the distribution of severity scores **114** for a cohort of subjects for whom aortic stenosis is not present. In addition, graph **660B** presents an analogous distribution of severity scores **114** for another cohort of subjects diagnosed with severe aortic stenosis. The severity score distributions shown in FIG. **6** were determined across fifteen minutes of data collection for each subject, in other words, during a fifteen minute sampling interval for each subject. It is noted that the reference subjects for the research resulting in the graphs shown in FIGS. **6**, **7**, and **8** are referred to as "subjects" rather than patients because at least some of those subjects may be voluntary research participants, rather than patients undergoing diagnosis and/or receiving treatment.

[0082] As shown in FIG. **6**, all subjects for whom aortic stenosis is not present were determined to have severity scores of less than 0.5. By contrast, most subjects having severe aortic stenosis were determined to have severity scores above 0.6, with many subjects having severity scores substantially higher than 0.6. Thus, based on severity score **114**, aortic stenosis may be classified as mild, moderate or severe. For example, severity score **114** of less than 0.3 may indicate a mild aortic stenosis, severity score **114** of between 0.3 and 0.6 may indicate a moderate aortic stenosis, and severity score **114** of more than 0.6 may indicate a severe aortic stenosis.

[0083] In moderate cases of aortic stenosis, echocardiography may be performed on the patient every 1-2 years to monitor the progression, possibly complemented with a cardiac stress test. In severe cases of aortic stenosis, echocardiography may be performed on the patient every 3-6 months. Also, in adult patients, a symptomatic severe aortic

stenosis usually requires aortic valve replacement (AVR). While AVR has been the standard of care for aortic stenosis for several decades, other options to AVR include open heart surgery, minimally invasive cardiac surgery (MICS) and minimally invasive catheter-based aortic valve replacement. For infants and children, balloon valvuloplasty may be used, where a balloon is inflated to stretch the valve and allow greater flow. Thus, in response to classification of severity score **114**, the patient having an increased risk for death may be treated within a sufficient lead time to decrease the patient's risk of death.

[0084] FIG. **7** shows the results of aortic stenosis classification using the methods and systems disclosed in the present application for subjects having mild or moderate aortic stenosis. Graph **770**A presents the distribution of severity scores **114** for subjects having mild aortic stenosis, while graph **770**B presents an analogous distribution of severity scores **114** for subjects having moderate aortic stenosis.

[0085] It is noted that the severity score distributions shown in FIG. **7** were determined across fifteen minutes of data collection for each subject in other words, during a fifteen minute sampling interval for each subject. It is further noted that none of the subjects represented in graph **770***a* or **770***b* was used to generate the cross validation results shown in FIG. **6**, or to train the classification model used by aortic stenosis diagnostic software code **110**/**210**/**310**. As shown in FIG. **7**, there is a statistically significant separation between subjects having moderate aortic stenosis and those having mild aortic stenosis, with the severity scores of those with moderate aortic stenosis trending higher than those of subjects having mild aortic stenosis.

[0086] FIG. **8** shows graph **880** of mean severity scores **114** determined using the methods and systems disclosed in the present application for four distinct cohorts of subjects **882**, **884**, **886**, and **888** having no aortic stenosis, mild aortic stenosis, moderate aortic stenosis, and severe aortic stenosis, respectively. The mean severity score distributions shown in FIG. **8** were determined across fifteen minutes of data collection for each subject in other words, during a fifteen minute sampling interval for each subject.

[0087] As shown in FIG. **8**, there is a statistically significant difference **893** between the mean severity score for cohort of subjects **882** having no aortic stenosis and the mean severity score for cohort of subjects **884** having mild aortic stenosis. As further shown in FIG. **8**, there are also statistically significant differences **895** and **891** between the mean severity score for cohort of subjects **886** having moderate aortic stenosis and the respective mean severity scores for cohort of subjects **884** having mild aortic stenosis and cohort of subjects **882** having no aortic stenosis. Moreover, graph **880** shows additional statistically significant difference **897** between the mean severity score for cohort of subjects **888** having severe aortic stenosis and the mean severity score for cohort of subjects **882** having no aortic stenosis.

[0088] Thus, by substantially automating aortic stenosis classification, the solution disclosed by the present application advantageously enables early detection of aortic stenosis by clinicians having little or no expertise in cardiac auscultation. In addition, by enabling performance of aortic stenosis diagnosis and classification based on arterial blood pressure measurements obtained non-invasively or minimally invasively from a to patient, the methods and systems disclosed in the present application advantageously enhance patient comfort and safety. Moreover, by enabling substantially continuous beat-to-beat monitoring of arterial blood pressure at an extremity of the patient, such as at the patient's finger, the present application discloses a compact, portable aortic stenosis classification solution suitable for deployment to cardiology offices or primary care sites.

[0089] From the above description it is manifest that various techniques can be used for implementing the concepts described in the present application without departing from the scope of those concepts. Moreover, while the concepts have been described with specific reference to certain implementations, a person of ordinary skill in the art would recognize that changes can be made in form and detail without departing from the scope of those concepts. As such, the described implementations are to be considered in all respects as illustrative and not restrictive. It should also be understood that the present application is not limited to the particular implementations described herein, but many rearrangements, modifications, and substitutions are possible without departing from the scope of the present disclosure.

What is claimed is:

1. A medical device comprising:

a display;

a blood pressure sensor configured to sense an arterial blood pressure of a patient and generate a blood pressure signal;

an analog-to-digital converter (ADC) configured to receive the blood pressure signal and convert the blood pressure signal to blood pressure data in digital form;

a hardware processor configured to execute an aortic stenosis diagnostic software code to:

receive the blood pressure data from the ADC;

identify a plurality of parameters indicative of aortic stenosis in the patient, based on the blood pressure data; and

classify a severity of aortic stenosis in the patient based on an exponential function of the plurality of parameters.

2. The medical device of claim **1**, wherein in response to classifying the severity of aortic stenosis in the patient, the patient having an increased risk for death is treated within a sufficient lead time to decrease the patient's risk of death.

3. The medical device of claim **1**, wherein the hardware processor is further configured to execute the aortic stenosis diagnostic software code to output a severity score corresponding to the severity of aortic stenosis in the patient to the display.

4. The medical device of claim **1**, wherein the hardware processor is further configured to execute the aortic stenosis diagnostic software code to activate a sensory alarm based on the severity of aortic stenosis in the patient.

5. The medical device of claim **1**, wherein the hardware processor is further configured to execute the aortic stenosis diagnostic software code to:

before classifying the severity of aortic stenosis in the patient, monitor the plurality of parameters indicative of aortic stenosis in the patient during a sampling interval lasting a plurality of minutes; and

identify an average value for each of the plurality of parameters during the sampling interval;

wherein the exponential function of the plurality of parameters is an exponential function of the average values.

6. The medical device of claim 1, wherein the exponential function of the plurality of parameters is an exponential function of a weighted sum of the average values.

7. The medical device of claim 1, wherein the blood pressure sensor is configured to sense the arterial blood pressure of the patient invasively.

8. The medical device of claim 1, wherein the blood pressure sensor is configured to sense the arterial blood pressure of the patient non-invasively.

9. The medical device of claim 1, wherein the blood pressure sensor is configured to sense a peripheral arterial blood pressure of the patient non-invasively at an extremity of the patient.

10. The medical device of claim 9, wherein the hardware processor is further configured to execute the aortic stenosis diagnostic software code to:

before identifying the plurality of parameters indicative of aortic stenosis in the patient, transform the blood pressure data to a central pressure data corresponding to a central arterial blood pressure of the patient, and

identify the plurality of parameters using the central pressure data.

11. A method of using a medical device including a display a blood pressure sensor, an analog-to-digital converter (ADC), and a hardware processor, the method comprising:

sensing, using the blood pressure sensor, an arterial blood pressure of a patient and generating a blood pressure signal;

converting, using the ADC, the blood pressure signal to blood pressure data in digital form;

receiving, using the hardware processor, the blood pressure data from the ADC;

identifying, using the hardware processor, a plurality of parameters indicative of aortic stenosis in the patient, based on the blood pressure data; and

classifying, using the hardware processor, a severity of aortic stenosis in the patient based on an exponential function of the plurality of parameters.

12. The method of claim 11 further comprising:

in response to the classifying of the severity of aortic stenosis in the patient, treating the patient having an increased risk for death within a sufficient lead time to decrease the patient's risk of death.

13. The method of claim 11, further comprising outputting, using the hardware processor, a severity score corresponding to the severity of aortic stenosis in the patient to the display.

14. The method of claim 11, further comprising activating, using the hardware processor, a sensory alarm based on the severity of aortic stenosis in the patient.

15. The method of claim 11, further comprising:

before classifying the severity of aortic stenosis in the patient, monitoring, using the hardware processor, the plurality of parameters indicative of aortic stenosis in the patient during a sampling interval lasting a plurality of minutes; and

identifying, using the hardware processor, an average value for each of the plurality of parameters during the sampling interval;

wherein the exponential function of the plurality of parameters is an exponential function of the average values.

16. The method of claim 11 wherein the exponential function of the plurality of parameters is an exponential function of a weighted sum of the average values.

17. The method of claim 11, further comprising sensing the arterial blood pressure of the patient invasively using the blood pressure sensor.

18. The method of claim 11, further comprising sensing the arterial blood pressure of the patient non-invasively using the blood pressure sensor.

19. The method of claim 11, further comprising sensing a peripheral arterial blood pressure of the patient non-invasively at an extremity of the patient, using the blood pressure sensor.

20. The method of claim 19, further comprising:

before identifying the plurality of parameters indicative of aortic stenosis in the patient, transforming, using the hardware processor, the blood pressure data to a central pressure data corresponding to a central arterial blood pressure of the patient, and

identifying, using the hardware processor, the plurality of parameters using the central pressure data.

* * * * *

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摘要(译)

根据一个实施方式，医疗设备包括显示器，用于感测患者的动脉血压并用于生成血压信号的血压传感器，用于接收血压信号的模数转换器（ADC）以及用于将血压信号转换为数字形式的血压数据，以及用于执行主动脉狭窄诊断软件代码的硬件处理器。硬件处理器执行主动脉狭窄诊断软件代码以接收来自ADC的血压数据，并基于血压数据识别指示患者的主动脉狭窄的参数。硬件处理器还执行主动脉狭窄诊断软件代码，以基于参数的指数函数对患者中的主动脉狭窄的严重程度进行分类。