Recent Cardiopulmonary Studies

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Over the period 2009 – 2010, Clinics has published a relatively large number of original studies dealing with the cardiovascular and pulmonary system. Twenty of these have attracted significant numbers of citations within this relatively short time span. This short review covers these aspects of recent research with direct interest to cardiologists. Articles were grouped under three headings: Cardiology, Pneumology and Multidisciplinary

Cardiology

It is interesting to note that Basic Research studies are the most frequent single research item represented in this sample and also the item to which the highest number of citations has been granted.

Two articles report experiments on ventricular remodeling. Zamo et al[1] examined the development of left ventricular hypertrophy, increased blood pressure and blood pressure variability, in spontaneously hypertensive rats. These are important determinants of heart damage. They investigated the effects of the time-course of hypertension on (a) hemodynamic and autonomic patterns (blood pressure; blood pressure variability; heart rate); (b) left ventricular hypertrophy; and (c) local and systemic Renin-Angiotensin response patterns. They conclude that autonomic dysfunction and modulation of Renin-angiotensin system activity are contributing factors to end-organ damage in hypertension and could be interacting. This result brings up the important message that the management of hypertensive disease must start before blood pressure reaches high stable levels and the consequent established end-organ damage is reached. This paper has received 8 citations over a one-year period.

Duarte et al[2] evaluated the roles of oxidative stress and lipid peroxidation in the ventricular remodeling induced by tobacco smoke exposure after myocardial infarction in a murine model and conclude that exposure to tobacco smoke, and oxidative stress are associated with the intensification of ventricular remodeling after myocardial infarction. This article has earned four citations in two years.

Keywords

Review, scientific and technical publications, periodicals, data analysis.

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The baroreflex was the object of a study by Valenti et al[3], which studied the variation of baroreflex sensitivity among conscious Male Wistar Kyoto rats. Baroreflex gain was calculated as the ratio between change in HR and MAP variation in response to a depressor dose of sodium nitroprusside and a pressor dose of phenylephrine. Approximately 37% of the rats showed a reduced bradycardic peak, bradycardic reflex and decreased bradycardic gain of baroreflex while roughly 23% had a decreased basal HR, tachycardic peak, tachycardic reflex and reduced sympathetic baroreflex gain. No significant alterations were noted with regard to basal MAP. Thus, baroreflex sensitivity was found to vary among Wistar Kyoto rats from the same laboratory. This paper has been cited 8 times over a one-year period.

Oxidative stress was the object of a project by Budin et al[4], who examined the effects of palm oil tocotrienol-rich fractions on streptozotocin-induced diabetic rats. Animals were divided into three groups: (i) normal non-diabetic (ii) diabetic treated with tocotrienol-rich fractions, and (iii) diabetic untreated. Blood glucose and lipid profiles, oxidative stress markers and morphological changes of the thoracic aorta were evaluated. The following results were observed in treated vs untreated animals: (a) reduced serum glucose and glycated hemoglobin concentrations; (b) lower levels of plasma total cholesterol, low-density lipoprotein cholesterol, and triglyceride; (c) higher levels of high-density lipoprotein cholesterol; (d) increased plasma levels of superoxide dismutase activity and vitamin C in plasma were increased in tocotrienol-rich fractions-treated rats. (e) lower levels of plasma and aorta malondealdehyde + 4-hydroxynonenal (MDA + 4-HNE) and oxidative DNA damage. Electron microscopic examination showed that the normal morphology of the thoracic aorta was disrupted in untreated diabetic rats, whereas Tocotrienol-rich fractions supplementation resulted in a protective effect on the vessel wall. They conclude that tocotrienol-rich fractions lower the blood glucose level and improve dyslipidemia. Levels of oxidative stress markers were also reduced by administration of tocotrienol-rich fractions. Vessel wall integrity was maintained due to the positive effects mediated by tocotrienol-rich fractions. This study obviously requires further confirmation, but has attracted 6 citations in 2 years.

The objective of a study by Carnieto Jr et al[5] performed in 48 mongrel dogs was to determine whether a selective cyclooxygenase-2 inhibitor (rofecoxib) could alter the evolution of acute myocardial infarction after reperfusion. The dogs underwent 180 minutes of coronary occlusion, followed by 30 minutes of reperfusion. Blood samples were collected from the venous sinus immediately before

coronary occlusion and after 30 minutes of reperfusion for measurements of CPK-MB, CPK-MBm and troponin I. During the experiment we observed the mean blood pressure, heart rate and coronary flow. The coronary flow and heart rate did not change, but in the control group, there was blood pressure instability, in addition to maximal levels of CPK-MB post-infarction. The same results were observed for CPK-MBm and troponin I. Authors conclude that in this canine model of myocardial ischemia-reperfusion, selective inhibition of Cyclooxygenase-2 with rofecoxib was not associated with early detrimental effects on the hemodynamic profile or the gross extent of infarction; in fact, it may be beneficial by limiting cell necrosis. This article attracted 4 citations in 2 years.

Meneghini et al[6] endeavored to evaluate the effects of memantine on nuclear size reduction in cardiac cells exposed to cold stress and found that the substance effectively prevents nuclear size reduction of cardiomyocytes in rats exposed to cold stress. This study has been cited 4 times in two years.

A single clinical study was widely cited. This is a highly interesting investigation performed by Guimarães et al[7] who sought to evaluate the neurohormonal activity in heart transplant recipients and compare it with that in heart failure patients and healthy subjects during rest and just after a 6-minute walking test. The study was performed in 20 heart transplantation patients, 11 heart failure patients and 7 healthy subjects. Blood samples were collected immediately before and during the last minute of the exercise. During rest, patients' norepinephrine plasma level was higher in heart transplant recipients and healthy subjects. Heart transplant recipient's norepinephrine plasma level was not different than that of healthy subjects. Just after the 6-minute walking test, the heart transplant recipient's norepinephrine plasma level was not different from that of heart failure patients. Both these groups had a higher level than healthy subjects had. It was concluded that neurohormonal activity remains increased after the 6-minute walking test after heart transplantation. This study has been granted 3 citations in one year.

Three prevalence studies are reported, on thyroid dysfunction, hemochromatosis and peripheral artery disease. Duarte et al[8] evaluated the prevalence of thyroid dysfunction in 399 elderly cardiac patients (268 women, age range 60-92 years) in an outpatient setting, through serum free T4, TSH, anti-Peroxidase antibodies, urinary iodine excretion measurements and thyroid ultrasound. It is recommended that ultrasound studies, tests for thyroid function and autoimmunity should be evaluated in elderly patients. This article has earned five citations over its two-year existence.

Hemochromatosis prevalence was studied by Bittencourt et al[9]. Approximately half of Brazilian patients with hereditary hemochromatosis (HH) are neither homozygous for the C282Y mutation nor compound heterozygous for the H63D and C282Y mutations associated with HH in Caucasians. Other mutations have been described in the *HFE* gene as well as in genes involved in iron metabolism, such as transferrin receptor 2 (TfR2) and ferroportin 1 (SCL40A1). To evaluate the role of HFE, TfR2 and SCL40A1 in mutations in Brazilian individuals with HH, a study was conducted with 19 male individuals with HH. The authors concluded that one-third of Brazilian individuals with the classical phenotype of HH do not carry HFE or other mutations that are currently associated with the disease in Caucasians. This observation suggests a role for other yet unknown mutations in the aforementioned genes or in other genes involved in iron homeostasis in the pathogenesis of HH in Brazil. This article received 4 citations in two years.

Zanati et al[10] examined the prevalence of cardiovascular risk factor profiles and 24-month mortality in patients with symptomatic peripheral arterial disease through a prospective observational study including 75 consecutive patients hospitalized for planned peripheral vascular reconstruction. Doppler echocardiograms were performed before surgery in 54 cases. Survival analysis at 24-month follow-up was performed Overall mortality over 24 months was 24% and was associated with age and lack of use of aspirin, as no deaths occurred among those using this drug. No association was found between cardiovascular death (11 cases) and the other risk factors. A high prevalence of uncontrolled (treated or untreated) cardiovascular risk factors was found in patients undergoing planned peripheral vascular reconstruction, and chronic use of aspirin is associated with reduced all-cause mortality. This article was cited 3 times in 2 years.

A single diagnostic study was reported: non-invasive detection of atherosclerosis is critical for its prevention, which led Bampi et al[11] to correlate non-invasively detectable indicators of coronary atherosclerosis, or Coronary Artery Disease (i.e., classical risk factors, hs-CRP test results, carotid intima-media thickness, endothelial function, ankle-brachial index and calcium score by computed tomography) with the extent of coronary disease assessed by the Friesinger index from conventional coronary angiography through a prospective study of 100 consecutive patients, mean age 55.1 ± 10.7 years, 55% men and 45% women. They conclude that it is possible to approximately determine the presence and extent of CAD by non-invasive methods, especially by calcium score, HDL-c and TG/HDL-c ratio assays. Four citations in two years were granted to this report.

We also wish to highlight two review articles on cardiology themes. Wichi et al[12] provide us with a highly interesting insight into the associations of aging with alterations in the cardiovascular and autonomic nervous systems. Autonomic changes related to aging involve parasympathetic and sympathetic alterations leading to a higher incidence of cardiovascular disease morbidity and mortality. Several studies have suggested that physical exercise is effective in preventing deleterious changes. Chronic exercise in geriatrics seems to be associated with improvement in the cardiovascular system and seems to promote a healthy lifestyle. In this review, we address the major effects of aging on the autonomic nervous system in the context of cardiovascular control. We examine the use of chronic exercise to prevent cardiovascular changes

during the aging process. Five articles have cited this report over 2 years.

Landim et al[13] supply interesting information on atherosclerotic coronary heart disease, which is the leading cause of morbidity and mortality in industrialized countries, and endothelial dysfunction is considered a precursor phenomenon. The nitric oxide produced by the endothelium under the action of endothelial nitric oxide synthase has important antiatherogenic functions. Its reduced bioavailability is the beginning of the atherosclerotic process. The addition of two methyl radicals to arginine, through the action of methyltransferase nuclear proteins, produces asymmetric dimethylarginine, which competes with L-arginine and promotes a reduction in nitric oxide formation in the vascular wall. The asymmetric dimethylarginine, which is itself considered a mediator of the vascular effects of the several risk factors for atherosclerosis, can be eliminated by renal excretion or by the enzymatic action of the dimethylarginine dimethylaminohydrolases. Several basic science and clinical research studies suggest that the increase in asymmetric dimethylarginine occurs in the context of chronic renal failure, dyslipidemia, high blood pressure, diabetes mellitus, and hyperhomocysteinemy, as well as with other conditions. Therapeutic measures to combat atherosclerosis may reverse these asymmetric dimethylarginine effects or at least reduce the concentration of this chemical in the blood. Such an effect can be achieved with competitor molecules or by increasing the expression or activity of its degradation enzyme. Studies are in development to establish the true role of asymmetric dimethylarginine as a marker and mediator of atherosclerosis, with possible therapeutic applications. The main aspects of the formation and degradation of asymmetric dimethylarginine and its implication in the atherogenic process are addressed in this article, which has been cited 3 times in two years.

Pneumology

Four articles on the pathophysiology of the pulmonary system are highlighted.

Bisanccioni et al[14] conducted a retrospective analysis of data obtained from electronic medical records of 245 patients with severe asthma between January 2006 and June 2008. Symptoms of rhinitis and gastroesophageal reflux disease were evaluated as well as intolerance to nonsteroidal anti-inflammatory drugs. The results of esophagogastroduodenoscopy, videolaryngoscopy and CT scans of the chest in order to confirm gastroesophageal reflux disease, nasal polyposis, vocal cord dysfunction and bronchiectasis were also evaluated Rhinitis symptoms were present in 224 patients (91.4%); 18 (7.3%) had intolerance to nonsteroidal anti-inflammatory drugs, and 8 (3.3%) had nasal polyposis. Symptoms of gastroesophageal reflux disease were reported for 173 (70.6%) patients, although the diagnosis of gastroesophageal reflux disease was confirmed based on esophagogastroduodenoscopy or laryngoscopy findings in just 58 (33.6%) patients. Vocal cord dysfunction was suspected in 16 (6.5%) and confirmed through laryngoscopy in 4 (1.6%). The patient records provided CT scans of the chest for 105 patients, and 26 (24.8%) showed bronchiectasis. Because rhinitis and gastroesophageal reflux disease were the most common comorbidities observed, in addition to bronchiectasis, authors recommend that in patients with severe asthma, associated diseases should be investigated as the cause of respiratory symptoms and uncontrolled asthma. This paper has received 7 citations in 2 years.

The within-breath analysis of respiratory mechanics is of interest in pathophysiology diagnosis of respiratory diseases. Veiga et al[15] evaluated within-breath mechanics of asthmatic individuals and the contribution of the monofrequency Forced Oscillation Technique in the asthma diagnosis in 22 healthy and 22 asthmatic subjects. Respiratory impedance values were significantly higher in asthmatics and identified the best parameters for detecting asthma, concluding that the technique permits a non-invasive and detailed analysis in different phases of the respiratory cycle, providing parameters that are adequate for the diagnosis of asthma with high accuracy. This article has received 5 citations in 2 years.

Sabino et al[16] investigated the impact of nutritional status on body composition, exercise capacity and respiratory muscle strength in 32 severe chronic obstructive pulmonary disease patients. Patients (nine women) were divided into three groups according to their body mass indices (BMI): overweight/obese, normal weight and underweight. Spirometry, bioelectrical impedance, a six-minute walking distance test and maximal inspiratory and expiratory pressures were assessed. Airway obstruction was similar among the groups; however, overweight/obese patients had a higher fat-free mass index, exercise capacity and maximal inspiratory pressure in comparison to normal weight and underweight patients, respectively. In addition, on backward multiple regression analysis, fat-free mass index was the sole independent predictor of exercise capacity. Authors claim that these characteristics of overweight or obese patients might counteract the drawbacks of excess weight and lead to an improved prognosis in COPD. In one year this paper has been cited three times.

Torquato et al[17] quantified the interaction between increased intra-abdominal pressure and Positive-End Expiratory Pressure in a cohort of 30 mechanically ventilated ICU patients with a fixed tidal volume, respiratory system plateau and abdominal pressure were measured at a Positive-End Expiratory Pressure level of zero and 10 cm H_2O. The measurements were repeated after placing a 5 kg weight on the patients' belly. They conclude that the addition of a 5kg weight onto the abdomen significantly increased both IAP and the airway plateau pressure, confirming that intra-abdominal hypertension elevates the plateau pressure. However, plateau pressure alone cannot be considered a good indicator for the detection of elevated intra-abdominal pressure in patients under mechanical ventilation using PEEP. In these patients, the intra-abdominal pressure must also be measured. This article was accorded 3 citations in 2 years.

Multidisciplinary

Three studies fall in this category. The aim of a study authored by Azeka et al[18] was to report a single center experience of organ and tissue transplantation. This is the first report of organ and tissue transplantation at the Hospital das Clínicas of the University of São Paulo Medical School. Data were collected from each type of organ transplantation from 2002 to 2007. The data collected were patient characteristics and actuarial survival Kaplan-Meier curves at 30 days, one year, and five years. There were a total of 3,321 transplants at the institution and the 5-year survival curve ranged from 53% to 88%. This report is claimed to show that solid organ and tissue transplants are feasible within the institution and allow us to expect that the quality of transplantation will improve in the future. This study has earned 4 citations over 2 years.

A prospective observational study was implemented by Silva et al[19] from February 2004 to October 2007 in a tertiary university hospital. A consecutive sample of 856 included patients was evaluated. Bivariate and multivariate analyses were performed to determine associations between in-patient mortality and gender, age, length of stay, number of prescribed medications and diagnoses at admission, history of heart failure, neoplastic disease, immobility syndrome, delirium, infectious disease, and laboratory tests at admission (serum albumin and creatinine). The overall mortality rate was 16.4%. The following factors were associated with higher in-hospital mortality: delirium, neoplastic disease, serum albumin levels at admission <3.3mg/dL, serum creatinine levels at admission ≥ 1.3mg/dL, history of heart failure, immobility, and advanced age. Authors claim that this study strengthens the perception of delirium as a mortality predictor among older inpatients. Cancer, immobility, low albumin levels, elevated creatinine levels, history of heart failure and advanced age were also related to higher mortality rates in this population. Three articles cited this report over 2 years.

Castro et al[20] addressed the risks of hypothermia and hypoglycemia during a 10-km open-water swimming competition in order to alert physicians to the potential dangers of this recently-introduced Olympic event through an observational cross-sectional study, conducted during a 10-km open-water event (water temperature 21ºC) in which the highest ranked elite open-water swimmers in Brazil (7 men, 5 women; ages 21 ± 7 years old) were submitted to anthropometrical measurements on the day before competition. Hypothermia may occur during open-water swimming events even in elite athletes competing in relatively warm water. Thus, core temperature must be a chief concern of any physician during an open-water swim event. Capillary glycemia may have positive effects on performance. This article collected 3 citations in 2 years.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any post-graduation program.

References

1. Zamo FS, Lacchini S, Mostarda C, Chiavegatto S, Silva ICM, Oliveira EM, et al. Hemodynamic, morphometric and autonomic patterns in hypertensive rats - renin-angiotensin system modulation. Clinics. 2010;65(1):85-92.
2. Duarte DR, Minicucci MF, Azevedo PS, Matsubara BB, Matsubara LS, Novelli EL, et al. The role of oxidative stress and lipid peroxidation in ventricular remodeling induced by tobacco smoke exposure after myocardial infarction. Clinics. 2009;64(7):691-7.
3. Valenti VE, Abreu LC, Imaizumi C, Petenusso M, Ferreira C. Strain differences in baroceptor reflex in adult wistar kyoto rats. Clinics. 2010;65(2):203-8.
4. Budin SB, Othman F, Louis SR, Bakar MA, Das S, Mohamed J. The effects of palm oil tocotrienol-rich fraction supplementation on biochemical parameters, oxidative stress and the vascular wall of streptozotocin-induced diabetic rats. Clinics. 2009;64(3):235-44.
5. Carnieto Jr A, Dourado PMM, Luz PL, Chagas ACP. Selective cyclooxygenase-2 inhibition protects against myocardial damage in experimental acute ischemia. Clinics. 2009;64(3):245-52.
6. Meneghini A, Ferreira C, Abreu LC, Valenti VE, Ferreira M, F-Filho C, et al. Memantine prevents cardiomyocytes nuclear size reduction in the left ventricle of rats exposed to cold stress. Clinics. 2009;64(9):921-6.
7. Guimarães GV, D' Avila V, Bocchi EA, Carvalho VO. Norepinephrine remains increased in the six-minute walking test after heart transplantation. Clinics. 2010;65(6):587-91.
8. Duarte GC, Tomimori EK, Camargo RYA, Rubio IGS, Wajngarten M, Rodrigues AG, et al. The prevalence of thyroid dysfunction in elderly cardiology patients with mild excessive iodine intake in the urban area of São Paulo. Clinics. 2009;64(2):135-42.
9. Bittencourt PL, Marin MLC, Couto CA, Cançado ELR, Carrilho FJ, Goldberg AC. Analysis of HFE and non-HFE gene mutations in Brazilian patients with hemochromatosis. Clinics. 2009;64(9):837-41.
10. Zanati SG, Mouraria GG, Matsubara LS, Giannini M, Matsubara BB. Profile of cardiovascular risk factors and mortality in patients with symptomatic peripheral arterial disease. Clinics. 2009;64(4):323-6.
11. Bampi ABA, Rochitte CE, Favarato D, Lemos PA, Luz PL. Comparison of non-invasive methods for the detection of coronary atherosclerosis. Clinics. 2009;64(7):675-82.
12. Wichi RB, De Angelis K, Jones L, Irigoyen MC. A brief review of chronic exercise intervention to prevent autonomic nervous system changes during the aging process. Clinics. 2009;64(3):253-8.
13. Landim MBP, Casella-Filho A, Chagas ACP. Asymmetric dimethylarginine (ADMA) and endothelial dysfunction: implications for atherogenesis. Clinics. 2009;64(5):471-8.
14. Bisaccioni C, Aun MV, Cajuela E, Kalil J, Agondi RC, Giavina-Bianchi P. Comorbidities in severe asthma: frequency of rhinitis, nasal polyposis, gastroesophageal reflux disease, vocal cord dysfunction and bronchiectasis. Clinics. 2009;64(8):769-73.

15. Veiga J, Lopes AJ, Jansen JM, Melo PL. Within-breath analysis of respiratory mechanics in asthmatic patients by forced oscillation. Clinics. 2009;64(7):649-56.

16. Sabino PG, Silva BM, Brunetto AF. Nutritional status is related to fat-free mass, exercise capacity and inspiratory strength in severe chronic obstructive pulmonary disease patients. Clinics. 2010;65(6):599-605.

17. Torquato JA, Lucato JJJ, Antunes T, Barbas CV. Interaction between intra-abdominal pressure and positive-end expiratory pressure. Clinics. 2009;64(2):105-12.

18. Azeka E, Auler-Júnior JOC, Fernandes PMP, Nahas WC, Fiorelli AI, Tannuri U, et al. Registry of Hospital das Clínicas of the University of São Paulo Medical School: first official solid organ and tissue transplantation report - 2008. Clinics. 2009;64(2):127-34.

19. Silva TJA, Jerussalmy CS, Farfel JM, Curiati JAE, Jacob-Filho W. Predictors of in-hospital mortality among older patients. Clinics. 2009;64(7):613-8.

20. Castro RRT, Mendes FSNS, Nobrega ACL. Risk of hypothermia in a new Olympic event: the 10-km marathon swim. Clinics. 2009;64(4):351-6.