

**THESES OF THE DOCTORAL DISSERTATION ( Ph. D. )**

**ECHOCARDIOGRAPHIC EXPERIENCES  
AND CLINICAL OBSERVATIONS  
IN ACUTE MYOCARDIAL INFARCTION**

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**DEBRECEN, 2002**

## **I. INTRODUCTION**

It is well-known that nowadays myocardial infarction is one of the most important mortality factors. In Hungary some 25000 people suffer acute myocardial infarction (AMI). Unfortunately, most of the deceases occur before arriving at hospital. In its entirety, more than 50% of the patients do not survive the acute phase of the myocardial infarction. The importance of the myocardial infarction in public health is reinforced by the fact that it is one of the diseases which most often require hospital admission.

Some decadas ago, before the coronary units were established, the inhospital mortality of the AMI had been about 30%. The introduction of the modern diagnostic techniques developing uninterruptedly, and the administration of effective, verified - supported by multifocal clinical examinations - medication (aspirin, systemic thrombolysis, early beta blockers and ACE-inhibitor treatment) decreased the in-hospital mortality to 7 - 12%.

The coronary disease causing myocardial infarction is of multifactoral origin. You can clearly identify the separately or multiply occurring factors which raise the hazard of the acute myocardial infarction in an increased degree: these are, first of all hyperlipidaemia, hypertension, smoking, diabetes mellitus, male gender and the old age. The primary and secondary prevention of the myocardial infarction is based on exerting favourable influence on the risk factors which can be influenced.

Over the past decade echocardiography virtually became a routinely used non-invasive diagnostic method. Waves necessary

for imaging are emitted by a special piezoelectric crystal placed in the transducer. The emitted beam is reflected from the acoustically denser surface, and the transducer detects the ultrasound beam of changed frequency, and transforms it into an electric signal, and then the equipment - with the help of a highly-developed computer technology - displays the heart on the screen in a wonderful way. By using a single beam of rays led along the time axis from the realistic, live (online), two dimensional image (2-D) appearing during the examination, the anatomical structure of the heart is delineated, and by continuous analysis of which we can gain, among others, data on the size of the cardiac cavities, the global left ventricular function and the wall motion of the ventricles. The essence of the left ventricular wall motion is the systolic thickening of the wall, and the dislocation of the endocardium from the contour of the epicardium. The Doppler examination, which completes the echocardiography, gives information on the intracardiac flow patterns on the basis of the Doppler effect.

The immediate inducing factor of the acute myocardial infarction is the sudden occlusion of a coronary artery, which is caused - with few exceptions - by thrombus formation. Due to the occlusion, the blood supply area of the given coronary artery in the myocardium becomes ischaemic, the involved ventricular wall motion is damaged, hypokinesis or dyskinesis develops, and in the most severe cases outward movement, that is, dyskinesis develops in the systole. The normal wall motion surely precludes the possibility of transmural infarction, but it does not rule out the other forms of myocardial ischaemia, like the angina pectoris and the stunned or hibernating myocardium.

It is obvious that the acute phase of the myocardial infarction is a condition immediately threatening life, so improving the diagnostic safety and the early detection of the so called

mechanical complications are essential for proper clinical decision making. During the intensive care of the patients further useful pieces of information can be obtained in connection with the risk analysis of the further life expectancy. Consequently, establishing the right diagnosis, detecting the complications and making the prognosis of the patients are essential tasks in the proper treatment of the AMI. Echocardiography offers indispensable help for the everyday medical practice in the implementation of these three objectives.

The transthoracic echocardiography can be carried out nearly in all hospitals in Hungary nowadays, and handled with the due expertise of a skilled examiner, it serves an irreplaceable tool in the acute cardiac diseases. At the beginning of the 1990-s cardiology teams in Hungary virtually were in the fever of excitement to purchase an echocardiography appliance. We also felt the same in Markhot Ferenc Hospital, Eger. After the initial enthusiastic collecting experience, we set ourselves the objective to perform transthoracic echocardiography as soon as possible in the patients admitted into the intensive care unit of our department with the presumed or the established diagnosis of the AMI.

During years we made an effort to report on the processed data of more and more patients suffering from acute myocardial infarction. First we reported in Hungarian, then in international congresses and scientific journals. My present dissertation is aimed at the summary of my experiences and some clinical observations gained during a decade with the help of echocardiography in the field of the treatment of the acute myocardial infarction.

## **II. OBJECTIVES**

### **A/ Studying the diagnostic significance of echocardiography in the acute phase of the myocardial infarction:**

**A/1.** Evaluation of the role of echocardiography in the improvement of diagnostic safety if it is performed in the patients with AMI within 72 hours after the admission.

**A/2.** Analysis of the experience gained by echocardiography in the detection of the mechanical complications in acute myocardial infarction.

### **B/ Looking for correlations between some echocardiographic parameters and the course of the acute myocardial infarction:**

**B/1.** Specification of the echocardiographic changes connected with the in-hospital mortality of the acute myocardial infarction.

**B/2.** Controlling the successful coronary reperfusion due to thrombolytic therapy with the help of repeated echocardiography.

### **C/ Examination of the incidence, clinical characteristics and prognostic significance of left ventricular thrombi and arterial embolism in acute myocardial infarction:**

**C/1.** Complex risk analysis of the early formation of left ventricular thrombi (detected within 72 hours after the hospital admission).

**C/2.** Processing the data of patients who suffered systemic embolism is acute myocardial infarction.

### **III. PATIENTS AND METHODS**

#### **III/A: Patient material**

I carried out the examinations outlined in the dissertation in the Intensive Cardiac Care Unit of Markhot Ferenc Hospital, Eger (named before as Department of Intensive Internal Medicine and then, since 1998 it is called Coronary Unit of the Department of Cardiology). The indications for the echocardiography were as follows: verification of the diagnosis of the AMI, differential diagnosis of the chest pain, determining the degree of the left ventricular wall motion abnormality and checking the left ventricular function, the size of cardiac cavities, excluding the haemodynamically significant vitiums and the detection of the possible complications of the infarction. The echo examinations were carried out not at the intensive bedside, but we had to carry the patients several floors higher. Under these circumstances I performed transthoracic echocardiography within 72 hours after the hospital admission in more than 2000 consecutive, non-selected patients during the 10-year period. The examination was performed in 20% of the cases within 24 hours after the admission, in 35% on the second day, and in 45% on the third day. The diagnosis of the AMI was established on the basis of the clinical symptoms, 12 lead ECG and the laboratory findings. We created a computer database from the material of 1833 patients treated because of Q-wave AMI. The data were processed in detail, regarding the left ventricular thrombus and the incidence of embolism. Studying this well-documented patient material gave an answer to the questions raised in the objectives.

### **III/B: The technique of the echocardiography**

We carried out the transthoracic echocardiography with Toshiba SSH-65A appliance with a 2.5 and 3.75 MHz transducers in the left lateral position, and the examination was completed with colour pulsatile Doppler and continuous wave (CW) Doppler. The diameter of the cardiac cavities and the left ventricular mural thickness were measured along the parasternal longitudinal axis on the two-dimensional M-mode echocardiographic images. Abnormalities in the left ventricular wall motion were evaluated both qualitatively and quantitatively. By using the 16 segment model suggested by the American Society of Echocardiography Committee. According to the accepted suggestions we examined four segments from the parasternal longitudinal view, 6-6 segments from the apical four and two cavity views. The above listed segments could be repeatedly delineated with parasternal short axis view.. The wall motion index was calculated on the basis of a generally used score system, by which normokinesis equals 1, hypokinesis 2, akinesis 3, dyskinesis 4, aneurysm 5 scores. Dividing the added up score by the number of the visible segments we get the wall motion abnormality index. The systolic and diastolic protrusion of the left ventricular wall involved was considered as the criterion of the left ventricular aneurysm. The global systolic left ventricular function was characterized via the linear ejection fraction (EF) calculated with the adjusted Quinones-formula. Ejection fraction lower than 40% was considered as diminished left ventricular ejection fraction. A LVT was diagnosed when an echodense mass was adjacent to an abnormally contracting myocardial segment, it was clearly distinguished from the underlying myocardium and was seen in at least two different transducer positions. The echocardiographic images were recorded with a Panasonic videorecorder, and they were archived on a videocassette.

### **III/C: Other complimentary examinations**

During the intensive cardiac care - in cases without complication it was the first 3 days of AMI in our practice - we carried out continuous ECG-monitoring, and as it was required, but at least in every 24 hours we performed a 12-lead ECG. In the diagnosis of the myocardial necrosis we used the traditional serum enzyme tests: CK, CK-MB, GOT and LDH values, which, depending on the clinical conditions, were repeated at least in every 24 hours. On-the-spot chest X-ray was generally carried out in the coronary unit with the purpose of checking the pulmonary circulation and excluding the possible pulmonary disease. In the differential diagnosis - especially in the case of aortic dissection - we were assisted by computed tomography, and sometimes, when acute abdominal symptoms developed, we performed abdominal ultrasonography. At the onset of neurologic complications - with the aim of deciding whether it was a cerebral ischaemia or haemorrhagia - cranial computed tomography was performed as soon as it was possible.

### **II/D: THE THERAPY OF AMI**

Considering the actual clinical status and the haemodynamic parameters, each patient received medication according to the international guidelines. After the initial strict bed-rest and sedative, analgetics - in the lack of contraindication - acetylsalicylic acid, heparin, beta blockers, ACE-inhibitors, nitrate as required and diuretics were administered. Almost 25% of the patients who suffered AMI underwent thrombolytic therapy, in all cases with streptokinase. We administered mainly Lidocain in infusion as the drug therapy for ventricular arrhythmias. In intracardiac conduction disorders we inserted a temporary pacemaker on the basis of the adequate indications.

### **III/E Statistical analysis**

Processing the numerical data we calculated the average and the standard deviation ( $\pm$ SD). I carried out the statistical analyses partly with a chi - square test, and in the case of continuous variables with Student *t*-test. Some statistical investigations were carried out by variance analysis, with univariate and multivariate logistic regression models (GB-STAT). A p value of  $< 0.05$  was considered to be significant.

## **IV. RESULTS**

### **Ad A/l.**

*Assessment of the role of echocardiography in the improvement of diagnostic safety, if it is performed within 72 hours after the admission in the patients with acute myocardial infarction.*

In connection with processing the data of the initial 512 cases of the patient material we disclosed that the abnormalities of the left ventricular wall motion (WMA) detected by echocardiography provide highly important information in the case of ECG deviations like left bundle branch block, ventricular pacemaker control, myocardial reinfarction, Q-waves which were caused not by myocardial infarction, and other repolarization deviations which make the diagnosis of AMI difficult. In addition, the echocardiography has a great part in the detection of the right ventricular infarction and in the differential diagnosis of the AMI:

- We found that the pathological examination of the patients who died in hospital due to AMI and had been examined by echocardiograph, too, verified acute myocardial necrosis in all cases (6).

- It is known that in the case of left bundle branch block the ECG signals of the myocardial infarction can not be detected in a reliable way. We could render the AMI probable in its early phase in all left ventricular localisations with the help of WMA detected by echocardiography in 51 patients with the ECG records of left bundle branch block from the 925 patients admitted in the intensive cardiac care unit. Then, in addition to the clinical pictures, on one hand the diagnosis was validated by the kinetics of the serum necroenzyme findings, and on the other hand by the pathological examinations (11 patients) (2).
  
- In Hungary we were among the first to report on an isolated right ventricular infarction, which was detected with echocardiography (4). In a case report we called the attention to the diagnostic characteristics of the left ventricular AMI which was spreading out to the right ventricle and was associated with pulmonary embolisation: the features of the right ventricular segmental wall motion abnormality and the differential diagnostic significance of the increased right ventricular systolic pressure calculated from the tricupsidal insufficiency (1).
  
- We summarized the clinical and diagnostic experiences of 8 aorta dissections detected during a ten-year period, in 6 cases of which the patients were sent to hospital with the diagnosis of AMI. With the help of echocardiography we managed to establish the appropriate diagnosis and avoid the thrombolytic therapy, which had been intended to administer (5) .
  
- In the numerous patient material we managed to detect a rare association of AMI, an atrial myxoma and its probable cause, which is considered as rarity in the technical literature (9).

## **Ad A/2.**

### ***Analysis of the experiences we gained by echocardiography in detecting the mechanical complications of the acute myocardial infarction.***

We could diagnose and document all the possible mechanical complications of the AMI (free wall rupture, defect of the ventricular septum, rupture of the papillary muscle, left ventricular aneurysm, pseudo-aneurysm) by early echocardiography. On the basis of our experiences, we must emphasize that the complications involving the rupture of the myocardium lead to the death of the patient without surgery, therefore the diagnosis established by non-invasive imaging technique can save the patient's life. In the cases of the deceased patients the autopsy findings were in compliance with the echocardiograms (6).

## **Ad B/1.**

### ***Specification of the echocardiography changes related to the in-hospital mortality of the acute myocardial infarction.***

Analysis carried out in the case of 552 patients support the data in the technical literature, by which the left ventricular dilatation ( $Dd > 60$  mm), the decreased systolic left ventricular function (linear  $EF < 40\%$ ), wall motion index higher than 2.0, pericardial effusion thicker than 5 mm in the time of the end-systole and right ventricular infarction occurred significantly more often in the patients who died in hospital because of AMI than who survived. We proved that the most severe left ventricular wall motion abnormality, that is the dyskinesis is a bad prognostic factor even if the left ventricular function is good (the frequency of dyskinesis in the case of good left ventricular function was 27.5% in the deceased patients versus 8.1% in the survivors;  $p < 0.01$ ) (6).

## **Ad B/2.**

### ***Checking the successful coronary reperfusion after thrombolytic therapy by repeated echocardiography.***

We studied the changes on the echocardiograms due to thrombolytic therapy in 78 patients with AMI. Using the three non-invasive markers of the successful coronary reperfusion - CK peak within 12 hours, within the first 90 minutes at least 50% reduction of the ST segment elevation representing the infarction on the ECG, reperfusion arrhythmias - we got to the following observations:

a.) At least 10% decrease of the left ventricular WMA index detected by echocardiography within 72 hours after the thrombolytic therapy in AMI, and repeated before the discharge from the hospital and,

b.) the improvement in the quality of the most severe wall motion abnormality detected by the first echo examination in the given patient refer to the successful coronary reperfusion (7).

## **Ad C/1.**

### ***Complex risk analysis of the development of left ventricular thrombi detected in the early stage ( within 72 hours after the admission to hospital ).***

We carried out the complex risk analysis of the early left ventricular thrombi in 1833 patients. From among them in 145 cases (7.9%) we detected left ventricular thrombus. In the patients with AMI complicated with left ventricular thrombus the myocardial infarction in the family history (3% versus 11%), hospital admission within 24 hours after the onset of the chest pain (17% versus 50%), thrombolytic therapy (8% versus 23%), smoking (24% versus 35%) were lower than in those without left

ventricular thrombus. In contrast, the anterior wall infarction (23% versus 10%), the aneurysm (22% versus 7%), and the decreased left ventricular function (28% versus 17%) were significantly more frequent than in the group of patients with left ventricular thrombus. By analyzing the risk factors of a significant patient material we could state that the hypercholesterolaemia, the hypertension and the diabetes mellitus do not increase the incidence of the left ventricular thrombus formation. We also observed seasonality, which has not been reported in the literature yet: left ventricular thrombus in AMI was significantly more frequent in spring and winter (8). These echocardiography and clinical parameters seem to be useful both in the determination of the hazard ratio of the left ventricular thrombus formation and in its prevention in the everyday clinical practice (10).

## **Ad C/2.**

### ***Processing the data of patients who suffered systemic embolism in acute myocardial infarction.***

Systemic embolism developing in AMI obviously further impairs the life-expectancy of the patients and delimitates the possibilities for the rehabilitation. In the first 4 years of our 10-year patient material we diagnosed 12 cerebral emboli from 942 AMI-s. Analysing the clinical data and the results of the examinations we found that in 50 percent of the patients left ventricular thrombus was detected by echocardiography, we also found that the cranial CT made the anticoagulant therapy safe. The in-hospital mortality of the patients was high (50%). It is known that left ventricular thrombi are very rare in the AMI of inferior localisation. On the basis of all these, it is noteworthy that from 12 patients one had inferior and four had inferolateral infarction. During the examinations we found that though the incidence of inferior and

inferolateral thrombi is significantly rarer than that of the anterior ones, they are significantly more likely to cause embolism (3). Later, as a result of the analysis of the data of 1833 patients during a ten-year period we found that the incidence of arterial embolisation in AMI was 2.9%, 77% of which was cerebral embolism. This analysis reinforced our observations, which we had stated before, based on a patient material with a lower number of cases. We found that the predisposing factors for arterial embolism are as follows: old age, lack of the thrombolytic therapy, more than 24-hour delay in hospital admission (it occurred in 90% of the cases), early left ventricular aneurysm (17%) and a left ventricular thrombus (36%).

## **V. DISCUSSION**

There has been a very fast development in the technique of the echocardiography during the past few years, the harmonic imaging, the colour kinesis, the tissue Doppler imaging and the contrast echocardiography are used more and more widely, the three-dimensional imaging has become available. These examination opportunities are further developing and make the evaluation of the wall motion abnormalities more objective. The appliances of different type offer more and more advanced programs for the users. In my work I have strived from the beginning to use the traditional, generally accepted echocardiographic parameters, which can easily be carried out and serve the everyday acute cardiac patient care well even today.

The diagnosis of AMI can usually unambiguously be established on the basis of the classical symptom complex (angina pectoris, ECG changes and the serum enzyme markers), but sometimes the chest pain can be atypical or the ECG has no diagnostic value. The elevation of the enzyme values, which refers to myocardial

necrosis, starts only hours later, so the echocardiography can decisively help the early diagnosis. It is 90% sure that the segmental left ventricular WMA can be detected in transmural AMI, and it indicates the localisation and the size of the infarction. The segmental wall motion abnormality caused by myocardial ischaemia develops earlier than the ECG deviation, therefore echocardiography is an especially useful examination in the clinical practice if the ECG has no diagnostic value, but the symptoms refer to AMI. The left ventricular segmental WMA in itself can be the consequence of either a new or a former myocardial infarction, so the clinical symptoms, the laboratory findings and the ECG should also be taken into consideration when you establish the diagnosis. It must be underlined that the segmental WMA is not exclusively the sign of the myocardial infarction, but it can develop due to the other reversible forms of myocardial ischaemia like "stunned" or "hibernating" myocardium. Repeated echocardiography or the viability examination can help to clarify such cases. Determining the size of the infarction in AMI we should also consider that the left ventricular segment detected as involved by the early echocardiography, can contain not only necrotic, but also stunned or hibernating myocardium. Returning of the contraction function of the stunned myocardium explains the fact that we could detect the improvement of the WMAI by echocardiography repeated between the 10<sup>th</sup> and 16<sup>th</sup> days after thrombolytic therapy.

In addition, the significance of the echocardiography in AMI is the evaluation of the left ventricular function and the detection of mechanical complications. Echocardiography has a primary part during the acute phase of the myocardial infarction, the transoesophageal examination is required only in emergency cases, when the transthoracic echocardiography can not be carried out or additional information is required before the

surgery of a mechanical complication. Echocardiography may be required for differential diagnostic reasons (suspected aorta dissection), for prognostic reasons (AMI involving a large area), and for the sake of the safety of some therapeutic decision making (critical cases of administration of thrombolytic and anticoagulant therapy, beta blockers, nitrate or diuretics). It is a fact that in the emergency patient care the echocardiographic triage of the patients hospitalized because of chest pain is considered to be a cost - effective procedure. Starting the adequate treatment or the reperfusion immediately will decrease the morbidity and the mortality, and if we can surely exclude the AMI, we can save the cost of the hospital treatment. Determining the localization of the myocardial infarction is important both from the point of view of choosing the therapy and making the prognosis (temporary pacemaker introduction was previously indicated in anterior AMI, the thrombolytic therapy and the direct PTCA are expected to be more useful in the case of the anterior localization). In clinical situations which make the diagnosis of the AMI more difficult, the determination of the localisation of the infarction detected by echocardiography, helps to increase the chance of survival.

In the case of our patients dyskinesia was a bad prognostic factor, even in the case of good systolic left ventricular function. It can probably be accounted for the effect of the dyskinesia causing haemodynamic and electric instability, and for the more severe ischaemic heart disease of these patients.

In right ventricular AMI even a minor hypovolaemia may cause severe hypotension, the decrease in the cardiac output. In such cases administration of diuretics or nitrate causes further haemodynamic disorders. Carrying out the early echocardiography may be a great help in establishing the exact diagnosis and in choosing the right therapy.

In the everyday practice we use the analysis of the mitral inflow Doppler spectrum for the evaluation of the left ventricular diastolic function. The relaxation flow patterns are influenced by several factors (the heart rate, the blood pressure, the left ventricular systolic function, the age). It is a fact that in AMI, even if the relaxation is obviously impaired, we can measure mitral inflow Doppler spectrum referring to normal diastolic function (the phenomenon of the so called pseudonormalization). On the basis of all these, during the retrospective study of the patient material I did not process the data of diastolic left ventricular function.

It can be considered to be an interesting and new observation that such known cardiovascular risk factors like hypercholesterolaemia, hypertension, diabetes mellitus and smoking do not increase the risk of the left ventricular thrombus formation, moreover, in the case of smoking patients we significantly more rarely detected the incidence of the left ventricular thrombus. These data suggest that the coronary thrombosis leading to AMI and the left ventricular thrombus formation have different predisposing factors. On the basis of all these, it can be stated that in the case of a left ventricular thrombus developing during the AMI, some clinical and echocardiographic parameters can be determined, and taking them in consideration in everyday practice serve the prevention.

Making the prognosis in acute myocardial infarction is a complex job, which depends on several factors. It is obvious that in AMI it is advisable to perform the first echocardiography as soon as possible and, if possible, in each patient, as most of the deaths occur during the first few days. Therefore, the early echocardiography facilitates to establish the right diagnosis and to detect the possible complications.

My observations support the fact that the qualitative and the quantitative data of the WMA provide very important information in the acute phase of the myocardial infarction. From the opportunities for using my results in practice - regarding the echocardiography - I underline the following ones.

1./ In AMI the segmental left ventricular WMA detected by echocardiography reliably helps to establish the diagnosis even by the side of left bundle branch block seen on the ECG.

2./ The development of dyskinesia in acute myocardial infarction leads to increased in-hospital mortality even if the global systolic left ventricular function is good.

3./ The routine use of the left ventricular WMAI in the practice of cardiology can be recommended, as according to our data, its value above 2.0 indicates the bad early prognosis of the AMI.

4./ At least 10% improvement of the left ventricular WMAI, and the improvement in the quality of the most severe WMA after the thrombolytic therapy refer to successful coronary reperfusion.

5./ Our results verify the observations that in AMI the lack of thrombolytic therapy, the anterior mural infarction, left ventricular aneurysm and the decreased systolic left ventricular function make the early left ventricular thrombus formation more frequent.

6./ It can be stated that from among the risk factors of the myocardial infarction the hypercholesterolaemia, the hypertension and the diabetes mellitus do not increase the frequency of the left ventricular thrombus formation, and incidence of the left ventricular thrombus is less frequent in smoking patients.

7./ In 145 cases seasonal fluctuation can be observed in the incidence of the left ventricular thrombus: it is significantly more frequent in winter and spring.

8./ According to our examinations the non-anterior LVT-s in AMI are more likely to cause embolism than those with the anterior wall localisation.

In the course of my work I was lead by the conviction that we should take the advantage of the technique available for us any time - in this case echocardiography - in the best possible way in the everyday patient care. The implementation of this objective is of special importance in such dramatical conditions like AMI. Avoiding a single wrong diagnosis, or detecting a severe complication in time can save life of patients. On the basis of my experiences I can state and recommend that the echocardiography performed in the early stage of the disease should be the integral part of the treatment of the acute myocardial infarction.

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