PART 4: GENERAL DISCUSSION, CONCLUSIONS, PERSPECTIVES
PART 4: GENERAL DISCUSSION, CONCLUSIONS, PERSPECTIVES

Stress echocardiography is a relatively new technique in equine cardiology. Since the late eighties and early nineties, when echocardiography and Doppler echocardiography became standard in equine medicine, no new diagnostic technique has been described (Reef et al., 1989, Reef, 1991, Long et al., 1992). However, there would be an evident need for diagnostic techniques allowing examination of the equine heart under exercising conditions. Stress echocardiography is certainly the only technique for the diagnosis of exercise-induced myocardial dysfunction, which occurs in about 5 to 8% of horses examined for poor performance and which is characterized by lack of significant lesions at resting examination (Reef, 1997; Martin et al., 2000). Furthermore, stress echocardiography might be useful in clinical settings for the assessment of the behaviour of valvular insufficiencies during exercise, in order to refine their prognosis (Gehlen, 2005). Stress echocardiography might also become a tool for the evaluation of the relationship between valvular disease and ventricular dysfunction in horses as it has been done in man (Lebrun et al., 2001, Lancellotti et al., 2003).

Stress echocardiography in the form of post-exercise stress echocardiography has already been described in the context of exercise-induced myocardial dysfunction in horses. Unfortunately, post-exercise stress echocardiography only partly mimics the conditions during exercise (Durando et al., 2002). Maximal or near-maximal exercise is needed to induce measurable changes in echocardiographic parameters in the immediate post-exercise period. It is a technically demanding procedure that has to cope with bad quality images due to intense respiration after strenuous exercise, and still a rapid drop in HR, which decreases the sensibility of the test. Pharmacological stress induction, in the same manner as used in human medicine for the diagnosis and prognosis of coronary artery disease, has been described to overcome the limitations of post-exercise stress echocardiography but proved to be cardiomyotoxic (Frye et al., 2003).

The pharmacological stress test described in our first study overcomes most of the disadvantages of exercise stress echocardiography and high-dose dobutamine stress echocardiography. However, echocardiographic measurements made during this atropine/low-dose dobutamine test in the second study and compared to those induced by exercise in the third study, we assumed that loading conditions and contractility, major determinants of myocardial performance, are different during the two different forms of cardiac stress induction.

Therefore, the evaluation of cardiac preload, afterload and contractility in response to the atropine/low-dose dobutamine stress test was the aim of the fourth study of this work. Systolic time intervals, although not completely independent of HR and loading conditions were evaluated as indicators of myocardial contractility and demonstrated that contractility is increasing with increasing stimulation. Mean velocity of circumferential fibre shortening is considered as a preload-independent measure of contractility, but it is affected by afterload (Atkins and Snyder, 1992). To overcome the influence of HR on Vcirc, a rate-correcting formula of Colan et al. (1984) was used in the present
Both, rate-corrected and uncorrected $V_circ$ significantly increased with dobutamine stimulation, which is similar to observations made in dogs (Lang et al., 1986) and humans (Colan et al., 1984) and demonstrating the positive inotropic effect of dobutamine.

Increased contractility can also be expected during exercise. The heart at rest is primarily under parasympathetic control. During exercise, increased sympathetic stimulation occurs and catecholamine are released leading to increased contractility (Sexton and Erickson, 1986). Shortly after exercise, the influence of the sympathetic system is diminished, as shown by Durando et al., (2002) who measured right ventricular pressure dynamics during and after exercise. The interpretation of our results in the light of their study, suggests that contractility during atropine/low-dose dobutamine better reflects the conditions during exercise than in the post-exercise period, when post-exercise stress echocardiography can be performed in horses.

Preload is often estimated by measurement of the LVIDd. During our studies, LVIDd decreased significantly with increasing atropine/low-dose dobutamine stimulation. On the contrary, during exercise, preload increases by sympathetic stimulation of veins and compression of capacitance vessels by abdominal musculature. In the post-exercise period, there may be conflicting control by the autonomic nervous system, as sympathetic tone and catecholamine tone decreases and parasympathetic system again predominates. For this reason and due to the missing compression of the capacitance vessels, venous return and preload decrease after cessation of exercise. Preload during pharmacological stimulation is certainly lower that during exercise, and probably still lower than in the immediate post-exercise period.

In clinical settings, SVR is commonly used as a measure of ventricular afterload. It is calculated as the mean aortic pressure minus the mean right atrial pressure multiplied by the conversion factor 80 dyne * cm$^{-2}$/mmHg divided by the thermodilution-derived cardiac output. This formula has been validated angiographically (Grossmann and McLaurin, 1980). Klabunde (2004) suggested that right atrial pressure can be neglected in order to facilitate measurements in clinical settings. Because in horses cardiac output increases approximately 4-fold (Thomas et al., 1983) and MAP increases approximately 1.7-fold (Hornicke et al., 1977) with sub-maximal exercise, the calculated sub-maximal SVR would be would approximately 40% of the resting value. Dobutamine is known to reduce SVR in humans and dogs (Leier et al., 1977). In the present study, dobutamine reduced SVR from 324 to 137 dyne * s/cm$^5$, which represents the same level of changes than those observed during submaximal exercise. However, SVR may not adequately assess left ventricular afterload (i.e. ventricular internal fibre load during systole) since it reflects only peripheral vasomotor tone (Lang et al., 1986).

Left ventricular afterload is defined as the force opposing ventricular fibre shortening during left ventricular ejection (Weber et al., 1982; Nichols and Pepine, 1982). It is not synonymous with peripheral arterial pressure, peripheral vasomotor tone, or SVR. It should rather be evaluated as left ventricular wall stress during ejection. It includes factors both internal and external to the myocardium. According to the La Place’s principle, left ventricular wall stress is directly related to
chamber dimension and pressure and inversely related to wall thickness (Gould et al., 1974; Grossmann et al., 1975; Weber and Janicki, 1980). In the present study, wall stress did not change significantly during the pharmacological stimulation which is probably due to the sum of effects of the decreasing left ventricular dimension, increasing LVFW and increasing MAP.

In conclusion, the fourth study demonstrated that changes in STI, PEP, ET, Vcirc and rate-corrected Vcirc are indicators of ventricular performance in horses undergoing dobutamine stress test. All these parameters change significantly with increasing stimulation. Afterload, decreases significantly during the test when measured as SVR but decreases only slightly when measured as left ventricular wall stress.

Even though these values during our studies behaved similar to what was described in other studies, it remains difficult to conclude how afterload is manipulated by atropine/low-dose dobutamine stress test in healthy horses. Nevertheless, this test induced significant changes in measurable variables of cardiac performance and has a great potential for the evaluation of the equine heart under exercising conditions. The test has been proven to be well tolerated and easy to perform. Therefore, it can be used in horses suffering from cardiac diseases. Future studies should evaluate of the semi-quantitative method used in human medicine, which is less time consuming and has a good sensibility when performed by an experienced user. Stress echocardiography has without doubt a great diagnostic potential, but might be interesting in prognosis as well. As demonstrated in the last study, CPO measured by Doppler echocardiography, is feasible in horses, and might allow refinement of prognosis in horses suffering from low or mid-grade cardiac disease.

Overall, stress echocardiography opens a new diagnostic and prognostic dimension in equine cardiology. The choice of exercise or pharmacological stress induction depends on availability of staff and material, cooperation of horses and the clinical problem investigated.

For the future, our studies could be expanded to evaluate the effect of various physiological factors, such as breed, age, sexe, and training on the pharmacological stress echocardiography developed during this work.

Furthermore, this test could be applied in a variety of clinical indications. It could be particular usefull in horses with poor performance without an evident cause of it. Moreover, this test could be applied to horses suffering from various degrees of mitral and/or aortic insufficiencies, in the aim of a better stratification of the degree of severity and of giving a more accurate prognosis.

The present work focussed on the systolic cardiac function. However, for some cardiac diseases, diastolic function is known to be altered before changes of systolic function can be measured. Therefore, it would be interesting to measure parameters of diastolic function during atropine/low-dose-dobutamine stress test in healthy horses and in horses suffering from various cardiac diseases.