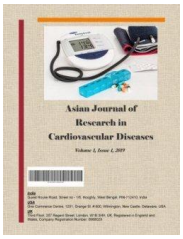

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# Features of Congestive Heart Failure in Moroccan Elderly Patients

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***Authors' contributions***

*This work was carried out in collaboration among all authors. Author HM designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript, managed the analyses of the study, managed the literature searches. Author MH helped designing the study and managing the analyses of the study. All authors read and approved the final manuscript.*

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## ABSTRACT

**Introduction:** Congestive heart failure (CHF) is associated with aging-related diseases. CHF in African elderly is a severe and frequent condition, responsible for a high mortality and hospitalization rate. However very few studies report particularities of CHF in this population. This study aims to characterize clinical and therapeutic features of CHF in the elderly in the region of Casablanca Morocco.
**Methods:** It's a transversal retrospective study conducted over 13 years, [May 2006- June 2019] covering all CHF patients beyond 14 years old, followed-up in the HF therapeutic unit of the cardiology department of Casablanca University hospital. We studied features of CHF among elderly patients (>= 65 years) compared with younger patients.
**Results:** Among 3412 patients, elderly patients accounted for 1701 (49.8%) with male predominance (62.5 %). 26,7% were smokers, 44.9% hypertensive, 31,6% diabetic, and 9,8% had dyslipidemia. In elderly vs youngsters: Ischemic-heart-disease was the most common etiology 59,9%vs57,4%, followed by non-ischemic-dilated-cardiomyopathy 9,4%vs1,2% and valvular heart disease 2.9%vs4,5%, *P*<0,001. Dyspnea stage III-IV was found in 25.5%vs7.2%, *P* <0,001. Elderly

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patients presented more clinical signs of HF, more atrial fibrillation, more cerebral stroke and were more likely to present chronic kidney disease. Mean LVEF was 36,18+10,34% vs 36+-9,88%, *P*:0,649. Critical elevation Doppler-filling-pressures was found in 22,5%vs18,3%, *P*:0,003. Therapeutically, ACE has been used in 78,50%, AT-II-receptor-antagonists in 7,47%, Beta-blockers in 80,32%, Furosémide in 46,64%, Spirinolactone in 58.2% and Ivabradine in 3,82%. The re- hospitalization rate in elderly patients was 53,5% vs 43,2%, *P* <0,001.

**Conclusion:** CHF is a major public health problem in Morocco and AFRICA in general. It's a major cause of death and re-hospitalization among elderly patients. Therefore, health strategies need to be accustomed and adjusted to the elderly patients in order to implant an optimal and appropriate therapeutic treatments.

*Keywords: Elderly; heart failure with reduced ejection fraction; NYHA functional class; hospitalization for heart failure; mortality.*

## 1. INTRODUCTION

Congestive heart failure (CHF) is a clinical syndrome caused by systolic or diastolic ventricular dysfunction. Despite the improvement in HF therapy in recent decades and the decrease in morbidity and mortality caused by cardiovascular disease, the prevalence of heart failure (HF) is still increasing because of the rising burden of cardiovascular risk factors [1,2].

Congestive heart failure (CHF) is associated with aging-related diseases and thus affects predominantly older patients. The incidence of HF doubles in the general population for each decade after the age of 40 years [3]. Aging causes a deconditioning of the skeletal muscles and a decrease in capillary density and coronary reserve responsible for a progressive loss of myocytes and hypertrophy of the remaining myocytes, as well as progressive decrease in maximal cardiac output, maximal heart rate and maximal VO2 [4,5]. "It is also responsible for increasing systemic vascular resistance along with blood pressure [4]. We observe significant changes in LV structure with aging, the LV stiffness is increased as a result of increased interstitial fibrosis, LV compliance is decreased, LV wall thickness is increased, early LV diastolic filling is decreased with a greater contribution to LV filling resulting from left atrial systole, and LV relaxation is impaired" [4,6]. "Approximately 80% of patients hospitalized with HF are older than 65 years" [7]. CHF in elderly is a quite frequent and severe condition worldwide, responsible for a high mortality and hospitalization rate as well as high cost. Yet few African data available take into account the specific profile of CHF in this population.

Among HF phenotypes, heart failure with reduced ejection fraction (HFrEF) patients have the worst outcomes and are challenging to manage. The difficulty of management is even greater in older patients, who often have co-existing multi-morbid illness, polypharmacy, cognitive impairment, and frailty, which may contribute to poor prognosis [8]. "Despite the important progress in HF management during recent years, elderly patients with HF are rarely included in randomized controlled trials, which explain scarce data about outcomes in elderly patients" [9].

More insights into particularities of HFrEF in elderly patients may aid to our knowledge about this complex disease and may eventually lead to better management in this age group of patients in order to improve outcomes.

This study aims to report features of HFrEF in the elderly compared to younger patients in a specialized cardiac facility in Casablanca, Morocco.

## *2.* MATERIALS AND METHODS

### 2.1 Study Population

We have conducted a transversal retrospective study over 14 years [May 2006 and June 2020] including patients with HFrEF beyond 14 years old, followed-up in the HF therapeutic unit of the cardiology department of IBN Rochd University hospital in Casablanca, Morocco.

HFrEF is defined as a left ventricular ejection fraction (LVEF) ≤40% according to 2021 Europen Society of Cardiology guidelines.

We excluded patients with insufficient echocardiography or examination data.

The echocardiography examination at discharge was kept when the initial cause of admission was

acute HF. This database was crossed with hospitalization records, clinical, echocardiographic and data were collected in order to study HF features in elderly patients with HFrEF compared to younger patients.

## 2.2 Follow Up

Follow-up was censored on 1st June 2020, and consisted of a retrieval of last consultation data and verification of hospitalization and mortality registers. For all patients, we recorded data on the occurrence of death and hospitalization for HF.

## 2.3 Echocardiographic Assessment

"Transthoracic echocardiograms were recorded on various generations of Vivid systems. Measurements were made according to guidelines" [10,11]. Simpson's approach was used to calculate the LV ejection fraction (LVEF). Mitral-pulsed Doppler inflow and tissue-Doppler imaging at the lateral mitral annulus were used to assess diastolic function. Left atrial area was measured from the apical four-chamber view.

## 2.4 Statistical Analysis

The data was gathered in Excel and analysed with the SPSS 2.0 software. All continuous variables are represented by means and standard deviations, whereas categorical variables are represented by frequencies. Patients were divided into two groups according to their age, group 1 included elderly patient (≥65years old) and group 2 included younger patients (<65ans). Comparisons of the occurrence of HF hospitalization or death according to the age group were realized with Student's t test for continuous variables and the Chi2 test for discrete variables. Differences were considered statistically significant when $P < 0.05$.

## 3. RESULTS

Among 3412 patients, 1710 (49.8%) were elderly patients (Group 1) and 1702 (50.2%) were young (Group 2). 62.6% of patients in group 1 were male versus 64.9% of patients in group 2 ($P$ =0.169).

Regarding cardiovascular risk factors: hypertension was represented in 44.9% versus 32.8% ($P$ <0.001), diabetes mellitus in 31.6% vs 29.2% ($P$ =0.127), dyslipidemia in 9.7% vs 10.1% ($P$ <0.514), tobacco use 26.7% vs 37.2% ($P$ <0.001).

Regarding etiologies of HFrEF: ischemic heart disease (IHD) was represented in 59.9% versus 57.4%, dilated cardiomyopathy (DCM) in 9.4% versus 11.2%, valvar hear disease (VHD) in 2.9% versus 4.5%, chemotherapy induced cardiomyopathy in 1.1% versus 2.5%, tachycardiomyopathy in 0.4% versus 0.2% ($P$ =0.001). Finding related to demographics, cardiovascular disease risk factors, comorbidities and etiologies of HF are represented in Table 1.

**Table 1. Demographics, cardiovascular disease risk factors, comorbidities and etiologies of heart failure**

| | **Group 1 (n=1710)** | **Group 2 (n=1702)** | ***P* value** |
|---|---|---|---|
| **Male Gender** | 62.5 % | 64.9% | 0.169 |
| **Age (Mean**±SD) [min;max] | 75.11±6.7 [65;104] | 54,65±8.69 [15;64] | <0.001 |
| **Male** | 75.22±6.82 [65;104] | 54.85±8.493 [14;64] | |
| **Female** | 74.92±6.49 [65;103] | 54.28±9.05 [15;64] | |
| **History of hypertension** | 44.9% | 32.8% | <0.001 |
| **History of diabetes mellitus** | 31.6% | 29.2% | 0.123 |
| **Dyslipidemia** | 9.7% | 10.1% | 0.514 |
| **Smoking** | 26.7% | 37.2% | <0.001 |
| **Etiologies of HF:** | | | |
| IHD | 59.2% | 57.4% | <0.001 |
| DCM | 9.4% | 11.2% | |
| VHD | 2.9% | 4.5% | |
| Chemotherapy induced cardiomyopathy | 1.1% | 2.5% | |
| Tachycardiomyopathy | 0.4% | 0.2% | |

*(HF: Heart Failure, IHD: Ischemic Heart Disease, DCM: Dilated Cardiomyopathy, VHD: Valvar Heart Disease)*

Regarding comorbidities and clinical status: Cerebral stroke occurred in 12.8% in Group 1versus 7.4% in Group 2 (*P* <0.001). Chronic kidney disease was observed in 14.4% versus 11.3% (*P* =0.008). Patients were classified according to NYHA class I in 15.2% in group 1 vs 25.6% in group 2, class II in 59.3% vs 57.2%, class III in 23.4% vs 15.4%, class IV in 2.1% vs 1.8% (*P* <0.001). we have observed left HF signs in 10.5% vs 7.8% (*P* =0.009) and right HF signs in 7.4% vs 5.6% (*P* =0.055). Therefore, elderly patients were more symptomatic. There was no statistical difference between the two groups concerning heart rate (HR). Group 1 patients presented a higher systolic and diastolic blood pressure, mean systolic blood pressure was 132.07±24.17 versus 128.12±21.02 mmHg (*P* <0.001) and diastolic blood pressure was 73.96±13.19 versus 71.18±11.40 (*P* =0.013). Results also showed more atrial fibrillation in elderly patients compared to Group 2 (13.3% vs 9.6%, *P* <0.001). Clinical and electrical data are reported in Table 2.

Echocardiographic data have shown that left ventricular (LV) function was similar in both groups, mean LVEF was 36.18±10.34% vs 36±9.88% (*P* =0.649). Elderly patients were more likely to have high LV filling pressure in 22.5% vs 18.3% (*P* =0.003). Transthoracic echocardiography data are reported in Table 3.

Regarding pharmacotherapy prescription: Betablockers were prescribed in 85.9% vs 88% (*P* <0.001), Ivabradine was prescribed in 3.8% vs 7% (*P* <0.001), loop diuretics were prescribed in 46.6% vs 43.6% (*P* <0.001), Spirinolactone was prescribed in 58.1% vs 55.2% (*P* <0.001), ACE-I were prescribed in 83.3% vs 76.9% (*P* <0.001), ARB were prescribed in 16.7% vs 19.4% (*P* <0.001). Pharmacotherapy prescription data are represented in Table 4.

Regarding HF hospitalization: The hospitalization rate for decompensated HF was 53.5% for Group 1 vs 43.2% for group 2 (*P* <0.001). Hospitalization rates are reported in Table 5.

**Table 2. Clinical and electrical data**

| | Group 1 (n=1710) | Group 2 (n=1702) | *P* value |
|---|---|---|---|
| **NYHA** | | | |
| Class I | 15.2% | 25.6% | <0.001 |
| Class II | 59.3% | 57.2% | |
| Class III | 23.4% | 15.4% | |
| Class IV | 2.1% | 1.8% | |
| **Signs of left HF** | 10.5% | 7.8% | 0.009 |
| **Signs of right HF** | 7.4% | 5.6% | 0.055 |
| **Mean HR** | 76.61±15.96 bpm | 78.45±14.82 bpm | 0.067 |
| **Mean SBP** | 132.07±24.17mmHg | 128.12±21.02mmHg | <0.001 |
| **Mean DBP** | 73.96±13.19 mmHg | 71.18±11.40mmHg | 0.013 |
| **Persistent atrial fibrillation** | 13.3% | 9.6% | <0.001 |

*(NYHA: New York Heart association classification of Dyspnea; HR: Heart Rate ; SBP: Systolic blood pressure ; DBP: Diastolic blood pressure)*

**Table 3. Transthoracic echocardiography data**

| | Group 1 (n=1710) | Group 2 (n=1702) | *P* value |
|---|---|---|---|
| **Mean LVEF** | 36.18±10.34% | 36±9.88% | 0.649 |
| **Elevated LVFP** | 22.5% | 18.3% | 0.003 |

*(LVEF: Left Ventricle Ejection Fraction, LVFP: Left Ventricle Filling Pressures)*

**Table 4. Heart failure medical therapy**

| | Group 1 (n=1710) | Group 2 (n=1702) | *P* value |
|---|---|---|---|
| **Beta-blockers** | 85.9% | 88% | <0.001 |
| **Ivabradine** | 3.8% | 7% | <0.001 |
| **Loop diuretics** | 46.6% | 43.6% | <0.001 |
| **Spironolactone** | 58.1% | 55.2% | <0.001 |
| **ACE-I** | 83.2% | 76.9% | <0.001 |
| **ARB** | 16.7% | 19.4% | <0.001 |

*(ACE-I: Angiotensin Converting Enzyme Inhibitors, ARB: angiotensin II receptor blockers)*

**Table 5. HF hospitalization rates**

| | Group 1 (n=1710) | Group 2 (n=1702) | *P* value |
|---|---|---|---|
| HF Hospitalization | 53.5% | 43.2% | <0.001 |

*(HF: heart failure)*

## 4. DISCUSSION

### 4.1 Heart Failure Features in Elderly Patients

The incidence of HF doubles in the general population for each decade after the age of 40 years [3]. Aging causes an impairment of LV compliance and LV relaxation with an increase of systemic vascular resistance and a progressive loss of myocytes [4-6]. Therefore, the incidence of diastolic dysfunction increases with aging as well an as increase of the incidence of atrial fibrillation (AF) [12,13]. In our study the prevalence of AF in elderly patients was 13.3% versus 9.6% in younger patients (P <0.001). AF is responsible for atrial systole loss, causing a reduction in LV diastolic filling and leading to pulmonary and systemic venous congestion and cardiac output decrease. In addition AF can be responsible for thromboembolic complications, in our study, the occurrence of ischemic stroke concerned 12.8% of group 1 and 7.4% of group 2 (P <0.001). AF can also lead in the long term to the development of tachcardiomyopathy.

With aging, the body doesn't handle the medicine in the same way. It metabolizes medicines differently, therefore taking too many medications can be a problem for older patients with heart failure [14].The elderly patients also show an increase in the occurrence of chronic kidney disease resulting from nephron loss secondary to aging as well as the chronic effects of arterial hypertension and diabetes mellitus. In our study chronic kidney disease concerned 14.4% of elderly patients and 11.3% of younger patients (*P* =0.008). This makes the elderly population fragile and candidate for close monitoring when introducing HF therapies. Medication doses must be adjusted according to renal filtration capacity, monitoring of medication effect on renal function must be rigorous and some medications may be contraindicated in advanced renal failure.

Congestive heart failure (CHF) is associated with comorbidities caused by aging. Elderly patients are more likely to present hypertension and coronary artery disease (CAD) which are the principles causes of HF in this age group of patients. In our study elderly patients had a higher prevalence of hypertension 44.9% than younger patients 32.8% (*P* =0.001). Hypertension, leads to arterial stiffness responsible for the acceleration of atherosclerosis, the destabilization of atherosclerotic plaques and leads to an increase in systemic vascular resistance and therefore in the afterload of the left ventricle and and leads to diastolic and systolic heart failure [15]. Elderly patients in our study were no different from younger patients concerning the prevalence of diabetes mellitus and dyslipidemia as shown in Table 1.

Elderly patients in our study had a worse clinical HF status as shown in Table 2 compared to younger patients. 23.4% of elderly patients were NYHA III and 2.1% were NYHA IV. Left signs of HF were present in 10.5% vs 7.8% (*P* =0.009) and Right HF signs in 7.4% vs 5.6% (*P* =0.055). LV filling pressure (LVFP) were elevated in 22.5% vs 18.3% (*P* =0.003) and the mean LVEF was 36.18±10.34 versus 36±9.88 (*P* =0.649). Elderly patients tend to have more advanced CHF than do younger patients because they tend to be more sedentary and thus do not note symptoms or do not receive a diagnosis of CHF until their cardiac limitation is advanced. Manifestation can be atypical, especially in frail or demented patients who may have lethargy, fatigue, or confusion. Concomitant illnesses tend to precipitate exacerbations of CHF due to excess load placed on the heart because of hypertension, renal disease with fluid retention, and high-output states due to anemia, thyroid disease, or infection [16].

Ischemic heart disease (IHD) represented the major cause of HF in elderly patients followed by dilated cardiomyopathy (DCM) and valvular heart disease (VHD) as shown in Table 1. According to literature, Elderly patients in comparison with younger patients, have more hypertensive heart disease causing diastolic dysfunction, the incidence of CAD also increases with age as well as degenerative aortic stenosis [16].

In the present study, we found that elderly HFrEF patients had a worse clinical status and presented a higher rate of hospitalizations for

decompensated HF compared to younger patients (53.5% vs 43.2% *P* <0.001). According to the literature, despite significant improvements in HF treatment in recent years, HF hospitalization in elderly patients have increased because of aging process [9].

## 4.2 Treatment of Heart Failure

### 4.2.1 General measures

Patients with HF should decrease their sodium intake and fluid intake. Drugs that may cause HF decompensation such as NSAIDs and antiarrhythmic drugs such as verapamil, diltiazem and flecaïne, should be stopped and alcohol intake must be avoided. Noncompliance for HF therapy in elderly patients may have multiples explanations, Elderly patients may not tolerate side effects caused by HF therapy especially hypotension or polyuria [16]. Elderly often have multiple treatments because of comorbidities that may be responsible for drug-drug interactions (warfarin and aspirin), drug–disease interactions (nonsteroidal anti-inflammatory drugs in HF), or drug–person interactions (digoxin use in older adults) [17]. Besides elderly patients may not always understand the importance of HF treatment because of dementia related to aging. HF patients should be encourage to maintain regular physical activity such as walking because of its benefice to improving symptoms and functional status [4]. In the same optic, HF patients who are very symptomatic at rest may benefit from a cardiac rehabilitation program [18].

### 4.2.2 Heart failure medical therapy

Medical therapy management can be challenging in older HF patients [17]. Diuretics treats volume overload. Loop diuretics such as furosemide are the main diuretic used in elderly. Thiazide diuretics such as hydrochlorothiazide may be used alone or in association with furosemide to treat volume overload. In case of severe HF symptoms, HF should be managed in hospitalization with intravenous diuretics. HF patients treated with diuretics need close monitoring of hypokalemia and hyponatremia. Diuretics must be prescribed at the minimum effective dose, then diuretic doses must be gradually decreased and stopped if possible when no longer needed to control fluid retention [19,4]. In our results 46.6% of elderly patients received Diuretics versus 43.6% of younger patients, this may be related to the worse HF clinical status in elderly as they were more symptomatic and had more fluid overload.

ACE inhibitors have many benefices as a HF treatment in HFrEF patients, the help decrease blood pressure, LV and RV filling pressures, systemic vascular resistance, and therefore decrease the myocardial oxygen consumption and improve cardiac output. They should be initiated in elderly patients with HF in low doses and gradually increased to the maximum tolerated dose. During titration, patients must be monitored closely in order to detect possible side effects including renal function impairment and hypotension, those should not cause automatic ACE-I discontinuation, but must lead the physician to recheck the doses of diuretics or ACE-I for eventual reduction of doses. In our study 83.2% of group 1 patients received an ACE inhibitor versus 76.9% (*P* <0.001), the higher use of ACE inhibitors in elderly patients can be explained by the higher incidence of hypertension in this age group of patients. 16.7% of our elderly patients received ARB because of secondary effects of ACE inhibitors versus 19.4% (*P* <0.001). Angiotensin II receptor blockers (ARB) should be considered in HFrEF patients who didn't tolerate or presented side effects of ACE inhibitors such as cough or angioneurotic edema [19]. In the PARADIGM-HF trial, the use of Sacubitril/valsartan, an angiotensin receptor-neprilysin inhibitor (ARNI), was shown to be superior to enalapril in reducing HF hospitalizations, mortality and improve symptoms in patients with HFrEF with LVEF <_35%., thus 2021 ESC guidelines of management of HF recommend using an ARNI straight away for the inhibition of renin-angiotensin system or as a replacement of ACE inhibitors [19].

Beta-blockers have been shown to improve symptom and reduce mortality and morbidity in patients with HFrEF in general and elederly patients in specifically [20]. Initiation of Blockers should be made with low dose and gradually increased each two to three weeks intervals. Monitoring of patients is important during the process of titration, in order to detect possible secondary effects of Blockers (HF symptoms, fluid retention, hypotension, and bradycardia) [19]. Ivabradine can be used in HFrEF<35% patients in sinus rhythm when the heart rate is still >70 pbm despite the use of maximal tolerated dose of beta-blockers or in case of contraindication of beta-blockers [19]. In our finding only 58.9% of elderly patients received a

Beta-bocker vs 88% (*P* <0.001) and 3.8% received Ivabradine versus 7% (*P* <0.001), this result can be explained by the importance of HF signs and the frequent elevation of LV filling pressure in the elderly, which makes it difficult to introduce beta-blockers in these patients.

The 2021 European society of cardiology (ESC) guidelines to the management of acute and chronic HF, recommend adding Mineralocorticoid receptor antagonists (MRAs), in all patients with HFrEF to reduce mortality and the risk of HF hospitalization, [21,22] and improve symptoms [21]. MRA use should be cautious in case of impaired renal function or increased serum potassium levels >5.0 mmol/L [19]. 58.1% of elderly patients received an MRA versus 55.2% in younger patients (*P*<0.001), this higher use of MRA in elderly is related to the higher incidence of left and right HF signs in elderly. Latest ESC guidelines highlight the benefice of diuretic/natriuretic properties of SGLT2 inhibitors (Dapagliflozin or empagliflozin) when added, regardless of diabetes status, in patients with HFrEF by reducing congestion and reducing loop diuretic doses [23].

Digoxin may be considered in patients with HFrEF in SR to reduce the risk of hospitalization, [24,19]. The therapeutic window of Digoxin is narrow, thus Digoxin serum levels should be checked with an objective <1.2 ng/mL [25]. Age-related decrease in renal function and drugs interactions in elderly helps increase digitalis toxicity risk in these patients [26].

Oral anticoagulation by direct oral anticoagulants (DOA) should be administered in HF patients with a history of atrial fibrillation, systemic or pulmonary embolism, or cardiac thrombi detected by echocardiography. Warfarin should be reserved for patients with mechanical prosthetic valves and significant mitral stenosis.

#### 4.2.3 Cardiac implantable devices

Intraventricular conduction delay in patients with HFrEF may lead an aggravation of LV systolic dysfunction caused by LV systolic asynchrony [27]. In patients with NYHA II-III, despite OMT who present an intraventricular conduction delay, cardiac resynchronization therapy can lead to significant clinical improvement [28]. In patients survivors from cardiac arrest, or who have experienced sustained ventricular arrhythmia and ischemic cardiomyopathy, Implantable cardioverter-defibrillators (ICDs) is indicated as a secondary prevention. It can also be indicated as a primary prevention in patients with HFrEF and ischemic cardiomyopathy to reduce mortality [29,30]. The decision of an automatic implantable cardioverter-defibrillator should take into account the stage of HF, comorbidities and life expectancy in elderly [31,32]. Elderly patients who have refractory and severe HF symptoms with limited life expectancy, and who are not eligible for a ventricular assist device (VAD) or cardiac transplantation shouldn't benefice from an ICD because they are more likely to die from pump failure [33,34].

## 5. CONCLUSION

CHF is a major public health problem in Morocco and AFRICA in general. Our study shows particularities of HF features in Moroccan elderly patients. Elderly patients accounted approximately for half of our population of study, they had a more severe clinical status and a higher risk of hospitalization for HF. Therefore, more focus should be given to this age group of patients, since they have more comorbidities, are more frail and HF treatment can be difficult to optimize because of concern about potential side effects. Preventive and public health strategies need to be defined according to the local characteristics in order to implant an optimal and appropriate therapeutic treatments.

## CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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