Impact of Noninvasive Studies to Distinguish Volume Overload From ARDS in Acutely Ill Patients With Pulmonary Edema*

Analysis of the Medical Literature From 1966 to 1998

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Study objective: To assess the impact of substituting noninvasive diagnostic studies for Swan-Ganz catheter (SGC) placement in the evaluation of acutely ill patients.

Design: Modified decision analysis.

Methods: Using published studies that define effectiveness of clinical examination, echocardiography, and SGC placement to diagnose pulmonary edema, an analysis of the impact of substituting three diagnostic approaches using (1) clinical assessment (CA), (2) M-mode two-dimensional transthoracic echocardiography (EC), or (3) CA then EC if necessary for SGC placement was considered.

Study population: Patients with acute respiratory distress and radiographic findings of pulmonary edema, and ICU patients with hypotension and/or pulmonary edema without acute cardiac ischemia.

Interventions: Three approaches using noninvasive studies were substituted for placement of SGC in the initial evaluation of pulmonary edema.

Measurements and results: The number of SGCs placed, the number of tests needed to diagnose (NTND) all cases of volume overload, and the total number of procedure-related adverse events were calculated for each diagnostic approach and compared to SGC placement. EC, and CA then EC approaches produced fewer procedure-related serious complications and deaths, compared to the SGC approach; however, these approaches also produced a higher NTND and total procedures performed than did the SGC or CA approaches. The CA approach led to reduced NTND and procedure-related adverse events.

Conclusions: Substituting noninvasive studies for SGC placement in the initial evaluation of acutely ill patients may slightly reduce procedure-related adverse events, but it may also increase the number of procedures performed. Studies of SGC use are warranted and need to include a clinical assessment control group and an analysis of resource utilization.

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Key words: clinical assessment; echocardiography; pulmonary edema; Swan-Ganz catheter; volume overload

Abbreviations: CA = clinical assessment; EC = two-dimensional transthoracic echocardiography; NTND = number of tests needed to diagnose; PCWP = pulmonary capillary wedge pressure; SGC = Swan-Ganz catheter

Patients presenting with acute onset of respiratory failure and pulmonary edema are a common and difficult clinical dilemma. Although caused by a variety of disease processes, pulmonary edema is produced by two pathophysiologic mechanisms: cardiogenic, due to increased pulmonary capillary hydrostatic pressures; or noncardiogenic, due to increased per-
meability of the alveolar capillary membrane. Current diagnostic approaches to pulmonary edema require that the clinician distinguish cardiogenic from noncardiogenic pulmonary edema, which is often accomplished by measuring pulmonary capillary wedge pressure (PCWP) with a Swan-Ganz catheter (SGC). Thus, placement of a SGC has become the standard of care in the evaluation of pulmonary edema.

The overall impact of SGC use on patient outcome in the evaluation of pulmonary edema has not been clearly defined. It would seem obvious that defining the underlying mechanism leading to pulmonary edema should result in improved patient care. However, several observational studies of critically ill patients, including patients with pulmonary edema, showed increased mortality rather than improved survival associated with SGC use. These studies have been criticized due to the lack of an appropriate control group in which placement of a SGC was withheld. A properly designed study of SGC placement in critically ill patients with a primary endpoint of survival was attempted; however, the study was terminated due to failure to accrue sufficient numbers of patients. Unwillingness of attending physicians to participate in a study in which placement of SGC was randomized was cited by the study authors as the major cause of low patient accrual.

The mechanism of pulmonary edema can also be assessed by noninvasive studies including simple clinical assessment (CA) and two-dimensional trans-thoracic echocardiography (EC). Use of noninvasive studies could provide important information as to the pathogenesis of pulmonary edema without any direct procedure-related morbidity or mortality. However, substituting noninvasive studies to evaluate pulmonary edema has not been widely accepted due to the lack of evidence establishing the accuracy of this approach. Moreover, SGC placement is perceived to provide definitive quantitative information, whereas noninvasive tests provide subjective and qualitative information.

Use of decision analysis, clinical case modeling, and other hypothetical methods of clinical analysis can provide useful clinical information when human studies are deemed unethical or infeasible. This study estimates whether alternative strategies to using SGC, particularly those relying on CA and/or EC, could be reasonably used to diagnose volume overload. This would allow treatment without invasive monitoring or the adverse events associated with SGC placement. The variables used in this analysis to compare strategies were the number of tests needed to diagnose (NTND) all cases of volume overload and the morbidity and mortality related to each diagnostic strategy.

**Materials and Methods**

**Analysis**

The baseline model considered the clinical scenario of adult patients presenting with acute respiratory failure, radiographic findings of pulmonary edema, and no evidence of acute myocardial ischemia. Four different diagnostic approaches were evaluated (Fig 1). The standard approach used SGC placement in all patients. An alternative approach relied on CA (based on a directed physical examination, chest radiograph, and ECG interpretation) to detect volume overload. If CA reflected volume overload, a trial of diuretics would be given. A response to diuretics would not require further assessment. Either no response to diuretics or a failure to detect volume overload on CA would lead to SGC placement. Another approach was to use EC in all patients with outcomes patterned after the CA approach. A third alternative approach was to use CA as the first step. If CA detected volume overload, then the approach described for CA alone would be used. If CA did not detect volume overload, the more sensitive diagnostic test, EC, would be performed. This reflects the currently accepted, conservative clinical management of this problem.

A decision analysis modified to focus on accuracy of diagnosis and on the specific performance characteristics of sensitivity and false-positive rate was used to calculate the overall number of procedures required to correctly diagnose the cause of pulmonary edema. A population with known prevalence of volume overload as the cause of pulmonary edema was assumed, and noninvasive studies with known performance characteristics of sensitivity and false-positive rate were used to derive the number of procedures required to make a correct diagnosis of volume overload. A study population size of 10,000 patients was assumed to yield outcome results that were easily interpreted. The total number of SGCs placed and total procedures performed for each approach were calculated from the performance characteristics (sensitivity and false-positive rate) of CA or EC to diagnose volume overload. CA and EC performance characteristics were derived from pooled data of relevant studies that were identified by search of the medical literature. Similarly, total numbers of SGC-related serious complications and deaths were calculated based on morbidity and mortality estimates derived from pooled data of relevant studies. The NTND all cases of volume overload was derived as a measure of workload and efficiency of evaluation that is easily interpreted by the clinician. The NTND was defined as the total number of diagnostic tests required to identify all cases of volume overload for each diagnostic approach.

**Baseline Estimates**

Performance characteristics of CA and EC for diagnosing volume overload were determined by review of the medical literature. The authors searched the MEDLINE database from 1966 to 1998 using the following combinations of key words: volume overload (or congestive heart failure) and sensitivity/ specificity of diagnosis, ARDS/diagnosis and PCWP, ARDS/diagnosis and volume overload (or congestive heart failure)/ diagnosis, respiratory insufficiency and PCWP, pulmonary edema and ARDS, precision and accuracy of diagnosis of pulmonary edema and CA, and precision and accuracy of diagnosis of pulmonary edema and echocardiography. Several criteria were used to identify relevant articles for analysis: (1) the study population had to consist of patients presenting with acute respiratory failure and diffuse infiltrates on chest radiography, (2) study patients had to have both CA and SGC placement or CA and EC placement to distinguish volume overload from...
ARDS, (3) hemodynamic and quantitative echocardiographic data had to be presented in either tabular or graphic form, and (4) direct correlation of all hemodynamic data to the diagnosis of volume overload by CA or EC had to be a focus of the article. All relevant articles were reviewed by the authors for quality. Only articles meeting high-quality standards including prospective study design and at least ≥ 20 patients studied consecutively were included for analysis. Articles were excluded if the data were obtained retrospectively, if the primary focus of the study was not on the accuracy of diagnosis of volume overload, if the article was a review article or meta-analysis, or if the article studied patients in a nonconsecutive fashion.

The hemodynamic standard for diagnosis of volume overload was a PCWP ≥ 18 mm Hg. This value was cited by the American-European consensus conference on the definition of the ARDS as the PCWP that distinguished ARDS from volume overload. Moreover, a PCWP ≥ 18 mm Hg was found by Forrester et al.1 to correlate closely with clinical evidence of pulmonary edema in patients with acute myocardial ischemia and volume overload. Criteria to diagnose volume overload by CA included the presence of elevated neck veins, displaced apical pulse, lower-extremity edema, bibasilar rales, enlarged cardiac silhouette, and/or prior myocardial infarction on an ECG.12,14 Criteria for the diagnosis of volume overload by EC included the presence of cardiac chamber enlargement and reduced stroke volume.12,14

The results of the searches were combined to yield 345 citations. Overall, 14 relevant articles were identified as meeting the study criteria and were reviewed by one of the authors. Specific data from these articles were pooled to derive the most reliable and accurate assumptions. Results showed a sensitivity of 73% and false-positive rate of 50% for diagnosing volume overload by CA (n = 98 pooled patients),16,20 and a sensitivity of 89% and false-positive rate of 67% to diagnose volume overload by EC (n = 20 patients; Table 1).14

To calculate the number of correct and incorrect diagnoses of volume overload that each approach produced, it was necessary to determine the prevalence of volume overload in the study population. The authors determined this by review of studies that diagnosed volume overload in patients presenting with acute respiratory failure and pulmonary edema. Pooled data from four studies with a total number of 224 patients showed that the prevalence of volume overload in this population was 30%.16,20–22 Similarly, morbidity and mortality rates due to SGC placement were derived from four studies involving > 5,000 patients. Pooled data from these studies showed SGC procedure-related serious complications and deaths were 4% and 0.1%, respectively.23–26

**Sensitivity Analysis**

All outcome calculations were repeated after making changes in study population characteristics and baseline estimates. The new study population consisted of critically ill patients in an ICU who were being evaluated for hypotension, pulmonary edema, or both. Study population exclusion criteria included age < 16 years and volume overload due to acute myocardial ischemia or infarction. Operating characteristics for CA and EC in diagnosing volume overload in this population were derived as previously described. Sensitivity and false-positive rates for diagnosing volume overload by CA were 40% and 21% (n = 290 pooled patients), and for EC were 77% and 62%, respectively (n = 40 patients; Table 1).14,27–29 Pooled data from four studies (n = 330 pooled patients) gave a prevalence of volume overload in this population of 40%.14,27–29 Assumed SGC-related morbidity and mortality were 4% and 0.1%, respectively.

Further analyses were conducted in which the performance characteristics of noninvasive tests were assumed rather than calculated from pooled data. Baseline assumptions for CA were changed to a sensitivity of 90% and a false-positive rate of 10%. For EC, baseline assumptions were changed to 95% sensitivity.

![Diagram](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21955/)
and 20% false prevalence rates. Changes in procedure-related adverse events were not altered because these changes would affect the outcome results of all diagnostic approaches equally.

**RESULTS**

**Diagnostic Approaches and Estimates**

According to the first diagnostic approach, all initial evaluations of patients would be by insertion of a SGC, and all diagnoses of volume overload by SGC placement (ie, PCWP ≥ 18 mm Hg) would be assumed to be true-positive. Thus, 3,000 patients (10,000 patients multiplied by the prevalence of volume overload in the population, 0.3) would have a PCWP ≥ 18 mm Hg and would receive a diagnosis of volume overload. The remaining 7,000 patients would have a PCWP < 18 mm Hg and would receive a diagnosis of no volume overload. There would be 10,000 SGCs placed to identify all cases of volume overload, which results in a NTND of 10,000 diagnostic tests (Table 2). Assuming a procedure-related morbidity of 4% and mortality of 0.1%, the initial evaluation of 10,000 patients with pulmonary edema by SGC placement would lead to 400 adverse events and 10 deaths.

Initial evaluation by the CA approach results in 5,690 patients with a diagnosis of volume overload (Fig 2). This value comes from the number of patients who received a correct diagnosis of volume overload (3,000 patients with volume overload multiplied by the sensitivity of CA to diagnose volume overload, 0.73), plus the number of patients who received an incorrect diagnosis of volume overload (7,000 patients without volume overload multiplied by the false-positive rate of CA to diagnose volume overload, 0.5). The 2,190 patients who received a correct diagnosis of volume overload would respond to diuretic therapy; however, the 3,500 patients who received an incorrect diagnosis of volume overload would not respond and would require SGC placement to further evaluate the cause of pulmonary edema. The remaining 4,310 patients would receive a diagnosis of no volume overload (simply calculated as 10,000 subtracted from 5,690 patients with a diagnosis of volume overload), and would have a SGC placed to evaluate the cause of pulmonary edema. Overall, there would be 7,810 SGCs placed, a NTND all cases of volume overload of 7,810 diagnostic tests (Table 2). Evaluation by CA would lead to 312 adverse events and 7.8 deaths from SGC.

Using similar steps as for CA, the EC approach leads to 7,360 SGCs placed, and a NTND all cases of volume overload of 17,360 diagnostic tests (Fig 3 and Table 2). Evaluation by EC would lead to 293 adverse events and 7.3 deaths from SGC. For the CA then EC approach, patients are initially evaluated by CA. If volume overload is diagnosed using CA, the patient is given a trial of diuretics. However, if no volume overload is diagnosed using CA, the patient is evaluated further by EC. This approach leads to 7,080 SGCs placed, and a NTND all cases of volume overload of 11,390 diagnostic tests (Fig 4 and Table 2). Evaluation by CA then EC results in 283 adverse events and 7.1 deaths from SGC.

As summarized in Table 2, all approaches involving CA or EC lead to a reduction in procedure-related serious complications and deaths, but affect the NTND variably when compared to the SGC approach. The fewest procedures are found in the CA approach, which also leads to 85 fewer serious complications and 2.2 fewer deaths, compared to the SGC approach. Similar results were obtained by the EC approach, but an additional 9,520 procedures were required to avoid 19 serious complications and 0.5 deaths, compared to the CA approach. The CA then EC approach required 3,580 additional procedures to avoid 29 serious complications and 0.7 deaths, compared to the CA approach.

**Sensitivity Analysis**

Outcome calculations were repeated for a new study population consisting of critically ill patients in an ICU with hypotension, pulmonary edema, or both. The prevalence of volume overload in this

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**Table 2—Impact on Procedure-Related Outcomes of the Different Approaches to Diagnose Volume Overload in Patients With Acute Respiratory Failure and Pulmonary Edema**

<table>
<thead>
<tr>
<th>Diagnostic Approach</th>
<th>NTND SGCs Placed</th>
<th>Volume Overload</th>
<th>Total Serious Complications</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGC only</td>
<td>10,000</td>
<td>10,000</td>
<td>400</td>
<td>10.0</td>
</tr>
<tr>
<td>CA</td>
<td>7,810</td>
<td>7,810</td>
<td>312</td>
<td>7.8</td>
</tr>
<tr>
<td>EC</td>
<td>7,360</td>
<td>17,360</td>
<td>293</td>
<td>7.3</td>
</tr>
<tr>
<td>CA then EC</td>
<td>7,080</td>
<td>11,390</td>
<td>283</td>
<td>7.1</td>
</tr>
</tbody>
</table>

*Data are presented as No.
population was derived to be 40%, and estimates of CA and EC performance characteristics were recalculated (Table 1). Again, the CA approach was the only approach that led to reductions in all adverse outcomes and in the NTND (Table 3). Compared to the first study population, a greater benefit in adverse outcomes occurred in the EC, and CA then EC approaches, compared to the CA-only approach. However, these benefits required the performance of an additional 8,520 diagnostic tests for the EC approach and 6,920 diagnostic tests for the CA then EC approach.

Outcome calculations were also repeated after assuming performance characteristics that strongly favored the noninvasive approaches over SGC placement (Table 4). Under these conditions, the CA approach results in 2,700 fewer diagnostic studies, a decrease in the NTND, and elimination...
of 108 serious complications and 2.7 deaths, compared to the SGC approach. Comparison of the three noninvasive approaches shows that the CA approach produced the fewest number of procedures and the lowest NTND. Compared to the CA approach, EC, and CA then EC approaches lead to 9,850 and 6,315 more diagnostic tests, respectively, and increases in the NTND, while producing only modestly fewer serious complications and deaths.

**Discussion**

Many outcome-based studies have shown that SGC use in critically ill patients leads to unexpected diagnoses, changes in patient management, and purported improved survival, although many of these studies lack statistical power to make valid conclusions.20,27,28,30,31 In contrast, several large observational studies have demonstrated increased mortality in patients managed with SGC, compared to patients managed without SGC.3,10,12,15 Conflicting results raise doubts about the benefits of SGC use and have led to an increased interest in other methods to obtain hemodynamic information. Echocardiography is an easy noninvasive test to obtain hemodynamic information and is clearly a safer alternative to

**Table 3—Impact on Procedure-Related Outcomes of the Different Approaches To Diagnose Volume Overload in ICU Patients With Hypotension, Pulmonary Edema, or Both**

<table>
<thead>
<tr>
<th>Diagnostic Approach</th>
<th>SGCs Placed</th>
<th>NTND</th>
<th>Volume Overload</th>
<th>Total Serious Complications</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGC only</td>
<td>10,000</td>
<td>10,000</td>
<td>400</td>
<td>10.0</td>
<td></td>
</tr>
<tr>
<td>CA</td>
<td>8,400</td>
<td>8,400</td>
<td>336</td>
<td>8.4</td>
<td></td>
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<tr>
<td>EC</td>
<td>6,920</td>
<td>16,920</td>
<td>277</td>
<td>6.9</td>
<td></td>
</tr>
<tr>
<td>CA then EC</td>
<td>6,552</td>
<td>13,692</td>
<td>262</td>
<td>6.5</td>
<td></td>
</tr>
</tbody>
</table>

*Data are presented as No.

**Table 4—Impact on Outcome Results as Baseline Estimates of CA and EC Are Changed**

<table>
<thead>
<tr>
<th>Diagnostic Approach</th>
<th>SGCs Placed</th>
<th>NTND</th>
<th>Volume Overload</th>
<th>Total Serious Complications</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGC only</td>
<td>10,000</td>
<td>10,000</td>
<td>400</td>
<td>10.0</td>
<td></td>
</tr>
<tr>
<td>CA†</td>
<td>7,300</td>
<td>7,300</td>
<td>292</td>
<td>7.3</td>
<td></td>
</tr>
<tr>
<td>EC‡</td>
<td>7,150</td>
<td>17,150</td>
<td>286</td>
<td>7.1</td>
<td></td>
</tr>
<tr>
<td>CA then EC§</td>
<td>7,015</td>
<td>13,615</td>
<td>280</td>
<td>7.0</td>
<td></td>
</tr>
</tbody>
</table>

*Data are presented as No.

†Sensitivity, 95%; false-positive rate, 10%.
‡Sensitivity, 95%; false-positive rate, 20%.
§CA sensitivity, 90%; false-positive rate, 10%. EC sensitivity, 95%; false-positive rate, 20%.
SGC placement from the standpoint of procedure-related adverse events. However, substituting echocardiography or any other noninvasive studies for SGC placement would be premature, since evidence is lacking that this could be done reliably and to the patient’s overall benefit. Moreover, completing such studies may be difficult and may be met with ethical concerns.

The purpose of this study was to better understand the impact of substituting noninvasive studies for SGC placement in the diagnosis of acutely ill patients without incurring ethical considerations. To accomplish this objective, we used a modified decision analysis design and data from relevant human studies on performance characteristics of SGC and noninvasive diagnostic studies to estimate the impact of substituting CA, EC, or both for SGC placement in the initial assessment of patients with acute pulmonary edema. The purpose in selecting the key performance characteristics studied was to maximize sensitivity, to detect the most patients possible with volume overload, to minimize the false-positive rate, and to reduce the number of patients misleadingly labeled as having volume overload. Our results suggest that a substantial number of patients would require SGC placement despite evaluation with noninvasive studies. However, by noninvasive methods, some patients receive a correct diagnosis of pulmonary edema due to volume overload and avoid SGC placement. Thus, substituting noninvasive studies for SGC placement leads to an overall reduction in the number of SGCs placed and a 10 to 30% reduction in procedure-related complications and deaths. However, in absolute numbers, the reductions in complications and deaths due to use of some noninvasive studies are small, while there are substantial increases in the NTND all cases of volume overload. The EC approach resulted in an additional 500 to 3,000 echocardiographic procedures to avoid one death, compared to the SGC approach. In contrast, the CA approach led to 1,200 to 2,700 fewer procedures while avoiding 1.6 to 2.7 deaths. The CA approach was the only noninvasive approach that produced reductions in the NTND all cases of volume overload. Approaches using EC had fewer serious complications and deaths, compared to the SGC approach, but EC approaches continued to have a high NTND all cases of volume overload. In further sensitivity analysis in which the operating characteristics of CA and EC were improved, results showed again that the CA approach led to substantial benefit in procedure-related complications and deaths that were similar to the EC, or CA then EC approaches. However, the CA approach was the only approach that produced reductions in the NTND all cases of volume overload.

Although in need of careful interpretation, our analysis leads to several considerations. Substituting noninvasive tests for placement of a SGC may have only a modest impact on overall patient care. Absolute reductions in procedure-related adverse events were very small, which is largely due to the small number of complications and deaths associated with insertion of a SGC. Our data also suggest that replacing the SGC with echocardiography in the initial evaluation of patients with pulmonary edema would reduce absolute procedure-related adverse events slightly, but substantially add to total number of procedures performed. In contrast, the results of the CA approach showed that procedure-related adverse events were reduced while also leading to reductions in the NTND volume overload and the total number of procedures performed. These findings raise the point that resource utilization may become an important determinant in assessing the overall value of replacing the SGC with noninvasive tests.

This study used the results of numerous reliable and well-designed studies to form assumptions and projections. However, our conclusions are limited in that the study focus was only on procedure-related events and on the initial evaluation of pulmonary edema and/or hypotension in the absence of acute myocardial ischemia. Also, study methods do not
take into account the clinical events following the decision to place a SGC or to perform a noninvasive test. As such, recommendations on the proper use of SGC cannot be formulated; however, our results do provide useful insights in an area in which studies have been limited by study design and ethical problems. Our results show that substituting noninvasive studies, particularly CA, may have a survival and resource utilization benefit and should reassure clinicians that controlled studies in which SGC placement may be withheld from some study patients are reasonable. Moreover, our sensitivity analysis demonstrates that improving the performance characteristics of CA for diagnosing volume overload may provide even greater benefit.

In summary, using a modified decision analysis of a specific clinical problem involving SGC placement, we found that substitution of noninvasive studies for SGC insertion reduces overall procedure-related adverse events. Substitution of echocardiography for SGC placement also results in an increase in the NTND all cases of volume overload and the total number of procedures performed. Use of CA only leads to reductions in both the NTND and in the total number of procedures performed. Future prospective, sufficiently powered studies aimed at replacing SGC placement with noninvasive tests could reasonably include a control group consisting of CA only, and should include measures of resource utilization.

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