



## EDITOR'S PAGE

# Pulmonary arterial hypertension and quality of life in cardiology. Do we really need more studies?



Cardiovascular medicine has significantly evolved over the past three decades, as reflected by the decreasing incidence of morbidity and mortality from myocardial infarctions and in the successful identification and modification of a series of cardiovascular risk factors.<sup>1–5</sup>

Significant accomplishments have also been achieved in understanding the diagnosis and treatment of pulmonary hypertension, especially pulmonary arterial hypertension, with the introduction of medicines in the clinical practice capable of modifying symptoms and the physical history of the disease.<sup>6,7</sup> These achievements have oriented research toward the improvement of the patient's status and quality of life. To this end, several studies have identified supervised exercise rehabilitation as capable of increasing functional capacity and quality of life.<sup>8,9</sup> However, these studies are based on small sample sizes, and we are unaware of the specific rehabilitation practices that may achieve the most significant and valuable improvements. Interestingly, in this issue of Hellenic J Cardiol, Laoutaris ID et al.<sup>10</sup> present the results of supervised inspiratory muscle training in the functional status and life quality of patients with pulmonary hypertension. According to this pilot study, high-intensity inspiratory muscle training may improve dyspnea, exercise capacity and quality of life, emphasizing the need for a holistic approach to managing this high-risk group of patients.

However, pulmonary arterial hypertension, especially in adults with congenital heart disease, remains relatively rare and is difficult for inexperienced physicians to manage (Table 1). These issues are elucidated by Giannakoulas G and Gatzoulis MA in the recent issue of Hell J Cardiol (9). These researchers propose the question of "whether the patients must be treated according to established guidelines or with more aggressive protocols by specialized

physicians in tertiary centers".<sup>11</sup> Finally, the authors note the need to further research this group of patients, especially patients with Eisenmenger syndrome, in tertiary centers in collaboration with pulmonary arterial hypertension and adult congenital heart disease specialists.

Another interesting topic discussed in this issue of Hellenic J of Cardiol is the Health Related Quality of Life in patients with coronary artery disease after coronary revascularization. Several studies have agreed on the superiority of revascularization over medicine treatment alone, especially in symptom relief, but also in survival.<sup>12,13</sup> Moreover, a series of scores have been introduced to select patients appropriate for coronary artery stenting or coronary artery by-pass grafting.<sup>14,15</sup> Nevertheless, the issue of Health Related Quality of Life after coronary artery stenting or coronary artery by-pass grafting has not been extensively addressed. Takousi M et al. have analyzed data from 34 publications involving 15,992 patients undergoing either type of revascularization to conclusively address this topic. Interestingly these researchers found that both types of revascularization may improve patient Health Related Quality of Life, an issue that may be of importance when patients are informed to decide whether to comply with medical management or to choose a revascularization procedure.<sup>16</sup> Taken together, these findings suggest that both the treatment of pulmonary arterial hypertension and the improvement in quality of the life after a cardiovascular event remain unresolved issues and further studies are needed.

Two interesting studies from the region of Crete further extend our knowledge concerning the quality of treatment in the management of patients with arrhythmias. Implantable cardioverter defibrillators (ICDs) have been established as the gold standard treatment for the management of patients with ventricular tachycardia.<sup>17</sup> However, patients with ICDs followed up for a long-term period present a significant number of complications. Therefore, real world data regarding the identification of patients most suitable for ICD therapy is of importance. According to this long term

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**Table 1** Main drugs used in the treatment of Pulmonary arterial hypertension.

Endothelin receptor antagonists	
Bosentan	Administration PO. The first molecule of its class. Dual endothelin receptor type A and B antagonist In patients at WHO-FC II, III or IV
Ambrisertan	Administration PO. Selective antagonists of endothelin receptor type A. In patients at WHO-FC II, III or IV
Macitentan	Administration PO. Newer Dual endothelin receptor type A and B antagonist with fewer side effects In patients at WHO-FC II, III or IV
Phosphodiesterase type 5 inhibitors (enhance the NO—cGMP pathway, slowing cGMP degradation)	
Sildenafil	Administration PO. t.i.d The first molecule of its class In patients at WHO-FC II, III or IV
Tadalafil	Administration PO. Once daily In patients at WHO-FC II, III or IV
Vardenafil	Administration PO. b.i.d In patients at WHO-FC II, III or IV
Guanylate cyclase stimulators (enhance cGMP production)	
Riociguat	Administration PO t.i.d The only molecule of its category It cannot be combined with Phosphodiesterase type 5 inhibitors In patients at WHO-FC II, III or IV
Prostacyclin analogues	
Epoprostenol	Administration IV. Short half-life (3–5 min) it requires cooling and continuous administration In patients at WHO-FC III or IV
Iloprost	Administration inhaled 6–8 times per day In patients at WHO-FC III or IV
Treprostinil	Administration mainly SC or IV In patients at WHO-FC III or IV
Beraprost	Administration PO Novel agent In patients at WHO-FC III
Prostacyclin receptor agonists	
Selexipag	Administration PO Novel agent In patients at WHO-FC III

registry<sup>18</sup> (21 years) the frequency of complications is relatively low (approximately 15%), while appropriate ICD therapies were more frequent in patients selected for secondary prevention. In addition, the time for the first appropriate therapy was longer in patients selected for primary prevention highlighting the need to extend the follow up period to make conclusions about the absolute beneficial effect of ICD therapy. Concerning atrial arrhythmias there is consistent data from the past several years that new oral

anticoagulants (NOAC) have a safer profile in patients with non-valvular atrial fibrillation.<sup>19–21</sup> However, as Papakonstantinou et al. observed,<sup>22</sup> based on data from the emergency department of a health center in southern Greece, the implementation of NOACs is low, despite evidence from the Danish registry showing a decline in the initiation of warfarin among oral anticoagulation-naïve atrial fibrillation patients.<sup>23</sup> Possible reasons for these inconsistencies may be the unwillingness of patients on previously established vitamin K antagonist therapies to convert to newer treatments, as well as the cost of NOACs.

Concerning coronary artery disease (CAD) management and interventional procedures significant data are discussed in the review article of Hahalis G et al.<sup>24</sup> Although the radial artery approach has been established as preferential over the femoral arterial access site in many centers,<sup>25</sup> especially due to the lower rates of complications and patient preferences, the ulnar artery is most often considered in cases in which the radial artery approach is unsuccessful. However, as the authors emphasize once arterial access is obtained the likelihood of a successful coronary procedure is similar between the two forearm arteries. Accordingly, based on a review of the literature the authors conclude on the need for radial operators to extend their skills and to adopt ulnar artery access as a reasonable alternative in patients with unfavorable femoral and radial artery characteristics. Despite the significant improvements in interventional procedures, concerns remain regarding the prevalence of high platelet reactivity due to aspirin and clopidogrel resistance. Nevertheless, based on previous reports and on data presented in this issue from Dušan AD et al. there is no straight-forward association between high platelet reactivity and cardiovascular events.<sup>26–28</sup> Moreover, cardiometabolic risk profile has been identified as a factor associated with high platelet reactivity that may shed light on previous reports between the association of platelet reactivity and arterial wall properties.<sup>29</sup>

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