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Model based analysis of the accuracy and precision of auscultatory blood pressure measurements in patients with atrial fibrillation

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ABSTRACT

Accurate measurement of blood pressure in the presence of atrial fibrillation remains an open problem. The present study combines the techniques of stochastic mathematical modeling with physiological models of the systemic circulation, cuff, and arm (1) to explore mechanisms underlying both the lack of accuracy and the lack of precision in cuff-based arterial pressure measurements during atrial fibrillation and (2) to develop strategies to correct for errors. Both the cardiovascular system and the measurement technique are described using mathematics, including both numerical techniques and analytical probability theory. Preliminary results with numerical models suggested that, despite variability, average systolic pressures tend to remain stable during atrial fibrillation, since longer inter-beat intervals are accompanied by greater filling of the pump, and in turn greater stroke volume, compensating for greater fall in arterial pressure during the previous beat. The mean or median of several repeated measures of systolic pressure is relatively precise and accurate. Individual diastolic pressure measurements also vary greatly from beat to beat; however, the average measured diastolic pressure underestimates true diastolic pressure to a clinically meaningful degree. To describe this phenomenon concisely an analytical model was created. Given the known statistical distribution of inter-beat intervals, it is possible to predict the distribution of potential diastolic endpoints. In turn, by modeling the rate of cuff deflation, it is further possible to predict the distribution of measured arterial pressure levels at which the last Korotkoff sound is heard. Exploration of the underlying patterns and mechanisms using such mathematical models leads to clinically useful insights, including a relatively simple equation to correct for the systematic underestimation of diastolic blood pressure during atrial fibrillation, based upon patient-specific average heart rate and the range of electrocardiographically derived cardiac cycle lengths. Future clinical tests are in order.

Key words: arrhythmia, bias, cuff, inaccuracy, model, sphygmomanometer, stochastic, supraventricular.

Word count: 8955
INTRODUCTION

Hypertension and atrial fibrillation often coexist[1]. Yet accurate auscultatory measurement of arterial blood pressure in the presence atrial fibrillation remains a challenge. Recommended guidelines are vague; there is no generally accepted method of determining auscultatory endpoints[2]; and the interactions between atrial fibrillation and blood pressure are insufficiently studied[3]. The challenge relates to the natural variation in true arterial blood pressure, caused by the arrhythmia itself, and also to the subtle features of the cuff-based auscultatory technique for measuring arterial pressure noninvasively. Further, accurate measurement of blood pressure using automated electronic devices for cuff inflation and deflation remains challenging in patients with atrial fibrillation, owing to the forgoing fundamental issues and to substantial differences among devices[4].

The key mechanisms driving the intrinsic variation in blood pressure during atrial fibrillation derive from the variable diastolic intervals between heartbeats, which correspond to the variable arrival times of fibrillation waves at the atrioventricular (AV) node. The arterial blood pressure falls more than average during longer intervals between ventricular systoles and less than average during shorter intervals. The major factor determining diastolic pressure is the cycle time from the last ventricular ejection, during which “diastolic runoff” of arterial blood from the aortic pressure/volume reservoir happens. Longer filling periods, however, produce greater stroke volumes, owing to Starling’s Law of the heart, which tend to compensate for the greater drop in diastolic pressure during the preceding beat. As a result, systolic pressures during atrial fibrillation, at least on average, should tend to be relatively stable compared to diastolic pressures.

The foregoing effects the arrhythmia upon systemic arterial pressure are further complicated by interaction between the right and left ventricles, which are connected in series through the pulmonary arteries, capillaries, and veins. The interaction works as follows. Right ventricular stroke volumes that are produced by beats following longer cardiac cycle lengths are greater than average. The transiently increased flow “feeds forward” through the pulmonary vasculature, causing transiently increased left ventricular output, after a short delay[5]. Obversely, shorter than average right ventricular filling times produce smaller than average right ventricular stroke volumes, which feed forward to cause smaller left ventricular stroke volumes and smaller systemic pulse pressures. This feed forward mechanism was first discovered by Einthoven and Korteweg[6] in the year 1915, who observed that in atrial fibrillation the amplitude of a beat was determined not only by the preceding cycle length, but also by the amplitude of the preceding beat. As will be shown, this phenomenon produces damped, beat-to-beat random variations in systolic arterial pressures, with little change in average systolic pressure.

Now consider the classical auscultatory technique for the non-invasive measurement of blood pressure, in which cuff pressure is released slowly from a starting point above the systolic level. Korotkoff sounds happen when cuff pressure is first greater than the time-varying internal arterial pressure, causing arterial flattening and collapse; and then, within the next fraction of a second during ventricular ejection, internal arterial pressure suddenly becomes greater than cuff pressure, allowing rapid re-expansion and audible vibration of the arterial wall (Figure 1). The cuff pressure reading at the time of the first detected arterial sound (Korotkoff sound) is regarded
as systolic pressure, and the cuff pressure reading at the time of the last detected Korotkoff sound is regarded as diastolic pressure[7]. This technique works well when the cardiac rhythm is regular. In control, sinus rhythm, with a random start time of cuff deflation, the first Korotkoff sound occurs just after cuff pressure dives below the steady level of peak arterial pressure for the first time. The cuff pressure at the time of appearance of the first heart sound is thus slightly less than true systolic, depending on the cuff deflation rate. Similarly, the cuff pressure at the time of the appearance of the last Korotkoff sound is slightly greater than true diastolic. Accordingly, cuff deflation rates progressively greater than 2 mmHg per second can cause the systolic pressure to appear slightly lower and the diastolic pressure to appear slightly higher than their actual values[8].

Figure 1. The auscultatory method.

The difficulty in atrial fibrillation lies in interpretation of the appearance and disappearance of the arterial sounds in the presence of widely varying time intervals between heartbeats. In the case of the systolic endpoint, the first Korotkoff sound happens when cuff pressure falls below maximal intra-arterial pressure for the first time. This endpoint will vary with fluctuations in true systolic pressure, causing variable readings, which on average, are only slight underestimates of the true systolic pressure.
In the case of the diastolic endpoint, the last Korotkoff sound happens just after diastolic pressure falls below cuff pressure for the last time. During atrial fibrillation diastolic endpoints will vary, depending on the local cycle length at the time cuff pressure falls below the prevailing diastolic level. In addition, the measured diastolic endpoints will be negatively biased. There will be an underestimation of true diastolic pressure, especially when using gradual cuff deflation technique. In the limiting case of exceedingly gradual cuff deflation and otherwise stable cardiovascular parameters, the sound disappearance rule for diastolic pressure would correspond to the longest possible cycle length and the lowest possible diastolic pressure.

Hence, there are necessarily both a lack of accuracy and a lack of precision in cuff-based measurements of diastolic blood pressure in patients with atrial fibrillation. The terms “accuracy” and “precision” have precise meanings[9]. Strictly, lack of accuracy refers to the difference between the mean of a large number of repeated measures of a stable phenomenon and the true or “gold standard” value. Lack of precision refers to variation among repeated measures, quantifiable for example as the standard deviation, regardless of accuracy. Hence a particular technique of measurement might be accurate but not precise, or precise but not accurate. Indeed, there are four logical possibilities: accurate, precise, both, or neither. In the case of auscultatory blood pressure readings in patients with atrial fibrillation, the forgoing a priori, qualitative reasoning suggests that typical measurements of diastolic blood pressure using the standard cuff-based method might well be both inaccurate and imprecise. International guidelines state that “in arrhythmias, such as atrial fibrillation, stroke volume and as a consequence blood pressure vary, depending on the preceding pulse interval … [and] … in such circumstances, there is no generally accepted method of determining auscultatory endpoints[2].”

Accordingly, the present study was conducted to explore quantitatively the lack of accuracy and the lack of precision of arterial pressure measurements using stochastic or probabilistic mathematical models to represent the pulmonary and systemic circulations, the brachial artery and surrounding cuff, and the widely and randomly varying cycle lengths during atrial fibrillation. One virtue of the modeling approach is that emergent properties of the time domain waveforms of the pulmonary and systemic arterial pulses can be calculated from fundamental principles, including the relevant anatomy and the definitions of vascular compliance and resistance. The resulting pulse amplitudes depend on pump filling, the Starling characteristic, timing, vascular resistance, and vascular compliance. Using stochastic techniques, one can compute the statistical distributions of measured systolic and diastolic pressures for many random sequences of AV-delay times over many runs of cuff deflation.

Another virtue of the modelling approach is that rational values for the “true” or “gold standard” systolic and diastolic blood pressures can be defined as those values obtained in the same model for a steady, constant ventricular rate corresponding to the median AV delay time in simulated atrial fibrillation. Thus, one can compare the measured pressures during atrial fibrillation for hundreds of different trials to measured pressures during the corresponding regular rhythm with exactly the same underlying cardiovascular parameters.
The goals of the present modeling effort are to identify critical variables in this complex system and also, if possible, to develop useful rules for interpreting the appearance and disappearance of Korotkoff sounds in more accurate and precise ways that are easy to implement and compatible with day-to-day clinical practice.

METHODS

Approach

To model cuff-based blood pressure measurement in atrial fibrillation one needs to take into account the random nature of the “irregularly irregular” cycle lengths, the level of systolic blood pressure, as influenced by the feed forward of variations in right heart stroke volume, the rate of descent of blood pressure during diastole, the expected level at which slowly vented cuff pressure first falls below systolic pressure (setting conditions for the first Korotkoff sound), and also the expected level at which rapidly falling arterial pressure falls below cuff pressure in late diastole (setting conditions for the last Korotkoff sound). In this problem random sampling from a defined probability distribution is needed to represent the time series of irregularly irregular heartbeats.

Such “stochastic” models, involving random sampling from a probability distribution, may be either numerical, implemented in computer code using random number generators, or analytical, implemented in paper-and-pencil mathematics using the calculus of continuous probability theory. In the present investigation the numerical approach was tried first, and provided key insights that allowed a simple analytical model to be subsequently constructed. Both models are based on experimentally determined distributions of cardiac cycle lengths in human patients with atrial fibrillation[10,11], such as those illustrated in Figure 2. Both models give estimates of typical first and last time-domain crossing points of arterial pressure and cuff pressure--corresponding to the first and last Korotkoff sounds--specified as functions of the cuff deflation rate, the rate of fall of arterial blood pressure in diastole, the average cycle length (computed clinically by counting the pulse for a full minute) and other variables as defined in Table 1.
Figure 2. Probability density functions for cycle length in a typical patient with atrial fibrillation according to the data of Tateno and Glass[11]. (a) The probability density is the probability of a random variable occurring in an interval or “bin” on the horizontal axis, divided by the width of the interval or bin. The area under the probability density curve equals 1.00 exactly. If the probability density function for a point, x, on the horizontal axis is large, that means the value of the random variable is likely to be close to x. If the probability density function for a point, x, on the horizontal is small, that means the value of the random variable is unlikely to be close to x. (b) The cumulative probability is the probability that a randomly selected value of the variable plotted on the horizontal axis will be less than or equal to that value. It is the integral of the probability density function in (a).
“True” reference pressures

For comparison to the systolic and diastolic endpoints measured in the presence of atrial fibrillation, the “true” or actual systolic and diastolic pressures are defined as those produced during a regular rhythm having a constant, mean valued cycle length during simulated atrial fibrillation with otherwise identical physiologic conditions. These “true” pressures are the steady-state pressures that the patient would have, given the same ventricular contractility, the same peripheral vascular resistance, and the same vascular and pump compliances, were it not for the presence of the arrhythmia.

Numerical model

Systemic and pulmonary circulations

The numerical model of the circulation is a variation of the 6-compartment model described by the author in detail previously[12], and one recently used by others in this context[13]. The model is based upon normal human anatomy and physiology, the definition of compliance (volume change / pressure change), and Ohm’s Law (flow = pressure / resistance). The version in Figure 3, used here, includes six compliant chambers, representing lumped systemic and pulmonary arteries, lumped systemic and pulmonary veins, a right ventricle, and a left ventricle, connected by resistances through which blood may flow. Definitions of model components are shown in Table 1.

The compliant vascular compartments correspond to the arteries, veins, and cardiac chambers. Conductance pathways with non-zero resistances, R, connect the vascular compartments. The values of $R_p$ and $R_{pc}$ are large and represent the systemic (peripheral vascular) and pulmonary capillary resistances. The values $R_{in}$, and $R_{out}$, are small and represent resistances of the “tricuspid”, “pulmonic”, “mitral” and “aortic” valves of the heart. The heart valves (triangles in Figure 3) permit only one-way flow of blood from the venous side to the arterial side of each ventricle. Blood flows between compartments of the model are indicated by the variables $f_1$, $f_2$, $f_3$, etc. with positive directions shown by the arrows. In this model blood ineritance, manifest mostly by ringing and small, high frequency oscillations in the aortic pulse contour, is neglected for the sake of simplicity.
Figure 3. Simple model of the circulatory system. Compliances of vascular compartments are denoted C. Resistances to blood flow are denoted R. Local instantaneous flows are denoted f. Subscripts: a = large arteries, v = large veins, pa = pulmonary arteries, pv = pulmonary veins, lv = left ventricle, rv = right ventricle, in = inlet, out = outlet, p = peripheral, pc = pulmonary capillary. Triangles indicate heart valves. Arrows indicate positive directions of blood flow.
Table 1. Definitions of variables in a simple model of the circulation.

<table>
<thead>
<tr>
<th>Resistances</th>
<th>Compliances</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R_p$ peripheral vascular resistance</td>
<td>$C_a, C_v$ lumped systemic arteries and veins</td>
</tr>
<tr>
<td>$R_{in}, R_{out}$ small in-line resistances of the cardiac valves</td>
<td>$C_{pa}, C_{pv}$ lumped pulmonary arteries and veins</td>
</tr>
<tr>
<td>$R_{pc}$ pulmonary capillary resistance</td>
<td>$C_{lv}, C_{rv}$ left and right ventricles</td>
</tr>
</tbody>
</table>

The governing first order differential equations for the system are based on the definition of compliance for a hollow elastic blood vessel, namely $C = \frac{\Delta V}{\Delta P}$, for blood volume increment $\Delta V$ and blood pressure increment $\Delta P$. The goal is to specify six coupled differential equations for the rates of change in pressure in each vascular compartment. For a typical compartment

$$\Delta P = \frac{1}{C} \Delta V,$$

(1)

and in turn

$$\frac{d(\Delta P)}{dt} = \frac{1}{C} \frac{d(\Delta V)}{dt} = \frac{1}{C} (f_{in} - f_{out}),$$

(2)

where in general $f_{in}$ is the flow rate of blood into a compartment with constant compliance $C$, and $f_{out}$ is the rate of outflow. This expression gives the change in compartment pressure caused by filling and emptying. In the model of Figure 3 one can use Ohm's law to substitute for $f_{in}$ or $f_{out}$ in terms of neighboring compartment pressures. In turn, for constant compliances, $C$, and constant resistances, $R$, one can generate a system of coupled differential equations for time-varying pressures, $P(t)$, in the six compartments of the circulatory model.

For systemic and pulmonary arteries

$$\frac{dP_a}{dt} = \frac{1}{C_a} \left[ \max(0,P_{lv}-P_a) - \frac{P_a-P_v}{R_p} \right], \quad \text{and} \quad \frac{dP_{pa}}{dt} = \frac{1}{C_{pa}} \left[ \max(0,P_{rv}-P_{pa}) - \frac{P_{pa}-P_{pv}}{R_{pc}} \right].$$

(3a, b)

For systemic and pulmonary veins

$$\frac{dP_v}{dt} = \frac{1}{C_v} \left[ \frac{P_a-P_v}{R_p} - \max(0,P_v-P_{rv}) \right], \quad \text{and} \quad \frac{dP_{pv}}{dt} = \frac{1}{C_{pv}} \left[ \frac{P_{pa}-P_{pv}}{R_{pc}} - \max(0,P_{pv}-P_{lv}) \right].$$

(4a, b)
For systemic and pulmonary pumps (left and right ventricles)

\[
\frac{dP_{LV}}{dt} = \frac{dP_{LV_{ext}}}{dt} + \frac{1}{C_{LV}} \left[ \max\left(0, P_{LV} - P_{LV_{int}}\right) - \frac{\max(0, P_{LV} - P_{a})}{R_{in}} \right], \quad \text{and}
\]

\[
\frac{dP_{RV}}{dt} = \frac{dP_{RV_{ext}}}{dt} + \frac{1}{C_{RV}} \left[ \max\left(0, P_{RV} - P_{RV_{int}}\right) - \frac{\max(0, P_{RV} - P_{a})}{R_{out}} \right].
\] (5a, b)

Here the max() function simulates the action of the valves, and \(P_{ext}\) represents the external pressure on intracavitary blood in each ventricle that is caused by periodic contraction of cardiac muscle. For example, one may assume that contraction and relaxation of cardiac muscle creates positive sinusoidal external pressure of the form

\[
P_{ext}(t) = \frac{\Delta P_{\text{max}}}{2} \left( 1 - \cos(\omega t) \right)
\] (6)

for angular frequency \(\omega = 2\pi f\), where \(f\) is pump frequency (or heart rate) in Hz, \(\Delta P_{\text{max}}\) is the peak pressure generated by either left or right ventricular contraction, and \(t\) is time. To simulate the Starling characteristics of the right and left ventricles the external pressure expression in Equation (6) was augmented by a value equal to the slope of Starling’s curve multiplied by the difference between the current end diastolic ventricular pressure minus the average end diastolic ventricular pressure over the preceding duration of the simulation. The slopes of Starling’s curves differed for the two ventricles. Here the Starling slope for the right ventricle was \(1.5\) mmHg peak systolic pressure per mmHg difference in filling pressure. The Starling slope for the left ventricle was \(8\) mmHg peak systolic pressure per mmHg difference in filling pressure.
Normal numerical values of the constants are obtained from textbook physiology[14].

- Normal cardiac output = 5 L/min
- Normal systemic perfusion pressure (mean arterial minus mean central venous pressure = (95 – 5) mmHg or about 90 mmHg
- Peripheral systemic vascular resistance, \( R_p = 90 \text{ mmHg/5 L/min} = 18 \text{ mmHg/(L/min)} \)
- Pulmonary capillary bed resistance, \( R_{pc} = (15 – 7) \text{ mmHg/5 L/min} = 1.6 \text{ mmHg/(L/min)} \)
- \( R_{in} = R_{out} = 1 \text{ mmHg/(10 L/min)} \) (during one half cycle) = 0.1 mmHg/(L/min)
- Total aortic and pulmonary artery compliances are estimated as 85% of stroke volume divided by pulse pressure: \((0.85) \times 0.0625 \text{ L/40 mmHg} = 0.00133 \text{ L/mmHg}, \) and \((0.85) \times 0.0625/15 \text{ mmHg} = 0.00354 \text{ L/mmHg}, \) respectively
- Systemic venous compliance = stroke volume divided by the fall in right atrial pressure during ventricular filling = 0.0625 L/4 mmHg = 0.0156 L/mmHg = right ventricular compliance
- Pulmonary venous compliance = stroke volume divided by the fall in left atrial pressure during ventricular filling = 0.0625 L/10 mmHg = 0.00625 L/mmHg = left ventricular compliance
- Slopes of Starling’s curves for the left and right ventricles = change in peak systolic pressure, divided by change in filling pressure: 8 mmHg/mmHg for the left ventricle and 1.5 mmHg/mmHg for the right ventricle
- Peak external pressures \( \Delta P_{LVmax} = 123 \text{ mmHg} \) for the left ventricle, and \( \Delta P_{RVmax} = 24 \text{ mmHg} \) for the right ventricle
- Left ventricular ejection time[15] = 0.50 sec
- Cardiac frequency \( f = 1.25 \text{ Hz} \) (75 beats/min)
- Angular cardiac frequency \( \omega = 7.85 \text{ Hz} \)
Activation of the rhythmic ventricular contraction causes a series of beats rapidly approaching equilibrium. To speed transition to a steady state equilibrium, initial left or right sided filling pressures (denoted MVP_{left} and MVP_{right}) were initialized at time \( t = 0 \) to their steady-state values under the regular rhythm test condition. Initial pressure in the aorta is 90 mmHg, representing the approximate state at end-diastole. Note that no atrial kick is modeled here, in keeping with the situation of atrial fibrillation.

The simple Euler method is used for solving the system of simultaneous linear differential equations (3), (4), and (5). If \( P(t) \) is an unknown function one wishes to determine, and an explicit expression for derivative \( y = dP/dt \) is known, as in Equations (3a) through (5b); then for a small finite time step \( \Delta t \), one can find \( P(t + \Delta t) \approx P(t) + y\Delta t \). A sufficiently small time-step for numerical integration, such as 0.0001 sec, assures stable results.

The total systolic interval, including ventricular ejection and relaxation times, was maintained constant at 0.5 sec, in keeping with published data[15,16]. For each cardiac cycle a random diastolic interval was selected such that the total cycle length was sampled from the distribution of Figure 2 and Equation (10) (subsequently described), representing a clinically realistic peaked triangular distribution with power 2.5.

**Auscultatory endpoints**

In this study Korotkoff sounds are assumed to be produced, as previously described[7] by the rapid expansion and ringing of the arterial wall beneath the cuff as it rebounds from a collapsed state, just after arterial pressure exceeds cuff pressure. For simplicity, declining cuff pressure is modeled as a simple linear function, falling at a rate of between 2 mmHg/sec and 5 mmHg/sec, as currently recommended[17]. The systolic endpoint is defined as the prevailing cuff pressure at the earliest time during cuff deflation when arterial pressure exceeds cuff pressure. The diastolic endpoint is defined as the prevailing cuff pressure at the final time during cuff deflation when arterial pressure is less than cuff pressure.

**Analytical model**

The companion analytical model, described here, can be used for checking the validity of the numerical model results, and also for computing the negative bias and corresponding correction factor for diastolic pressure readings in a particular patient.

**Continuous probability distributions of cycle times**

The analytical model was inspired by early numerical results showing that, despite irregular fluctuations, relatively accurate levels of average systolic blood pressure in atrial fibrillation were obtained. However, there were clearly inaccurate and negatively biased average diastolic blood pressure readings. (See Figures 4 through 9.) The lack of precision in both systolic and
diastolic pressure data can be dealt with by combining results of multiple, repeated measures. Further, assuming that the average systolic pressure is relatively accurate, sufficient simplifying assumptions can be made to predict the negative bias of the diastolic auscultatory endpoint, based upon continuous probability distributions for cycle lengths, such as those shown in Figures 2(a) and 2(b). These peaked triangular distributions can be described concisely using the normalized separation, u, between the current instantaneous cycle time, T, and the maximal value of cardiac cycle length, $T_{\text{max}}$, namely

$$u = \frac{T_{\text{max}} - T}{a},$$ (7)

in which value of $u$ represents the absolute difference between $T$ and $T_{\text{max}}$, divided by the half range, a, of the distribution. (In Figure 2 we have $a = \frac{1}{2} (0.6 \text{ sec}) = 0.3 \text{ sec}.$) When $T = T_{\text{max}}$, then $u = 0$. When $T_{\text{max}} - T = a$, at the peak of the distribution, then $u = 1$.

The probability density function in the $u$-domain has the form

$$f(u) = \frac{n}{2} u^{n-1}, \quad 0 \leq u \leq 1$$ (8a)

$$f(u) = \frac{n}{2} (2 - u)^{n-1}, \quad 1 < u \leq 2$$ (8b)

and cumulative probability

$$F(u) = 1 - \frac{1}{2} u^n, \quad 0 \leq u \leq 1$$ (9a)

$$F(u) = \frac{1}{2} (2 - u)^n, \quad 1 < u \leq 2,$$ (9b)

where $n$ is the exponent of $u$, and a family of probability distributions is defined by the various possible values of $n$. For $n = 1$ the function gives a uniform distribution, and for $n = 2$ the function gives a straight-sided triangular distribution. For $n = 3$ the function gives a more sharply peaked triangular distribution with curved sides. All of these distributions are symmetrical about the mean or median value at the peak, in keeping with the overall trend of empirical data[11]. Although the human data are distributed with different points of peak probability density and different maximum and minimum nonzero values (i.e. different ranges) depending on average heart rate; the shapes of the distributions are similar, regardless of heart rate. That is, each heart-rate dependent distribution can be described by characteristic values of the parameters $T_{\text{max}}$ and $a$ in Equation (7).

Non-integer values of $n$ are also allowed. Indeed, by deduction from Equation (8), as shown in the Appendix 1, the value of $n$ is equal to the peak probability density multiplied by the range, $2a$, of the distribution of the cardiac cycle lengths in the T-domain. Using this property, one can determine the empirical value of $n$ that describes published distributions of cycle lengths in actual human patients with atrial fibrillation[11]. As shown in Table 2, for the data of Tateno and Glass[11] one can obtain a value $n \approx 2.5$, regardless of the average heart rate in beats/min.
In turn, the following probability density functions can be used to represent the mid to late diastolic portions of the continuous probability distributions of cycle lengths in atrial fibrillation:

\[ f(u) = \frac{2.5}{2} u^{1.5}, \quad 0 \leq u \leq 1 \]  
\[ \text{and} \]

\[ F(u) = 1 - \frac{1}{2} u^{2.5}, \quad 0 \leq u \leq 1. \]

At the maximum possible value of cardiac cycle time, \( T_{\text{max}} \), \( u = 0, f(u) = 0 \) and \( F(u) = 1 \). At the mean or median of value of cardiac cycle time, \( \bar{T} \), \( u = 1, f(u) = 1.25 \), and \( F(u) = 0.5 \). In the subsequent discussion of the diastolic end point, the range of values from \( u = 0 \) to \( u = 1 \) is of most interest and the expressions for \( 1 < u \leq 2 \) are omitted for the sake of brevity.

Table 2. Experimental fitting of exponent \( n \) (described in Appendix 1) using data from Figure 4 in reference [11].

<table>
<thead>
<tr>
<th>Histogram label</th>
<th>Mean cardiac cycle length (sec)</th>
<th>Mean heart rate (beats/min)</th>
<th>Computed exponent ( n = 2a \times (\text{peak pdf}) )</th>
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<td>0.375</td>
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</tr>
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<td>2.52</td>
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</table>
**Prediction of the negative bias and corresponding correction factor for mean or median diastolic pressure**

From inspection of the time domain record of Figure 1, describing the process of auscultatory blood pressure measurement[18], one can define the following variables:

- $T =$ instantaneous time from onset of the last heartbeat (time from preceding R wave of the ECG)
- $dT =$ incremental time from onset of last heartbeat
- $\overline{T} =$ average period of the cardiac cycle in sec, namely $60/(\text{heart rate in beats/min})$
- $t =$ clock time during cuff deflation
- $dt =$ incremental time step
- $s =$ late diastolic slope of instantaneous arterial pressure as a function of time, $dP_a/dt$
- $E_K =$ the expected number of Korotkoff sounds during a specified time interval
- $dE_K =$ incremental expected number of Korotkoff sounds in sample time $dt$
- $F(T) =$ cumulative probability distribution of cardiac cycle lengths in atrial fibrillation.

**Expected value of the diastolic endpoint**

To determine the most likely diastolic endpoint using conventional cuff deflation technique, one can begin by calculating the expected number of Korotkoff sounds, $E_K$, in a particular time interval. This value is the product of the probability that a heartbeat (a ventricular ejection producing a sharp rise in arterial pressure and consequent arterial expansion) would occur in a sample time interval, $dt$, multiplied by the probability that the previous beat would have a cycle length long enough to allow blood pressure to fall below cuff pressure. Because cycle lengths occur randomly and are “irregularly irregular” they are not correlated with each other, and so the rule for multiplying probabilities applies. Thus, the expected number of late diastolic Korotkoff sounds in time increment, $dt$, equals the expected number of heartbeats in $dt$ multiplied by the fraction of heartbeats with diastolic pressure less than the prevailing cuff pressure. In symbols,

$$dE_K = \frac{dt}{\overline{T}} (1 - F(T)) \ .$$

(12)

Now let $|s|$ represent the absolute value of the slope of the blood pressure vs. time curve in late diastole. For an approximately constant value of $|s|$ the relationship between the incremental local cycle time, $T$, and the incremental clock time, $t$, is

$$r dt = |s|dT \ ,$$

(13)

so that in terms of the local cycle time, $T$, the incremental expected value

$$dE_K = \frac{|s|}{r} \frac{dT}{\overline{T}} (1 - F(T)) \ .$$

(14)

In general, the cumulative distribution of random values $u$ or $T$ is known from Equation (9a),
F(T) = 1 - \frac{1}{2} u^n , \quad (15)

as previously described. Substituting for \( u = \left( \frac{T_{\text{max}} - T}{a} \right) \),

\[ F(T) = 1 - \frac{1}{2} \left( \frac{T_{\text{max}} - T}{a} \right)^n . \quad (16) \]

Combining Equations (14) and (16) and integrating, the expected number of Korotkoff sounds in a particular late diastolic interval from \( T^* \) to \( T_{\text{max}} \) is

\[ E_K = \frac{1}{2} |s| \int_{T^*}^{T_{\text{max}}} \left( \frac{T_{\text{max}} - T}{a} \right)^n \, dT. \quad (17) \]

With the change of variable \( u = \frac{T_{\text{max}} - T}{a} \), and \( du = -\frac{1}{a} \, dT \), where variable, \( a \), is the half range of the statistical distribution of \( T (\sim 0.3 \text{ sec}) \),

\[ E_K = \frac{a |s|}{2 r T (n+1)} u^* , \quad (18a) \]

or

\[ E_K = \frac{a |s|}{2 r T} \left( \frac{T_{\text{max}} - T^*}{a} \right)^{n+1} . \quad (18b) \]

This is the number of late diastolic Korotkoff sounds expected in the range of cycle times from \( T^* \) to \( T_{\text{max}} \).

Here there are two subtle features to consider. First, because in this analytical model we assume that the average systolic blood pressure levels are constant; the maximum value, \( T_{\text{max}} \), corresponds to the lowest measurable average diastolic blood pressure under the given physiologic conditions. Considering the range from \( T^* \) to \( T_{\text{max}} \) as extending in reverse, from \( T_{\text{max}} \) to \( T^* \), if the expected number of Korotkoff sounds is set equal to 1, the range from \( T^* \) to \( T_{\text{max}} \) represents the range over which the last Korotkoff sound, that is the diastolic endpoint, is expected to appear.

Second, as the cuff pressure is deflated over a time \( t^* \) to \( t_{\text{diastolic}} \), corresponding to \( T^* \) to \( T_{\text{max}} \), the last heart sound may appear randomly anywhere in this range. The critical question is what is the best estimate of the time, \( t^* \), or cycle length, \( T^* \), when the last sound or diastolic endpoint is most likely to occur. Here it is proposed that a middle value for the time or cycle length at which the last sound would most likely occur would be one for which the expected number of Korotkoff sounds = 0.5 or one half. For example, in the case of a straight-sided triangular distribution and linear probability density function, one half of the last sounds would be expected at times less than \( t^* \) and one half would be expected at times greater than \( t^* \). For the nonlinear distributions characterized by exponent \( n > 2 \), sounds would be more likely at earlier times, when the probability density is larger. However, a middle value would still correspond to a cumulative expected number representing \( \frac{1}{2} \) of sounds before, and \( \frac{1}{2} \) of sounds after, the most characteristic time of occurrence, \( t^* \), of the last sound. According to this reasoning the best theoretical choice
of diastolic endpoint T* can be found by solving E(T*) = 0.5 for T*, where T* is the most likely value of cardiac cycle time associated with the appearance of one last diastolic Korotkoff sound. So, in this case

\[ E_K = \frac{a |s| (T_{\text{max}} - T^*)^{n+1}}{rn^2} = \frac{1}{2}, \quad \text{and} \]

\[ u^* = \frac{T_{\text{max}} - T^*}{a} = \sqrt{\frac{n+1}{a|s|} rT}. \]  

Hence, the correction factor, representing the absolute value of the expected underestimate of diastolic blood pressure, is

\[ c = |s| a (1 - u^*) = |s| a - \sqrt{n+1} a^n |s| n rT. \]  

Finding the late diastolic slope from clinical data

The last step of the analytical approach is to create a practical method for evaluating the correction formula of Equation (21) using clinical data. Here one assumes that the middle values for several repeated measurements (≥ 3) of systolic and diastolic endpoints for a particular patient are available, as well as the average heart rate counted over a period of one full minute to provide a stable mean value, and ideally, the range of cycle lengths from a particular patient’s electrocardiogram, which is equal to 2a. (In the absence of patient individualized values, literature values of 2a could be used for purposes of estimation.) Clinically, exponent n = 2.5 (Table 2).

All that is needed, therefore, is a reasonable estimate of the magnitude of the late diastolic slope of instantaneous arterial pressure as a function of time. This slope will critically depend (inversely) upon peripheral vascular resistance, which is difficult to measure. A work-around, however, is possible. As shown in Appendix 2, a reasonable clinical estimate of the absolute value of the late diastolic slope is

\[ |s| \approx \frac{P_d}{T} \ln \left( \frac{P_s}{P_d} \right), \]  

where \( \ln() \) is the natural logarithm function, \( P_d \) is measured diastolic pressure, \( P_s \) is measured systolic pressure, and \( \bar{T} \) is the mean cardiac period (60 divided by heart rate in beats/min).

Having determined the late diastolic slope magnitude, the diastolic pressure correction factor, which equals the absolute value of the negative bias, in terms of easily measured variables in the clinic becomes

\[ c \approx |s| a - \sqrt{n+1} (n+1) a^n |s| n rT. \]
RESULTS

Time domain records

Figure 4(a) illustrates a typical pattern of the systemic arterial pressure in the time domain for the standard normotensive model of atrial fibrillation. This record is plotted at an expanded time scale to show details of the arterial pulse waveform for comparison with published records[3,5,19-21]. The rhythm is classically irregularly irregular. There is variation in pulse pressure associated with variable delays between heartbeats and variable forward feeding of right heart output through the lungs to the left ventricle. Figure 4(b) shows a characteristic record of cuff-based blood pressure determination at a more compressed time scale. The thick straight line represents linear cuff deflation. The systolic peaks exhibit oscillations with a relatively stable average value near 120 mmHg. The diastolic minima vary more widely in a random way, depending on the duration of each local period between beats.

(a)

(b)
Figure 4. (a) Time domain record of arterial pressure for the standard, normotensive numerical model of atrial fibrillation. Pulse amplitudes vary irregularly in patterns quite similar to those recorded in human patients. Parameter values are as follows: Resistances (mmHg/L/sec) Rp 1080, Rin 0.1, Rout 0.1; Compliances (L/mmHg) Ca 0.0013, Cv 0.0156, CLR 0.00625, CRV 0.0156; Delay range (sec) 0.6; Pump contraction time (sec) 0.5; PmaxLV (mmHg) 123; PmaxRV (mmHg) 24; MVPright (mmHg) 4; MVPleft (mmHg) 6; time step for integration (sec) 0.0001. (b) Compressed scale time domain record of arterial pressure, Pao, venous pressure, Pv, and cuff pressure, Pcuff, in the standard normotensive model of atrial fibrillation. (c) Pulmonary venous compliance equal to one-tenth the standard value; the oscillations are greatly increased. (d) Pulmonary venous compliance equal to ten times the standard value; the oscillations are greatly reduced.
Figures 4(c) and 4(d) illustrate the effects of the feed forward mechanism on systolic blood pressure. When pulmonary venous compliance is $1/10^{th}$ normal, greatly reducing the damping of peaks and valleys in right ventricular output, the systolic oscillations are much greater. (A similar state may well occur in patients with congestive left heart failure, when pulmonary venous congestion and distension stiffen the walls of the pulmonary veins, reducing their compliance; although the effect could well be blunted by reduced myocardial contractility.) When pulmonary venous compliance is ten times normal, greatly increasing the damping of peaks and valleys in right ventricular output, the systolic oscillations are much less. (A similar state might well occur in hypovolemia, when pulmonary venous unloading causes walls of pulmonary veins to become more compliant; although the effect could well be blunted by reactive increased adrenergic drive and increased myocardial contractility.)

Figure 5 shows the corresponding control simulation for a steady, regular rhythm at 75 beats/min (median and mean cycle length = 0.8 sec). Both systolic and diastolic pressure levels are steady and uniform. This state defines the “true” or control systolic and diastolic pressures for purposes of this study, namely, the systolic and diastolic pressures that would be measured under identical physiological conditions in the absence of atrial fibrillation.

Figure 5. *Time domain record of arterial pressure, venous pressure, and cuff pressure in the standard normotensive model with regular rhythm at 75 beats/min. Parameter values are identical to those in Figure 4.*
Figure 6 is a similar time domain plot for a hypertensive model during simulated atrial fibrillation. In this model peak left ventricular pressure is increased, peripheral resistance is doubled, and aortic compliance is halved. A similar pattern of irregularly irregular beats is obtained. In this simulation the constancy of average systolic pressure levels is maintained, despite gradual beat-to-beat fluctuations. However, the randomness of the diastolic pressure levels is exaggerated in the presence of larger pulse pressures and steeper slopes of “diastolic runoff” of aortic pressure. In this example the last Korotkoff sound near 40 sec in the time domain occurs at a cuff pressure near 93 mmHg.

![Graph](image)

**Figure 6.** Time domain record of arterial pressure, venous pressure, and cuff pressure in the hypertensive model. Parameter values are identical to those in the normotensive model except as follows: Rp twice normal; Cao one half normal; PmaxLV 140 mmHg.

Figure 7 shows the control, regular rhythm time domain plot for the hypertensive model, in which the heart rate is kept constant at the median value. The “true” or gold-standard diastolic pressure that would have been obtained in the absence of the arrhythmia is 98 mmHg, suggesting that in the presence of atrial fibrillation and hypertension the measured diastolic pressure is underestimated using the cuff-based, auscultatory technique. The cardiac output, however, is reduced from 5.3 to 3.3 L/min in the hypertensive model.
Figure 7. Time domain record of arterial pressure, venous pressure, and cuff pressure in the hypertensive model with regular rhythm. Parameter values are identical to those for Figure 6.

Histograms

To explore the lack of accuracy (measured minus “true” value) and lack of precision (standard deviation of repeated measurements) series of 100 separate trials of simulated cuff deflation were tested for both the normotensive and hypertensive models. In these trials each AV-delay time and corresponding total cycle length was selected randomly from the peaked triangular distribution of Figure 2 and Appendix 1, which describes published histograms of cycle times in patients with atrial fibrillation[11], having a specified heart rate and a specified range of cardiac cycle lengths.

Figures 8 and 9 show histograms of simulated auscultatory blood pressure measurements for the normotensive and hypertensive models, based on the criteria that the systolic end-point is the cuff pressure at the time of the appearance of the first Korotkoff sound (when cuff pressure is less than maximal arterial pressure for the first time) and the diastolic end-point is the cuff pressure at the time of the appearance of the last Korotkoff sound (when cuff pressure is greater than the minimum arterial pressure for the last time). To simulate repeated trials in a clinical setting, the starting point of cuff deflation in time is chosen randomly over the interval of t = 5.0 to 7.0 sec after the onset of pumping. The vertical axes represent the empirical probability density function, and are scaled so that the areas under each histogram, describing either systolic or diastolic endpoints, equal 1.00 exactly. In these simulations the rate of cuff deflation rate is 3 mmHg/sec. Straight vertical lines represent the actual or true values of systolic and diastolic blood pressure.
Figure 8. Histograms demonstrating accuracy and precision of auscultatory blood pressure measurements in the normotensive model simulating atrial fibrillation (a), and corresponding regular rhythm (b). Curves represent distributions of measured systolic and diastolic endpoints; vertical lines represent actual values of systolic and diastolic pressure.
Figure 8(a) shows the distributions of measured systolic and diastolic endpoints for the normotensive model with atrial fibrillation. Figure 8(b) shows the distributions of measured systolic and diastolic endpoints for the normotensive model with a regular rhythm at 75 beats/min. Note the differing vertical scales of probability density. In atrial fibrillation there is variability in the systolic, and especially in the diastolic end-points. The straight vertical lines indicate the maxima and minima of the time domain functions of arterial pressure over the time range of 10 to 30 sec, for the stable, regular rhythm condition (i.e. true systolic and diastolic pressures). These histograms of measured values may be used to assess both accuracy and precision.

Accuracy refers to the agreement between the mean of measured data points and the actual value. Lack of accuracy refers to the difference between the mean of measured data points and actual value. The simulated results in Figure 8(a) indicate that during normotension and atrial fibrillation, auscultatory blood pressure readings are underestimates of the actual values of both systolic pressure (0.18 mmHg below actual) and diastolic blood pressure (2.41 mmHg below actual). In contrast, when the rhythm is regular (Figure 8(b)) the auscultatory readings are underestimates for systolic pressure (1.28 mmHg below actual systolic pressure) and overestimates for diastolic pressure (1.12 mmHg above actual diastolic pressure).

Precision refers to the tightness, or agreement, of repeated measures of the same phenomenon. Lack of precision is quantified by the magnitude of the standard deviation of repeated measures. The simulated results in Figure 8(a) indicate that during normotension and atrial fibrillation systolic blood pressure readings are moderately precise; however, diastolic blood pressure readings are substantially less precise. The coefficient of variation (standard deviation/mean) of systolic readings is 1.98 percent. However, the coefficient of variation for diastolic readings is 4.67 percent in this example. In contrast, when the rhythm is regular (Figure 8(b)) the coefficients of variation for systolic and diastolic pressure measurements are each less than 1 percent (0.53 and 0.93, respectively).
Figure 9. Histograms demonstrating accuracy and precision of auscultatory blood pressure measurements in the hypertensive model simulating atrial fibrillation (a) and corresponding regular rhythm (b). Curves represent distributions of measured systolic and diastolic endpoints; vertical lines represent actual values of systolic and diastolic pressure.
The lack of accuracy in auscultatory measurements of diastolic arterial pressure is greater in hypertension than in normotension, as illustrated in Figure 9. As before, with a regular rhythm, the auscultatory method slightly underestimates systolic pressure and slightly overestimates diastolic pressure. However, with atrial fibrillation there is a significant underestimation of diastolic pressure, which in this example is 2.99 mmHg.

**Cuff deflation rate dependence**

As shown in Figure 10, the degree of inaccuracy in the numerical hypertensive model with atrial fibrillation is dependent on the rate of cuff deflation in an interesting way. Whereas it is well known that the accuracy of auscultatory readings decreases with faster cuff rate deflation during a regular rhythm[22,23], with atrial fibrillation the accuracy of diastolic readings actually increases with faster deflation. This phenomenon appears to happen because, as cuff deflation rate increases, the expected number of beats with below average diastolic pressure decreases. The cuff pressure “powers past” a zone of even lower diastolic pressures after the last Korotkoff sound is heard. Alternatively, with very slow cuff deflation, described by a nearly horizontal cuff pressure versus time curve, it is likely that one of the lowest diastolic pressure points will be detected, causing a maximally large underestimate of true diastolic pressure. (A more exact formulation of this idea can be found in Equations (14) and (18), which show that the expected number of Korotkoff sounds in a given late diastolic time interval is inversely proportional to the cuff deflation rate, r.)
Figure 10. Numerical computations of the errors in accuracy as a function of cuff deflation rate for the hypertensive model with atrial fibrillation. Parameters as in Figure 6 unless otherwise noted. SBP = systolic blood pressure; DBP = diastolic blood pressure.

Analytical solutions

To explore the full matrix of possibilities regarding the accuracy of diastolic readings in an efficient way, the analytical model of Equations (12) through (21) was exercised. Figure 11 shows the calculated error in accuracy of the diastolic endpoint for the hypertensive model during atrial fibrillation.
Figure 11. Solutions from the analytical model showing the error in accuracy of the diastolic endpoint for the hypertensive model during atrial fibrillation. Parameter values corresponding to those used in the numerical model are $T_{\text{max}}$ 1.1 sec, $T_{\text{min}}$ 0.5 sec, SBP 152 mmHg, DBP 98 mmHg, HR 75 beats/min, $\bar{T}$ (mean) 0.8 sec, late diastolic slope 54 mmHg/sec.

Figure 12 shows the additive correction factors required to adjust the average of 100 measured diastolic pressures during atrial fibrillation to the true value for a typical hypertensive model, as predicted by the companion numerical and analytical methods.
DISCUSSION

Accurate and precise measurement of blood pressure using the cuff-based auscultatory method in patients with atrial fibrillation is difficult, owing to intrinsic variability in the pulse amplitude, caused by the arrhythmia. There are complex beat-to-beat variations in ventricular rate, filling volume, afterload, and ejection, which make determination of the auscultatory endpoints challenging. The present paper presents a physics based and physiology based theoretical analysis of the accuracy and precision of auscultatory measurements of blood pressure in the presence of atrial fibrillation.

The patterns of variability in the computed time domain waveforms for arterial blood pressure in the present study (Figures 4 and 6) are very similar to those reported previously in human patients[3,5,19-21,24], providing clinical validation of the present mathematical modeling approach. There is also remarkable similarity with the original animal study of Lewis[25] in the year 1912, which included a smoked drum recording of blood pressure in an anesthetized cat after the "auricle was faradized" with asymmetric alternating electric current, produced by an induction coil, to cause transient atrial fibrillation (Figure 13).
The present modeling results are consistent with a much more recent clinical study of Olbers and coworkers[3], who described high beat-to-beat blood pressure variability in patients with atrial fibrillation compared to those with sinus rhythm. They found that systolic beat-to-beat blood pressure variability roughly doubled in the atrial fibrillation group compared to the sinus rhythm group; whereas diastolic beat-to-beat blood pressure variability was approximately 6 times as high in the atrial fibrillation group compared to the sinus rhythm group. These measures of variability correspond to those reported here in Figures 8 and 9. Measured systolic arterial pressures tend to be relatively accurate but imprecise. However, readings of diastolic arterial pressure are both inaccurate and imprecise. Lack of accuracy in the diastolic endpoint is the more vexatious problem in the diagnosis of patient with mild hypertension and perhaps also in the medical management of patients with established mild, moderate, or severe hypertension. (Although, it is possible that larger variations of treatment effectiveness and timing in the medical management scenario may tend to mask variations caused by the atrial fibrillation itself[26].)

One approach to dealing with such variability is to discount diastolic readings and base assessment of hypertension in patients with atrial fibrillation only on multiple measures systolic pressure. Another approach, suggested here, is first to measure pressure several times in the usual way, and use the middle values for systolic and diastolic pressure. (Note here the importance of complete cuff deflation between readings and of raising the arm to drain excess trapped venous blood in order to prevent the build-up of excessive venous back-pressure between readings[8,23].) Then, second, apply a formula-based correction factor, c, to the median measured diastolic value, using the algebraic expressions of Equations (22) and (23):
\[ c = |s|a - \sqrt[2.5]{(n + 1)a^n|s|^n r \bar{T}}. \]

where

\[ |s| = \frac{P_s}{\bar{T}} \ln \left( \frac{P_s}{P_d} \right), \]

\( P_s \) = the median measured systolic pressure,

\( P_d \) = the median measured diastolic pressure,

\( n = 2.5, \)

\( a = \) the half range of cycle length values,

\( r = \) cuff deflation rate, and

\( \bar{T} = \) mean cycle time.

Nowadays, it is easy to imagine and to implement a simple cell phone-based application to compute the correction factor. Moreover, an automated blood pressure measuring system might be able to estimate the width, 2a, of the distribution of cardiac cycle lengths from the standard deviation of recorded time intervals between Korotkoff sounds, allowing automatic computation of the correction factor. This approach holds promise for estimation of “true” systolic and diastolic pressures in patients with atrial fibrillation, even in the presence of large variations in pulse rate and pulse pressure introduced by the arrhythmia itself.
APPENDIX 1: Peak probability density × range product as a measure of the exponent for a peaked triangular distribution

Peaked triangular distributions can be described by a family of cumulative probability density functions for the upper halves of the distributions having the form

\[ F(u) = 1 - \frac{1}{2} u^n , \quad (24) \]

where

\[ u = \frac{T_{\text{max}} - T}{a} , \quad (25) \]

\( T \) is the instantaneous time from the preceding R-wave, \( T_{\text{max}} \) is the maximal possible of \( T \), and \( 2a = T_{\text{max}} - T_{\text{min}} \) is the complete range of cardiac cycle times during atrial fibrillation. In turn,

\[ \frac{du}{dT} = -\frac{1}{a} . \quad (26) \]

The probability density function for the upper half of the distribution in the \( u \)-domain is

\[ f(u) = -\frac{dF}{du} = \frac{n}{2} u^{n-1} . \quad (27) \]

The probability density function in the \( T \)-domain is

\[ f(T) = \frac{dF}{dT} = -\frac{dF}{du} \cdot \frac{du}{dT} = \frac{n}{2a} u^{n-1} . \quad (28) \]

When cycle length, \( T \), equals the mean value, then the probability density is at its peak value, and \( u = a/a = 1 \). So, the exponent

\[ n = 2a \cdot f(T_{\text{peak}}) . \quad (29) \]

Thus, for experimentally measured distributions of cycle lengths, \( T \), as reported in the literature[11], the empirical value of the exponent, \( n \), can be estimated as the product of the empirical range of cycle lengths, \( 2a \), and the peak probability density.
APPENDIX 2: Late diastolic slope in terms of clinical data

Let $P_s$ be the measured peak systolic pressure, occurring at time $t_s$, and $P_d$ be the measured diastolic pressure, occurring at time $t_d$. The diastolic phase of any particular arterial pressure pulse in the time domain can be described approximately by the falling exponential function

$$P(t) = P_s e^{-(t-t_s)/\tau}, \quad (30)$$

where $\tau$ is the exponential time constant. This expression can be solved for $\tau$, and in turn for the magnitude of the late diastolic slope, $\left|\frac{dP}{dt}\right|_{t_d}$, as follows.

$$\ln\left(\frac{P_d}{P_s}\right) = -(t_d - t_s)/\tau, \quad (31a)$$

$$\tau = \frac{t_d - t_s}{\ln\left(\frac{P_s}{P_d}\right)}. \quad (31b)$$

Now,

$$|s| = \left|\left(\frac{dP}{dt}\right)_{t_d}\right| = \frac{1}{\tau} P_s e^{-(t_d-t_s)/\tau} = \frac{1}{\tau} P_s e^{-(t_d-t_s)} \ln\left(\frac{P_s}{P_d}\right), \quad (32)$$

or

$$|s| = \frac{\ln\left(\frac{P_s}{P_d}\right)}{t_d-t_s} P_s e^{-(t_d-t_s)} \ln\left(\frac{P_s}{P_d}\right) = \frac{\ln\left(\frac{P_s}{P_d}\right)}{t_d-t_s} P_d. \quad (33)$$

Practically, one can estimate the average value of the difference $t_d - t_s$ for the measured diastolic end point as $T = 60$ divided by the average heart rate in beats/min. Thus, a reasonable clinical estimate of the absolute value of the slope would be

$$|s| \approx \frac{P_d}{T} \ln\left(\frac{P_s}{P_d}\right). \quad (34)$$
REFERENCES


