

Podemos prever doenças?

“A menor distância entre dois pontos não é uma linha reta.” Albert Einstein

Prezado Editor,

Li com muito interesse o artigo de Sá et al. [1]: “Validation of MagedanzSCORE as a predictor of mediastinitis after coronary artery bypass graft surgery”, publicado na Rev Bras Cir Cardiovasc. 2011;26(3):386-92. O assunto em si é muito relevante, mas algumas considerações são pertinentes.

Cito Escrivão Jr. [2]: “*Cresce também a exigência para que os serviços de saúde, tanto privados quanto da área pública, organizem-se de modo a responder às necessidades das pessoas e ofereçam um cuidado efetivo e humanizado, provendo todas as informações que o usuário necessita*”. E cito, também, Dobrow et al. [3]: “... *sugerem ser necessário fazer uma distinção entre o “impacto das evidências” nos resultados das organizações e a simples “utilização das evidências” no processo de tomada de decisão.*”

O tema central seria: Podemos prever doenças? Se podemos, a quem participar destas informações? Este tema e estas dúvidas também tive quando descrevi um relato de caso utilizando o EuroSCORE (1999) para a avaliação de risco operatório e o escore de Fowler et al. (2005) na análise de risco para mediastinite [4]. Neste caso estudado, a utilização das duas escalas não apresentou poder em prever no pré-operatório os problemas cirúrgicos que se seguiram no pós-operatório.

Se a precisão dos dados avaliados em detectar complicações graves como a mediastinite entrar em nossa avaliação prática de rotina, qual seria o momento ideal desta apresentação ao paciente? Na fase de pré-operatório? No período de pós-operatório? E, mais importante, nesta era de informação, o paciente deveria saber que ele apresenta risco alto para o desenvolvimento de infecção pós-operatória (uma complicação cirúrgica?), mesmo com risco pré-operatório baixo?

Concordo com Turpin et al. [5] que indicadores de desempenho não são medidas diretas da qualidade e sim “...*flags to alert users to possible opportunities for improvement in processes and outcomes*”.

Diante destas incertezas, acompanho Vallet et al. [6]: “*Ces publications ne sont compréhensibles que par un public de professionnels avertis qui dénonce massivement les exploitations des données telles qu’elles sont faites et les carences méthodologiques de la presse grand public*”.

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An overview of basic research articles recently published by Clinics

Introduction

This is an insight on articles on basic research recently published by Clinics with direct or indirect interest to the cardiopulmonary system. We believe they may be of interest to readers of Revista Brasileira de Cirurgia Cardiovascular.

Cardiovascular

The most cited article of this collection describes the effects of hypertension time course in spontaneously hypertensive rats. Spontaneously hypertensive rats develop left ventricular hypertrophy, increased blood pressure and blood pressure variability, which are important determinants of heart damage, like the activation of renin-angiotensin system. Zamo et al. [1] investigated the effects of the time-course of hypertension over 1) hemodynamic and autonomic patterns (blood pressure; blood pressure variability; heart rate); 2) left ventricular hypertrophy; and 3) local and systemic Renin-angiotensin system of the spontaneously hypertensive rats. They observed that autonomic dysfunction and modulation of Renin-angiotensin system activity are contributing factors to end-organ damage in hypertension and could be interacting. Our findings suggest that the management of hypertensive disease must start before blood pressure reaches the highest stable levels and the consequent established end-organ damage is reached.

Memantine, a drug used in the treatment of Alzheimer's disease was tested by Meneghini et al. [2] to evaluate its effects on nuclear size reduction in cardiac cells exposed to cold stress in rats and conclude that memantine prevented the nuclear size reduction of cardiomyocytes in rats exposed to cold stress.

Duarte et al. [3] induced myocardial infarction in rats in order to evaluate the roles of oxidative stress and lipid peroxidation in the ventricular remodeling that is induced by tobacco smoke exposure after myocardial infarction. They found that tobacco smoke induced oxidative stress is associated with the intensification of ventricular remodeling after myocardial infarction.

The microcirculation was the object of most articles in this collection. The degree of vascular occlusion, vascular recanalization, and necrosis of the vascular wall caused by polyvinyl alcohol-covered polyvinyl acetate particles compared to trisacryl particles after renal embolization was evaluated by Barbosa et al. [4] in female albino New Zealand rabbits. Their conclusion is that polyvinyl alcohol-covered polyvinyl acetate particles exhibited adequate tissue reactions, more expressive vascular occlusion and necrosis, and less recanalization than the trisacryl material.

Coelho da Mota et al. [5] investigated the effects of buflomedil and pentoxifylline, both of which are used in reconstructive surgery of hamster skin flap microcirculation of hamsters, and evaluated the skin flap survival rate by orthogonal polarization spectral imaging. Their results show that functional capillary density values were higher in the buflomedil group compared to the control and pentoxifylline groups in this model.

The interaction between liver steatosis and ischemia reperfusion in rats was the object of Andraus et al. [6] who hypothesized that S-nitroso-N-acetylcysteine (SNAC), an NO donor component, can ameliorate cell damage from IR injury. They suggest that SNAC effectively protects against IR injury in the steatotic liver but not in the normal liver.

The classic rat paw edema model for the study of inflammatory agents was studied by Hajhashemi et al. [7] who further investigated the effect of amitriptyline, a classical tricyclic antidepressant, on carrageenan-induced paw edema in rats. They found that amitriptyline has a considerable anti-inflammatory effect on carrageenan-induced paw edema in rats and suggest that at least a part of this property could be mediated through supraspinal sites. Moreover, it seems unlikely that the investigated adrenergic and opioid receptors have a significant role in this effect of amitriptyline.

Mechanical ventilation with positive end expiratory pressure (PEEP) improves oxygenation and treats acute pulmonary failure. However, increased intrathoracic pressure may cause regional blood flow alterations that

may contribute to mesenteric ischemia and gastrointestinal failure. Aikawa et al. [8] investigated the effects of different PEEP levels on mesenteric leukocyte-endothelial interactions in male Wistar rats. They found that high intrathoracic pressure was harmful to mesenteric microcirculation in the experimental model of rats with normal lungs and stable systemic blood pressure, a finding that may have relevance for complications related to mechanical ventilation.

The aortic wall structure was studied by Adam et al. [9] who observed the effects of consuming repeatedly heated soy oil on the aortic tissues of estrogen-deficient rats in female Sprague Dawley rats and found that fresh soy oil offered protection in the estrogen-deficient state, as these rats had similar features to those of the NC group. The damage to the tunica intima and the increase in the ratio of tunica intima/media thickness showed the deleterious effect of consuming repeatedly heated soy oil in castrated female rats.

Two highly interesting and intensely cited physiological studies in conscious rats are by Valenti et al. are included in this series. In the first [10], a subset of normotensive Sprague-Dawley rats show lower baroreflex sensitivity; however, no previous study investigated whether there are differences in baroreflex sensitivity within this subset. The study compared baroreflex sensitivity among conscious rats of this specific subtype and found there is variability regarding baroreflex sensitivity among WKY rats from the same laboratory. In the second [11], the importance of oxidative stress on the cardiovascular system was studied. The effects of central catalase inhibition on cardiopulmonary reflex in conscious Wistar rats was evaluated. It is claimed that catalase injected into the fourth cerebral ventricle increases sympathetic inhibition but does not change the parasympathetic component of the cardiopulmonary reflex in conscious Wistar rats.

Two interesting exercise murine models are described. Ferreira et al. [12] analyzed the effects of exhausting long-duration physical exercise (swimming) sessions of different durations and intensities on the number and phagocytic capacity of macrophages and neutrophils in sedentary rats and conclude that exercise intensity, duration and frequency are important factors in determining immune response to physical effort: neutrophils and macrophages of sedentary rats respond differently to exercise-induced stress. Adaptation sessions reduce exercise-induced stress on the immune system.

Malysz et al. [13] investigated the effects of treadmill training (10 weeks) on hindlimb motor function and nerve morphometric parameters in diabetic rats submitted to sciatic nerve crush. And found that the diabetic condition promoted delay in sciatic nerve regeneration. Treadmill training is able to accelerate hindlimb motor function

recovery in diabetic injured rats and prevent or revert morphometric alterations in proximal nerve portions in non-diabetic and diabetic injured rats.

Two articles cover the ever interesting subject of the interaction of shock with hypertonic saline. Rocha Filho et al. [14] evaluated the effects of terlipressin versus fluid resuscitation with normal saline, hypertonic saline or hypertonic-hyperoncotic hydroxyethyl starch, on hemodynamics, metabolism, blood loss and short-term survival in hemorrhagic shock in pigs subjected to severe liver injury. They show that hyperkalemia accompanies hemorrhagic shock and, in addition to providing an early sign of the acute ischemic insult severity, may be responsible for cardiac arrest related to hemorrhagic shock.

Costantini et al. [15] designed a study to combine the hemodynamic and immune benefits of hypertonic saline with the anti-inflammatory effects of the phosphodiesterase inhibitor pentoxifylline as a hemorrhagic shock resuscitation strategy to reduce lung injury in Male Sprague-Dawley rats. They conclude that the decreases lung inflammation following hemorrhagic shock compared with conventional.

Two articles cover themes in microcirculation. The previously described Aikawa et al. [8] study shows that high intrathoracic pressure was harmful to mesenteric microcirculation in the experimental model of rats with normal lungs and stable systemic blood pressure, a finding that may have relevance for complications related to mechanical ventilation.

Pulmonary system

Pulmonary lung development in the preterm rabbit was the object of a study by Mascaretti et al. [16]: elastic and collagen fiber deposition is known to increase throughout normal lung development, and this fiber network significantly changes when development of the lung is disturbed. In preterm rats and lambs, prolonged hyperoxic exposure is associated with impaired alveolization and causes significant changes in the deposition and structure of elastic fibers. The study evaluated the effects of hyperoxic exposure on elastic and collagen fiber deposition in the lung interstitial matrix and in alveolarization in preterm rabbits. And found that prolonged oxygen exposure impaired alveolization and also lowered the proportion of collagen fibers, with an evident fiber network disorganization.

Nutrition and dislipidemia have become highly significant themes in contemporary medical investigation. Four reports are included in this review. Toscano et al. [17] investigated the effect of fetal undernutrition on the passive mechanical properties of skeletal muscle of weaned and young adult rats. A poor nutrition supply during fetal development is known to affect physiological functions of

the fetus. They find that the increase in passive stiffness in skeletal muscle of weaned rat submitted to intrauterine undernutrition it is most likely due to changes in muscle passive stiffness.

Nutrition

An original article by von Wilmsdorff et al. [18] investigated the impact of typical and atypical antipsychotic drugs on leptin concentration in blood and changes in the receptor expression in the hypothalamus of male Wistar rats. And found that haloperidol and ziprasidone induced a significantly decrease in weight gain and food consumption. No differences were seen in the alcove test, but locomotor activity was significantly reduced in the haloperidol group. Except for rats in the clozapine and ziprasidone groups, after 2 weeks of drug application, no changes were found in the leptin blood concentrations among the four groups or among animals within each group. No specific differences in hypothalamic leptin receptor expression occurred among the groups. Thus, the treatment did not act directly on the leptin regulatory system.

Rodrigues et al. [19] investigated the effect of carnitine supplementation on alcoholic malnourished rats' hepatic nitrogen content. And found: (i) no difference between the alcohol/no alcohol groups, with or without carnitine, regarding body weight gain, diet consumption, urinary nitrogen excretion, plasma free fatty acids, lysine, methionine, and glycine. (ii) Liver nitrogen content was highest in the carnitine recovery non-alcoholic group (from 1.7 to 3.3 g/100 g, $P < 0.05$) and lowest in alcoholic animals (about 1.5 g/100g). (iii) Hepatic fat content (similar to 10 g/100 g, $P > 0.05$) was highest in the alcoholic animals. They conclude that Carnitine supplementation did not induce better nutritional recovery.

The effects of natural product on diabetic rats were the object of two papers: Budin et al. [20] examined the effects of palm oil tocotrienol-rich fractions on streptozotocin-induced diabetic rats. And found that such 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.

Movahedian et al. [21] studied the effects of *Peucedanum pastinacifolium*, an antihyperlipidemic vegetable used in Iranian folk medicine and found that there were significant ($P < 0.05$) increases in total serum cholesterol, triglyceride and low-density lipoprotein cholesterol and a decrease in high-density lipoprotein cholesterol in streptozotocin-induced diabetic rats. Treatment of diabetic rats with the extract over a period of a month returned these levels close to control levels, suggesting that it has hypolipidemic effects in streptozotocin-induced diabetic rats.

Neuro-psychiatric themes

Learning and memory were the subject of four murine model studies. Because of the well-established severe cognitive impairment which follows thyroid hormone deficiency during the neonatal period and the role of nitric oxide in learning and memory Hosseini et al. [22] investigated the effect of hypothyroidism during neonatal and juvenile periods on NO metabolites in the hippocampi of rats and on learning and memory. Their results suggest that the increased NO level in the hippocampus may play a role in the learning and memory deficits observed in childhood hypothyroidism.

The consequences of ill studied consequences of the very widespread use of mobile phones Narayanan et al. [23] exposed male Wistar rats to 50 missed calls/day for 4 weeks from a GSM (900/1800MHz) mobile phone in vibratory mode (no ring tone). Animals were subsequently tested for spatial memory performance using the Morris water maze test. They claim that mobile phone exposure affected the acquisition of learned responses in Wistar rats.

Mobile phone emissions on free radical metabolism and sperm motility in rats was studied by Mailankot et al. [24] in an often cited paper: Their results show that in animals sacrificed 24 hours after the last exposure mobile phones emissions negatively affect semen quality and may impair male fertility.

Still on the subject of the mobile phone, Hosseini et al. [25] evaluated the effect of L-arginine on the learning and memory of estradiol-treated ovariectomized rats. And propose that chronic treatment with estradiol enhances the spatial learning and memory of ovariectomized rats, and that long term L-arginine treatment attenuates the effects of improvement produced by estradiol in OVX rats.

Kumar et al. [26] studied the protective effects of ascorbic acid in memory loss induced by chronic restraint stress in rats exposed to restraint stress alone and in animals pretreated with vehicle solution before restrained stress: both groups showed deficits in learning and impaired memory retention in the memory tests when compared to animals in other experimental groups. Animals pretreated with ascorbic acid before restraining showed significant improvement in memory retention in the same memory tests.

Other neuro-psychiatric studies include a previously cited study by von Wilmsdorff et al. [18] on the impact of typical and atypical antipsychotic drugs on leptin concentration in blood and changes in the receptor expression in the hypothalamus of male Wistar rats. Haloperidol and ziprasidone induced a significantly decrease in weight gain and food consumption. With listle or no effect on leptin blood concentrations or on hypothalamic leptin receptor expression. Suggesting the treatment did not act directly on the leptin regulatory system.

A second study by von Wilmsdorff et al. [27]

investigated sex-dependent differences in motor coordination and activity as well as in cognitive and social behavior in Fisher rats (postnatal days, PD 56-174) that had received intracerebroventricular injections of kainic acid. These results demonstrate important differences between males and females in terms of weight gain, response to fear, working memory and social behavior. Sex-dependent differences in the lengths of hippocampal neurons were also found.

Natural products

Apart from their effects on the cardiovascular system and and nutrition, natural product were studied for a number of different effects. Hajhashemi et al. [28] investigated the antianxiety and sedative effects of the essential oil of *Ducrosia anethifolia*. Boiss. (Apiaceae). In elevated plus maze, *Ducrosia anethifolia* essential oil at doses of 25-200 mg/kg increased the percentage of open arm time and entries. Unlike diazepam, *ducrosia anethifolia* essential oil could not suppress spontaneous motor activity and did not alter ketamine-induced sleep parameters. They claim that these results are indicative of antianxiety effect of *Ducrosia anethifolia* essential oil without sedative effect.

Paval et al. [29] evaluated the anti-arthritis potential of the plant *Justicia gendarussa* using two different rat models and claim that it showed significant anti-arthritis activity that was statistically similar to that of aspirin.

Wahab et al. [30] examined the ability of *Eurycoma longifolia* Jack to reverse the inhibitory effects of estrogen on testosterone production and spermatogenesis. And claim that the natural product acts as a potential agent for reversing the effects of estrogen by increasing spermatogenesis and sperm counts in rats after fourteen consecutive days of treatment.

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