REVIEW ARTICLE

# The Use of Mechanical Circulatory Support – Early Experiences in the Czech Republic

Kettner J., [1]Pirk J., [1]Netuka I., [2]Březina A., [2]Říha H., [1]Malý J., [1]Mašín J.

*Department of Cardiology IKEM, Prague*
*[1] Department of Cardiovascular Surgery IKEM, Prague*
*[2] Department of Anaesthesiology and Resuscitation IKEM, Prague, Czech Republic*

## ABSTRACT

**Background.** Implantation of mechanical assist device is widely accepted modality of treatment of patients with refractory heart failure. In the present study we evaluated our first one-year experiences with this method for bridging patients to heart transplantation.
**Methods and Results.** Between April 2003 and May 2004, the Thoratec® VAD (Thoratec, Pleasanton, CA, USA) was implanted in 6 patients ( males; age 28-61 years) as a bridge-to-transplant procedure after having received maximum inotropic support and who were at imminent risk of death. In all patients was performed VAD as biventricular device (BiVAD).
During a week after placement recovery of organs function was observed in all patients. The primary goal, which was bridging of the critical period to heart transplantation, was achieved in 5 patients who, after explantation of the assist device, underwent orthotopic heart transplantation. One patient died 21 days after BiVAD placement due to massive bleeding into the respiratory tract. In post-transplantation period 1 patient died due to acute graft failure and other patients died 34 days after because of intracranial bleeding. Three patients have been discharged from the hospital and they are surviving more than 1 year.
**Conclusions.** Analysis of our first experiences with the Thoratec BiVAD implantation as bridging to heart transplantation suggests that it is well suited method in our conditions with the largest potential with respect to long-term prognosis, in spite of substantial costs.
**Key words:** heart failure, mechanical assist devices, heart transplantation.

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## INTRODUCTION

Heart failure is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the heart to fill with or eject blood. It is a progressive process, and even though modern pharmacotherapy can slow it down by influencing neurohormonal compensatory mechanisms, the further course of the disease remains unfavourable. Incidence and prevalence of this "21st century epidemic" increase with more sophisticated treatment of cardiac diseases.

Often the end-stage of heart failure cannot be influenced only by pharmacological treatment. Specialized non-pharmacological procedures are the next possibilities. At present, heart transplantation is the only proved and recognized solution to the terminal phase of heart failure with a long-term acceptable effect. It has a clearly defined position in the treatment of heart failure refractory to pharmacological treatment, without the possibility of standard cardiosurgical operation.

The criteria for indication and contraindication concerning both recipients and donors and mainly the absolute lack of donors are the reasons why this therapeutical method still remains available for only a limited number of patients. This is despite the fact that the candidate for heart transplantation may be at risk of acute worsening while waiting for a suitable donor, a worsening which is refractory to intravenous inotropic treatment. For all these reasons, further non-pharmacological methods that would support the activity of the failing heart are being researched. Mechanical cardiac supports (MCS) are among the most effective approaches. The purpose of their use in this indication is to bridge the critical waiting time, to improve or normalize the function of hypoperfused organs and to achieve better results in cardiac transplantation.

The history of mechanical circulatory supports dates back to the 1930s. The greatest progress in this endeavour was the development and use of what was dubbed extracorporeal circulation (a heart-lung apparatus), which meant a revolution in cardiosurgery. After 20 years of experiments, John Gibbon was the first to use it in 1953 during an operation to remedy an atrial septal defect in an 18-year-old girl.

The Texas Heart Institute in Houston in the USA is a cradle of mechanical devices. Names such as Domingo Liotta, John Norman, Tetsuzo Akutsu, Denton A.Cooley and O. H. Frazier are firmly associated with the development and application of these systems.

Essentially, there are three types of mechanical circulatory support:

1. Intraaortal balloon counterpulsation (IABC)
2. Mechanical pumps supporting or replacing the function of one or both heart ventricles (pulsatile, non-pulsatile, paracorporeal, implantable, univentricular and biventricular)
3. Artificial heart as a total cardiac replacement.

A detailed review of mechanical circulatory supports has been published formerly (1).

A clinical programme of orthotopic heart transplantations (OHT) was started in the Institute of Clinical and Experimental Medicine (IKEM) in Prague as early as 1984. One of the problems which per-

sists to date has been the impasse for those candidates for transplantation who have developed serious exacerbation of heart failure during the waiting time. Even though complex therapy including administration of catecholamines, phosphodiesterase inhibitors III or levosimendan can improve the health of these patients temporarily, it usually cannot avert multiorgan failure, and every further deterioration results in fatal consequences. Even IABC in the case of severe mechanical failure fails to produce satisfactory results due to the low efficiency of this support in the given indications. After many years of attempts to introduce this very costly programme, in 2003 the conditions were created in IKEM that would suit the implantation of mechanical circulatory support for the purpose of bridging the critical phase of heart failure in candidates for heart transplantation. The main indication and contraindication criteria for mechanical assist devices are stated in Table 1.

## PATIENTS AND METHODS

From 03. 04. 2003 to 30. 05. 2004, the Thoratec ® VAD (Thoratec, Pleasanton, CA, USA; Fig. 1) was implanted in 6 patients (all males, age 28-61) in indication "bridge to heart transplantation", for whom all possibilities of conservative treatment had been exhausted and who were in imminent risk of death.

Basic diagnosis and causes of heart failure were nonischaemic dilated cardiomyopathy in 3 patients, 1 case of ischaemic cardiomyopathy, 1 case of heart failure due to congenital valvular disorder and 1 case of heart failure after corrected valvular disease in association with refractory ventricular fibrillation (Tab. 2). All the patients were treated with a combination of dopamine and dobutamine; 4 patients were additionally treated with milrinone and one patient with levosimendan. Two patients underwent cardiopulmonary cerebral resuscitation, IABC was applied in 2 patients, the necessity of hemodialysis occurred in 2 patients during waiting time and 2 patients were subjected to the artificial pulmonary ventilation during transfer. We chose the Thoratec ® VAD (Thoratec, Pleasanton, CA, USA) from several existing devices. The blood pump is situated outside the patient's body (paracorporeally) and it is connected with the patient's heart by the cannulas. The pump consists of a rigid plastic case containing a flexible pumping blood sack (Fig. 2). The blood is expelled from the pump by compression of the sack with air from an externally placed compressor in the control system (Fig. 3). Blood flow direction is controlled by mechanical valves in the inflow and outflow part of the pump.

Stroke volume of the blood pump is fixed (65 cc), and pumping rate may reach 100 beats per minute, which leads to minute volume 6-7 L/min. The external monitoring system includes the compressor responsible for air supply and vacuum creation, and it also images all the important parameters such as eject pressure, eject time, beat rate, flow and vacuum value. This system also contains a portable unit enabling mobility and rehabilitation of the patient (Fig. 4). The device can be used both for univentricular and biventricular support (see Fig. 1).

The implantation is performed in general anaesthesia and in extracorporeal circulation under strictly sterile conditions. After usual preparation of the operative field, sternotomy and systemic heparinization, the cannulas for extracorporeal circulation in standard configuration are introduced – arterial cannula to the distal ascending aorta and venous two-stage atriocaval cannula through the auricle of the right atrium into vena cava inferior. After iniciation of extracorporeal circulation, mild hypothermia of 34 degrees Centigrade is induced. In decompressed beating heart after circular excision of a part of the left ventricle wall, apical inflow cannula of the left ventricular assist device (LVAD) is introduced parallel to the interventricular septum with subsequent stitch fixation (Fig. 5). Then follows suture of the anastomosis between the outflow cannula of LVAD and ascending aorta with classical continuous suture, the outflow cannula of a right ventricular assist device (RVAD) being attached to pulmonary

**Tab. 1.** General indications and contraindications for implantation of MHS

**Indications of mechanical heart support**

**General inclusion criteria**

1. HF refractory to pharmacological treatment - organ hypoperfusion
   - *high doses of inotropics (at least 2 drugs)*:
     - dopamine ≥ 10 ug/kg/min
     - dobutamine ≥ 10 ug/kg/min
     - epinephrine (adrenalin) ≥ 0.02 ug/kg/min
     - isoprenaline ≥ 0.05 ug/kg/min
     - milrinon ≥ 0.75ug/kg/min
     - PGE1

2. Haemodynamic parameters:
   - CI < 2 l/min
   - MAP < 65 mmHg
   - PCWP ≥18 mmHg
   - PAPd > 20 mmHg
   - CVP > 20 mmHg

**Contraindications of mechanical circulatory support**

1. Absolute contraindications
   - S-Cr > 440 umol/l or S-urea > 17 mmol/l
   - total bilirubin > 85 umol/l (5mg/dl)
   - serious infection
   - coagulopathy in patient's history
   - tumour (in bridge to OHT)
   - cerebrovascular disease
   - aortic diseases
2. Relative contraindications
   - parenchymatous pulmonary disease (e. g. sarcoidosis)
   - fixed pulmonary hypertension
   - mechanical valvular replacement
   - heparin-induced intolerance (HIT)
   - peripheral vasculary disease

Notes:
CI - cardiac index; MAP - mean arterial pressure; PCWP – pulmonary capillary wedge pressure; PAPd - pulmonary artery diastolic pressure; CVP- central venous pressure; S-Cr – serum creatinin; S-urea – serum urea; HIT - heparin-induced thrombocytopaenia

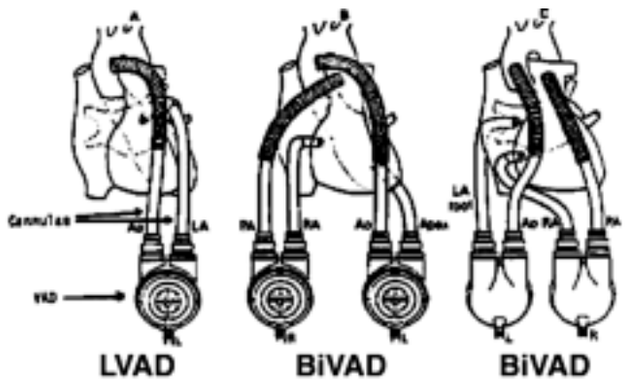


**Fig. 1.** Schematic diagram of the extracorporeal univentricular (left ventricular - LVAD) and biventricular (BiVAD) assist device – Thoratec VAD. The cannulas are led out through the chest wall and connected to the pump that is situated on the anterior area of the abdomen

**Tab. 2.** List of patients with MHS ( state on May 30, 2004)

| Patients | Age (years) | Basic dg | Type of MHS | Duration of MHS (days) | Serious complications | Successful bridging to OHT | Health state |
|---|---|---|---|---|---|---|---|
| 1. | 58 | DCMP | BiVAD | 29 | bleeding, tamponade, infection | yes | living |
| 2. | 54 | IHD | BiVAD | 21 | bleeding, tamponade | no | died with BiVAD |
| 3. | 48 | DCMP | BiVAD | 60 | 0 | yes | living |
| 4. | 46 | DCMP | BiVAD | 64 | tamponade; infection | yes | died 34 days after OHT |
| 5. | 59 | Ao disorder | BiVAD | 49 | tamponade; infection | yes | died 2nd day after OHT |
| 6. | 28 | Ao disorder | BiVAD | 13 | 0 | yes | living |

Notes:
DCMP - dilated cardiomyopathy; IHD - ischaemic heart disease; BiVAD - biventricular assist device; OHT – orthotopic heart transplantation

artery similarly. All cannules are led out transcutaneously in upper epigastrium (Fig. 6). The last step is the introduction of an atrial cannula of RVAD into the right atrium with the tip of the cannula being directed to the junction of the atrium and orifice of the inferior vena cava. The cannulas are successively connected with the chambers of circulatory support and then follows careful deflation of all components of the system. In all the patients a biventricular assist device (BiVAD) with cannulation of the apex of the left ventricle was implanted for the purpose of achieving better flow parameters in comparison with cannulation of the left atrium through the auricle. The action of the drive unit Thoratec VAD is usually started in the fixed mode and the flow of extracorporeal circulation is gradually decreased to complete cessation with careful monitoring of haemodynamic parameters. Assist device at that time provides a required minute volume 4-5 L/min. Usual serious diffuse bleeding demands long careful hemostasis, and subsequent wound closure is performed as usual. After the patient's transport to the recovery room, if there are satisfactory flow parameters the system is switched to the volume controlled mode for assuring the flow 5-6 L/min. In these patients the immediate postoperative period is characterized first of all by the struggle with blood coagulation disorders and with the risk of infection. Heparin administration in continuous infusion is standard procedure if discharge from the chest drains is minimal, after several days administration of warfarin is begun and this treatment continues for the whole time of activity of the device whose parts are mechanical valves. In addition to observance of strict sterile conditions, in the first period antibiotic prophylaxy with combination vancomycin and ciprofloxacin is applied. Both these procedures have to be modified in case of more severe bleeding and renal failure.

**Tab. 3.** List of the most often used mechanical assist devices in clinical practice with respect to the indications

| | | |
|---|---|---|
| After cardiosurgical operation | Extracoporeal membrane oxygenator (ECMO)<br>Abiomed BVS 5000 VAD<br>Centrifugal pumps (BioMedicus pump)<br>Thoratec VAD | |
| Bridge-to-heart transplantation | Thoratec VAD<br>HeartMate – VAD<br>Novacor LVAD<br>Jarvik 2000<br>MicroMed DeBakey VAD | |
| Bridge to recovery | BerlinHeart EXCOR<br>Novacor LVAD<br>HeartMate VAD | |
| Permanent or replacement | LionHeart LVD 2000<br>CardioWest TAH<br>AbioCor TAH | support |

**Fig. 2.** Detail of the pumping chambers, either of them replacing function of one heart ventricle

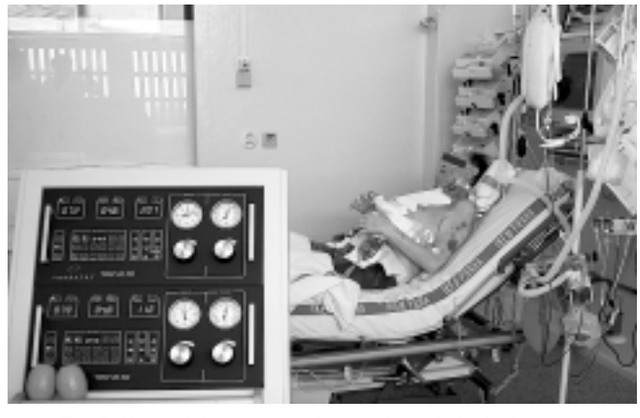

**Fig. 3.** External drive units with control panels for both pumps

**Fig. 4.** Wearable drive unit Thoratec VAD. One of our patients going for a walk

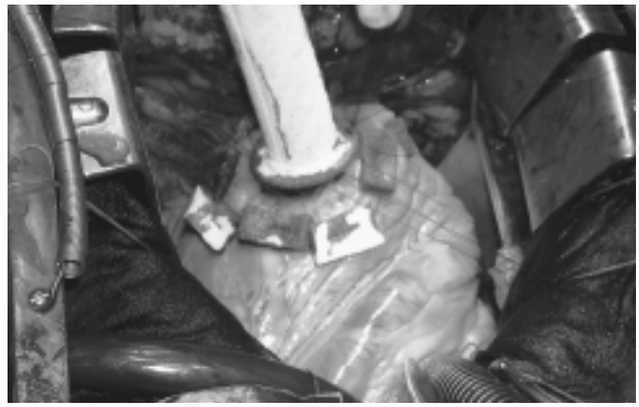

**Fig. 5.** Detail of the operational field – apical inflow cannula of the left ventricle assist device (LVAD)

## RESULTS

Despite the high risk, the mechanical assist device was successfully implanted in all patients without perioperational death. Total time of mechanical cardiac support was 236 days. There was significant improvement or normalization of organ functions in all the patients within a week. Primary goal, i.e. bridge to heart transplantation was fulfilled in 5 patients, in whom - after explantation of mechanical heart device - orthotopic cardiac transplantation was performed. One patient died on 21st day after BiVAD implantation due to massive bleeding into the respiratory tract.

The main challenge in the early postoperative period after implantation BiVAD were bleeding complications that necessitated surgical revision for cardiac tamponade in 4 patients. For these reasons we lastly prefer delayed definitive closure of sternotomy. In 2 patients contemporary continuous veno-venous hemofiltration (CVVH) for oliguria in consequence of preoperative renal failure was used. In one patient there was serious infection in the vicinity of outlet of BiVAD cannula, and after the management with combined antibiotic therapy the patient was filed in the waiting list of candidates for OHT.

Postoperative care after MCS implantation may be extraordinarily challenging. The basis for successful detection and resolution of all situations is long-term experience with management of patients after complicated cardiosurgical operations and heart transplantations. Therefore we assume that these surgical operations should be performed only in the centres with this experience.

Five patient were successfully brought to OHT, and thus the primary goal was achieved. Of these, one patient died on postoperative day 2 due to graft failure, in one patient perioperative ischaemic brain stroke was diagnosed with partial permanent residual. Table 2 shows further fate of our patients – 3 patients survived 1 year, 2 patients are still living and the course of their illness is quite uncomplicated. One patient died 34 days after OHT due to cerebral haemorrhage in consequence of undiagnosed vascular malformation and another patient died 14 months after OHT – he was the first patient in whom BiVAD was used and of whom it was previously reported (2).

## DISCUSSION

Mechanical assist devices represent the most significant therapeutical approach to patients with terminal heart failure, if all possibilities of pharmaceutical treatment have been exhausted and who are waiting for heart transplantation. This indication, so called bridging to heart transplantation, is the second most common indication of implantation of these devices. The first indication is post-cardiotomy temporary mechanical support, the other indications are less frequent.

The selection of this type of mechanical support was performed after assessing our needs, after a series of consultations with foreign specialists and with awareness that there is world-wide experience with that support devices used in more than 2000 patients, of whom more than half were indicated for bridging the time for heart transplantation. Every year in the USA the mechanical cardiac support is used for this indication in 300-400 patients, of which 50-70% successfully undergo the heart transplantation. The application of mechanical heart devices for cases of refractory acute heart failure without consequent transplantation, e.g. in fulminant myocarditis, dilated cardiomyopathy or cardiogenic shock in acute myocardial infarction, are used with frequency 5-15% (3).

In all our patients, we used the BiVAD system for serious manifestations of biventricular failure. In 5 patients with subsequent OHT, the duration of mechanical support was 13-64 days: considering the critical condition in which the patients were in the time of indication of the heart support, we believe that they lived to receive their graft only thanks to this therapeutical approach.

There are still many obstacles and complications in programme of MCS implantations. Bleeding that occurs due to necessary combined anticoagulant therapy, infection and sepsis with multiorgan failure, thromboembolism and mechanical failure of the devices are among the most frequent complications of the treatment (4). The

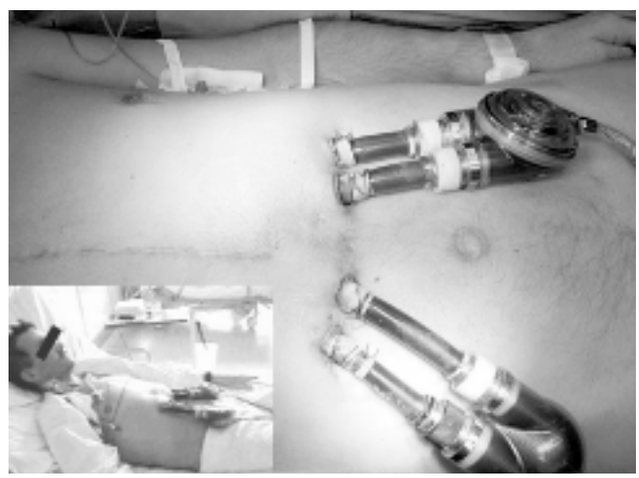

**Fig. 6.** Transcutaneous outlet of the cannulas in the epigastrium and connection on the externally (paracorporeally) situated chambers of mechanical assist device Thoratec VAD. Details in the text

biggest problem in our small sample was bleeding which caused death in one of our patients during the waiting time for OHT. Frequent surgical revisions because of bleeding made us apply the above-mentioned procedure with delayed definitive suture of sternotomy. Neither any clinically significant thromboembolic event nor any malfunction of the devices were observed.

## CONCLUSION

Mechanical assist devices constitute the most important approach to patients with terminal heart failure, in which pharmacological treatment exhausted its possibilities. Use of mechanical assist devices in bridging-to-heart transplantation is fully justifiable, despite the high cost, in our conditions, because of its biggest potential with respect to long-term prognosis.

**Abbreviations**

BiVAD - biventricular assist device
MCS - mechanical cardiac support
IABC - intraaortic balloon counterpulsation
OHT - orthotopic heart transplantation
IKEM - Institut klinické a experimentální medicíny
LVAD - left ventricle assist device
RVAD - right ventricle assist device
CVVH - continuous veno-venous hemodialysis

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*Address for correspondence:*
*J. Kettner, MD, PhD*
*Dept. of Cardiology, IKEM*
*Vídeňská 1958/9*
*140 00 Prague 4*
*Czech Republic*
*Fax: +420 241 728 225*
*E-mail: jiri.kettner@medicon.cz*

*Translation: Oldřich Louthan*

COMMENTARY

# Do We Really Need a Mechanical Circulatory Support Program in the Czech Republic? Comments upon the Article by J. Kettner: "The Use of Mechanical Circulatory Support – Early Experiences in the Czech Republic"

Heart failure is known as the 21st century ailment. The number of patients with this condition keeps on growing, as do medical care costs. Despite considerable progress in pharmacotherapy, which has undoubtedly improved the fate of patients with advanced stages of heart failure, the prognosis still remains very unfavorable. Recently published data from the Swedish register showed that patient mortality has been decreasing there over the last twelve years (1). Apparently mortality has been essentially influenced by the expansion of classical pharmacotherapy, firstly by the introduction of ACE inhibitors and later by the addition of betablockers and the wider application of spironolactone. Undoubtedly significant results have been achieved by the improvement of medical care for patients, with subsequent favorable results, wider application of revascularization procedures, the introduction of cardiac resychronization treatment and, last but not least, the improvement of outpatient care. In the patients with the most severe stages, the usage of calcium-sensitizer levosimendan is increasing, as is the case with mechanical circulatory support (2, 3). Nevertheless, in many patients, heart transplantation remains the final solution. However, this procedure entails not only financial and organizational challenges (including lack of suitable donors), but also first of all the necessity for complex preoperational and postoperational care. It is above all preoperational care that we tend to forget. In most cases, patients with severe forms of heart failure suffer from multiorgan failure, in addition to congestion in the lesser circulation, when the patients are affected by low cardiac output, which alters renal and hepatic functions and brings about the state of advanced malnutrition. Thus many patients will not live to see heart transplantation, or they will develop a critical health condition that compromises their further prognosis. Mechanical circulatory support, such as left ventricular or biventricular assist devices, is becoming increasingly popular. The recently published REMATCH study proved unequivocally that implantation of the left ventricular assist device leads to an improved prognosis in the most severe cases (4). One-year survival was 50% in patients with mechanical support, in comparison with 28% survival in patients submitted to the pharmacological treatment, and two-year survival was 29% vs. 13%. Nevertheless, malfunction of the system occurs frequently, and during the first year it was necessary to replace it in 13% cases: during the second year the figure was as high as 63%. Thus it appears that this method is beneficial for the patients primarily as a bridge to cardiac transplantation, covering a relatively short time. In addition to left ventricular assist devices, the most severe cases in particular will require implantation of biventricular assist devices (5).

In this issue Kettner et al. report on the first Czech experience with biventricular mechanical support implantation in patients indicated for heart transplantation. Even though the number of patients concerned is relatively small, the report unequivocally shows the benefit of the system. In 5 out of 6 patients, the primary goal, i. e. performing heart transplantation, was achieved. Three patients survived for one year. It is significant that no patient died of multiorgan failure, which is what cardiac support is specifically aimed at preventing. At the same time, the authors show how postoperational care for the patients is challenging, mainly with respect of bleeding complications.

It seems that if we accept the existence of a heart transplantation program, we will have to accept the necessity of wider usage of mechanical heart devices in selected patients. Undoubtedly we will face the concomitant financial problems. But this was initially the case with many modern therapeutical approaches. The introduction of mechanical heart devices need not lead to a dramatic increase of medical care costs for patients with terminal heart failure, as it might seem at first sight. And it may well enable us to prevent the very complications that increase the price of the care for these patients and ultimately, in many cases, thwart our efforts to save their lives.

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Translation: Oldřich Louthan

Address for correspondence:
Prof. Aleš Linhart, MD., D.Sc.
2nd Clinic of Internal Medicine, 1st Medical Faculty of the Charles University and the General Teaching Hospital
128 00 Prague 2, U Nemocnice 2
Czech Republic
E-mail: alinh@lf1.cuni.cz