Safety of right heart catheterization for pulmonary hypertension in very elderly patients

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Abstract
Right heart catheterization (RHC) is the reference test in diagnosing pulmonary hypertension (PH). The increasing age of patients at the time of diagnosis raises the issue of the morbidity of this invasive test in elderly individuals. We hypothesized that the morbidity associated with RHC would be increased in elderly patients and highlight differences in hemodynamic characteristics compared to younger patients. A retrospective study was conducted in a regional referral center for PH. Data for all consecutive RHCs performed during the study period were analyzed. Over a five-year period, 1060 RHCs were performed. Of the patients, 228 (21.5%) were aged ≥75 years and 832 (78.5%) were aged <75 years. Duration of the procedure and site of puncture did not differ according to age group (all P > 0.05). Nine procedures (0.9%) led to complications: three (1.3%) in patients aged >75 years and six (0.7%) in younger patients aged >75 years. Pulmonary arterial pressure and cardiac output were lower in patients aged >75 years than in younger patients (P = 0.001). RHC may be performed regardless of patient age. The rate of RHC complications is not increased in individuals aged ≥75 years. As most complications were related to femoral vein puncture, this route should be avoided whenever possible.

Keywords
hemodynamics, morbidity, pulmonary hypertension

Introduction
Right heart catheterization (RHC) is the reference test in diagnosing pulmonary hypertension (PH). In addition, it indicates hemodynamic severity and mechanism, pulmonary circulation vasoreactivity to inhaled nitric oxide, and assesses the benefit of therapeutic intervention. When performed in an experienced center, RHC in patients with PH is associated with 1.1% morbidity and 0.055% mortality. Patient age at diagnosis of PH is steadily increasing. This trend raises the question of whether to perform RHC in very elderly patients.

The present study assessed the risks associated with RHC in patients aged ≥75 years and their hemodynamic characteristics.

Methods
A retrospective, observational, single-center study was conducted in the Rhône-Alpes (France) regional PH referral center. Data for all consecutive RHCs performed by the same practitioner over a five-year period were collected. Recorded data included patients’ demographic characteristics, procedure duration, puncture site, number and type of adverse events (AEs), and hemodynamic values.

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Once the patient’s consent was obtained, and if the international normalized ratio (INR) was <3 and platelet count >50,000/mm³, RHC was performed with a 6- or 7-French Swan-Ganz catheter. A humeral approach was preferred when possible, otherwise a femoral or internal jugular approach was adopted. PH was defined as mean pulmonary arterial pressure (mPAP) ≥25 mmHg. Pre-capillary PH was defined by pulmonary artery wedge pressure (PAWP) ≤15 mmHg, isolated post-capillary PH by PAWP >15 mmHg with diastolic pressure gradient (DPG; diastolic PAP [dPAP] minus mean PAWP) <7 mmHg, and combined pre- and post-capillary PH for PAWP and DPG >15 mmHg and ≥7 mmHg, respectively. A fluid challenge was performed when pre- or post-capillary status was unclear. The duration of the procedure was assessed by measuring dose-length product (DLP) X-rays. Patients were divided into two groups according to their age: “elderly” (aged ≥75 years) and “non-elderly” (aged <75 years) groups. Elderly participants were defined by the World Health Organization (WHO) as individuals aged ≥65 years or older. In this study, we chose the threshold of 75 years because it is the age used in France for admission to geriatric institutions. In clinical practice, it is also the age above which diagnostic and treatment strategies are usually reassessed.

Categorical variables were described by frequency (n) and percentage (%). Comparison between groups was performed using chi-square or Fisher’s exact tests. Median and interquartile ranges were used to describe quantitative variables, compared by Student’s t-test. A value of P < 0.05 was considered statistically significant. Analysis used IBM SPSS Statistics 20 software.

**Results**

Between 1 November 2010 and 31 October 2014, 1102 RHCs were performed and 1060 were included for analysis. Forty-two were excluded because PAWP values were not available. Patient characteristics and procedural details are shown in Table 1. The median age was 66 years (± 14.2; range = 18–94 years). 21.5% of RHCs (n = 228) were

### Table 1. Characteristics of patients and RHC procedures.

|                          | Total (n = 1060) | Age < 75 years (n = 832) | Age ≥75 years (n = 228) | P     |
|--------------------------|-----------------|-------------------------|------------------------|-------|
| Age (years)              | 66 ± 14.2       | 61 ± 12.7               | 79 ± 3.5               |       |
| Female gender (n (%))    | 580 (54.7)      | 458 (55.0)              | 122 (53.5)             | 0.679 |
| BMI (kg/m²)              | 25.8 ± 6.34     | 25.6 ± 6.5              | 26.3 ± 5.7             | 0.199 |
| RHC (n (%))              | <0.001          |                        |                        |       |
| Vascular access site (n (%)) | 513 (49.4)      | 397 (48.5)              | 116 (52.7)             | 0.553 |
| Humeral vein             |                |                         |                        |       |
| Femoral vein             |                |                         |                        |       |
| Internal jugular vein    | 3 (0.3)         | 3 (0.4)                 | –                      |       |
| Dose length product (Gy/cm²) | 6 ± 16.7        | 5 ± 15.8                | 6 ± 19.7               | 0.090 |
| Hemodynamic diagnosis    |                |                         |                        | 0.475 |
| RHC (n)                  | 369             | 272                     | 97                     |       |
| Normal (n (%))           | 92 (25.0)       | 71 (26.1)               | 21 (21.6)              |       |
| Pre-capillary PH (n (%)) | 224 (60.8)      | 165 (60.7)              | 59 (60.8)              |       |
| Post-capillary PH (n (%))| 33 (8.9)        | 23 (8.4)                | 10 (10.4)              |       |
| Combined PH (n (%))      | 18 (4.9)        | 12 (4.4)                | 6 (6.2)                |       |
| Hyperdynamic state (n (%)) | 2 (0.5)         | 1 (0.4)                 | 1 (1.0)                |       |
| PH etiological group (n) | 242             | 177                     | 65                     | 0.03  |
| Group 1 (n (%))          | 110 (45.5)      | 86 (48.6)               | 24 (36.9)              |       |
| Group 2 (n (%))          | 75 (31.0)       | 52 (29.4)               | 23 (35.4)              |       |
| Group 3 (n (%))          | 38 (15.7)       | 22 (12.4)               | 16 (24.6)              |       |
| Group 4 (n (%))          | 19 (7.8)        | 17 (9.6)                | 2 (3.1)                |       |
| Adverse events (n (%))   | 9 (0.9)         | 6 (0.7)                 | 3 (1.3)                | 0.513 |
| Local vascular injury    | 8 (0.8)         | 5 (0.6)                 | 3 (1.3)                |       |
| Cardiac complications    | 1 (0.1)         | 1 (0.1)                 | –                      |       |

BMI, body mass index; RHC, right heart catheterization; PH, pulmonary hypertension.
performed in patients aged ≥ 75 years. A total of 369 RHCs (34.8%) were performed as part of initial assessment. Pre-capillary PH was diagnosed in 224 cases (60.8%): 165 non-elderly (60.7%) and 59 elderly (60.8%). Proportions of patients with no PH, pre-, or post-capillary PH did not differ according to age group (P = 0.475). Among patients with pre-capillary and combined PH (n = 242), elderly individuals exhibited a chronic thromboembolic PH (group 4) twice as much as younger ones (24.6% vs. 12.4%). Group 1 PH was found less often in elderly patients (36.9%) than in younger patients (48.6%).

Procedure-related morbidity
In total, 513 (49.4%) RHCs were performed via the humeral vein and 522 (50.2%) via the femoral vein. According to age, there was no difference in the use of the different venous access (humeral, femoral, or jugular veins, P = 0.55). The complexity of the procedure was indirectly estimated by the DLP, which was not significantly different between age groups (5 ± 15.8 Gy/cm² for non-elderly patients and 6 ± 19.7 Gy/cm² for elderly patients; P = 0.09). Serious AEs occurred in nine patients (0.9%): three (1.3%) were elderly and six (0.7%) were non-elderly (P = 0.5). In all these cases, access had been femoral (odds ratio [OR] = 64.1; 95% confidence interval = 31.9–128.9; P < 0.001). Older age, gender, body mass index, or co-morbidity were not significantly associated with occurrence of complications (P > 0.05), which comprised eight local vascular injuries (one femoral phlebitis and seven hematomas, including two associated with pseudoaneurysm and two with arteriovenous fistula) and one pulmonary edema in a patient with pre-existing post-capillary PH and elevated filling pressure. Atrial and ventricular tachyarrhythmias were not systematically collected because they did not require treatment unless they resolved quickly after catheter pull-back and did not induce hemodynamic instability. There were no vasovagal episodes, hypotensive episodes after inhalation of nitric oxide, or infections. There were no deaths implicating the procedure.

Baseline hemodynamic parameters
Data from RHC at baseline, in patients with pre-capillary PH (n = 224), showed comparable results for RAP, systolic PAP, and PAWP throughout the ages. In contrast, mPAP, dPAP, and DPG were lower in elderly patients. A fluid challenge was performed for 81 patients and revealed a post-capillary hemodynamic profile for 29 of them. This result was not different between age groups (P = 0.09).

Furthermore, if we consider means values of cardiac index (CI), right ventricular function was impaired in patients aged > 75 years (CI = 2.4 L.min⁻¹.m⁻² ± 0.7) when it was preserved in those aged <75 years (CI = 2.6 L.min⁻¹.m⁻² ± 0.7) (P = 0.012). These geriatric characteristics were also found when only group 1 PH patients were considered (CI = 2.3 L.min⁻¹.m⁻² ± 0.7 for elderly patients and CI = 2.7 L.min⁻¹.m⁻² ± 0.8 for non-elderly patients; P = 0.03) (Table 2).

When patients were treated for PH, elderly patients had significantly less hemodynamic re-evaluation than non-elderly patients (P < 0.001).

Discussion
In our department, 21.5% of RHCs were performed in elderly patients (aged ≥ 75 years). The overall rate of serious AEs was low (0.9%) and very similar to previous reports (1.1–1.7%).2,12 The rate of RHC-related complications was not higher in individuals aged >75 years. The vast majority of AEs (hematoma, pseudoaneurysm, arteriovenous fistula) were associated with femoral venous access. Our practice has been modified in the light of this finding. Humeral vein access is preferred whenever possible, and we use smaller catheters via smaller sheaths (6-French), with ultrasound to locate the humeral vein if necessary. International guidelines fail to specify the preferred venous access route,1 but it seems that femoral vein puncture should be avoided, in favor of humeral or internal jugular approaches. Almost 14% of RHCs done at baseline evaluation (n = 51) showed isolated or combined post-capillary PH, comparable to

| Table 2. Baseline hemodynamic parameters in pre-capillary and group 1 PH. |
|---------------------|---------------------|---------------------|
| Age < 75 years     | Age ≥ 75 years     | P                   |
| Pre-capillary PH (n) | 165                | 59                  |
| mPAP (mmHg)       | 39 ± 13.2          | 37 ± 8.7            | 0.003           |
| sPAP (mmHg)       | 64 ± 21.6          | 61 ± 15.3           | 0.660           |
| dPAP (mmHg)       | 26 ± 9.9           | 22 ± 5.8            | <0.001          |
| PAWP (mmHg)       | 8 ± 3.4            | 9 ± 3.2             | 0.726           |
| DPG (mmHg)        | 18 ± 9.8           | 13 ± 6.1            | <0.001          |
| CO (L.min⁻¹)      | 4.8 ± 1.4          | 4.3 ± 1.1           | 0.003           |
| CI (L.min⁻¹.m⁻²)  | 2.6 ± 0.7          | 2.4 ± 0.7           | 0.012           |
| PVR (WU)          | 6.1 ± 4.2          | 6.3 ± 3.6           | 0.923           |
| RAP (mmHg)        | 5.0 ± 3.6          | 5.5 ± 3.5           | 0.470           |
| PH group 1 (n)    | 76                  | 17                  |
| mPAP (mmHg)       | 40.5 ± 16.6        | 38.0 ± 7.5          | 0.020           |
| sPAP (mmHg)       | 68.0 ± 27.2        | 62.0 ± 13.8         | 0.112           |
| dPAP (mmHg)       | 27.0 ± 11.8        | 22.0 ± 4.3          | 0.001           |
| PAWP (mmHg)       | 8.0 ± 3.3          | 10 ± 3.4            | 0.423           |
| DPG (mmHg)        | 19.5 ± 11.6        | 11.0 ± 4.7          | <0.001          |
| CO (L.min⁻¹)      | 4.9 ± 1.4          | 3.7 ± 1.1           | 0.009           |
| CI (L.min⁻¹.m⁻²)  | 2.7 ± 0.8          | 2.3 ± 0.7           | 0.030           |
| PVR (WU)          | 6.4 ± 5.2          | 6.3 ± 3.2           | 0.810           |
| RAP (mmHg)        | 6.0 ± 3.3          | 6.0 ± 3.5           | 0.936           |

PH, pulmonary hypertension; mPAP, mean pulmonary arterial pressure; sPAP, systolic pulmonary artery pressure; dPAP, diastolic pulmonary arterial pressure; PAWP, pulmonary artery wedge pressure; DPG, diastolic pressure gradient; CO, cardiac output; CI, cardiac index; PVR, pulmonary vascular resistance; RAP, right atrial pressure; WU, Wood unit.
previous reports of 11.7–34.6%. Although a left-heart component is known to be more frequent in elderly patients, no such difference was found in the present series, possibly due to special care taken in patient selection before RHC in a dedicated PH center. At follow-up, elderly patients treated for PH had significantly fewer control RHCs than non-elderly patients. However, RHC should be performed to confirm diagnosis of PH regardless of patient age. Decision to perform iterative RHC for patients under treatment should be based on opportunities of alternative therapeutic strategies.

In healthy individuals, aging may be associated with a slight increase in mPAP and a decrease in cardiac output. In contrast, pulmonary arterial hypertension literature supports the fact that patients aged >65 years have significantly lower mPAP and similar CI than patients aged <65 years. In our study, the population of very elderly patients (≥75 years) exhibited lower cardiac output, suggesting that the capacity of the right ventricle to support high PAPs declines with aging.

The present study involved certain limitations. It was a single-center retrospective study. However, analysis was carried out on a large number of procedures performed in a pulmonary vascular disease center. Furthermore, RHCs were performed by a single practitioner over a limited period of time, avoiding operator-related bias.

**Conclusion**

RHC may be performed regardless of patient age, to confirm the diagnosis of PH and guide management. The rate of RHC-related complications was not higher in individuals aged >75 years. As most complications were related to femoral vein puncture, this route should be avoided whenever possible.

**Conflict of interest**

JFM reports receiving consulting fees and research grants from LFB Biomédicaments, CSL Behring, and travel and meeting support and lecture fees from Actelion, Pierre Fabre, BoehringerIngelheim, Pfizer, GSK, Chiesi, Novartis, Almirall, MSD, and Bioprojet outside the submitted work. VC reports personal fees from Actelion, Bayer, Biogen Idec, BoehringerIngelheim, Gilead, GSK, Intermune, Lilly, Novartis, Pfizer, Roche, Sanofi, and grants from Actelion, BoehringerIngelheim, GSK, Pfizer, and Roche outside the submitted work. The other authors have nothing to disclose.

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**References**

1. Galie N, Humbert M, Vachiery J-L, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS). *Eur Respir J* 2015; 46(4): 903–975.
2. Hoeper MM, Lee SH, Voswinckel R, et al. Complications of right heart catheterization procedures in patients with pulmonary hypertension in experienced centers. *J Am Coll Cardiol* 2006; 48(12): 2546–2552.
3. Rich S, Dantzker DR, Ayres SM, et al. Primary pulmonary hypertension. A national prospective study. *Ann Intern Med* 1987; 107(2): 216–223.
4. Humbert M, Sitbon O, Chaouat A, et al. Pulmonary arterial hypertension in France: results from a national registry. *Am J Respir Crit Care Med* 2006; 173(9): 1023–1030.
5. Frachon I, Barnier A, Jobic Y, et al. Hypertension artérielle pulmonaire du sujet âgé. La cohorte d’un centre régional. *Rev Mal Respir* 2010; 27(1): 30–36.
6. Badesch DB, Raskob GE, Elliott CG, et al. Pulmonary arterial hypertension: baseline characteristics from the REVEAL Registry. *Chest* 2010; 137(2): 376–387.
7. Frost AE, Badesch DB, Barst RJ, et al. The changing picture of patients with pulmonary arterial hypertension in the United States: how REVEAL differs from historic and non-US Contemporary Registries. *Chest* 2011; 139(1): 128–137.
8. Hurdman J, Condliffe R, Elliott CA, et al. ASPIRE registry: assessing the Spectrum of Pulmonary Hypertension Identified at a Referral centre. *Eur Respir J* 2012; 39(4): 945–955.
9. Hoeper MM, Huscher D, Ghofrani HA, et al. Elderly patients diagnosed with idiopathic pulmonary arterial hypertension: results from the COMPERA registry. *Int J Cardiol* 2013; 168(2): 871–880.
10. McGoon MD, Benza RL, Escribano-Subias P, et al. Pulmonary arterial hypertension: epidemiology and registries. *J Am Coll Cardiol* 2013; 62(25 Suppl): D51–59.
11. SANT4- Bulletin Officiel No. 2007-4: Annonce No. 58. Available at: http://social-sante.gouv.fr.
12. Ranu H, Smith K, Nimako K, et al. A retrospective review to evaluate the safety of right heart catheterization via the internal jugular vein in the assessment of pulmonary hypertension. *Clin Cardiol* 2010; 33(5): 303–306.
13. Pugh ME, Sivarajan L, Wang L, et al. Causes of pulmonary hypertension in the elderly. *Chest* 2014; 146(1): 159–166.
14. Vachiéry J-L, Adir Y, Barberà JA, et al. Pulmonary hypertension due to left heart diseases. *J Am Coll Cardiol* 2013; 62(25 Suppl): D100–108.
15. Granath A and Strandell T. Relationship between cardiac output, stroke volume and intracardiac pressures at rest and during exercise in supine position and some anthropometric data in healthy old men. *Acta Med Scand* 1964; 176: 447–466.
16. Kovacs G, Berghold A, Scheidl S, et al. Pulmonary arterial pressure during rest and exercise in healthy subjects: a systematic review. *Eur Respir J* 2009; 34(4): 888–894.
17. Naeije R. Physiology of the pulmonary circulation and the right heart. *Curr Hypertens Rep* 2013; 15(6): 623–631.
18. Ling Y, Johnson MK, Kiely DG, et al. Changing demographics, epidemiology, and survival of incident pulmonary arterial hypertension: results from the pulmonary hypertension registry of the United Kingdom and Ireland. *Am J Respir Crit Care Med* 2012; 186(8): 790–796.
19. Rose JA, Cleveland JM, Rao Y, et al. Effect of age on phenotype and outcomes in pulmonary arterial hypertension trials. *Chest* 2016; 149(5): 1234–1244.