The Accuracy of Pulmonary Angiography in Assessing Resolution of Experimental Thromboemboli

By Phillip S. Wolf, M.D., and Edward Genton, M.D.

SUMMARY
Quantification of pulmonary emboli has become important in assessing the results of thrombolytic therapy and in following the natural history of thromboemboli. This study evaluated angiography as a quantitative procedure by comparing sequential changes in emboli of known size and weight with alterations on angiograms.

Twenty-four aged thrombi formed in vivo were embolized intact into 12 recipient dogs. Serial angiograms showed the location of each thrombus and allowed evaluation of its changes. Urokinase was administered to some animals to produce a spectrum of lysis.

Quantification proved accurate when thrombolysis exceeded 80% When less, angiograms over or underestimated lysis in 11 of 18 instances (61%). Postmortem dissection suggested four reasons for these discrepancies: (1) downstream movement impacted emboli and increased obstruction; (2) coiling of an embolus compromised more vessel area and increased obstruction; (3) circumferential flow of contrast material obscured some emboli; and (4) second emboli redistributed flow to an area with prior embolus, producing apparent improvement.

These data suggest that quantifying changes in emboli by angiography are frequently misleading when less than 80% lysis occurs. The discrepancy, when present, usually results in overestimation of the amount of embolus remaining.

Additional Indexing Words:
Necropsy study Thrombolysis Urokinase

ANGIOGRAPHY is the diagnostic procedure of choice for establishing the presence of pulmonary emboli and estimating the degree of obstruction in the pulmonary circulation.1,2 The potential application of angiography has increased with current interest in defining the natural history of thromboemboli and in evaluating the results of thrombolytic therapy.3-7 The use of serial angiography for such purposes requires that the procedure permits quantification of embolic material within the pulmonary circulation rather than merely documentation of the fact that obstruction has occurred or persists. The present study was undertaken to examine the accuracy of angiography in quantifying emboli under conditions simulating clinical pulmonary embolism.

Theoretically, there is reason to anticipate limitations in using the angiogram as a quantitative procedure. For example, when there is total obstruction of a pulmonary artery, one cannot estimate the amount of embolus extending distally. On angiogram, a small embolus, critically located, might produce as much obstruction as one impacted in a large stretch of the vessel. On the other hand, even a sizable embolus might allow laminar flow to proceed circumferentially and the embolus thus would either be totally obscured on
angiogram or appear to be producing a minimal degree of obstruction. Even emboli which produce filling defects on angiogram but allow laminar flow may be difficult to characterize as to length and circumference and certainly to mass. Difficulty may also be anticipated in evaluating the success of thrombolytic therapy since removal of a significant percentage of an embolus may fail to reestablish flow. Conversely, an embolus undergoing very little lysis may so alter its position within the vessel as to improve laminar flow and correspondingly the appearance of the angiogram.

Methods

Thrombi were formed in the caudal cava of donor dogs by the method of Sabiston et al.8 and permitted to age for 5 to 14 days. They were then harvested, photographed, weighed and measured. They varied in length from 1.2 to 8 cm and in weight from 0.2 to 5.2 g. One to three thrombi harvested from separate donors were then embolized without disruption into the pulmonary circulation of healthy recipient dogs over a 1 to 2-hour period through a specially constructed cannula which was inserted into the external jugular vein. A base-line angiogram was obtained prior to embolization in each animal. Angiograms were made after insertion of each embolus to verify the site and extent of obstruction produced by thrombi of varying sizes. Animals were observed for 8 to 48 hours to study changes in the appearance of the angiogram. To produce a spectrum of lysis, a sustained infusion of urokinase was administered for 8 to 17 hours in some studies.

Following the experimental period a final angiogram was obtained, and within minutes the animal was heparinized and killed with pentobarbital. The heart and lungs were removed en bloc, and emboli were removed from the pulmonary arteries by careful dissection. To avoid loss of weight through drying, the emboli were carefully handled and kept in a humidified petri dish during characterization. The emboli were again photographed, weighed, and measured to evaluate the actual changes in size with that suggested on angiogram.

Angiograms were reviewed separately by two observers unaware of the actual change which had occurred in the embolus mass. The areas of obstruction were classified by arbitrary division of the pulmonary circulation (fig. 1). The magnitude of block was estimated as partial (0 to 50% obstruction), subtotal (over 50%), or total (100%). The estimates of location and extent of obstruction, determined angiographically, were correlated with actual changes in the embolic mass confirmed by autopsy. The angiograms were categorized further as showing good correlation or as underestimating or overestimating the amount of residual embolus.

Results

Histologic examination revealed the thrombi to have partial degrees of organization which allowed them to be embolized to the pulmonary vessels of recipient animals without disruption. In this respect, the embolism in the animal model was thought to simulate closely pulmonary embolism encountered clinically.

The reproducibility of angiograms was consistent in animals having three consecutive angiograms within a 2-hour period. The accuracy of angiography was established as autopsy examination regularly confirmed the

Figure 1

Areas of obstruction classified by arbitrary division of the pulmonary circulation. MPA = main pulmonary artery; RPA = right pulmonary artery; LPA = left pulmonary artery.
ANGIOGRAPHY IN ASSESSING THROMBOEMBOLI

Table 1
Correlation Between Angiograms and Actual Changes in Embolus Size

<table>
<thead>
<tr>
<th>Thrombolysis (%)</th>
<th>Thrombus weight (g)</th>
<th>Size of vessel* obstructed on angiogram</th>
<th>Magnitude of obstruction</th>
<th>Angiographic correlation</th>
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*1, 2, 3, = 1st, 2nd and 3rd order vessel (see fig. 1).

Abbreviations: T = total; ST = subtotal; P = partial; OE = overestimation of actual size of embolus; UE = underestimation of actual size of embolus.

presence of thrombi within the pulmonary circulation at the site suggested by angiography.

Dissection of the pulmonary arteries revealed no examples of distal propagation of embolus despite occlusion of the pulmonary arteries for periods up to 48 hours.

The correlation between angiograms and actual changes in embolus size is depicted in table 1. Serial angiographic observations in several animals demonstrated improvement in flow commensurate with reduction in the embolus mass. As illustrated, correlation was good when the amount of dissolution exceeded 80%. Figure 2 is an example of such a correlation. This animal received urokinase as a sustained infusion for 8 hours. Thrombus B embolized intact into the left pulmonary artery (fig. 2b) decreased 99% in size with thrombolytic therapy. Thrombus A which was embolized to the right upper lobe of the lung (fig. 2b) underwent a similar degree of lysis. Angiograms suggested virtually complete clearing of embolic material (fig. 2c) with residual obstruction confined to a third order left lower lobe branch.

With lesser degrees of lysis, estimates of embolus size from the angiogram often proved inaccurate. Emboli of similar size led to dissimilar patterns of obstruction on serial angiograms (fig. 3). The first panel depicts total occlusion of the right lower and middle lobe arteries by a 4.1-g embolus. Partial return in flow as suggested by angiogram was accompanied by a 50% reduction in embolic weight. In a separate study, a 3.5-g embolus also obstructed the main and lower lobe vessels. Despite nearly equal lysis (47.5%), the
final angiogram demonstrated minimal return in flow to the lower lobes and actually a decrease in flow of contrast material to the right upper lobe.

When lysis was less than 80%, the amount of embolus as recovered at autopsy was overestimated or underestimated in 11 of 18 instances (61%) from the angiograms. Some of the reasons for discrepancy between actual change and that suggested by angiogram were apparent at postmortem examination.

In some instances, the embolus underwent lysis and moved slightly more distally within the vessel. This produced the paradoxical effect of increased obstruction on the angiogram when, in fact, embolus weight had decreased substantially. An example of this is demonstrated in figure 4 in which the embolus weight decreased by 70% over a 48-hour period of observation while sequential x-ray studies demonstrated that obstruction had, if anything, worsened.

A similar discrepancy resulted from the embolus altering its configuration within the vessel (fig. 5). A 14-day-old thrombus led to subtotal occlusion of the right lower lobe artery. Twenty-two hours later, the angiographic appearance had worsened. At autopsy, the embolus was found to have coiled within the vessel, obstructing the right middle and lower lobe arteries. Although embolus weight decreased by 25%, the effective cross-sectional area had probably almost doubled and resulted in substantial worsening of the angiographic appearance. Thrombus B, located in the right main and right upper lobe arteries, actually increased in size although serial angiograms suggested improvement of flow to that area. Thrombus C, having fragmented from thrombus B between the second and third angiograms, was found impacted in a distal vessel of the left lower lobe.

On the other hand, in two instances, the amount of embolic material recovered at autopsy was greater than suggested by angiograms. An example is given in figure 6, in which an initial embolus (B) caused partial obstruction of a left lower lobe artery. A second larger thrombus (A) was then embolized to the right lower lobe with immediate improvement in flow on the left. The serial x-ray studies suggested almost total clearing of embolus B, while in fact, two thirds of the original embolus was found at postmortem dissection. The sudden increase in vascularity to an area previously obstructed indicates that subsequent thromboemboli can substantially

Figure 2
Base-line angiogram. Urokinase treatment with 80% lysis of emboli. Nearly complete return of flow was suggested by the angiograms.
Angiograms. (a) A 4.1-g embolus totally occludes the right middle and lower lobe arteries. This lysed 50%, and the angiogram (b) exhibited improved perfusion. In contrast (c), an embolus of similar weight (3.5 g), which lysed 47.5%, was associated with considerable worsening of the final angiogram (d).

Figure 3

Alter flow within the pulmonary circulation. The hyperperfusion of contrast material into a previously obstructed segment appeared to conceal smaller emboli; consequently the amount of residual embolus was underestimated from the angiographic appearance.
Figure 4
(a) Base-line angiogram. (b) A 2.8-g embolus subtotally occludes a left lower lobe artery. (c) The embolus underwent 70% lysis. The final angiogram suggested that obstruction had actually increased.

Figure 5
Angiograms. (a) Base-line. (b) Subtotal occlusion of right lower lobe branch was produced by embolus A. (c) Despite 25% lysis, increased obstruction was apparent on the final angiogram. (See text.)
angiography in assessing thromboemboli


gonography. (a) Base-line view. (b) Embolus (B) subtotally obstructed the left lower lobe artery. (c) Embolus (A) totally occluded right middle and lower lobe vessels, redirecting flow to other areas including left lower lobe. Although the left lower lobe embolus lysed only 31%, almost complete clearing of embolic material was suggested from this angiogram.

Discussion

This study confirms the reliability of angiography for localizing pulmonary emboli. Angiography consistently demonstrated obstruction of flow in areas where embolus was recovered at autopsy. Substantial degrees of thrombolysis were associated with return of flow as suggested by the angiogram. Correlation was particularly good when lysis exceeded 80%.

With lesser degrees of thrombolysis, there were often striking discrepancies between the size of the remaining embolus and the amount of obstruction shown on the angiogram. Analysis of angiograms led to both over and underestimation of the amount of embolus. Some of the reasons for these differences were made clear at postmortem dissection. A decrease in the diameter of some emboli allowed downstream migration and produced impaction within the vessel. Even subtle movements of emboli tended to worsen the angiographic appearance by reducing laminar flow around the periphery of the embolus and thereby decreasing filling of distal branches. Downstream migration with impaction of pulmonary emboli probably occurs commonly in patients. In this circumstance, one would predict overestimation of the amount of remaining embolus from the angiogram.

In patients, long thrombi from the deep veins of the lower extremities often enter the pulmonary circulation without disruption and might be expected to alter their shape within the pulmonary vessels. As seen in this animal model, an embolus that folds over and compromises more cross-sectional vessel area may worsen the angiographic appearance while its size is actually decreasing. The uncoiling of a previously folded embolus would produce the opposite effect. Angiograms in these instances would grossly misrepresent the amount of embolus actually contained.

In these studies, the regional flow of contrast material within the pulmonary circu-
lation was affected by subsequent emboli. Alteration in flow tended to improve the changes produced by some emboli and worsen others, as shown in figure 6. The initial embolus in the left lower lobe of the lungs was almost obscured when a second larger embolus blocked flow to the right lower lobe and diverted contrast material to other vessels including the area of initial obstruction. In fact, one might well have difficulty in identifying the initial obstruction without benefit of the previous angiograms. Since under clinical circumstances emboli enter the pulmonary circulation sequentially, flow of contrast material might well shift from sites of major occlusion to areas either not obstructed or incompletely occluded. One would interpret the angiogram as showing more lysis than in fact had occurred.

There were no "false negatives" in this study as all emboli could be accounted for and produced either filling defects or obstruction. A single "false positive" result was observed in which a thrombus, thought to have migrated to a right lower lobe artery, was in reality caught in the trabeculations of the right ventricle.

This study confirmed that angiograms are capable of demonstrating the site of clinically significant emboli, both large and small, within the pulmonary circulation. Quantification of embolic material by angiography was less accurate, and in the majority of instances in which the results were misleading angiographic diagnosis erred in the direction of overestimating the amount of residual embolus found at autopsy. This information becomes relevant when determining the results of thrombolytic therapy and the rate of spontaneous resolution of thromboemboli in man. The results of this study suggest that the use of angiography to estimate both the size of the initial embolus and the serial changes occurring with lysis must be regarded with caution.

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References


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