Pulmonary Embolism: is Echo of Any Use?

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Important Facts on PE

- High morbidity
- Mortality is (still) high
- Low detection rate before death
- Frequent overdiagnosis & overtreatment
- Aggressive therapy required
## Incidence of PE

<table>
<thead>
<tr>
<th>Country</th>
<th>Annual estimated rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>600 000</td>
</tr>
<tr>
<td>France</td>
<td>100 000</td>
</tr>
<tr>
<td>England and Wales</td>
<td>65 000</td>
</tr>
<tr>
<td>Italy</td>
<td>60 000</td>
</tr>
</tbody>
</table>

Dalen JE et al. Prog Cardiovasc Dis 1975
ESC Guidelines, Eur Heart J 2000
Survival of Pts with Pulmonary Embolism

- Medicare enrollees with DVT and PE
- Enrollees matched for age, sex and race

Kniffin WD Jr et al, Arch Intern Med 1994
Important Facts on PE

• Prevalence of PE at autopsy is 12-15%
  ✓ unchanged during last 30 yrs

• Numerous cases unrecognized/untreated

• Mortality if untreated is ~30%
  ✓ could be reduced to 2-8%

ESC Guidelines, Eur Heart J 2000
Stein PD et al, CHEST 1995
Mortality Associated to Pulmonary Embolism Can Be Reduced!

- Majority of “preventable deaths” due to PE (range 27-68%) can be ascribed to missed Dg rather than existing therapies failure

Fedullo PF et al, NEJM 2003
Goldhaber SZ et al, Lancet 1999
Diagnostic Evaluation in Suspected PE

- D-dimer, BNP, troponin
- Chest x-ray, ECG
- V/P lung scan
- Spiral-CT
- Pulmonary angiography
- Angioscopy
- MSCT
- Duplex ultrasonography
- Echocardiography (TTE, TEE)

No single noninvasive diagnostic test is sensitive or specific enough! Sequential diagnostic approach is necessary!
Rational for Echo in PE

- Pathophysiological responses to increased pulmonary pressure can be easily detected by echo (indirect signs)
- Rarely, direct visualization of thrombus in the right heart and/or PA is possible
- Noninvasive, available, portable
Acute obstruction >25% of pulmonary vascular bed

- Acute pulmonary hypertension
  - Acute RV pressure overload
  - RV hypokinesis, dilation, dysfunction
  - Tricuspid regurgitation

Displacement of the septum towards LV cavity

- Reduced LV preload
- LV dysfunction
- Low CO, shock

Pathophysiology of Acute PE
Pathophysiology of Acute PE

Acute obstruction >25% of pulmonary vascular bed

Doppler & 2D Echo

Acute pulmonary hypertension

- Acute RV pressure overload
- RV hypokinesis, dilation, dysfunction
- Tricuspid regurgitation

Displacement of the septum towards LV cavity

Reduced LV preload

LV dysfunction

Low CO, shock
Role of Echo in Suspected PE

- Diagnosis
- Identification of high-risk pts
- Monitoring the effect of therapy
- Differential diagnosis
Echo Signs of PE

- RV dilatation/hypokinesis and subsequent TR
- RA dilation
- Dilation of PA and its branches
- Dilated (>20mm), non-collapsing (insp) IVC
- Flattened interventricular septum
- Decreased LV size
- Increased RV/LV end-diastolic diameter ratio
- TR jet >2.5 m/s (mild-moderate PA hypertension)
- RVOT mid-systolic “notching” pattern (AcT<80 ms, with mid-systolic deceler)

- Direct thrombus visualization in the right heart or PA
• Direct sign of PE, thrombus in RVOT

Only in 4% of pts in ICOPER* (International Cooperative Pulmonary Embolism Registry)

* Goldhaber SZ et al, Lancet 1999
• RV dilation / hypokinesis
• LV geometrical changes
- RV dilation / hypokinesis
- Flattened IVS
• **Acute pulmonary hypertension**

TV systolic gradient typically $\leq 60$ mmHg

*(TR jet velocity, modified Bernoulli equation)*
Characteristic alteration of pulmonary ejection flow pattern

- AcT < 60 ms
- Midsystolic deceleration ("notching")
“60/60” sign

Pulmonary ejection acceleration time in RVOT of $\leq 60$ ms in the presence of tricuspid insufficiency pressure gradient $\leq 60$ mmHg

$AcT \leq 60$ ms  $\quad$  $TIPG \leq 60$ mmHg
• Dilated IVC, non-collapsible in inspirium
• Dilated IVC, non-collapsable in inspirium
Regional RV Dysfunction in Acute PE

McConnell’s sign

“distinct echocardiographic pattern of RV dysfunction”

McConnell MV, et al. AJC 1996
What is the real diagnostic value of echo signs suggesting pulmonary embolism?
# Major Studies Evaluating Diagnostic Value of Echo Signs Suggesting Pulmonary Embolism

<table>
<thead>
<tr>
<th>Source</th>
<th>n</th>
<th>Screened population</th>
<th>Echocardiographic criteria used</th>
<th>Sens</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nazeyrollas et al(^{10})</td>
<td>132</td>
<td>Out-patients, no known previous serious cardio-respiratory disease</td>
<td>RV/LVEDD &gt; 0.5 (parasternal M-mode echo) TPA jet velocity &gt; 2.5 m/s</td>
<td>93%</td>
<td>81%</td>
<td>78%</td>
<td>93%</td>
</tr>
<tr>
<td>Grifoni et al(^{11})</td>
<td>117</td>
<td>Consecutive patients seen at emergency department</td>
<td>One or more of four signs: 1. Right heart thrombus 2. RV &gt;30 mm parasternal view or RV/LVED &gt; 1.3 3. Systolic flattening of inter-ventricular septum 4. AcT or &lt;90 ms or TIPG &gt;30mmHg but no RV hypertrophy</td>
<td>51%</td>
<td>87%</td>
<td>82%</td>
<td>60%</td>
</tr>
<tr>
<td>Perrier et al(^{12})</td>
<td>50</td>
<td>Consecutive patients, mostly from emergency ward</td>
<td>RV dilation ‘by visual inspection’ on 2-D echo and TPA jet velocity &gt;2.6 m/s</td>
<td>67%</td>
<td>94%</td>
<td>86%</td>
<td>83%</td>
</tr>
<tr>
<td>McConnell et al(^{17})</td>
<td>85</td>
<td>Hospitalized patients with RV dysfunction</td>
<td>Hypokinetic RV free wall but normo/hyperkinetic RV apex</td>
<td>77%</td>
<td>94%</td>
<td>71%</td>
<td>96%</td>
</tr>
<tr>
<td>Torbicki et al(^{19})</td>
<td>86</td>
<td>Hospitalized patients with precapillary pulmonary hypertension</td>
<td>AcT &lt;60 ms with TIPG &lt;60 mmHg</td>
<td>48%</td>
<td>98%</td>
<td>n.a</td>
<td>n.a</td>
</tr>
<tr>
<td>Miniati et al(^{13})</td>
<td>110</td>
<td>Consecutive patients with clinically suspected APE</td>
<td>Two of the following: signs: 1. RV hypokinesis, 2. RV diameter &gt;27 mm, long parasternal 3. TI velocity &gt;2.7 m/s</td>
<td>56%</td>
<td>90%</td>
<td></td>
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</tr>
</tbody>
</table>
Diagnostic Value of Echo in PE

Possible sources of confusion:

- There are only few prospective studies.
- Major differences in:
  - patient’s selection
  - severity of PE
  - previous cardiorespiratory disease
  - diagnostic echo criteria

- Enrolled pts were not a representative sample of the severity spectrum of the disease
  - majority had massive and submassive PE
Diagnostic Value of Echo in PE

**Echo Dg of PE, if any 2 of 3:**
- RV EDD > 27 mm
- RV hypokinesis
- TR velocity > 2.7 m/s

**At least 2/3 echo criteria were present in:**
- 24/43 pts with angio-proven PE
- 7/67 pts without PE

Sn 56%
Sp 90%


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**ROC Curve**
- Sensitivity vs 1-Specificity
- RV end-diastolic diameter (mm)
- TR velocity (m/s)

**Post-test probability of PE (%)**
- Pretest (clinical) probability of PE (%)
Diagnostic Value of Echo in PE

- TTE has **limited diagnostic value**: it fails to identify ~ 50% of pts with angio-proven PE in a prospective study of *unselected pts*

- Should **not be used** for PE screening

Regional RV Dysfunction in Acute PE

McConnell’s sign

RV free wall hypokinesis with normal wall motion of the RV apex →

- 14 pts with PE
- 9 pts with PPH
- 18 normal controls

McConnell sign:

Sn 77%
Sp 94%
PPV 71%
NPV 96%

for diagnosis of PE

McConnell MV, et al. AJC 1996
Prevalence of McConnell Sign in pts with Acute PE and RV Infarction

- 161 pts with RV dysfunction
- PE or RV infarction
- Restrospective blinded study

p = 0.657

McConnell sign:

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sn</td>
<td>70%</td>
</tr>
<tr>
<td>Sp</td>
<td>33%</td>
</tr>
<tr>
<td>PPV</td>
<td>67%</td>
</tr>
<tr>
<td>NPV</td>
<td>36%</td>
</tr>
</tbody>
</table>

for diagnosis of PE

Casazza F et al, EJE 2005
TEE in PE
TEE in Diagnosis of PE

- Direct visualization of thrombus in proximal parts of pulmonary arteries and right heart

- Good sensitivity in selected pts

- High specificity
  - *If intraluminal mass with distinct borders, different in echodensity from the vascular wall is considered as thrombus*

- Experience/learning curve (left PA?)
  - *special care to avoid overdiagnosis of acute PE*
  - *TEE result often serves as justification of aggressive Th*
Diagnosis of Central Massive PE by TEE

Popovic AD, Neskovic AN, et al. Cardiology 1992
Improvement of Diagnostic Accuracy of TEE by Color Doppler in Cases With Incomplete Obstruction

Diagnostic value of TEE in pts with suspected PE and signs of RV overload at TTE?

PA thrombi
- 11 right
- 15 left
- 25 bilateral

Sn 80.5%
Sp 97.2%


Value of TOE in the diagnosis of PE and RV strain
Sensitivity 80.5%
Specificity 97.2%
• TEE can be used for bedside confirmation of significant PE in 80% of cases.

• However, due to topographic limitations it cannot rule out PE.

• Bedside TEE: 1\textsuperscript{st} choice Dg test in \textit{selected} pts with RV dysfunction, shock, or during CPR.
Echo Identification of High-Risk Pts with Confirmed PE

High-Risk Features:

• RV dysfunction
• Free-floating RH thrombi
• PFO
RV dysfunction
Echo Signs of RV dysfunction

- RV / LV EDD > 1
- RV EDD > 30 mm (RV dilation)
- RV hypokinesis
- Paradoxical RV septal motion
- McConnell’s sign
RV dysfunction

- Dilation
- Hypokinesis
- McConnell’s sign
RV Dysfunction as a Marker of Worse Outcome in Pts with PE

- 126 pts with PE
- RV function assessed by WMA analysis

P = 0.003 in hospital

P = 0.02 1-year F/U

# Prognostic Significance of RV afterload stress in Pts with Suspected PE

- 317 pts with clinically suspected PE
- Echo for the presence of RV afterload stress

<table>
<thead>
<tr>
<th>In-hospital events</th>
<th>RV afterload stress +</th>
<th>RV afterload stress -</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total mortality</td>
<td>16 (18.4%)</td>
<td>13 (5.7%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mortality due to PE</td>
<td>11 (12.6%)</td>
<td>2 (0.9%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CPR</td>
<td>16 (18.4%)</td>
<td>5 (2.1%)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1-year mortality due to PE</th>
<th>RV afterload stress +</th>
<th>RV afterload stress -</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>11 (12.6%)</td>
<td>3 (1.3%)</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
</tbody>
</table>

Impact of RV Dysfunction on Survival* in Pts with Acute PE and Preserved Systolic Arterial Pressure

- 1035 ICOPER pts with PE
- SBP ≥ 90 mmHg at presentation
- Baseline echo for RV hypokinesis

RV hypokinesis in pts with PE and SBP ≥90mmHg:

Log-rank p<0.001

96.4%

91.0%

Independent predictor of 30-day mortality

HR 1.94 (1.23-3.06)

*, Survival adjusted for: cancer, CHF, COPD, age, and TA

Right Heart Thrombi
Right Heart Thrombi
### Characteristics of Pts With and Without Right Heart Thrombi on Baseline Echo

- **2452 ICOPER pts with PE**
- **1113 have baseline ECHO**
- **42 RHTh+ and 1071 RHTh -**

<table>
<thead>
<tr>
<th></th>
<th>Right Heart Thrombi + (42 pts)</th>
<th>Right Heart Thrombi - (1071 pts)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHF</td>
<td>26%</td>
<td>13%</td>
<td>0.024</td>
</tr>
<tr>
<td>Heart rate</td>
<td>107±19</td>
<td>101±22</td>
<td>0.030</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>116±29</td>
<td>126±25</td>
<td>0.008</td>
</tr>
<tr>
<td>Systolic BP &lt;90</td>
<td>14%</td>
<td>5%</td>
<td>0.012</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>28±8</td>
<td>25±10</td>
<td>0.037</td>
</tr>
<tr>
<td>RBBB</td>
<td>27%</td>
<td>13%</td>
<td>0.023</td>
</tr>
<tr>
<td>RV hypo (Echo)</td>
<td>64%</td>
<td>40%</td>
<td>0.002</td>
</tr>
<tr>
<td>Mortality at 14 d</td>
<td>21%</td>
<td>11%</td>
<td>0.032</td>
</tr>
<tr>
<td>Mortality at 3 mo</td>
<td>29%</td>
<td>16%</td>
<td>0.036</td>
</tr>
</tbody>
</table>

3-Month Survival According to the Presence or Absence Of Right Heart Thrombi on Baseline Echo

PFO

patent foramen ovale
PFO is Important Predictor of Adverse Outcome in Pts with Major PE

- 139 consecutive with major PE
- Contrast Echo for PFO detection at presentation
- F/U: in-hospital death and complications

PFO in 48/139 pts (35%)

- Ischemic stroke: 13% vs 2.2%, p=.02
- Peripheral artery embolism: 15% vs 0%, p<.001

Thrombus Lodged in PFO
Differential Diagnosis of PE

- Secondary pulmonary hypertension
- RV infarction
- Atrial septal defect
- Pulmonary stenosis
- Primary pulmonary hypertension
- Aortic dissection
- Tamponade
- ARDS
- ARVD
Acute Pulmonary Hypertension

vs. chronic:

- Dilated, hypokinetic RV  \textit{(McConnell?)}

- Absence of RV hypertrophy

- Absence of significant left heart pathology

- TR, with flow velocities indicating mild to moderate elevation of PAP
Cor pulmonale
Echo in Monitoring
Effects of Therapy for PE

- Reversal of RV dysfunction
- Normalization of RV ejection flow
- Reduction of PA systolic pressure
- Disappearance of thrombi
Day 1, before Th  Day 3, after thrombolysis
Day 1, before Th  

Day 3, after thrombolysis
Day 1, before Th  Day 3, after thrombolysis
Day 1, before Th

Day 3, after thrombolysis
Echo in PE

• Should not be used as a screening test for PE due to low sensitivity in unselected pts.

• May be useful in identifying pts with poor prognosis (RV dysfunction, PFO, right heart thrombus).

• TEE allows bedside direct confirmation of PE in selected pts with RV strain (in ~80% of cases).