

6. Bölüm

KARDİYAK İSKEMİ REPERFÜZYON

Ülkü SABUNCU¹

Işın GÜNEŞ²

6. 1. MİYOKARD İSKEMİ REPERFÜZYON HASARI

Kalbe gelen kan akımının kesilmesi ya da azalması sonucu miyokardın oksijen sunum ve tüketim dengesi bozulur ve bunun sonucunda miyokard iskemisi meydana gelir. Takibinde kan akımının çeşitli tekniklerle restorasyonu miyokardda gelişen hasarı azaltır ancak reperfüzyon olarak tanımlanan bu süreç yine miyokard hasarına neden olabilir. Bu durum miyokard iskemisi reperfüzyon (İ/R) hasarı olarak tanımlanmıştır. Miyokard İ/R hasarı miyokard iskemisi, kardiyak arrest ve kardiyak cerrahiye takiben olumsuz sonuçlara neden olmaktadır (1).

6.2. KARDİYAK ANATOMİ ve FİZYOLOJİ

Kalp toraks boşluğundaki 3 kaviteden biri olan perikardiyal kavitenin içinde, 2. ve 5. interkostal mesafe arasında yer alır. Bu kavite koni şeklindedir, kalbin tamamını ve büyük damarların proksimal kısımlarını barındırır (2,3). İki atriyum ve 2 ventrikülden oluşur. Diğer organ ve dokularımızın perfüzyonunu sağlamak için 7/24 kan pompalarken bu esnada kendi perfüzyonunu da sağlar. Kalp her defasında kanı sağ ve sol pulmoner arterler ile pulmoner dolaşıma, aort ile sistemik dolaşıma pompalar. Atriyumlar özelleşmiş iletim sistemini içerirken, kalbin uyarılarını başlatan başlangıç pompası gibi görev yapar, ventriküller ise, asıl pompa görevini yapar (2,3).

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Kaynaklar

1. Frank A, Bonney M, Bonney S, Weitzel L, Koeppen M, Eckle T. Myocardial ischemia reperfusion injury: from basic science to clinical bedside. *Semin Cardiothorac Vasc Anesth* 2012;16(3):123-32.
2. Frank H. Netter. The Netter Collection Of Medical Illustrations, Volume 5: Heart Bölüm 1, Anatomy 2007:2-33.
3. Pollock JD, Makaryus AN. Physiology, Cardiac Cycle. 2020 Oct 7. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. PMID: 29083687.
4. Strobeck JE, Sonnenblick EH. Myocardial and ventricular function. Part II: Intact heart. *Herz* 1981;6(5):275-87.
5. Little RC, Little WC. Cardiac preload, afterload, and heart failure. *Arch Intern Med* 1982;142(4):819-22.
6. John F. Butterworth, David C. Mackey, John D. Wasnick, Morgan and Mikhail's Clinical Anesthesiology, Chapter 20: Cardiovascular Physiology and Anesthesia; McGraw Hill Medical Books, 6th edition, 2018.
7. Schofield ZV, Woodruff TM, Halai R, Wu MC, Cooper MA. Neutrophils--a key component of ischemia-reperfusion injury. *Shock* 2013;40(6):463-70.
8. Muir WW, Hamlin RL. Myocardial Contractility: Historical and Contemporary Considerations. *Front Physiol* 2020;11:222. doi: 10.3389/fphys.2020.00222.
9. Maxwell JT, Blatter LA. A novel mechanism of tandem activation of ryanodine receptors by cytosolic and SR luminal Ca^{2+} during excitation-contraction coupling in atrial myocytes. *J Physiol* 2017;595(12):3835-45.
10. Saxton A, Tariq MA, Bordoni B. Anatomy, Thorax, Cardiac Muscle. 2021 Feb 9. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. PMID: 30570976.
11. Eisner DA, Caldwell JL, Kistamás K, Trafford AW. Calcium and Excitation-Contraction Coupling in the Heart. *Circ Res* 2017;121(2):181-95.
12. Feher J. The Cardiac Action Potential. In *Quantitative Human Physiology*. Elsevier, 2012;458-66.
13. Pinnell J, Turner S, Howell S. Cardiac muscle physiology, Continuing Education in Anaesthesia Critical Care & Pain 2007;7(3):85-8.
14. Higgins CB, Vatner SF, Braunwald E. Parasympathetic control of the heart. *Pharmacol Rev* 1973;25(1):119-55.
15. JP Howard Fee, James G Bovill, Physiology for Anesthesiologist, Part 1: Cardiovascular Physiology. Taylor and Francis Group, United Kingdom. 2004:1-33.
16. Leslie RA, Johnson EK, Goodwin AP. (Eds.). Dr Podcast Scripts for the Primary FRCA. Chapter 1.2. Cardiovascular Physiology. Cambridge University Press. 2011:30-52.
17. Rehman S, Khan A, Rehman A. Physiology, Coronary Circulation. [Updated 2020 May 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK482413>.
18. Bassenge E, Heusch G. Endothelial and neuro-humoral control of coronary blood flow in health and disease. *Rev Physiol Biochem Pharmacol* 1990;116:77-165.
19. Ibáñez B, Heusch G, Ovize M, Van de Werf F. Evolving therapies for myocardial ischemia/reperfusion injury. *J Am Coll Cardiol* 2015;65(14):1454-71.
20. Kumar V, Abbas AK, Aster JC. (2017). Robbins basic pathology e-book. Chapter 11 Heart. Elsevier Health Sciences. 2017:399-441.
21. Halladin NL. Oxidative and inflammatory biomarkers of ischemia and reperfusion injuries. *Dan Med J* 2015;62(4):B5054.
22. Eltzschig HK, Eckle T. Ischemia and reperfusion--from mechanism to translation. *Nat Med* 2011;17(11):1391-401.

23. Dong Y, Chen H, Gao J, Liu Y, Li J, Wang J. Molecular machinery and interplay of apoptosis and autophagy in coronary heart disease. *J Mol Cell Cardiol* 2019;136:27-41.
24. Liu XM, Yang ZM, Liu XK. Fas/FasL induces myocardial cell apoptosis in myocardial ischemia-reperfusion rat model. *Eur Rev Med Pharmacol Sci* 2017;21(12):2913-18.
25. Cadenas S. ROS and redox signaling in myocardial ischemia-reperfusion injury and cardioprotection. *Free Radic Biol Med* 2018;117:76-89.
26. Zhou T, Chuang CC, Zuo L. Molecular Characterization of Reactive Oxygen Species in Myocardial Ischemia-Reperfusion Injury. *Biomed Res Int* 2015;2015:864946. doi: 10.1155/2015/864946.
27. Moens AL, Claeys MJ, Timmermans JB, Vrints CJ. Myocardial ischemia/reperfusion-injury, a clinical view on a complex pathophysiological process. *Int J Cardiol* 2005;100(2):179-90.
28. Agrawal V, Gupta JK, Qureshi SS, Vishwakarma VK. Role of cardiac renin angiotensin system in ischemia reperfusion injury and preconditioning of heart. *Indian Heart J* 2016;68(6):856-61.
29. Escobales N, Nuñez RE, Javadov S. Mitochondrial angiotensin receptors and cardioprotective pathways. *Am J Physiol Heart Circ Physiol* 2019;316(6):H1426-38.
30. Vinten-Johansen J. Involvement of neutrophils in the pathogenesis of lethal myocardial reperfusion injury. *Cardiovasc Res* 2004;61(3):481-97.
31. Schanze N, Bode C, Duerschmied D. Platelet Contributions to Myocardial Ischemia/Reperfusion Injury. *Front Immunol* 2019;10:1260. doi: 10.3389/fimmu.2019.01260.
32. Yang BC, Virmani R, Nichols WW, Mehta JL. Platelets protect against myocardial dysfunction and injury induced by ischemia and reperfusion in isolated rat hearts. *Circ Res* 1993;72(6):1181-90.
33. Yang BC, Mehta JL. Platelet-derived adenosine contributes to the cardioprotective effects of platelets against ischemia-reperfusion injury in isolated rat heart. *J Cardiovasc Pharmacol* 1994;24(5):779-85.
34. Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium. *Circulation* 1986;74(5):1124-36.
35. Tomai F, Crea F, Chiariello L, Giorfrè PA. Ischemic preconditioning in humans: models, mediators, and clinical relevance. *Circulation* 1999;100(5):559-63.
36. Cohen MV, Liu GS, Downey JM. Preconditioning causes improved wall motion as well as smaller infarcts after transient coronary occlusion in rabbits. *Circulation* 1991;84(1):341-9.
37. Downey JM, Cohen MV. Mechanisms of preconditioning: correlates and epiphenomena. In: Marber MS, Yellon DM, eds. *Ischemia: Preconditioning and Adaptation*. Oxford, UK: BIOS Scientific Publishers Limited. 1996:21-34.
38. Yellon DM, Baxter GF. A "second window of protection" or delayed preconditioning phenomenon: future horizons for myocardial protection? *J Mol Cell Cardiol* 1995;27(4):1023-34.
39. Auchampach JA, Gross GJ. Adenosine A1 receptors, KATP channels, and ischemic preconditioning in dogs. *Am J Physiol* 1993;264(5 Pt 2):H1327-36.
40. Yao Z, Mizumura T, Mei DA, Gross GJ. KATP channels and memory of ischemic preconditioning in dogs: synergism between adenosine and KATP channels. *Am J Physiol* 1997;272(1 Pt 2):H334-42.
41. Sengul İ, Sengul D. Place of Mitochondrial Potassium-ATP Channels in The Mechanism of Effect of Ischemic Conditionings. *J Clin Anal Med* 2012;3(3): 370-3.
42. Zhao ZQ, Corvera JS, Halkos ME, Kerendi F, Wang NP, Guyton RA, et al. Inhibition of myocardial injury by ischemic postconditioning during reperfusion: comparison with ischemic preconditioning. *Am J Physiol Heart Circ Physiol* 2003;285(2):H579-88.
43. Argaud L, Gateau-Roesch O, Raïsky O, Loufouat J, Robert D, Ovize M. Postconditioning inhibits mitochondrial permeability transition. *Circulation* 2005;111(2):194-7.
44. Tsang A, Hausenloy DJ, Yellon DM. Myocardial postconditioning: reperfusion injury revisited. *Am J Physiol Heart Circ Physiol* 2005;289(1):H2-7.

45. Kin H, Zhao ZQ, Sun HY, Wang NP, Corvera JS, Halkos ME, et al. Postconditioning attenuates myocardial ischemia-reperfusion injury by inhibiting events in the early minutes of reperfusion. *Cardiovasc Res* 2004;62(1):74-85.
46. Sun HY, Wang NP, Kerendi F, Halkos M, Kin H, Guyton RA, et al. Hypoxic postconditioning reduces cardiomyocyte loss by inhibiting ROS generation and intracellular Ca²⁺ overload. *Am J Physiol Heart Circ Physiol* 2005;288(4):H1900-8.
47. Tsang A, Hausenloy DJ, Mocanu MM, Yellon DM. Postconditioning: a form of “modified reperfusion” protects the myocardium by activating the phosphatidylinositol 3-kinase-Akt pathway. *Circ Res* 2004;95(3):230-2.
48. Mastitskaya S, Marina N, Gourine A, Gilbey MP, Spyer KM, Teschemacher AG, et al. Cardioprotection evoked by remote ischaemic preconditioning is critically dependent on the activity of vagal pre-ganglionic neurones. *Cardiovasc Res* 2012;95(4):487-94.
49. Donato M, Buchholz B, Rodríguez M, Pérez V, Inserte J, García-Dorado D, et al. Role of the parasympathetic nervous system in cardioprotection by remote hindlimb ischaemic preconditioning. *Exp Physiol* 2013;98(2):425-34.
50. Pickard JM, Davidson SM, Hausenloy DJ, Yellon DM. Co-dependence of the neural and humoral pathways in the mechanism of remote ischemic conditioning. *Basic Res Cardiol* 2016;111(4):50. doi: 10.1007/s00395-016-0568-z.
51. Basalay MV, Mastitskaya S, Mrochek A, Ackland GL, Del Arroyo AG, Sanchez J, et al. Glucagon-like peptide-1 (GLP-1) mediates cardioprotection by remote ischaemic conditioning. *Cardiovasc Res* 2016;112(3):669-76.
52. Bosnjak ZJ, Ge ZD. The application of remote ischemic conditioning in cardiac surgery. *F1000Res* 2017;6:928. doi: 10.12688/f1000research.11018.1.
53. Thielmann M, Kottenberg E, Boengler K, Raffelsieper C, Neuhaeuser M, Peters J, et al. Remote ischemic preconditioning reduces myocardial injury after coronary artery bypass surgery with crystalloid cardioplegic arrest. *Basic Res Cardiol* 2010;105(5):657-64.
54. Thielmann M, Kottenberg E, Kleinbongard P, Wendt D, Gedik N, Pasa S, et al. Cardioprotective and prognostic effects of remote ischaemic preconditioning in patients undergoing coronary artery bypass surgery: a single-centre randomised, double-blind, controlled trial. *Lancet* 2013;382(9892):597-604.
55. Davies WR, Brown AJ, Watson W, McCormick LM, West NE, Dutka DP, et al. Remote ischemic preconditioning improves outcome at 6 years after elective percutaneous coronary intervention: the CRISP stent trial long-term follow-up. *Circ Cardiovasc Interv* 2013;6(3):246-51.
56. Hoole SP, Heck PM, Sharples L, Khan SN, Duehmke R, Densem CG, et al. Cardiac Remote Ischemic Preconditioning in Coronary Stenting (CRISP Stent) Study: a prospective, randomized control trial. *Circulation* 2009;119(6):820-7.
57. Heusch G, Gersh BJ. ERICCA and RIPHeart: two nails in the coffin for cardioprotection by remote ischemic conditioning? Probably not! *Eur Heart J* 2016;37(2):200-2.
58. Collard CD, Gelman S. Pathophysiology, clinical manifestations, and prevention of ischemia-reperfusion injury. *Anesthesiology* 2001;94(6):1133-8.
59. Canbaz S, Duran E, Ege T, Sunar H, Cikirikcioglu M, Acipayam M. The effects of intracoronary administration of vitamin E on myocardial ischemia-reperfusion injury during coronary artery surgery. *Thorac Cardiovasc Surg* 2003;51(2):57-61.
60. Lassnigg A, Punz A, Barker R, Keznickl P, Manhart N, Roth E, et al. Influence of intravenous vitamin E supplementation in cardiac surgery on oxidative stress: a double-blinded, randomized, controlled study. *Br J Anaesth* 2003;90(2):148-54.
61. Guan W, Osanai T, Kamada T, Hanada H, Ishizaka H, Onodera H, et al. Effect of allopurinol pretreatment on free radical generation after primary coronary angioplasty for acute myocardial infarction. *J Cardiovasc Pharmacol* 2003;41(5):699-705.

62. González-Montero J, Brito R, Gajardo AI, Rodrigo R. Myocardial reperfusion injury and oxidative stress: Therapeutic opportunities. *World J Cardiol* 2018;10(9):74-86.
63. Wang X, Yang L, Kang L, Li J, Yang L, Zhang J, et al. Metformin attenuates myocardial ischemia-reperfusion injury via up-regulation of antioxidant enzymes. *PLoS One* 2017;12(8):e0182777. doi: 10.1371/journal.pone.0182777.
64. Liang S, Ping Z, Ge J. Coenzyme Q10 Regulates Antioxidative Stress and Autophagy in Acute Myocardial Ischemia-Reperfusion Injury. *Oxid Med Cell Longev* 2017;2017:9863181. doi: 10.1155/2017/9863181.
65. Wang W, Kang PM. Oxidative Stress and Antioxidant Treatments in Cardiovascular Diseases. *Antioxidants (Basel)* 2020;9(12):1292. doi: 10.3390/antiox9121292.
66. Claustrat B, Leston J. Melatonin: Physiological effects in humans. *Neurochirurgie* 2015;61(2-3):77-84.
67. Sun H, Gusdon AM, Qu S. Effects of melatonin on cardiovascular diseases: progress in the past year. *Curr Opin Lipidol* 2016;27(4):408-13.
68. Carreira RS, Monteiro P, Gon Alves LM, Providência LA. Carvedilol: just another Beta-blocker or a powerful cardioprotector? *Cardiovasc Hematol Disord Drug Targets* 2006;6(4):257-66.
69. Dandona P, Ghanim H, Brooks DP. Antioxidant activity of carvedilol in cardiovascular disease. *J Hypertens* 2007;25(4):731-41.
70. Li XS, Uriuda Y, Wang QD, Norlander R, Sjöquist PO, Pernow J. Role of L-arginine in preventing myocardial and endothelial injury following ischaemia/reperfusion in the rat isolated heart. *Acta Physiol Scand* 1996;156(1):37-44.
71. Pernow J, Bohm F, Beltran E, Gonon A. L-arginine protects from ischemia-reperfusion-induced endothelial dysfunction in humans in vivo. *J Appl Physiol* (1985) 2003;95(6):2218-22.
72. Moens A, Claeys M, Bosmans J, Herman A. VC. Folate improves endothelial function after ischemia/reperfusion. *Circulation* 2002; 106 (Ref Type: Abstract): II-297.
73. Moens A, Claeys M, Bosmans J, Timmermans JP, Vrints C. Pretreatment with folic acid prevents ischemia/reperfusion induced endothelial dysfunction. *J Am Coll Cardiol* 2003;41(6):330A.
74. Sack S, Mohri M, Schwarz ER, Arras M, Schaper J, Ballagi-Pordány G, et al. Effects of a new Na⁺/H⁺ antiporter inhibitor on postischemic reperfusion in pig heart. *J Cardiovasc Pharmacol* 1994;23(1):72-8.
75. Xue YX, Aye NN, Hashimoto K. Antiarrhythmic effects of HOE642, a novel Na⁽⁺⁾-H⁺ exchange inhibitor, on ventricular arrhythmias in animal hearts. *Eur J Pharmacol* 1996;317(2-3):309-16.
76. Boyce SW, Bartels C, Bolli R, Chaitman B, Chen JC, Chi E, et al; GUARD During Ischemia Against Necrosis (GUARDIAN) Study Investigators. Impact of sodium-hydrogen exchange inhibition by cariporide on death or myocardial infarction in high-risk CABG surgery patients: results of the CABG surgery cohort of the GUARDIAN study. *J Thorac Cardiovasc Surg* 2003;126(2):420-7.
77. Liem DA, Verdouw PD, Ploeg H, Kazim S, Duncker DJ. Sites of action of adenosine in interorgan preconditioning of the heart. *Am J Physiol Heart Circ Physiol* 2002;283(1):H29-37.
78. Ely SW, Berne RM. Protective effects of adenosine in myocardial ischemia. *Circulation* 1992;85(3):893-904.
79. Mahaffey KW, Puma JA, Barbagelata NA, DiCarli MF, Leeser MA, Browne KF, et al. Adenosine as an adjunct to thrombolytic therapy for acute myocardial infarction: results of a multicenter, randomized, placebo-controlled trial: the Acute Myocardial Infarction Study of Adenosine (AMISTAD) trial. *J Am Coll Cardiol* 1999;34(6):1711-20.
80. Díaz R, Paolasso EA, Piegas LS, Tajer CD, Moreno MG, Corvalán R, et al. Metabolic modulation of acute myocardial infarction. The ECLA (Estudios Cardiológicos Latinoamérica) Collaborative Group. *Circulation* 1998;98(21):2227-34.
81. Li H, Wang C, Sun J, Liu C, Li N, Chen J. Pravastatin Decreases Infarct Size Induced by Coronary Artery Ischemia/Reperfusion with Elevated eNOS Expression in Rats. *Int Heart J* 2018;59(1):154-60.

82. Abarbanell AM, Herrmann JL, Weil BR, Wang Y, Tan J, Moberly SP, et al. Animal models of myocardial and vascular injury. *J Surg Res* 2010;162(2):239-49.
83. Verdouw PD, van den Doel MA, de Zeeuw S, Duncker DJ. Animal models in the study of myocardial ischaemia and ischaemic syndromes. *Cardiovasc Res* 1998;39(1):121-35.
84. Ytrehus K. The ischemic heart--experimental models. *Pharmacol Res* 2000;42(3):193-203.
85. Chorro FJ, Such-Belenguer L, López-Merino V. Modelos animales de enfermedad cardiovascular [Animal models of cardiovascular disease]. *Rev Esp Cardiol* 2009;62(1):69-84.
86. Zornoff LA, Paiva SA, Minicucci MF, Spadaro J. Experimental myocardium infarction in rats: analysis of the model. *Arq Bras Cardiol* 2009;93(4):434-40, 426-32.
87. Ytrehus K. Models of myocardial ischemia. *Drug Discovery Today: Disease Models* 2006;3(3):263-71.
88. Tang J, Xie Q, Pan G, Wang J, Wang M. Mesenchymal stem cells participate in angiogenesis and improve heart function in rat model of myocardial ischemia with reperfusion. *Eur J Cardiothorac Surg* 2006;30(2):353-61.
89. Lv X, Lu P, Hu Y, Xu T. miR-346 Inhibited Apoptosis Against Myocardial Ischemia-Reperfusion Injury via Targeting Bax in Rats. *Drug Des Devel Ther* 2020;14:895-905.
90. Litwin SE. The rat model of postinfarction heart failure. *Heart Fail* 1995;11:182-95.
91. Wu Y, Yin X, Wijaya C, Huang MH, McConnell BK. Acute myocardial infarction in rats. *J Vis Exp* 2011;(48):2464. doi: 10.3791/2464.
92. Liu P, Xu B, Cavalieri TA, Hock CE. Age-related difference in myocardial function and inflammation in a rat model of myocardial ischemia-reperfusion. *Cardiovasc Res* 2002;56(3):443-53.
93. Conci E, Pachinger O, Metzler B. Mouse models for myocardial ischaemia/reperfusion *Journal Für Kardiologie - Austrian Journal of Cardiology* 2006;13(7-8):239-44.
94. Camacho P, Fan H, Liu Z, He JQ. Large Mammalian Animal Models of Heart Disease. *J Cardiovasc Dev Dis* 2016;3(4):30. doi: 10.3390/jcdd3040030.
95. Schott RJ, Rohmann S, Braun ER, Schaper W. Ischemic preconditioning reduces infarct size in swine myocardium. *Circ Res* 1990;66(4):1133-42.
96. Chen Y, Shao DB, Zhang FX, Zhang J, Yuan W, Man YL, et al. Establishment and evaluation of a swine model of acute myocardial infarction and reperfusion-ventricular fibrillation-cardiac arrest using the interventional technique. *J Chin Med Assoc* 2013;76(9):491-6.
97. Crisóstomo V, Maestre J, Maynar M, Sun F, Báez-Díaz C, Usón J, et al. Development of a closed chest model of chronic myocardial infarction in Swine: magnetic resonance imaging and pathological evaluation. *ISRN Cardiol* 2013;2013:781762. doi: 10.1155/2013/781762.
98. Suzuki Y, Lyons JK, Yeung AC, Ikeno F. In vivo porcine model of reperfused myocardial infarction: in situ double staining to measure precise infarct area/area at risk. *Catheter Cardiovasc Interv* 2008;71(1):100-7.
99. Jones SP, Tang XL, Guo Y, Steenbergen C, Lefer DJ, Kukreja RC, et al. The NHLBI-sponsored Consortium for preclinicaL assESsment of cARdioprotective therapies (CAESAR): a new paradigm for rigorous, accurate, and reproducible evaluation of putative infarct-sparing interventions in mice, rabbits, and pigs. *Circ Res* 2015;116(4):572-86.
100. Sharp TE 3rd, Gong Z, Scarborough A, Goetzman ES, Ali MJ, Spaletta P, et al. Efficacy of a Novel Mitochondrial-Derived Peptide in a Porcine Model of Myocardial Ischemia/Reperfusion Injury. *JACC Basic Transl Sci* 2020;5(7):699-714.
101. Duan T, Song R, Zhang J, Kong R, Lei H, Xiang D. Continuous balloon occlusion has more influence on microcirculation function assessed by the index of coronary microcirculatory resistance in a pig model. *Int J Clin Exp Med* 2018;11(12):13003-13.
102. Lindsey ML, Bolli R, Canty JM Jr, Du XJ, Frangogiannis NG, Frantz S, et al. Guidelines for experimental models of myocardial ischemia and infarction. *Am J Physiol Heart Circ Physiol* 2018;314(4):H812-38.