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EDITORIAL

Cardiovascular research in CLINICS

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CLINICS is a multidisciplinary medical journal. This editorial highlights the field of cardiovascular research. We have selected papers published from 2011-2012 and focused on the concept of Continuously Variable Rating, which we have recently introduced as an alternative and hopefully superior method for evaluating published scientific papers (1).

Ciolac and Greve (2) compared the heart rate response to exercise and exercise-induced improvements in muscle strength, cardiorespiratory fitness, and the heart rate response between 79 normal-weight and 76 overweight/obese women, all of whom were postmenopausal. The overweight/obese women exhibited an impaired heart rate in response to exercise. Both groups improved in muscle strength, but only normal-weight women improved in cardiorespiratory fitness and the heart rate response to exercise. The results suggested that exercise-induced improvements in cardiorespiratory fitness and the heart rate response to exercise may be impaired in the overweight/obese group.

Farinatti et al. (3) evaluated heart rate, systolic blood pressure, and the rate-pressure product during and after large and small muscle-group flexibility exercises performed simultaneously with the Valsalva maneuver. The researchers found that only systolic blood pressure and the rate-pressure product increased throughout the exercises but did not detect post-exercise hypotension. They concluded that the stretched muscle mass and the Valsalva maneuver influenced acute cardiovascular responses to multiple-set passive-stretching exercise sessions.

Perim et al. (4) compared relative oxygen pulse (absolute value/body weight) curves in 180 elite soccer players at a maximal heart rate during treadmill cardiopulmonary exercise testing. The players were categorized into quartiles according to their maximal heart rate values. The authors reported that the relative oxygen pulse curve slopes, which serve as an indirect, noninvasive surrogate for stroke volume, suggested that stroke volume is similar in young, aerobically fit subjects, regardless of the maximal heart rate reached.

Oliveira et al. (5) retrospectively calculated the relative O_2 pulse (absolute value/body weight) of 100 adults (80 males; mean age, 59 ± 12 years) who underwent two cardiopulmonary exercise tests (median interval, 15 months) for clinical and exercise prescription reasons. The researchers concluded that excluding the rest-exercise transition, the relative O_2 pulse exhibited a stable linear increase throughout maximal exercise in adults who were retested under the same clinical conditions at a 15-month interval.

Christofoletti et al. (6) assessed the effects of physical activity on neuropsychiatric disturbances in 59 demented patients (evaluated with the Neuropsychiatric Inventory, the Mini-Sleep Questionnaire, and the Baecke Questionnaire) and the mental burden of the patients' caregivers. The researchers observed that regular physical activity contributes to a reduction in neuropsychiatric symptoms in patients and attenuates the burden of the patients' caregivers.

Medeiros et al. (7) investigated hemodynamic responses to mental stress before and after a bout of exercise in subjects with prehypertension. The authors reported that subjects with prehypertension had an elevated blood pressure and a blunted vasodilator response during mental stress and that the subjects' blood pressure was attenuated and vasodilator response was normalized after a single bout of maximal dynamic exercise.

Casonatto et al. (8) investigated the effects of aerobic exercise on the acute blood pressure response and indicators of autonomic activity after exercise in 10 male subjects (aged 25 ± 1 years) who underwent four experimental exercise sessions and a control session on a cycle ergometer. Although the authors did not find decreased blood pressure, measurements of the indicators of autonomic activity revealed that in intense exercise, parasympathetic recovery tends to be slower, and sympathetic withdrawal can apparently compensate for this delay in recovery.

Bombarda et al. (9) examined and compared conscious rats' hemodynamic responses after the intrathecal administration of sildenafil, 8-bromo-cGMP (an analog of cGMP), forskolin (an activator of adenylate cyclase), or dibutyryl-cAMP (an analog of cAMP) to elucidate the possible role of sympathetic preganglionic neurons in the observed hemodynamic responses (namely, an increase in both lumbar sympathetic activity and heart rate, with no change in the mean arterial pressure). The authors concluded that the cardiovascular response involves the inhibition of phosphodiesterases other than phosphodiesterase type 5, which increases the cAMP level and the activation of sympathetic preganglionic neurons.

Ferreira-Melo et al. (10) investigated the influence of sildenafil on cardiac contractility and diastolic relaxation and examined the distribution of phosphodiesterase type 5 in the hearts of hypertensive rats that were treated with nitro-L-arginine methyl ester (L-NAME) and sildenafil for eight weeks. They found that the sildenafil-induced

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attenuation of the deleterious hemodynamic and cardiac morphological effects of L-NAME in cardiac myocytes is mediated, at least in part, by the inhibition of phosphodiesterase type 5.

Rodrigues et al. (11) investigated the effects of hyperglycemia on left ventricular dysfunction, morphometry, myocardial infarction area, hemodynamic parameters, oxidative stress profile, and mortality rate in diabetic and nondiabetic rats that had undergone seven days of myocardial infarction. The authors observed that the myocardial infarction area and mortality were reduced, whereas the ejection fraction, velocity of circumferential fiber shortening, and left ventricular isovolumetric relaxation time were increased in the diabetic animals compared with the myocardial infarction group. The researchers suggested that short-term hyperglycemia initiates compensatory mechanisms that culminate in improvements in the ventricular response, infarcted area, and mortality rate in diabetic rats exposed to ischemic injury.

Schifelbain et al. (12) analyzed changes in cardiac function using a Doppler echocardiogram in 24 critical patients during weaning from mechanical ventilation, using two different weaning methods: pressure support ventilation and a T-tube. The researchers compared success with failure in weaning, and seven patients failed in the first weaning attempt. Moreover, the authors reported that no differences were observed between Doppler echocardiographic variables and electrocardiographic and other cardiorespiratory variables during pressure-support ventilation and T-tube weaning. However, cardiac structures were smaller, the isovolumetric relaxation time was larger, and the oxygen level was higher in successfully weaned patients.

Konrad et al. (13) evaluated cardiovascular autonomic function in a murine obesity model induced by monosodium glutamate injections during the first seven days of life. Body weight, Lee index, and epididymal white adipose tissue values were higher in the monosodium glutamate-treated group compared with the control group. The monosodium glutamate-treated rats displayed insulin resistance and a higher mean arterial pressure, whereas heart rate variability, bradycardic responses, and vagal and sympathetic effects were reduced compared with the control group. The researchers argued that the obesity induced by neonatal monosodium glutamate treatment impairs cardiac autonomic function and contributes to increased arterial pressure and insulin resistance.

Hoe et al. (14) investigated the cardiovascular effects of a butanolic fraction of *Gynura procumbens* in rats. Intravenous administrations of the butanolic fraction elicited significant dose-dependent decreases in the mean arterial pressure. A significant decrease in heart rate was observed only at higher doses (10 mg/kg and 20 mg/kg). The authors concluded that the butanolic fraction contains putative hypotensive compounds that may inhibit calcium influx via receptor-operated, voltage-dependent calcium channels, causing vasodilation and a consequent decrease in blood pressure.

Jaarin et al. (15) aimed to determine the possible mechanism involved in the blood pressure-raising effect of heated vegetable oils. Adult male Sprague-Dawley rats were fed with rat chow or with chow mixed with palm or soy oils, which were either in a fresh form or heated once, twice, five, or 10 times. Plasma nitric oxide levels were assessed prior to treatment and at the end of the study. The authors concluded that the blood pressure-raising effect of heated vegetable cooking oils is associated with increased vascular reactivity and a reduction in nitric oxide levels.

Myers et al. (16) examined the association between cardiac performance during recovery and the severity of heart failure, as determined by clinical and cardiopulmonary exercise test responses. They found that impaired cardiac output recovery kinetics can identify heart failure patients with more severe disease, lower exercise capacity, and inefficient ventilation. The authors suggested that estimating cardiac output in recovery from exercise may provide insight into the cardiovascular status of patients with heart failure.

Correale et al. (17) aimed to determine whether statin administration influenced prognosis, inflammatory activation, and tissue Doppler imaging-evaluated myocardial performance in 353 patients with chronic heart failure (mean follow-up, 384 days). The researchers reported that patients who received statin treatment had fewer hospital readmissions for adverse events; experienced blunted inflammatory activation; and exhibited improved left ventricular performance, as assessed by tissue Doppler imaging.

Ochiai et al. (18) aimed to identify the predictors of low cardiac output and mortality in 452 patients with decompensated heart failure (ejection fraction of <0.45). The researchers concluded that in patients with severe decompensated heart failure, the predictors of low cardiac output are Chagas disease, a low ejection fraction, hyponatremia, and renal dysfunction. The authors also reported that patients with Chagas disease have higher B type natriuretic peptide levels and a poor prognosis, independent of the lower ejection fraction.

Martins et al. (19) investigated high-sensitivity C-reactive protein levels as a predictor of acute myocardial infarction in patients undergoing high-risk noncardiac surgery. The authors concluded that patients undergoing high-risk noncardiac surgery, and especially vascular surgery, and presenting elevated baseline high-sensitivity C-reactive protein levels are at increased risk of perioperative acute myocardial infarction.

Sadeghi et al. (20) investigated the relationship between major depressive disorder and metabolic risk factors for coronary heart disease in 153 patients with major depressive disorder and 147 healthy individuals. The researchers reported that depression was a negative predictor of apolipoprotein A and a positive predictor of apolipoprotein B. They concluded that considering the relationship between apolipoproteins A and B and depression, in addition to psychological interventions, screening for these metabolic risk factors is necessary in depressed patients.

Faa et al. (21) evaluated S100B protein expression in the human heart and this expression's correlation with drug-related death. Preliminary data showed that S100B protein accumulates in injured cardiomyocytes during drug-related sudden death, which suggests that S100B immunopositivity may be used as a new ancillary screening tool for the postmortem diagnosis of overdose-related cardiac death.

Pimentel et al. (22) evaluated the role of carvedilol in cardiac remodeling and mortality in Chagas' cardiomyopathy in 55 Syrian hamsters, divided into the following groups: control, infected, and infected+carvedilol. The left ventricular diastolic and diastolic diameters, fractional shortening, and collagen accumulation in the interstitial

space were measured. The diameters and collagen accumulation were larger, whereas shortening was smaller, in the infected groups. The survival rate was significantly higher in the control group, but no benefit from carvedilol was observed for any of these parameters. However, in the acute phase (up to 100 days of infection), carvedilol did reduce mortality.

Borges et al. (23) evaluated structural and functional heart abnormalities in 18 women with mitral regurgitation during pregnancy (12th and 36th weeks through a longitudinal, prospective case-control study). The researchers concluded that pregnancy causes unfavorable structural alterations, which are associated with an aggravation of the hemodynamic overload, in women with mitral regurgitation.

Yuan et al. (24) investigated the biological functions of transforming growth factor-beta signaling with respect to coronary artery bypass grafts. The authors studied remnants of saphenous veins and radial and mammary arteries. The saphenous veins showed more severe intimal degeneration, smooth muscle cell proliferation, and collagen deposition than arterial grafts. Transforming growth factor-beta1 signaling cytokines were found in all three types of grafts, whereas ectopic transforming growth factor-beta1, the type I receptor of transforming growth factor-beta, and Smad7 were observed in the saphenous veins and radial arteries. Enhanced transforming growth factor-beta1 signal transduction with medial smooth muscle cell proliferation and the presence of ectopic transforming growth factor-beta1, the type I receptor of transforming growth factor-beta, and Smad7 may provide primary evidence for early or late graft failure.

Astudillo et al. (25) aimed to determine the predictors of patient prosthesis mismatch, an independent predictor of mortality, in patients with aortic stenosis who used bioprosthetic valves. The authors analyzed 2,107 sequential surgeries, from which 311 patients with bioprotheses were identified. The incidence of nonsignificant, moderate, and severe patient prosthesis mismatch was 41%, 42%, and 16%, respectively. The researchers concluded that severe patient prosthesis mismatch is more common in females but not in those females with minimal available body surface area. Although operative times were shorter in these patients, intensive care unit and hospital lengths of stay were longer.

Rocha-e-Silva et al. (26,27) described a novel approach for the correction of hypoplastic left heart syndrome, which simplifies the surgery by forming the autologous pulmonary trunk and ascending aorta tissue into flaps to create a posterior wall for a neo-aorta. Moreover, a reconstructive procedure constructs a valved pulmonary outlet.

Khazaei et al. (28) evaluated the effects of diabetes on myocardial capillary density and several serum angiogenic factors, including nitric oxide, vascular endothelial growth factor, and soluble vascular endothelial growth factor receptors in a murine model. Diabetes was induced with a single dose of streptozotocin, and the capillary density in the myocardial tissue was evaluated. The authors suggested that reduced serum nitric oxide and vascular endothelial growth factor receptor 2 levels and increased serum vascular endothelial growth factor receptor 1 levels may be responsible for decreased myocardial capillary density in diabetic rats.

Silva et al. (29) aimed to evaluate cheek-pouch microvessel morphological characteristics, reactivity, permeability, and expression of cytoskeletal and extracellular matrix components in hamsters with streptozotocin-induced diabetes. The authors reported precocious changes that were related to cell-matrix interactions and may contribute to the pathological remodeling that was already underway one week after the induction of experimental diabetes.

Tibirica et al. (30) investigated the day-to-day repeatability of measurements of systemic microvascular reactivity in 24 healthy volunteers using laser Doppler perfusion monitoring. The researchers performed this monitoring in combination with skin iontophoresis using acetylcholine and sodium nitroprusside and post-occlusive reactive and thermal hyperemia twice within two weeks. The post-occlusive vasodilatory response showed marked variability, whereas the responses to acetylcholine sodium nitroprusside and thermal treatment were less variable. Given the importance of random error to the day-to-day repeatability of laser Doppler perfusion monitoring, the authors proposed a new robust statistical method for use in designing prospective clinical studies.

da Conceicao et al. (31) evaluated vascular permeability in a hamster cheek-pouch preparation using either short ischemic periods or bradykinin as preconditioning stimuli, followed by 30 min of ischemia/reperfusion in male hamsters. The researchers reported that short ischemic periods and bradykinin can function as preconditioning stimuli for the ischemia/reperfusion response in the hamster cheek-pouch microcirculation. Short ischemic periods also reduced histamine-induced macromolecular permeability.

Faa et al. (32) evaluated myocardial histological changes in an experimental animal model of neonatal hypoxia-reoxygenation in 40 male Landrace/Large White piglets. Reoxygenation (FiO_2 of 18%, 21%, 40%, and 100%) was initiated when the animals developed bradycardia (HR of $<$60 beats/min) or severe hypotension (MAP of $<$15 mm Hg). There was no correlation between the severity of histological changes and FiO_2, whereas myocardial changes correlated with recovery time, which suggests an unreported individual susceptibility of myocardiocytes to hypoxia. According to the authors, the significant myocardial histological changes suggested that this research might be a reliable model for investigating human neonatal cardiac hypoxia-related injury.

Karetsi et al. (33) compared the expression of hypoxia-inducible factor-1alpha and vascular endothelial growth factor in small-cell lung cancer and subtypes of nonsmall-cell lung cancer and examined the expression's relationships with clinicopathologic factors, the response to treatment, and survival. In particular, the expression of hypoxia-inducible factor-1alpha differed significantly between subtypes of lung cancer. This finding could help to elucidate the biology of different types of inoperable lung carcinomas and have implications for the design of new therapeutic approaches to lung cancer.

Santos et al. (34) investigated changes in the vascular reactivity of the rabbit femoral artery and nitric oxide metabolites under partial ischemia/reperfusion conditions after cilostazol administration. The authors found that hind-limb ischemia/reperfusion yielded an impaired endothelium-dependent relaxation of the femoral artery. Furthermore, cilostazol administration prior to ischemia exerted a protective effect on endothelium-dependent vascular reactivity under ischemia/reperfusion conditions.

Belczak et al. (35) evaluated the feasibility of using endovascular repair to treat penetrating arterial injuries with covered stents in 20 white male domestic pigs. Feasibility was examined according to the circumferential extent of the injury. The authors concluded that repairing an arterial injury is possible and that success depends on the circumferential extent of the arterial lesion. Their experimental model, involving endovascular techniques, highlights important factors that must be considered in future studies on similar animals and materials.

Cabral et al. (36) investigated the effect of L-thyroxine replacement on the association between subclinical hypothyroidism and coronary arteries in 32 subclinical hypothyroid female patients who were randomly assigned to 12 months of L-thyroxine replacement or no treatment. Endothelial function was measured by the flow-mediated vasodilatation of the brachial artery and the mean carotid artery intima-media thickness. Additionally, lipid profiles were studied at baseline and after 12 months of follow-up. The replacement therapy prevented a decline in flow-mediated vasodilatation, with continuation of the subclinical hypothyroidism state. Further studies are necessary to define the role of L-thyroxine therapy in improving endothelial function in these patients.

Florence et al. (37) studied the vascular beds of 29 solar keratoses, 30 superficially invasive squamous cell carcinomas, and 30 invasive squamous cell carcinomas. Panendothelial and neoangiogenic immunohistochemical markers were specifically compared. The vascular bed of non-neoplastic adjacent skin was evaluated for eight solar keratoses, 10 superficially invasive squamous cell carcinomas, and 10 invasive squamous cell carcinomas. The angiogenic switch occurred early in the development of cutaneous squamous cell carcinoma, and the rate of neovascularization was parallel to tumor progression. In contrast to panendothelial markers, CD105 use allowed a dynamic evaluation of tumor angiogenesis. This study demonstrates the dependence of skin carcinogenesis on angiogenesis.

Machado et al. (38) compared the effects of glimepiride and metformin on the vascular reactivity, hemostatic factors, and glucose and lipid profiles of patients with type 2 diabetes. Glimepiride and metformin were effective in improving glucose and lipid profiles and norepinephrine levels. Metformin afforded more protection against macrovascular diabetic complications, increased the systolic carotid artery diameter and total and systolic blood flow, and decreased insulin levels. As both therapies increased plasminogen levels but reduced t-PA activity, a coagulation process was likely to be ongoing.

Park et al. (39) aimed to determine the prevalence of and most frequent risk factors for carotid stenosis through a transversal study. The study was conducted in the form of a stroke prevention campaign held on three nonconsecutive Saturdays. Carotid stenosis diagnostic procedures were performed on 500 individuals aged 60 years or older and who had systemic arterial hypertension, diabetes mellitus, coronary heart disease, and a family history of stroke. There was a 7.4% prevalence of carotid stenosis in the population studied, and the most frequent risk factors identified were a mean age of 70 years, carotid bruit, peripheral obstructive arterial disease, coronary insufficiency, and smoking. The authors concluded that a senior population with peripheral obstructive heart disease and carotid bruit should undergo routine screening for carotid stenosis.

Dogan et al. (40) examined the separate and combined effects of tobacco and biomass smoke exposure on pulmonary histopathology in rats. They concluded that exposure to cigarette smoke causes serious damage to the respiratory system, particularly with concomitant exposure to biomass smoke.

Castro et al. (41) measured the inspiratory capacity, sensation of dyspnea, peripheral oxygen saturation, heart rate, and respiratory rate of 19 patients with chronic obstructive pulmonary disease at rest and after the patients performed activities of daily living. The patients with chronic obstructive pulmonary disease exhibited reductions in inspiratory capacity and increases in dyspnea perception during the commonly performed activities of daily living, which may limit physical performance in these patients.

Medeiros et al. (42) presented ex vivo lung perfusion as a new model for the study of lung preservation because using human lungs instead of animal models may bring the results of experimental studies closer to clinical practice. In this study, brain-dead donors whose lungs had been declined by transplantation teams were used. Two perfusion solutions (Perfadex and LPDnac) were implemented. LPDnac proved to be as good as Perfadex and may reduce costs in Brazilian centers. Moreover, the ex vivo model may be useful for studying lung preservation.

Sener et al. (43) compared hemodynamic responses and upper airway morbidity after tracheal intubation via conventional laryngoscopy or after intubating the laryngeal mask airway in 42 hypertensive patients. The intense and repeated oropharyngeal and tracheal stimulation resulting from intubating the laryngeal mask airway induced greater pressor responses than did stimulation, which results from conventional laryngoscopy in hypertensive patients.

Zhang et al. (44) explored the effect of M2 macrophages on the proliferation and migration of mouse Lewis lung carcinoma cells and tumor-induced lymphangiogenesis. The researchers found that M2-polarized macrophages promoted the metastatic behavior of Lewis cells by inducing vascular endothelial growth factor-C expression. Thus, the interruption of signaling between M2 macrophages and Lewis cells may be considered to be a new therapeutic strategy.

REFERENCES

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. CA: a cancer journal for clinicians. 2009;59(4):225-49, http://dx.doi.org/10.3322/caac.20006.
2. Ciolac EG, Greve JM. Exercise-induced improvements in cardiorespiratory fitness and heart rate response to exercise are impaired in overweight/obese postmenopausal women. Clinics (Sao Paulo). 2011;66(4):583-9.
3. Farinatti PT, Soares PP, Monteiro WD, Duarte AF, Castro LA. Cardiovascular responses to passive static flexibility exercises are influenced by the stretched muscle mass and the Valsalva maneuver. Clinics (Sao Paulo). 2011;66(3):459-64, http://dx.doi.org/10.1590/S1807-59322011000300017.
4. Perim RR, Signorelli GR, Myers J, Arena R, de Araujo CG. The slope of the oxygen pulse curve does not depend on the maximal heart rate in elite soccer players. Clinics (Sao Paulo). 2011;66(5):829-35, http://dx.doi.org/10.1590/S1807-59322011000500020.
5. Oliveira RB, Myers J, Araujo CG. Long-term stability of the oxygen pulse curve during maximal exercise. Clinics (Sao Paulo). 2011;66(2):203-9, http://dx.doi.org/10.1590/S1807-59322011000200004.
6. Christofoletti G, Oliani MM, Bucken-Gobbi LT, Gobbi S, Beinotti F, Stella F. Physical activity attenuates neuropsychiatric disturbances and caregiver burden in patients with dementia. Clinics (Sao Paulo). 2011;66(4):613-8, http://dx.doi.org/10.1590/S1807-59322011000400015.

7. Medeiros RF, Silva BM, Neves FJ, Rocha NG, Sales AR, Nobrega AC. Impaired hemodynamic response to mental stress in subjects with prehypertension is improved after a single bout of maximal dynamic exercise. Clinics (Sao Paulo). 2011;66(9):1523-9, http://dx.doi.org/10.1590/S1807-59322011000900003.
8. Casonatto J, Tinucci T, Dourado AC, Polito M. Cardiovascular and autonomic responses after exercise sessions with different intensities and durations. Clinics (Sao Paulo). 2011;66(3):453-8, http://dx.doi.org/10.1590/S1807-59322011000300016.
9. Bombarda G, Sabino JP, Silva CA, Fazan Jr R, Salgado MC, Salgado HC. Role of cGMP and cAMP in the hemodynamic response to intrathecal sildenafil administration. Clinics (Sao Paulo). 2011;66(8):1407-12, http://dx.doi.org/10.1590/S1807-59322011000800017.
10. Ferreira-Melo SE, Demacq C, Lacchini S, Krieger JE, Irigoyen MC, Moreno H. Sildenafil preserves diastolic relaxation after reduction by L-NAME and increases phosphodiesterase-5 in the intercalated discs of cardiac myocytes and arterioles. Clinics (Sao Paulo). 2011;66(7):1253-8, http://dx.doi.org/10.1590/S1807-59322011000700022.
11. Rodrigues B, Figueroa DM, Fang J, Rosa KT, Llesuy S, De Angelis K, et al. Short-term diabetes attenuates left ventricular dysfunction and mortality rates after myocardial infarction in rodents. Clinics (Sao Paulo). 2011;66(8):1437-42, http://dx.doi.org/10.1590/S1807-59322011000800022.
12. Schifelbain LM, Vieira SR, Brauner JS, Pacheco DM, Naujorks AA. Echocardiographic evaluation during weaning from mechanical ventilation. Clinics (Sao Paulo). 2011;66(1):107-11, http://dx.doi.org/10.1590/S1807-59322011000100019.
13. Konrad SP, Farah V, Rodrigues B, Wichi RB, Machado UF, Lopes HF, et al. Monosodium glutamate neonatal treatment induces cardiovascular autonomic function changes in rodents. Clinics (Sao Paulo). 2012;67(10):1209-14, http://dx.doi.org/10.6061/clinics/2012(10)14.
14. Hoe SZ, Lee CN, Mok SL, Kamaruddin MY, Lam SK. Gynura procumbens Merr. decreases blood pressure in rats by vasodilatation via inhibition of calcium channels. Clinics (Sao Paulo). 2011;66(1):143-50, http://dx.doi.org/10.1590/S1807-59322011000100025.
15. Jaarin K, Mustafa MR, Leong XF. The effects of heated vegetable oils on blood pressure in rats. Clinics (Sao Paulo). 2011;66(12):2125-32, http://dx.doi.org/10.1590/S1807-59322011001200020.
16. Myers JN, Gujja P, Neelagaru S, Hsu L, Burkhoff D. Noninvasive measurement of cardiac performance in recovery from exercise in heart failure patients. Clinics (Sao Paulo). 2011;66(4):649-56, http://dx.doi.org/10.1590/S1807-59322011000400021.
17. Correale M, Brunetti ND, Totaro A, Montrone D, Russo AR, Fanigliulo AM, et al. Statin therapy blunts inflammatory activation and improves prognosis and left ventricular performance assessed by Tissue Doppler Imaging in subjects with chronic ischemic heart failure: results from the Daunia Heart Failure Registry. Clinics (Sao Paulo). 2011;66(5):777-84.
18. Ochiai ME, Cardoso JN, Vieira KR, Lima MV, Brancalhao EC, Barretto AC. Predictors of low cardiac output in decompensated severe heart failure. Clinics (Sao Paulo). 2011;66(2):239-44, http://dx.doi.org/10.1590/S1807-59322011000200010.
19. Martins OM, Fonseca VF, Borges I, Martins V, Portal VL, Pellanda LC. C-Reactive protein predicts acute myocardial infarction during high-risk noncardiac and vascular surgery. Clinics (Sao Paulo). 2011;66(5):773-6.
20. Sadeghi M, Roohafza H, Afshar H, Rajabi F, Ramzani M, Shemirani H, et al. Relationship between depression and apolipoproteins A and B: a case-control study. Clinics (Sao Paulo). 2011;66(1):113-7, http://dx.doi.org/10.1590/S1807-59322011000100020.
21. Faa A, Senes G, Locci A, Pampaloni P, Pais ME, Piras B, et al. S100B protein expression in the heart of deceased individuals by overdose: a new forensic marker? Clinics (Sao Paulo). 2012;67(7):821-6, http://dx.doi.org/10.6061/clinics/2012(07)19.
22. Pimentel Wde S, Ramires FJ, Lanni BM, Salemi VM, Bilate AM, Cunha-Neto E, et al. The effect of beta-blockade on myocardial remodelling in Chagas' cardiomyopathy. Clinics (Sao Paulo). 2012;67(9):1063-9, http://dx.doi.org/10.6061/clinics/2012(09)14.
23. Borges VT, Matsubara BB, Magalhaes CG, Peracoli JC, Rudge MV. Effect of physiological overload on pregnancy in women with mitral regurgitation. Clinics (Sao Paulo). 2011;66(1):47-50, http://dx.doi.org/10.1590/S1807-59322011000100009.
24. Yuan SM, Wang YQ, Shen Y, Jing H. Transforming growth factor-beta in graft vessels: histology and immunohistochemistry. Clinics (Sao Paulo). 2011;66(5):895-901, http://dx.doi.org/10.1590/S1807-59322011000500029.
25. Astudillo LM, Santana O, Urbandt PA, Benjo AM, Elkayam LU, Nascimento FO, et al. Clinical predictors of prosthesis-patient mismatch after aortic valve replacement for aortic stenosis. Clinics (Sao Paulo). 2012;67(1):55-60, http://dx.doi.org/10.6061/clinics/2012(01)09.
26. Rocha-e-Silva R. A new technique for the correction of hypoplastic left heart syndrome. Clinics (Sao Paulo). 2012;67(5):521-4, http://dx.doi.org/10.6061/clinics/2012(05)20.
27. Rocha-e-Silva R, De Mola R, Santos Ede S, Martins DM, Pesciotto VR, Hatori DM, et al. Surgical correction of hypoplastic left heart syndrome: a new approach. Clinics (Sao Paulo). 2012;67(5):535-9, http://dx.doi.org/10.6061/clinics/2012(05)24.
28. Khazaei M, Fallahzadeh AR, Sharifi MR, Afsharmoghaddam N, Javanmard SH, Salehi E. Effects of diabetes on myocardial capillary density and serum angiogenesis biomarkers in male rats. Clinics (Sao Paulo). 2011;66(8):1419-24, http://dx.doi.org/10.1590/S1807-59322011000800019.
29. Silva JF, Cyrino FZ, Breitenbach MM, Bouskela E, Carvalho JJ. Vimentin and laminin are altered on cheek pouch microvessels of streptozotocin-induced diabetic hamsters. Clinics (Sao Paulo). 2011;66(11):1961-8, http://dx.doi.org/10.1590/S1807-59322011001100018.
30. Tibirica E, Matheus AS, Nunes B, Sperandei S, Gomes MB. Repeatability of the evaluation of systemic microvascular endothelial function using laser doppler perfusion monitoring: clinical and statistical implications. Clinics (Sao Paulo). 2011;66(4):599-605.
31. da Conceicao FG, Conde CM, Svensjo E, Bottino DA, Bouskela E. Preconditioning of the response to ischemia/reperfusion-induced plasma leakage in hamster cheek pouch microcirculation. Clinics (Sao Paulo). 2012;67(8):923-9, http://dx.doi.org/10.6061/clinics/2012(08)12.
32. Faa A, Iacovidou N, Xanthos T, Locci A, Pampaloni P, Aroni F, et al. Hypoxia/reoxygenation-induced myocardial lesions in newborn piglets are related to interindividual variability and not to oxygen concentration. Clinics (Sao Paulo). 2012;67(5):503-8, http://dx.doi.org/10.6061/clinics/2012(05)16.
33. Karetsi E, Ioannou MG, Kerenidi T, Minas M, Molyvdas PA, Gourgoulianis KI, et al. Differential expression of hypoxia-inducible factor 1alpha in non-small cell lung cancer and small cell lung cancer. Clinics (Sao Paulo). 2012;67(12):1373-8, http://dx.doi.org/10.6061/clinics/2012(12)05.
34. Santos MR, Celotto AC, Capellini VK, Evora PR, Piccinato CE, Joviliano EE. The protective effect of cilostazol on isolated rabbit femoral arteries under conditions of ischemia and reperfusion: the role of the nitric oxide pathway. Clinics (Sao Paulo). 2012;67(2):171-8, http://dx.doi.org/10.6061/clinics/2012(02)13.
35. Belczak S, Silva ES, Aun R, Sincos IR, Belon AR, Casella IB, et al. Endovascular treatment of peripheral arterial injury with covered stents: an experimental study in pigs. Clinics (Sao Paulo). 2011;66(8):1425-30, http://dx.doi.org/10.1590/S1807-59322011000800020.
36. Cabral MD, Teixeira P, Soares D, Leite S, Salles E, Waisman M. Effects of thyroxine replacement on endothelial function and carotid artery intima-media thickness in female patients with mild subclinical hypothyroidism. Clinics (Sao Paulo). 2011;66(8):1321-8.
37. Florence ME, Massuda JY, Brocker EB, Metze K, Cintra ML, Souza EM. Angiogenesis in the progression of cutaneous squamous cell carcinoma: an immunohistochemical study of endothelial markers. Clinics (Sao Paulo). 2011;66(3):465-8, http://dx.doi.org/10.1590/S1807-59322011000300018.
38. Machado HA, Vieira M, Cunha MR, Correia MR, Fukui RT, dos Santos RF, et al. Metformin, but not glimepiride, improves carotid artery diameter and blood flow in patients with type 2 diabetes mellitus. Clinics (Sao Paulo). 2012;67(7):711-7, http://dx.doi.org/10.6061/clinics/2012(07)03.
39. Park JH, Razuk A, Saad PF, Telles GJ, Karakhanian WK, Fioranelli A, et al. Carotid stenosis: what is the high-risk population? Clinics (Sao Paulo). 2012;67(8):865-70, http://dx.doi.org/10.6061/clinics/2012(08)02.
40. Dogan OT, Elagoz S, Ozsahin SL, Epozturk K, Tuncer E, Akkurt I. Pulmonary toxicity of chronic exposure to tobacco and biomass smoke in rats. Clinics (Sao Paulo). 2011;66(6):1081-7, http://dx.doi.org/10.1590/S1807-59322011000600027.
41. Castro AA, Kumpel C, Rangueri RC, Oliveira MD, Dornelles RA, Brito ER, et al. Daily activities are sufficient to induce dynamic pulmonary hyperinflation and dyspnea in chronic obstructive pulmonary disease patients. Clinics (Sao Paulo). 2012;67(4):319-25, http://dx.doi.org/10.6061/clinics/2012(04)04.
42. Medeiros IL, Pego-Fernandes PM, Mariani AW, Fernandes FG, Unterpertinger FV, Canzian M, et al. Comparison of lung preservation solutions in human lungs using an ex vivo lung perfusion experimental model. Clinics (Sao Paulo). 2012;67(9):1101-6, http://dx.doi.org/10.6061/clinics/2012(09)19.
43. Sener EB, Ustun E, Ustun B, Sarihasan B. Hemodynamic responses and upper airway morbidity following tracheal intubation in patients with hypertension: conventional laryngoscopy versus an intubating laryngeal mask airway. Clinics (Sao Paulo). 2012;67(1):49-54, http://dx.doi.org/10.6061/clinics/2012(01)08.
44. Zhang B, Zhang Y, Yao G, Gao J, Yang B, Zhao Y, et al. M2-polarized macrophages promote metastatic behavior of Lewis lung carcinoma cells by inducing vascular endothelial growth factor-C expression. Clinics (Sao Paulo). 2012;67(8):901-6, http://dx.doi.org/10.6061/clinics/2012(08)08.