A Mathematical Model for the Estimation of Heart Volumes from Indicator Dilution Curves

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ABSTRACT

The estimation of ventricular volumes by indicator dilution methods is subject to errors resulting from incomplete mixing and nonuniform sampling. A mathematical model is proposed which theoretically permits calculation of these errors. The model allows for nonuniform distribution of indicator in the ventricle and for nonuniform representation of the end-diastolic volume (EDV) in the systolic ejectate. It is assumed that the concentration of indicator and the flow at a given cross section of the aorta are uniform but not necessarily the same at a different cross section, or at different times during the cardiac cycle. In respect to the validity of the popular formula, \[ EDV = SV/K \] \((K = \text{average residual fraction})\), it was shown that the conditions traditionally believed to be satisfying for accurate measurements of EDV are neither sufficient nor necessary. Less restrictive alternative conditions sufficient for accurate measurements are proposed.

ADDITIONAL KEY WORDS

- errors in estimation of end-diastolic volume
- indicator mixing
- indicator sampling
- washout technique for estimation of end-diastolic volume

This paper has a twofold purpose: (1) to define necessary and sufficient conditions for the validity of classical equations used in determining end-diastolic volume and (2) to suggest a way of estimating the error when the classical equations are not valid.

We imagine an experiment in which an indicator is injected into the left ventricle during diastole by means of a catheter, and the outflow of the indicator is recorded as a function of time by means of a probe located in the aorta just distal to the valves; thus, the concentration of the indicator can be measured. We will use the following definitions:

- \( Q_i \) is the quantity of indicator in the ventricle just prior to the \( i \)th systole after injection of the indicator.
- \( EDV_i \) is the diastolic volume of the ventricle just prior to the \( i \)th systole, called end-diastolic volume.

\( SV_i \) is the stroke volume ejected during the \( i \)th ejection period.

\( ESV_i = EDV_i - SV_i \), the end-systolic volume.

Holt(1, 2) and Lewis(3) have pointed out that if mixing of the indicator is complete within the ventricle two formulas might be used for estimating the end-diastolic volume. The first is

\[ EDV_1 = \frac{Q_1}{C_1} \]  

where \( C_1 \) is the concentration measured on the first beat after injection. The second is,

\[ EDV_2 = \frac{(C_i - C_{i+1})}{(C_i)} (SV_i) \]  

if an estimate of \( SV_i \) is available. Since then, the use of these formulas has been criticized because it has become apparent that the indicator is, in fact, rarely if ever well mixed within the ventricle(4). Several workers have pointed out that these formulas may give reliable estimates of EDV even if mixing is not complete but no one has proposed explicitly necessary and sufficient conditions for their use.

We will: (1) generalize slightly Holt's model to allow for the effects of incomplete...
mixing and nonuniform sampling of ventricular contents; (2) derive necessary and sufficient conditions for the use of the formulas mentioned, and (3) propose a means of determining experimentally whether these conditions are met in practice and to measure the magnitude of the error in estimating end-diastolic volume if they are not met.

**Theory**

We divide $EDV_i$ into $N$ equal but arbitrarily small volumes and define $q_i$ to be the fraction of indicator present in the $i$th volume.

\[ \sum_{i=1}^{N} q_i = 1.0. \] (1)

\[ 1 \geq q_i \geq 0. \] (2)

Each small volume is identified by its own set of solvent and indicator molecules rather than by a fixed geometric location within the ventricle. We denote by $f_i(t)$ the fraction of the $i$th volume contributing to flow during the $i$th systole at time $t$.

\[ \sum_{i=1}^{N} f_i(t) \geq 0. \] (3)

The flow at time $t$ during the $i$th systole we denote by $F_i(t)$. If we take backflow to be negligible, then the flow in the aorta is:

\[ F_i(t) = \frac{EDV_i}{N} \sum_{i=1}^{N} f_i(t). \] (4)

If we allow $T_1$ to denote the beginning of the ejection period, and $T_2$ its end, we have,

\[ SV_i = \int_{T_1}^{T_2} F_i(t) dt, \quad T_2 \geq t \geq T_1. \] (5)

\[ SV_i = \frac{EDV_i}{N} \int_{T_1}^{T_2} \sum_{i=1}^{N} f_i(t) dt. \] (6)

If we assume that transfer of indicator is principally bulk transfer, so that we may neglect diffusion, then each volume of fluid moved carries with it its aliquot of indicator and we may write,

\[ Q_{i+1} = Q_i - \frac{1}{T_2 - T_1} \int_{T_1}^{T_2} C_i(t) dt. \] (7)

This also assumes that the concentration of indicator within the $i$th partitioned volume is uniform, though not necessarily the same as the concentration of some other sample of $EDV_i$. We assume that the concentration of indicator, and flow at a given cross section of the aorta are uniform, but not necessarily the same as at a different cross section. This presumes that the ejection process accomplishes mixing. Then we have for the concentration of indicator,

\[ C_i(t) = \frac{Q_i \sum_{i=1}^{N} q_i f_i(t)}{F_i(t)}, \] (8)

which will be measured by our probe since $C_i(t)$ is uniform across a single cross section.

The "ventricular" volumes represent all the volume of fluid proximal to the probe and distal to mitral valve and hence will, in practice, include a small dead space of aortic volume lying between the probe and the valves of the ventricle. Neither $q_i$ nor $f_i(t)$ need be uniform. They are defined here explicitly with the thought that, in general, the indicator in the ventricle is not well mixed, and the fluid ejected at any time is probably not derived from all parts of the ventricle in equal proportions and that the proportion of any volume of the ventricle contributing to flow may change with time. For example, one may imagine that fluid close to the valves will tend to be ejected early in systole while apical contents may be more heavily represented late in systole.

If the average concentration measured in the aorta were exactly equal to the concentration in the ventricle prior to systole which would be present if the contents were well mixed, then knowing the amount of indicator injected one could calculate $EDV_i$. We define the average concentration, $\bar{C}_i$, in the aorta as,

\[ \bar{C}_i = \frac{1}{T_2 - T_1} \int_{T_1}^{T_2} C_i(t) dt. \] (9)

The question then becomes what is a necessary and sufficient condition for,

\[ \bar{C}_i = \frac{Q_i}{EDV_i}. \] (10)
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In order to solve this problem, we define:

\[ \rho_{\text{II}} = \frac{Q_i}{T_2 - T_1} \int_{T_1}^{T_2} \sum_{j=1}^{N} \left( \frac{1}{N} - q_j \right) \frac{f_0(t)}{F_i(t)} \, dt. \]  

Theorem 1

\[ \bar{C}_i = \frac{Q_i}{EDV_i} \] if, and only if, \( \rho_{\text{II}} = 0. \)

Proof:

By equations 8 and 9,

\[ \bar{C}_i = \frac{Q_i}{T_2 - T_1} \int_{T_1}^{T_2} \sum_{j=1}^{N} \frac{q_j f_0(t)}{F_i(t)} \, dt. \]

Rearranging equation 11 we obtain

\[ \rho_{\text{II}} = \frac{Q_i}{T_2 - T_1} \int_{T_1}^{T_2} \sum_{j=1}^{N} \left( \frac{1}{N} - q_j \right) \frac{f_0(t)}{F_i(t)} \, dt. \]

which using the definition of \( \bar{C}_i \) and \( F_i(t) \) becomes,

\[ \rho_{\text{II}} = \frac{Q_i}{EDV_i} - \bar{C}_i. \]

From 14 it is evident that \( \bar{C}_i = \frac{Q_i}{EDV_i} \) if, and only if, \( \rho_{\text{II}} = 0 \), which proves the assertion. In particular, \( \rho_{\text{II}} = 0 \), if the indicator is uniformly
distributed \( (q_j = \frac{1}{N}) \) or if the contents of
each volume of the ventricle is uniformly sampled \( (f_0(t) = f_k(t) \) for all \( j, k, t \) arbitrary). Neither of these, however, is necessary. Looking
once more at equation 11 we see that the condition, \( \rho_{\text{II}} = 0 \), merely states that the time
average of the \( f_0 \) weighted by \( F_i \) must be un-
correlated with the distribution of indicator. Put
another way, if sampling normalized for
total flow is large from some portion of the
ventricle having a high concentration of indi-
cator then there must be some compensation
by heavy sampling from areas of low concen-
tration. In practice this condition might be
satisfied if, although concentration were not
uniform in the ventricle, the inhomogeneities
were randomly distributed with respect to the
contributions to outflow.

Holt(1, 2) has pointed out that with
uniform mixing in the ventricle, one may ex-
pect that,

\[ \frac{C_{i+1}}{C_i} = \left( 1 - \frac{SV_i}{EDV_i} \right). \]

If one can determine \( SV_i \) as well as \( C_{i+1}, \)
\( C_i \), then equation 15 may be used to estimate
\( EDV_i \). Accordingly, we now seek necessary
and sufficient conditions for equation 15. To
that end we define,

\[ \rho_{\text{II}} = \frac{Q_i}{T_2 - T_1} \int_{T_1}^{T_2} \sum_{j=1}^{N} \left( \frac{1}{N} - q_j \right) f_0(t) \, dt. \]

\[ \beta_i = \left( 1 - \frac{SV_i}{EDV_i} \right) \]

and

\[ \phi_i = \left( \frac{\rho_{\text{II}}}{\beta_i EDV_{i+1}} + \frac{Q_i}{EDV_i - \rho_{\text{II}}} \right). \]

Theorem 2

\[ \frac{C_{i+1}}{C_i} = \beta_i \] if, and only if, \( \phi_i = 1. \)

Proof:

By equation 14, we have

\[ \frac{C_{i+1}}{C_i} = \frac{Q_{i+1}}{EDV_{i+1}} \frac{EDV_i}{EDV_{i+1}} \left( 1 - \rho_{i+1} \right) \frac{EDV_i}{Q_i} \left( 1 - \rho_{II} \right). \]

Rearranging equation 16, solving, and using
equations 7 and 4 we obtain,

\[ \rho_{\text{II}} = \frac{Q_i SV_i}{EDV_i} - (Q_i - Q_{i+1}). \]

Solving equation 20 for \( Q_{i+1} \) we have,

\[ Q_{i+1} = \rho_{\text{II}} - \frac{Q_i SV_i}{EDV_i} + Q_i \]

\[ Q_{i+1} = \rho_{\text{II}} + Q_i \beta_i. \]
We now substitute equation 22 into 19,

\[ \frac{\bar{C}_{t+1}}{\bar{C}_t} = \frac{Q_i}{EDV_i - \rho_{t+1}}. \]  

(23)

Factoring \( \beta_i \) from equation 23 gives us,

\[ \frac{\bar{C}_{t+1}}{\bar{C}_t} = \beta_i \frac{Q_i}{EDV_i - \rho_{t+1}} = \beta_i \phi_i. \]  

(24)

We see that \( \frac{\bar{C}_{t+1}}{\bar{C}_t} = \beta_i \) if, and only if, the term in brackets is 1, which proves our assertion.

If \( \rho_{t+1} = \rho_{t+1} = 0 \) and \( EDV_i = EDV_{i+1} \), then \( \rho_{2i} = 0 \) is required in order to satisfy \( \phi = 1 \).

Once again we see from equation 16 that either homogenous concentration or uniform sampling are sufficient to assure \( \rho_{t+1} = \rho_{t+1} = 0 \). The condition that \( \rho_{2i} = 0 \) may be interpreted as an assertion that the distribution of indicator is uncorrelated with that of the sampling variable.

Perhaps more insight can be obtained into the meaning of equation 24 by noting

\[ \rho_{t+1} = \frac{Q_i}{T^* T_1} \int_{t_1}^{T^*} \sum_{j=1}^{N} \left( \frac{1}{N} - q_{ij} \right) f_0(t) \frac{f_0(t)}{F_i(t)} \, dt \]

Let \( \alpha = \sum_{j=1}^{N} \left( \frac{1}{N} - q_{ij} \right) f_0(t) \alpha > 0, \, T^* \geq t \geq T_1. \)  

(27)

that if \( \bar{C}_{i+1}/\bar{C}_i \) and \( \bar{Q}_i/\bar{Q}_i \) are approximately equal to \( \beta_i \) and \( EDV_i \) is approximately equal to \( EDV_{i+1} \), then \( \rho_{t+1} \) is approximately equal to \( \beta_i \rho_{t+1} \). From equation 14 we have

\[ \rho_{t+1} = \frac{Q_{i+1}}{EDV_{i+1}} - \bar{C}_{i+1}. \]

Letting

\[ \bar{C}_{i+1} = \beta_i \bar{C}_i, \]

\[ EDV_{i+1} = EDV_i, \]

\[ Q_{i+1} = \beta_i Q_i, \]

and substituting into the expression for \( \rho_{t+1} \) gives us

\[ \rho_{t+1} = \beta_i \left( \frac{Q_i}{EDV_i - \bar{C}_i} \right) = \beta_i \rho_{t+1}. \]

If we can take \( \rho_{t+1} \) to be approximately equal to \( \beta_i \rho_{t+1} \), then equation 24 requires that \( \rho_{2i} = 0 \), in order that \( \bar{C}_{i+1}/\bar{C}_i \) be equal to \( \beta \). That \( \rho_{t+1} \) will be less than \( \rho_{t+1} \) if \( q_{ij} \), \( f_0 \) are the same as \( q_{ij} \), \( f_0 \) for all \( i, k \) may be seen from the definition of \( \rho_{t+1} \), since in equation 11 \( \rho_{t+1} \) decreases as \( Q_i \) decreases. A similar result may be obtained by assuming that \( \rho_{t+1} \) is proportional to \( \rho_{t+1} \).

INDEPENDENCE OF \( \rho_{t+1} \) AND \( \rho_{t+1} \)

Since the expression for \( \rho_{t+1} \) and \( \rho_{t+1} \) are similar, the question arises, does \( \rho_{t+1} = 0 \) imply that \( \rho_{t+1} \) is also zero, or perhaps does \( \rho_{t+1} = 0 \) imply that \( \rho_{t+1} = 0 \)? The answer is no, they are independent. This can be shown as follows.

Define:

\[ T^* = \frac{T^* T_1}{2}, \]

(25)

Choose \( n_1, n_2 > 0 \) and consider the case where

\[ \alpha(t + T') = -n_1 \alpha(t), \]  

(28)

\[ F_i(t + T') = +n_2 F_i(t), \]  

(29)

Then, let \( n_1 = n_2 = 1 \),

\[ \rho_{t+1} = \frac{Q_i}{T^* T_1} \int_{t_1}^{T^*} \frac{\alpha}{F_i(t)} - \frac{n_1 \alpha}{n_2 F_i(t)} \, dt. \]  

(30)

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\( \rho_{11} \), in equation 30 is clearly zero, but
\( \rho_{21} = \varrho_i \int_{T_1}^{T_2} (1 - n_1) \alpha dt \neq 0. \) (31)

This shows that \( \rho_{11} = 0 \) need not imply that \( \rho_{21} = 0 \). Now consider in similar fashion \( n_1 = 1, n_2 \neq 1, \rho_{21} \) in equation 31 is now obviously zero, but \( \rho_{11} \) in 30 is clearly not. Then \( \rho_{21} = 0 \) need not imply that \( \rho_{11} \) is zero. This shows that \( \rho_{21} = 0 \) and \( \rho_{11} = 0 \) are truly independent conditions.

A SUFFICIENT CONDITION FOR \( \rho_{11} = \rho_{21} = 0 \)

If we define,

\[ \varrho_i = \frac{Q_i}{T_2 - T_1} \int_{T_1}^{T_2} \frac{\rho_{21}}{P_i(t)} dt, \] (32)

\[ \rho_{21} = \varrho_i \int_{T_1}^{T_2} \rho_{21} dt. \] (33)

Then

\[ \rho_{11} = \varrho_i = 0. \] (34)

Proof:

\[ \varphi_i = \frac{Q_i}{T_2 - T_1} \int_{T_1}^{T_2} \rho_{21} dt, \] (35)

If we set \( \rho_{21} = 0 \) in equations 34 and 35, \( \rho_{11} \) and \( \rho_{21} \) are also zero. Then the condition \( \rho_{21} = \varrho_i \) satisfies for \( C_i = \frac{Q_i}{EDV_i} \), \( \bar{C}_{i+1} = \frac{Q_{i+1}}{EDV_{i+1}} \), and \( \frac{\bar{C}_{i+1}}{C_i} = \beta_i \).

The condition \( \rho_{11} = 0 \) implies that \( C_i(t) = \frac{Q_i}{EDV_i} \), so that it can only hold if the concentration is constant during the whole of systole. Of course even if the concentration during systole is not constant we are not assured that \( \rho_{11} = 0 \). Since this is not a necessary condition, both \( \rho_{11} \) and \( \rho_{21} \) may be zero even if \( \rho_{11} \) is not and the concentration is not constant during systole.

A CONDITION THAT IS NEITHER SUFFICIENT NOR NECESSARY

Holt(5) has proposed, in a model less general than the one presented here, that for \( m + 1 \) beats in which

\( SV_i = SV_k \) for all \( i, k = 1, 2, \ldots, m + 1 \) (36)

and

\( EDV_i = EDV_k \) for all \( i, k = 1, 2, \ldots, m + 1 \), (37)

that

\[ \sum_{i=1}^{m} \frac{Q_{i+1}}{Q_i} = \sum_{i=1}^{m} \frac{\bar{C}_{i+1}}{C_i} \] (38)

is sufficient to assure that

\[ \beta = \frac{1}{m} \sum_{i=1}^{m} \frac{\bar{C}_{i+1}}{C_i}. \] (39)

That equation 38 is not sufficient to assure 39 may be shown as follows.

First let,

\[ \rho_{1i} = 0 \quad i = 1, 2, \ldots, m + 1. \] (40)

Equation 38 must be true, by theorem 1 and equation 37.

Under these circumstances \( \phi_i \) becomes,

\[ \phi_i = \frac{\rho_{2i}}{\beta Q_i} + 1. \] (41)

If we choose \( \frac{\rho_{2i}}{Q_i} = a > 0 \) which implies only that the distribution of indicator and the sampling distribution are the same at each beat, then

\[ \phi_i = \phi_k \quad \text{for all } i, k = 1, 2, \ldots, m + 1, \] (42)

and we have using equation 41 and equation 24,

\[ \frac{C_{i+1}}{C_i} = a + \beta. \] (43)

Equation 39 cannot possibly be correct. That it is possible to so choose \( \rho_{2i} \) and \( \rho_{1i} \) follows from their independence. To show that equation 38 is not necessary for 39 to hold, we choose

\[ \rho_{1i} = \rho_{2i} = 0 \quad i = 2, 3, \ldots, m + 1 \] (44)

and

\[ \frac{\rho_{2i}}{EDV_i} = -\beta \rho_{1i}, \quad \rho_{11} \neq 0. \] (45)

Then

\[ \phi_i = 1, i = 1, 2, \ldots, m + 1, \] (46)
and so equation 39 holds by theorem 2, and equations 36 and 37. Also by theorem 1 and equations 44 and 37,
\[ \frac{C_{i+1}}{C_i} = \frac{Q_{i+1}}{Q_i} \quad i = 2, 3, \ldots, m. \] (47)
But,
\[ \frac{C_2}{C_1} = \frac{Q_2}{Q_1} \frac{EDV - \rho_{12}}{EDV - \rho_{11}}. \] (48)
Since \( \rho_{12} = 0 \) (equation 44), 48 becomes
\[ \frac{C_2}{C_1} = \frac{Q_2}{Q_1} \frac{EDV}{EDV - \rho_{11}}. \] (49)
Factoring our \( Q_2/Q_1 \) we obtain,
\[ \frac{C_2}{C_1} = \frac{Q_2}{Q_1} \left( \frac{1}{1 - \rho_{11}EDV} \right). \] (50)
Since \( \frac{C_2}{C_1} \neq \frac{Q_2}{Q_1} \) and all other \( \frac{C_{i+1}}{C_i} = \frac{Q_{i+1}}{Q_i} \),
equation 38 cannot hold so that it is not a necessary condition for 39.

**Applications**

The model presented here may be used to assess the magnitude of the error in estimating end-diastolic volume using current formulas. If \( \rho_{11} \) and \( \rho_{21} \) are known then theorems 1 and 2 indicate the manner in which corrections may be made in obtaining an estimate of end-diastolic volume.

One way of obtaining estimates of \( \rho_{11} \) and \( \rho_{21} \) is as follows. From equation 20
\[ \rho_{21} = \frac{QSV_i}{EDV_i} - (Q_i - Q_{i+1}), \]
and from equation 14
\[ \rho_{11} = \frac{Q_i}{EDV_i} - C_i. \]
Combining these two expressions we obtain
\[ \rho_{21} = SV_i(\rho_{11} + C_i) - (Q_i - Q_{i+1}). \] (51)
With a flowmeter on the aorta, a curve fol-
lower and an analogue computer, we may obtain an estimate of \( SV_i \), call it \( X_{1i} \).
\[ X_{1i} = \int_{r_{i-1}}^{r_i} F_i(t) \, dt. \] (52)
With the concentration curve we obtain an estimate of \( C_i \), call it \( X_{2i} \).
\[ X_{2i} = \frac{1}{T_2 - r_{i-1}} \int_{r_{i-1}}^{r_i} C_i(t) \, dt. \] (53)
Finally \( Q_i - Q_{i+1} \) is just the amount of indicator ejected during the \( i \)th systole, call its estimate \( X_{8i} \).
\[ X_{8i} = \int_{r_{i-1}}^{r_i} F_i(t)C_i(t) \, dt. \] (54)
Substituting \( X_{1i} \), \( X_{2i} \), and \( X_{8i} \) into equation 51 we obtain
\[ \rho_{21} = X_{1i}(\rho_{11} + X_{2i}) - X_{8i}. \] (55)
Finally, we note from the definitions of \( \rho_{11} \) and \( \rho_{21} \) that their magnitude depends on \( Q_i \).
If we know the amount of indicator injected \( (Q_i) \), and can calculate the amount lost at each step, then we can estimate \( Q_i \). Call the estimate \( X_{4i} \). Let
\[ \rho_{11} = b_1X_{4i}, \]
\[ \rho_{21} = b_2X_{4i}, \]
and substitute these expressions into equation 55.
\[ b_2X_{4i} = X_{1i}(b_1X_{4i} + X_{2i}) - X_{8i}. \] (56)
Rearranging equation 56 we have
\[ (X_{1i}X_{2i} - X_{8i}) = -b_1(X_{1i}X_{4i}) + b_2(X_{4i}). \] (57)
Now \( b_{11} \) and \( b_{21} \) may be estimated by linear regression. The reason for choosing to estimate \( b_{11} \) and \( b_{21} \) rather than \( \rho_{11} \) and \( \rho_{21} \) is that the former may be expected to have mean values which are independent of \( i \), while \( \rho_{11} \) and \( \rho_{21} \) clearly will tend to be larger during earlier beats. With estimates of an average \( b_1 \) and \( b_2 \) it becomes possible to evaluate the error to be expected in applying the currently popular formulas.
Discussion

While it is now clear that the assumption of uniform concentration of indicator in the ventricle cannot, in general, be safely made, investigators have continued to use formulas a and b which were mentioned at the beginning of this paper for calculating cardiac volumes. Various arguments have been used to justify this. Some have proposed that mixing becomes progressively more complete with each successive beat and have suggested that only the later portions of a record of outflow concentrations be used in calculating cardiac volumes. This proposal is based on the observation that concentration differences within the ventricle diminish with each successive beat. Since it is the distribution of indicator rather than the absolute concentration difference that will determine the error in estimating, this is not an appropriate rationalization of the use of Holt's formulas. It is not a priori clear that the distribution of indicator should improve with time as it might in a closed container, since every beat brings with it a new inflow of unlabeled blood which must be mixed with the labeled portion remaining. One might expect that after a beat or two the distribution remains relatively stable although not uniform. Holt has proposed an alternate condition which, in our model, proved neither necessary nor sufficient. One could contend that each volume of the ventricle is uniformly sampled, but there is evidence against this also. We have here established alternative rationalizations for the use of Holt's formulas. If blood which has just entered through the mitral valves is either more or less likely to be ejected at the next systole than the residual contents with which it is incompletely mixed, then method b could lead to substantial errors in the estimation of end-diastolic volume. It may be possible for method a to be nearly independent of heart action. By injecting the indicator late in diastole, through a multihole catheter which will distribute the inhomogeneities of indicator concentration throughout the ventricle, it may be possible to make $p_{11}$ very small. By obtaining estimates of $p_{21}$ and $p_{11}$ it should be possible to evaluate the errors in estimating end-diastolic volume which are due to incomplete mixing and nonuniform sampling. A scheme for obtaining such estimates is outlined in the previous section.

We review briefly the assumptions we have made in developing the model. We assume that the transfer of indicator out of the ventricle is principally by bulk flow so that we may neglect transfer by diffusion. This does not assume that diffusion is negligible in the ventricle during diastole. We also assume that it is possible to partition the end-diastolic volume of the ventricle into a finite number of smaller volumes each with its own approximately uniform concentration. In order to make measurements with present instrumentation practical, we further assume that concentration of indicator and flow are approximately uniform at the cross section of the aorta at which measurements are to be made. Finally, an analysis is proposed which assumes that the distribution of indicator and the outflow pattern are approximately the same for all beats to be included in the analysis. Constancy of SV and EDV need not be assumed.

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