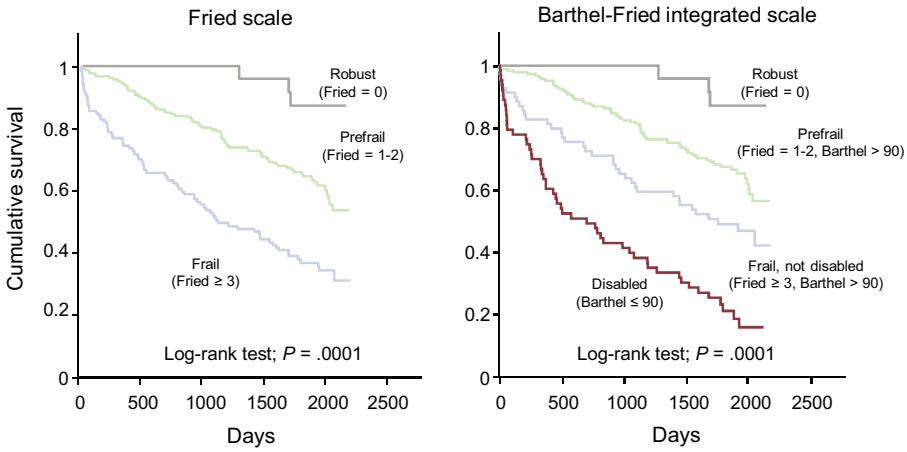

Figure 2. Risk stratification according to frailty using the Fried score (left), and according to the Barthel-Fried integrated scale (right).

All disabled patients were also frail, while 100 out of 279 (36%) nondisabled patients were frail. Accordingly, we built a new scale integrating disability and frailty: disabled (Barthel $\leq$ 90, n = 63), frail nondisabled (Green $\geq$ 5, Barthel $>$ 90, n = 100) and robust (Green $<$ 5, Barthel $>$ 90, n = 179). The mortality rate progressively decreased from disabled, to frail nondisabled, and robust categories: 81%, 56% and 27% (log-rank test; P = .0001, Figure 1). Likewise, mortality risk progressively decreased after adjustment for the clinical model (compared with the disabled subgroup; frail nondisabled: hazard ratio, 0.70; 95% confidence interval, 0.47-1.05; P = .08; robust: hazard ratio, 0.41; 95% confidence interval, 0.25-0.66; P = .0001). The integrated frailty/disability scale also performed well using the predefined categories of robust, prefrail and frail, in the Fried scale (Figure 2).[5]

This study proposes a simple geriatric scale, integrating frailty and disability, which has proven to be of prognostic value after acute coronary syndrome. The scale attempts to optimize patient classification according to age-related vulnerability.

There is little information about the Barthel index as a prognostic factor in acute coronary syndromes. In our population, only 18% of the patients had at least moderate disability (Barthel index $\leq$ 90 points). This might reflect the selection bias of patients admitted to a cardiology ward. The small number of disabled patients would explain the lack of predictive value of the Barthel index. However, the incorporation of the disabled subgroup into the frail classification provided a more comprehensive risk gradient. Disabled patients had the highest mortality risk, followed by frail and robust patients. Therefore, the main contribution of the integrated scale, unlike the simple frailty scale, is the distinction between high (disabled) and intermediate (frail but nondisabled) risk subgroups. Additionally, categorization of the nondisabled patients into frail and nonfrail subgroups was also useful for risk stratification. Our study confirms that disability and frailty can be considered in aggregate and result in a gradation in long-term outcomes after acute coronary syndrome. Conceivably, frailty scales other than Green's and Fried's, using alternative definitions of frailty, might also fit this mixed frailty/disability scale.

A major concern is to decide on the best management of these patients. Potentially, geriatric assessment might lead to a more personalized approach to the elderly patient with acute coronary syndrome. Further trials targeting elderly patients with geriatric conditions and acute coronary syndrome are warranted.[6]

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Juan Sanchis,[a,*] Vicente Ruiz,[b] Albert Ariza-Solé,[c] Arantxa Ruescas,[d] Clara Bonanad,[a] and Julio Núñez[a]

[a]*Servei de Cardiologia, Hospital Clínic Universitari, Institut d'Investigació Sanitària Clínic València (INCLIVA), Universitat de València, Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Valencia, Spain*
[b]*Facultat d'Infermeria, Universitat de València, Valencia, Spain*
[c]*Servei de Cardiologia, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain*
[d]*Departament de Fisioteràpia, Universitat de València, Valencia, Spain*

* Corresponding author:
E-mail address: sanchis_juafor@gva.es (J. Sanchis).

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REFERENCES

1. Muruet W, Rudd A, Wolfe CDA, Douiri A. Long-term survival after intravenous thrombolysis for ischemic stroke: A propensity score-matched cohort with up to 10-year follow-up. *Stroke.* 2018;49:607–613.
2. van Kan AG, Rolland YM, Bergman H, Kritchevsky SB, Vellas B. The I.A.N.A. task force on frailty assessment of older people in clinical practice. *J Nutr Health Aging.* 2008;12:29–37.
3. Sanchis J, Bonanad C, Ruiz V, et al. Frailty and other geriatric conditions for risk stratification of older patients with acute coronary syndrome. *Am Heart J.* 2014;168:784–791.
4. Sanchis J, Ruiz V, Bonanad C, et al. Prognostic value of geriatric conditions beyond age after acute coronary syndrome. *Mayo Clin Proc.* 2017;92:934–939.
5. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci.* 2001;56:M146–M156.
6. Sanchis J, Ariza-Solé A, Abu Assi E, et al. Invasive versus conservative strategy in frail patients with non-ST elevation myocardial infarction: The MOSCA-FRAIL Clinical Trial. *Study design Rev Esp Cardiol.* 2019;72:154–159.

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Val30Met Familial Amyloid Polyneuropathy, Heart Failure, and Chylous Ascites: An Unexpected Combination

Polineuropatía amiloidótica familiar Val30Met, insuficiencia cardiaca y ascitis quilosa: una combinación inesperada

To the Editor,

Hereditary transthyretin-related amyloidosis (ATTR) with Val30Met mutation (V30 M) is the most common form of familiar amyloid polyneuropathy (FAP). Although usually considered mainly a neurological disease, cardiac involvement is increasingly recognized. We describe a patient with endemic-type V30M-FAP admitted for decompensated congestive heart failure (HF) with impressive cardiac involvement and an extremely rare complication with chylous ascites (CA). We discuss the phenotypic variability of ATTR, the mechanisms that explain CA in HF and the challenging management of patients with severely impaired cardiac compliance.

We present the case of a 70-year-old Portuguese man with endemic-type V30M-FAP. The disease presented 10 years previously (late-onset) with polyneuropathy. The patient was the index case in his family, although his father was an asymptomatic mutation carrier. Past medical history included atrial fibrillation, pacemaker implantation due to atrioventricular block, chronic kidney disease, and New York Heart Association class II HF with no previous hospitalizations. He was transferred to our center due to decompensated HF. In the previous month, he developed generalized edema unresponsive to oral diuretics, rapidly worsening dyspnea, and symptomatic orthostatic hypotension. Upon arrival, he was in anasarca with tension ascites and needed urgent paracentesis. Surprisingly, the peritoneal liquid had a milky appearance and its analysis revealed high triglycerides (444 mg/dL; triglycerides serum-to-ascites ratio: 3.2) meeting criteria for CA. N-terminal pro-B-type natriuretic peptide was extremely high (140 454 pg/mL). Echocardiography revealed severely increased biventricular wall thickness (maximal at the interventricular septum with 30 mm), moderate systolic impairment, low systolic tissue velocities, and small pericardial effusion. The myocardium had a granular appearance compatible with infiltration (Figure A).

After this initial evaluation we struggled to understand our findings. The striking cardiac involvement was atypical for V30 M and had been "silent" with no previous HF decompensations, and the CA did not seem to fit in this clinical puzzle. Given these discrepancies, we decided to exclude any underlying disease that could explain the CA and also contribute to the myocardial infiltration.

Thoracic-abdominal-pelvic tomography showed diffuse severe ascites causing intestinal compression but ruled out neoplastic, obstructive, or lymphatic causes of CA (Figure B). Scintigraphy with ^{99m}Tc-3,3-diphosphono-1,2-propanodicarboxylic acid revealed severe myocardial tracer uptake that was strongly suggestive of ATTR deposition and made other infiltrative causes and hypertrophic cardiomyopathy unlikely (Figure C). Extensive laboratory work-up was also negative. After reviewing the literature for similar cases, we assumed CA caused by HF as a diagnosis of exclusion.

Fluid management was difficult due to symptomatic hypotension with small increases in intravenous loop diuretics. Balance was achieved by using subcutaneous (SC) furosemide combined with metolazone and spironolactone, scheduled paracentesis and fluid intake restrictions. The patient slowly improved and was discharged after 3 weeks. At home, he self-administered SC furosemide using a SC catheter changed every week.

Because of wide genotypic and phenotypic variability, ATTR is still a challenging diagnosis. V30M-FAP is the most common

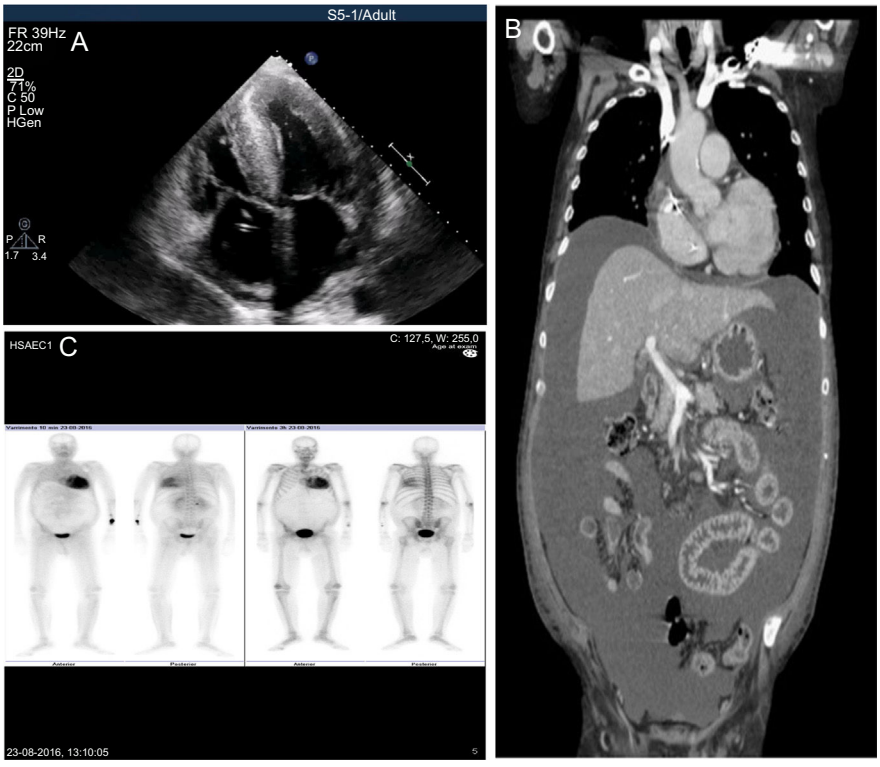

Figure. A: echocardiography: severe hypertrophy, biatrial enlargement, pericardial effusion and myocardial granular appearance. B: thoracic-abdominal-pelvic tomography: large diffuse ascites with intestinal compression. C: DPD-scintigraphy: severe tracer uptake in the myocardium and carpal tunnel. DPD, ^{99m}Tc-3,3-diphosphono-1,2-propanodicarboxylic acid.

mutation and neurological manifestations usually dominate the clinical picture. Heart involvement is most frequently related to conduction abnormalities but infiltration (usually mild to moderate) and diastolic dysfunction have been increasingly reported, mainly in late-onset and sporadic cases.[1–3] This highlights the need for systematic echocardiographic screening in all V30M-FAP patients. The severe cardiac infiltration seen here is atypical for endemic-type V30M-FAP and warrants the exclusion of other causes for cardiac hypertrophy or infiltration.

^{99m}Tc-3,3-diphosphono-1,2-propanodicarboxylic acid-scintigraphy is useful given its high sensitivity and specificity for TTR-amyloid. The high visual score obtained confirmed that the severe cardiac infiltration was caused by TTR-amyloid deposition, although it cannot distinguish between mutated and wild-type TTR-amyloid forms.[1]

CA related to HF is extremely rare. A PubMed search retrieved only 6 relevant articles and, to our knowledge, this is the first report of the association between ATTR cardiac amyloidosis and CA. The underlying mechanism relates to high venous pressures that cause increased abdominal lymph production (secondary also to augmented capillary filtration) and reduced thoracic lymphatic drainage due to the high pressures in the left subclavian vein.[4,5] HF should be considered in the differential diagnosis of CA in suitable patients.

Third-space fluid removal was quite challenging in this case. The normal initial depletion of intravascular volume by loop diuretics could not be counteracted by the autonomic nervous system and angiotensin-aldosterone system since these were impaired. The failure of compensation mechanisms, combined with the small and noncompliant ventricular cavity, caused abrupt decreases in preload with diuretic usage. This led to diminished cardiac output that induced symptomatic hypotension and thus prevented sufficient fluid removal. Careful diuretic dosing and SC furosemide were crucial to overcome the decreased oral absorption and improve edema. Using an elastomeric pump for SC furosemide infusion would also be effective.[6]

In conclusion, this case is remarkable because of 3 important messages: *a)* The late-onset and exuberant cardiac infiltration are uncommon in endemic-type V30M-FAP. *b)* HF is an extremely rare cause of CA and should be a diagnosis of exclusion. *c)* Impaired compliance creates a challenge to achieving diuretic dosing that permits third-space fluid removal without major intravascular depletion. Using SC furosemide can be very helpful.

Maria Trêpa,[a,*] Raquel Baggen Santos,[a] Marta Fontes Oliveira,[a] Inês Silveira,[a] Joana Pires,[b] and Severo Torres[a]

[a]*Cardiology Department, Centro Hospitalar do Porto, Porto, Portugal*
[b]*Medicine Department, Centro Hospitalar do Baixo Vouga, Aveiro, Portugal*

* Corresponding author:
E-mail address: maria_trp@hotmail.com (M. Trêpa).

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REFERENCES

1. Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. *Orphanet J Rare Dis.* 2013;8:31.
2. Rapezzi C, Quarta CC, Riva L, et al. Transthyretin-related amyloidoses and the heart: a clinical overview. *Nat Rev Cardiol.* 2010;7:398–408.
3. Ripoll-Vera T, Buades J, Cisneros E, et al. Cardiac Involvement in a Patient Cohort With Val30Met Mutation Transthyretin Amyloidosis. *Rev Esp Cardiol.* 2019;72:92–94.
4. Hurley MK, Emiliani VJ, Corner GM, Patel A, Navarro C, Maiki CO. Dilated cardiomyopathy associated with chylous ascites. *Am J Gastroenterol.* 1989;84:1567–1569.
5. Ridruejo E, Mandó OG. Chylous ascites as the main manifestation of left ventricular dysfunction: a case report. *BMC Gastroenterol.* 2005;5:25.
6. Zatarain-Nicolás E, López-Díaz J, Fuente-Galán L, et al. Subcutaneous infusion of furosemide administered by elastomeric pumps for decompensated heart failure treatment: initial experience. *Rev Esp Cardiol.* 2013;66:1002–1004.

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Thrombotic and Bleeding Events After Percutaneous Coronary Intervention in Out-of-hospital Cardiac Arrest With and Without Therapeutic Hypothermia

Eventos trombóticos y hemorrágicos después de una intervención coronaria percutánea tras parada cardiaca extrahospitalaria con y sin hipotermia terapéutica

To the Editor,

Mild therapeutic hypothermia (MTH) has been linked to an increased risk of both thrombotic and bleeding events in comatose survivors after out-of-hospital cardiac arrest (OHCA) and in patients with acute coronary syndrome (ACS) after OHCA who undergo percutaneous coronary intervention (PCI).[1,2] Controversially, MTH is associated with an increased risk of stent thrombosis (ST).[3] The postcardiac arrest (CA) state by itself might increase the thrombotic/bleeding risk regardless of MTH, so that the clinical effects of MTH by itself have been debated.[3,4] Thus, the aim of this study was to assess the incidence of thrombotic/bleeding events in patients with ACS after an OHCA, depending on whether they received MTH.

This was a single-center observational study. We screened consecutive patients admitted to our hospital between 2005 and January 2016 with ACS and OHCA undergoing PCI. Since 2010, the MTH protocol has been used in our center for comatose patients after OHCA of presumed cardiac cause regardless of the initial rhythm. We compared outcomes in these patients with those in other patients not undergoing MTH from 2005 to 2009.

Exclusion criteria included OHCA patients with contraindications for MTH (pregnancy, temperature on admission $< 30\ ^{\circ}C$, the use of coumadin products, previous use of a fibrinolytic, suspected or known acute intracranial hemorrhage, or stroke), and patients who died before the index procedure. The study was approved by the Ethics Committee of our center (retrospective data collection).

All surviving OHCA patients with high suspicion of ACS (electrocardiogram changes, initial shockable rhythm, or previous chest pain) were admitted to the cardiac catheterization laboratory. Patients were treated with aspirin and heparin. PCI was attempted if there was an acute coronary atherothrombotic lesion. A loading dose of $P2Y_{12}$ inhibitors was crushed and administered by nasogastric tubing immediately after PCI. The loading dose was followed by a maintenance dose. Since 2010, patients received MTH to 33 °C according to the local intensive cardiac unit protocol.

The primary endpoint was the occurrence of thrombotic events including definite and probable ST, as well as the incidence of bleeding events according to the Bleeding Academic Research Consortium criteria during hospitalization.

From 2005 to 2016, 204 patients were treated after OHCA in the intensive cardiac unit. Of these, 145 had an ACS. From 2005 to