Symposium Highlight

PHYSIOLOGY AND FUNCTIONAL PATHOLOGY OF THE LYMPHATIC SYSTEM WITH IMPLICATIONS FOR THE FONTAN PATIENT

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ABSTRACT

Contractile function of the collecting lymphatic vessels depend on smooth muscle cells, one-way valves, surrounding tissues, and regulation by the autonomic nervous system. The potentially deleterious effects of the Fontan procedure and elevated central venous pressure on lymphatic function leading to life-threatening complications are described.

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PHYSIOLOGY AND FUNCTIONAL PATHOLOGY OF THE LYMPHATIC SYSTEM

The lymphatic system is a vital component of the human body's immune system, playing a crucial role in maintaining fluid balance, absorbing fats from the digestive system, and facilitating the body's immune response. Comprised of a network of lym-

phatic vessels this system functions to transport lymph – a clear fluid containing white blood cells – throughout the body.

The lymphatic system helps maintain fluid balance by collecting interstitial fluid from tissues and returning it to the bloodstream. This process prevents the build-up of fluids in the tissues, known as edema (1).

The contractile function of collecting lymphatic vessels is a crucial aspect of the lymphatic system's operation. Unlike the cardiovascular system, which relies on the heart's pumping action to circulate blood, the lymphatic system does not have a central pump. Instead, lymphatic vessels have intrinsic contractile properties that enable them to propel lymph fluid throughout the body. Here are some key points regarding the contractile function of collecting lymphatic vessels:

- Smooth Muscle Cells: Collecting lymphatic vessels are lined with endothelial cells and surrounded by layers of smooth muscle cells. These smooth muscle cells exhibit rhythmic contractions, known as lymphangion contractions, that propel lymph along the vessels (1).
- 2) One-Way Valves: Similar to veins in

- the circulatory system, collecting lymphatic vessels contain one-way valves that prevent backflow of lymph. As the smooth muscle cells contract, these valves open to allow lymph to flow in one direction and then close to prevent retrograde movement.
- 3) Influence of Surrounding Tissues:
 The contractile function of collecting lymphatic vessels can be influenced by external factors, including changes in tissue pressure, local concentrations of substances like nitric oxide, and neural inputs. These factors can modulate the frequency and strength of lymphatic contractions (2).
- 4) Role in Fluid Transport: By contracting rhythmically, collecting lymphatic vessels propel lymph fluid from the interstitial spaces towards larger lymphatic vessels and eventually into the bloodstream. This process helps maintain fluid balance, remove waste products, and transport immune cells throughout the body.
- 5) Regulation by Autonomic Nervous System: The contractile activity of lymphatic vessels is regulated, in part, by the autonomic nervous system (3,4).

THE FONTAN CIRCULATION

In the context of a Fontan circulation, which is a surgical procedure used to treat univentricular heart defects, there are distinctive lymphatic changes that can occur. The Fontan procedure involves diverting venous blood directly to the pulmonary arteries, bypassing the right ventricle. This alteration in circulation can have implications for the lymphatic system, as it is intricately connected to the cardiovascular system. Here are some key aspects of lymphatic changes in the context of Fontan circulation:

 The altered hemodynamics in Fontan circulation, characterized by increased central venous pressure and reduced

- cardiac output, can lead to impaired lymphatic drainage (5,6).
- 2) The combination of venous congestion and reduced cardiac function associated with Fontan circulation can result in increased interstitial fluid in tissues. This excess fluid may overwhelm the lymphatic system's capacity to drain it efficiently, contributing to tissue edema.
- 3) Fontan patients are at an increased risk of the lymphatic vessels establishing new transport channels aiming for locations with low pressures such as, the intestinal tract, the airways, the pleural space and the peritoneum.

Given the impact of Fontan circulation on the lymphatic system, there is emerging interest in exploring lymphatic interventions to improve fluid balance and overall outcomes in Fontan patients. Strategies such as lymphatic imaging, lymphatic vessel bypass procedures, or pharmacological interventions targeting lymphatic function are areas of active research.

CONFLICT OF INTEREST AND DISCLOSURE

The author declares no competing financial interests exist.

REFERENCES

- 1. Mohanakumar, S, N Telinius, B Kelly, et al: Reduced lymphatic function predisposes to calcium channel blocker edema: A randomized placebo-controlled clinical trial. Lymphat. Res. Biol. 18 (2020), 156-165.
- Kelly, B, CL Smith, M Saravanan, et al: Spontaneous contractions of the human thoracic duct-Important for securing lymphatic return during positive pressure ventilation. Physiol. Rep. 10 (2022), e15258.
- Boedtkjer, DB, J Rumessen, U Baandrup, et al: Identification of interstitial Cajal-like cells in the human thoracic duct. Cells Tissues Organs 197 (2013), 145-158.
- 4. Telinius, N, U Baandrup, J Rumessen, et al: The human thoracic duct is functionally

- innervated by adrenergic nerves. Am. J. Physiol-Heart C. 306 (2014), H206-H213.
- Mohanakumar, S, N Telinius, B Kelly, et al: Morphology and function of the lymphatic vasculature in patients with a fontan circulation. Circ. Cardiovasc. Imaging 12 (2019), e008074.
- 6. Telinius, N, VE Hjortdal: Role of the lymphatic vasculature in cardiovascular medicine. 12 (2019), e008074.

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