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Original article

Implementation of a systematic comprehensive geriatric assessment for elderly patients suspected of pulmonary hypertension

C. Duvillard[a], L. Lafaie[b,*], É. de Magalhaes[a,c,i], S. Bezzeghoud[a,i], S. Accassat[a,c,i], P.B. Poble[d], P.B. Bonnefoy[e], C. Tulane[f], T. Célarier[b,g,h], L. Bertoletti[a,c,i,j]

[a] *Service de médecine vasculaire et thérapeutique, CHU de Saint-Étienne, Saint-Étienne, France*
[b] *Département de gérontologie clinique, CHU de Saint-Étienne, Saint-Étienne, France*
[c] *INSERM, UMR1059, Équipe dysfonction vasculaire et hémostase, université Jean-Monnet, 42055 Saint-Étienne, France*
[d] *Service d'explorations fonctionnelles, CHU de St-Étienne, Saint-Étienne, France*
[e] *Service de médecine nucléaire, CHU de St-Étienne, Saint-Étienne, France*
[f] *Département de cardiologie, CHU de Saint-Étienne, Saint-Étienne, France*
[g] *Gérontopôle Auvergne-Rhône-Alpes, Saint-Étienne, France*
[h] *Chaire santé des ainés, université Jean-Monnet, Saint-Étienne, France*
[i] *INSERM, CIC-1408, CHU de Saint-Étienne, 42055 Saint-Étienne, France*
[j] *F-CRIN INNOVTE network, Saint-Étienne, France*

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ABSTRACT

Background. – The phenotype of patients seen for a suspicion of pulmonary hypertension has changed, with an increasing age and frequency of comorbidities. Selection of elderly patients, in whom a classical work-up is mandatory, is challenging. Comprehensive geriatric assessment (CGA) has modified the management of elderly patients with cancer. Pulmonary hypertension (PH) shares with cancer a functional impact and may evolve rapidly, depending on the group of PH. We assessed the impact of a systematic CGA in patients over 70 years old referred for a suspicion of PH.
Methods. – A standardised CGA was performed on every patient older than 70 years old, referred for a PH suspicion, before considering invasive tests for diagnosis and treatment, between July 2014 and May 2019. Our primary aim was to describe the impact of CGA on the decision to stop or pursue the recommended diagnostic work-up for PH.
Results. – Among the thirty-one patients evaluated [mean age 81,5 (72–91) years], a negative CGA leads to stop the diagnostic work-up in eleven patients. Among the nineteen remaining patients, sixteen had confirmed PH, with half being chronic thromboembolic pulmonary hypertension.
Conclusions. – Our study indicates that comprehensive geriatric assessment could be an excellent first screen for elderly patients referred for a PH suspicion. Involving a geriatric physician stopped the investigations in one third of patients. In patients with a favourable CGA, PH was confirmed in most of the cases, with chronic thromboembolic pulmonary hypertension being the first cause of PH.

1. Introduction

Pulmonary hypertension (PH) is a severe condition, linked to an increase in pulmonary vascular resistances, which can lead to right heart failure and death. On the functional level, the impact on daily life and autonomy is important, with dyspnea limiting the activities of daily life. The etiologies of PH are diverse and classified into several major groups: related to chronic respiratory (group 3) or cardiac (group 2), chronic thromboembolic (group 4), and pulmonary arterial hypertension (group 1) [1]. Therapeutic management varies according to these etiologies. For group 1 and group 4, specific drug treatments were developed. For group 4, it is also recommended to be treated by pulmonary endarterectomy and balloon pulmonary angioplasty [1]. Without treatment, the median

Abbreviations: ADL, Activities of Daily Living; BMI, Body mass index; CGA, Comprehensive Geriatric Assessment; CTEPH, Chronic Thromboembolic Pulmonary Hypertension; ECOG, Eastern Cooperative Oncology Group; GDS, Geriatric Depression Scale; IADL, Instrumental Activities of Daily Living; LVEF, Left ventricular ejection fraction; MMS, Mini Mental State; MNA, Mini Nutritional Assessment; NYHA, New York Hearth Association; PAH, Pulmonary Arterial Hypertension; PH, Pulmonary Hypertension; sPAP, systolic pulmonary artery pressure; TTE, Transthoracic Echocardiogram; V/Q lung scan, Ventilation/Perfusion lung scan.

* Corresponding author at: Département de gérontologie clinique, CHU de Saint-Étienne, Saint-Étienne, France.
E-mail address: lafaie.ludovic@gmail.com (L. Lafaie).

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survival rate is less than 3 years for pulmonary arterial hypertension [2–4].

These specific PAH drug treatments have, on the one hand, potential side effects (hypotension, headache, digestive disorders for the most frequent) with, on the other hand, potentially serious drug interactions (bleeding accident with oral anticoagulants, for example [5]). Regarding thrombo-endarterectomy, the only curative treatment for chronic thromboembolic pulmonary hypertension (CTEPH) [6], a significant mortality rate (between 2 and 4% perihospital) was observed [6]. Thus, it is crucial to concentrate and improve management of these vulnerable PH patients in a specialised PH centre.

It is well recognised that medical advances contributed to an increase in life expectancy. For instance, the proportion of patients over 75 years of age rose from 6.3% (3.7 million) in 1996 to 9.1% (6.1 million) in 2016 [7]. At the same time, the epidemiology of patients with PH has moved from young females to older patients in their 6th decade [8,9]. This phenotype's modification is marked in patients seen for a suspicion of pulmonary hypertension, with an increasing age and high frequency of comorbidities. The development of transthoracic echocardiogram (TTE) has increased the number of patients suspected of being diagnosed with elevated right pressures. However, the sensitivity and specificity of this examination remains modest [10]. This is one problem in elderly patients with associated comorbidities, causing frequent false positives when the patient is brought to right cardiac catheterisation.

In the elderly patient, the most frequent causes of PH are groups 2 or 3 (cardiac or respiratory pathology) [11]. CTEPH (group 4) and PAH (group 1) are not known to be one of the most common causes, but management and prognosis may be different, as it is potentially curable for CTEPH patients. In fact, in the case of individual comorbidities, a precise diagnostic procedure must be carried out in the event of suspected PH [12]. Regardless of the etiology, the confirmation of the diagnosis of hypertension requires the realisation of a right cardiac catheterisation, an invasive examination. The pertinence of this exam can be discussed if it does not lead to the initiation of a dedicated therapy. Selection of elderly patients, in whom a classical work-up is mandatory, is challenging. In this population, there is a balance between futility (because most suspected PH is assumed to be post-capillary PH, with no need for introduction of specific therapy), and loss of chance (some patients may have pre-capillary PH that can be effectively improved by dedicated therapy).

The Comprehensive Geriatric Assessment (CGA) is a multidimensional diagnostic process and an interdisciplinary approach to the frail elderly subject. It provides a complete assessment of medical issues, as psychosocial and functional capacities for each patient.

Its development has deeply proven track in elderly patients with cancer, where it is important to differentiate between what results from the determinants of fragility and/or comorbidities and what results from cancer pathology. In cancer, CGA provides a better approach to physiological age and comorbidities [13]. Moreover, knowledge of side effects of specific treatments (chemotherapy, radiotherapy) can be used to estimate a patient's ability to tolerate them, as well as the impact on his quality of life.

For this frail population with a PH and other comorbidities, no specific guidelines about how identify and manage them is available. An invasive test must not be automatic (compared with younger patients), particularly because they have a systemic and pulmonary vasculature less responsive to vasodilation [14]. So, it is unlikely to give them a profit with a PAH treatment [15]. It is first necessary to understand their life expectancy and their quality of life, because expectations of each patient for any therapy should always be considered and a case-by-case assessment is recommended.

Based on this point of view, we decided to evaluate the impacts of a systematic CGA in consecutive patients of 70 years of age and older referred for suspected pulmonary hypertension.

2. Materials and methods

This study was monocentric, prospective and descriptive, carried out in the Pulmonary Hypertension Centre of Saint-Étienne University Hospital, between July 2014 and May 2019.

All consecutive patients over 70 years of age, referred for suspected PH, were seen in consultation or hospitalisation before considering invasive tests for a diagnosis of PH. At the time of this consultation, the evaluating physician had a complete clinical examination (including an assessment of dyspnea according to the NYHA functional class modified by WHO), history and available paraclinical data (transthoracic echocardiogram).

The comprehensive geriatric evaluation was standardised, carried out by a specialized doctor during a dedicated consultation. The assessment was made using the following scales: Katz ADL autonomy scale, Lawten IADL scale, Mini MNA (Mini Nutritional Assessment), monopod support, walking speed, mini GDS (Geriatric Depression Scale), MMS (Mini Mental State), 5-word test, amongst others. The CGA also included an analysis of comorbidities, socio-economic data (lifestyle, environment, and resources) and capacities to adapt to possible specific therapies. These scales are presented in the Appendix.

The complete evaluation was notified to the referring doctor, including the conclusion of the CGA (positive evaluation, negative evaluation).

In the case of a positive evaluation, the patient pursued the recommended diagnostic work-up with an initial assessment in hospitalisation: right cardiac catheterisation (including a fluid challenge in patients with pulmonary hypertension and wedge pressure superior between 12 and 16 mmHg), 6 min walking test, pulmonary function tests, blood gas analysis, and thoracic iconography (V/Q lung scan, thoracic CT). Additional advice from the national PH centre was taken any time it was required. Adaptation of therapies was made during the initial hospitalisation.

The management of patients with confirmed pre-capillary PH was realised in accordance with the international recommendations [1].

In case of a negative CGA evaluation, no more tests were realised, and symptomatic treatments were proposed.

3. Results

3.1. Population

From July 2014 to May 2019, 31 elderly patients were referred for a suspicion of PH. The median age was 81 [72–91] years. Twenty (64,5%) of these patients had a comprehensive geriatric evaluation favourable to further investigations, one of them refused to continue the examinations. Thus, 19 patients (61,3%) received additional examinations for diagnosis and 11 (35,5%) were rejected on the basis of the geriatric assessment.

In the patients with a CGA favourable to further investigations, all patients were still alive 12 months after the PH suspicion. Regarding the 11 patients not evaluated after CGA, 1 died at 6 months, and the remaining 10 were alive at 12 months.

The population is described in Table 1.

3.2. Clinical profile of PH

Of the 19 patients with complementary assessment for suspected PH, more than two-thirds were female, and the median

Table 1
Population.

	Patients evaluated after CGA $n = 19$	Patients not evaluated after CGA $n = 11$	Total population $n = 31$[a]
Age (in years) [median (Boundaries)]	81 [72–91]	82 [74–90]	81 [72–91]
Female sex	14 (73,7%)	6 (54,5%)	20 (64,5%)
Polymedication	10 (52,6%)	9 (81,8%)	19 (61,3%)
Anticoagulant treatment	13 (68,4%)	7 (63,6%)	21 (67,7%)
Isolation	2 (10,5%)	7 (63,6%)	9 (29%)
Performans status			
PS0	3 (15,8%)	0 (0%)	4 (12,9%)
PS1	9 (47,4%)	4 (36,4%)	13 (41,9%)
PS2	5 (26,3%)	2 (18,2%)	7 (22,5%)
PS3	2 (10,5%)	3 (27,3%)	5 (16,1%)
PS4	0 (0%)	2 (18,2%)	2 (6,4%)
Institutionalisation	0 (0%)	3 (27,3%)	3 (9,6%)
Risk factor for PH			
Group 1	6 (31,6%)	2 (18,2%)	9 (29%)
Group 2	4 (21,1%)	7 (63,6%)	11 (35,5%)
Group 3	6 (31,6%)	5 (45,5%)	11 (35,5%)
Group 4	11 (57,9%)	1 (9,1%)	13 (41,9%)
NYHA Functional class		($n = 8$)	($n = 28$)
I/II	5 (26,3%)	2 (25%)	8 (28,6%)
III	14 (73,7%)	2 (25%)	16 (57,1%)
IV	0 (0%)	4 (50%)	4 (14,3%)
sPAP/TTE (mmHg) [median (Boundaries)]	60 [43–100]	67,5 [45–90] ($n = 10$)	62,5 [43–100] ($n = 30$)
Sensory disorders			
Visual	3 (15,8%)	2 (18,2%)	5 (16,1%)
Auditive	3 (15,8%)	3 (27,3%)	7 (22,6%)
Functional evaluation [median (Boundaries)]	6 [5,6]	5 [1–6]	6 [1–6]
ADL/6	4 [2–4]	2 [0–4]	3 [0–4]
IADL/4			
Nutrition [median (Boundaries)]	14[6–14] ($n = 15$)	10 [9–11] ($n = 2$)	14 [6–14] ($n = 18$)
Mini MNA/14	26,8 [16,5–43] ($n = 17$)	25,7 [20,6–49] ($n = 7$)	26,7 [16,5–49] ($n = 25$)
BMI kg/m^2	35 [29,1–43] ($n = 14$)	36,5 [36,37] ($n = 2$)	35,5 [29,1–43,0] ($n = 16$)
Albumin g/L			
Cognition (median [Boundaries])	29 [26–29] ($n = 18$)	25 [13–29] ($n = 7$)	28 [13–29] ($n = 27$)
MMS/30	10 [9,10] ($n = 18$)	9 [9,10] ($n = 4$)	10 [9,10] ($n = 23$)
5 words/10			
Mini GDS/4 (median [Boundaries])	0 [0–3] ($n = 17$)	1 [0–4] ($n = 7$)	0 [0–4] ($n = 25$)
Sleeping disorder	11 (68,8%) ($n = 16$)	3 (42,9%) ($n = 7$)	15 (62,5%) ($n = 24$)
Risk of falling			
Fall history < 1 year	4 (21,1%)	1 (11,1%) ($n = 9$)	5 (17,2%) ($n = 29$)
Positive orthostatic	6 (35,3%) ($n = 17$)	2 (40%) ($n = 5$)	9 (39,1%) ($n = 23$)
hypotension test	6 (26,7%) ($n = 15$)	2 (66,7%) ($n = 3$)	8 (42,1%) ($n = 19$)
Monopodal support < 5sec	4 (26,7%) ($n = 15$)	1 (25%) ($n = 4$)	5 (25%) ($n = 20$)
Walking test < 1 m/sec			
Survival rate			
At 6 months	19 (100%)	10 (90,9%) ($n = 11$)	29 (96,7%) ($n = 30$)
At 1 year	19 (100%)	10 (90,9%) ($n = 11$)	29 (96,7%) ($n = 30$)

[a] One patient refused explorations despite a favourable CGA

age was 81 [72–91]. For 3 patients (15,8%) the diagnosis of PH was refuted by a right cardiac catheterisation.

Of the 16 patients with confirmed PH (Table 2), eight had chronic thromboembolic pulmonary hypertension, three PAH (pre-capillary pulmonary hypertension with both negative fluid challenge and etiological assessment), two group 2 PH (PH due to heart failure with preserved LVEF) and three had group 3 PH (2 restrictive and 1 obstructive lung diseases). Two patients combined a group 1 (1 anorexigenic intake and 1 scleroderma) and group 4 PH. The NYHA functional class was between II and III for all patients. The median cardiac index was 1,75 L/min/m^2 [1,3,3], the PAPm (median) was 36 mmHg [25–47], the right atrium pressure (median) was 9,5 mmHg [2–16], and the 6-minute walk test (median) was 264 meters [104–444]. The median PaO_2 was 58,5 mmHg in room air [44–93].

3.3. Additional treatment

Specific treatment of PH has been initiated for 13 of the 16 patients. 3 patients did not receive specific treatment. Three patients in group 1 received a phosphodiesterase 5 inhibitor and 1 of them received an endothelin receptor inhibitor in addition.

In group 2 PH, 1 patient has benefited from an improvement in his diuretic treatment.

One patient in group 3 benefited from the introduction of non-invasive ventilation in the context of advanced Obstructive Sleep Apnea Syndrome.

Finally, all patients with group 4 PH were eligible for specific invasive treatment (pulmonary endarterectomy or balloon pulmonary angioplasty). Two of them refused invasive treatment and stayed on with drug treatment. For the two patients with mixed

Table 2
PH diagnosis and treatment.

	Total PH $n=16$	PH group 1 $n=3$	PH group 2 $n=2$	PH group 3 $n=3$	PH group 4 $n=8$
Age [median (Boundaries)]	81 [72–91]	81 [72–82]	78 [78]	76 [76–85]	82,5 [77–91]
Female sex	12 (75%)	1 (33,3%)	2 (100%)	3 (100%)	6 (75%)
NYHA [median (Boundaries)]	3 [2,3]	3 [2,3]	3 [3]	3 [2,3]	3 [2,3]
sPAP/TTE [median (Boundaries)]	70 [43–100]	80 [70–83]	65 [60–70]	50 [48–75]	65 [43–100]
Risk factor Group 1 Group 2 Group 3 Group 4					
	6 (37,5%)	1 (33,3%)	1 (50%)	2 (66,7%)	2 (25%)
	3 (18,8%)	2 (66,7%)	1 (50%)	0	0
	6 (37,5%)	2 (66,7%)	0	3 (100%)	1 (12,5%)
	10 (62,5%)	0	1 (50%)	1 (33,3%)	8 (100%)
Walking test/6 min [median (Boundaries)]	264 [104–444]	272 [143–341]	263 [224–302]	224 [200–282]	288 [104–444]
mPAP/mmHg [median (Boundaries)]	36 [25–47]	42 [40–47]	33,5 [31–36]	32 [25–51]	35,5 [28–46]
Cardiac index/L/mn (median [Boundaries])	1,75 [1,3,3]	1,7 [1,7]	2 [1.9-2.1]	3,1 [2,4–3,3]	1,55 [1,3–1,9]
Right atrium pressure/mmHg [median (Boundaries)]	9,5 [2–16]	10 [6–16]	9,5 [9,10]	9 [2–11]	8 [3–16]
PaO_2/mmHg [median (Boundaries)]	58,5 [44–93]	46 [44–51]	84 [75–93]	52 [46–61]	61 [4,56]
Introduction of specific treatment after evaluation		1 sildenafil 1 tadalafil 1 silde- nafil + ambrisentan	1 diuretics	1 non-invasive ventilation	1 surgery 2 balloon pulmonary angioplasty 5 riociguat

group 1 and group 4 PH, both were treated as group 4 PH, one by balloon pulmonary angioplasty twice and the other with riociguat.

All the information concerning diagnosis and treatment are summarised in Table 2.

4. Discussion

In our monocentre prospective study, the implementation of a dedicated Comprehensive Geriatric Assessment in elderly patients referred for a suspicion of PH leads to stop the investigation in one third of the patients. In the remaining patients, pre-capillary PH was confirmed in most of them, with CTEPH representing half of the patients.

CGA was initially developed in oncology and is an integral part of international recommendations [16]. By specifying what is related to the clinical manifestations of fragility by what is related to cancer pathology, CGA predicts treatment tolerance, hospitalisation times, dependence and survival [17–19]; an approach which is increasingly validated for areas other than cancer, such as post-hip fractures [20]. A literature review of 10 recent studies found a change in initial oncologic treatment after a CGA for 39% of patients [21], and 2/3 of patients had a less intensive treatment. Our results suggest that implementation of a systematic CGA in patients admitted for PH suspicion was possible, and had a similar impact in the field of PH than in oncology, since 35% of patients did not have a favourable CGA, and therefore did not have additional investigations. One has to remember that right heart catheterisation is an invasive procedure, exposing the patients to the risk of complications as haematoma at puncture sites, pneumothoraces, arrhythmias, vasovagal episodes, hypotensive episodes, and pulmonary haemorrhage [22]. If these risks are acceptable in a patient with a high likelihood of PAH, it is most debatable in elderly patients with a lower likelihood.

Our suspected PH patients with more often functionally dependent (ADL and low IADL and high ECOG Performans Status), more isolated, having more polydrug therapy and having a lower BMI were not examined. Interestingly, all these factors (including patient functional status [ADL], undernutrition [17], and number of comorbidities [23]) are statistically significant to modify oncology treatment in patients with cancer; results which supported our investigation well.

Currently, two major cohorts are underway in oncogeriatric to clarify how the CGA affects the initiation of specific treatment. The GERICO cohort [24] evaluates the benefit of the CGA in terms of chemotherapy, morbidity and mortality versus conventional treatment in colorectal cancer in the elderly; and the EGeSOR cohort [25] evaluates the impact of a CGA in survival, functional status and nutrition for elderly patients with head and neck cancer. To our knowledge, there are no ongoing studies in the field of PH. Moreover, some concerns have been raised about a potential under-screening of PH after pulmonary embolism in patients with cancer [26].

Concerning our PH older patients detected, the etiologies of the PH found were mainly from group 4, which is inconsistent because the main causes of PH after 65 years are rather from group 2, group 3 or mixed [11]. This can be explained by the selection of patients and the monocentric nature of the study.

However, in another French monocentre cohort, nearly a quarter of patients with 75 years and more had a CTEPH [27]. The increasing risk of pulmonary embolism with age [28] may explain these results. Larger multicentre cohorts are needed.

The only curable cause of PH was that of group 4, thanks to a surgical procedure: pulmonary endarterectomy. According to the European CTEPH register, survival at 3 years was better for operated patients than for non-operated patients (89% versus 70%) [29]. This management improved survival, but also functional abilities and dyspnea [30]. Most sick patients in our study were therefore eligible for curable treatment. However, among these patients, two refused invasive management, but all were able to receive specific treatment, which is known to improve exercise capacity and reduce dyspnea, despite few elderly patients being included [31].

Our inclusive population had severe PHs. Regarding functional impact: the average walking distance for 6 minutes was 250 m, all patients were with a function class III according to the NYHA functional class and the average cardiac index was less than 2 L/min/m^2. These investigations were useful because they allowed the initiation of a specific treatment, offered to 13 out of 16 patients. The main outcome of most targeted therapies is the functional improvement (increase in 6-minute walk distance) on elderly patients, while the effect on survival may be more debatable than in younger population.

Finally, PH group 1 in our study was as frequent as PH group 2 or 3, which is inconsistent with data from other studies [11]. This may be explained by the under-representation of group 2 and group 3 PAHs in our series, probably due to a recruitment bias.

Nevertheless, our work has many limits. This monocentric study is representative of patients referred to the unit, such as its endogenous recruitment. However, the patients referred in the PH centre came from several diverse situations, in a metropolitan area of 1 million of inhabitants. Our department is also specialised in

thromboembolic venous disease, so a recruitment bias is possible: half of the patients were carriers of chronic thromboembolic pulmonary hypertension. Nevertheless, the prospective nature of the collection has limited the number of lost views and follow-up is still ongoing.

CGA could not be multidisciplinary. Due to the limited resources of the unit, we could not have a dedicated physiotherapist, occupational therapist or neuropsychologist time. The assessment was based on subjective statements; no assessment of the patient in his or her environment was possible. The caregivers' appreciation was collected if possible, but not systematically. The collection was standardised for all patients, which limited the missing information.

PH has a significant impact on patient autonomy through the dyspnea it causes. The functional capacity assessment may have been biased by this confounding factor. The assessment was as exhaustive as possible, also based on other functional reserves, such as mental reserves, and integrating, if possible, the assessment of those around them. However, it should be noted that the distance covered by the walking test (in patients with a positive opinion) was low, objectifying the handicap felt by the patients.

5. Conclusion

Our study suggests that the implementation of CGA in patients admitted for a PH suspicion is feasible and may lead to stop the investigation in one third of the patients. Most of the remaining patients had PH, with CTEPH being the main cause of PH. Further research are needed to assess the efficacy on such implementations in the clinical practice, as the evolution of patients is according to CGA conclusion.

Disclosure of interest

The authors declare that they have no competing interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.resmer.2020.100785.

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