The Impact of Limited Biventricular Stimulation on Cardiac Hemodynamics in Patients with Reduced Left Ventricular Function

Healthcare

Keywords: Biventricular Pacing, Cardiopulmonary Bypass, and Heart failure.

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Abstract

Background: Patients with severely impaired left ventricular (LV) function often demonstrate prolonged inter- and intraventricular conduction. This prospective study investigates hemodynamic effects and outcomes of perioperative temporary biventricular pacing in patients with heart failure undergoing heart surgery. **Methods:** 100 consecutive cardiac surgery patients with a LV ejection fraction below 35% received biventricular stimulation via temporary myocardial electrodes. Group 1 consisted of 50 patients with LV dilatation (mean-LVEDD 65±5 mm), group 2 of 50 patients with normal or slightly dilated LV (mean-LVEDD 52±4 mm). **Results:** Hemodynamic parameters were measured immediately, 6 and 24 hours after operation. An increase of cardiac index (CI) and arterial blood pressure with biventricular pacing was observed in 27 patients (group 1/67.5%) versus 22 patients (group 2/55%) from 2.4±0.7 l/min/m2 to 3.5±0.5 l/min/m2 ($p<0.01$). This benefit persisted 6 and 24 hours postoperatively. The remaining patients already showed higher cardiac index prior to pacing (3.7±0.9 l/min/m2). In-group 1, responding patients required shorter times for ventilation support and intensive care. QRS duration before surgery was not predictive for the response to biventricular pacing. **Conclusions:** In the majority of patients with reduced LV function, temporary biventricular pacing improves CO and arterial blood pressure after surgery, especially when LV-dilatation is present.

Introduction

In centuries men have attempted to recognize themselves and this is a process that continues even to this day. It is very interesting the fact that cardiovascular surgery dates much earlier than we thought or studied.

Cardiac diseases today represent the first cause of mortality in the developed countries. Only a few thousand Albanians in Albania, Macedonia and Kosovo need to perform cardiac catheterizing or cardiac surgery just over a year. The number of patients who have an indication for cardiac surgery is 1100 patients out of a million people each year.

The aim of this paper is to explain the biventricular stimulation during surgical treatment of patients with heart insufficiency. With this treatment it will be possible that in this group of patients will be given the option of reducing complications during their treatment with open heart surgery. Especially in patients with heart failure, their departure phase of extracorporeal circulation is more subtle phase and a phase in which cardiologists encounter a series of problems.

Description of the research project

100 patients with a reduced LVEF of 35%, who underwent cardiac intervention were consecutively included in this research project and are divided into two groups.

In the first group were analyzed 50 patients with significant enlargement of the left ventricle (LVEDD ≥ 55 mm) while in the second group were analyzed patients who had no significant enlargement of the left ventricle (LVEDD ≤ 55 mm).

The average diameter of the left ventricle in the first group was LVEDD = 65 ± 5 mm, while the average diameter of the left ventricle in the second group was LVEDD = 52 ± 4 mm. All patients were stimulated with the help of the temporal electrodes in both ventricles and in the same place in epicardium.

This study had as hypothesis the improvement of the function of ventricles (EF) with the help of biventricular stimulation during surgery and 24 hours after cardiac inetrvention.

Patients and Methodology

In our prospective clinical study were analyzed 100 patients who had an elective cardiac intervention necessity and who were suffering from cardiac insufficiency. The age of all patients was over 50, and all of them had *Echocardiographic Examination* in a reduced function of ventricles EF <35%. After measuring the diameter of the left ventricle with the help of *Echocardiography* prior to the surgical intervention patients were divided into two groups of 50.

Prior to the cardiac intervention, each patient was made general and cardiac anamnesis, examination with the aid of a 12 ditches ECG, examination of the echoradioography and coronarography with the ventriculography of the left ventricle.

Based in end diastolic diameter of the left ventricle, patients were divided into two groups:

	LVEDD	Number of patients
Group I	≥ 55 mm	50
Group II	≤ 55 mm	50

Table 1. *Distribution of patients*

The purpose of this research project was to analyze the effect of biventricular stimulation based on the diameter of the left ventricle in the operational phase and 24 hours after that by taking data on the hemodynamics of patients.

In each patient during cardiac inetrvention were incorporated three electrodes each for temporary stimulation with the pacemaker of type TME OSYPKA 66L (Fa. Dr. OSYPKA Rheinfelden-HERTEN, Germany). Fixation countries were as follows:

- At the base of the lateral wall of the left ventricle, left atrial parotid
- In the vicinity of the pulmonary valve in the right ventricle
- At The basic part of the left atrium, below aorta

Stimulation was done with the temporary pacemaker also taken from the firm OSYPKA (P300)

At the end of each operation, transesophageal echocardiography was performed with Vivid 7 device (GE Medical), to control the syncronization of ventricles in orden to measure LVEF, and to verify the impact of biventricular stimulation in the improvement of LVEF.

During biventricular stimulation that began immediately during the operation and lasted 24 hours after surgical intervention were verified the following parameters below constant influence among kateholamin with the positive inotropic action after 1 hour, 6 hours and 24 hours:

- Arterial invasive pressure AIP =
- Central Venous Pressure = CVP

- Pulmonalo Arterial Pressure = PAP
- Pulmonalo Capillary Pressure-Wedge = PCPW
- Cardiac Output = CO

All parameters were recorded as follows:

- During the patient's own pace without Peacemeaker
- During AAI stimulation at a frequency of 100 per minute
- During biventricular stimulation with a frequency of 100 per minute and AV-Delay 80 mesc.

As patients with a positive response to biventricular therapy were verified patients who during stimulation in both ventricles showed an increase to more than half a liter of Cardiac Index (CI ≥ 0.5 l / min / kg).

Compilation of statistical data

Preoperative data

The following will be listed the preoperative data which are taken for each patient, irrespective of the group in which s(he) is listed. These data are written analogously and later are digitized which then they could be valued through statistical tests that were mentioned above.

Preoperative statistical data were as follows:

- Age
- Gender
- Attached Diseases
- classification according to Nyhan
- cardiac rhythm
- duration of the QRS
- The value of LVEF
- The value of LVEDD

All these parameters are taken from the archives of the patient and standardized perioperative procedures.

Hemodynamic Parameters

During follow-up of patients within this scientific work, a specific role for the hemodynamic cardiac outcomes was played which is measured during 1 hour, 6 hours and 24 hours after the cardiac intervention. Following are the hemodynamic values marked:

- invasive ABP Arterial Pressure
- HR heart frequency
- Central Venous Pressure ZVD
- Cardiac Ouput CO
- Pulmonalo Capillary Pressure PCWP
- Pulmonalo Arterial Pressure PAP

All these parameters were recorded in the three modalities of stimulation with the pacemaker and and then through it are digitized for statistical assessments

Clinical Parameters

In addition to hemodynamic parameters, from each patient were taken clinical data on the current state in one hand, whereas on the other hand were marked data that were evaluated during surgical inetervention. The following clinical parameters were taken as relevant for this scientific paper:

- The total duration of extracorporeal circulation
- duration of cardiac arest
- Time of intubation
- perioperative complications
- duration of stay in the intensive station
- The need of patient for medications with positive inotropic action (Katholamine)
- ejektiv fraction LVEF
- All these parameters are listed in the general documentation on the patient and later are crystallized and digitized.

Statistics

Satistics took place at the statistical office. As the results were applied data on medians and standard movements. Parameters were treated according to the normal distribution of Gauss's and were verified with the Kolmogoroff-Smirnoff test Index.

If numeric data were normally distributed, then the statistical evaluation could be applied in a global level with a Validity of alpha = 0.05 with T-test for two groups.

Analysis of variance (ANOVA) was done with the help of ANOVA and attached Schefft Test. As significant is applied the p value <0:05.

Digital statistical evaluation was done with the software program "BiAS for Windows 8.0" (Epsilon Verlag, Darmstadt, Germany).

Results

1. Population of Patients

A total of 124 patients agreed to participate in this research project, each patient was informed about the methods and scope of this project and signed willingnessly to actively participate in this study (Annex 1). Out of 124 patients only 100 fullfilled all the conditions for participation in this project. 24 patients were dropped from this procedure since they didn’t accomplish the defined conditions.

The table below gives an overview of the patients' preoperative data:

Parameters	Group I (n = 50)	Group II (n=50)	Value "p"
Age (years)	67 ± 11	67 ± 9	ns
Males (n)	32	34	ns
Females (n)	18	16	ns
Kidney insufficiency	6	6	ns
COPD	11	13	ns
Patients with arterial hypertension	7	13	ns
Patients with pulmonary hypertension	27	24	ns
pAVK	8	7	ns
Hypertriglikemie	17	21	ns
Diabetes mellitus	18	16	ns
Anamnesis for Miocard heart attack	41	37	ns
Anterior wall	22	16	ns
Posterior wall	11	9	ns
Lateral wall	8	12	ns
NYHA	3,05 (0,64)	2,90 (0,63)	ns
Sinusoidal pace (n)	48	47	ns
Atrial fibrilation (n)	2	3	ns
QRS prolongation (sec)	119,60 (14,78	127,82 (20,3)	ns
LVEF Angio (mean SD %)	26,63 (4,85)	26,92 (5,24)	ns
LVEF Eho (mean SD %)	27,44 (5,24)	28,23 (5,09)	ns
LVEDD (mean SD mm)	64,75 (4,72)	52,32 (3,76)	< 0,05

Table 2 preoperative data: COPD = Chronic obstructive pulmonary Disease, Nyhan = New York Heart Association, LVEF = Left Ventricular Ejection Fraction, LVEDD = Left Ventricular End diastolic diameter, ns = non Significant.

Demographic data, except LVEDD which were with no significant changes in both the same groups.

Aortocoronary bypass was applied to 80% of patients (n = 160), 5% of patients had a change in prosthetic aortic valve with biological replacement, 13.75% of patients had a combined intervention in the valles and bypass, 1, 26% of patients had mitral valve intervention.

2. Clinical results

Echocardiography examinations which were performed prior to cardiac intervention showed in front of all patients who had undergone prior myocardial heart attack disorders in the ventricular wall motility. A paradoxical movement of the intraventricular septum was observed to 50% of patients (n = 50).

Postoperative data	Group 1 (n 50)	Group 2 (n 50)	p-value
Intensive stay in the station (days)	1,75 (1,10)	1,7 (1,13)	ns
Time of intubation (min)	14,5 (13,9)	14,5 (11,7)	ns
Equipment with IABP (n)	4	7	ns
LVEF (%)	34,63 (4,06)	33,84 (4,79)	ns
Time of hospitalization (days)	9,46 (6,50)	9,05 (5,15)	ns
Initropic support (n)	36	43	ns
Serum CK (U/l)	279,59 (353,99)	192,48 (187,45)	ns

Complications (n)			
Neurologic complications	1	1	ns
Infection of injury	2	3	ns
Emboli	0	1	ns
Re-Torkotomi	1	1	ns
Respiratory failure	1	1	ns
Renal disfunction	1	1	ns
Cardiac arrest/ventricular fibrilation	1	0	ns
Mortality in hospital (n)	2	1	ns

Tab. 3: *Postoperative data*

Except the planned effective cardiac intervention, to 35 patients was performed a surgical remodeling in the left ventricle (geometric cavitar correction of the left ventricle with the help of the perpendicular sewing of Apex Cordis). This intervention was applied with a very significant difference with the first group, where patients had a significant dilatation of the left ventricle.

Duration of extracorporeal circulation, cardiac arrest duration and the amount of preoperative bleeding had no significant statistical change between the two groups. Significant statistical change was found in the application with red blood cells. They were applied with a greater amount of patients of the second group.

Implantation of the electrode for left ventricular stimulation was applied without major complications. In twelve patients it was observed after the implantation of this electrode a diaphragmatic stimulation, which helped to avoid the establishment of a special gauze (Tabotamb®) in this realm.

In the following table is provided a detailed visualization of the data listed after the application of cardio surgical intervention.

Hospital mortality was 3% in both groups without significant difference between them. The cause of death was a multiorganic failure in three patients and a persistence of a severe cardiac insufficiency with drastic reduction of CO (low cardiac output syndrome) in three other patients. None of the deaths were related to the implantation procedure of the temporal pacemaker.

Postoperative treatment and the results were in both groups, except for erythrocyte need for the second group, with no statistical significant difference. We noted no significant statistical difference regarding the duration of treatment in hospital and the need for isotropic medications.

67.5% of patients in the first group and 55% of patients in the second group benefited biventricular significant stimulation by increasing CI over 1 compared with preoperative installment stimulation and compared with the AAI's temporal peacemaker or with the rhythm of the patient himself.

These results with the positive effect of biventricular stimulation were present in 6 and 24 hours after inetrvention (Fig. a. Group I and Fig. b Group II)

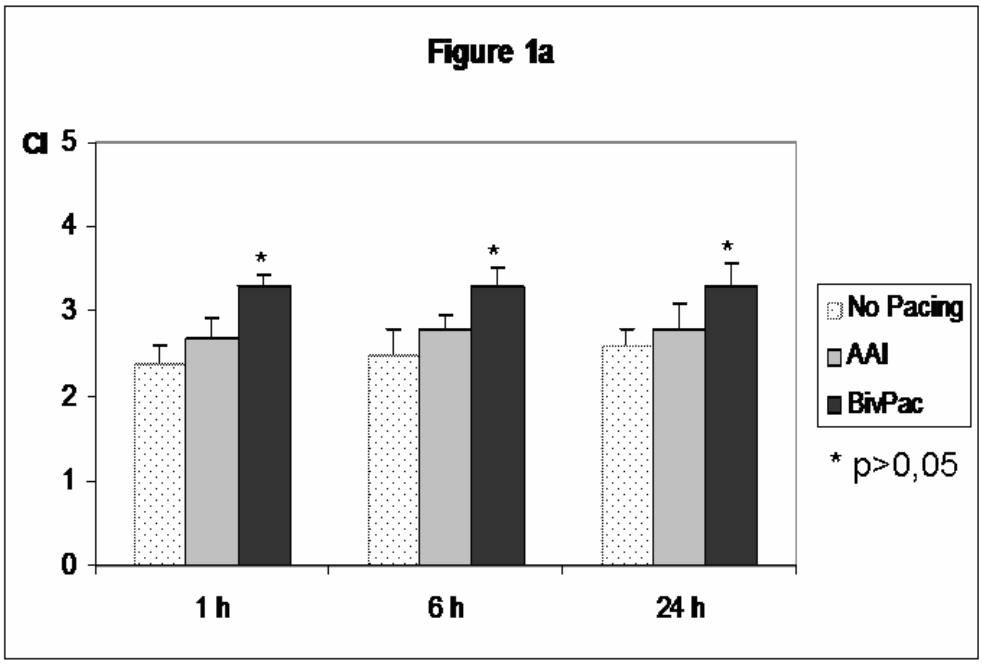

Fig. a: CI = cardiac index 1, 6 and 24 hours after the intervention of the Group I of patients - Responder.

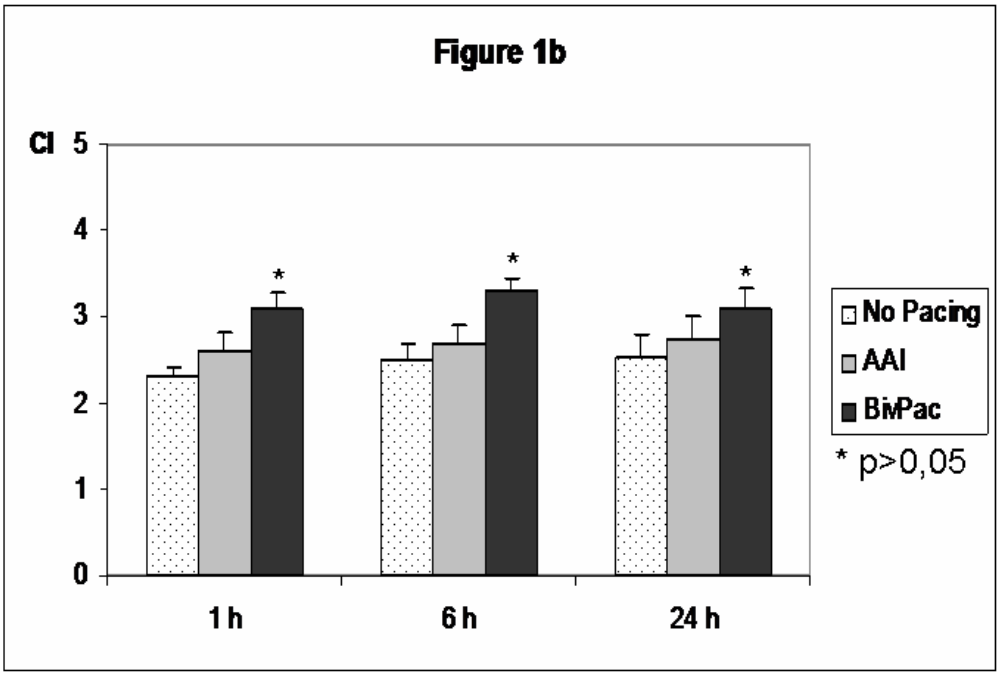

Fig. a: cardiac index 1, 6 and 24 hours after the intervention of the Group II of patients - Responder.

Fifty-six (56) patients belonging to the group of so-called "Responder" so patients who had significant statistical benifit from biventricular stimulation, also after surgery had medications with positive inotropic action, but this effect remained even after removal of the drugs, ie 6 and 24 hours after cardiac intervention.

Most of the patients to whom during the operation was applied a surgical remodeling of the left ventricle also showed a positive effect of biventrikular stimulation (77% of these patients).

Patients who showed no positive effect of this kind of therapy (biventricular Perioperative stimulation) were ranked in the group of so-called "Non Responders". In this group of patients wasn't noticed cardiac index increase during biventricular stimulation in all measurements applied (Fig. a. Group I and b. Group II).

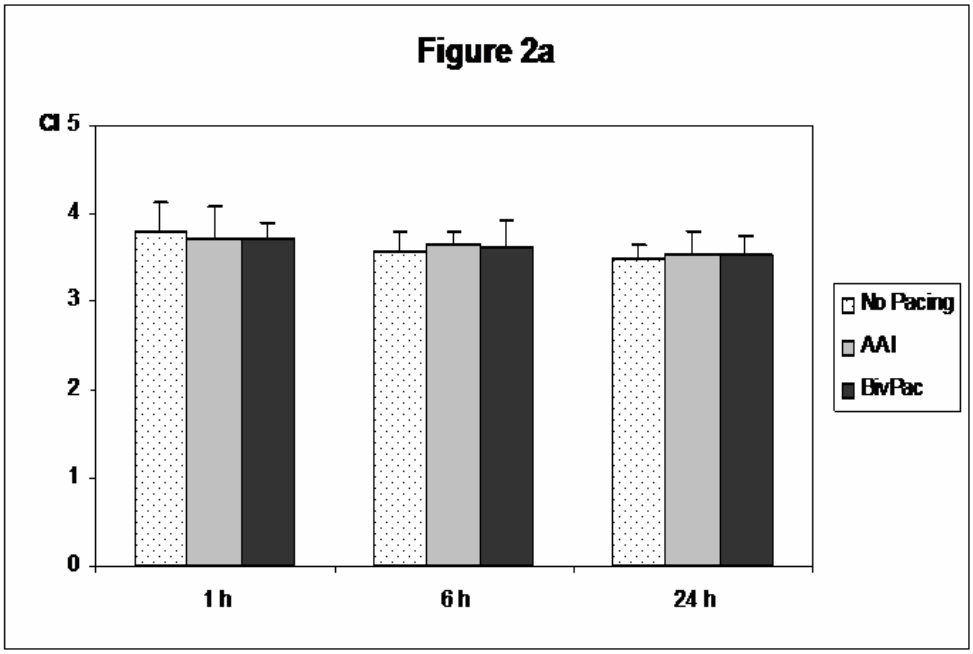

Fig. a: *CI = cardiac index 1, 6 and 24 hours after intervention of patients of Group I - Non Responders.*

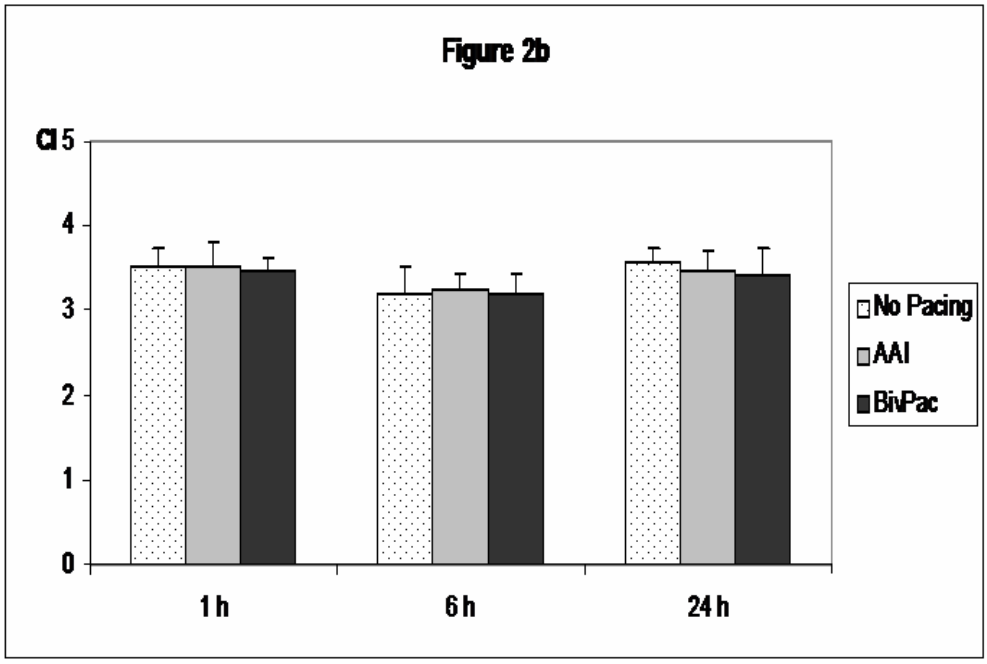

Fig. b: *CI = cardiac index 1, 6 and 24 hours after intervention of patients of Group II - Non Responders.*

In this group of patients "non-responders", CO was even before the intervention with biventricular stimulation with 6.51 ± 1.84 l / min increased and with significant statistical difference compared with the group of patients belonging to "Responder" who had in the beginning a CO = 4.4 ± 1.3 l / min.

In the following table is provided a detailed information on patients' hemodynamic situation during different modus of peacemaker stimulation or during the phase with no stimulation. A singnificant statistical difference was seen in systemic arterial pressure increase, while other hemodynamics parameters showed a positive tendency but with no significant statistical difference.

	1 hour postoperatively					6 hours postoperatively					24 hours postoperatively				
	Heart rate	RR (mmHg)	CVP (mmHg)	PAP (mmHg)	pcwp (mmHg)	Heart rate	RR (mmHg)	CVP (mmHg)	PAP (mmHg)	pcwp (mmHg)	Heart rate	RR (mmHg)	CVP (mmHg)	PAP (mmHg)	pcwp (mmHg)
Group 1 No Pacing	76±15	96/43/60	9.5±2.5	31/16/21	11±3.0	77±13	103/51/66	11.5±3	36/17/24	10,7±2	82±16	114/55/74	8.6±1.4	37/16/24	10.0±2.9
Group 1 AAI	100	102/48/65	10.5±3	33/17/22	12±3.2	100	107/55/71	10.9±3.1	38/18/25	11,2±2.5	100	118/57/77	8.5±3	37/17/24	10.3±2.6
Group 1 DDD_{bivpac}	100	**116/56/75***	11±2.5	35/18/25	11.5±2.8	100	**121/62/81***	11.2±2.4	37/17/24	12±2.9	100	**128/62/85***	8.2±2.8	37/17/24	10.6±3.4
Group 2 No pacing	76±13	103/51/67	10.1±3.3	31/16/21	11.5±3.1	79±16	106/52/68	10.6±3.3	36/16/23	11±3.2	85±13	11/52/71	9.3±2.2	32/15/20	9.3±3.2
Group 2 AAI	100	108/52/70	10.2±3.5	30/16/21	11.6±2.8	100	113/55/73	10.6±2.9	37/18/23	11.3±3.2	100	116/56/74	10±3.4	32/16/21	9.2±3.2
Group 2 DDD_{bivpac}	100	**121/61/80***	10.3±3.2	32/17/21	1.6±3.0	100	**125/62/82***	10.6±3.2	38/19/25	11.8±3.6	100	**130/63/85***	9.1±3.1	32/16/21	10.4±2.8

Tab. 4: $p \leq 0,05$; RR = Systemic arterial pressure; CVP = central venous Pressure.

In the last table are provided key preoperative and after perioperative data even after cardiac intervention.

	Group 1		**Group 2**	
	Responder	Non-Responder	Responder	Non-Responder
Age (years)	66±11	70±10	68±9	66±9
Sex (m/f)	21/6	11/2	18/4	16/2
Heart attack (%)	63 %	69%	63%	**28%***
Bypass grafts	2.9±1.1	3.2±1.2	3.1±1.2	3.0±1.4
NYHA class	3.0±0.7	3.1±0.5	2.9±0.5	2.9±0.7
LVEF preop (%)	26±5	28±3	26±5	28±5
LVEDD (mm)	**32±5****	**33±5****	26±5	27±2
QRS-width (msec)	60±7	57±8	64±10	64±7
LBBB (%)	22%	23%	50%	33%
RBBB (%)	19%	15%	0	39%
Bypass time (min)	47±19	49±26	43±12	47±14

X-Clamp (min)	27±13	26±13	25±14	25±8
ICU stay (d)	1.5±0.6	**2.2±0.7*** **	1.7±1.1	1.7±1.2
Ventilation (h)	11.7±4.5	**20.2±23**** **	13±5	16±17
Inotropi (n)	11	12	13	14
EF postop (%)	17±2	13±1	16±2	17±2
Hospital stay (d)	4.3±1	6±5	5±3	4±1

Tab. 5: Comparison of preoperative and postoperative data of the two groups respnder and nonresponder.

The data in the table shows that non-responder patients of grup I stayed longer in the intensive station and had a longer intubation compared with other patients. In non-responder patients of group II were noted more Myocard heart attacks. Other data showed no significant statistical difference, particularly in terms of the length of the QRS complex of ECG in both groups. In echocardiographic examination after biventricular stimulation was observed a difference in motility of different parts of the myocardial wall in both ventricles. This phenomenon was observed normally in the "Responder" group. A positive difference showed patients with LSB while thoshe patients who had preoperative a RSB showed no benifit during temporal biventricular stimulation.

Discussion

Congestive heart failure (CHF) is a major health care problem, associated with a high mortality rate of up to 50% at one year in New York Heart Association (NYHA) class IV patients. Patients suffering from severe impairment of LV function and biventricular dilatation often demonstrate prolonged inter-and intraventricular conduction. Asynchrononous ventricular contraction, shortened diastolic filling times at a given heart rate, and mitral regurgitation are adverse consequences of this pathology. Widening of QRS complexes to more than 130 ms has been identified as an indipendet risk factor for cardiac mortality in patients with poor LV function. Especially an underlying complete left bundle branch block leads to interventricular septal wall motion abnormalities. In these patients, ventricular resynchronizatin by means of biventricular stimulation leads to immediate improvement of cardiac function and NYHA class.

Perioperative mortality in patients undergoing open heart surgery with impaired LV function is considerable. Especially weaning from extracorporal circulation (ECC) can be difficult due to prolonged impairment of LV contractility caused by the ischemic period and following reperfusion damage. Possible therapeutic strategies besides biventricular pacing focus on maximizing CI by administration of adrenergic drugs and in sevese cases implantation of intraaortic ballon pumps. A beneficial effect of cardiac resynchronization therapy (CRT) has been reported in individual cases of patients with open heart surgery and reduced LV Function 8,9. The present study systematically evaluated the use of temporary biventricular pacing after open heart surgery in patients with reduce LV function.

200 consecutive cardiac surgery patients with a LV ejection fraction below 35% recived biventricular stimulation via temporary myocardial electrodes. Group 1 cosisted of 100 patients with LV dilatation (meen-LVEDD 65+/-5mm), Group 2 100 patients with normal or slightly dilated LV (meen-LVEDD 52+/-4mm). Hemodynamic parameters were measured immediately, 6 and 24 hours after operation.

An increase of cardiac index (CI) and arterial blood pressure with biventricular pacing was observed in group 1 67.5%)versus group 2 55% from 2.4+/-0.7l/min/m2 to 3.5+/-0.5l/min/m2($p<0.01$). This benefit persisted 6 and 24 hours postoperatively. The remaining patients alredy showed higher cardiac index prior to pacing

(3.7+/-0.9l/min/m2). In group 1, responding patients required shorter times for ventilation support and intensive care. QRS duration before surgery was not predictive for the response to biventricular pacing.

In the group with severely enlarged LV (Group 1) more then 2/3 of our patients (67%) demonstrated a signifikant rise in CI, which was comparable to the hemodynamic benefit of intraaortic ballon pump implantation. Thus, intraoperative biventricular stimulation may be conciderated as a less invasive alternative to intraaortic ballon pump therapy. The hemodynamic benefit persisted for 24 hours, although the improvement in CI became less significant. Further more significantly higher postoperative arterial blood pressure values could be observed for the responding patients. In the group of patients with Impaired ventricular function and maintained ventricular dimensions the rate of responding patients was lower (55%), again response to biventricular stimulation led not only to a rise in cardiac output but also in arterial blood pressure. Of note, especially patients with a history of myocardial infarction responded to the resynchronization therapy, although the etiology of ventricular dilatation in the remaining patients must have been ischemic too. Comparing the resonce to biventricular pacing in the two groups the higher success rate in group 1 was related to their initially larger ventricules, which profited more frequently from resynchronization, rather than the effect of the LV remodeling, as there was not a higher percentage of resonce in those ten patients, who had undergone such surgery. In summary, biventricular pacing helps many patients with reduce LV function not with standing presence or absence of LV-dilatation.

Conclusion

Based on the results obtained during this research paper we can conclude that the therapy of cardial resincronization with the temporary biventricular help shows positive effects to a significant number of patients.

Based on these experiences, we prefer in the future to develop other studies, randomized now, with a larger number of patients and with a longer follow-up time frame to be given the opportunity to be able to verify results and the same be more defined.

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