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Effects of Hypothermia on Left Ventricular Ejection Time: Case Report and Review of The Literature

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Abstract

Accidental hypothermia is a relatively rare condition, whereas therapeutic hypothermia is commonly used for resuscitated patients. However, cardiac effects of hypothermia are still incompletely understood, in particular echocardiographic changes remain poorly evaluated. We report the case of a 66-year-old man who underwent unintentional hypothermia. His electrocardiogram showed sinus bradycardia and Osborn J waves. The most remarkable echocardiographic abnormality was a prolonged left ventricular ejection time, whereas other echocardiographic parameters were within normal range, especially a preserved left ventricular systolic function. Electrocardiographic and echocardiographic changes were reversible after rewarming.

We compared tissue Doppler measurements of our hypothermic patient with his own control echocardiography after recovery and with a healthy normothermic patient with similar heart rate. Comparative pictures helped highlight the differences in distribution of cardiac cycle phases.

Prolonged left ventricular ejection time might be a specific echocardiographic finding in hypothermia, since it has not been described in other clinical conditions. Our observations are consistent with previous reported data and may be of clinical relevance for the diagnosis and therapeutic management of hypothermic patients. Indeed, the prolongation of systole at the expense of diastole during hypothermia might induce an impaired left ventricular filling and a potential diastolic dysfunction. This case report is interesting as it relates to an ambulatory patient, thus with no confounding hemodynamic modification induced by vasoactive drugs, mechanical ventilation or previous cardiac injury.

Introduction

Accidental hypothermia is a relatively rare condition. Cardiac effects of hypothermia have been studied in animal models or in humans especially during therapeutic hypothermia, which has been shown to improve neurological and cardiac outcome in critically ill patients, including resuscitation after cardiac arrest [1]. Although electrocardiographic abnormalities induced by hypothermia are well known, echocardiographic changes have been less evaluated. We describe herein electrocardiographic and echocardiographic data from a patient who suffered from unintentional hypothermia. The interest of this case report lies in the fact that the patient was not under any medication that could interfere with echocardiographic parameters.

Case report

In January 2018, a 66-year-old African man was admitted in neurovascular intensive care unit for suspicion of stroke because of psychomotor retardation, dysphasia, initially decreased verbal fluency and then mutism. However, brain MRI excluded any ischemic or hemorrhagic stroke and electroencephalogram argued in favour of a metabolic or toxic encephalopathy.

Indeed, the patient's body temperature, measured at the tympanic membrane, was 33°C (91.4°F), which could explain his neurological symptoms. He had no prior illness and took no medications. He was homeless and usually housed by family or friends but nobody could say where he was in the hours before his hospital admission. His hypothermia was therefore probably induced by time spent outdoors.

Physical examination showed normal blood pressure (111/77 mmHg) and bradycardia (40 beats per minute). Apart from hypothermia and neurological signs, there was no other physical abnormality. Laboratory results found no electrolytic disorders (serum sodium level 141 mmol/l, serum potassium level 3.6 mmol/l and creatinine 72 µmol/l) and no toxic in the urine test. They only indicated a mild hyperglycemia (glycemia 9.7 mmol/l then 6.7 mmol/l but A1C 5.6%), a mild inflammatory syndrome (CRP 63 mg/l and fibrinogen 7.7 g/l but white blood cells 4 700 /mm^3 and sterile blood cultures), an isolated moderate thrombocytopenia (platelets 79 000 /mm^3), a mild hepatic cytolysis (ASAT 49 U/l, ALAT

42 U/l and GGT 87 U/l), a mild increased serum level of CPK and LDH (217 U/l and 244 U/l respectively) and folate deficiency (folic acid 3.4 nmol/l). Cardiac biomarkers were normal (HS troponin T 6.4 pg/ml and NT-pro-BNP < 50 pg/ml).

His electrocardiogram (figure 1) displayed sinus bradycardia (heart rate of 37 beats per minute), first degree atrio-ventricular block (PR interval 220 ms) with no other conductive disorder (QRS complex duration 104 ms, QRS axis 70°), mild prolonged QT interval (576 ms measured / 454 ms corrected) and Osborn J waves.

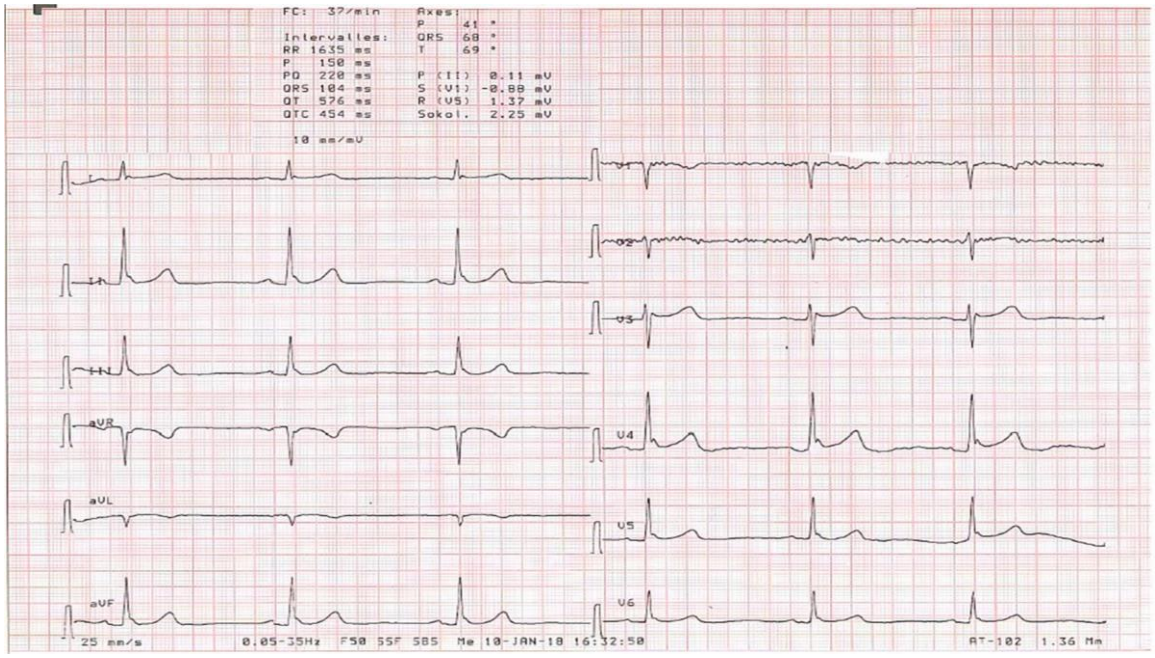

Figure 1: Patient's electrocardiogram during hypothermia.

A transthoracic echocardiography was performed, showing almost all parameters within normal range (normal left ventricular mass, end-diastolic volume and end-diastolic diameter, normal wall motion and systolic function with a left ventricular ejection fraction of 64%, moderate dilatation of left atrium, which indexed volume was 43 ml/m², no significant valvular heart disease, normal pulmonary pressures with a systolic pulmonary pressure of 24 mmHg, compliant inferior vena cava and no pericardial effusion).

The most remarkable abnormality was an increased duration of the systole, which was visually detectable on two-dimensional videos and documented by time-related measurements (please note that all the pictures below were registered at a scanning speed of 100 mm/s):

- Left ventricular M-mode: increased wall contraction duration (figure 2);
- Pulsed wave Doppler through aortic and mitral valves: prolonged left ventricular ejection time (610 ms) and shortened left ventricular filling time (800 ms) (figure 3);
- Tissue Doppler imaging at lateral and septal mitral annulus: increased S' wave duration (figure 4).

Finally, the patient's condition quickly improved after external rewarming. He was treated with antibiotics for pneumonia due to Haemophilus influenzae. This septic condition may have contributed to hypothermia, in addition to environmental exposure. No other potential triggers of hypothermia (such as acute adrenal insufficiency, hypothyroidism and ketoacidosis) were found. The patient was discharged after a few days.

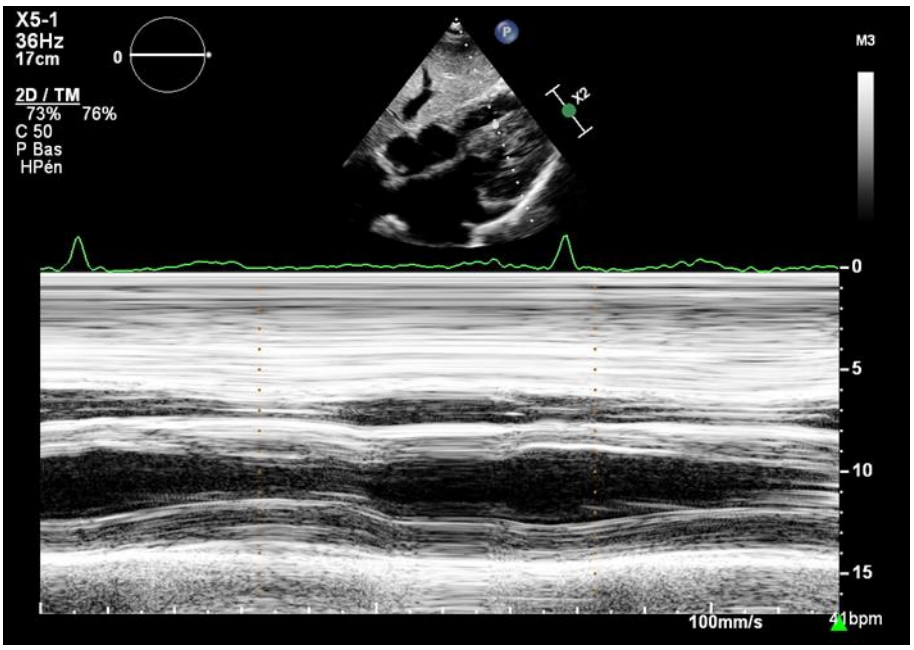

Figure 2: Left ventricular M-mode: increased wall contraction duration.

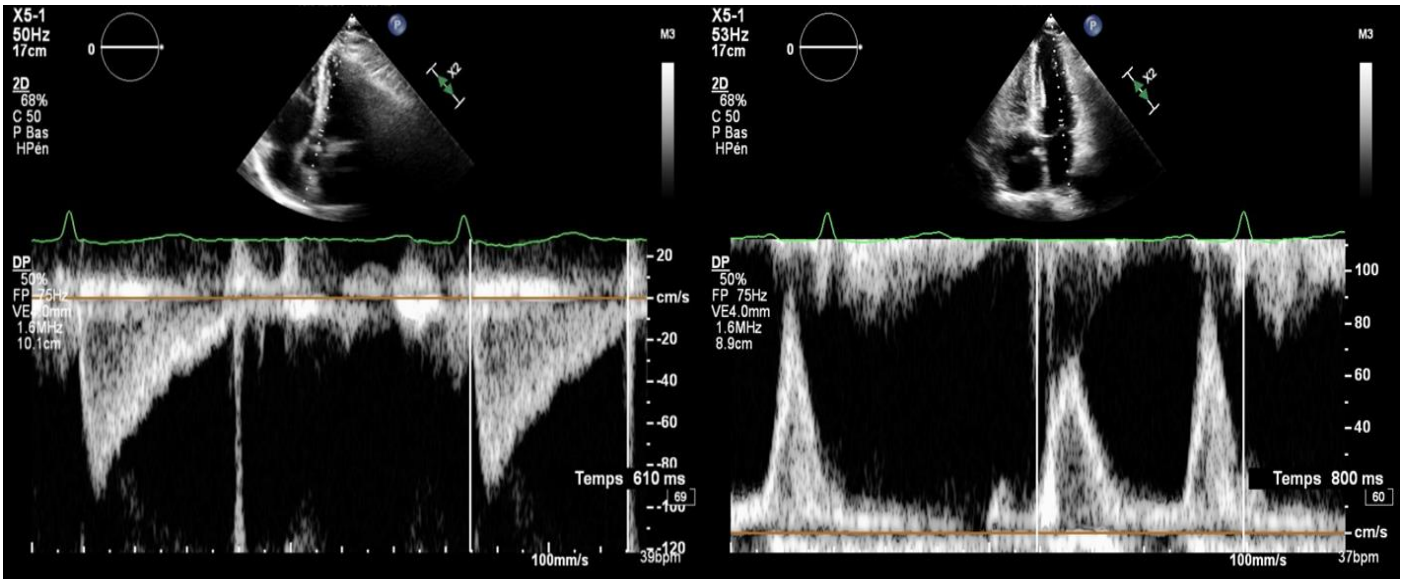

Figure 3: Pulsed wave Doppler through aortic and mitral valves: prolonged left ventricular ejection time (610 ms) and shortened left ventricular filling time (800 ms).

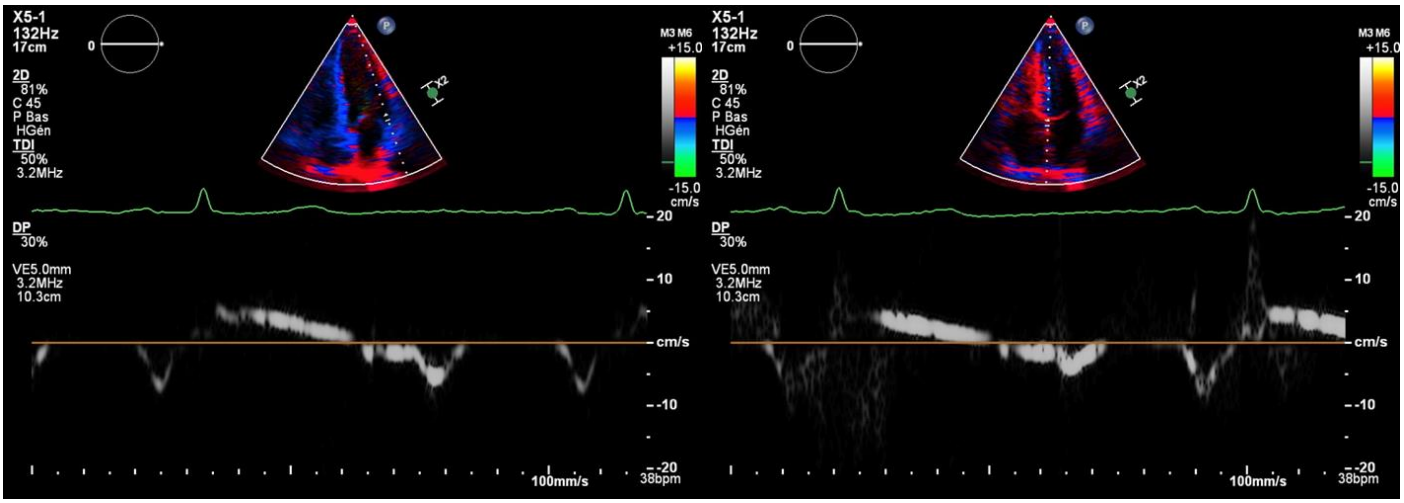

Figure 4: Tissue Doppler imaging at lateral and septal mitral annulus: increased S' wave duration.

Comparison

1- Comparison with the physiological cardiac cycle.

Ventricular systolic and diastolic duration physiologically depends on the heart rate: Lance et al. reported that the normal left ventricular ejection time is 320 to 340 ms when the heart rate is 40 beats per minute. However, diastolic duration is much more influenced than systolic duration and represents the main adjustment variable: it decreases in case of tachycardia whereas it increases in case of bradycardia. In contrast, systolic ejection time shows relatively low variability within physiological heart rate range, with a normal value at around 300 ms [2].

Systole includes ventricular isovolumic contraction time and ventricular ejection time. Similarly, diastole includes ventricular filling time and ventricular isovolumic relaxation time. Since isovolumic contraction and relaxation are very short, we can provide the approximation that ventricular ejection time reflects systolic duration and ventricular filling time reflects diastolic duration.

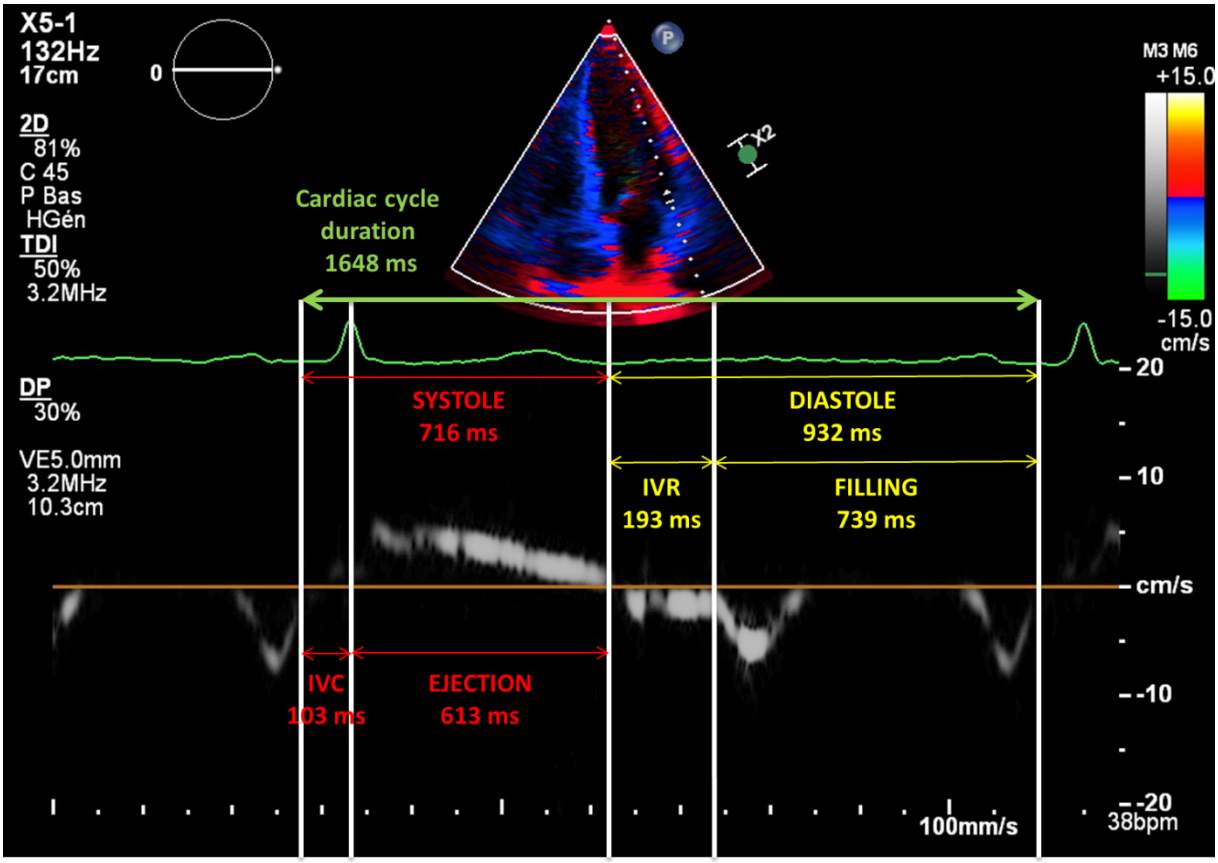

Figure 5: Tissue Doppler imaging at lateral mitral annulus, showing the different phases of the cardiac cycle in our hypothermic patient. IVC: isovolumic contraction time, IVR: isovolumic relaxation time.

Tissue Doppler imaging measurements at mitral annulus in our hypothermic patient (figure 5 and table 1) showed a left ventricular ejection time of 613 ms, a left ventricular filling time of 739 ms, an isovolumic contraction time of 103 ms and an isovolumic relaxation time of 193 ms. It led to a systolic duration of 716 ms and a diastolic duration of 932 ms, which accounted for only 57% of the cardiac cycle duration (1 648 ms). The shortened diastole might induce an impaired left ventricular filling, leading to a potential diastolic dysfunction, or a reduced coronary perfusion.

2- Comparison with a healthy normothermic patient.

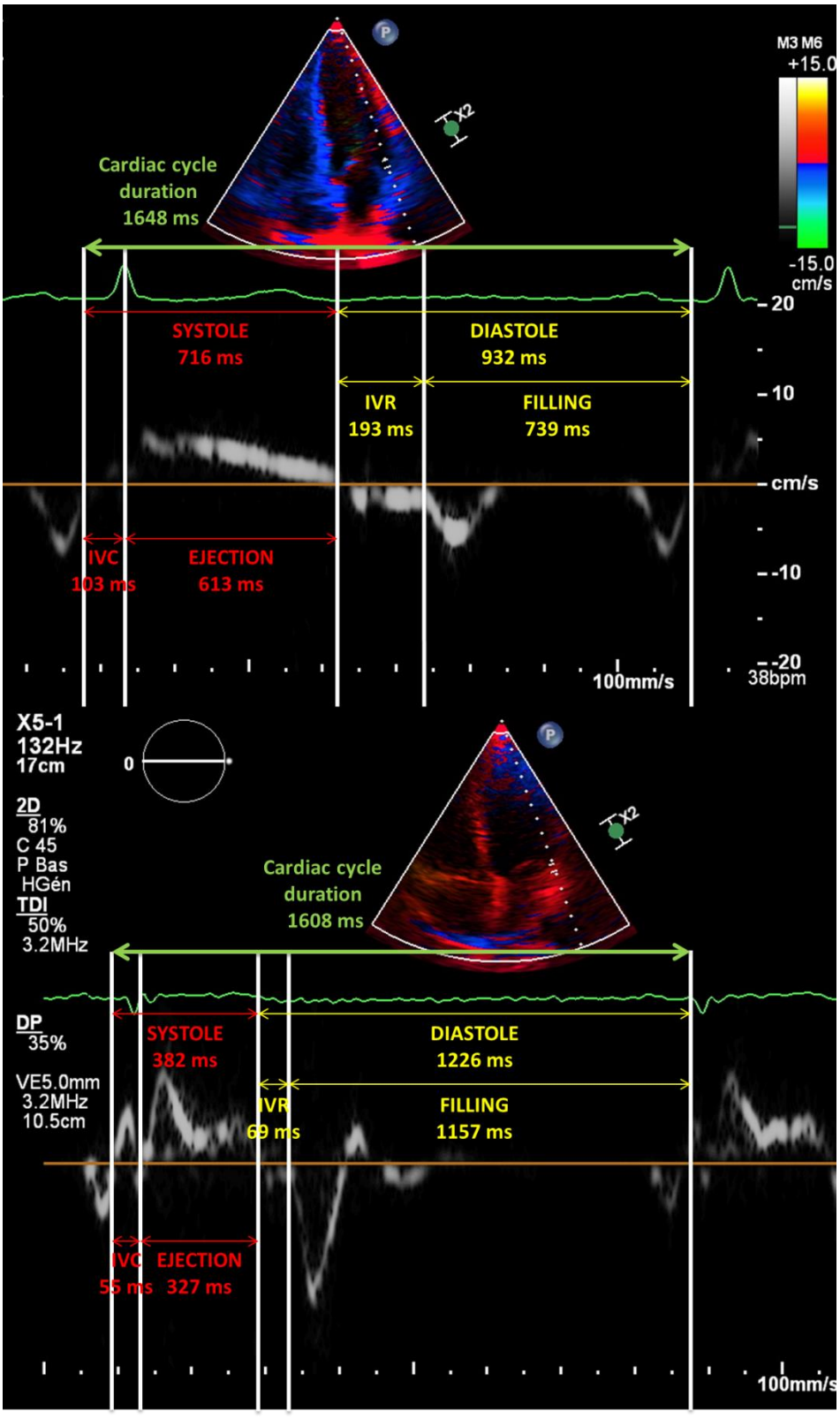

Figure 6: Comparison of tissue Doppler imaging at lateral mitral annulus between our hypothermic patient (at the top) and a normothermic patient (below). IVC: isovolumic contraction time, IVR: isovolumic relaxation time.

In order to illustrate echocardiographic changes during hypothermia, our hypothermic patient's data were compared with echocardiographic findings from a healthy normothermic patient whose heart rate was within a similar range of 40 beats per minute. His tissue Doppler imaging parameters at mitral annulus were: left ventricular ejection time 327 ms, left ventricular filling time 1 157 ms, isovolumic contraction time 55 ms and isovolumic relaxation time 69 ms. Thus, systolic duration was 382 ms and diastolic duration 1 226 ms, which is well within physiological range, and diastolic duration accounted for 76% of the cardiac cycle duration (1 608 ms). The following pictures (figures 6 and 7 and table 1) help highlight

the differences in the distribution of cardiac cycle phases between the two patients, especially left ventricular ejection time lengthening, which was twice as long in our hypothermic patient as in the normothermic patient, and thus was even visually detectable on two-dimensional videos. Isovolumic contraction and relaxation times also seemed to be prolonged in hypothermia.

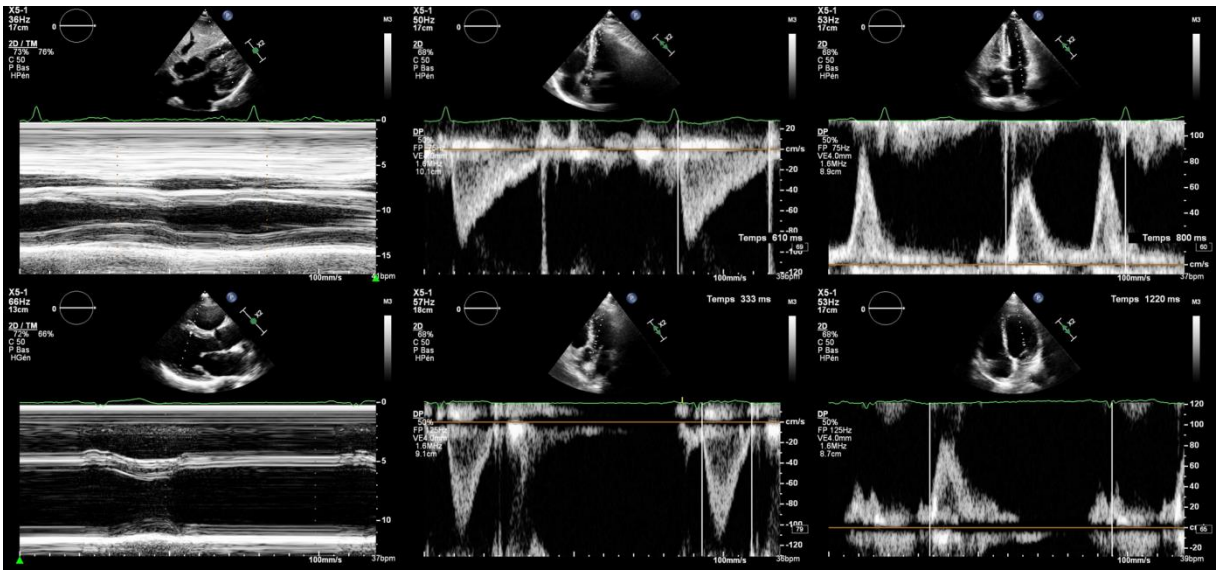

Figure 7: Comparison of left ventricular M-mode and pulsed wave Doppler through aortic and mitral valve between our hypothermic patient (at the top) and a normothermic patient (below).

3- Comparison with his own echocardiography in normothermia.

In October 2019, our patient underwent control electrocardiogram and echocardiography. He was asymptomatic and reported no intercurrent event since his previous hospitalization. His body temperature, measured at the tympanic membrane, was 36.4°C (96.8°F). His electrocardiogram (figure 8) displayed sinus rhythm (heart rate of 59 beats per minute), with no conductive disorder (PR interval 182 ms, QRS complex duration 76 ms, QRS axis 30°), with normalization of the QT interval (384 ms measured / 380 ms corrected). As expected, Osborn J waves disappeared, but a residual notch remained on the terminal part of the QRS complex with ST-segment elevation from V1 to V6, related to an early repolarization pattern.

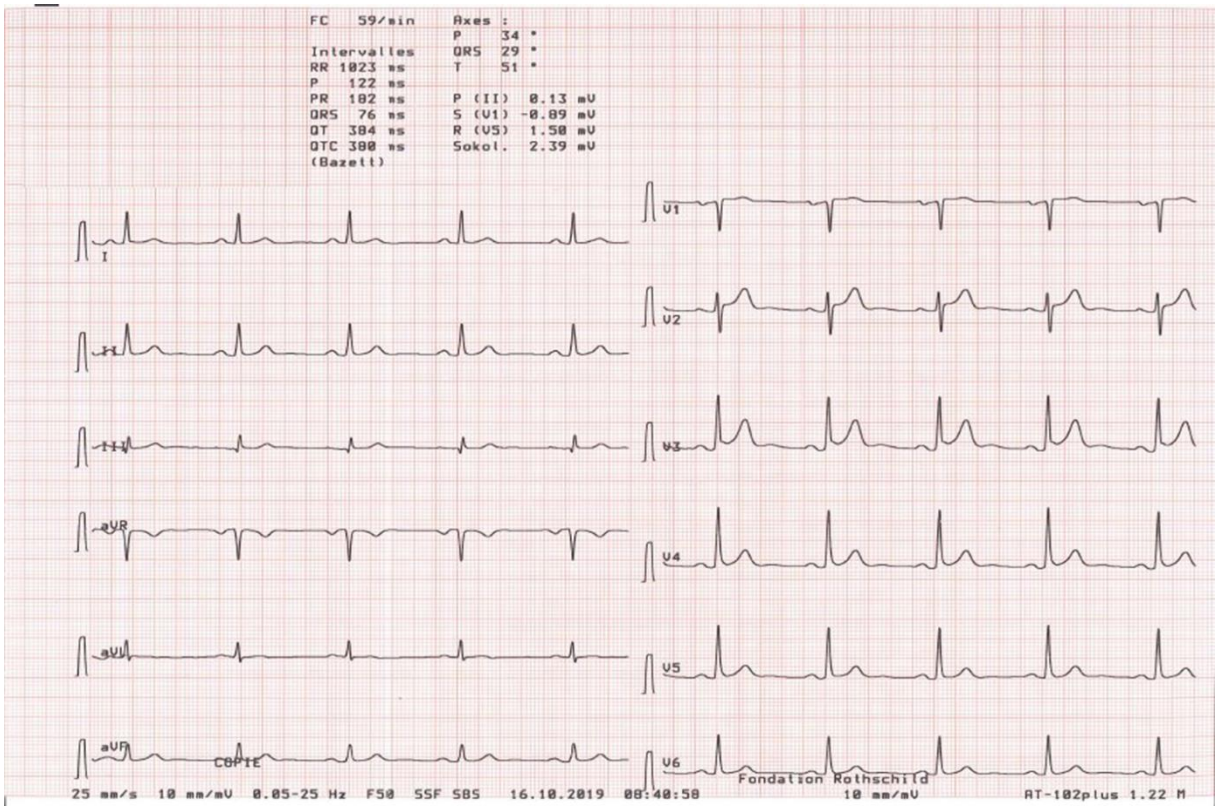

Figure 8: Patient's electrocardiogram in normothermia.

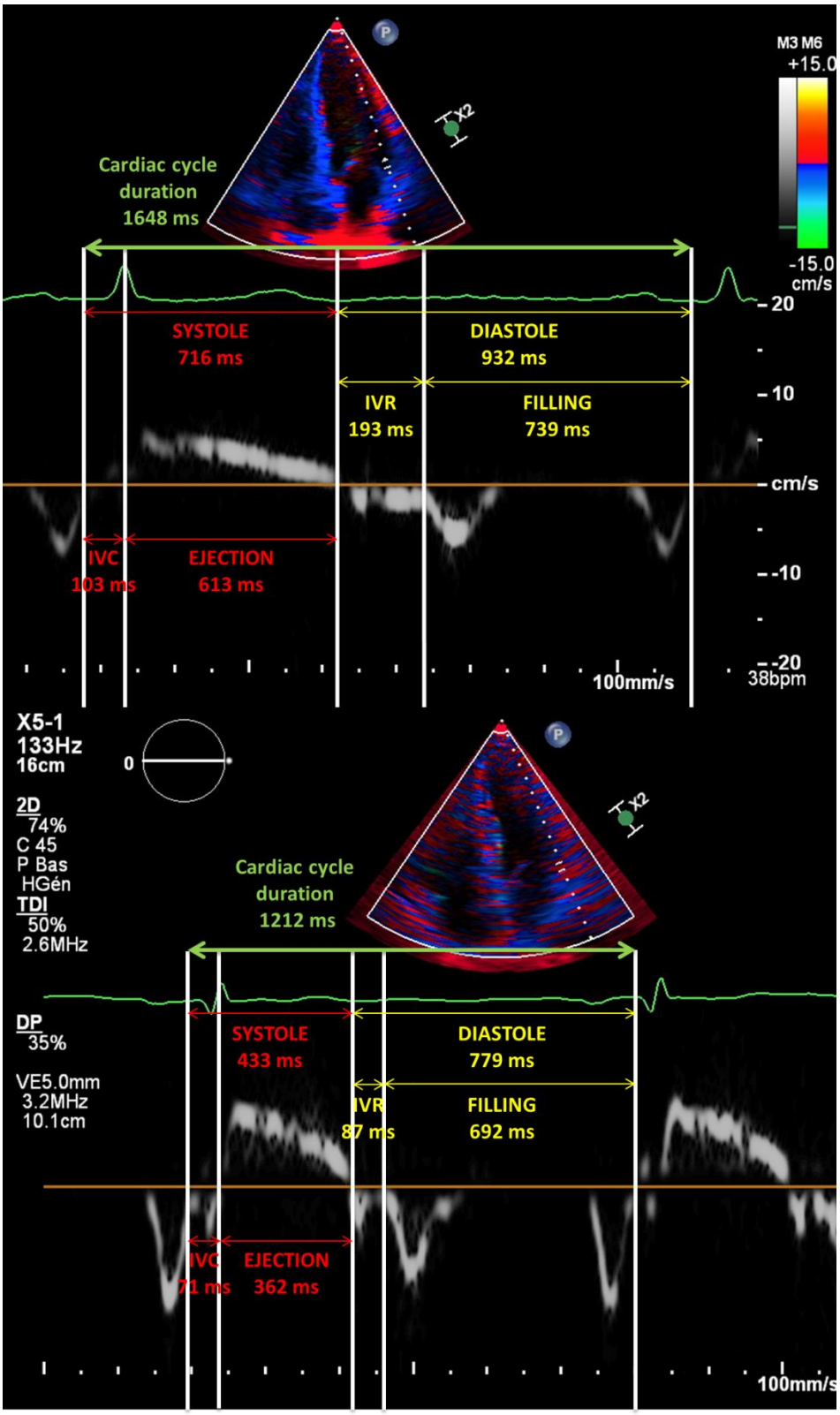

Figure 9: Comparison of tissue Doppler imaging at lateral mitral annulus in the same patient in hypothermia (at the top) and in normothermia (below). IVC: isovolumic contraction time, IVR: isovolumic relaxation time.

As before, almost all his echocardiographic parameters were within normal range (normal cardiac chambers size except from a moderate dilatation of left atrium, which indexed volume was 40 ml/m², normal left ventricular wall motion and systolic function with a left ventricular ejection fraction of 64%, mitral inflow E/A ratio of 0.8 suggesting impaired left ventricular relaxation without elevated filling pressure, no significant valvular heart disease, normal pulmonary pressures with a systolic pulmonary pressure of 28 mmHg and no pericardial effusion). The only difference was a normalization of the left ventricular ejection time. Indeed, his tissue Doppler imaging parameters at mitral annulus showed a left ventricular ejection time of 362 ms, a left ventricular filling time of 692 ms, an isovolumic contraction time of 71 ms and an isovolumic relaxation time of 87 ms. Thus, systolic duration was 433 ms and diastolic duration 779 ms, which is well within

physiological range, and diastolic duration accounted for 64% of the cardiac cycle duration (1 212 ms). Figures 9 and 10 and table 1 depict his time-related echocardiographic measurements in normothermia compared with previous hypothermia. These observations suggest that hypothermia may impact the distribution of cardiac cycle phases, especially leading to ventricular ejection time lengthening, which is reversible after rewarming.

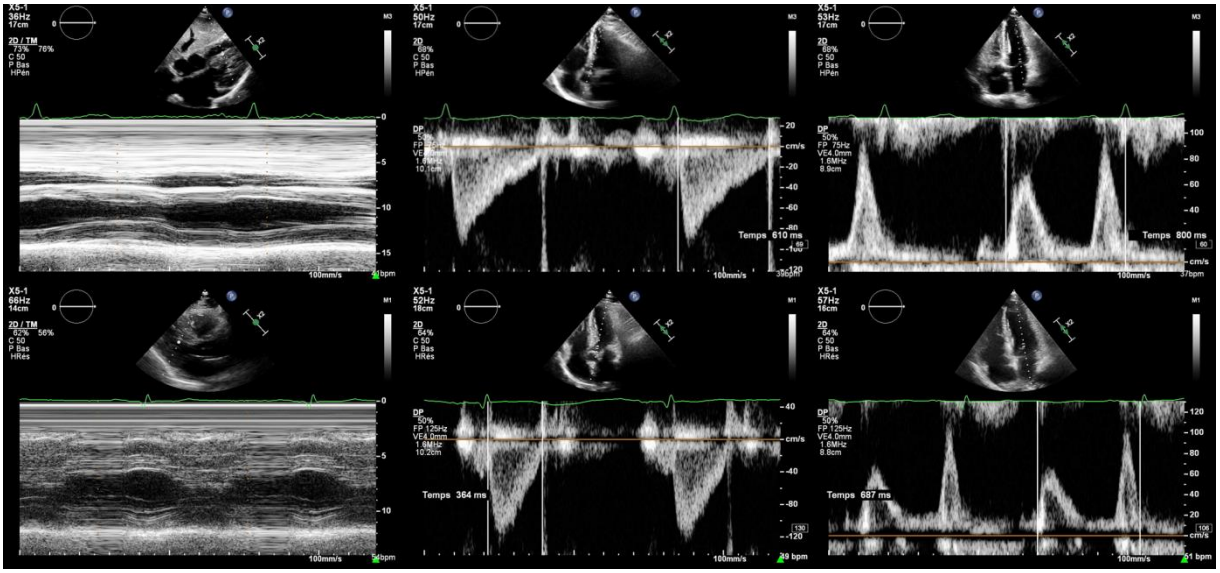

Figure 10: Comparison of left ventricular M-mode and pulsed wave Doppler through aortic and mitral valve in the same patient in hypothermia (at the top) and in normothermia (below).

Phase duration (ms)	Cardiac cycle duration	Systole duration	IVC	Ejection	Diastole duration	IVR	Filling
Hypothermic patient	1648	716	103	613	932	193	739
Normothermic control	1608	382	55	327	1226	69	1157
Normothermic patient	1212	433	71	362	779	87	692

Table 1: Comparison of cardiac cycle phases duration between our hypothermic patient, a normothermic control subject and our normothermic patient. IVC: isovolumic contraction time, IVR: isovolumic relaxation time.

Discussion

Hypothermia is defined as core body temperature below 35°C (95°F). It is mild between 35 and 32°C (95 and 90°F), moderate between 32 and 28°C (90 and 82°F) and severe below 28°C (82°F) [3, 4, 5]. Hypothermia induces characteristic electrocardiographic changes, such as sinus bradycardia, sometimes junctional rhythm (especially below 32°C), atrial fibrillation with slow ventricular response (especially below 29°C), prolonged PR interval, prolongation of measured QT and corrected QT intervals, widening and low amplitude of P waves, widening of QRS complex with an increased risk of ventricular tachycardia or ventricular fibrillation (especially below 28°C) and widened, flattened or negative T waves. Another typical electrocardiographic feature is Osborn J wave, which has been described as a positive deflection at the terminal part of the QRS complex, also named “camel hump” or “hump-like deflection”. Osborn J waves are detectable in 80% of hypothermic patients with core body temperature below 30°C, they generally correlate with the degree of hypothermia and regress gradually with rewarming. Their amplitude is most prominent in inferior and precordial leads. The presence of Osborn J waves is associated with higher incidence of ventricular fibrillation and sudden cardiac death. Differential diagnoses are repolarization abnormalities induced by hypercalcemia, early repolarization syndrome, Brugada syndrome, right ventricular arrhythmogenic dysplasia and intoxication by tricyclic antidepressants [3].

Although hypothermia-related electrocardiographic abnormalities are well known, its specific effects on echocardiographic parameters have been less described. Prolonged ventricular ejection time during hypothermia, assessed by ventriculography or echocardiography, has previously been reported in animal studies.

The first study involved seventeen dogs in the setting of a myocardial infarction model. Although systolic ejection time was similar at baseline (200 ms for heart rate of 90 beats per minute), it was significantly prolonged in the hypothermic group (240 ms for heart rate of 100 beats per minute at 34°C and 270 ms for heart rate of 86 beats per minute at 32°C) compared with normothermic groups (170 ms for heart rate of 130 beats per minute at 37.5°C).

Similarly, isovolumic relaxation time was similar at baseline (42 ms) and significantly prolonged in the hypothermic group (62 ms at 34°C and 87 ms at 32°C) compared with normothermic groups (39 ms) [6]. More recently, Espinoza et al. provided relevant information about the effects of therapeutic hypothermia on left ventricular systolic and diastolic function in a porcine model. They performed invasive measurements of cardiac output and pressure (thermodilution, ultrasonic transit-time flow probe, micromanometer), ultrasonographic measurements (left ventricular anterior wall thickening and thinning velocities recorded by epicardial ultrasonic transducers) and echocardiographic measurements (left ventricular volume and ejection fraction, mitral inflow, tissue Doppler imaging and 2-dimensional strain), at 38°C and 33°C, at spontaneous and paced heart rates (100 and 120 beats per minute). They found that hypothermia induced a decrease in systolic wall thickening velocity, a decrease in early diastolic wall thinning velocity and an increased systolic duration (338 ms to 465 ms during spontaneous heart rate, 322 ms to 397 ms during paced heart rate of 100 beats per minute and 301 ms to 368 ms during paced heart rate of 120 beats per minute, at 38°C and 33°C respectively). Left ventricular systolic function was preserved through this prolonged systolic duration, which compensated for slow contraction. On the other hand, hypothermia led to a decrease in relative diastolic duration at spontaneous heart rate, which was further shortened with atrial pacing. It suggested a reduced tolerance to increasing heart rate during hypothermia [5, 7].

Furthermore, they investigated the effects of esmolol and epinephrine on myocardial function during therapeutic hypothermia. This issue is of clinical relevance since resuscitated patients commonly receive beta-blocker before cardiac arrest and frequently require vasopressors and inotropic medication after cardiac arrest. As expected, esmolol infusion exacerbated the effects of hypothermia on active myocardial contraction and relaxation by an additive negative inotropic effect, inducing both left ventricular systolic and diastolic function impairment [8]. In contrast, epinephrine infusion reversed the myocardial effects of hypothermia by shortening systolic duration and allowing complete relaxation, leading to enhanced left ventricular systolic and diastolic function and improved tolerance to increasing heart rate [9].

Human studies in hypothermia are rare but provide similar results. In seven patients with severe head injuries who underwent therapeutic hypothermia, M-mode, tissue Doppler imaging and pulsed Doppler echocardiography showed that hypothermia increased left ventricular ejection time and reciprocally reduced left ventricular filling period, whereas spatial parameters such as fractional shortening or stroke volume index were not affected [10].

Only a few cases of accidental hypothermia were reported. In an early echocardiographic study published in 1982 [11], M-mode echocardiography was performed in ten patients with accidental hypothermia (rectal temperature 34°C or lower). The left ventricular ejection time, which approximately correlated to the interval from the onset to the peak of the posterior wall forward movement, was prolonged in hypothermia (mean value 434 ms after correction for heart rate according to Bazett formula). The maximal systolic endocardial velocity, determined by drawing a tangent to the steepest portion of the systolic excursion and measuring the slope, was decreased in hypothermia. These abnormalities were particularly remarkable when body temperature was below 26°C and returned toward normal when body temperature rose, whereas stroke volume did not change significantly.

Although left ventricular systolic function is usually preserved in mild therapeutic hypothermia, some authors described transient reduced left ventricular ejection fraction in accidental hypothermia, which is often deeper. It remains uncertain whether this systolic dysfunction is related to hypothermia itself or to an intercurrent disease, hence various mechanisms may be involved. Nevertheless, it is usually reversible within a few days. A Japanese team reported the case of an 88-year-old man found in a coma, with heart failure associated with hypothermia (body temperature, measured at the tympanic membrane, below 34°C). His electrocardiogram showed sinus arrest and junctional rhythm, with a heart rate of 40 beats per minute, and Osborn J waves in leads V4 to V6. Echocardiography performed on admission indicated left ventricular dysfunction (left ventricular ejection fraction of 25%) and lengthened ejection time (710 ms). These parameters gradually normalized during rewarming (his left ventricular ejection fraction improved to 43% then 45% and the ejection time shortened to 530 ms then 450 ms three hours and five days later respectively) [12]. Two case reports described Tako Tsubo cardiomyopathy following severe unintentional hypothermia [13, 14]. In another case, echocardiography showed global hypokinesia with a left ventricular ejection fraction of 25%. Further investigation by cardiac MRI revealed diffuse late gadolinium enhancement of left ventricular myocardium, which was compatible with interstitial oedema and presumably related to abnormalities in the microcirculation [4].

Limitations of our study

Our findings are consistent with previous reported observations. However, they concern only one case compared with himself and with one healthy normothermic patient with the same heart rate. Further studies are therefore needed to improve the understanding of hypothermia's physiopathology.

Conclusions

Prolonged left ventricular ejection time might be a specific echocardiographic finding in hypothermia, since it has not been reported in other clinical conditions. Slow myocardial contraction is visually detectable on two-dimensional videos by an experienced operator and confirmed by tissue Doppler imaging, M-mode or pulsed-wave Doppler. Most of the electrocardiographic and echocardiographic changes induced by hypothermia are reversible after rewarming. This case report is interesting because it relates to an ambulatory patient, thus without confounding hemodynamic modifications induced by vasoactive drugs, mechanical ventilation or previous cardiac injury. The prolongation of systole at the expense of diastole during hypothermia leads to a shortened left ventricular filling time and a potential diastolic dysfunction. A comprehensive assessment of cardiac effects of hypothermia might thus help therapeutic management of critically ill patients.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Patient's consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying image.

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