

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.

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Available online 5 June 2018

REFERENCES

- Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. *Orphanet J Rare Dis*. 2013;8:31.
- Rapezzi C, Quarta CC, Riva L, et al. Transthyretin-related amyloidosis and the heart: a clinical overview. *Nat Rev Cardiol*. 2010;7:398–408.
- 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.
- 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.
- Ridruejo E, Mandó OG. Chylous ascites as the main manifestation of left ventricular dysfunction: a case report. *BMC Gastroenterol*. 2005;5:25.
- 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.

<https://doi.org/10.1016/j.rec.2018.04.019>

1885-5857/

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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 cardíaca 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 °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 P2Y₁₂ 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

2009, 40 patients (38%) did not received MTH, whereas from 2010 to 2016, 105 patients (62%) were treated with MTH. Baseline clinical and procedural characteristics are presented in Table 1. During hospitalization, no differences among groups were seen for thrombotic events, any or major bleeding, and mortality (Table 2). All ST occurred in patients receiving clopidogrel. In those patients who received clopidogrel there were no significant differences in the incidence of ST with MTH: 14% vs no MTH 8.8%; $P = .52$. In a multivariable logistic regression model incorporating covariates such as MTH, thromboaspiration, stent type, and clopidogrel use, MTH was not a significant predictor of ST with an adjusted odds ratio, 1.1; 95% confidence interval, 0.24–4.95; $P = .89$.

The incidence of ST in OHCA patients has been poorly studied with variable results ranging from 1.4 to 45.5% in small series.³ This study shows a high incidence in ST in OHCA patients after PCI (6.8% overall). In most studies, the relationship between MTH and ST is studied without an OHCA patient control group not undergoing MTH.

Our study did not show a higher incidence of thrombotic events in patients under MTH compared with the control group, similar to a previous report³ suggesting that the post-CA state by itself could be the trigger for ST. In the present study, the new P2Y₁₂ inhibitors were used more often in the last years. Previously, our group has reported a reduction in the incidence of ST in patients with ACS after OHCA and MTH with the use of ticagrelor compared with clopidogrel.⁵ The present study shows high rates of any and major bleeding events (11%) in ACS patients after OHCA undergoing PCI. There were no differences depending on the use of MTH. The bleeding rate in patients is in keeping with that of previously published studies in OHCA patients.² Thus, the clinical effects of MTH in addition to the post-CA state remain controversial. The comatose state of patients hampers the administration of oral P2Y₁₂ inhibitors, and multiorgan failure can result in delayed absorption and metabolism of antiplatelet drugs and a subsequent increased risk of ST. OHCA patients often present with acidosis, tissue damage, and high levels of intrinsic or therapeutically

Table 1
Baseline Clinical and Procedural Characteristics

	Hypothermia (n = 105)	No hypothermia (n = 40)	P
Age, y	57.2 ± 10.8	62.5 ± 12.6	.015
Male sex	90 (85.7)	34 (85)	.91
Smoking	50 (47.6)	19 (47.5)	.99
Hypertension	44 (41.9)	19 (47.5)	.54
Diabetes mellitus	19 (18.1)	6 (15)	.65
Hypercholesterolemia	44 (41.9)	16 (40)	.26
Renal failure	6 (5.7)	3 (7.5)	.24
Initial shockable rhythm	81 (77.1)	26 (65)	.13
ST-segment elevation myocardial infarction	84 (80)	29 (72.5)	.33
Postresuscitation shock	71 (67.6)	29 (72.5)	.57
LVEF	42.9 ± 1633	41.3 ± 13	.66
Culprit coronary artery			.90
LAD	46 (43.8)	19 (47.5)	
LCX	27 (25.7)	8 (20)	
RCA	29 (27.6)	12 (30)	
Other	3 (2.9)	1 (2.5)	
Grace risk score	158.2 ± 35	165.0 ± 42.9	.55
Crusade risk score	20.6 ± 9.6	23.8 ± 17	.48
TIMI flow 0–1 pre-PCI	73 (69.5)	34 (85)	.26
TIMI flow 3 post-PCI	92 (87.6)	35 (87.5)	.53
Femoral access	54 (51.4)	33 (82.5)	.001
Thromboaspiration	50 (47.6)	12 (30)	.05
Heparin doses (U)	7542 ± 2068	7100 ± 1816	.64
Glycoprotein IIb/IIIa receptor inhibitors used	13 (21.3)	6 (18.7)	.77
Anti P2Y ₁₂ inhibitor regimen			.001
Clopidogrel	57 (54.3)	37 (92.5)	
Ticagrelor	42 (40)	2 (5)	
Prasugrel	6 (5.7)	1 (2.5)	
Number of implanted stents	1.28 ± 0.52	1.25 ± 0.43	.78
Patients treated with DES	43 (41)	6 (15)	.003
Maximum stent diameter, mm	3.72 ± 1.83	3.33 ± 1.73	.30
Total stent length, mm	23.4 ± 10.2	20.7 ± 4.9	.12
Bifurcation lesions	14 (18.7)	6 (15.4)	.66
No reflow	9 (9.2)	5 (12.5)	.55
IABP	19 (18.1)	7 (17.5)	.20

DES, drug-eluting stent; IABP, intra-aortic balloon pump; LAD, left descending artery; LCX, left circumflex artery; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; RCA, right coronary artery; TIMI, Thrombolysis In Myocardial Infarction.

Data are expressed as No. (%) or mean ± standard deviation.

Table 2
Outcomes

	Hypothermia (n = 105)	No hypothermia (n = 40)	P
Thrombotic events			
Stent thrombosis	7 (6.7)	3 (7.5)	.86
Deep vein thrombosis/pulmonary embolism	4 (3.8)	1 (2.5)	.69
Total thrombotic events	11 (10.4)	4 (10)	.93
Bleeding			
Any	24 (22.9)	8 (20)	.71
BARC type 3 or 5	12 (11.4)	4 (10)	.80
Gastrointestinal	9	2	
Cerebral	2	1	
Alveolar	1	0	
Vascular access	0	1	
Mortality	29 (27.6)	16 (40.0)	.15

BARC, Bleeding Academic Research Consortium.
Data are expressed as No. (%).

administered catecholamines that might facilitate hemorrhagic complications.

The present study has several limitations. It is a single-center nonrandomized study that includes patients treated in a long period and heterogeneous groups with changes in treatment protocols (MTH, thromboaspiration, radial access, new P2Y₁₂ inhibitors, drug-eluting stents). The MTH group showed a reduction in mortality. These patients were those included in the last years of the study and probably benefited from advances in the treatment. Although this reduction was not statistically significant, this was probably due to the small sample size of this study.

In conclusion, the incidence of thrombotic/bleedings events in this study was high in patients with ACS undergoing PCI after an OHCA. The use of MTH was not associated with an increased risk of thrombotic/bleeding events. The results are hypothesis-generating and there is a need for further randomized data.

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Available online 26 May 2018

REFERENCES

1. Penela D, Magaldi M, Fontanals J, et al. Hypothermia in acute coronary syndrome: brain salvage versus stent thrombosis? *J Am Coll Cardiol*. 2013;61:686–687.
2. Rosillo SO, Lopez-de-Sa E, Iniesta AM, et al. Is therapeutic hypothermia a risk factor for stent thrombosis? *J Am Coll Cardiol*. 2014;63:939–940.
3. Shah N, Chaudhary R, Mehta K, et al. Therapeutic hypothermia and Stent Thrombosis. *JACC Cardiovasc Interv*. 2016;9:1801–1811.
4. Aboal J, López de Sá E, Martín-Asenjo R, Masip J, Sionis A. Selection of the Best of 2017 on Acute Cardiac Care. *Rev Esp Cardiol*. 2018;71:123–124.
5. Jiménez-Brítez G, Freixa X, Flores-Umanzor E, San Antonio R, Caixal G, García J. Out-of-hospital cardiac arrest and stent thrombosis: Ticagrelor versus clopidogrel in patients with primary percutaneous coronary intervention under mild therapeutic hypothermia. *Resuscitation*. 2017;114:141–145.

<https://doi.org/10.1016/j.rec.2018.04.022>
1885-5857/

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