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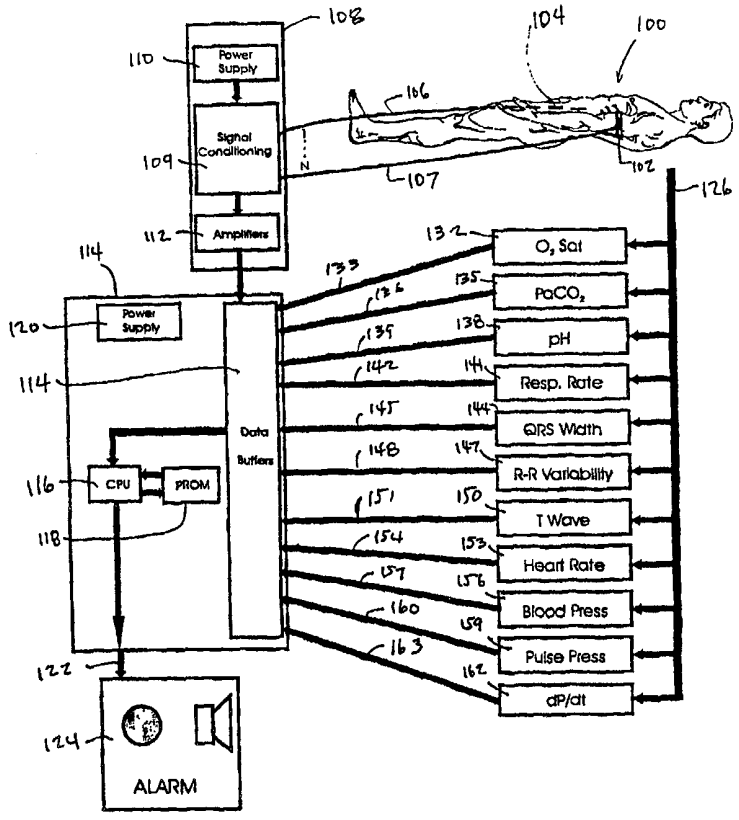
(54) **Title**: METHOD AND APPARATUS FOR PREDICTING MORTALITY IN CONGESTIVE HEART FAILURE PATIENTS

(57) **Abstract**

Method, and apparatus for predicting mortality or imminent death in patients with congestive heart failure, includes detecting changes in the patient's temperature, and/or the detection of hypothermia. The apparatus includes a cutaneous sensor (102), an indwelling sensor (104), analyzer (114), and CPU (116).



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METHOD AND APPARATUS FOR PREDICTING MORTALITY IN CONGESTIVE HEART FAILURE PATIENTS

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention generally relates to methods of predicting mortality in patients with congestive heart failure, and more particularly to such methods including detection of hypothermia in a congestive heart failure patient. The invention also relates to apparatus, devices and kits for carrying out the methods.

Description of the Background Art

Congestive heart failure (CHF) is a leading, and increasing, cause of morbidity and mortality. Numerous predictors of mortality in patients with CHF have been described in the literature,including symptoms(e.g., exercise duration, as measured been identified by New York Heart Association class, peak oxygen uptake (VO_2) and treadmill time , including left ventricular ejection fraction (LVEF), age, atrial fibrillation(AF), ventricular tachycardia (VT), loss of R-R (heart rate)variability, cachexia ,serum levels of interleukins 1 and 6 and tumor necrosis factor alpha (TNF) and its receptors, creatinine, right ventricular ejection fraction (RVEF), hyponatremia, bilirubin, and recently, lymphocyte count. Nevertheless, these variables together account for only a portion of the variance, with the strong predictors usually applying to only a few patients, leaving prognosis uncertain for the individual patient.

See, e.g,, Ommen SR, Hodge DO, Rodeheffer RJ, McGregor CG, Thomson SP, Gibbons RJ., *Predictive power of the relative lymphocyte concentration in patients with advanced heart failure* [see comments]. CIRCULATION 1998; 97:19-22; Pierpont GL, Parenti CM., *Physician risk assessment and APACHE scores in cardiac care units*, CLIN CARDIOL 1999; 22:366-8; Vranckx P, Van Cleemput J., *Prognostic assessment of end-stage cardiac failure*, ACTA CARDIOL 1998; 53:121-5; Parameshwar J, Keegan J, Sparrow J, Sutton GC, Poole-Wilson PA, *Predictors of prognosis in severe chronic heart failure*, AM HEART J 1992; 123:421-6; Bonaduce D, Petretta M, Marciano F, et al. *Independent and incremental prognostic value of heart rate variability in patients with chronic heart failure,* AM HEART J 1999; 138:273-84; Teerlink JR, Jalaluddin M, Anderson S, et al. *Ambulatory ventricular arrhythmias in patients with heart failure do not specifically predict an increased risk of sudden death*, PROMISE (Prospective Randomized Milrinone Survival Evaluation) Investigators, CIRCULATION 2000; 101:40-6; Rouleau J, Shenasa M, de Champlain J, Nadeau R, *Predictors of survival and sudden death in patients with stable severe congestive heart failure due to ischemic and nonischemic causes: a prospective long term study of 200 patients*. CAN J CARDIOL 1990; 6:453-60; Cohn JN, Rector TS, *Prognosis of*

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The ability to accurately predict which patients are likely to have the shortest survival times is particularly needed in the selection of patients for heart transplantation or left ventricular assist device (LVAD) implantation (Hunt S, op cit). An accurate prognosis helps physicians optimize therapies for their patients. Even if in the circumstances a more accurate prognosis would not improve therapy (e.g., when the therapy has already been optimized), most patients and their families want as accurate a prognosis as possible (Fox E, op cit).

SUMMARY OF THE INVENTION

The invention contemplates a method, apparatus and kit devices for detecting a drop in a patient's body temperature as a means of predicting imminent death in congestive heart failure patients.

In accordance with this invention, a method of monitoring a patient with congestive heart failure for prognosis of survival comprises: obtaining an initial body temperature which is not elevated above normal, then obtaining subsequent body temperatures of the patient and determining whether the subsequent temperatures fit any of predetermined criteria showing a condition of congestive heart failure hypothermia. A method of warning of imminent mortality in a patient suffering from congestive heart failure absent therapeutic intervention comprises sensing internal and/or external temperatures of a patient, analyzing the temperatures to determine a data set conforming to a predefined condition signifying congestive heart failure hypothermia; and issuing an alarm reporting said condition.

Such criteria include any one or more of: (i) a decrease in temperature of about 2° F or more from said initial temperature, (ii) a decrease in temperature of 1° F or more within a 12 hour period, (iii) a decrease in temperature of about 1° F or more over 24 hours if the patient's mean temperature is at or below 96.5° F, and (iv) a decrease in mean temperature of two standard deviations below the patient's mean temperature over the prior 24 hours.

Body core and/or surface (cutaneous) temperatures may be utilized. For cutaneous temperatures, the method advantageously obtains a cutaneous temperature pattern of base line temperatures from a plurality of surface sites on the patient, and analyzes subsequent temperatures to determine variation of heat distribution over the body, outputting an alarm if said heat distribution over the body exceeds a predetermined pattern indicative of congestive heart failure hypothermia.

An embodiment of the method of the invention involving a staged or multi-step manner of monitoring for risk of imminent mortality in a patient suffering from congestive heart failure, comprises (a) determining an initial body temperature which is not in excess of 97° F, (b) obtaining subsequent body temperatures of the patient and determining whether the subsequent temperatures fit any of a first set of predetermined criteria for a condition of developing congestive heart failure hypothermia, and if so, (c) monitoring the patient under a second set of predetermined criteria for a developed condition of congestive heart failure hypothermia and determining whether the subsequent temperatures fit any of said second set of predetermined criteria, and if so; (d) triggering an alarm for intensive therapy.

A preferred embodiment measures the patient's temperature at more than one site, analyzes the detected temperatures and triggers an alarm should a temperature decline be detected. In a particular of this method, the temperature gradient between the patient's core and body surface

is measured. In accordance therewith, a preferred method of the invention comprises (a) determining an initial body temperature which is not in excess of 97° F, (b) obtaining at least one temperature sensor for measuring a cutaneous body temperature and at least one sensor for measuring a core body temperature; (c) positioning said sensors to be in direct contact with a patient having said initial temperature; (d) transmitting said core body temperature and said cutaneous body temperature at predetermined timed intervals to a processor programmed to analyze said temperatures; (e) analyzing said core body temperature and said cutaneous body temperature to determine if said temperatures fall outside of a predetermined criteria for a decrease in the patient's temperature signifying a condition of congestive heart failure hypothermia ; and (f) triggering an alarm if said temperatures fall outside of said predetermined criteria.

In one aspect the invention includes a method of monitoring a patient with congestive heart failure for prognosis of time remaining to death absent intervention, by obtaining an initial body temperature which is not elevated above normal, obtaining subsequent body temperatures of the patient and determining whether the subsequent temperatures fit any of predetermined criteria showing a condition of congestive heart failure hypothermia, and if so, predicting time to death according to the formula: time to death (hours) = 12.5 (°F – 95.24), where °F represents the current temperature of the patient.

The invention embodies apparatus, kits and temperature sensor devices for implementation of the invention. One such implement analyzes temperature measurements and comprises a processor programmed to activate an alarm if a temperature gradient between a core body temperature and a surface body temperature exceeds a predetermined criteria determined to signify congestive heart failure hypothermia.

A device useful in the present invention for monitoring body temperature preferably includes a temperature sensor included in an indwelling medical device, suitably a needle, tube, catheter, line, pacemaker, implanted pump and implanted defibrillator, adapted for monitoring the core body temperature of the patient. Suitable such tubes are a nasogastric tube, Dubbhoff tube, endotracheal tube, rectal tube, T-tubes, drain, and nasal probe. A suitable such catheter is a urinary catheter, pulmonary artery catheter, triple-lumen catheter, dialysis catheter, Hickman catheter, and infusion catheter . The temperature sensor may be a device for placement on the surface of the body such as a umbilical sensor, skin electrode, tympanic ear sensor, pulse oximeter, and casts. The temperature detector may be a thermocouple, thermistor, thermosensitive chromophore, thermosensitive liquid crystal, infrared detector or ultrasound detector

Another useful temperature sensor comprises a temperature measuring device having means for notifying a patient diagnosed with congestive heart failure when the patient's temperature decreases below a predetermined criteria.

In a greater particular, an apparatus useful in the practice of the invention includes a temperature detector for sensing temperature of a patient and generating a signal representative of the sensed temperature, a mount of said temperature sensor for indwelling or external placement on the patient, a data recorder for receiving said detector signals at timed intervals and using the signals to produce and store data representing temperatures of the patient sensed over time, an analyzer for processing said stored data to determine a data set conforming to a predefined condition signifying congestive heart failure hypothermia and outputting a signal indicative of the condition, and an alarm for receiving and reporting said output signal indicative of said condition. The apparatus can also include means of furnishing therapeutic warming to the patient.

It is further useful for the apparatus to include means providing one or more additional predictors including one or more of O_2 saturation, P_ACO_2, pH, respiratory rate, QRS width, R-R variability and T wave alternans, heart rate, blood pressure, pulse pressure and dP/dt, as a composite index to maximize sensitivity and specificity. Because most patients experience a fall in cardiac output and blood pressure before death (e.g. patients without known heart disease who are dying of sepsis, stroke, trauma, or failure of the kidneys, liver, or respiratory system) a temperature monitoring apparatus of the present invention augmented by e monitoring devices of the latter type also serves to warn of a risk of imminent death in these latter patients.

Yet another embodiment of the invention is a kit comprising a device having at least one temperature sensor for transmitting a signal indicative of the temperature of a patient with congestive heart failure, the means of receiving the signal indicative of the temperature of a patient and analyzing such signal to determine whenever the patient experiences a decline in temperature outside of a predetermined normal range, and a means for triggering an alarm if such a temperature decline occurs.

The core temperature measuring device of the kit suitably includes a temperature detecting means attached to an indwelling or attached medical device. If the latter, it is suitably an umbilical sensor, skin electrode, and tympanic ear sensor. The kit analyzer includes a processor programmed to identify when the temperature measurement transmitted to the analyzing means fall outside of a predetermined criteria. The predetermined criteria include any one of: (i) a decrease in temperature of about 2° F or more from said initial temperature, (ii) a decrease in temperature of 1° F or more within a 12 hour period, (iii) a decrease in temperature of about 1° F or more over 24 hours if the patient's mean temperature is at or below 96.5° F, and (iv) a decrease in mean temperature of two standard deviations below the patient's mean temperature over the prior 24 hours. The temperature monitoring kit alarm suitably notifies a person of a change in the patient's temperature, said notification including a text display, noise, shock, change in color or shape, warmth, or vibration. Advantageously the temperature monitoring kit includes means providing one or more additional predictors including one or more of O_2 saturation, P_ACO_2, pH, respiratory rate, QRS width, R-R variability and T wave

alternans, heart rate, blood pressure, pulse pressure and dP/dt, as a composite index to maximize sensitivity and specificity.

BRIEF DESCRIPTION OF THE DRAWINGS

The accompanying drawings, which are incorporated in and form a part of the specification, illustrate the embodiments of the present invention, and with the description, serve to explain the principles of the invention. In the drawings:

FIG. 1 is a graph illustrating that the temperature of a congestive heart failure patient upon admission into the hospital is predictive of that patient's survival;

FIG. 2 illustrates the consequences of hypothermia in a congestive heart failure patient;

FIG. 3 represents an embodiment of placement of cutaneous/core temperature monitoring devices;

FIG. 4 is a schematic of one embodiment of a staged or two step process of identifying patients at risk of imminent death.

FIG. 5 is a graph illustrating a time to death calculation in hypothermic congestive heart patients.

FIG. 6 is a depiction of a temperature sensing device incorporated with a Foley catheter suitable for indwelling use in the invention.

FIG. 7 is a depiction of a temperature sensing device wrist watch device wearable by a patient for remote signaling of an alarm of a hypothermic condition in accordance with the invention.

FIG. 8 is a depiction of a temperature sensing device beeper device wearable by a patient for remote signaling of an alarm of a hypothermic condition in accordance with the invention.

FIG. 9 is a schematic showing a preferred embodiment of the invention in which temperature measurement for occurrence of hypothermia is coupled with other predictors.

It is to be noted that the drawings illustrate only typical embodiments of the invention and are therefore not to be considered limiting of its scope, for the invention admits to other equally effective embodiments.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

In the descriptions which follow, abbreviations are employed for clarity and convenience, as set forth in the following list:

List of Abbreviations

Congestive heart failure	CHF
Left ventricular ejection function	LVEF

Right ventricular ejection fraction	RVEF
Peak oxygen uptake	VO_2
Left ventricular assist device	LVAD
Temperature	T
International Classification of Diseases, 9th Revision, Clinical modification	ICD-9 CM
Systolic blood pressure	SBP
Creatinine	CR
Leukocyte count	WBC
Lymphocyte count	lymph
Diastolic blood pressure	DBP
New York Heart Association	NYHA
Atrial fibrillation	AF
Ventricular tachycardia	VT
Systemic vascular resistance	SVR
Pulmonary capillary wedge pressure	PCWP
Reactive oxygen species	ROS
Cardiac output	C.O.
Myocardial oxygen consumption	MVO_2

A. Discovery: Hypothermia Is An Indicator of Imminent Death in Congestive Heart Failure

Initially, it was observed that one patient's temperature (T) fell from 97°F to 91.7°F two hours prior to death from severe congestive heart failure (CHF) despite maintenance of normal heart rate, blood pressure and mentation. A similar situation was noted in two more patients. In the third patient, medical treatment (nitrates, enalapril, digoxin) was intensified, the patient was warm, and the patient survived. This led to the novel hypothesis that some patients become hypothermic prior to death from congestive heart failure. This hypothesis is in contrast to teachings in the field suggesting that CHF is characterized by normal and slightly elevated temperatures.

Hypothermia was investigated as an indicator of imminent death from congestive heart failure. The outcomes of a number of patients admitted to the hospital with a diagnosis of congestive heart failure (CHF) were investigated to correlate their body temperature with death.

Hypothermia is generally defined as a core body temperature of 35°C (95°F) or below and is classified as mild (35-32°C), moderate (<32 to 28°C), or severe (<28°C). See Petty, K.J. "Hypothermia" in *Cardinal Manifestations and Presentation of Diseases*, McGraw-Hill Companies, 1998.

The Department of Medical Records at Hermann Hospital in Houston, Texas, USA, was the source of the data reported herein. A case-control retrospective study of patients who were admitted with CHF as one of the principal diagnoses was performed. The diagnosis was in accordance with the International Classification of Diseases, 9th Revision, Clinical modification

(ICD-9 CM). Information about CHF admissions, deaths and discharges between January 1, 1996 till June 1, 1998 was collected.

The cases were selected on the basis of having pure CHF without any other condition known to affect temperature. Exclusion criteria included all the deaths and discharges that were complicated with temperature confounders such as hepatic failure, infections, acute stroke, sepsis, thyroid disease, alcohol intoxication, exposure to cold or heating blankets. Medications were not causes for exclusion (aspirin, non-steroidal anti-inflammatory drugs, acetaminophens, steroids, vasopressors). Cardiovascular diseases were not causes for exclusion either.

Patients who died were selected as cases and were divided into two groups; those who died with hypothermia and those who died without it. Controls were randomly selected patients discharged alive with CHF as a primary diagnosis who fulfilled the same inclusion criteria as the cases. Controls were divided into two groups in a manner identical to the cases (i.e., those having hypothermia and those without hypothermia). Overall 148 patients (53 cases and 95 controls) were analyzed by SPSS software (1998).

TABLE 1

UNIVARIATE ANALYSIS

VARIABLES	CASES (N=53)	CONTROLS (N=96)	*P* VALUE
Age (Years)	73.45 +/-13.8	69.3 +/-14.3	0.088
Sex (M:F)	24:29	52:44	
Race(W,B,O)	W:29, B:19, O:05	W:41, B:46, O:4, H:5	
Systolic BP	118.4 +/-28.1	136.9 +/-26.7	.0001
Diastolic BP	70 +/-17.5	75.7 +/-17.5	.060
HR	88.1 +/-21.9	84.6 +/-19.9	.320
Creatinine (Cr)	1.9 +/-1.4	1.4 +/-1.1	.014
Sodium (Na)	137.9 +/-3	138 +/-3.2	.941
LVEF (%)	37 +/-17.7	42.4 +/-14.9	.364
RVF	↓↓	↓	
Leukocytes (WBCs)	8.8 +/-2.1	8.1 +/-1.8	0.022
Lymphocyte Count	15 +/-6.8	20.1 +/-9.3	.001
Last Temp (T2)	96.5 +/-2.3	97.6 +/-0.9	.0001
Adm.Temp (T1)	97.2 +/-1.8	97.7 +/-0.8	.025
Ave. Temp	97.1 +/-1.5	97.6 +/-0.7	.003
T ↓ (last 12 hrs)	-0.6 +/-1.9	-0.01 +/-1.0	.009
ΔT (T2-T1)	-0.7 +/-2.7	-0.1 +/-1.1	.066

Table 1 gives patient demographics of cases (deaths) and controls (patients discharged alive with CHF) and univariate analysis of differences (2 tailed P; equal variances assumed). Patients who died of CHF had lower systolic blood pressure, serum sodium, leukocyte count and higher creatinine. Age and diastolic blood pressure were borderline predictors. The most

significant predictors were the last recorded oral temperature, lymphocyte count, temperature fall over the last 12 hours, average temperature and admission temperature.

TABLE 2

MULTIVARIATE LOGISTIC REGRESSION ANALYSIS

VARIABLE	ODDS RATIO	95% CI	P
Systolic Blood Pressure	0.972	0.94 - 0.99	0.042
Diastolic Blood Pressure	1.023	0.98 - 1.06	0.247
Creatinine	1.570	1.10 - 2.23	0.011
Leukocytes	1.343	1.04 - 1.71	0.019
Lymphocyte Count	0.920	0.86 - 0.97	0.005
Last Temp	10.254	3.74 - 28.10	0.00001

Table 2 gives the multivariate logistic regression analysis of variables of systolic blood pressure (SBP), creatinine (CR), leukocyte count (WBC), lymphocyte count (lymph), last temperature (temp, indicating the last recorded temperature divided categorically into $\geq 97^{\circ}$ F. and $< 97^{\circ}$ F.) and diastolic blood pressure (DBP). Variables with a P value above 0.1 in the univariate analysis were not included. The odds ratio and 95% confidence intervals are shown. The strongest predictor of death during the patient's hospital stay was the last recorded oral temperature, followed by the lymphocyte count. In this case-control study, hypothermia emerged as a strong predictor of death in patients admitted with congestive heart failure.

This was surprising because temperature is not listed as a prognostic variable in any of the dozen of papers prognosis of CHF. Indeed, it was not even been included in the data sets. Nor is CHF listed as a cause of hypothermia though age, stroke, medications and shock which often coexists with CHF are known risks for hypothermia. Therefore, we undertook a second study to see if the first could be confirmed.

Because case-control studies have well-known limitations, including missing data and can be confounded by unsuspected associations, a second type of study was performed, a retrospective cohort study. All of the 1998 admissions to Hermann Hospital whose primary discharge diagnosis (or death) was congestive heart failure were analyzed, using the same International Classification of Disease coding as in the previous study. For patients admitted more than once during the year, only the last admission was studied. Potential confounders of temperature, such as sepsis, acute stroke, thyroid disease, alcohol intoxication or cold exposure, resulted in the exclusion of 35 of the original 423 patients. Medications were not used to exclude patients. Another 97 were excluded because of multiple admissions to the hospital during that year. Medications were not cause for exclusion. The remaining 291 charts were reviewed according to the following prospective criteria, which include the reported prognostic variables for CHF, in groupings that conform to the

usual stages of clinical assessment of the patient. Analysis was by Cox regression. David W., Jr. Hosmer, Stanley Lemeshow. *Applied survival Analysis: Regression of Time to Event Data*; John P. Klein, M. L. Moeschberger (Contributer). *Survival Analysis: Techniques for Censored and Truncated Data (Statistics for Biology and Health)*.

Bedside variables were considered first. These included age, sex, a history of hypertension or diabetes or coronary artery disease or symptoms thereof, New York Heart Association (NYHA) CHF class, valvular disease, heart rate, blood pressure and temperature.

In situations of missing data, the variable was dropped if more than a third of the patients were lacking that particular variable. Of the remaining variables, missing data were handled by assuming the mean of the cohort for that particular variable.

A second analysis examined the prognostic ability of admission temperature compared to arrhythmia (ventricular tachycardia and/or atrial fibrillation) and RR variability. No analysis for T-wave alternans was undertaken because arrhythmic death was not the focus of the study.

A third analysis compared temperature to echocardiographic and angiographic variables.

A fourth analysis compared temperature to laboratory variables, including creatinine, serum sodium, lymphocyte count, glucose, potassium and carbon dioxide.

In the comparison of bedside variables (shown in Table 5), hypothermia was the best predictor of in-hospital mortality (P=.004), followed by systolic blood pressure (P=.015) NYHA class (P=0.47) and female sex (P=.047). Tricuspid regurgitation a trend toward significance (P=.06), but hypertension, diabetes, coronary artery disease, diastolic BP, mitral regurgitation and heart rate on admission did not.

Table 5

Multivariate analysis of bedside variables (derived from history and exam) predicting in-hospital mortality of CHF patients. Temperature is mean of hospital stay; NYHA = New York Heart Association; CHF = Congestive Heart Failure: TR = Tricuspid valve regurgitation; SBP = Systolic Blood Pressure on admission. Variables not associated with mortality were age, history of hypertension, diabetes, or coronary atherosclerosis; findings of aortic or mitral valve disease, heart rate, and diastolic blood pressure.

Variable	Odds Ratio	P Value
Temperature	0.3296	0.0042
Sex (Female)	3.6733	0.0468
NYHA	2.3920	0.0469
TR	31.6312	0.0604
SBP	0.9561	0.0154

Compared to electrocardiographic variables, such as arrhythmia and variability in the RR interval (P=.88 and .89, respectively), temperature was more significant, with a borderline P value of .06. Most charts locked on LVEF or RV dimension for that specific hospitalization. Analysis of just those cases that did have the data revealed that, compared to LVEF, temperature was of borderline significance (OR=0.45, P= 0.06) while LVEF was not a significant predictor (P=0.77). However, among cases with data on RV enlargement (OR=8.8, P=0.014), temperature lost predictive value. This must be interpreted with caution because it is a subset analysis (only 2 variables) on a subset of patients (96 of 291) that may have a selection bias. In any event RV function can not be evaluated at the bedside or monitored non-invasively.

Compared to laboratory variables, temperature was of borderline significance (P=.077), and creatinine, a well-recognized prognostic factor, was the most significant, with a P value of .003. In this data set, hyponatremia and lymphopenia were not significant (P=.53 and P=.70, respectively). Bilirubin, a recently described predictor, was not measured in enough patients to be included in the multivariate analysis. In a subset analysis of 193 patients, T remained predictive (OR=0.32, P=0.0008) but bilirubin (P=0.27) was not.

Other variables with too many missing data points for inclusion in the multivariate analysis, which were compared in subset analyses to temperature were VT(OR=8.7,p=0.0000, vs OR=0.44, p=0.046 for T) and variables which did not predict mortality (AF,R-R variability, and use of beta-blockers, ACE inhibitors, aspirin, or amiodarone) though in each comparison T remained significantly and inversely associated with mortality.

Taken together, these different analyses of different data sets demonstrate with considerable consistency an association of hypothermia with CHF mortality. Hence, the data presented in the present application, derived from two different types of analysis, are robust. Indeed it is likely that standardizing the T data, i.e. per rectum, aural or oral etc., normalizing to correct for circadian variation, and collecting continuous T, will increase the sensitivity and specificity of T as a prognostic variable.

Temperature, shown in Table 1 with a P value of 0.025, was also shown to correlate with survival. FIG. 1 plots the temperature at the time of admission against the survival time of the patient in hours. As can be seen in the graph shown in FIG. 1, temperature at the time of admission is related to the patient's survival time. Moreover, a core temperature decrease from the patient's baseline temperature (e.g., average temperature or temperature upon admission to the hospital) is predictive of imminent death in the patient (i.e., within 24 hours) and suggests that the patient needs more intensive medical therapy or consideration for heart transplantation or left ventricular assistance.

A regression analysis of the data shown in FIG. 1 produces the graph illustrated in FIG. 5, which yields the formula for time to death once hypothermia commences in a congestive heart failure patient.

The literature suggests that several competing mechanisms may be operating in the observed temperature decrease. Factors that are expected to increase temperature in congestive heart failure, as noted in prior reports, are listed in Table 3. These reports also suggest that a number of factors may contribute to the decrease in temperature in patients with congestive heart failure, as listed in Table 4.

TABLE 3

FACTORS THAT MAY DECREASE TEMPERATURE IN CHF

- Vasodilator therapy
- Inactivity
- Decreased metabolism due to hypoxemia and severe vasoconstriction
- Decreased liver/intestinal metabolism due to venous congestion
- Anti-inflammatory effect of hypercortisolemia
- Malnutrition
- Cell senescence
- Down regulation of mitochondrial uncoupling proteins
- Down regulation of adenylate cyclase
- Down regulation of β adrenergic receptors
- Decreased metabolism due to CNS effects of norepinephrine, epinephrine, angiotensin II
- Uncoupling of receptors from G proteins
- Increased neurotensin

TABLE 4

FACTORS THAT MAY INCREASE TEMPERATURE IN CHF

- Tachycardia
- Tachypnea
- Vasoconstriction
- "Oxygen-wasting" effect of norepinephrine, epinephrine
- B_3- adrenergic stimulation
- Pyrogenic cytokines (interleukins no 1,6,8 and TNF-α)
- Oxidation by myocardial macrophages
- Increased β adrenergic receptors due to increased cortisol

B. Consequences of Hypothermia in CHF

It is not known whether hypothermia adds to a patient's risk of death or whether it is solely a marker of imminent death. The excess vasoconstriction caused by hypothermia may initiate local tissue death, hepatic congestion or a hypothalamic effect. As shown in FIG. 2, hypothermia causes an increase in systemic vascular resistance (SVR), which can precipitate or complicate the symptoms of myocardial infarction such as decreased cardiac output (C.O.) and increased pulmonary capillary wedge pressure (PCW). Such effects are known to increase the levels of norepinephrine (NE), angiotensin II (AII), epinephrine (EP), central nervous tissue (CNS), interleukin (IL), tumor necrosis factor (TNF) and the production of reactive oxygen species (ROS). Hypothermia also decreases the myocardial oxygen consumption (MVO_2).

It is proposed that the reasons some of the CHF patients develop hypothermia at the very end stage of their disease include a decline in heat production due to adrenergic receptor uncoupling, inactivity, anorexia, hypoxemia, and other factors, as shown in Table 3. (Gong DW, et al.,*Uncoupling protein 3 is a mediator of thermogenesis regulated by thyroid hormone,beta3 agonists and leptin.* J BIOL CHEM 1997, 272:24129-24132; Wilson KM,Fregly MJ., *Factors affecting angiotensin II- induced hypothermia in rats.* PEPTIDES 1985, 6:695-701; Hissa R, et al., *Noradrenaline-induced hypothermia is suppressed in the vagotomized cold-exposed pigeon*, COMP BIOCHEM PHYSIOL 1995, 111:89-97; Gully D et al., *Biochemical and pharmacological activities of a new potent neurotensin receptor antagonist.* J PHARMACOL EXP THER 1997;280:802-812.)

In addition, since stable CHF patients have relatively higher resting basal metabolic rates and oxidative stress (Keith M et al., *Increased oxidative stress in patients with congestive heart failure*, J AM COLL CARDIOL 1998, 31:1352-1356), the bodies of these patients may well use an inefficient f-oxidative pathway (such as glycolysis). Increased lactate level is another indicator that these patients are not using oxygen efficiently. This evidence, considered in light of Shellock FG, Rubin SA. *Mixed venous blood temperature response to exercise in heart failure patients treated with short-term vasodilators*, CLIN PHYSIOL 1985; 5:503-14, and Shellock FG, Rubin SA, Ellrodt AG, Muchlinski A, Brown H, Swan HJ, *Unusual core temperature decrease in exercising heart-failure patients*, J APPL PHYSIOL 1983, 54:544-50, regarding the effects of vasodilators and the core temperature decrease with exercise in heart-failure patients, strongly suggests that in pre-terminal CHF there is decompensation of sympathetic constriction of the peripheral vascular bed. Little by little the warm core blood circulates into cool extremities and muscles resulting in a drop in core temperature. By comparing the peripheral cutaneous temperatures of hypothermic and normothermic patients, it can be determined whether there is relatively more peripheral vasodilation in congestive heart failure patients. A suitable parameter for comparison is the gradient of temperature between peripheral and core areas in the two groups.

Thus, a core temperature decrease from the patient's baseline temperature (e.g., average temperature or temperature upon admission to the hospital) is predictive of imminent death in the patient (i.e., within 24 hours) and suggests a need for intensive medical therapy or consideration for heart transplantation or left ventricular assistance. In addition to the successful intervention in one patient described above, the complications of vasoconstriction caused by cold suggest that hypothermia may not only be a prognostic marker and a stimulus to intervene with medicines, devices or transplantation, but also an indication to warm the patient, indeed a recent paper described an improvement in symptom when CHF patients (who were not hypothermic) were warmed (Tei C et al., *Acute hemodynamic improvement by thermal vasodilation in congestive heart failure,* CIRCULATION 1995, 91:2582-2590. These findings differ from the medical literature in that:

1) Very mild hypothermia, such as was observed in terminal CHF patients, has not been associated with increased mortality (perhaps because most of the patients in those hypothermia reports did not have CHF).

2) Warming did not just relieve symptoms and signs of CHF but also prolonged life.

C. Identifying Patients at Risk of Imminent Death from Congestive Heart Failure

Hypothermia, as shown above, is a clinically significant sign that a patient needs more intensive medical therapy or consideration for heart transplantation or left ventricular assistance.

One embodiment of the present invention provides one or more sensors that patients diagnosed with CHF can wear at home to warn them or their caretakers when they need to call their physician or go to the hospital for observation and/or treatment. The sensors may be fiber or plastic strips containing thermosensitive chromophores or liquid crystals, similar to conventional fever strips used in the home for measuring a child's temperature. Any suitable temperature measuring device, such as a remotely monitored thermistor or thermocouple assembly, could be substituted. Such sensors may be skin electrodes that are taped onto the body or strapped onto the body (see U.S. Pat. No. 4,763,112, which is incorporated herein by reference as if set forth verbatim), or built into clothing or accessories that are worn by the patient. For example, a temperature sensor may be built into a hearing aid or eyeglasses for those patients that wear one or the other. In addition, wristwatches, beepers, caps, belts, underwear, socks, shoes, rings, necklaces and other types of clothing or clothing accessories may be adapted to measure body temperature.

Another embodiment of the present invention provides multiple sensors for the measurement of cutaneous and core temperatures of a patient. For an example of a core temperature measurement device, see U.S. Pat. No. 4,981,139, which by reference is incorporated

herein as if set forth in the entirety. The placement of temperature sensors at any or all of the locations shown in FIG. 3 is envisioned. In addition, bilateral temperature sensors may be placed on each leg and each arm. One or more cutaneous sites, such as fingers 32, toes 34, upper arms 36, thighs 38 and neck 39 are monitored. Additional sites such as the upper arm 36 and the lower leg 37 may also be monitored. Each strip is not necessarily connected to another, and may be monitored separately or simultaneously.

The patient is preferably scored on his overall temperature compared to a general reference criteria, or the patient's own reference criteria if known. Additionally, or alternatively, the pattern of heat distribution over the body, reflecting variations in vasoconstriction, can be considered against reference data for each respective point. Although the lability in temperature is also likely to predict death because it is a sign of autonomic dysfunction, the devices described herein are disclosed for use in monitoring CHF patients, these devices may also be used in a number of other situations such as monitoring peripheral vascular circulation.

Temperature sensors can be directly attached to or inserted into any medical device that comes into direct contact with the patient such as a nasogastric tubes, Dobbhoff and endotracheal tubes, pulmonary artery catheters (e.g., Swan-Ganz catheter), urinary catheters, T-tubes, drains, rectal tubes, arterial lines, triple-lumen and dialysis catheters, pacemakers (both temporary and permanent), intra-aortic balloon pumps, implantable defibrillators, remote (EGIR) monitors, Hickman and similar chronic infusion catheters, pulse oximetry probes, nasal probes for carbon dioxide monitoring, intravenous needles, and other invasive devices. Such indwelling or attached devices preferably include on the instrument a thermistor or thermocouple device to remotely monitor the core temperature of the patient. The core temperature may also be monitored by any suitable non-invasive technique, such as by placement of a sensor in the umbilicus 31 or ear 33. Cutaneous temperature measurements can be taken by including temperature sensors in skin electrodes, casts, hearing aids, and the like.

D. Patient Monitoring

Whenever a patient diagnosed with CHF is admitted to a hospital, the patient's temperature is taken. If the patient's admitting temperature is less than about 96.5° F, the patient is identified as a candidate for constant temperature monitoring.

A process of patient temperature monitoring is illustrated in FIG. 9. Referring to FIG. 9, a patient 100 is fitted with at least one, and preferably multiple temperature sensors (a plurality is indicated by "1...N" on FIG. 8), suitably a cutaneous sensor as at 102 and indwelling sensor as indicated by the dashed line 104, for example as provided by the temperature sensor applied to a Foley's catheter as depicted in FIG. 6) entered through a femoral artery. The signals collected from these temperature monitors are transmitted by conductors 106, 107 to connectors on a printed

circuit card 108 where signal conditioning circuitry 109 energized by power supply 110 process the signals and route them to amplifiers 112 that output the amplified signals to an analyzer 114 that incorporates data buffers for receiving and retaining the amplified signals until the signals are accessed and processed by a central processing unit (CPU) 116 acting under the control of a program suitably incorporated into a programmable read only memory (PROM) chip 118. Power supply 120 energizes analyzer . Under the control of the PROM, the CPU compares follows the temperature history of the patient, suitably comparing the current temperature data represented by the signals from buffer 114 to the patient's reference data suitable also entered (not shown) and held in buffer memory. The data can be compared as a whole, or it can be compared for each temperature sensor in place.

The temperature detected by the temperature sensor suitably is analyzed at predetermined time intervals, or averaged over specific time intervals and then the average analyzed. The temperature measurements are analyzed to detect deviations from the patient's baseline information and the usual core-to-surface temperature gradient. Specifically, an elevated gradient (core T minus cutaneous T) indicates the sympathetic vasoconstriction response to CHF, unless the air is cold or the vessels are constricted by mucosal sympathetic tone due, for example, to anxiety, or constricted by medication. A falling (normalizing) gradient is a sign of vasodilator therapy, a cornerstone of CHF therapy. A low gradient in CHF patient with a cool core T indicates high risk of death.

Whenever a change in temperature is detected that falls outside of preselected criteria a signal 122 is transmitted to an alarm device to notify the patient, the nurse, or the physician that a significant change in temperature has occurred. The alarm may be any means which can be perceived, locally and/or remotely. Examples of potential preselected criteria are when the patient's temperature decreases: a) more than 2° F degrees from the admitting temperature, b) about 1° F. or more within 12 hours, c) about 2° F. or more over a 24 hour period, or d) about 1° F. or more over 24 hours if the baseline temperature of the patient is below 96.5° F. or falls two standard deviations below that patient's mean for the prior 24 hours.

As shown in FIG. 4 an optional dual signaling system may be used. A first signal is sent when a first predetermined criteria is met or surpassed. This signal would most likely be sent to the nurses station to identify the patient as needing more intensive monitoring. This first signal may also initiate a change in the analysis program used to analyze the collected data. For example, the time criteria for taking measurements may be changed or the rate of temperature change allowed decreased to represent a stricter criteria. Whenever the patient's temperature falls beyond a second criteria, a second signal is transmitted or an alarm triggered indicating the patient may need left ventricular assistance or other more intensive therapy.

Also depicted in FIG. 9 are signals (generally indicated by reference numeral 126) from a plurality of sensors for selectively and continuously sensing various vital signs indicative of physiological conditions, including one or more of O_2 saturation sensor 132, P_ACO_2 sensor 135, pH sensor 138,, respiratory rate sensor 141, QRS width sensor 144, R-R variability and T wave alternans sensors 147 and 150, heart rate, blood pressure, pulse pressure and dP/dt sensors 153, 156, 159 and 162, respectively,. The sensed signals are fed by conductors 133, 136, 139, 142, 145, 148, 151, 154, 157, 160, 163 respectively, to data buffers 114 of analyzer 114, where CPU 116 processes these received signals according to instructions from PROM and outputs a composite index of physiological predictors to maximize sensitivity and specificity of the monitoring process.

FIG. 7 depicts a wrist watch device 200 adapted to be worn again the skin of a congestive heart failure patient (as at home) to monitor the temperature of the patient (indicated at 202) and emit a local (sound or vibration) and remote (telemetry) signal warning if cutaneous temperature at the wrist at has dropped to a level, show at display 204 for example as 36.02 °C, signaling onset of a potentially dangerous hypothermia. The alarm may be text displays, noises, mild electric shocks, changes in color or shape, vibrations, warmth, or an electronic signal to a remote location such as a computer (including palm held device) or telephone system. Referring to FIG. 8, another device wearable by an out-patient is depicted at 300. This device is a beeper worn against skin that emits an alarm to the wearer and by telemetry to a station where action can be taken in aid of the wearer. The devices of FIGS. 7 and 8 are merely exemplary and other suitable devices with the scope of this invention for ascertaining a condition of hypothermia will be apparent to those skilled in the art and are deemed with in the scope of the hypothermia detection invention.

The ability to carefully monitor a CHF patient's body temperature may well help to save these patient's lives by providing notice of a change in prognosis in time to alter the therapy being administered. It may also provide a more accurate prognosis for the patients and their families.

E. Mortality Predictive Kit

Preferably a set of temperature monitoring devices are provided in an easy-to-use kit for identifying patients at imminent risk of dying from congestive heart failure. A suitable kit would include at least one device for monitoring the core body temperature of the patient, such as a Swan-Ganz catheter, IV needle, urinary catheter or the like, equipped with a temperature sensor such as a thermistor or thermocouple. A conventional tympanic ear temperature monitoring device or umbilicus temperature monitoring device could also be included for measuring the core body temperature. In addition, the kit would include at least one device for monitoring the temperature of cutaneous sites, such as the fingers, toes, upper arms, thighs, and optionally calves and forearms. The kit could also include electronic equipment for analyzing temperature signals and triggering an alarm if a dangerous decline in temperature is detected in the patient.

Alternatively, temperature sensors may be incorporated into other monitoring devices such that temperature and O_2 saturation and/or pCO_2 and/or blood pressure, change in width of the QRS or QT interval, or other parameters would be measured simultaneously and used to enhance the prediction of CHF mortality.

Although the present invention and its advantages have been described in detail, it should be understood that various changes, substitutions, and alterations can be made to the described methods and apparatus without departing from the spirit and scope of the invention as defined by the appended claims.

CLAIMS

1. A method of monitoring a patient with congestive heart failure for prognosis of survival, which comprises:
   (a) obtaining an initial body temperature which is not elevated above normal,
   (b) obtaining subsequent body temperatures of the patient and determining whether the subsequent temperatures fit any of predetermined criteria showing a condition of congestive heart failure hypothermia.

2. The method of claim 1 in which upon detection of a temperature less than normal temperature, core body temperature is monitored in step (b).

3. The method of claim 1 further characterized in that the initial body temperature is cutaneous and obtained as a pattern of base line temperatures from a plurality of surface sites on the patient, and step (b) includes analyzing the subsequent temperatures to determine variation of heat distribution over the body, and further including the step of (c) outputting an alarm if said heat distribution over the body exceeds a predetermined pattern indicative of congestive heart failure hypothermia.

4. The method of claim 1 in which said predetermined criteria showing a condition of congestive heart failure hypothermia include any one or more of:
   (i) a decrease in temperature of about 2° F or more from said initial temperature,
   (ii) a decrease in temperature of 1° F or more within a 12 hour period,
   (iii) a decrease in temperature of about 1° F or more over 24 hours if the patient's mean temperature is at or below 96.5° F,
   (iv) a decrease in mean temperature of two standard deviations below the patient's mean temperature over the prior 24 hours.

5. A method of predicting time remaining to death absent intervention for a patient with congestive heart failure, which comprises:
   (a) obtaining an initial body temperature which is not elevated above normal,
   (b) obtaining subsequent body temperatures of the patient and determining whether the subsequent temperatures fit any of predetermined criteria showing a condition of congestive heart failure hypothermia, and if so,
   (c) predicting time to death according to the formula:
   Time to Death (hours) = 12.5 (°F – 95.24)

where °F represents the current temperature of the patient.

6. A method of warning of imminent mortality in a patient suffering from congestive heart failure absent therapeutic intervention, comprising:

(a) sensing internal and/or external temperatures of a patient

(b) analyzing the temperatures to determine a data set conforming to a predefined condition signifying congestive heart failure hypothermia; and

(c) issuing an alarm reporting said condition.

7. A method of predicting imminent mortality in a patient suffering from congestive heart failure, comprising:

(a) determining an initial body temperature which is not in excess of 97° F,

(b) obtaining subsequent body temperatures of the patient and determining whether the subsequent temperatures fit any of a first set of predetermined criteria for a condition of developing congestive heart failure hypothermia, and if so,

(c) monitoring the patient under a second set of predetermined criteria for a developed condition of congestive heart failure hypothermia and determining whether the subsequent temperatures fit any of said second set of predetermined criteria, and if so;

(d) triggering an alarm for intensive therapy.

8. A method of predicting imminent mortality in a patient suffering from congestive heart failure, comprising:

(a) determining an initial body temperature which is not in excess of 97° F,

(b) obtaining at least one temperature sensor for measuring a cutaneous body temperature and at least one sensor for measuring a core body temperature;

(c) positioning said sensors to be in direct contact with a patient having said initial temperature;

(d) transmitting said core body temperature and said cutaneous body temperature at predetermined timed intervals to a processor programmed to analyze said temperatures;

(e) analyzing said core body temperature and said cutaneous body temperature to determine if said temperatures fall outside of a predetermined criteria for a decrease in the patient's temperature signifying a condition of congestive heart failure hypothermia : and

(f) triggering an alarm if said temperatures fall outside of said predetermined criteria.

9. The method of claim 8 in which said predetermined criteria in step (e) comprise at least one of:

(i) a decrease in temperature of about 2° F or more from said initial temperature,

(ii) a decrease in temperature of 1° F or more within a 12 hour period,

(iii) a decrease in temperature of about 1° F or more over 24 hours if the patient's mean temperature is at or below 96.5° F,

(iv) a decrease in mean temperature of two standard deviations below the patient's mean temperature over the prior 24 hours.

10. Apparatus for monitoring a patient with congestive heart failure for prognosis of survival, comprising:

(a) a temperature detector for sensing temperature of a patient and generating a signal representative of the sensed temperature

(b) a mount of said temperature sensor for indwelling or external placement on the patient,

(c) a data recorder for receiving said detector signals at timed intervals and using the signals to produce and store data representing temperatures of the patient sensed over time,

(d) an analyzer for processing said stored data to determine a data set conforming to a predefined condition signifying congestive heart failure hypothermia and outputting a signal indicative of the condition, and

(e) an alarm for receiving and reporting said output signal indicative of said condition.

11. The apparatus of claim 10 in which said predefined condition signifying congestive heart failure hypothermia is any one or more of:

(i) a decrease in temperature of about 2° F or more from said initial temperature,

(ii) a decrease in temperature of 1° F or more within a 12 hour period,

(iii) a decrease in temperature of about 1° F or more over 24 hours if the patient's mean temperature is at or below 96.5° F,

(iv) a decrease in mean temperature of two standard deviations below the patient's mean temperature over the prior 24 hours.

12. The apparatus of claim 10 in which said mount is an indwelling medical device selected from the group consisting of a needle, tube, catheter, line, pacemaker, implanted pump and implanted defibrillator.

13. The apparatus of claim 12, wherein said tube is selected from the group consisting of a nasogastric tube, Dobbhoff tube, endotracheal tube, rectal tube, T-tubes, drain, and nasal probe.

14. The apparatus of claim 12, wherein said catheter is selected from the group consisting of a urinary catheter, pulmonary artery catheter, triple-lumen catheter, dialysis catheter, Hickman catheter, and infusion catheter.

15. The apparatus of claim 10, wherein said mount for external placement is selected from the group consisting of umbilical sensor, skin electrode, tempanic ear sensor, pulse oximeter, and casts.

16. The apparatus of claim 10 in which said temperature detector is selected from the group consisting of a thermocouple, thermistor, thermosensitive chromophore, thermosensitive liquid crystal, infrared detector and ultrasound detector.

17. The apparatus of claim 10 further including means providing one or more additional predictors including one or more of O_2 saturation, P_ACO_2, pH, respiratory rate, QRS width, R-R variability and T wave alternans, heart rate, blood pressure, pulse pressure and dP/dt, as a composite index to maximize sensitivity and specificity.

18. Apparatus comprising:

(1) means for monitoring a patient with congestive heart failure for prognosis of survival, including:

(a) a temperature detector for sensing temperature of a patient and generating a signal representative of the sensed temperature

(b) a mount of said temperature sensor for indwelling or external placement on the patient,

(c) a data recorder for receiving said detector signals at timed intervals and using the signals to produce and store data representing temperatures of the patient sensed over time,

(d) an analyzer for processing said stored data to determine a data set conforming to a predefined condition signifying congestive heart failure hypothermia and outputting a signal indicative of the condition, and

(e) an alarm for receiving and reporting said output signal indicative of said condition; and

(2) means of furnishing therapeutic warming to the patient.

19. A temperature monitoring kit for identifying a patient at risk of imminent death due to congestive heart failure, the kit comprising:

(a) at least one device for measuring a core temperature of a patient;

(b) at least one device for measuring a cutaneous temperature of the patient;

(c) means for transmitting the temperature measurements taken by said core temperature measuring device and said cutaneous temperature measuring device;

(d) means for analyzing the transmitted temperature measurements; and

(e) an alarm for reporting a dangerous decline in temperature in said patient.

20. The temperature monitoring kit of claim 19, wherein said core temperature measuring device includes a temperature detecting means attached to an indwelling or attached medical device.

21. The temperature monitoring kit of claim 19, wherein said cutaneous measuring device is selected from the group of umbilical sensor, skin electrode, and tympanic ear sensor.

22. The temperature monitoring kit of claim 19, wherein said analyzing means includes a processor programmed to identify when the temperature measurement transmitted to the analyzing means fall outside of a predetermined criteria.

23. The temperature monitoring kit of claim 22, wherein said predetermined criteria include any one of:

(i) a decrease in temperature of about 2° F or more from said initial temperature,

(ii) a decrease in temperature of 1° F or more within a 12 hour period,

(iii) a decrease in temperature of about 1° F or more over 24 hours if the patient's mean temperature is at or below 96.5° F,

(iv) a decrease in mean temperature of two standard deviations below the patient's mean temperature over the prior 24 hours.

24. The temperature monitoring kit of claim 19 wherein the alarm notifies a person of a change in the patient's temperature, said notification including a text display, noise, shock, change in color or shape, warmth, or vibration.

25. The temperature monitoring kit of claim 19 further including means providing one or more additional predictors including one or more of O_2 saturation, P_ACO_2, pH, respiratory rate, QRS width, R-R variability and T wave alternans, heart rate, blood pressure, pulse pressure and dP/dt, as a composite index to maximize sensitivity and specificity.

26. A temperature monitoring kit for identifying a patient at risk of imminent death due to congestive heart failure, the kit comprising:

(a) at least one device for measuring a core temperature of a patient, wherein said core temperature measuring device includes a temperature detecting means attached to an indwelling or attached medical device;

(b) at least one device for measuring a cutaneous temperature of the patient, wherein said cutaneous measuring device is selected from the group of an umbilical sensor, skin electrode, and tympanic ear sensor;

(c) means for transmitting the temperature measurements taken by said core temperature measuring device and said cutaneous temperature measuring device;

(d) means for analyzing the transmitted temperature measurements, wherein said analyzing means includes a processor programmed to identify when the temperature measurement transmitted to the analyzing means has decreased about 1° F or greater within a 12 hour period, about 2° F or greater over a 24 hour period, or about 1° F or greater if the patient's baseline temperature is at or below 96.5° F or two standard deviations below the patient's mean temperature for the prior 24 hours; and

(e) an alarm for reporting a dangerous decline in temperature in said patient, wherein the alarm notifies a person of a change in the patient's temperature, said notification including a text display, noise, shock, change in color or shape, warmth, or vibration.

27. A device for analyzing temperature measurements comprising a processor programmed to activate an alarm if a core body temperature of a patient suffering from congestive heart failure and exhibiting a hypothermic baseline temperature of 97° F or less has

(i) a decrease in temperature of about 2° F or more from said initial temperature,

(ii) a decrease in temperature of 1° F or more within a 12 hour period,

(iii) a decrease in temperature of about 1° F or more over 24 hours if the patient's mean temperature is at or below 96.5° F,

(iv) a decrease in mean temperature of two standard deviations below the patient's mean temperature over the prior 24 hours.

28. A device for analyzing temperature measurements comprising a processor programmed to activate an alarm if a temperature gradient between a core body temperature and a surface body temperature exceeds a predetermined criteria determined to signify congestive heart failure hypothermia.

29. Apparatus for providing alarm of imminent mortality in a patient suffering from congestive heart failure, comprising means for initially and subsequently obtaining body temperatures of

a patient of 97° F and lower and determining whether the subsequent temperatures lower than 97° F fit any of a first set of predetermined criteria for a condition of developing congestive heart failure hypothermia, and if so, monitoring the patient under a second set of predetermined criteria for a developed condition of congestive heart failure hypothermia and determining whether the subsequent temperatures fit any of said second set of predetermined criteria, and if so; triggering an alarm for intensive therapy.

30. A temperature sensor comprising a temperature measuring device, said measuring device having means for notifying a patient diagnosed with congestive heart failure when the patient's temperature decreases below a predetermined criteria.

31. The temperature sensor of claim 29, wherein said sensor is attached to the patient's wristwatch, clothing, or clothing accessories.

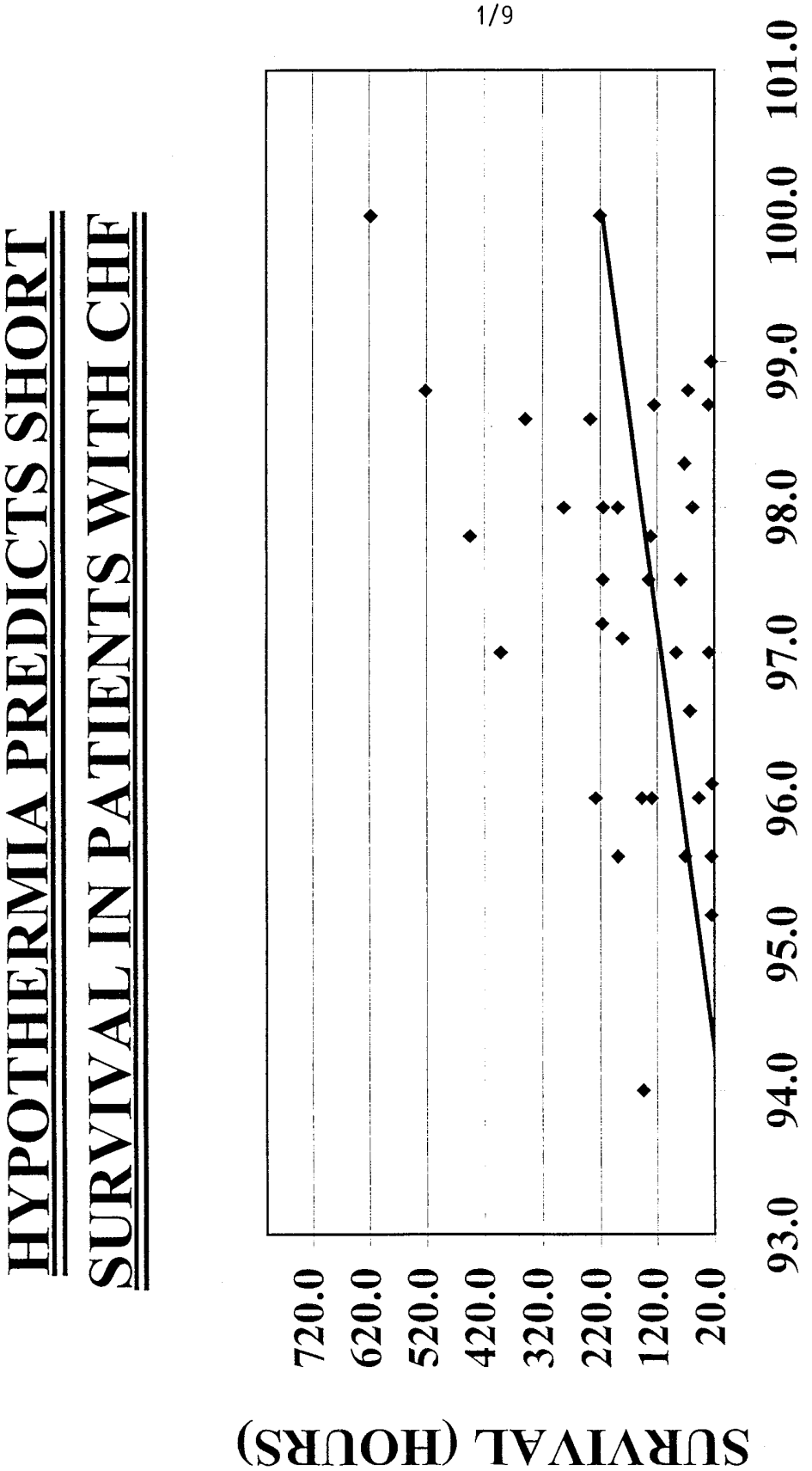

HYPOTHERMIA PREDICTS SHORT
SURVIVAL IN PATIENTS WITH CHF
SURVIVAL (HOURS)
720.0
620.0
520.0
420.0
320.0
220.0
120.0
20.0
93.0
94.0
95.0
96.0
97.0
98.0
99.0
100.0
101.0
TEMPERATURE AT TIME OF ADMISSION (°F)

FIG. 1

CONSEQUENCES OF HYPOTHERMIA IN CHF

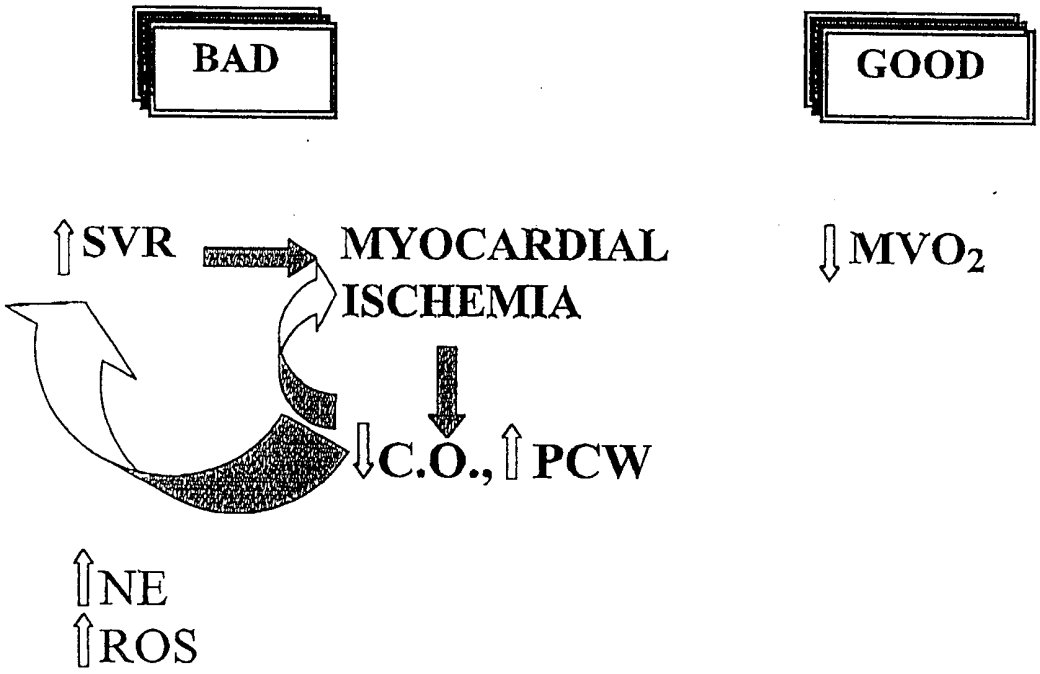


FIG. 2

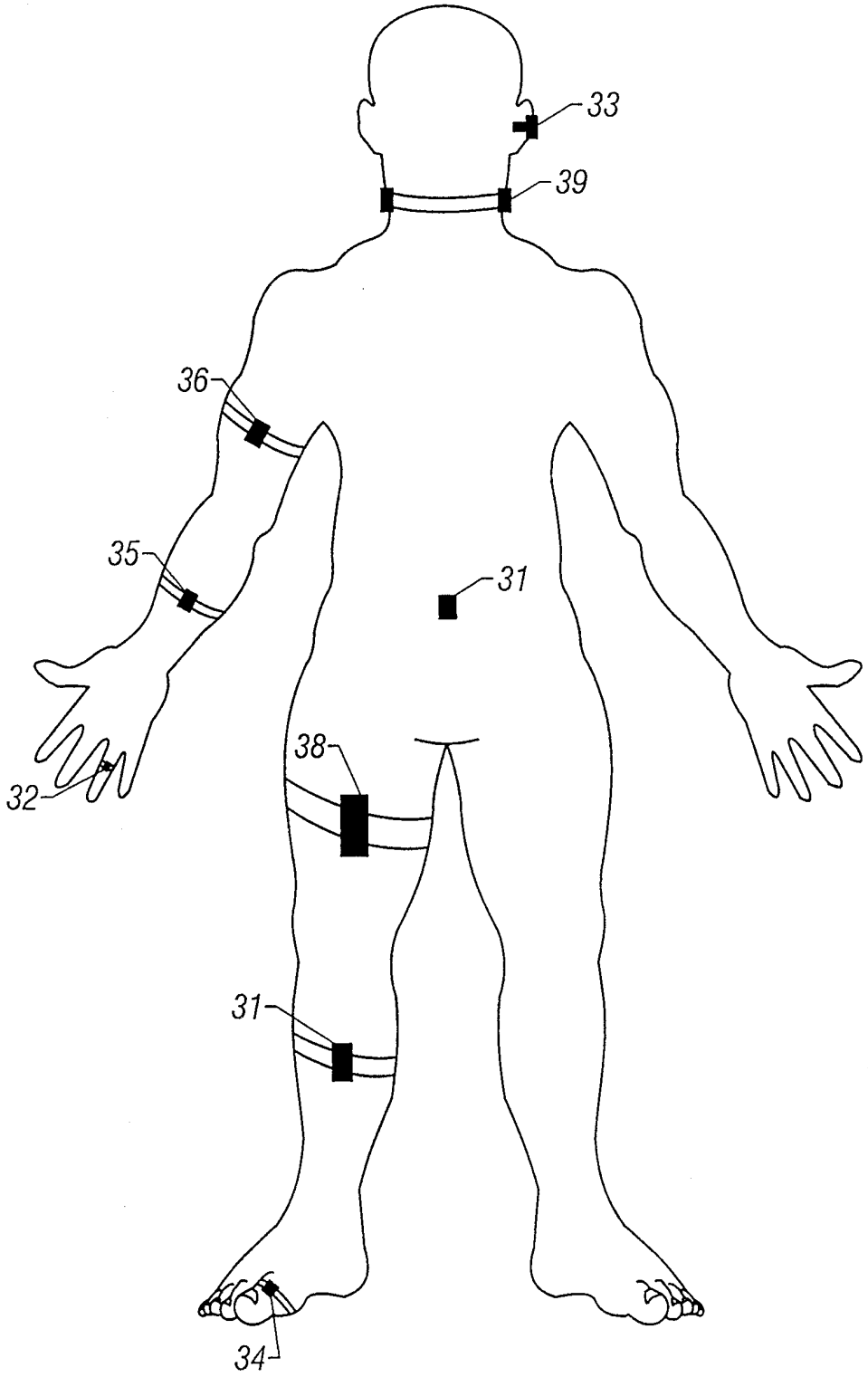


FIG. 3

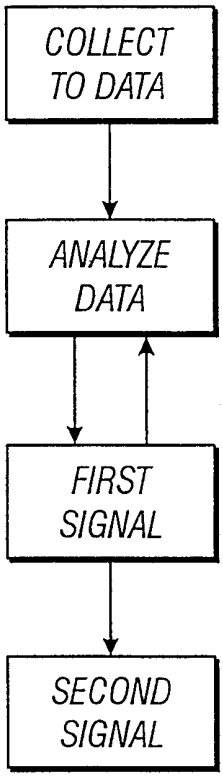


FIG. 4

Time to Death = 12.5 (Temp – 95.24)
(hr) (F)

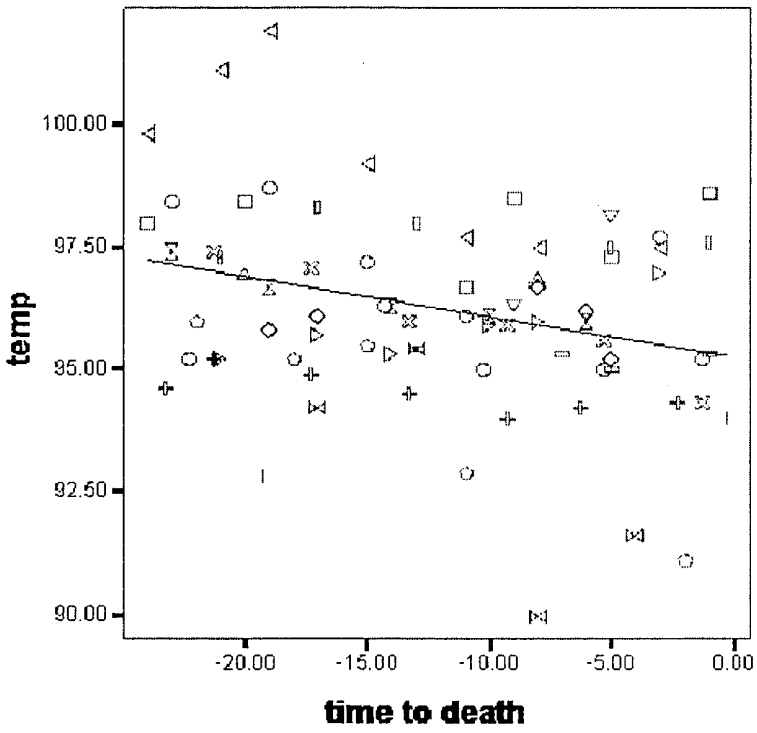


FIG. 5

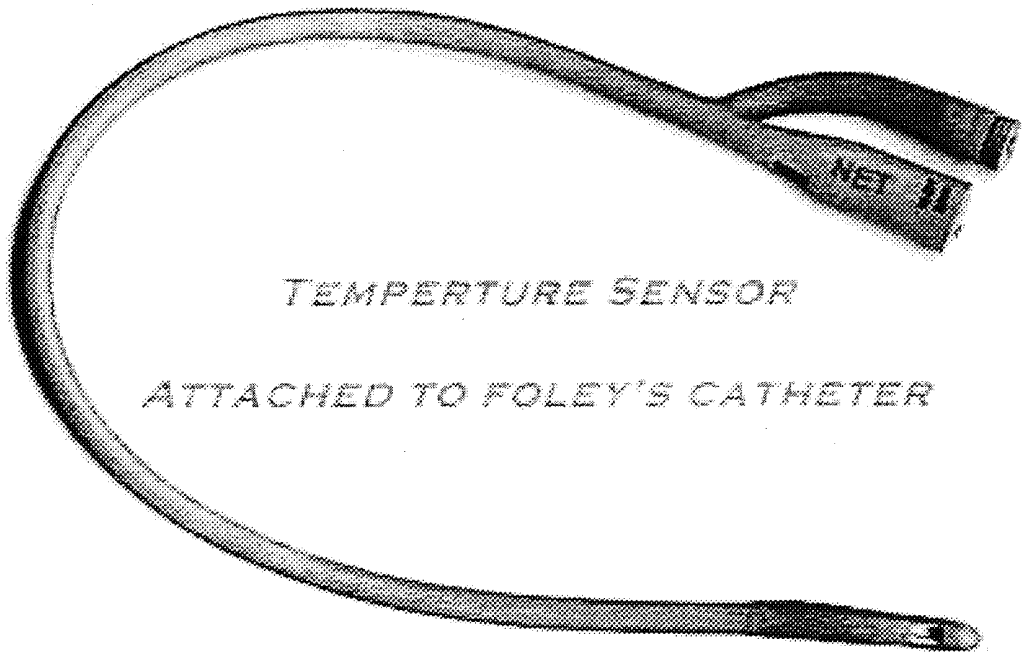


FIG. 6

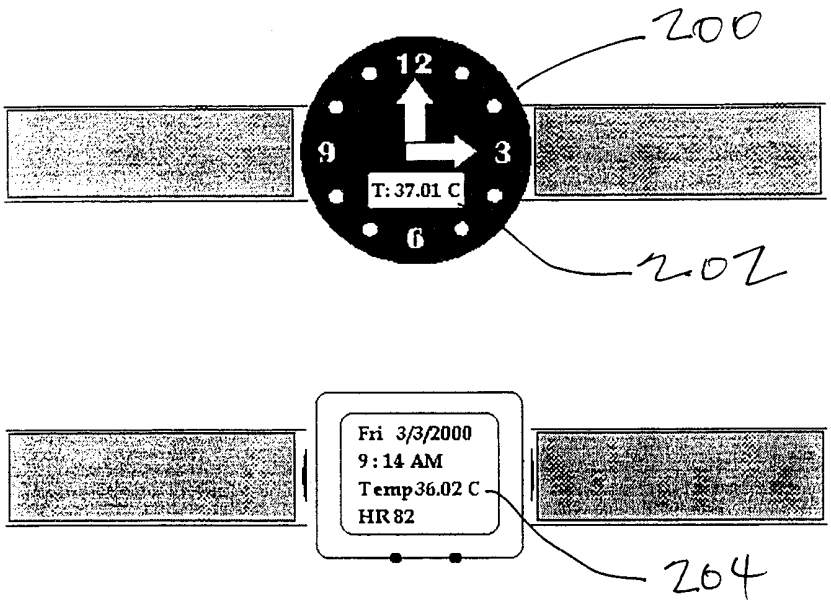


FIG. 7

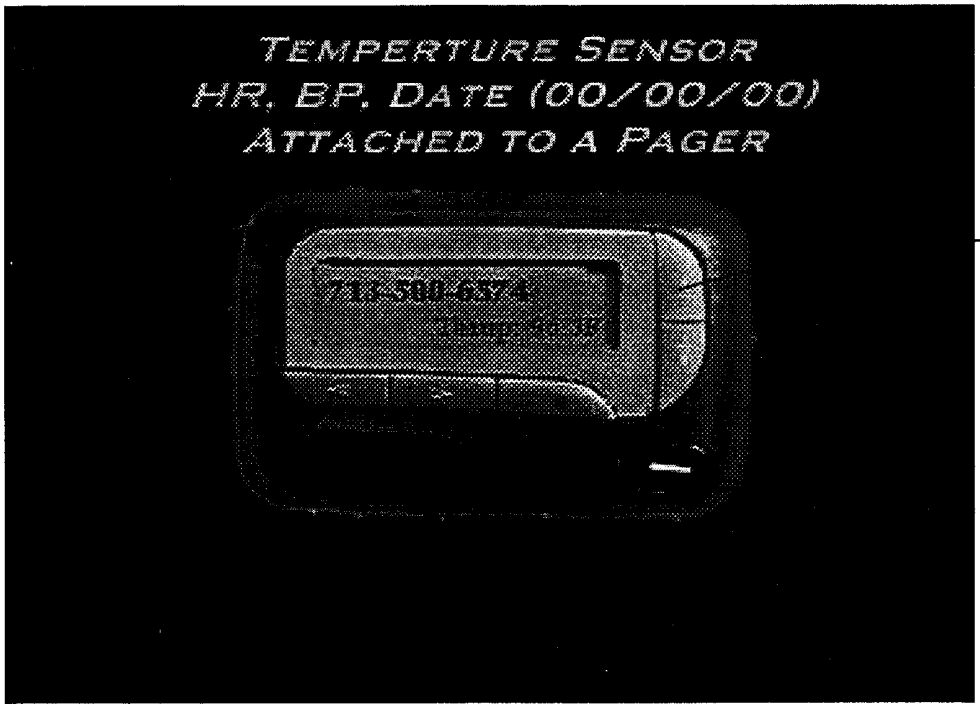
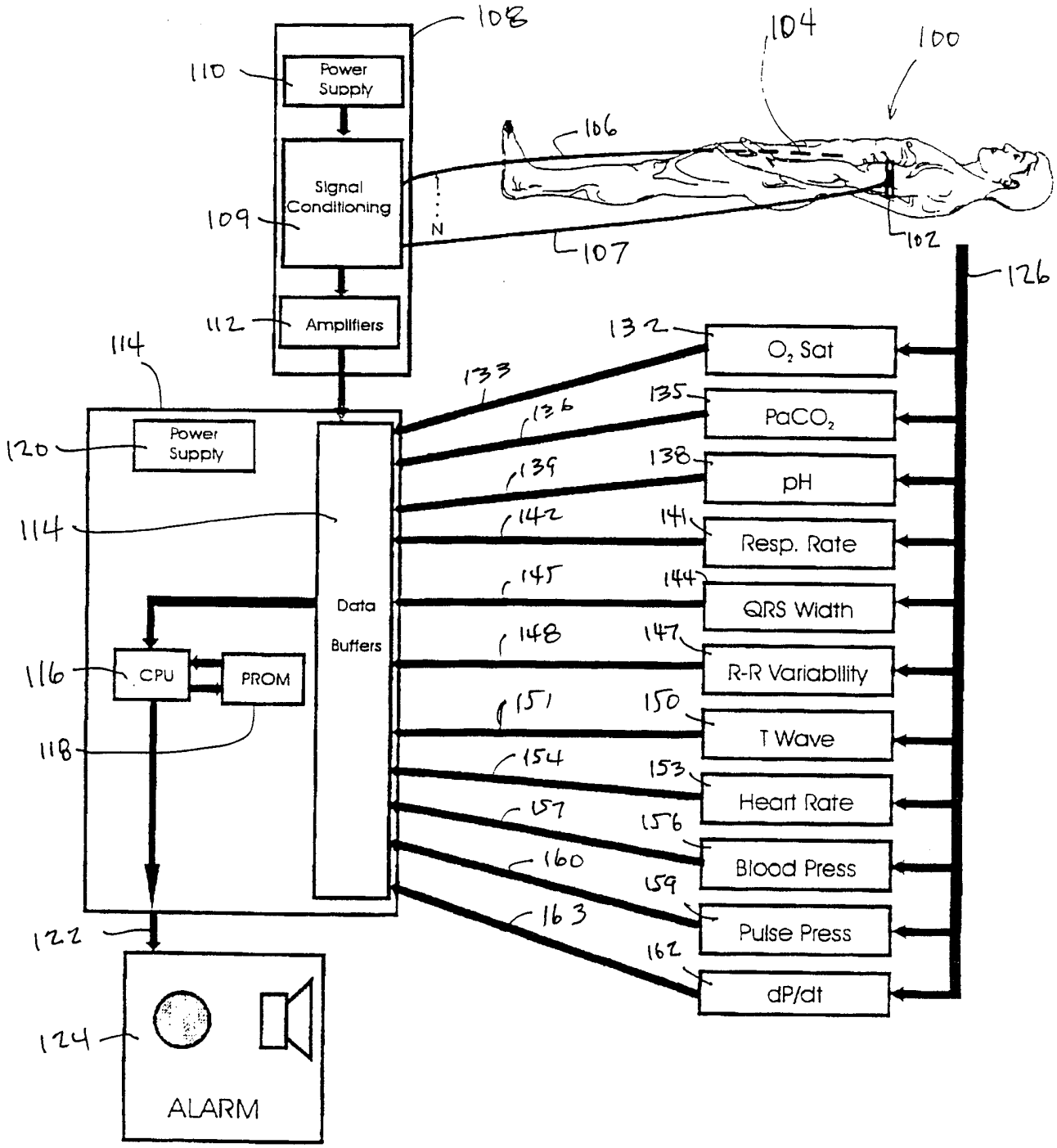


FIG. 8


108
110
Power Supply
Signal Conditioning
109
112
Amplifiers
N
104
100
106
107
102
126
114
120
Power Supply
114
Data Buffers
116
CPU
PROM
118
122
124
ALARM
132
O2 Sat
133
136
135
PaCO2
139
138
pH
142
141
Resp. Rate
145
144
QRS Width
148
147
R-R Variablity
151
150
T Wave
154
153
Heart Rate
157
156
Blood Press
160
159
Pulse Press
163
162
dP/dt

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/06081

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) :A61B 5/00
US CL :600/549
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 600/549

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,464,012 A (FALCONE) 07 November 1995, Fig. 1.	30
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Y		31
A	US 4,508,103 A (CALISI) 02 April 1985.	1-31
A	US 5,241,965 A (MICK) 07 September 1993.	1-31
A	US 4,216,462 A (McGRATH et al.) 05 August 1980.	1-31

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
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"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 14 JUNE 2000	Date of mailing of the international search report 10 JUL 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MAX HINDENBURG Telephone No. (703) 308-3130

Form PCT/ISA/210 (second sheet) (July 1998)★