Heliyon 10 (2024) e37816

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Case report

Extracorporeal cardiopulmonary resuscitation for Takotsubo cardiomyopathy triggered by coronary vasospasm complicated with gastrointestinal bleeding: A case report

Haotian Lu [a], Anke Shi [a], Mingshuai Ai [b], Shengtao Yan [c,*]

[a] China-Japan Friendship Hospital (Institute of Clinical Medical Sciences), Chinese Academy of Medical Sciences & Peking Union Medical College, China
[b] Peking University Fist Hospita, China
[c] Department of Emergency, China-Japan Friendship Hospital, China

ARTICLE INFO

Keywords:
Takotsubo cardiomyopathy
Extracorporeal cardiopulmonary resuscitation
Coronary vasospasm
Anticoagulation
Case report

ABSTRACT

Takotsubo cardiomyopathy is typically triggered by excessive catecholamine release. Here, we present a case of Takotsubo cardiomyopathy following gastrointestinal bleeding. The patient experienced cardiac arrest, necessitating extracorporeal cardiopulmonary resuscitation. Coronary angiography revealed severe coronary vasospasm, and echocardiography showed left ventricular dysfunction with ballooning. The patient was transferred out of the emergency intensive care unit on the ninth day with improved consciousness.

1. Introduction

Takotsubo cardiomyopathy is often induced by stressful events and severe acute critical illnesses. It presents as acute coronary syndrome with possible complications, including cardiogenic shock, cardiac arrest, and heart failure. The main characteristic is the ballooning of the left ventricle in the absence of coronary artery obstruction, with cardiac function usually returning to normal spontaneously [1]. In extracorporeal membrane oxygenation (ECMO) treatment, anticoagulation is crucial for thrombosis prevention, with unfractionated heparin being the most commonly used anticoagulant. Additionally, activated partial thromboplastin time (aPTT) is the primary monitoring parameter [2]. We report a case of Takotsubo cardiomyopathy triggered by coronary vasospasm following gastrointestinal bleeding, in which extracorporeal cardiopulmonary resuscitation was performed without anticoagulation during treatment.

2. Case report

A 65-year-old Chinese man was admitted to the emergency department with melena lasting 1 day, accompanied by dizziness, palpitations, and fatigue. The patient reported a 20-year history of coronary atherosclerotic heart disease and hypertension and had been taking long-term oral medications, including aspirin, clopidogrel, isosorbide mononitrate, metoprolol, and sacubitril/valsartan. The patient had no history of diabetes or cerebrovascular disease. Blood tests revealed moderate anemia (hemoglobin, 64 g/L).

* Corresponding author. Department of Emergency, China-Japan Friendship Hospital, No. 2 East Yinghua Street, Chaoyang District, Beijing, 100029, China.
E-mail address: yanshengtaozrr@126.com (S. Yan).

https://doi.org/10.1016/j.heliyon.2024.e37816
Received 25 July 2024; Received in revised form 29 August 2024; Accepted 10 September 2024
Available online 19 September 2024

Continuous intravenous infusion of omeprazole and oral lyophilizing thrombin powder were administered along with fluid replacement. An emergency gastroscopic examination was performed for possible hemostatic therapy, revealing multiple ulcers in the gastric antrum and duodenal bulb, with no active bleeding observed (Fig. 1a).

After gastroscopic examination, the patient complained of precordial pain. A 12-lead electrocardiogram (ECG) revealed ST-segment depression in leads V1-V4 (Fig. 1b), with an elevated cardiac troponin T level of 0.025 ng/mL (Fig. 2a). Thus, acute coronary syndrome was suspected, and a continuous intravenous infusion of isosorbide mononitrate was administered to dilate the coronary arteries. Subsequently, the patient experienced a sudden cardiac arrest. Standard cardiopulmonary resuscitation with mechanical ventilation was immediately initiated. Ventricular fibrillation was observed, and there was no return of spontaneous circulation despite three attempts at defibrillation and administration of amiodarone. Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was successfully initiated an hour post cardiac arrest (right femoral vein and left femoral artery, 3500 rpm; blood flow 3.8 L/min, air flow 4 L/min, FiO2 100 %). Cyanosis and decreased skin temperature were noted in the left lower extremity; therefore, an extra-arterial cannula was placed in the distal left superficial femoral artery to increase the blood supply. Coronary angiography was conducted with ECMO support, revealing severe spasms in both the left and right coronary arteries (Fig. 1c–f, Supplementary material 1). Following the administration of 100 μg nitroglycerin for spasmolysis, chronic occlusion in the mid-distal left circumflex artery (LCx) with collateral circulation was identified, and mild stenosis in the left anterior descending artery (LAD) was detected, with no other blockage or stenosis observed (Fig. 1g–j).

After angiography, the patient was transferred to the emergency intensive care unit (EICU) for further treatment. Neurological examination revealed upward gaze in both eyes, bilateral sluggish pupillary light reflex, absence of myoclonus, and negative pathological signs. No cerebral edema was observed on computed tomography (CT) (Fig. 1k). Bedside echocardiography revealed left ventricular dysfunction and wall motion abnormalities with ballooning corresponding to the typical manifestations of Takotsubo cardiomyopathy (Fig. 1m–n, Supplementary material 2). ECMO was continued without an anticoagulant strategy because of ongoing melena, potential active bleeding, and coagulation disorders. Simultaneous interventions included blood transfusion (Fig. 2e and g), vasopressors, continuous renal replacement therapy, targeted temperature management, lung-protective ventilation, sedation and

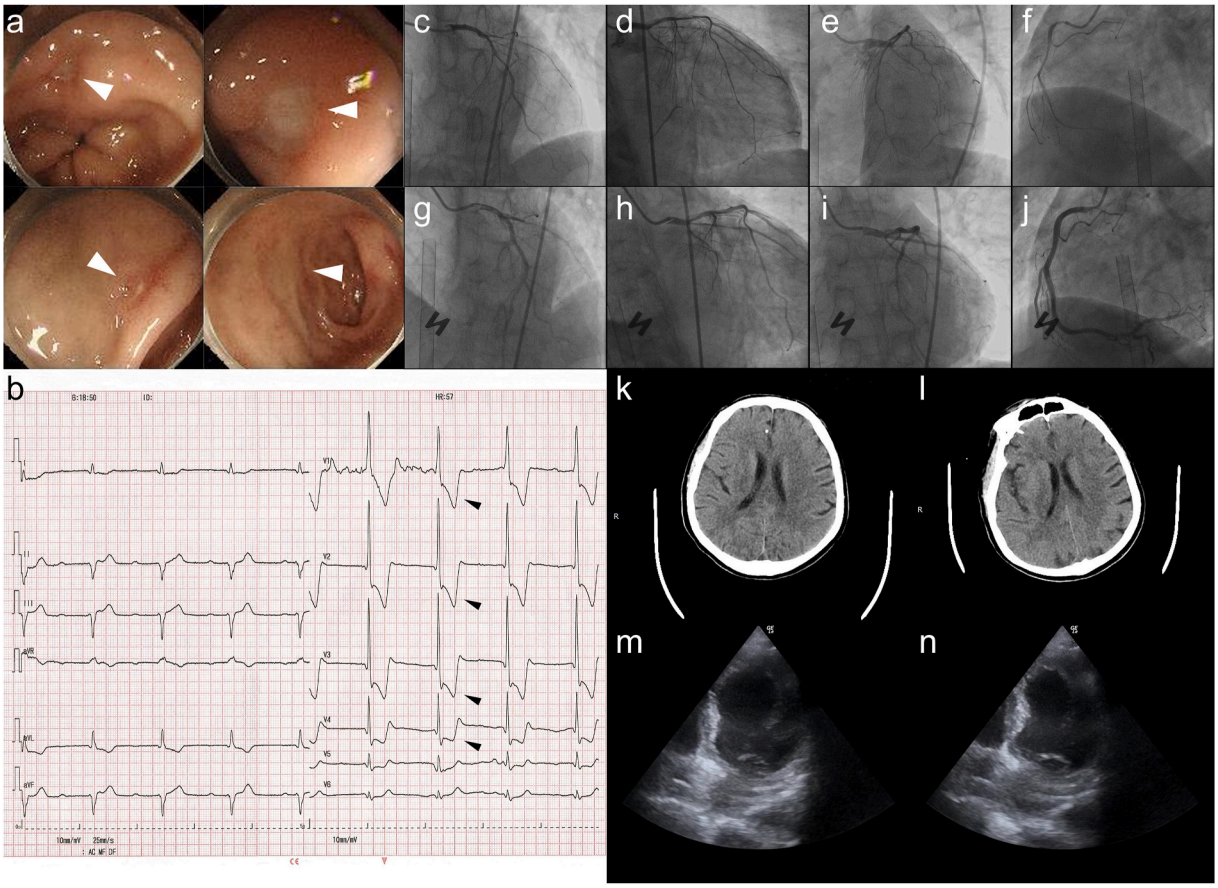

Fig. 1. a. Multiple ulcers in the gastric antrum and duodenal bulb. b. Sinus rhythm with ST-segment depression in leads V1-V4. c-f. Severe spasm observed in both the left and right coronary arteries. g-j. Chronic occlusion in the mid-distal LCx with collateral circulation following nitroglycerin administration; mild stenosis in the LAD. k. No cerebral edema was observed after cardiac arrest. l. No cerebral edema was observed on day 4. m-n. Left ventricular dysfunction and wall motion abnormalities with ballooning, resembling the shape of an octopus trap.

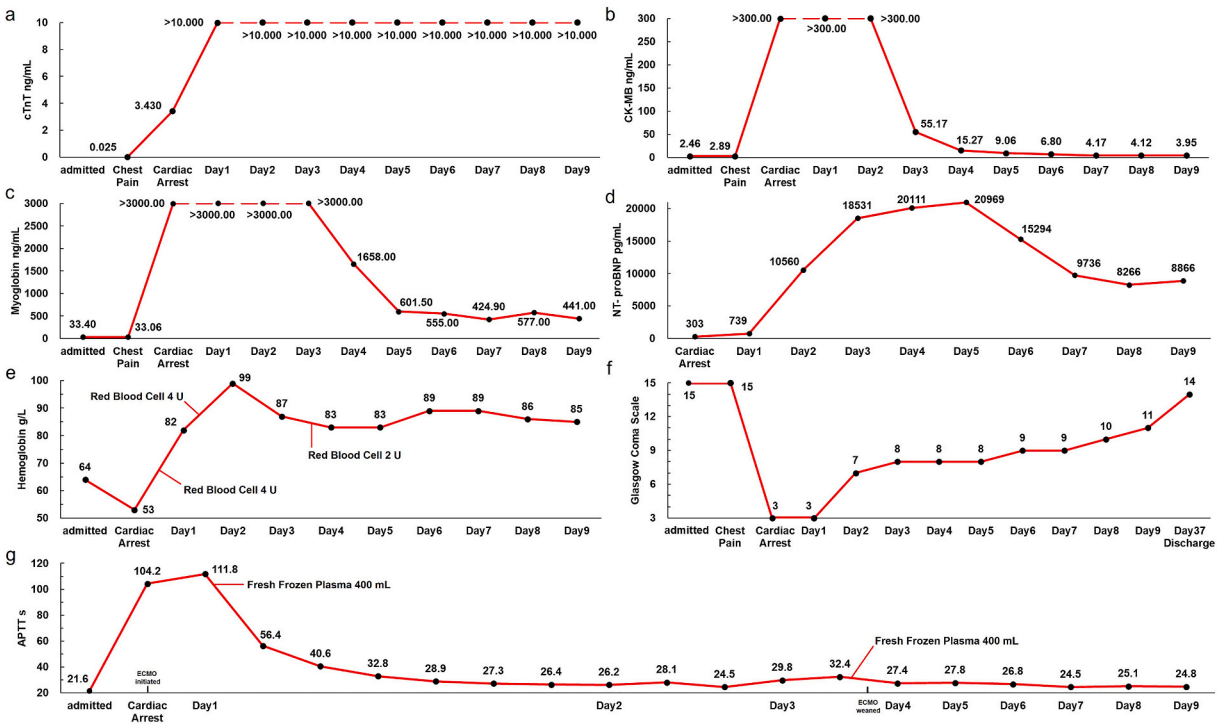

Fig. 2. a. cTnT level increased to >10.000 ng/mL and remained elevated beyond the measurable range on day 9; b. creatine kinase MB level increased to >3000.00 ng/mL; c. myoglobin level increased to >3000.00 ng/mL; d. NT-proBNP level increased to 20969 pg/mL; e. hemoglobin level decreased to 53 g/L post-cardiac arrest, gradually increasing and stabilizing with blood transfusion; f. GCS score gradually improved from 3 to 11, and increased to 14 on the discharge day; g. aPTT level normalized with blood transfusion and remained stable without anticoagulant strategy.

analgesia, isosorbide mononitrate, mannitol, anti-infection, hepatoprotection, acid suppression, and parenteral nutrition with high doses of vitamin C. The cardiac troponin T level (cTnT) increased to >10.000 ng/mL, and the creatine kinase MB (CK-MB) level increased to >300.000 ng/mL (Fig. 2a–b).

Forty hours after cardiac arrest, the patient regained spontaneous respiration, showed responsiveness by opening eyes and making slight movements, and scored 7 (E3V1M3) on the Glasgow Coma Scale (GCS) (Fig. 2f). The extent of life support treatment was gradually reduced as the patient's vital signs stabilized. The aPTT was monitored and maintained at 24.5–32.4 s, and no significant thrombosis was observed on the membrane (Fig. 2g). Successful ECMO weaning was achieved on the third day. Continuous intravenous infusion of landiolol was administered to control heart rate and minimize myocardial oxygen consumption. The patient passed the spontaneous breathing trial and was extubated on the fourth day. No cerebral edema was observed on CT (Fig. 1i). Stable hemoglobin levels enabled the initiation of enteral nutrition on the fifth day (Fig. 2e). The left ventricular ejection fraction was 39 % as measured with bedside echocardiography, and no ballooning was observed. The patient was transferred from the EICU to the general ward on day nine with a GCS score of 11 (E4V3M4) (Fig. 2f). Treatments including isosorbide mononitrate, beta-blockers, clopidogrel, diuresis, anti-infection, and acid suppression were continued. Nutritional support was gradually transitioned from nasal to oral feeding, and lower-limb rehabilitation exercises were initiated. The patient was discharged home 4 weeks later (day 37) with a GCS score of 14 (E4V4M6) (Fig. 2f) and a modified Rankin Scale score of 3.

3. Discussion

Currently, an endogenous catecholamine surge is considered the primary mechanism underlying the pathogenesis of Takotsubo cardiomyopathy. High concentrations of catecholamines induce calcium dysregulation, signaling pathway changes, hypoxia, and necrosis of myocardial cells, leading to impaired contractile function. In addition, multivessel coronary artery spasm and microvascular dysfunction may contribute to the pathogenesis of Takotsubo cardiomyopathy, although this remains uncertain [1,3]. Accordingly, many physicians have empirically used beta-blockers in clinical practice [1,4]. For acute complications such as heart failure, pulmonary edema, and thromboembolism, nitrates and anticoagulants are necessary. For shock and pump failure, a left ventricular assist device and VA-ECMO are recommended [1,5]. Previous studies have primarily reported stress events [6–8], infection (mostly virus) [9–11], drug treatment (catecholamines and chemotherapeutic agents) [12,13], and surgery [14,15], as precipitating factors of Takotsubo cardiomyopathy. In these reports, most patients presented with elevated cardiac troponin levels and non-specific ECG changes, with echocardiography indicating ventricular ballooning and significantly reduced ejection fraction, with or without chest pain, dyspnea, or hemodynamic instability. Most coronary angiography were negative, and patients received treatments similar

to those of acute coronary events, including anticoagulants and antiplatelet agents, which often led to a spontaneous return of normal cardiac function [6–15]. In our report, the patient experienced gastrointestinal bleeding and subsequent cardiac arrest. Gastrointestinal bleeding was considered the inducing factor in this case. It resulted in discomfort, blood loss, and subsequent hypovolemia and led to a significant hemodynamic impact, including hypotension and reduced perfusion to vital organs. The resulting severe physiological stress may have triggered an adrenergic surge, especially with the elevated levels of catecholamines such as adrenaline, which further contributed to Takotsubo cardiomyopathy. Additionally, the treatment of gastrointestinal bleeding often involves endoscopic examination, intensive care, and continuous monitoring, which can exacerbate physiological and mental stress. In addition to the general clinical findings, significant and extremely severe spasms in both the left and right coronary arteries were detected using coronary angiography, and obvious relief was observed after the administration of nitroglycerin. This manifestation has not been commonly reported in previous cases of Takotsubo cardiomyopathy. Continuous nitrate treatment was effective, suggesting that Takotsubo cardiomyopathy in this patient may have been triggered by coronary spasms. Our case highlights the importance of coronary angiography in identifying various coronary artery abnormalities beyond obstruction, emphasizing the need to distinguish coronary artery spasm in cardiac arrest events. Considering that coronary artery spasm could be a trigger factor in the pathogenesis of Takotsubo cardiomyopathy, nitrates may be necessary in addition to beta-blockers for managing the condition during its diagnosis and treatment.

Despite the requirement for anticoagulation in Takotsubo cardiomyopathy and VA-ECMO, we did not implement anticoagulation measures owing to gastrointestinal bleeding. Reportedly, the absence of systemic anticoagulation in VA-ECMO and VV-ECMO is not associated with higher mortality, pump failure, or thrombotic complications, and patient may have a lower requirement for blood transfusion, with no risk of heparin-induced thrombocytopenia [16,17]. In our case, the aPTT was maintained between 24.5 and 32.4 s, well below the recommended range of 1.5–2.5 times the patient's pre-therapy baseline [18]. No apparent thrombus formation was observed on the membrane, and no thrombotic or embolic events occurred. Performing ECMO without anticoagulants may be practical in situations with significant bleeding risks, such as gastrointestinal bleeding and other contraindications to anticoagulation, even if aPTT is maintained at normal levels. Regular monitoring and customized anticoagulation strategies are required for patients with severe bleeding.

4. Conclusion

Takotsubo cardiomyopathy may be triggered by coronary artery spasms. Coronary angiography can not only assist in differential diagnosis but also help identify the possible pathogenesis of stress cardiomyopathy to adopt appropriate treatment strategies. Additionally, ECMO may be performed without implementing anticoagulation measures in patients with clear contraindications to anticoagulation therapy.

Ethics statement

This study was approved by the Ethics Committee and Institutional Review Board of China-Japan Friendship Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, China (2022-KY-206). All the procedures complied with the principles of the Declaration of Helsinki. The authors confirm that the patient signed an informed consent form for the publication of anonymized case details and images.

Data availability statement

The data associated with this study have not been deposited in a publicly available repository. The authors confirm that all data in this study are available within the article and supplementary materials.

CRediT authorship contribution statement

Haotian Lu: Writing – original draft, Investigation, Formal analysis, Data curation. **Anke Shi:** Writing – original draft, Visualization, Data curation. **Mingshuai Ai:** Data curation, Writing – original draft, Writing – review & editing. **Shengtao Yan:** Writing – review & editing, Validation, Supervision, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This work was supported by the National High Level Hospital Clinical Research Funding of China (2022-NHLHCRF-YS-03-01, 2022-NHLHCRF-YS-03-02, and 2022-NHLHCRF-YS-03-03) and the National Key Research and Development Program of China (2021ZD0200200).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e37816.

References

[1] T. Singh, H. Khan, D.T. Gamble, C. Scally, D.E. Newby, D. Dawson, Takotsubo syndrome: pathophysiology, emerging concepts, and clinical implications, Circulation 145 (13) (2022) 1002–1019, https://doi.org/10.1161/circulationaha.121.055854.

[2] M.M. Chlebowski, S. Baltagi, M. Carlson, J.H. Levy, P.C. Spinella, Clinical controversies in anticoagulation monitoring and antithrombin supplementation for ECMO, Crit. Care 24 (1) (2020) 19, https://doi.org/10.1186/s13054-020-2726-9.

[3] Y.H. S, P. Tornvall, Epidemiology, pathogenesis, and management of takotsubo syndrome, Clin. Auton. Res. 28 (1) (2018) 53–65, https://doi.org/10.1007/s10286-017-0465-z.

[4] K. Milinis, M. Fisher, Takotsubo cardiomyopathy: pathophysiology and treatment, Postgrad Med J 88 (1043) (2012) 530–538, https://doi.org/10.1136/postgradmedj-2012-130761.

[5] H. Medina de Chazal, M.G. Del Buono, L. Keyser-Marcus, L. Ma, F.G. Moeller, D. Berrocal, et al., Stress cardiomyopathy diagnosis and treatment: JACC state-of-the-art review, J. Am. Coll. Cardiol. 72 (16) (2018) 1955–1971, https://doi.org/10.1016/j.jacc.2018.07.072.

[6] A. Ahmadjee, K. Herzallah, Y. Saleh, G.S. Abela, Takotsubo Cardiomyopathy presenting with different morphological patterns in the same patient: a case report and review of the literature, Cardiovasc. Pathol. 47 (2020) 107204, https://doi.org/10.1016/j.carpath.2020.107204.

[7] V. Patel, S. Levy, I. Malik, M.B. Fertleman, L.J. Koizia, Takotsubo cardiomyopathy in elderly female trauma patients: a case series, J. Med. Case Rep. 15 (1) (2021) 451, https://doi.org/10.1186/s13256-021-03056-1.

[8] H. Herath, S.P. Pahalagamage, L.C. Lindsay, S. Vinothan, S. Withanawasam, V. Senarathne, et al., Takotsubo cardiomyopathy complicated with apical thrombus formation on first day of the illness: a case report and literature review, BMC Cardiovasc. Disord. 17 (1) (2017) 176, https://doi.org/10.1186/s12872-017-0616-0.

[9] C.W. Tsao, J.B. Strom, J.D. Chang, W.J. Manning, COVID-19-Associated stress (takotsubo) cardiomyopathy, Circ Cardiovasc Imaging 13 (7) (2020) e011222, https://doi.org/10.1161/circimaging.120.011222.

[10] M.T. Chou, W.L. Yu, Takotsubo cardiomyopathy in a patient with dengue fever, J. Formos. Med. Assoc. 115 (9) (2016) 818–819, https://doi.org/10.1016/j.jfma.2016.06.010.

[11] J. Buzon, O. Roignot, S. Lemoine, P. Perez, A. Kimmoun, B. Levy, et al., Takotsubo cardiomyopathy triggered by influenza A virus, Intern. Med. 54 (16) (2015) 2017–2019, https://doi.org/10.2169/internalmedicine.54.3606.

[12] K. Kido, M. Guglin, Drug-induced takotsubo cardiomyopathy, J. Cardiovasc. Pharmacol. Therapeut. 22 (6) (2017) 552–563, https://doi.org/10.1177/1074248417708618.

[13] A. Ioannou, Iatrogenic adrenaline induced mid-ventricular Takotsubo cardiomyopathy: a case-based review, Ir. J. Med. Sci. 192 (1) (2023) 125–129, https://doi.org/10.1007/s11845-022-03000-2.

[14] G.A. Chiariello, P. Bruno, C. Colizzi, F. Crea, M. Massetti, Takotsubo cardiomyopathy following cardiac surgery, J. Card. Surg. 31 (2) (2016) 89–95, https://doi.org/10.1111/jocs.12675.

[15] H. Zhang, X. Liao, Takotsubo cardiomyopathy following pericardiectomy: a case report, J. Card. Surg. 36 (11) (2021) 4413–4415, https://doi.org/10.1111/jocs.15948.

[16] K.L. Wood, B. Ayers, I. Gosev, N. Kumar, A.L. Melvin, B. Barrus, et al., Venoarterial-extracorporeal membrane oxygenation without routine systemic anticoagulation decreases adverse events, Ann. Thorac. Surg. 109 (5) (2020) 1458–1466, https://doi.org/10.1016/j.athoracsur.2019.08.040.

[17] C. Kurihara, J.M. Walter, A. Karim, S. Thakkar, M. Saine, D.D. Odell, et al., Feasibility of venovenous extracorporeal membrane oxygenation without systemic anticoagulation, Ann. Thorac. Surg. 110 (4) (2020) 1209–1215, https://doi.org/10.1016/j.athoracsur.2020.02.011.

[18] A.B.V. McMichael, L.M. Ryerson, D. Ratano, E. Fan, D. Faraoni, G.M. Annich, ELSO adult and pediatric anticoagulation guidelines, Asaio j 68 (3) (2021) 303–310, https://doi.org/10.1097/mat.0000000000001652, 2022.