Patient and Family Experience With Transthyretin Amyloid Cardiomyopathy (ATTR-CM) and Polyneuropathy (ATTR-PN) Amyloidosis: Results of Two Focus Groups

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Abstract

Background: Patients with transthyretin amyloidosis manage a chronic, life-threatening condition that severely affects their quality of life. Although the primary symptoms and diagnostic criteria for transthyretin amyloid cardiomyopathy (ATTR-CM) and transthyretin amyloid polyneuropathy (ATTR-PN) are well established in the medical literature, very little has been published on patient and family experience of these conditions. Two focus groups, one for ATTR-CM and one for ATTR-PN, were asked to describe the diagnostic process, symptoms, and impact on quality of life that they experienced from these illnesses.

Results: Patients in both ATTR groups often experienced a long and difficult diagnostic odyssey characterized by misdiagnoses, inadequate interventions and delay in establishing the correct diagnosis leading to the specialized treatment they needed. Collectively, patients with ATTR-CM reported 26 different symptoms and patients with ATTR-PN reported 24 different symptoms. The ATTR-CM group identified intolerance to activity, inability to exercise, insomnia and fatigue as the most challenging symptoms. The ATTR-PN group identified fatigue, diarrhea/constipation, sensory symptoms as the most difficult symptoms. In general, ATTR was reported to be highly stressful for both patients and their families. Spouses of patients with ATTR-CM were often in a caregiver role and experienced considerable anxiety. Patients with ATTR-PN were stressed not only by the physical consequences of their illness, but also by its effects on their parents and other relatives, and their worry about children and grandchildren inheriting their disease-causing mutations associated with ATTR. Despite these challenges, family members were also appreciated as a source of coping, motivation, inspiration and support.

Conclusions: Several steps can be taken to reduce the challenges and burdens of living with ATTR, including more education for primary care physicians and specialists who encounter ATTR, ready access to mental health services and support, patient advisory groups to help guide clinical trials and additional studies of patients’ experience.

Background

Transthyretin amyloidosis, or ATTR, is caused by the dissociation of the transthyretin tetramer into its constituent monomers and subsequent accumulation as misfolded protein deposits, or amyloid, in organs and tissues.\(^1,2\) Transthyretin amyloid polyneuropathy (ATTR-PN) is a genetic form of the illness characterized by a generalized, length-dependent (or ascending) peripheral neuropathy involving the sensory, motor, and autonomic nervous systems. Transthyretin amyloid cardiomyopathy (ATTR-CM) is the result of amyloid deposits in the myocardium causing progressive heart failure and can occur in individuals with or without inherited mutations.\(^3,4\) All forms of TTR amyloidosis lead to reduced functionality (effort tolerance and activities of daily living) and premature death.\(^4\)

The symptoms and diagnostic criteria of ATTR amyloidosis are well established.\(^4-8\) Quality of life (QOL) of people living with ATTR has been measured by validated instruments (e.g., Kansas City
Cardiomyopathy Questionnaire; Norfolk Quality of Life Questionnaire-Diabetic Neuropathy), most often in recent interventional clinical trials studying disease-modifying agents. Studies have reported lower quality of life for people living with ATTR as compared to the general population and compared to people living with other diseases including multiple sclerosis, diabetic neuropathy, and irritable bowel syndrome.\textsuperscript{7,9} QOL scores in ATTR have been reported to decrease with worsening illness.\textsuperscript{10,11}

Despite the profound effect ATTR has on patients' lives, we know of no previous qualitative studies on the nature of patients' lived experience with the illness. The Amyloidosis Research Consortium's report on testimony to the FDA does include a highly useful thematic analysis of patient reports, however.\textsuperscript{13} Qualitative research can inform treatment providers about patients' needs and identify opportunities for improvements in patient care. The current qualitative study of responses in two focus groups with patients with ATTR-CM and ATTR-PN and their family caregivers provides new insights into the patients' lived experience of ATTR.

**Methods**

In collaboration with two patient organizations, the Northern California Amyloidosis Support Group (affiliated with the Amyloidosis Research Consortium), and the Alianza Argentina de Pacientes, we convened a focus group for ATTR-CM patients and family members in San Francisco, California, and ATTR-PN patients and their family members in Buenos Aires, Argentina. The ATTR-CM group included the following: 4 male patients with wild-type ATTR cardiomyopathy (ATTR\textsubscript{wt}-CM), 2 male patients and 1 female patient with hereditary (mutant) ATTR cardiomyopathy (ATTR\textsubscript{m}-CM), and the partners of three of the patients in the group. The ATTR-PN focus group included 10 patients and 5 family members. Several of the ATTR-PN patients also had relatives (including their children) with ATTR-PN who they referenced in their discussion of the disease. Altogether, 5 participants in the Buenos Aires group had immediate and/or extended family with ATTR-PN and 3 participants had children who had been diagnosed with ATTR-PN. Since the patient organization recruited the participants, no identifying data were collected, so ages of the participants are not known. An application for Institutional Review Board approval was made to the Western Institutional Review Board, who issued an exemption. The groups were facilitated by a licensed psychologist (first author). We developed discussion guides for semi-structured focus groups. Among the topics discussed were the following:

1. The patient's experience of seeking and establishing a correct diagnosis
2. Physical or psychological symptoms experienced
3. Impact on the quality of life of the patient and family

The format allowed time for participants to communicate freely about living with ATTR, and to express concerns about daily functioning, family relationships, and overall health. Participants in each group also participated in an exercise in which they were asked to list the symptoms of ATTR that affected their physical health and quality of life and to choose the top three that had the most effect on their lives.
The group discussions were transcribed. The Buenos Aires focus group was conducted in Spanish, and simultaneous translation was provided. Two members of the research team conducted a content analysis of the transcripts, using first cycle and second cycle coding techniques described elsewhere. Each of the two team members independently conducted preliminary *a priori* coding on both transcripts based on the interview guides while noting potential patterns and themes that would likely emerge from second cycle coding. The researchers met to compare codes and discuss emerging themes. After finalizing the coding scheme, a second cycle of coding was completed and organized into larger themes representing the greatest density of responses from participants. Three of the themes that are most closely related to symptoms and quality of life were identified as: 1) diagnostic odyssey; 2) symptoms and impact; 3) family reaction and dynamics. This article discusses these themes with support from quotes from the focus groups. Identifying information was removed or changed to protect patient confidentiality.

**Results**

Participants from both focus groups provided detailed information about what was often a long and difficult diagnostic process. They identified a wide range of symptoms stemming from the effects of ATTR and described the major impact the disease had on their quality of life. They talked openly about the stresses on their marital relationships and family as well as the ways in which these relationships helped them cope with the illness.

**Diagnostic Odyssey**

As with many people living with rare diseases, several participants in each of the focus groups reported that they endured long periods of time searching for answers, receiving misdiagnoses, and often inappropriate or ineffective treatment before their illness was accurately diagnosed. Many primary physicians, neurologists and cardiologists remain unfamiliar with ATTR and are not attuned to this disease as part of the differential diagnosis of patients’ presenting symptoms. This is common for individuals with rare diseases and is often described as the “diagnostic odyssey.”

**ATTR-CM:** The diagnostic process for ATTR-CM is often long and difficult. Patients reported that they were misdiagnosed and given inappropriate treatments, sometimes multiple times.

*It took them [the doctors] eight months before they came up with something, still out of – out of left field. They’re still off.*

*going to...my GP... and it was “we'll, give you a shot of testosterone.” It’s kind of like there’s no answer. They keep trying to find out what is wrong with you. You’re constantly trying to find what’s wrong with you*

One patient reported retrospectively finding signs of amyloidosis in previous test results.
I have good medical exams that tell me it almost certainly started in 2006 because I just had some x-rays before for other reasons, and so I know pretty much when this started.

Because the disease is rare, doctors may delay taking actions that would speed the diagnostic process:

*He [the doctor] had tissue [for a biopsy]. He could have sent it, but he doesn't do that regularly, and with good reason because it's a rare disease.*

Even when there was a suspicion of ATTR from the outset, it could take time to reach a diagnosis:

*My story's a little bit different because I knew I was gene positive before the symptoms started, so we were able to catch it pretty early... I still had to talk to multiple cardiologists and get to the point where somebody would diagnose it.*

I made an appointment with my primary care physician and he knew my history and he gave me an EKG and he says, "I see a blip here and I don't understand it." So, he referred me to a cardiologist. And from there, the in-house cardiologist suspected that I had something similar to amyloidosis, so he sought his colleagues at the...[research hospital]...and they came back and say, "It sounds like amyloidosis, but we don't know which one it is." So, I got a referral to the [research hospital], ... And I saw a hematologist...; he got right to the point. He says, "Okay...any familial involvement?" I said, "My mother." He said, "I think you have hereditary." So, at that point I had all the tests and sure enough it was – that was late.

For two patients, serendipity shortened the diagnostic odyssey. They were fortunate to have a non-physician identify ATTR when their healthcare professionals had missed the diagnosis:

*Tom [a friend] got word...about me not being able to find out what's wrong with me...He said,... you got what I got, amyloidosis. ... See [a doctor who with specialized knowledge of amyloidosis]," and she [that doctor] saved my life. Whoa, she saw my chart. She said, "Who's been diagnosing you?" She said, "No, no. You're going to need a heart right off the bat. You need a heart." She went straight to the point. I was shocked, but I was happy.*

*I went into Afib and wound up going to the emergency room...they had me have an echocardiogram, and the technician who did the echocardiogram was really the one that diagnosed me, not the doc. She told the doc "this looks like, you know" – the echocardiogram has that speckled appearance that is typical. [But initially] the doc knew nothing, and I went to see my local GP, who is a friend of mine, and...and he doesn't know that much about that kind of stuff. I just said, "Well, let's wait and see. It didn't go away." And finally, I heard back from the ER doc. He said, "It looks like amyloidosis."*

Receiving a diagnosis of ATTR-CM did not guarantee that the patient would receive appropriate treatment:
So, I kind of messed around locally... for a while, and they prescribed Metoprolol and Lisinopril, and those are not appropriate drugs for amyloidosis, and...kind of went to various docs kind of that I knew and worked around. Finally, I realize I'm not getting anywhere with this.

Patients were actively involved in the search for answers, often using the Internet as a tool. As a result, they sometimes knew more than their physicians about amyloidosis, and found a specialist themselves. One spouse was proud of her partner's burgeoning expertise:

[He] became an amyloidosis expert by looking everything up online, and he was telling... the cardiologist – his cardiologist admitted he didn't know anything about it, either.

So, I self-referred to [a research hospital]. Got into [the hospital] right away. That's a great place to go.

**ATTR-PN**: Diagnosis did not come readily for patients with ATTR-PN either. Some were diagnosed rapidly because of their family history, but others did not know their family history or did not understand it. A number of ATTR-PN patients were repeatedly misdiagnosed.

It took 3 years for a proper diagnosis. Doctors make incorrect diagnosis without hesitating. In [Name of city] a doctor said something was odd because I had an ulcer in my foot, and I wasn't diabetic; and he referred me. I lost 3 years of treatment. That's why I want the genetic test for my son, for him not to lose time.

It's kind of like there's no answer. They keep trying to find out what is wrong with you...you're constantly trying to find what's wrong with you.

I had pain in my legs and back. I thought it was my job. I saw a traumatologist and back specialist, who said I was fine, but I could not walk with the pain.

I saw many doctors. Urologist, backbone specialists, I had an MRI. A neurologist diagnosed me with amyloidosis. I got tested and the result was positive.

One patient had a family member who was diagnosed with ATTR, but doctors did not tell the family that the illness was heritable:

...one of my cousins had symptoms and went to [name of hospital in Argentina]. They said he had amyloidosis. But they didn't say it was inherited and that all the family could have it. Doctors make an incorrect diagnosis without hesitating.

Other patients knew about their family history but endured years of anxiety because they had to wait until adulthood to be tested.

I asked to have the genetic test, but I was told I should wait until I was 18. At that time, I had to wait for years, I felt very anxious about it. ...I got my genetic test at [hospital in Argentina] and it was positive. My sister-in-law was negative, and they called to tell her. I didn't get a call in two months, so I suspected I was
positive, because we were tested at the same time. Then they came home with a group of psychologists, and I knew.

I wanted to test...but had to wait until age 18...I got the results at, when my son was 6 months old. I would have prevented getting pregnant if I had known because my son could inherit the disease. I had to reach out to doctors, the doctors didn't follow up on my mother or me.

The fact that ATTR-PN manifests at different ages and under different circumstances for different family members could complicate the diagnostic process:

My sister and I have the disease, but she had it actively, and I didn't. They tested the tendon on our left legs and the result was not positive. Then they tested our stomachs and my sister got a positive result. [The doctor] called because of my aunt. I had an ulcer on my right foot. First it was just a callus, then it became a big hole. There was no solution, and it wasn't diabetes. I got a lot of tests. Then the doctor repeated the test and said the disease [ATTR-PN] was triggered because of my emotional situation.

Thus, patients and their family members in both ATTR groups often experienced a long and difficult diagnostic process. Misdiagnosis was common in both groups and seemingly unnecessary or inappropriate treatment occurred. It took time and effort in both groups to find physicians with expertise in treating the illness.

**Symptoms and Impact**

Because ATTR can affect multiple organ systems, it can lead to a variety of symptoms. ATTR-PN typically involves the sensory, motor and autonomic nervous systems to varying degrees, so patients with ATTR-PN tend to have a wide range or mixture of symptoms. People with ATTR-CM, on the other hand, suffer from chronic and progressive heart failure with its typical clinical manifestations. Participants were asked to identify the symptoms which had the greatest effect on their physical health, and those which had the greatest effect on their quality of life, defined as the ability to participate in the tasks and activities that were important to them. Patients with ATTR-CM reported 26 different symptoms and patients with ATTR-PN reported 24 different symptoms. Thirteen of those symptoms were reported in both groups. Table 1 lists the symptoms identified by patients and family members by organ system, and Figure 1 shows the frequency of symptoms within each organ system for each group.

**ATTR-CM**: Participants in the ATTR-CM focus group reported several conditions directly related to the disease’s effect on the heart including shortness of breath, atrial fibrillation, and arrhythmias. Several patients with ATTR-CM suffered from carpal tunnel syndrome. One patient with ATTR-CM experienced sharp abdominal pain, and others reported pains in their back or feet, “heavy legs” and vomiting. Male patients with ATTR-CM experienced decreased sexual interest and erectile dysfunction. Mood changes and depression were widely mentioned, as patients and family members faced an uncertain future and a dramatically reduced life expectancy. Several patients experienced insomnia.
Patients with ATTR-CM experienced dramatic loss of strength and stamina. Patients reported low energy, malaise, and “heaviness” in their limbs, ‘twitching,’ clumsiness, buckling knees, and trouble maintaining their balance. The ATTR-CM group identified intolerance to activity and inability to exercise as well as insomnia and fatigue as the most troubling symptoms they experienced. Several patients with ATTR-CM had a life-long devotion to sports and exercise that they had to curtail dramatically because of fatigue and weakness. As one spouse of an ATTR-CM patient related, “We went to Yosemite a couple years ago... it took us about fifteen minutes to go about ten feet.” The illness continually interfered with everyday tasks and with activities that brought them enjoyment. As one spouse said, “He walks our Labrador retriever every day...and he would double over from...abdominal pain...it was painful to watch him.” Even the effort to put up holiday decorations could be too much, “My wife loves Christmas decorations, so I was outside trying to put the lighted candy canes in the ground and every time I'd bend over and stand up, I'd get dizzy. [It's] just like a big effort just to stick things in the ground.”

**ATTR-PN.** Patients with ATTR-PN reported a wider range of symptoms than those with ATTR-CM. Patients and family members reported dysesthesias described as burning sensations or cold skin. They experienced both heightened sensitivity to touch, numbness, and lack of sensitivity. One patient had increased sensitivity in his upper body – “I couldn't use a towel after showering because it felt like sandpaper.” – but his feeling in his feet was so minimal that he had sprained his ankle without even realizing it. One patient had experienced multiple burns because of lack of sensitivity.

Due to autonomic dysfunction, ATTR-PN patients reported constipation, diarrhea, “lazy bladders” that did not void completely, or urinary incontinence sometimes leading to multiple urinary tract infections. Some reported blockage in their digestive system, and frequent vomiting. Decreased visual or hearing acuity was also a problem for some ATTR-PN patients. Some male patients experienced decreased sexual interest and erectile dysfunction.

Several patients experienced symptoms consistent with orthostatic hypotension and other experienced dizziness. One ATTR-PN patient reported fainting. For several ATTR-PN patients, food was no longer appetizing, they lost their appetite, experienced early satiety, or frequently had an upset stomach. At one point, one patient had lost almost half his body weight, decreasing from 200 to 135 pounds. Mood changes, depression and insomnia were also common in the ATTR-PN group.

ATTR-PN patients were forced to make dramatic changes in their employment and lifestyle. Two men who worked with their hands were forced to retire early because of the illness— one patient's numbness in his hand and bent fingers made him continually drop his tools. One patient had diarrhea so severe that he had to leave his job because he did not have a bathroom nearby.

Fatigue was identified as one of the most challenging symptoms in both groups. Otherwise, the ATTR-PN group identified gastrointestinal symptoms and sensory symptoms as having the greatest effect, which were notably different from the most impactful symptoms for the ATTR-CM group, intolerance to activity, inability to exercise, and insomnia. It should be noted that four of the symptoms identified as most impactful for ATTR-PN are related to gastro-intestinal dysfunction (chronic diarrhea, weight loss,
vomiting, and constipation), and an additional symptom (loss of muscle mass) is likely to be at least partially explained by digestive difficulties.

The Family System

The importance of the family system arose as a theme in several ways across the two focus groups. The illness was highly stressful for both patients and their families, and group members were open about the emotional sequelae of the illness. Spouses experienced considerable stress associated with the illness but also played a major role in coping with it. When patients had heritable forms of ATTR, patients experienced stress not only from the physical effects of the illness, but also from watching their parents, children and other family members cope with the illness as well.

ATTR-CM: In the ATTR-CM group, the partners’ active participation in the focus groups demonstrated the critical role that carers play in supporting their spouse's well-being. Spouses often took responsibility for the monitoring and management of medication. Patients and their spouses were sometimes overcome emotionally as they tried to come to terms with the effect of the disease on their lives:

...you spend a lot of time in that depression/mood/mortality thing wondering what your future is going to be like.

The participants talked about the fear and anxiety spouses felt.

Right of out of the blue somebody said to us "you're going to have to have a heart transplant," and ...that - - in 2013, maybe even still, that's a huge thing. It involves all kinds of preparation. Those of you who have had it probably understand the feelings that – when you first hear about it. It's terrifying, and I was just totally knocked off balance. Crying, not knowing what are we going to do. He's too young to die. I just – it's just – so my anxiety and fear is very strong

Speaking on my wife's behalf, she went through the same thing. When the cardiologist said to me "well, I think you're going to need a heart transplant and she said to me in passing "can't you just wait?" I mean, it's one of those things is fear. And I said, "Hon, it's not going to get any better," but from her mind's eye, you know, maybe if you just wait longer, maybe you won't need a heart transplant, but – it doesn't sound realistic, those were thoughts that caregivers go through…"

I can't sleep at night with worry and he's sleeping like a baby. Yes, the spouse, significant other, experiences extreme worry. Are you kidding me?

One wife's anxiety was mixed with frustration over limitations in her ability to help her husband.

I worry about him – that he has all these medications he takes. He's very concerned that he does them properly, and I – I don't know how I can help make that happen. He's very organized, so I really don't worry that much about it, but I worry that his lifestyle has changed for him so much, he gets frustrated at it -
and I hate to see that. I have anxiety -- I want him to be well...I want to reach in and take that amyloidosis outside of his heart.

Sometimes she felt guilty: "And sometimes I feel bad that I -- I'm healthy. I like being healthy."

But patients and their caregivers adapted to the limitations and that helped them cope:

...As a caregiver we tend to modify things, you know. We make it so that it works for what you're going to do. You're going to go on a hike. Well, maybe you're not going to hike ten miles. You're only going to hike one. So, you modify everything. You do that with food, as well. You don't make a big deal. You make, you know, half. So, you're only walking the one mile. You modify it so that it's not a big bone of contention.

I wouldn't call myself depressed. I think we modify so that we don't have that...I can't do the Christmas lights all at one time. Maybe I'll take three days to do it. Which is fine. You try to do as much as you can and not let this – yes, it's going to change the quality of your life, but it's not going to end having quality to your life.

Family members were invariably a source of coping, motivation, inspiration and support.

You try to do as much as you can and not let this – yes, it's going to change the quality of your life, but it's not going to end having quality to your life.

[Name of patient] is a grandfather to five beautiful children and they want Pops around for many more Christmases. So, we're in it to win it.

**ATTR-PN:** In the ATTR-PN group, much of the discussion revolved around the history of the illness in the family and its effects across family members. Heritable ATTR-PN is “a family disease” as one participant who had lost her husband to the disease observed. Patients had witnessed parents and other relatives failing to receive an accurate diagnosis and subsequently dying. Patients talked about their parents’, relatives’, and children's illness in conjunction with their own. Some asymptomatic Buenos Aires participants who attended as supportive family members felt considerable anxiety over the possibility that they might test positive, or, having already tested positive, the likelihood that they might develop the disease. The greatest concern of parents who had been diagnosed with ATTR-PN was passing the illness on to their children. Their concern about themselves paled when thinking about the diagnosis in one of their children. Some parents with ATTR-PN expressed regret over having children:

*For me, it's not hard to have a positive result, what really concerns me is my children. If I had known I had the disease, I wouldn't have had any children.*

Family members without ATTR-PN actively participated in the focus groups because they felt the impact of relatives passing away or because they were concerned about a family member who had elected not to attend the group. One group member explained her participation in this way
My father and brother have the disease. I had a negative test result. Another brother is also negative. But today I am here with my mother because of my father and brother who are positive.

Families with ATTR-PN coped with the inevitable progression of the disease in different ways. While some families worked to ensure that other members were tested, other families preferred to postpone acquiring that knowledge.

I have a 9-year-old daughter. I don’t want her to be genetically tested, because I can’t do anything about it anyway.

In my family it was a taboo topic, although we knew we could carry the disease in the family. 2 sisters died because of it. We are sure one had amyloidosis and had the genetic test done too late. Another had breast cancer. Amyloidosis has marked me forever.

They were troubled by the deaths of family members they had lost to the illness and their family’s history of misdiagnosis and inadequate care.

My mother died at 61, without knowing why. All the family died young but didn’t know why.

My mother died of [the] disease when I was 17. I started with symptoms at 25. My mother was wrongly diagnosed with psychiatric problems. Now we know it was amyloidosis.

My mother died at 55. Doctors said she was crazy. She had surgeries and remained the same. They did not discover the disease.

I inherited the condition from my mother’s side. Uncles and grandparents died because of it, but without knowing why. We had wrong diagnosis. My mother was diagnosed with multiple sclerosis, and uncles with other conditions.

Yet family was also the motivation to continue to battle their illness...

My daughter is positive. I wanted to know, and I want to continue until there is a solution for her.

I’m married, two kids, 10 and 5; that’s the kind of reason to stick around.

Discussion

The demands of living with ATTR and managing its effects are considerable for patients and their families. In order for clinicians to understand how best to treat patients, and for researchers to design clinical trials that are optimally meaningful and clinically successful, it is important to understand the patients’ and family members’ experiences. To the best of our knowledge, this is the first study that reports the lived experience of amyloidosis patients and their families.
Patients with ATTR-CM and ATTR-PN experience a wide range of debilitating symptoms that have a profound effect on their ability to function and participate in activities of daily life. Their reports are consistent with information on symptoms from previous studies.\textsuperscript{4-8} Patients with ATTR typically underwent a long, confusing and uncertain diagnostic odyssey in which they experienced symptoms with no explanation and inadequate treatment. Patients with ATTR-PN often witnessed their families undergoing a diagnostic odyssey, and then experienced their own diagnostic challenge. Sometimes patients did not know or understand their family history or were not told by doctors about its importance. At other times, they realized they could have the illness but had to wait to be tested. Or they had tested positive but had to wait to see if the disease emerged. Accurate diagnosis did not automatically lead to appropriate treatment. Many patients went through multiple steps just to find the treatment they needed in a specialized center requiring long distance travel.

The courage and fortitude of these people living with ATTR and their families is evident. Their experience should serve to offer several lessons about how to reduce their arduous challenges. First, more education is needed for physicians and specialists who may unknowingly treat ATTR patients, are unfamiliar with the early signs and symptoms or may not be aware of advances in the field relating to diagnosis, treatment options and ongoing clinical trials. Knowing when to evaluate or refer to subspecialists (e.g., cardiologists, gastroenterologists, and urologists) is also an important learning for the continued health and well-being of these amyloidosis families and the patients themselves. This could reduce the likelihood that patients undergo a protracted diagnostic odyssey or at least shorten its duration. Second, patients with ATTR amyloidosis need ready access to mental health services and informal sources of support such as support groups and patient advocates. Third, greater access and awareness of patient advocacy groups is needed to help guide clinical trials and other treatment options. Such groups help to hold professionals accountable for intervening in ways most attuned to patients’ needs. Fourth, additional studies of the experience of patients can help health care providers gain a greater understanding of this still inadequately understood disease and inform institutions about simple methods to address patients’ needs and lessen patients’ stress.

This study has limitations that need to be considered. The focus groups were small convenience samples consisting of patients who were known to patient organizations and may not be representative of all patients with ATTR, particularly those who do not participate in these organizations. Some patients expressed themselves more in the focus groups than other patients, so every patient’s experience was not necessarily represented equally. Despite these limitations, these focus groups provide a broad preliminary look at the lived experiences of patients with ATTR and their families.

The results of our study may serve to provide preliminary information for a conceptual model of the effects of ATTR on patients’ lives. Conceptual models have the potential to elucidate the effects of a disease helping to elaborate the causal relationships linking symptoms, functioning, health perceptions and quality of life.\textsuperscript{15} A conceptual model can inform the development of patient-reported outcomes (PRO) measures for future clinical trials\textsuperscript{16} and ultimately promote the design of effective treatments.\textsuperscript{14} Using published studies, patient and expert interviews, and patient blogs, Lin and colleagues developed a
conceptual model of the manifestations of AL amyloidosis.\textsuperscript{16} Many of the symptoms and impacts included in Lin and colleagues’ conceptual model are similar to those of the current study. As data on patients’ experience of ATTR accumulate, we recommend the development of a conceptual model for this form of amyloidosis.

The impact of amyloidosis is enormous for families with ATTR-PN, who deal with the effect of the illness on multiple generations and the dynamics of an entire extended family living at risk. It is also substantial for families with ATTR-CM because of its emotional effects on spouses and the caregiving role it often thrusts them into. Professionals need to develop a more sophisticated understanding of the family dynamics of the illness and provide more substantive support to family members as well as patients. Professionals also need to ally with families because of their importance in helping patients adapt to changes in their functioning and coping strategies given the social and emotional toll of TTR amyloidosis.

**Conclusion**

Our clinical understanding of TTR amyloidosis is expanding rapidly and our understanding of the effects of the illness on patients’ lives needs to keep pace. Patient groups are an important resource both to support patients and their families and to provide critical information to treatment providers and clinical researchers. The stories of the patients and family members living with the illness are an essential asset for understanding how best to respond to the illness.

**Abbreviations**

- ATTR-CM: Transthyretin Amyloid Amyloidosis with Cardiomyopathy
- ATTR-PN: Transthyretin Amyloidosis with Polyneuropathy
- QOL: Quality of Life
- GP: General Practitioner
- ATTR: Transthyretin Amyloidosis
- Afib: Atrial fibrillation
- EKG: Electrocardiogram

**Declarations**

Ethics approval and consent to participate
An application for Institutional Review Board approval was made to the Western Institutional Review Board, who determined that this study was exempt from IRB approval. All participants signed a consent to participate in the focus groups.

**Consent for publication**

Not applicable

**Availability of data and materials**

The data that support the findings of this study are available on request from the corresponding author DR. The data are not publicly available due to information that could compromise research participant privacy/consent.

**Competing interests**

The authors declare that they have no competing interests

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**Authors’ contributions**

David Rintell wrote focus group manual, conducted focus groups, oversaw project, writing, editing

Dena Heath recruited participants for the study, reviewed drafts of the paper, and provided advice and guidance to the project

Florence Braga Menendez recruited participants for the study, reviewed drafts of the paper, and provided advice and guidance to the project

Elizabeth Cross and Theodore Cross performed qualitative analysis of the data produced through conducting the focus group

Vincent Knobell and Bruno Gagnon supported the planning, focus group manual, and conducting of the focus group, and presented information at the focus groups

Cameron Turtle, Alan Cohen and Jonathan Fox conceptualized and planned the study, oversaw the activities of the study, and carefully edited and suggested changes in the manuscript. Dr. Fox presented information at the focus groups.

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### Tables

#### Table 1:

| Symptoms Reported by Organ System | ATIR-CSM | ATIR-FN |
|-----------------------------------|----------|---------|
| Cardiac                           |          |         |
| Anychthmia                        | ✓        | ✓       |
| Atrial Fibrillation               | ✓        |         |
| Enlarged heart                    |          |         |
| Fluid retention/Swelling          | ✓        |         |
| "Hunting" own heartbeat           | ✓        |         |
| Increased fatigue with altitude   | ✓        |         |
| Intolerance to activity           | ✓        |         |
| Orthostatic hypotension           |          |         |
| Passing out/painting              | ✓        |         |
| Shortness of breath               | ✓        |         |
| Gastrointestinal                  |          |         |
| Abdominal pain                    | ✓        |         |
| Bloating                          |          |         |
| Bowel problems                    | ✓        |         |
| Changes in taste of food/loss of taste in food | ✓ |         |
| Constipation                      | ✓        | ✓       |
| Diarrhea (chronic)                |          |         |
| Feeling full quickly              | ✓        |         |
| Loss of appetite                  | ✓        |         |
| Low bloated obesity/"slow digestion" | ✓ |         |
| Painful feeling in mouth          | ✓        |         |
| Upset stomach                     | ✓        |         |
| Vomiting                          | ✓        |         |
| Weight loss                       | ✓        | ✓       |
| Integumentary                     |          |         |
| Night sweats                      | ✓        |         |
| Rash                              | ✓        |         |
| Musculoskeletal                   |          |         |
| Back pain                         | ✓        |         |
| Balance when walking              | ✓        | ✓       |
| Bi Lateral Carpal Tunnel          |          |         |
| Chillingness/Dropping tools       | ✓        |         |
| Contracture of fingers            |          |         |
| Heaviness in legs                 | ✓        |         |
| Inability to exercise             | ✓        |         |
| Loss of muscle mass               | ✓        |         |
| Loss of muscle tone               | ✓        |         |
| Loss of stability                 | ✓        |         |
| Muscle twitching, cramps and spasms | ✓ |         |
| Weakness                          | ✓        |         |
| Weakness/Knee buckling            |          |         |
| Neurological                      |          |         |
| Burning sensation in feet and hands | ✓ |         |
| Cold skin, hands, feet            |          |         |
| Decreased sensitivity             |          |         |
| Dizziness                         | ✓        | ✓       |
| Dry eyes                          |          |         |
| Essential Dysfunction             | ✓        | ✓       |
| Fatigue                           |          |         |
| General malaise                   | ✓        | ✓       |
| Hearing loss                      |          |         |
| Heat intolerance                  | ✓        |         |
| Increased sweating               |          |         |
| Lower back pain                   | ✓        |         |
| Memory loss                       |          |         |
| No sensation with full bladder    |          |         |
| Numbness in hands                 |          |         |
| Pain in feet                      | ✓        |         |
| Pain and needles                  |          |         |
| Reduced sexual desire             |          |         |
| Sensitive to touch/numbness       | ✓        | ✓       |
| Urinary incontinence (nocturia)   |          |         |
| Urinary retention                 |          |         |
| Vision impairment                 | ✓        |         |
| Psychiatric                       |          |         |
| Depression                        | ✓        | ✓       |
| Mood changes                      |          |         |
| Sleep disorders/insomnia          |          |         |

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**Figures**

![Bar chart showing reported symptoms by organ system for ATTR-CM and ATTR-PN](image)

**Figure 1**

ATTR-CM & ATTR-PN Reported Symptoms by Organ System.