Haemodynamic Monitoring in Space

Monitorização Hemodinâmica no Espaço

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ABSTRACT: *Despite the fact that, during the last decade, modern countermeasure systems and preventive medicine have been proven useful in reducing the effects of microgravity upon the human body, they are likely to become outdated in forthcoming space missions. With space becoming gradually more accessible to the general public and with missions usually taking longer than six months, the risk of severe medical conditions increases significantly. In this context, medical autonomy will be the cornerstone for achieving good healthcare outcomes, and adequate medical equipment will be a determinant factor influencing both diagnosis and treatment. Reliable dedicated haemodynamic monitoring systems must therefore be available in orbit so as to guide patient management in critical medical situations. The equipment available in orbit, however, is unsuitable for emergency health care, either providing incomplete haemodynamic information or delivering it in an intermittent fashion. Furthermore, there exist a number of haemodynamic monitoring systems approved for terrestrial use which have the potential to bring about significant benefits for space medicine and which have never been tested in microgravity. This paper means to provide an overview of the physiological determinants of cardiovascular function and its adaptation to weightlessness, as well as précis the pathophysiological phenomena that define shock states. It also aims to review the existing haemodynamic monitoring capabilities in orbit and to explore new points for their improvement.*

KEYWORDS: *cardiovascular system; shock; weightlessness; microgravity; space medicine.*

RESUMO: *Ainda que durante a última década os sistemas de contramedida modernos e a medicina preventiva tenham se provado úteis na redução dos efeitos da microgravidade sobre o corpo humano, é provável que os mesmos acabem ultrapassados nas próximas missões espaciais. Com o espaço se tornando gradualmente mais acessível para o público geral e com as missões normalmente levando mais de seis meses, o risco de sofrer de condições clínicas graves aumenta de forma significativa. Neste contexto, a autonomia médica será o alicerce para que se atinjam bons resultados em termos de assistência médica, e o equipamento médico adequado será um fator determinante que influenciará tanto o diagnóstico quanto o tratamento. Sistemas de monitorização hemodinâmica dedicados confiáveis devem, portanto, estar disponíveis em órbita para orientar a gestão de pacientes em*

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situações clínicas críticas. O equipamento disponível em órbita é, entretanto, impróprio para tratamento médico de emergência, fornecendo informações hemodinâmicas incompletas ou apresentando estas de forma intermitente. Além disso, existem vários sistemas de monitorização hemodinâmica aprovados para uso terrestre que têm potencial para gerar benefícios significativos para a medicina espacial e que nunca foram testados em ambiente de microgravidade. Este trabalho intenciona proporcionar uma visão geral dos determinantes fisiológicos da função cardiovascular e sua adaptação à ausência de gravidade, fazer um resumo dos fenômenos fisiopatológicos que definem os estados de choque, revisar as capacidades de monitorização hemodinâmica existentes em órbita e explorar novos ângulos para promover sua melhora.
PALAVRAS-CHAVE: *sistema cardiovascular; choque; ausência de gravidade; microgravidade; medicina espacial.*

1 Background

Hemodynamic monitoring is recommended for adequate management of critically ill patients with cardiovascular insufficiency who do not respond to initial resuscitation treatment (ANTONELLI et al, 2007; FINFER et al., 2013). A broad spectrum of systems are currently available in hospitals to help clinicians diagnose and manage patients in Intensive Care Units (ICU) and Emergency Departments (ED) around the world. Haemodynamic Monitoring systems are required to evaluate cardiovascular status of critically ill patients, perform accurate diagnosis, decide appropriate management and monitor patient responses to treatment.

In forthcoming space exploration missions, and with the rise of space tourism, crews and medical teams will have to deal with unprecedented medical challenges. Conditions common on Earth but yet rare in space, such as acute myocardial infarction, sepsis, major trauma, severe respiratory failure and shock will have to be incorporated into space medicine textbooks (BILLICA et al., 1996). As mission duration and age of space travellers increases, the risk of occurrence of severe medical conditions leading to haemodynamic disarrangements rises significantly. Furthermore, cardiovascular responses to physiological and pathological situations are likely to be modified in space. Diagnosis and treatment of such severe medical conditions may be radically different in microgravity than it is on Earth and may be influenced by adaptive physiological changes induced by prolonged exposure to weightlessness.

In this new scenario, reliable hemodynamic monitoring systems will be determinant to guide cardiovascular management. Dedicated systems will be needed to unveil the underlying haemodynamic pattern and to monitor patient evolution and response to treatment. However, few if not any appropriate haemodynamic monitoring systems have been tested or validated for this purpose in space.

Finding the ideal space haemodynamic monitoring system is challenging and many factors need to be taken into account. Potential candidate systems should preferably be minimally invasive, provide continuous information, and be accurate and reliable. Spaceflight intrinsic limitations and constrains such as time, resource availability and insufficient in-situ medical expertise must also be considered. Monitoring systems should provide sufficient but not excessive cardiovascular information so less trained caregivers can easily understand and interpret data. Information displayed should be user-friendly and incorporated into a decision-making algorithm to maximize autonomy from Earth. Any space haemodynamic monitoring systems should also be able to follow patient evolution and warn the medical team well in advance so required treatment options can be undertaken in time. Finally, data relay and storing capabilities should be available so necessary information can be sent back to Earth-based medical teams for its evaluation in order to provide appropriate ground support to crews.

2 Main haemodynamic variables

Cardiac Output (CO) is a principal haemodynamic variable used to determine human cardiovascular profile and is commonly used in physiological research and clinical practice. CO can be defined by the product of Stroke Volume (SV) and Heart Rate (HR) and is determined by three factors being preload, afterload and contractility. Preload is referred as the initial stretching of the cardiac cells prior to contraction. The Frank - Starling relationship determines that changes in preload conditions cause increases in SV following an almost linear relation while the heart is in a preload-dependent condition. However, when muscular fibers from cardiac myocites reach a certain level of stretching, the heart becomes preload-independent, meaning that preload increases do not cause significant increases in SV. Preload is related to venous return, which is in turn related to venous volume and venous system capacitance. Its precise measure poses significant challenges but changes in Central Venous Pressure (CVP) or in ventricular end-diastolic volumes can be used for its estimation. Afterload is generally conceived as the “load” against which the heart must contract to eject blood. An increase in afterload reduces contraction velocity of cardiac myocytes, which reduces stroke volume if contraction time is kept constant. Afterload mainly depends in Systemic Vascular Resistances (SVR) and aortic compliance. While aortic compliance is rather stable and depends on age, SVR are generated in small arterioles in response to sympathetic nerve stimulation controlling distribution of blood flow to different tissues. Interaction between CO and SVR generate arterial blood pressure (systolic, diastolic and mean arterial blood pressure; SBP, DBP and MAP). SVR can be estimated from the determination of CO, MAP and CVP using the following simplified equation based on the Ohms law:

$$SVR = \frac{(MAP - CVP)}{CO}$$

Formula 1: relation between SVR, CO, MAP and CVP

Nevertheless, since CVP is often markedly inferior to MAP it can be omitted from the equation, so SVR can be calculated directly from CO and MAP alone. Finally, contractility is defined as intrinsic ability of the myocardial fibres to generate work independent of changes in loading conditions and can be modified by sympathetic nerve activation but also by many forms of cardiac injury. CO, SVR and Preload estimators provide crucial information on cardiovascular system responses and adaptation to physiological and pathological situations and are cornerstone when defining main patterns of cardiovascular insufficiency in critically ill patients (Table 1) (RICHARD, 2011; FINFER et al., 2013).

	Hypovolemic	Cardiogenic / Obstructive[3]	Distributive	Neurogenic
CO	N or ↓	↓	↑ (or ↓)	N or ↓
SVR	↑	↑	↓	↓
Preload	↓	N or ↑	↓	N or ↓

Table 1: Different haemodynamic patterns in shock states.

In table 1, cardiogenic shock can be divided depending on its origin in primary cardiogenic shock (myocardial infarction, myocarditis, arrhythmias etc.) and obstructive shock (massive pulmonary embolism and cardiac tamponade). Distributive shock can be further divided into septic (i.e. due to severe infections) and anaphylactic shock states (i.e. massive allergy reactions), which both share common haemodynamic profiles. Distributive shock usually presents with increased CO, however it may be initially reduced if hypovolemia is present. Neurogenic shock is a type of distributive shock in which CO is not increased due to the lack of neural cardiac stimulation (i.e. spine trauma or cranial trauma)

3 Shock and Resuscitation objectives

The main function of the cardiovascular system is to deliver oxygen and nutrients to cells. Oxygen is required for producing ATP (adenosine tri-phosphate), which is used as an energy exchange molecule and required in most cellular processes. Oxygen delivery mainly depends on blood haemoglobin content, haemoglobin saturation, and CO. It can be calculated using the following formula:

[3] CO: Cardiac Output ; SVR: systemic vascular resistances.

$$DO_2 = \overbrace{[(1.39 \times Hb \times \frac{SO_2}{100}) + 0,003 \times PO_2]}^{CaO_2} \times \overbrace{HR \times SV}^{CO}$$

Formula 2: Arterial oxygen content (CaO_2) is calculated by multiplying haemoglobin concentration (*Hb*) in gr/dL by arterial oxygen saturation (SO_2), and 1.39 mL/gr, which is the maximum amount of oxygen transportable by haemoglobin if fully saturated. A minor quantity of oxygen is also transported dissolved in plasma (0.003 ml of O_2 per each mmHg of arterial oxygen partial pressure or PO_2). DO_2 is obtained from the product of CO (heart rate by stroke volume) and CaO_2.

Additionally, arterial pressure must be sufficient to assure adequate tissue blood flow. MAP is generally used for estimating tissue perfusion pressure. Failure of the cardiovascular system to deliver enough oxygen to cope with tissue demands causes cellular hypoxia and impedes normal ATP production. In order to maintain cellular activity, anaerobic metabolism is used to obtain ATP, which in turn enhances production of lactate and free protons. The onset of anaerobic cellular metabolism can be detected by increases in blood lactate levels and drop of serum pH or bicarbonate. However, prior to the appearance of increased blood lactate levels, progressive misbalance between oxygen delivery and consumption can be detected by decreases in central venous saturation obtained from a venous catheter placed in a central venous vessel near the right atrium. Therefore, high lactate levels and low central venous saturation are markers of insufficient tissue perfusion and oxygen delivery (ANTONELLI et al, 2007; FINFER et al., 2013).

Pathologic situations leading to persistent hypo-perfusion, determined as low central venous saturation and high lactate levels despite initial corrective measures, define a state of cardiovascular shock. Clinical features such as cutaneous signs (cold and clammy skin, and distal cyanosis) reduced urinary output (< 0.5 ml/Kg of body weight), reduced mental status and persistent hypotension (MAP < 65 mmHg) despite initial resuscitation measures are also considered as markers of shock. Therefore, objectives of haemodynamic “resuscitation” will be recovery of a sufficient organ perfusion pressure (MAP > 65 mmHg) and compensation of oxygen demands by increasing oxygen delivery (ANTONELLI et al, 2007; FINFER et al., 2013).

Intravascular volume expansion by administration of an intravenous fluid load is the first therapeutic approach in most shock states however different origins of shock require different treatments for stabilisation. Initial basic haemodynamic monitoring should consist on blood pressure measure (either non-invasively by an inflatable arm cuff or invasively by an indwelling arterial catheter), central venous pressure (by placement of a central venous catheter via jugular or subclavia veins), urine output monitoring, heart rate and oxygen saturation (using finger pulsioximetry). An initial goal-directed simple echocardiographyic assessment is usually recommended. Together with accurate medical history this approach should help determining the underlying haemodynamic pattern

leading to shock. When patients fail to respond to initial therapeutic approaches advanced haemodynamic monitoring systems should be used for confirming haemodynamic diagnosis and monitor treatment responses (ANTONELLI et al., 2007; FINFER et al., 2012).

4 Cardiovascular adaptation to spaceflight

Microgravity induces a cephalic fluid shift that occurs early into spaceflight. This central compartment fluid overload is the main determinant of human cardiovascular adaptation to microgravity. Fluid shift varies throughout time, being maximal after a few hours in space for later decreasing progressively. The loose of craneo-caudal gravitational pull exerted to the peripheral venous system on Earth leads to a reduced venous system capacitance and increases venous return. Consequently, preload is increased in microgravity during initial phases of spaceflight, so are SV and CO (BUCKEY, 2006; BARRAT, POOL, 2008).

Plasma volume decreases rapidly after few days in orbit. Part of the reduction in plasma volume is caused by extravasation of fluids to the interstitial and intracellular spaces. Neither CVP nor urine output are increased in microgravity during initial phases of spaceflight. Changes in thoracic volumes and pressure explain maintenance or even reduction of CVP levels making its measures less reliable of venous return, while plasma extravasation and reduced fluid intake after first days in space explain the reduced urinary output. As intravascular plasma volume decreases haematocrit levels increase. Erythropoietin secretion is down-regulated in response, and absolute red blood cell mass is therefore decreased. These compensatory mechanisms return central venous volume, SV and CO to pre-flight values after some weeks in space (BUCKEY, 2006; BARRAT, POOL, 2008).

The lack of a craneo-caudal gravitational gradient causes inhibition of baroreceptor induced-reflexes aimed at maintaining arterial blood pressure and adequate organ perfusion pressure on Earth. In consequence, a reduction of SVR can be observed early in microgravity and a slight decrease in blood pressure has been reported during spaceflight.

Finally, as mission duration extends to several weeks or months cardiovascular adaptation evolves towards a reduction in total plasma volume, total blood cell mass, inappropriate baroreceptor activation, reduction in SV, CO and cardiac mass in some cases. Nevertheless, these changes represent an adaptive response to a new environment and do not generally impede human activity or reduce astronaut physical performance in orbit. Overall, cardiovascular performance and aerobic capacity is maintained in space and can even increase due to intensive physical training. However, upon return to Earth, reductions in effective intravascular fluid, SV / CO, baroreceptor responsiveness and red blood cell mass cause well known syndromes such as Post-flight Orthostatic Intolerance and Space Induced Anaemia. In current missions, a significant portion of time is devoted to countermeasure programmes, which aim at minimizing deleterious cardiovascular effects of microgravity on astronauts and improve rehabilitation after missions. Although different strategies may be present depending on nationality, a

combined approach implementing both restrictive and aerobic intensive exercise programmes, nutritional supplementation and a number of pre-landing procedures such as Low Body Negative Pressure and Fluid Load have proven to be effective (BUCKEY, 2006; BARRAT, POOL, 2008).

Despite extensive knowledge about human adaptation to spaceflight is currently available, physiological responses of the human body in severe medical conditions are not yet available. Abovementioned adaptive changes induced by microgravity may lead to radically different responses to shock states during spaceflight. Furthermore, variables considered as endpoints for cardiovascular resuscitation should also be evaluated in space to confirm their reliability. Similarly, main treatment options for shock states may not be applicable in orbit or may not prove to be as beneficial as they are on ground. However, specific validation studies are not likely to be feasible in space. In this context, haemodynamic monitoring systems are necessary to confirm effectiveness of medical management.

5 Haemodynamic monitoring in space

Few methods are available in orbit for performing an accurate hemodynamic evaluation. As previously mentioned, CO, SVR and fluid shifts are the main variables determining cardiovascular performance, hemodynamic physiological responses, and cardiovascular adaptation to spaceflight.

Determination of cardiac output has been given special importance in space physiology research due to its main role determining cardiovascular performance. As technology has evolved non-invasive methods for estimating CO have taken over invasive and more complex systems. Gas re-breathing systems were the first to provide accurate hemodynamic evaluation of astronauts during space missions. CO intermittent monitoring during spaceflight showed increases in CO (18% to 29%) coupled with reductions in systemic vascular resistances (SVR) (-24%) with minimal hear rate (HR) decrease (PRISK et al., 1993; SHYKOFF et al., 1996; NORSK et al., 2006) in short duration missions. These findings represented the first evidence of stroke volume (SV) increase during initial phases of spaceflight. During the decade of the ‘90 bio-impedance technology for continuous non-invasive hemodynamic monitoring was a promising new method. Bio-impedance systems used changes in thoracic electrical impedance for determining SV and CO continuously. First results were comparable to those published in previous reports and showed increases in CO (+1-1,7 L/min) during microgravity phases of parabolic flights (JOHNS, et al., 1994; HAMILTON, et al., 2011). Despite its advantages, bio-impedance based hemodynamic monitoring systems were dramatically affected by numerous factors such as surrounding electrical noise, patient movement, subcutaneous fat content and sensor positioning which limited their applicability in both spaceflight and real clinical scenarios on the Earth. As ultrasound technology evolved, echocardiography was introduced in spaceflight and permitted estimation of hemodynamic parameters offering a number of advantages over gas re-breathing methods. Recent results have confirmed previous observations and demonstrated on-orbit echocardiography evaluation is feasible and could be accurate enough even if performed by non-

specialized examiners, provided ground support is available (MUKAI, 1991; LONNIE, 2011). Despite its benefits, echocardiography has two important drawbacks, which are image acquisition and interpretation that require a certain degree of expertise, and the lack of continuous monitoring capability. Echocardiography is the only method currently implemented in space for advanced hemodynamic monitoring (BARRAT, POOL, 2008).

Significant research efforts have been conducted in microgravity for precisely determining fluid shift due to its principal role in human cardiovascular adaptation to spaceflight. Fluid shift modifies venous return and preload, and influences all other haemodynamic variables early in microgravity. However, its estimation using CVP is not reliable mainly due to intrathorathic pressure changes in microgravity. Early studies using leg girth measurements reported cephalic fluid displacement originated in lower extremities to range from 0.9 to 2L, and become complete 1.5h to 6h after microgravity ingress in space missions (THORNTON, 1987; MOORE, 1987). However, parabolic flight measures and bed-rest results differed from those obtained in real spaceflight for both leg volume loss and its distribution (THORNTON, 1992). By using strain gauge plethysmography a scarce 225ml leg volume loss was measured after 20s of microgravity when subjects where standing in parabolic flights (BAILLIART, 1998). Observed discrepancies in thoracic fluid shift origin and magnitude were explained by a different relevance of leg and abdominal compartments. The abdominal venous blood compartment constitutes an important whole blood pool, whereas legs provide a delayed but substantial fluid/plasma volume from interstitial space (JOHANSEN, 1997). Both compartments seem to contribute to total fluid delivery in a similar proportion as recently reported (LONNIE, 2011). Thereafter, measuring leg volume changes can only provide half of the information when trying to quantify thoracic fluid shift and a different approach is required to quantify the exact magnitude of thoracic fluid displacement. Studies based on bio-impedance have showed that transition to microgravity was associated with Thoracic Fluid Content increase in parabolic flights (THORNTON, 1987; MUKAI, 1991, 1994). TFC was decreased by 3.2% during 2G phases whereas a 3.4% increase was observed in microgravity (IWASE, 1999). Bio-impedance was also used in microgravity simulation studies for determining TFC and leg, pelvic and arm volumes during bed-rest. Although on-ground results of segment volumes did not match real spaceflight observed changes, overall thoracic fluid shift reached similar values (MONTGOMERY, 1993). Nevertheless, due to the reduced accuracy levels and low signal to noise ratio of Bio-impedance based monitoring systems their use in both terrestrial and space medicine has been limited. Finally, thoracic fluid shift and consequent preload increases are transient and may be different throughout spaceflight. Therefore its interpretation should be made with caution and duration of exposure to microgravity should be taken into account when determining different patterns of shock.

6 New potential systems for non-invasive haemodynamic monitoring in space

6.1 Bio-reactance

Bio-reactance based CO monitoring methods using electrical frequency modulation, as opposed to amplitude modulation of bio-impedance, offer a promising solution for enabling accurate and reliable space hemodynamic monitoring capabilities. Bio-reactance based systems have been proven to substantially increase signal to noise ratio, improve precision, present smaller bias, faster response and higher sensitivity and specificity for detecting directional changes (SQUARA, 2007). These systems have shown good correlation of measures when compared against standard haemodynamic monitoring systems in various clinical settings (Medical, Surgical and Cardiac Intensive Care Units) (RAVAL, 2008). Bio-reactance was found to be equivalent to other methods for minimally invasive haemodynamic monitoring such as arterial pulse contour analysis (MARQUÉ, 2009), help on diagnosis of acute pulmonary oedema (GARCÍA, 2011) and was able to predict fluid responsiveness in patients after cardiac surgery (BENOMAR, 2010).

Furthermore, by implementing software analysis and correction algorithms, noise problems of previous measurement methods based in bio-impedance could be overcome. A 2 $k\Omega^{-1}$ increase in thoracic bio-impedance has been correlated with 250-300ml thoracic fluid shifts during passive leg raising in critically ill patients on Earth (BENOMAR, 2010), and during haemodialysis, a 1 $k\Omega^{-1}$ change has been established to be equivalent to approximately 200 mL change in total thoracic water (JABOT, 2009). This parameter, could be used as an estimator of preload changes following volume expansion in haemodynamic resuscitation. If validated for spaceflight use, Bio-reactance based haemodynamic monitoring systems may offer unprecedented level of accuracy for measuring continuously both CO and TFC in space. Their use in microgravity may permit a new and totally non-invasive reliable advanced haemodynamic diagnosis and monitoring capabilities in orbit. However, its reliability and applicability in space health care systems have not yet been explored in microgravity.

6.2 Finger tonometry

Real-time, beat-to-beat information on blood pressure, CO, SV and SVR, and other hemodynamic parameters can be obtained from finger tonometry. An inflatable wrap is used to clamp pulsating finger artery by applying equivalent counter pressure. Arterial waveform can be read and analyzed, and serves as the basis for the measurement of SV and CO. This system has been validated during major abdominal, thoracic and cardiac surgery (CHEN et al., 2012). Its reliability was compared against transpulmonray thermodilution in patients undergoing elective cardiac surgery and good correlation of measures was found between the two methods. Furthermore, it can estimate values for predicting fluid responsiveness and has been found to detect changes in CO and SV induced by abrupt changes in preload after a passive leg raising (BROCH et al., 2010). Finger tonometry has the

potential for providing significant benefits for both research and space medicine by enabling real-time, easy-to-use, totally non-invasive and cheap blood pressure and CO monitoring. However it has not yet been validated in other medical scenarios, especially in shock states where peripheral circulation may be reduced. Further Earth-based research should be performed before it can be used for human health care in orbit.

6.3 Aortic ultrasonography

Measurements of CO, SV and SVR can be estimated by Doppler analysis of the ascending aorta blood flow, measured for the suprasternal notch without the need for direct structure visualization. Reliability of aortic ultrasonography systems for advanced haemodynamic monitoring of patients in the ED, Operation Room, and ICU has been evaluated. Correlation between pulmonary artery catheter and aortic ultrasonography measures was acceptable, although relevant systematic and variable errors were detected in critically ill patients in the ICU. Furthermore, it was able to differentiate between different shock types in these patients (VAN LELYVELD-HAAS et al., 2008). Although aortic ultrasonography requires a certain level of training its use in the ICU setting was reported to be easy and may be easier to learn than echocardiography. If validated for its use in orbit, aortic ultrasonography could provide valuable information for initial assessment of shock states as well as monitoring response to emergency treatment. However, this technique is not a continuous monitoring system and its measurement ability depends on operator skills and patient's echographic window. Other methods should then be chosen for continuous haemodynamic monitoring in patients at higher risks of treatment failure or with persistent shock states.

7 Conclusions

Critical medical situations may occur in forthcoming space missions due to the increasing number of space flights, astronaut's and space tourist's age, and extended mission duration. Prolonged exposure to microgravity induces cardiovascular adaptation, which may lead to significantly different responses to pathological situations. In this context, reliable haemodynamic monitoring systems may be necessary for diagnosis and guide therapy of severely ill crewmembers. Many factors determine characteristics of the ideal space monitoring system but minimally invasive, reliable and easy to use systems should be prioritised. In addition to basic parameters such as heart rate and blood pressure, cardiac output and systemic vascular resistances are informative variables that should be monitored in microgravity in critical medical situations. Furthermore, accurate measure of thoracic fluid shift and thoracic fluid content may help in the diagnosis. Few methods for estimating these variables are currently available in space and are either difficult to use, do not provide continuous information or highly depend on the operator. New totally non-invasive haemodynamic monitoring systems based on bio-reactance, finger tonometry or ultrasonic aortic flow measures may overcome limitations of

current methods and may prove to be very useful in space. However, their utility and applicability in microgravity is yet to be explored. Preliminary evaluation in Earth-based microgravity platforms such as parabolic flights is recommendable before these systems can be implemented into space medical systems.

References

ANTONELLI, M. et al. Hemodynamic monitoring in shock and implications for management. International Consensus Conference, Paris, France. **Intensive Care Med**, v. 33, p. 575-590, 2007.

BAILLIART, O. Changes in lower limb volume in humans during parabolic flight. **J Appl Physiol**, v. 85, n. 6, p. 2100-5, 1998.

BARRAT, M.; POOL, S. **Principles of Clinical Medicine for Space Flight**. Various Chapters. Springer Science + Business Media, LLC 2008. ISBN: 9780387988429

BENOMAR, B. Fluid responsiveness predicted by noninvasive Bioreactance-based passive leg raise test. **Intensive Care Med**, v. 36, p. 1875-81, 2010.

BILLICA, R.D. et al. Perception of the medical risk of spaceflight. **Aviation, Space, and Environmental Medicine**, v. 67, n. 5, p. 467-73, 1996.

BROCH, O. et al. A comparison of the Nexfin and transcardiopulmonary thermodilution to estimate cardiac output during coronary artery surgery. **Anesthesia**, 2010.

BUCKEY, J.C. Space Physiology. Various Chapters. Oxford University Press 2006. ISBN: 9780195137255.

CHEN, G. et al. Comparison of noninvasive cardiac output measurements using the Nexfin monitoring device and the esophageal Doppler. **Journal of Clinical Anesthesia**, v. 24, p. 275–283, 2012.

FINFER, S. et al. Circulatory Shock. **N Engl J Med**, v. 369, n. 18, 2013.

GARCÍA, X. Are Dynamic Changes In Cardiac Output And Thoracic Fluid Content Useful In Acute Heart Failure Diagnosis? **Am J Respir Crit Care Med**, v. 183:A2648, 2011.

HAMILTON, D. et al. On-Orbit Prospective Echocardiography on International Space Station Crew. **Echocardiography**, v. 28, n. 5, p. 491-501, 2011.

IWASE, S. Sympathetic outflow to muscle in humans during short periods of microgravity produced by parabolic flight. **Am J Physiol**, v. 277(2 Pt 2), p. R419-26, 1999.

JABOT, J. Passive leg raising for predicting fluid responsiveness: importance of the postural change. **Intensive Care Med**, v. 35, p. 85-90, 2009.

JOHANSEN, L.B. Contribution of abdomen and legs to central blood volumen expansión in humans during immersion. **J Appl Physiol**, v. 83, p. 695-699, 1997.

JOHNS, J.P. et al. Doppler evaluation of cardiac filling and ejection properties in humans during parabolic flight. **J Appl Physiol**, v. 76, n. 6, p. 2621-6, 1994.

LONNIE, G. Mechanisms of increase in cardiac output during acute weightlessness in humans. **J Appl Physiol**, v. 111, n. 2, p. 407-11.

MARQUÉ, S. Comparison between Flotrac-Vigileo and Bioreactance, a totally noninvasive method for cardiac output monitoring. **Critical Care**, v. 13:R73, 2009.

MONTGOMERY, L.D. Body volume changes during simulated microgravity. II: Comparison of horizontal and head-down bed rest. **Aviat Space Environ Med**, v. 64, n. 10, p. 899-904, 1993.

MOORE, T.P. Space shuttle inflight and postflight fluid shifts measured by leg volumen changes. **Aviat Space Environ Med**, v. 58 (9 Pt 2), p. A91-6, 1987.

MUKAI, C.N. Acute hemodynamic responses to weightlessness during parabolic flight. **J Clin Pharmacol**, v.31, n. 10, p. 993-1000, 1991.

_____. Cardiovascular responses to repetitive exposure to hyper- and hypogravity states produced by parabolic flight. **J Clin Pharmacol**, v.34, n. 5, p. 472-9, 1994.

NORSK, P. et al. Vasorelaxation in space. **Hypertension**, v. 47, n. 1, p. 69-73, 2006.

PRISK, G. et al. Pulmonary diffusing capacity, capillary blood volume, and cardiac output during sustained microgravity. **J Appl Physiol**, v. 75, n. 1, 15-26, 1993.

RAVAL, N.Y. Multicenter evaluation of noninvasive cardiac output measurement by bioreactance technique. **J Clin Monit Comput**, v. 22, p. 113-9, 2008.

RICHARD, E. Klabunde. **Cardiovascular Physiology Concepts** (2nf Ed.). Various Chapters. Lippincott Williams & Wilkins 2011. ISBN: 9781451113846

SHYKOFF, B.E. et al. Cardiovascular response to submaximal exercise in sustained microgravity. **J Appl Physiol**, v. 81, p. 26-32, 1996.

SQUARA, P. Noninvasive cardiac output monitoring (NICOM): a clinical validation. **Intensive Care Med**, v. 33, p. 1191-94, 2007.

THORNTON, W.E. Changes in leg volumen during microgravity simulation. **Aviat Space Environ Med**, v. 63, n. 9, p. 789-94, 1992.

_____. Fluid shifts in weightlessness. **Aviat Space Environ Med**, v. 58, (9 Pt 2), p. A86-90, 1987.

VAN LELYVELD-HAAS, L.E. et al. Clinical validation of the non-invasive cardiac output monitor USCOM-1A in critically ill patients. **Eur J Anaesthesiol**, v. 25, n. 11, p. 917-24, 2008.