Echocardiographic and invasive measurements of pulmonary artery pressure correlate closely at high altitude

YVES ALLEMANN,1 CLAUDIO SARTORI,2 MATTIA LEPORI,2 SÉBASTIEN PIERRE,3 CHRISTIAN MÉLOT,3 ROBERT NAEIJÉ,3 URS SCHERRER,2 AND MARCO MAGGIORINI4

1Swiss Cardiovascular Center Bern, University of Bern, 3010 Bern, Switzerland; 2Department of Internal Medicine, Centre Hospitalier Universitaire Vaudois, 1011 Lausanne, Switzerland; 3Laboratory of Cardiovascular and Respiratory Physiology, Erasme University Hospital, 1070 Brussels, Belgium; and 4Medical Intensive Care Unit of the Department of Internal Medicine, University Hospital Zürich, 8091 Zürich, Switzerland

Received 14 March 2000; accepted in final form 9 May 2000

METHODS

Study design and subjects. Thirty otherwise-healthy mountaineers were recruited for the study, and twenty-eight were finally included. Among them, 14 [3 women and 11 men, mean (±SD) age 40 ± 6 yr] had previously developed at least one episode of clinically and radiographically documented HAPE (HAPE susceptible; HAPE-S group). The 14 other subjects (4 women and 10 men, mean age 30 ± 2 yr) were known to be resistant to HAPE (HAPE-R group; repeated alpine-style climbing to peaks above 4,000 m without symptoms of pulmonary edema). Two HAPE-S subjects who developed pulmonary hypertension (57 ± 4, 559 m) were radical and invasive measurements of systolic pulmonary arterial pressure in HAPE-susceptible and HAPE-resistant mountaineers.

Allemann, Yves, Claudio Sartori, Mattia Lepori, Sébastien Pierre, Christian Mélot, Robert Naeije, Urs Scherrer, and Marco Maggiorini. Echocardiographic and invasive measurements of pulmonary artery pressure correlate closely at high altitude. Am J Physiol Heart Circ Physiol 279: H2013–H2016, 2000.—Exaggerated hypoxia-induced pulmonary hypertension is a hallmark of high-altitude pulmonary edema (HAPE) and plays a major role in its pathogenesis. Many studies of HAPE have estimated systolic pulmonary arterial pressure (SPAP) with Doppler echocardiography, whereas at low altitude, Doppler echocardiographic estimation of SPAP correlates closely with its invasive measurement. No such evidence exists for estimations obtained at high altitude, where alterations of blood viscosity may invalidate the simplified Bernoulli equation. We measured SPAP by Doppler echocardiography and invasively in 14 mountaineers prone to HAPE and in 14 mountaineers resistant to this condition at 4,559 m. Mountaineers prone to HAPE had more pronounced pulmonary hypertension (57 ± 12 and 58 ± 10 mmHg for noninvasive and invasive determination, respectively; means ± SD) than subjects resistant to HAPE (37 ± 6 and 37 ± 6 mmHg, respectively), and the values measured in the two groups as a whole covered a wide range of pulmonary arterial pressures (30–83 mmHg). Spearman test showed a highly significant correlation ($r = 0.89, P < 0.0001$) between estimated and invasively measured SPAP values. The mean difference between invasively measured and Doppler-estimated SPAP was 0.5 ± 8 mmHg. At high altitude, estimation of SPAP by Doppler echocardiography is an accurate and reproducible method that correlates closely with its invasive measurement.

Doppler echocardiography; right heart catheterization; high-altitude pulmonary edema

HIGH-ALTITUDE PULMONARY EDEMA (HAPE) is a life-threatening condition occurring in predisposed subjects at altitudes above 2,500 m (7, 9–11). An exaggerated hypoxia-induced vasoconstriction of the pulmonary arterial bed is a hallmark of HAPE and is thought to play a major role in its pathogenesis (7, 9–11). For obvious reasons, in almost all of the studies performed and correlate well with invasively measured pulmonary arterial pressures (2, 3, 12, 14). At high altitude, whole blood viscosity is altered (8), and whether these alterations are of sufficient magnitude to invalidate the simplified Bernoulli equation (which ignores viscous friction) (13) is unknown. We therefore performed at a high-altitude research laboratory (4,559 m) direct invasive and Doppler echocardiographic measurements of systolic pulmonary arterial pressure in HAPE-susceptible and HAPE-resistant mountaineers.

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
oped acute HAPE were not included in the study (because of insufficient quality of Doppler-derived gradients across the tricuspid valve in one case and because oxygen had been delivered between the echocardiographic and invasive determinations of pulmonary pressures in the other case). All subjects ascended in groups of two to four from 1,130 to 4,559 m within a period of 24 h. The ascent consisted of a transport by cable car to an altitude of 3,200 m; a 1.5-h climb to an altitude of 3,611 m, where the subjects stayed overnight; and, on the next day, a 4.5-h climb to the high-altitude research laboratory at Capanna Regina Margherita. The subjects then spent 2 days and 2 nights at this hut. Doppler echocardiographic estimations and invasive measurements of systolic pulmonary arterial pressure were performed after the first night spent at the Margherita hut or earlier if the subject had developed HAPE. Seven HAPE-S subjects had acute pulmonary edema at the time of the determinations of pulmonary arterial pressure. The experimental protocol was approved by the Institutional Review Boards on Human Investigation (University Hospitals, Lausanne and Zürich, Switzerland), and all subjects provided written informed consent before ascent.

**Doppler echocardiography.** Echocardiographic recordings were obtained with a real-time, phased array sector scanner (model Sonos 2500 or 5000; Hewlett-Packard, Andover, MA) with an integrated color Doppler system and a transducer containing crystal sets for imaging (2.5 MHz) and for continuous-wave Doppler recording (1.9 MHz). The recordings were stored on S-VHS videotape for analysis by an investigator (the study echocardiographer), who was unaware of the subject’s clinical history. The recordings were analyzed two times (analyses 1 and 2), at least 3 mo apart, by the study echocardiographer. All reported values represent the mean of at least three measurements. After tricuspid regurgitation had been localized with Doppler color flow imaging, the peak flow velocity of the tricuspid jet ($V_{TR}$) was measured with the use of continuous-wave Doppler (Fig. 1), and the pressure gradient between the right ventricle and the right atrium was calculated by use of the modified Bernoulli equation: $\Delta P_{RV-RA} = 4(V_{TR})^2$, where $\Delta P$ is pressure difference, RV is right ventricle, and RA is right atrium (4). Systolic pulmonary arterial pressure was estimated by adding the clinically determined mean jugular venous pressure (14) to the pressure gradient between the right ventricle and atrium.

**Right heart catheterization.** Right heart catheterization was performed immediately after Doppler echocardiography with the use of a standard thermodilution balloon-tipped pulmonary arterial catheter (131H-7F Baxter) inserted via an internal jugular vein. To enhance safety of the procedure, the internal jugular vein was first located by use of an ultrasound Doppler device (SonoGuide2; Darbomed, Fehraltorf, Switzerland). After localization of the vein and local anesthesia (lidocaine 1%), the vein was canulated with a sheath (Arrow, Erding, Germany) by use of the Seldinger technique. Thereafter, the pulmonary arterial catheter was floated under constant-pressure wave monitoring into the pulmonary artery for the measurements of right atrial and pulmonary arterial pressure. A small polyethylene catheter (Vygon, Ecouen, France) was inserted into a radial artery or a femoral artery to measure systemic arterial pressure. Pulmonary and systemic arterial pressures were measured with the use of transducers (Homedica, Cham, Switzerland) connected to a hemodynamic and electrocardiographic monitoring system (Sirecust 404; Siemens, Erlangen, Germany). The pressure transducers were zero-referenced at midchest, and vascular pressures were measured at end expiration. The vascular pressure signals were sampled at 200 Hz by use of an analog-to-digital converter (RTI 800, Analog Device) and stored on a personal computer (Fig. 1). For pulmonary arterial pressure measurements, the subjects were asked to stop breathing at the end of a normal tidal volume for a period of 8 s. Heart rate was determined by a continuously monitored electrocardiogram. Cardiac output (Q) was measured by thermodilution with the use of injections of 10 ml of 5% cold dextrose in water (8–10°C) and a computer (Vigilance, Baxter, Switzerland) and was calculated as the mean of three to five determinations.

**Statistics.** Statistical analysis was performed with the help of the Statistical Analysis System software package (version 6.12; SAS Institute, Cary, NC). The unpaired Student’s $t$-test

---

**Fig. 1.** Representative Doppler tricuspid regurgitation signals and superimposed pulmonary arterial waveforms from a subject susceptible to high-altitude pulmonary edema (HAPE susceptible; left) and from a subject resistant to this condition (HAPE resistant; right). SPAP, systolic pulmonary arterial pressure; $TR V_{max}$, peak flow velocity of tricuspid jet; Pk Grad, peak gradient.
was used for the comparisons between the HAPE-S and HAPE-R groups. A paired $t$-test was used for the comparisons between invasively measured and Doppler echocardiographically estimated parameters. Spearman correlation and Bland-Altman analysis were performed. $P$ value < 0.05 was considered statistically significant. Values are means ± SD.

RESULTS

Heart rate (82 ± 11 vs. 79 ± 11 beats/min) and systemic blood pressure (141/76 ± 18/10 vs. 132/78 ± 9/8) did not significantly differ between the HAPE-S and the HAPE-R subjects. Pulmonary vascular resistance index and invasively measured or Doppler echocardiographically estimated systolic pulmonary arterial pressures, as expected, were significantly higher in HAPE-S than in HAPE-R subjects (Table 1, Fig. 1).

Systolic pulmonary arterial pressure was 58 ± 10 mmHg in HAPE-S but only 37 ± 6 mmHg in HAPE-R subjects ($P < 0.0001$). When all subjects were analyzed together, the mean difference between invasively measured and Doppler echocardiographically estimated systolic pulmonary arterial pressures was $-0.5 ± 8$ mmHg (Fig. 2). Figure 3 shows that there was a strong relationship ($r = 0.89$, $P < 0.0001$) between invasively and echocardiographically obtained measurements of systolic pulmonary arterial pressure. The intraobserver variability between the first and the second Doppler analyses was very small. The $r$ values for the correlation coefficients between invasively measured pulmonary arterial pressure and the first and second Doppler echocardiographic measurements were 0.89 ($P < 0.0001$) and 0.85 ($P < 0.0001$), respectively; the $r$ value for the correlation coefficient between the first and the second Doppler measurements was 0.92 ($P < 0.0001$).

DISCUSSION

The present results show, for the first time at high altitude, that Doppler echocardiographically estimated systolic pulmonary arterial pressure correlates very well with its invasive measurement in both HAPE-susceptible mountaineers and subjects resistant to such edema. These findings indicate that Doppler echocardiography is an accurate and reproducible method for estimating pulmonary arterial pressure at high altitude, the most important predictor of an augmented susceptibility to HAPE. They also indicate that despite alterations of blood viscosity at high altitude...

### Table 1. Some pulmonary hemodynamic parameters

<table>
<thead>
<tr>
<th></th>
<th>HAPE-S</th>
<th>HAPE-R</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac index, l·min⁻¹·m⁻²</td>
<td>3.7 ± 0.6</td>
<td>3.7 ± 0.9</td>
<td>NS</td>
</tr>
<tr>
<td>Pulmonary vascular resistance index, dyn·s·cm⁻⁵</td>
<td>624 ± 175</td>
<td>360 ± 93</td>
<td>0.0001</td>
</tr>
<tr>
<td>Right atrial pressure, mmHg</td>
<td>7.5 ± 2</td>
<td>7 ± 2</td>
<td>NS</td>
</tr>
<tr>
<td>SPAP, mmHg</td>
<td>58 ± 10</td>
<td>37 ± 6</td>
<td>0.0001</td>
</tr>
<tr>
<td>Doppler echocardiographic measurements</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transtricuspidal pressure gradient, mmHg</td>
<td>50 ± 12</td>
<td>30 ± 8</td>
<td>0.0001</td>
</tr>
<tr>
<td>SPAP, mmHg</td>
<td>59 ± 12</td>
<td>37 ± 8</td>
<td>0.0001</td>
</tr>
<tr>
<td>ΔSPAP, mmHg</td>
<td>1.1 ± 10.3</td>
<td>-0.1 ± 5.2</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are means ± SD. HAPE-S, group susceptible to high-altitude pulmonary artery edema (HAPE); HAPE-R, group resistant to HAPE; SPAP, systolic pulmonary arterial pressure; ΔSPAP, difference between invasively measured and Doppler echocardiographically estimated SPAP; NS, not significant.
(8), the simplified Bernoulli equation, which ignores viscous friction, remains valid.

Measured peak velocity of tricuspid regurgitation jet was used to estimate pulmonary arterial pressure in this study, because this technique is easy to perform and correlates well with invasive measurements at low altitude (2, 3, 12, 14). At lowland, reported \( r \) values for correlation coefficients between Doppler-estimated and invasively measured systolic pulmonary arterial pressures vary between 0.95 and 0.97 (2, 3, 12, 14). None of these reports, however, included a Bland-Altman analysis. Although Doppler estimates of pulmonary pressure are operator dependent (2–4, 7, 12, 14), the slightly smaller \( r \) values in the present field study may be related, at least in part, to the difficulties of examining severely dyspneic and tachypneic subjects, with seven of them suffering full-blown HAPE. Moreover, the fact that echocardiography and right heart catheterization were performed sequentially may also have contributed to slightly larger differences between the estimated and invasively measured pressures than those observed in studies at low altitude using strictly simultaneous measurements. Nevertheless, our data indicate that at high altitude, provided sufficient individual echogenicity, a broad spectrum of systolic pulmonary arterial pressures can be reliably estimated by the Doppler-derived transtricuspid pressure gradient. In conclusion, Doppler echocardiography represents an accurate and reproducible method for estimating pulmonary arterial pressure at high altitude.

We are indebted to our subjects; to the Sezione Varallo del Club Alpino Italiano for providing the locations in the Capanina Regina Margherita; to our mountain guides Andrea Enzio, Osvaldo Antonietti, and Bruno Brand for leading our subjects safely to the hut; to Hewlett-Packard for providing the echocardiographic equipment; and to the Swiss Army for transporting part of the material.

This work was supported, in part, by grants from the Swiss National Science Foundation, the International Olympic Committee, the Fondazione Dottor PierLuigi Crivelli, the Hamasil Foundation, the Placide Nicod Foundation, the Olga Mayenfisch Foundation, and the Hermann Kurz Foundation, Zürich, Switzerland.

Parts of this work were presented at the 71st Scientific Sessions of the American Heart Association, Dallas, Texas, November 1998, and at the 11th International Hypoxia Symposium, Jasper, Alberta, Canada, February 1999.

REFERENCES