The Measurement of Pericardial Effusion Volume*

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A quantitative measurement of pericardial effusion volume was developed using an indicator dilution method. The technique was verified in animals and clinical subjects and applied to nine patients with pericardial effusions. The method was also utilized effectively in pleural effusion (two patients) and with modification, in ascites (one patient). The method allowed confirmation of aspiration site and recognition of loculation. The volume measurement was available during the aspiration and was found to be rapid, safe and of practical value in the management of patients with effusion.

The direct means of demonstrating the presence of pericardial effusion is by pericardiocentesis. Indirect methods, such as angiocardiography with radiopaque contrast medium,¹ radioisotope scanning,² negative contrast angiocardiography after injection of carbon dioxide³ and ultrasound⁴ have been used to establish the diagnosis of pericardial effusion and distinguish it from cardiac enlargement.

However, while these methods are reasonably accurate for qualitative assessment, quantitation of the volume of fluid cannot be obtained. Even after pericardiocentesis, incomplete removal of fluid may cause difficulty in distinguishing relative contribution to the radiologic cardiac silhouette by an enlarged heart and by the residual effusion. Further difficulty in this assessment is attendant on the peculiarity of fluid distribution about the heart.⁵ Quantitative assessment of ascitic fluid has been carried out by determining the concentration of an indicator completely mixed in the peritoneal fluid. The indicators used have been vital red, Evans blue,⁶ sodium sulfobromophthalein (Bromsulphalein),¹⁰¹I and para-aminohippurates and polyvinylpyrrolidone.⁹ There is no report in the literature, however, of measurement of pericardial effusion by this dilution technique.

This communication describes the use of a simple and rapid dilution technique in the direct measurement of pericardial effusion and demonstrates practical advantages of carrying out such measurements in the management of patients with this disorder.

**METHOD**

If a known quantity of an indicator is injected into the fluid-filled sac and its concentration determined after complete mixing has occurred, the volume of fluid is given by the relationship:

\[
\text{volume} = \frac{\text{amount of indicator injected}}{\text{concentration of indicator}}
\]

Under local anesthesia, a Teflon catheter is introduced over a needle into the pericardial sac with electrocardiographic monitoring. The needle is then withdrawn and the Teflon catheter left in place for the rest of the procedure. One hundred ml of pericardial fluid is removed to provide calibration and blank samples. A set volume (1-2 ml) of indocyanine green solution is injected into the pericardial sac from a Cornwall automatic syringe (Becton and Dickinson, Rutherford, N.J.) through a three-way stop-cock connected to the Teflon catheter. A 30 ml syringe is then affixed to the catheter and alternately filled with pericardial fluid and emptied back into the sac. This process is repeated eight to ten times over a period of five minutes until complete mixing of indicator with pericardial fluid has occurred. Then a sample of pericardial fluid containing diluted indicator is withdrawn for measurement of fluid volume.

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The same set volume of indocyanine green indicator is injected into a 25 ml graduated flask, which is then filled to the 25 ml mark with plasma. One ml of this plasma/dye mixture is added to 19 ml of pericardial fluid in a beaker. This gives a concentration equivalent to the amount of injected indicator diluted in 500 ml of effusion fluid. To provide the blank sample, 1 ml of plain plasma is added to 19 ml of pericardial fluid in another beaker. The blank and dyed samples are then alternately drawn through a cardiac output densitometer and the height of the dye deflection recorded. This deflection from blank base line, expressed in millimeters, is termed "the calibration deflection" (Fig 1A). A sample of pericardial effusion fluid obtained following complete mixing of the indicator is then drawn through the densitometer and its deflection over the base line (the sample deflection) is the recorded (Fig 1B). The volume of pericardial effusion is given by comparing the calibration and sample deflections in the following relationship:

\[
\text{Total volume of effusion} = \frac{\text{calibration deflection} \times 500 \text{ ml}}{\text{sample deflection}} + 100 \text{ ml}
\]

where 100 ml is the volume of fluid aspirated initially for calibration.

The densitometer deflections are recorded on portable equipment during aspiration of the effusion, and the volume estimate is available to the operator during the procedure.

Verification of Technique

This technique was used to measure effusion volume in 12 patients, and the accuracy of the method was tested in both experimental animals and clinical subjects.

The animal experiments were conducted in anesthetized open-chested dogs. A no. 5 French catheter was introduced into the pericardial sac through a fine incision and secured in position by a purse string suture. Further ligatures were tied around the catheter to minimize leakage. Sixty ml of plasma was then introduced into the pericardium through the catheter, followed by 0.5 ml of indocyanine green. After allowing a short time for mixing, a sample was withdrawn, and a further 30 ml of plasma was added. A second sample was removed after a mixing period. These samples were calibrated against a sample containing 0.5 ml in 25 ml of plasma. The actual "effusion volumes" were corrected for the volume of samples removed and indicator introduced. The calculated values were obtained, as above, for both the levels of experimental effusion and comparison with the known instilled volumes. The calculated volumes were 94.5 percent and 98 percent of the instilled volumes. However, total aspiration of the pericardial space following the experiments yielded only 94 percent and 96 percent of the volume introduced.

A second pair of animal experiments was conducted in a similar fashion. After the catheter was secured in the pericardial space, 100 ml of plasma was introduced, followed by 0.5 ml of indocyanine green. After mixing, a sample was obtained, and a total of 20 ml was extracted from the pericardial space. Another 0.5 ml of indicator was injected, and after allowing time for mixing, further samples were obtained. Samples were calibrated as in the first set of experiments, and volumes were calculated to correspond to both the 100 ml and 80 ml effusion. As before, the calculated values were 7 percent and 10 percent below the instilled volumes, but again, less than the instilled volume could be recovered by aspiration. In all the experiments, difficulty was experienced in eliminating leakage around the catheter, particularly when the pericardium was stretched by the larger infused volumes. The deficiencies in both the calculated and aspirated volumes are considered primarily due to this slight, but unmeasured, loss of plasma prior to uniform mixing of the indicator.

This experiment was repeated in man. The initial measurement of pericardial effusion volume was performed as described in the method section. After a further aspiration of 500 ml of pericardial fluid, a second injection of indicator was made, and a second sample of pericardial fluid was withdrawn following another five minutes of mixing. Using the first sample as a blank, the relative deflection of the second sample was recorded, and the result of the second test showed the volume of fluid to be 500 ml less than the previously aspirated volume. The accuracy also was confirmed in one instance when pericardial fluid volume was estimated at 900 ml by the above technique, and 550 ml was removed by aspiration. The subsequent chest x-ray film (Fig 2) demonstrated "complete" removal of the fluid.

The dilution principle measures a body fluid space only if mixing is complete at the time of sampling and if the indicator does not enter or leave the space under study. To establish that these limiting conditions are met in man, serial samples of pericardial fluid were withdrawn at one minute intervals for 20 minutes following injection of indicator in one patient. The concentration changes with respect to time are plotted in Figure 3, showing the stability of concentration (ie, complete mixing) has occurred at the end of five minutes. The concentration of indicator remained stable thereafter, showing that there was no transfer of indicator to other body compartments during this time.

Although the indicator indocyanine green is albumin bound, lowering of the plasma proteins in disease does not limit the applicability of the technique. Two of the patients in the series had albumin levels of 2.4 and 2.5 gm percent at the time of study. Neither patient demonstrated any loss of indicator from the pericardium, which, in the unbound state, might theoretically have passed out into the general circulation.

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This experiment was repeated in two dogs with normal pericardial tissues. After complete mixing had been effected, samples of experimental plasma effusion withdrawn over a 15-minute period demonstrated no change in indicator concentration.

**DISCUSSION**

Volume of pericardial fluid has been semiquantitatively assessed by correlation of x-ray film and \(^{131}\)I iodipamide methylglucamine (Cholografin) and iodinated human serum albumin \(^{131}\)I heart scan by Sklaroff, Charkes and Morse.\(^{10}\) These investigators measured the pericardial contents in 23 patients undergoing open heart surgery and in 11 patients at autopsy or by pericardiocentesis. Isotopic photoscans of the heart were made, and these were superimposed on the chest films of the patients. The ratio of the maximum transverse cardiac diameters on scan and roentgenogram was taken as an index for diagnosis and quantitation of pericardial fluid. In patients with less than 100 ml of pericardial fluid, this ratio of internal to external transverse cardiac diameter was greater than 0.8; it was less than 0.8 in cases of effusion of 200 ml or more. This technique appears to be fairly accurate for diagnosis of pericardial effusion and semiquantitation of volume. Correlation of the diameter ratio with volume of effusion was not possible, since the full pericardial contents were not always measured.

Moreover, cardiac dilation and/or hypertrophy decreases the sensitivity of the technique.

The ability to predict this volume has been found to be of considerable value in the management of pericardial effusion. The most significant aid is the knowledge of volume remaining when aspiration...
becomes difficult or ceases.

Depending on the comparison of volume aspirated to that calculated to be present, the operator will be guided to check for blockage or to reposition the aspiration needle on one hand, or to desist in his efforts to aspirate, on the other.

It may be argued that only a small amount of fluid need be removed to eliminate tamponade and consequently, no knowledge of the fluid volume is necessary. It is our experience, however, in circumstances of repeated effusions for a limited time period (as in renal failure at the onset of dialysis or terminal carcinoma with pericardial metastasis) that the reaccumulation rate is inversely, although not linearly, related to the amount of fluid aspirated. Small aspirations require frequent repetitions with proportional increase in all attendant risks, including super-added infection. Even when, for technical or elective reasons, all the available fluid was not aspirated, knowledge of the remaining volume has been of considerable practical value in planning further aspirations or alerting the physicians to anticipate tamponade-related problems.

The measurement has been of further practical value in determining the need to progress to formal surgical transthoracic drainage of the pericardial sac. A decreasing rate of accumulation, not necessitating a pericardial window, or an increasing accumulation, requiring surgery, provides a rational and prognostic approach to this intervention.

The method is also valuable in the consideration of loculation. When the size of the cardiac chambers can be determined, and the remaining cardiac silhouette suggests an effusion volume out of proportion to the calculated volume, it can be presumed that loculation is present. Further, in patients with repeated pericardial effusions, certain radiologic overall heart sizes are associated with relatively constant figures for fluid volume. Effusion volume measurements were obtained on two occasions in one patient with uremic pericarditis when the radiologic heart size appeared similar. Values of 1,550 ml and 1,700 ml were obtained. Loculation can be determined when on a repeated examination with the same heart size, the calculated effusion volume is significantly lower. Patients with repeated pericardial effusions can be followed with assurance that loculation is not occurring, when, at reproducible radiologic heart sizes, similar estimations of fluid volume are obtained.

Despite all precautions during pericardiocentesis, the needle may inadvertently be inserted into a cardiac chamber. In cases of hemorrhagic effusion, when the hematocrit difference between the circulating blood and the effusion may be as small as 3 percent, it may be difficult for the operator to know whether the aspirated material is from the heart or from the pericardial space. If indicator is injected into a cardiac cavity and sampled after five minutes, virtually no indicator can be recovered. Recovery of measurable concentrations of indicator after the five-minute mixing confirms the catheter position in the pericardial space.

The above technique can also be used for measurement of ascitic fluid and pleural effusion. Our experience with these measurements is limited to one patient with ascites and two with pleural fluid. Technical difficulty in measuring peritoneal fluid was shown by Baker et al, who found that equilibrium of mixing took more than two hours, and the estimated volume was in the range of 440 ml greater than could be physically recovered, which is similar to our own experience.

The measurement of pleural fluid was obtained in two patients with the same ease and reproducibility as with the pericardial effusion. Not only does the measurement aid diagnosis of loculation and radiologically confusing pleural thickening, but with effusions over 2 liters, prior knowledge of the volume avoids the tendency to cease aspiration at some arbitrary volume around a liter, a commonly observed practice. Although x-ray affords a qualitative assessment of pleural effusion, it is generally not feasible to expose films during the aspiration, and the dilution measurement is of far greater practical aid.

The technique performed 12 times in our laboratory, is safe and without complications. As demonstrated, it can be applied to bloody as well as clear fluid, as long as the same fluid is used for blank and standard specimens.

The accuracy of effusion volume measurements was tested in animals and man. In the former, a consistent underestimation of volume was found. This might have been due to leakage of plasma at the point of entry of the catheter into the pericardial sac, or possibly to some absorption of the plasma, under conditions of high pressure confinement within normal pericardial tissues, as in all instances, less plasma could be reaspirated than had been introduced. Nevertheless, even this (two percent to 10 percent) degree of underestimation found in the animal experiments would not interfere with the practical value of the measurement in a clinical setting. In man, with relatively chronic, lower pressure effusions and diseased pericardial tissues, the technique appeared to be more accurate.

The validity of the method is dependent on the retention of the indicator within the pericardial...
fluid volume. That this condition is fulfilled during the time interval of the measurement is demonstrated by the maintenance of a constant concentration of indicator after mixing. Had protein-bound indicator moved out of the pericardial space and been replaced with indicator-free protein, the indicator concentration would fall. If indicator had moved out without alteration in protein equilibrium, the concentration would have again fallen. Had the passage of indicator and protein been unidirectional out of the pericardium, then the concentration would be maintained, but the volume of fluid would diminish in response to the altered osmotic forces. The most convincing proof, however, of the retention of indicator within the space, is afforded by its total or near-total recovery from the aspirated fluid, as determined by the balancing of the equation:

\[ m = C \cdot V \]

where \( m \) is the mass of indicator injected, \( C \) is the final concentration of the indicator and \( V \) is the volume of the space. As the calculated volume is not significantly different from the aspirated volume, no significant amount of indicator can have been lost from the space. If indicator was lost in significant quantities prior to mixing, the final concentration would be reduced, and the calculated volume would be significantly in excess of the recoverable volume. As it is known that other indicators, such as vital red and radioactive isotopes, move from the pericardial space to the systemic circulation, it is not suggested that indocyanine green would be confined totally and indefinitely within the space, but the study demonstrates that no significant movement occurs during the time course of the measurement.

The safety of the procedure is confirmed by the uncomplicated record of the series. The method provides not only quantitative evaluation of the effusion, but information regarding position and patency of the aspirating needle. Obtaining this knowledge by using injection of carbon dioxide or contrast materials requires further equipment, limits the procedure to catheterization or x-ray laboratories, and utilizes a time not appreciably less than the mixing period of this technique.

REFERENCES
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