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Pharmaceutical guidance and the impact on medication adherence in patients with Amyloidosis

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Abstract

Objectives: To identify medication adherence in patients with Cardiac Amyloidosis (CA) before and after pharmaceutical guidance and investigate its association with quality of life. **Methods:** This is a before-and-after, single-arm, non-randomized study. The selection was among patients with transthyretin (TTR) cardiac amyloidosis included in research protocols of the Instituto do Coração do Complexo do Hospital das Clínicas da Universidade de São Paulo (InCor HCFMUSP). Five pharmaceutical visits were performed, the first in person and the others by telehealth. The Kansas City Cardiomyopathy Questionnaire (KCCQ) and Brief Medication Questionnaire (BMQ) quality of life questionnaires were used. Medication adherence was identified and classified into four categories: adherent, probable adherent, probable low adherent, and low adherent. To estimate the association between medication adherence and quality of life, analysis was performed using ANOVA and unpaired t-test. **Results:** 11 participants agreed to participate in all study visits. Mean age was 74.2 years (SD= 8.4), 95.2% were male, and 47.6% had completed college education. The mean number of medications in use was 8 (dp= 2.9). 54.5% of participants were classified as adherent. The association between medication adherence and quality of life was significant for the Total Symptom Score and Clinical Summary domains. There was no significance in the correlations between the number of medications and KCCQ. **Conclusions:** Pharmacotherapy follow-up mediated by telehealth for patients with Cardiac Amyloidosis can improve in at least one domain of KCCQ.
Keywords: amyloidosis, drug adherence, pharmaceutical services, telemedicine.

Orientação farmacêutica e o impacto sobre a adesão medicamentosa em pacientes com Amiloidose

Resumo

Objetivos: Identificar a adesão medicamentosa de pacientes com Amiloidose Cardíaca (AC), antes e após orientações farmacêuticas e investigar sua associação com a qualidade de vida. **Métodos:** Trata-se de um estudo do tipo antes e depois, de braço único e não randomizado. A seleção ocorreu entre pacientes com Amiloidose Cardícada por transtirretina (ATTR) incluídos em protocolos de pesquisa do Instituto do Coração do Complexo do Hospital das Clínicas da Universidade de São Paulo (InCor HCFMUSP). Realizou-se cinco consultas farmacêuticas, sendo a primeira de forma presencial e as demais por teleconsulta. Foram utilizados os questionários de qualidade de vida *Kansas City Cardiomyopathy Questionnaire* (KCCQ) e de adesão medicamentosa *Brief Medication Questionnaire* (BMQ). A adesão medicamentosa foi identificada e classificada em quatro categorias: aderente, provável aderente, provável baixa adesão e baixa adesão. Para estimar a associação entre adesão medicamentosa e qualidade de vida foi realizada uma análise por meio de ANOVA e teste *t* não pareado. **Resultados:** 11 participantes aceitaram participar de todas as consultas do estudo. A idade média foi de 74,2 anos (dp= 8,4), 95,2% eram homens e 47,6% possuíam ensino superior completo. A média do número de medicamentos em uso foi de 8 (dp= 2,9). 54,5% dos participantes foram classificados como aderentes. A associação entre a adesão medicamentosa e a qualidade de vida obteve significância para os domínios de Escore Total dos Sintomas e Sumário Clínico. Não houve significância nas correlações entre o número de medicamentos e KCCQ. **Conclusões:** O acompanhamento farmacoterapêutico mediado pela teleconsulta de pacientes com Amiloidose Cardíaca podem melhorar em pelo menos um domínio do KCCQ.

Palavras-chave: amiloidose, adesão ao medicamento, cuidados farmacêuticos, telemedicina.

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Introduction

Amyloidosis is a disease characterized by the atypical infiltration of structurally abnormal proteins, known as amyloid fibrils, in various tissues, such as the heart muscle, gastrointestinal tract, and nervous[1,2] system. Thirty proteins have been identified, with two predominantly affecting the cardiac phenotype: one with deposits of light chain immunoglobulin proteins, known as AL amyloidosis, and another with deposits of transthyretin, called ATTR[2,3] amyloidosis. The AL form is derived from the inappropriate increase in the production of monoclonal antibody light chain fragments, designated as primary amyloidosis[4].

In ATTR, the accumulation is due to alterations in the folding of the transthyretin protein, which originally has a tetrameric form and is responsible for transporting vitamin A and the hormone thyroxine. ATTR amyloidosis is the most common subtype, occurring in two forms: hereditary (type h) and wild-type (type w). The former has more than 130 described mutations, including T80A. Val142Ile, Val50Met, and Val30Met, with the last being the most frequent. The clinical presentation varies from pure polyneuropathy (ATTR-PN) to exclusive cardiomyopathy (ATTR-CM), which is the most widespread worldwide and the most common in Brazil. The latter form has a higher prevalence in men over 70 years old, with cardiac involvement as the main clinical feature, associated with spinal stenosis and carpal[5,6,7] tunnel syndrome.

It is known that the cardiac phenotype has a 95% prevalence and affected individuals develop cardiac hypertrophy progressing to heart failure with preserved ejection fraction (HFpEF), along with signs and symptoms such as shortness of breath, peripheral edema, fatigue, and eventually cachexia[8]. It should be noted that heart failure is a significant health problem, responsible for an annual cost of R$ 166,242,99 to the public health system (SUS)[9].

The pharmacotherapy for Cardiac Amyloidosis (CA) includes supportive medications for symptoms associated with heart failure (HF). To reduce amyloidogenesis in the ATTR form, the use of transthyretin RNA silencers (Patisiran) and selective transthyretin stabilizers (Tafamidis)[10,12] is considered. In AL, the therapy consists of chemotherapy with melphalan, bortezomib, and/or lenalidomide and stem[13] cell transplantation.

The estimated time from symptom onset to diagnosis is approximately two years, with patients typically consulting five different[6] professionals on average, Late diagnosis and limited therapeutic options can lead to a decline in quality of life due to complications from advanced heart disease. The median survival estimate for ATTRw is 3,6 years, and in ATTRh, the prognosis depends on the mutation[14,15]. Thus, initiatives are needed to disseminate knowledge about CA, especially adequate therapeutic guidance, to improve medication adherence, prognosis, and quality of life for patients.

According to the Pan American Health[16] Organization, the medication adherence rate for chronic diseases is around 50% in developed countries, as medication therapy requires discipline, awareness, and pharmaceutical guidance. Resolution No. 585 of August 29, 2013, of the Federal Council of Pharmacy (CFF)[17], regulates the clinical responsibilities of pharmacists, allowing professionals to have direct contact with patients to promote effective behavioral changes regarding medication adherence.

The clinical pharmacist promotes care through the provision of services such as pharmacotherapy review, health education, pharmacotherapeutic follow-up, and health[18] screening. To assess patients' medication adherence, this professional uses indirect methods of clinical interviews, such as the Brief Medication Questionnaire (BMQ), which identifies barriers regarding regimen, beliefs, and recall of treatment from the patient's[19] perspective.

Regarding the provision of integrated and safe care, the Ministry of Health[20] provided a document on the "Digital Health Strategy for Brazil 2020-2028" with the help of the telehealth service, considering the care difficulties faced during the Covid-19 pandemic. From this document, several resolutions were created, allowing the practice of teleconsultation by health professionals, including resolution No. 727/2022, which defines Telepharmacy as the practice of Clinical Pharmacy mediated by Information and Communication Technology (ICT)[21].

Thus, pharmaceutical guidance via teleconsultation can significantly contribute to medication adherence associated with improved quality of life in patients with amyloidosis. In this context, this study aimed to identify and classify medication adherence in patients with amyloidosis before and after pharmaceutical counseling, investigate the association between medication adherence and quality of life, and evaluate the correlation between the number of medications and quality of life.

Methods

This is a before-and-after study with a single arm and non-randomized design. The study population comprised patients diagnosed with ATTR Amyloidosis who were included in research protocols at the Scientific Committee of the Heart Institute of the University of São Paulo Medical School Hospital Complex (InCor HCFMUSP) and were continuously using medications for chronic non-communicable diseases. Patients of both genders, aged 18 years or older, were included. Individuals who were unavailable for scheduling or lacked internet access for teleconsultation follow-up were excluded from the study.

Study Development

Five pharmaceutical consultations were conducted, The first consultation was in-person, and the remaining consultations were conducted via teleconsultation. The intervals between the first (D0), second (D15), and third consultations (D30) were 15 days. The subsequent consultations were conducted with 30-day intervals (D60 and D90). Teleconsultations were scheduled by phone, and on the scheduled day, a link was sent to the patient via email by the technical team for access to the digital platform.

1) First consultation- in-person (D0)

Initially, to characterize the population, the following information was collected through self-report: sex, age, educational level. ATTR type (w or h and their mutations), comorbidities. New York Heart Association classification for predicting the prognosis and survival of heart failure patients, stratifying patients from I to IV, current smoking, and use of transthyretin stabilizers. This in-person consultation was conducted on the same day as the medical consultation at the Clinical Cardiomyopathy Unit or Scientific Committee.

Subsequently, two questionnaires were administered as described below:

Brief Medication Questionnaire (BMQ): This aims to evaluate medication adherence using an indirect clinical interview method that assesses barriers related to the use of home medications from the perspective of three domains: Regimen (1). Beliefs (2), and Recall (3). The Regimen domain evaluates adherence by comparing the medical prescription with the patient's practice; the Beliefs domain investigates the patient's perception of the necessity and effectiveness of the medications, as well as concerns about side effects; and the Recall domain examines the patient's ability to remember to take medications and identifies practical and psychological barriers. Based on the responses, the BMQ assists healthcare professionals in implementing specific and targeted interventions to improve treatment adherence as needed. Stratification is distributed into four categories: Adherent. Probable Adherent. Probable Low Adherence, and Low Adherence, as validated by Svarstad et al. (1999)[42].

Kansas City Cardiomyopathy Questionnaire (KCCQ): This assesses health-related quality of life (HRQoL) through an instrument with 23 questions divided into five domains: Physical Limitation (question 1). Symptom Stability (question 2). Symptoms (Frequency - questions 3. 5. 7, and 9; Severity- questions 4. 6, and 8). Quality of Life (questions 12. 13, and 14). Self-efficacy (questions 10 and 11), and Social Limitation (question 15), as validated by Green et al. (2000)[44].

The medications used by the patients were classified according to the Anatomical Therapeutic Chemical (ATC) classification, which stratifies medications based on the organ or system they act on: A- Digestive system and metabolism; B- Blood and blood-forming organs; C - Cardiovascular system; G - Genitourinary system and sex hormones; H - Systemic hormonal preparations; M - Musculoskeletal system; N - Central nervous system; and R - Respiratory system.

Finally, a "Pharmaceutical Guidance Table" was developed with the medications used by the patient. This table aims to guide the patient's therapy regarding dosage, therapeutic regimen, and other pharmaceutical guidance, considering the patient's beliefs and habits, as well as the pharmacokinetics of the medications and drug interactions, to establish the best time for medication administration.

2) Second consultation- teleconsultation (D15)

Assessment of prior knowledge about continuous-use medications and evaluation of understanding of pharmaceutical guidance related to the table provided on D0.

3) Third consultation – teleconsultation (D30)

The BMQ and KCCQ questionnaires were re-administered to evaluate the guidance provided on D0 and D15 and to provide new pharmaceutical guidance based on the information obtained from the tests.

4) Fourth consultation- teleconsultation (D60)

General review of the guidance addressed in the previous stages and identification of any doubts regarding the medication treatment.

5) Final consultation- teleconsultation (D90)

Re-administration of the BMQ and KCCQ questionnaires to evaluate the final results.

Data Analysis

Continuous variables will be presented using measures of central tendency (mean) and dispersion (standard deviation), and categorical variables will be presented using frequency distribution. To identify and classify medication adherence among study participants, frequency distribution was performed in four categories: 1) Adherent. 2) Probable Adherent. 3) Probable Low Adherence, and 4) Low Adherence.

To assess the quality of life of participants at the beginning and end of the study (at the in-person consultation (D0) and the fourth teleconsultation (D90), respectively), a paired t-test was used. To estimate the association between medication adherence and quality of life before and after pharmaceutical guidance, an analysis was conducted using ANOVA and an unpaired t-test, respectively. The correlation between the number of medications used and quality of life was assessed using Pearson's test.

Differences were considered significant at the level of $p<0.05$ to reject the null hypothesis. All analyses were performed using Jamovi® software version 2.3.21.0.

Ethical Aspects

The project was approved by the Regulatory Coordination of the Scientific Committee of InCor HCFMUSP and by the Ethics Committee for the Analysis of Research Projects (CAPPesq) of HCFMUSP. No. 5,605,306. Considering respect for human dignity and the special protection due to participants in scientific research involving human beings, the entire study was conducted in accordance with resolution 466/2012, with the signing of the informed consent form (TCLE) by all participants.

Results

In the research protocols at the Scientific Committee. 25 participants were in follow-up; of these, four were not invited to participate in this study due to unavailability for the initial consultation with the clinical pharmacist, and 21 participants agreed to participate in the study by signing the TCLE and responding to the questionnaires administered during the in-person consultation.

From the in-person consultation (D0) to the fourth teleconsultation (D90). 10 patients did not continue the study; six patients did not participate in the first teleconsultation, three did not participate in the second, and one did not participate in the third (Figure 1). The losses were due to participants dropping out and the unavailability of time and/or internet access for teleconsultation follow-up.

Of the total 21 participants included in this study, approximately 95.2% were men and 4.8% were women; however, the final population consisted only of male individuals (n=11). The mean age was 74.2 years (sd=8.4) at the first consultation and 73.5 years (sd=9.7) at follow-up. The frequency of participants with a bachelor degree was 47.6% initially and 63.6% at follow-up. Slightly more than half of the participants (52.4%) had a diagnosis

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Figure 1. Flowchart of participant recruitment throughout the study follow-up.
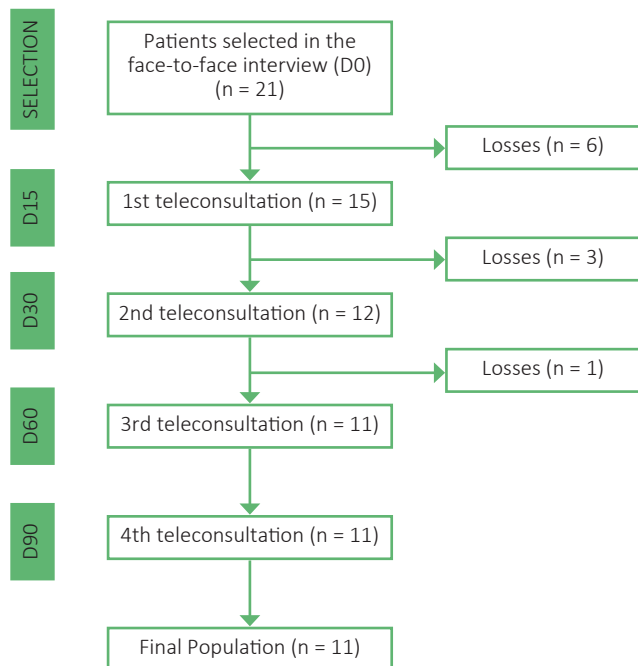
of ATTRw (wild-type), with a higher difference observed in the follow-up (63.6%). Among patients with ATTRh, the Val142Ile mutation predominated (60%). In the functional class (FC) NYHA (New York Heart Association) stratification, patients were identified only in classes I and II, with a majority in FC II with 66.7% at the in-person consultation and 54.5% at the end of the study. The percentage of participants who reported not smoking at the time of the study was 100% in all consultations. The average number of medications in use was 8 (sd=2.9) at the beginning and 7.7 (sd=3.4) at follow-up. Only 3 participants (14.3%) were using Tafamidis at the start of the study, and of these, only 2 completed the follow-up. Among comorbidities, arrhythmias had the highest frequency (66.7%), followed by diabetes mellitus (54.4%) and carpal tunnel syndrome (47.6%) at the in-person consultation. At follow-up, a high percentage of gastrointestinal disorders (54.5%) was observed, along with arrhythmias and diabetes mellitus (Table 1).

The application of the BMQ questionnaire and the analysis of medical records enabled the evaluation of medications used by participants according to the Anatomical Therapeutic Chemical (ATC) classification (Figure 2). Among physiological systems, there was a higher frequency (45%) of medications used for the cardiovascular system, given that the population consisted of patients with a cardiac pathology. This was followed by the use of medications for the digestive system and metabolism (27%) and for blood coagulation and blood-forming organs (13%).

When evaluating the medication adherence of participants who completed the study (n=11). 54.5% were classified as adherent and 45.4% as probable adherents at the end of the follow-up (D90). Only two participants (18.2%) were classified as having probable low adherence at the in-person consultation, and they showed improvement in category at D30 and D90. Although there was a reduction in the frequency of adherents between D30 (63.6%) and D90 (54.5%), there was a noted progression in the

classification of probable adherence across all three time points (Table 2). Among the barriers to medication adherence, the recall barrier had the highest frequency (27.3%) at the end of the follow-up, corresponding to participants with probable adherence. The belief barrier remained constant at D0 and D30 at 18.2%; however, it was not identified at D90. Regarding the number of barriers identified, seven barriers to medication adherence were found at D0: two (18.2%) for regimen and belief, and three (27.3%) for recall. By the end of the follow-up, only five barriers were identified: two (18.2%) for regimen and three (27.3%) for recall.

Table 1. Distribution of participants assessed at the first in-person consultation (N=21) and participants who completed all study consultations (N=11), according to sociodemographic characteristics, morbidities, and health-related behaviors. São Paulo, SP, 2022.

Characteristics	First Consultation (in-person) n = 21	All consultations n = 11
Age, mean ± SD	**74.2 ± 8.4**	**73.5 ± 9.7**
Gender, n (%)		
Male	20 (95.2)	11 (100)
Female	1 (4.8)	-
Education, n (%)		
Up to elementary school degree	6 (28.6)	2 (18.2)
High school degree	5 (23.8)	2 (18.2)
Bachelor degree and above	10 (47.6)	7 (63.6)
ATTR, n (%)		
Type w	11 (52.4)	7 (63.6)
Type h	10 (47.6)	4 (36.4)
T80A	3 (30.0)	1 (25.0)
Val142Ile	6 (60.0)	2 (50.0)
Val50Met	1 (10.0)	1 (25.0)
NYHA[1] Functional Class, n (%)		
I	7 (33.3)	5 (45.5)
II	14 (66.7)	6 (54.5)
Current smoking, n (%)		
No	21 (100)	11 (100)
Number of medications in use, mean ± SD	8.0 ± 2.9	7.7 ± 3.4
Use of Tafamidis, n (%)	3 (14.3)	2 (18.2)
Comorbidities, n (%)		
Arrhythmias	14 (66.7)	6 (54.5)
Atrial fibrillation	12 (57.1)	6 (54.5)
Diabetes mellitus	11 (54.4)	6 (54.5)
Carpal Tunnel Syndrome	10 (47.6)	4 (36.4)
Gastrointestinal disorders	9 (42.9)	6 (54.5)
Systemic arterial hypertension	9 (42.9)	4 (36.4)
Heart failure	8 (38.1)	3 (27.3)
Sleep apnea	5 (23.8)	2 (18.2)
Benign[2] Prostatic Hyperplasia	5 (25.0)	3 (27.3)
Pacemaker	4 (19.0)	2 (18.2)
Dyslipidemias	4 (19.0)	1 (9.1)
Hypothyroidism	4 (19.0)	0
Chronic kidney disease	3 (14.3)	1 (9.1)
Asthma/COPD[3]	3 (14.3)	1 (9.1)
Ischemic Stroke	3 (14.3)	0

[1.] New York Heart Association (NYHA) Functional Classification. [2.] % relative to the total of 20 male individuals. [3.] COPD: Chronic Obstructive Pulmonary Disease

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Table 2. Assessment of medication adherence among participants (N=11) at three time points, during the in-person consultation (D0), at the 2nd Teleconsultation (D30), and at the 4th Teleconsultation (D90), according to the Brief Medication Questionnaire, São Paulo, SP, 2022.

Medication Adherence	Inquiry		
	D0 n (%)	D30 n (%)	D90 n (%)
Adherent	6 (54.5)	7 (63.6)	6 (54.5)
Probable adherence	3 (27.3)	4 (36.4)	5 (45.4)
Probable low adherence	2 (18.2)	0	0
Barriers to medication adherence			
Regimen barrier	2 (18.2)	1 (9.1)	2 (18.2)
Belief barrier	2 (18.2)	2 (18.2)	0
Memory barrier	3 (27.3)	1 (9.1)	3 (27.3)

No patient was classified as "low adherence".

In the assessment of quality of life using the KCCQ among the 11 participants, it was observed that at D90, the average scores for the domains of Quality of Life. Social Limitation, and Functional Status were lower than at D30. In contrast, the averages at D90 were higher than at D0 in all domains except Symptom Stability. For the domains of Physical Limitation and Clinical Summary, a continuous progression in average scores was observed throughout all consultations. Notably, the Self-Efficacy domain achieved the highest average score (87.6) at the end of the follow-up (Table 3). However, in none of the domains was the difference between the averages at the initial consultation (D0) and the final teleconsultation (D90) statistically significant ($p > 0.05$).

The association between quality of life and medication adherence was evaluated before and after pharmaceutical counseling, at the initial consultation (D0) and the fourth teleconsultation (D90). At the initial consultation, participants were classified into three adherence categories: adherent, probable adherent, and probable low adherence. When comparing quality of life, it was observed that among the adherent and probable adherent participants, there was a reduction in average scores across all Kansas questionnaire domains. However, this pattern was not observed among participants with probable low adherence, which

may explain the lack of significance between the values. Unlike the initial consultation, at the fourth teleconsultation, participants were classified into only two adherence categories: adherent and probable adherent. There was a significant reduction in values for the Total Symptom Score domain (0.046) and the Clinical Summary (0.048) (Table 4).

No statistically significant correlation was observed between the number of medications taken by participants during the follow-up and the KCCQ domains ($p > 0.05$).

Table 3. Evaluation of participants' (N=11) quality of life at three time points: initial consultation (D0). 2nd Teleconsultation (D30), and 4th Teleconsultation (D90), according to the Kansas City Cardiomyopathy Questionnaire, São Paulo, SP, 2022.

Dominance	Inquiry		
	D0	D30	D90
	Mean (±dp)	Mean (±dp)	Mean (±dp)
Physical Limitation	78.7 (16.1)	82.8 (13.5)	83.7 (15.4)
Symptom Stability	79.5 (24.5)	70.5 (27)	77.3 (23.6)
Total Symptom Score	83.9 (21.5)	81.9 (21.7)	85.6 (14.1)
Self-Efficacy	83 (23.9)	80.5 (14.7)	87.5 (12.5)
Quality of Life	61.4 (19.1)	71.2 (17.2)	68.2 (15.7)
Social Limitation	69.3 (26.1)	76.7 (22.6)	72.7 (16.1)
Functional Status	73.5 (18.6)	78.5 (13.9)	77 (13.8)
Clinical Summary	81.7 (16.4)	83.1 (12.0)	83.5 (14.6)

Discussion

This study highlighted a higher percentage of participants classified as adherent or probable adherents during the second (D30) and fourth (D90) teleconsultations, suggesting a possible relationship with a higher level of education among participants who attended all consultations, as 63.6% had bachelor degree. A Brazilian study observed that medication adherence in patients with Heart Failure was directly related to literacy levels, the degree of ability to understand basic health information, which is associated with educational[22] attainment.

Table 4. Association between medication adherence and quality of life of participants (N=11) before and after pharmaceutical counseling, São Paulo, SP, 2022.

Dominance (Kansas)	Medication Adherence (D0)			Pvalue*	Medication Adherence (D90)		Pvalue**
	Adherent (n=6)	Likely adherent (n=3)	Likely low adherence (n=2)		Adherent (n=6)	Likely adherent (n=5)	
Physical Limitation	82.8 (±12.51)	68.9 (±18.72)	81.3 (±26.52)	0.511	91 (±8.89)	75 (±17.9)	0.086
Symptom Stability	87.5 (±20.92)	66.7 (±28.87)	75 (±35.36)	0.516	79.2 (±24.58)	75 (±25.0)	0.787
Total Symptom Score	93.5 (±6.69)	74 (±25.54)	69.8 (±42.72)	0.281	93.1 (±7.64)	76.6 (±15.5)	0.046
Self-Efficacy	87.5 (±13.69)	62.5 (±37.5)	100	0.186	89.6 (±9.41)	85 (±16.3)	0.573
Quality of Life	66.7 (±9.13)	47.2 (±24.06)	66.7 (±35.36)	0.358	73.6 (±14.36)	61.7 (±16.2)	0.228
Social Limitation	77 (±7.74)	58.3 (±38.19)	62.5 (±53.03)	0.606	79.2 (±9.41)	65 (±20.1)	0.156
Functional Status	79.7 (±5.95)	61.2 (±26.44)	73.5 (±34.68)	0.413	83.8 (±8.07)	69 (±15.6)	0.073
Clinical Summary	87.6 (±9.12)	69.5 (±22.21)	82.3 (±25.05)	0.329	91.1 (±6.86)	74.3 (±16.7)	0.048

*p – ANOVA. **p- teste t não pareado

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Regarding the barriers to medication adherence, regimen, belief, and recall barriers were present at D0, with the recall barrier being the most frequent. This frequency was also observed at D90, which contrasts with findings from a previous study[22] that evaluated the association between medication adherence and literacy level, showing a higher frequency for regimen barriers. That study concluded that the result was related to patients' difficulty understanding prescriptions and treatment instructions.

Contrary to this study, our results suggest that the level of medication adherence among participants is related to the recall barrier, which suggests the use of multiple doses and difficulties in answering question 3c of the BMQ. This question includes factors such as access to the medication, literacy, simultaneous intake of pills, and the ability to remember to take medications. Furthermore, it is important to note that the BMQ question evaluating the recall barrier—"Does the patient receive a multiple-dose regimen (2 or more times/day)?"—does not directly assess patient medication adherence but rather identifies a barrier that may impact it. Another point to emphasize is the constant shortage of medications in Brazil, such as Tafamidis.

Treatment with Tafamidis for managing cardiac amyloidosis (CA) is a promising therapy, as seen in studies[23-24] that showed a reduction in the risk of all-cause mortality and supported FDA approval in 2019. However, the number of participants reporting Tafamidis use was only 14.3%. This is due to the high cost of the medication (Factory Price: R$27.947.09 to Average Consumer Price: R$37.234.14 – as of 01/2023)[25] and the lack of incorporation by the National Commission for the Incorporation of Technologies (CONITEC) into the Unified Health System (SUS) for the treatment of both wild-type and hereditary ATTR in patients over 60 years old, leaving legal action as the only recourse for treatment[26].

Although no significant correlations were found between the number of medications and quality of life, it is notable that the higher the number of medications used, the lower the scores for the domains of Physical Limitation. Quality of Life. Self-Efficacy, and Functional Status, impacting participants' health. Chen and colleagues[27] reported in their study that respondents who consumed a greater number of medications per day were more likely to report problems with mobility, self-care, pain/discomfort, and depression/anxiety.

The association between medication adherence and the KCCQ for the Total Symptom Score and Clinical Summary domains, after all pharmaceutical counseling, was statistically significant. This highlights the critical role of the pharmacist in supporting individuals with cardiac amyloidosis, leading to a lower frequency and severity of daily symptoms and, consequently, better quality of life.

Studies conducted in the United States[28] reveal that pharmaceutical services have a significant impact on overall health, using the Short Form (SF-36) questionnaire as a measure of quality of life. A meta-analysis[29] observed that pharmaceutical interventions can significantly improve at least one domain of Health-Related Quality of Life (HRQoL) in various medical conditions.

The benefits of pharmaceutical counseling for patients with chronic non-communicable diseases are reported in several studies. For instance. Parajuli and colleagues[30] demonstrated that pharmacists involved in the care of heart failure patients promoted improvements, such as reduced hospitalizations and increased medication adherence.

American researchers demonstrate the crucial role of pharmacists in mediating medication adherence for hypertensive patients through telehealth services, minimizing barriers to accessing care[31]. This finding supports the results presented in this study, as the highest adherence percentage was observed during teleconsultation follow-ups, with no participants classified as having probable low adherence at the end of the follow-up.

A meta-analysis of 34 studies showed that the most commonly used pharmaceutical care model in an outpatient setting was chronic disease management, such as Diabetes and Hypertension, through phone calls. The results demonstrated a positive impact on medication adherence, achieving therapeutic goals, self-monitoring of blood pressure, and the technique of using inhalation[32] devices.

Teleconsultation implies changes in the typical professional-patient relationship, replacing in-person contact with virtual interactions, challenging the traditional view of healthcare professionals' practices, as described by Maldonado and colleagues[33]. This impact was observed during the follow-up of this study, as attrition occurred during the transition between the in-person consultation and the first teleconsultation, as well as in other stages conducted through technological resources.

It is necessary to highlight that patients who did not participate in this study due to unavailability or lack of internet access might differ in sociodemographic characteristics and health-related behaviors compared to those who accepted pharmacotherapeutic follow-up. Da Silva & Santos[34] note that difficulties in handling computers, smartphones, and tablets, along with a lack of internet access or poor connection quality, result from Brazilian socioeconomic inequality, hindering access to health services via technology. It is noteworthy that more than half of the participants in the follow-up had bachelor degree, suggesting that education level may be associated with access to information and ease of handling technology. Moreover, there may be a correlation between health commitment, represented by medication adherence, and willingness to contribute to scientific studies. Despite this, we believe that the difficulty in extrapolating data to individuals not eligible for inclusion criteria is inherent to studies where the study population is selected by convenience.

Although cardiac amyloidosis (CA) is one of the causes of heart failure with preserved ejection fraction (HFpEF), this study showed that the prevalence of heart failure (HF) was only 38%, and most participants were stable in NYHA class II (66.7%), suggesting that over half were diagnosed early, as HF in CA typically presents with advanced impairment. Additionally. 47.6% of the participants had bachelor degree, implying they have greater access to information and probably to health[3] services.

Some studies indicate that atrial fibrillation is very common in CA due to amyloid infiltration in the atria, leading to increased blood stasis even when the patient is in sinus rhythm, and impairing atrial[35.36.37] mechanical function. In this study, the most frequent comorbidity was arrhythmias (66.7%), with atrial fibrillation representing 57.1%.

According to Feng et al[38]., increased left ventricular (LV) filling pressure, contractile dysfunction caused by atrial amyloid infiltration, and atrial fibrillation are risk factors for thromboembolism development, which justifies that 13% of the medications reported by participants were for blood coagulation disorders.

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A study[39] observed that cardiac involvement is frequently associated with carpal tunnel syndrome in both hereditary (h) and wild-type (w) forms of CA, corroborating the results of this research, where 47.6% of the 21 participants had the diagnosis.

European researchers[40] demonstrated that the presentation of ATTR in the wild-type was common among male participants with a mean age of 77 years, a result also observed in this study, where 95.2% were men with a mean age of 74.2 years, and more than half (52.4%) had ATTRwt.

This work is innovative in studying a population group that is still not well explored. However, some limitations need to be presented: 1) The absence of a control group to validate the follow-up process; 2) The frequent medical consultations (every 21 days) of the participants in the research protocols may overestimate the quality of life and consequently promote better medication adherence, compared to the outpatient follow-up of SUS patients, which occurs every 6 months to a year; 3) Data collection was through self-report, which may have contributed to information bias; 4) The study's sample size was relatively small, although it deals with a rare disease with a still high rate of underdiagnosis; and 5) The small number of participants limits us in seeking statistical association between medication adherence, quality of life, and follow-up, so larger studies should be conducted to investigate such associations.

Finally, we can highlight the relevance of our results in the scientific scenario, given the late diagnosis of cardiac amyloidosis and the lack of available treatment in the Brazilian public health system, as this condition has the potential for cardiovascular worsening and can affect other physiological systems. These results emphasize the importance of pharmacotherapeutic follow-up for these patients to ensure a better quality of life and may stimulate future studies on this topic.

Conclusion

The results of this study suggest that pharmacotherapeutic follow-up mediated by teleconsultation for patients with cardiac amyloidosis can improve at least one domain of the KCCQ. Despite some limitations, this study represents an awakening about the possibility of including clinical pharmacists in the care of patients with cardiac amyloidosis and the potential use of technologies for the multiprofessional follow-up of patients with chronic non-communicable diseases.

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Author Contributions

AL – Project conception, data analysis and interpretation, manuscript writing. MGG – Data analysis and interpretation, critical revision for intellectual content. SLL – Project conception, data analysis and interpretation, critical revision for intellectual content. FF – Critical revision for intellectual content.

Conflict of Interests

The authors declare no conflicts of interest regarding this article.

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