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Letter to the Editor

Research Articles

Review

Case Report

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Isn't it time for us to leave our habit of not anticoagulating the patients with paroxysmal atrial fibrillation?

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In previous trial, the development of thromboembolic event was detected to get easier with the slowing down of atrial appendix flow rates and observation of spontaneous echo contrast in TEE, the development of thrombotic process is considered to be quite short (24-48 hours). Therefore, theorically a quite short-lasting atrial fibrillation episode has been suggested to cause thrombogenic events in case of predisposition.

In fact in a recently updated meta-analysis, oral anticoagulation was found to be more effective than aspirin in thromboembolism prophylaxis in atrial fibrillation both persistent and paroxysmal. However, it is a known fact that in routine clinical practice, anticoagulation is commonly discontinued in the presence of paroxysmal atrial fibrillation.

The main reason for this practice is thinking that sometimes there is no recurrence in the clinical follow-up of the patients with paroxysmal atrial fibrillation. However it is known that unnoticed atrial fibrillation attacks occur due to acceptable ventricular response, especially in patients taking anti-arrhythmic therapy.

"Euro Heart Survey on Atrial Fibrillation" observational trial is a study aiming to detect the attitude of the physicians in Europe towards atrial fibrillation, and the results of this attitude.

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This trial concerns more than 4000 patients with atrial fibrillation, and shows that the type of atrial fibrillation should not affect the choice of anti-thrombotic therapy. All atrial fibrillation types (paroxysmal, persistent, permanent) have similar rates of stroke risk. Thus, the decision of anticoagulation for atrial fibrillation, should be made according to the additional risk factors for stroke rather than the type of atrial fibrillation.[1,2]

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The significance of cardiac rhythm variability value assessment in partients wiht enfective endocarditis

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Summary

Objective: To assess heart rate variability (HRV) by the results of 24-hours ESG monitoring in patients with infection endocarditis (IE) before surgery and over a 6-month period after the surgical correction of valve heart pathology.

Material and Method: In 35 patients included into the study, an assessment of initial HRV (before surgery, I test) was performed by the results of 24-hours ECG monitoring on the 11,0±1,0 day after the surgery; in 3 and 6 months after the surgery.

Results: More than a half of IE patients in pre-and early postoperative periods (56% and 57% respectively) were found to have hypersympaticotonia which was associated with the reduction of cardiac rhythm variability temporary indices (standard deviation NN intervals - SDNN, standard deviation average NN intervals - SDANN- i). In early postoperative period acute reduction of HRV was revealed in patients with severe complications, such as myocarditis, valvular abscesses, severe heart failure associated with cardiac valve destruction as well as the perioperation myocardial infarction. In 3 and 6 months after the IE surgical treatment the number of patients with significant HRV reduction decreased. The significant hypersympaticotonia maintained in patients with previous MI and myocarditis that led to the development of heart failure with the reduction of global left ventricle (LV) contractility. The evidence of significant hypersympaticotonia in patients with type II diabetes mellitus was subject to diabetic neuropathy progressing underlying secondary immune failure in the settings of IE.

Conclusion: The low level of HRV can be used as a complication marker in IE patients including the post-operative period.

Keywords: Infectious endocarditis, heart rate variability, myocarditis, heart failure.

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Introduction

Heart rhythm variability analysis (HRV) is one of the leading evaluation methods of heart vegetative regulation condition as it reflects the extent of regulatory system strain in response to any stressful effect and cardiovascular system adaptation capacities.

There are results of selected data that investigated clinical value of HRV in arterial hypertension, in congenital heart failure, chronic mitral regurgitation, myocardial infarction. Data are absent on HRV clinical significance in evaluating complication risks during IE. To study HRV by the temporary test results in IE patients prior to the surgery, 6 months after heart valve abnormality surgical correction and to compare that to the progression of complications during the underlying disease.

Materials and methods

35 IE patients submitted to surgical treatment have been studied; they were on a hospital stay in cardiosurgical departments of GU RSPC "Cardiology" from January 1, 2009 till March 1, 2010.

The study involved IE patients in active disease phase. IE diagnosis was estimated according to standard criteria [Duke,1994] in the presence of positive blood culture and (or) echocardiographic approvals of heart valve lesions. The study includes patients without hemodynamically significant coronary artery lesions according to the data of coronary angiographies performed at the age of 19 to 70 (mean-age 43,6±2,4). The subjects examined were 27 (73,3%) males and 8 (26,7%) females. The primary IE was diagnosed in 22 (62,9%) patients, secondary - in 13 (37,1%) from 35 patients who were included in the study. Aortal valve damage (AVD) in IE was revealed in 11 (31,4%) from 35 patients, mitral valve (MV) – in 11 (31,4%) from 35 subjects, simultaneous mitral and aortal valve damage was revealed in 9 (25,7%), tricuspid valve (TV) – in 4 (11,5%) patients.

Chronic heart failure symptoms (CHF) of different severity were noted in 100% of cases. Symptom onset time was different. However, in 18 (60%) of 30 patients IV FC CHF was detected (FC) by New York Heart Association Classification (NYHA), in 8 (26,7%) patients - III FC and in 4 (13,3%) patients' CHF clinical manifestations corresponded to II FC.

Complications during the IE in pre- and post-operational periods, myocarditis, perioperational MI were revealed in 11 (31,4%) out of 35 patients. Intraoperational pyaemic cardiac loci were revealed in 7 (20%) out of 35 subjects: they had their aortic root and/or valve leaflet abscesses. One patient was CT-diagnosed with abscess forming pneumonia. 1 patient of 35 died of heart failure in pre-operation period.

34 patients underwent valve replacement surgery. Six ones (17,6 %) were implanted with biological prostheses (SJM mitral and tricuspid positions, Sorin tricuspidal position), 28 (82,4%) – mechanical were implanted in mitral and or aortic positions (Planix – E MDM, Planix - T MDM, Planix - T). Moreover, 14 of 34 patients (41,2%) received bivalvular correction- aortic valves (AV) and/or MV prosthesis, tricuspid valve plasty using Plankor rings. 10 ones (29,4%) underwent monovalvular correction in mitral or aortal positions. One patient (2,9%) had MV anterior leaflet quadriangular resection with the advancement onto the leasion region anterior leaflet and MV plasty and hard Plankor ring implantation.

Patient state evaluation who were included into the study was implemented initially (prior to the surgery) – test 1, on 11,0±1,0 day after the valvular correction surgery – test 2, within 3 months after the surgery – test 3, in 6 months after the surgery – test 4. HRV was reckoned based on the results of daily ECG Holter monitoring (ECGHM). ECGHM was done using Medilog FD 5 cardiomonitor system by Oxford Instruments Medical. Results of temporary test based on were studied. It was based on statistic programs for reckoning of pronounced quantity of RR interval rates with further interpretation of data obtained.

HRV data interpretation was done according to ESC and North American Society of Pacing and Electrophysiology Working Group (1996). Temporary HRVtest results were evaluated (Time Domain) recommended for usage:

- SDNN (ms) – standard deviation of all RR intervals analyzed (for total HRV assessment).
- SDANN - I (ms) – standard deviation of 5-minute averaged RR interval values which the observation period is divided by (for evaluating of low-frequency variability component).

• rMSSD (ms) – square root of difference sum of subsequent RR intervals (for evaluating of low-frequency variability component).

Indicators selected were offered by the ESC and North American Society of Pacing and Electrophysiology Working Group for universalization of physiological and clinical studies. The following parameters of temporary test were taken for norm:: SDNN -141±39 ms, SDANN – I -127±25 ms, rMSSD 27±12 ms. The fall-off criterion of 24-hour HRV was con-sidered to be a SDNN value of < 50 ms. A moderate drop criterion of 24-hour HRV was SDNN value of < 100 ms. Two patient groups were singled out by us on every step of examination: group I having a drop of SDNN < 100 ms, group II with fall-off of SDNN < 50 ms.

All reckons were done using personal computer with Excel 7.0 electronic charts («Microsoft», USA). Data obtained have been presented as M±m, where M – arithmetic mean, m − standard error of arithmetic mean. Differences between the groups were considered as statistically evident when p<0,05.

Results

Prior to the surgery, the HRV temporary test assessment was done in 25 patients. HRV was reduced in most cases − in 14 (56%) patients out of 25 examined subjects. Group I included 10 (72%) patients, Group II – 4 (28%) patients.

Group I demonstrated the reduction in mean indicators reflecting sympathetic activity: SDNN down to 77±4,5 ms, SDANN-i to 62,6±4,3 ms. The indicator of rMSSD that reflects parasympathetic activity fluctuated between normal values and made up on average 39,0±7,3 ms (the increase of this indicator was noted in 4 (40%) of patients having atrial fibrillation and/or premature beats). 4 patients having severe drop in HRV (Group II) had their temporary test rates evidently different form the mean of Group I and made up: SDNN -35,56±4,0 ms (p<0,001), SDANN-i− 32,3±4,5 ms (p<0,001) and rMSSD 17,2±0,5 ms (p<0,001).

Mean rates were beyond lower rates of this group of so called “parting points” which is associated with poor prognosis and high death risk. Two of four patients died who had a significant drop in HRV. One patient died of heart failure progression before the operation. The second one (female) died on a first day after the surgery had been performed. The cause of death was gastrointestinal bleeding that had developed during the preoperational DIC syndrome. One female patient had sepsis with the developing DIC syndrome in preoperational period, myocarditis. One more IE patient had aortic root abscess, myocarditis complication as well as severe aortal insufficiency in preoperational period. Group I did not show any of these complications.

Data of the second examination demonstrated that the situation (compared to the first ex-amination) has not changed substantially. Heart rhythm variability reducing tendencies maintained in 15 (57%) patients of 26 (test 1– 56 %, p>0, 05). The average reduction in SDNN (Group I) was revealed in 67% of patients (test 1– 72%, p>0,05). Severe drop (Group II) was revealed in 5 (33%) patients (test 1 28%, p>0,05).

SDNN and SDANN- I indicators were evidently different in Group I and II and made up: SDNN 75,9±3,0 ms and 45,0±2,1 ms (p<0,05) accordingly, SDANN-i 64,1±4,6 ms and 42,5±2,4 ms (p<0,001), accordingly. rMSSD value was 28,7±6,2 ms and 16,8±1,1 ms (p>0,05), accordingly in Groups I and II and it flits between the normal values. Retrospective analysis showed that in the second examination in group 2 that had a moderated decrease of HRV there were no significant complications in the course of in-patient period.

Among those having a significant drop in HRV – one out of 5 (20%), demonstrated a persistent sepsis with progressive DIC syndrome in early post-operational period (2 weeks after the surgery), heart failure accompanied by developing postoperational myocarditis. He died 3 months later after the surgical valve correction. Two ones (40%) developed perioperational postoperational myocardial infarction (MI). Maintenance of postoperational hypersymathicotonia can be perhaps explained by preserved and/or progressive heart failure and postoperation MI development.

Past MI is inevitably accompanied by left ventricular (LV) remodeling. The latter is able to cause LV dysfunction. It is considered that changes in heart geometry may cause sympathetic fiber afferent impulsation acceleration due to mechanical extension of receptors. This sympathetic activation weakens vagal effects on heart. There data present on the relations of daily SDNN drop and LV dysfunction. It is worth pointing

that any acute MI (including the perioperational) is itself accompanied by hypersympathicotonia. According to one of the hypotheses, during the HRV drop, after the past MI, cardio-cardinalsympatho-sympathic and sympatho-vagal reflexes get involved. So, detection of pronounced hypersympathicotonia in IE patients can be one of criteria of poor prognosis in the progression of complications in pre- and postoperational periods.

In 3 months after the operation the heart rhythm variability is noted in 9 (45%) of 20 patients examined (tests 1 and 2 56% and 57%, accordingly, $p>0,05$). In the third checkup a severe drop was noted in 2 put of 9 (22%) patients – Group II, moderate in 7 (78%) – Group I.

SDNN, SDANN- i indices were evidently different in groups I and II (pronounced according to the qualitative values of dividing values of SDNN) and made up correspondingly: SDNN 70,2±6,7 ms and 43,9±3,0 ms ($p<0,01$), SDANN- i – 61,5±5,9 ms and 40,7±1,6 ms ($p<0,01$). Mean values rMSSD reflecting parasymapthic activity were significantly lower in group II than in group I and made up 39,8±13,0 ms and 9,5±0,7 ms, ($p<0,05$), accordingly. In group I the rMSSD value was above 39 ms in 2 (22,2%) subjects who were registered with atrial fibrillation.

One female patient having a severe drop of HRV registered during the third checkup developed postoperation myocardial infarction that contributed to heart failure with LV global contractility reduction (EF – 22/24 %). Another patient having a severe drop of HRV was diagnosed with myocarditis in preoperational period.

Six months later (the fourth checkup) 5 of 14 (35%) subjects having their HRV parameters evaluated maintained temporary BCP test indices drop: HRV drop incidence was lower than in tests 1 and 2, 56% and 57% accordingly, $p<0,05$). A moderate reduction in HRV was registered in 4 (80%) of 5 patients, severe – in one (20%). Mean-values of HRV in group I were the following: SDNN –79,5±6,2 ms, SDANN- i –70,8±6,1 ms, rMSSD 25,3±4,4 ms. A patient with a severe drop of HRV turned out to have diabetes mellitus, and such a notable HRV drop that emerged in 6 months after the surgery could have been an outcome of progressive diabetic neuropathy accompanied by a secondary immune insufficiency.

In general it might be said that 3 and 6 months later after the operation the hypersympath-icotonia frequency had reduced according to the HRV data. A huge drop in SDNN, SDANN- i values maintained in subjects having severe heart failure or a concomitant diabetes mellitus.

Conclusion

1. A sudden drop in HRV was noted in subjects having severe complications, as my-ocarditis, valvular abscesses, severe heart failure associated with heart valvular apparatus destruction and perioperational myocardial infarction.

2. Three and six months after the operative treatment of IE the number of patients having a considerable HRV rate drop decreased. A pronounced hypersympathicotonia was preserved in patients who underwent myocardial infarction and myocarditis which contributed to , heart failure with global LV contractility reduction. The appearance of severe hypersympathicotonia in patient with II type diabetes mellitus was subject to diabetic neuropathy progression accompanied by a secondary IE immune insufficiency.

3. Low HRV may be used as a marker of complications in IE subjects including the post-operation period.

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Percutaneous coronary revascularization in diabetics

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Summary

Objective: Diabetics with coronary artery disease face a high risk of adverse events following coronary revascularization. However, recurrence rates of after the first revascularization have never been appraised. The aim of this study was to evaluate recurrent events in diabetics undergoing percutaneous coronary intervention (PCI) in the current era.

Material and Method: Authors collected baseline and outcome data of consecutive type-2 diabetics treated with PCI (January 2005-December 2008). End-points of interest were the long-term rates of major adverse cardiac events (MACE: cardiac death, myocardial infarction [MI], percutaneous target vessel revascularization [TVR-PCI], or coronary artery bypass grafting [CABG]), non-TVR PCI, and stent thrombosis.

Results: A total of 429 diabetics were included, 191 (44%) insulin-dependent, with drug-eluting stents implanted in 232 (54%). After a median of 38 months, events were as follows: MACE in 167 (38.9%) subjects, cardiac death in 38 (8.8%), MI in 42(9.8%), TVR PCI in 130 (30.3%), CABG in 11 (6.2%), non-TVR PCI in 52 (12.1%), and definite stent thrombosis (2.1%). Among the 129 patients undergoing TVR PCI as first event, as many as 28 (21.7%) underwent a second TVR PCI, 7 (5.4%) underwent a third TVR PCI, and a further 2 (1.5%) underwent a fourth TVR PCI, whereas CABG was performed in 2 (1.5%)and non-TVR PCI in 4 (3.1%).

Conclusion: This work, originally reporting on risk of recurrent repeat revascularization events among diabetics treated with PCI, showed that adverse events occur frequently in these patients, but can be managed in most cases safely and successfully by means of repeat PCI only.

Keywords: Stroke, coronary artery disease, diabetics.

Introduction

Many complications develop in diabetics: microvascular complications, including retinopathy, nephropathy, and neuropathy, and macrovascular complications, and including cardiac, cerebrovascular, and peripheral vascular complications.[1] Cardiovascular disease is the principal cause of death and disability in people with diabetes as it recognizes a unique pathophysiology.[2] Several features of atherosclerosis make diabetic patients 2 to 4 times more likely to develop coronary artery disease than non-diabetic patients and to manifest this condition earlier in life. moreover, many observational and experimental data showed a worse prognosis for diabetics experiencing a myocardial infarction

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(MI) or undergoing coronary revascularization.[3] The presence of several comorbidities, multivessel and diffuse coronary disease with small vessel diameter, long lesions and plaques prone to rupture, together with accelerated atherosclerosis progression, compromises periprocedural and long-term outocomes of both coronary artery bypass grafting or percutaneous coronary intervention (PCI).[4] Indeed, owing to its unique pathophysiologic milieu and unfavorable anatomical pattern, diabetes makes either revascularization approach seemingly suboptimal. Diabetic patients thus clearly need, in addition to optimal medical therapy, various therapeutic strategies for myocardial ischemia tailored to the different stages of disease.

In such a setting, many studies have explored the long-term risk of single or first ever adverse events after coronary revascularization in diabetics,[5] but none sistematically appraised to date the risk of date the risk of recurrent and repeat adverse events, e.g., PCI followed in the same patient by bypass grafting and then another PCI. We thus aimed to retrospectively assess intermediate and long-term recurrences of major adverse cardiac events and repeat target vessel revascularizations in a cohort of diabetic subjects undergoing PCI.

Materials and methods

Specifically, a series of 429 consecutive patients were enrolled according to the following criteria: 1) previous or new diagnosis of type 2 diabetes mellitus according to contemporary American Diabetes Association criteria,[6] with patients classified as "non-insulin requiring", including patients treated with diet and/or oral hypoglycemic drugs but no insulin, and "insulin requiring", including patients treated with insulin regardless of other therapies; and 2 treatment with PCI between July 1, 2002, and December 31, 2005 at our Center, with implantation of bare-metal stents and/or drug eluting stents. Age, acute ST-elevation MI, combined treatment with the implantation of both bare-metal and drug eluting stents in the index procedure were not exclusion criteria.

All patients completed a written informed consent form, and institutional Ethic Committee approval was waived given the observational design of the study. All procedures were performed according to standard guidelines for PCI,[7] but interventional strategy and choice of device were decided by the attending physician Patients who were not chronically receiving aspirin, were pretreated with a 500 mg oral loading dose at least three hours before the procedure, or a 300 mg intravenous loading dose directly before the procedure. Premedication included also a loading dose of 300 mg of clopidogrel the day before a planned procedure or 600 mg at least two hours before a procedure for non-ST- elevation acute coronary syndrome. All patients received intra-arterial unfractioned heparin to maintain an activated clotting time longer than 250 seconds.

The use of glycoprotein IIb/IIIa inhibitors was left at the operator's preference. Angiographic success was defined as residual diameter stenosis<30% by visual estimate in the presence of a thrombolysis in MI grade 3 flow. Revascularization was considered functionally complete in case of effective treatment of all epicardial vessel with diameter >2.25 mm, supplying viable areas of left ventricular myocardium, and affected by a diameter stenosis 75% by visual estimate. After the procedure all patients were prescribed lifelong aspirin (70-325 mg/d). In addition, one month of clopidogrel (75mg/d) or ticlopidine (250 mg twice a day) was recommended for patients treated with bare-metal stents, at least three-six months following drug-eluting stent implantation, and, in any case, at least 9-12 months following a non-ST-elevation acute coronary syndrome.

The primary outcome measure of this study was the cumulative incidence in hospital and at follow-up of major adverse cardiac events (MACE), defined as the composite of 1) cardiac death (all death were considered cardiac unless an unequivocal non-cardiac cause could be established); 2) MI;[8] 3) target vessel revascularization (TVR, any repeat percutaneous intervention or surgical bypass of any segment of the target vessel). The target vessel was defined as the entire major coronary vessel proximal and distal to the target lesion, which includes upstream and downstream branches and the target lesion itself. Any percutaneous procedure planned to complete the index revascularization was considered part of the index procedure, not a repeat revascularization.

Predefined secondary outcome measures were: 1) non cardiac death (non-cardiovascular death or vascular non-

cardiac death); 2) MI; 3) percutaneous TVR; 4) percutaneous non -TVR (i.e., a repeat percutaneous intervention driven by any lesion located in a epicardial vessel ferent from the target vessel); 4) surgical revascularization by means of coronary artery bypass grafting; 5) stroke; 6) stent thrombosis (divided into definite, probable and possible according to the Academic Research Consortium recommendations).[9] For each patient, baseline demographic data, cardiovascular risk profile, treatment for risk factor control, other medical history data, as well as procedural and angiographic follow-up details were obtained from the institutional database, visits at the outpatient clinic or telephone interviews. All previous mentioned data were collected using individualized case report forms and entered into a dedicated database.

Statistical analysis

Continuous variable are presented as mean standard deviation or median and interquartile range. Student's test and/or analysis of variance were performed to determine differences between mean values. Categorical variables are reported as absolute values and percentage with 95% confidence intervals, with comparisons made with the chi-square test or Fisher exact test where appropriate. Two-tailed probability values <0.05 were considered statistically significant. Data were analysed with CIA, EpiInfo ad SPSS softwares.

TABLE I.—*Baseline clinical characteristics of patients according to treatment group.*

Variable	DES (N.=133)	Both (N.=99)	BMS (N.=197)	Overall (N.=429)	P
Age (mean±SD), y	64.8±10.6	65.9±10.0	69.7±9.5	67.3±10.2	0.0001
Male gender N. (%)	86 (65)	74 (75)	138 (70)	298 (69)	0.2489
Duration of diabetes (mean±DS), y	14.9±10.0	16.8±9.8	14.2±10.2	16.7±10.9	0.3395
Ejection fraction (mean±DS), %	54.3±10.7	49.9±11.6	50.6±12.0	52.0±11.6	0.0070
Hypertension N. (%)	117 (88)	91 (92)	171 (87)	379 (88)	0.4269
Dyslipidemia N. (%)	108 (81)	76 (77)	139 (71)	323 (75)	0.0826
Family history of coronary disease N. (%)	26 (20)	12 (12)	37 (19)	75 (17)	0.2729
Current smoker N. (%)	13 (10)	16 (16)	27 (14)	56 (13)	0.3368
Former smoker N. (%)	54 (40)	37 (37)	80 (41)	171 (40)	0.8470
Body mass index (mean±SD) kg/mÇ	27.8±4.8	27.5±3.8	28.1±4.5	27.9±4.4	0.7200
Renail failure N. (%)					
Serum creatinine ? 2mg/dL	10 (8)	10 (10)	23 (12)	43 (10)	0.4672
Dialysis	3 (2)	5 (5)	9 (5)	17 (4)	0.4685
Peripheral vasculopathy N. (%)	19 (14)	28 (28)	60 (30)	107 (25)	0.0026
Chronic obstructive pulmonary disease N. (%)	4 (3)	6 (6)	14 (7)	24 (5)	0.2754
Severe valvulopaty N. (%)	6 (4)	4 (4)	20 (10)	30 (7)	0.0605
Previous myocardial infarction N. (%)	47 (35)	39 (39)	87 (44)	173 (40)	0.2704
Previous coronary angioplasty N. (%)	43 (32)	24 (24)	43 (22)	110 (26)	0.0941
Previous bypass surgery N. (%)	22 (16)	22 (22)	35 (18)	79 (18)	0.5165
Previous stroke N. (%)	4 (3)	3 (3)	9 (4)	16 (4)	0.6997
Admission diagnosis N. (%)					
Stable angina or silent ischemia	35 (26)	35 (35)	56 (28)	126 (29)	0.3025
Unstable angina	64 (48)	28 (28)	62 (31)	154 (36)	0.0016
Non-ST-elevation myocardial infarction	21 (16)	20 (20)	46 (23)	87 (20)	0.2456
ST-elevation myocardial infarction	13 (10)	16 (16)	33 (17)	62 (14)	0.1799
Medical therapy N. (%)					
Oral antidiabetic agents	62 (47)	43 (43)	81 (41)	186 (43)	0.6131
Insulin	57 (43)	46 (46)	92 (47)	195 (46)	0.7687
Angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers	99 (74)	67 (68)	124 (63)	290 (67)	0.0912
Calcium-channel blockers	33 (25)	25 (25)	51 (26)	109 (25)	0.9752
blocker	114 (86)	73 (74)	138 (70)	325 (76)	0.0043
Nitrates	34 (25)	31 (31)	64 (32)	129 (30)	0.3858
Statins	87 (65)	63 (63)	109 (55)	259 (60)	0.1389
Antiplatelet agents	129 (97)	97 (98)	179 (91)	405 (94)	0.0125
Dual antiplatelet therapy duration after index procedure (mean±SD), months	5.0±2.7	4.9±2.6	1.0±2.6	3.2±2.6	<0.0001

Defined as combined treatment with bare-metal stents (BMS) and drug eluting stents (DES).

Results

A total of 429 subjects met the study inclusion criteria. Baseline characteristics according to sent type are presented in **Table I**. Overall, age was 67.3 10.2 years, and 69% of the patients were male. The clinical characteristics of the present cohort of patients than for diabetics in previously reported studies. Indeed, 88% (379 patients) had hypertension, 75% (323) had dyslipidemia, and their body mass index was 27.9 4.4 kg/m². Insulin-requiring diabetes was observed in 46% (195) of subjects and often the index procedure was not their first original revascularization procedure, as 40% (173) had experienced, as 40% (173) had experienced a previous MI, 26% (110) a previous coronary angioplasty and 18% (79) a prior bypass surgery. Diagnosis at admission was stable angina or silent ischemia for 29% (126) of patients. Compared with subject who received drug-eluting stents, those who received bare-metal stents had a more severe clinical profile: they were older (P<0.01), ha poorer left ventricular ejection fraction (P<0.01) and more diffuse atherosclerosis (ie concomitant peripheral artery disease, P<0.01). The duration of dual antiplatelet therapy was 5.0 2.7 month after drug-eluting stent implantation, 1.0 2.7 month after bare-metal stenting, and 4.9 2.6 months after combined treatment with both drug-eluting and bare-metal stents. In 6% (24) of cases dual antiplatelet therapy was not administered at discharge because of drug intolerance.

As show in **Table II**, multivessel disease was present in 73.6% (316) of subjects, 3 1.7 lesions were treated per patient, and 3 1.8 stents were implanted per patient. Concerning stent type, 197 (46%) received only bare-metal stents, 133 (31%) received only drug-eluting stents (sirolimus or paclitaxel-eluating stents), and 99 (23%) received both bare-metal and drug-eluating stents. There were significant differences between these groups in terms of angiographic characteristics, with a more complex procedural profile for patients treated with both stent types, and an excess of drug-eluting stent implantation at bifurcation lesions and unprotected left main (all P<0.05). Follow-up duration was thus 41.0 12.2 months (median 38.5 months,interquartile renge).

The three-year cumulative incidence of MACE was 38.9% (167) with a significantly better outcome in the drug-eluting stent only group. The overall rate of MI was 9.8% (42), with only 1 (0.2%) patient facing a second MI. Revascularization procedures occurred as follows: bypass grafting in 2.6% (11), first percutaneous TVR in 6.7% (29), third percutaneous interventions on epicardial vessels not previously treated: 1.1% (52) of patients underwent a first percutaneous non TVR, 1.6%(7) a second percutaneous non TVR, 0.5% (2) a third percutaneous non- TVR. Comparisons between groups showed that patients treated with bare-metal

TABLE II.—*Angiographic and procedural characteristics according to treatment group.*

Variable	DES (N.=133)	Both (N.=99)	BMS (N.=197)	Overall (N.=429)	P
Multivessel disease N. (%)	92 (69.2)	90 (90.9)	134 (68.0)	316 (73.6)	<0.0001
N. of diseased vessels/patient (mean±SD)	2.0±0.8	2.4±0.6	2.0±0.8	2.1±0.8	<0.0001
N. of treated vessels/patient (mean±SD)	1.6±0.9	2.1±0.6	1.6±0.7	2.0±0.7	0.0001
N. of treated lesions/patient (mean±SD)	2.6±1.6	4.1±1.8	2.5±1.4	3.0±1.7	<0.0001
Vessel treated N. (%)					
Left anterior descending	84 (63.1)	83 (83.8)	117 (59.4)	284 (66.2)	0.0001
Left circumflex	64 (48.1)	67 (67.7)	104 (52.8)	235 (54.8)	0.0093
Right coronary artery	53 (39.8)	47 (47.5)	86 (43.6)	186 (43.3)	0.5074
Venous graft	3 (2.2)	4 (4.0)	15 (7.6)	22 (5.1)	0.0821
Unprotected left main N. (%)	14 (10.5)	17 (17.2)	5 (2.5)	36 (8.4)	<0.0001
Chronic total occlusion N. (%)	24 (18.0)	25 (25.5)	36 (18.3)	85 (19.8)	0.3013
In-stent restenosis N. (%)	18 (13.5)	7 (7.1)	15 (7.6)	40 (9.3)	0.1310
Bifurcation lesions N. (%)	32 (24.1)	27 (27.3)	28 (14.2)	87 (20.3)	0.0132
Stent implanted/patient (mean±SD)	2.4±1.8	4.0±1.7	2.4±1.6	3.0±1.8	0.0001

Defined as combined treatment with bare-metal stents (BMS) and drug eluting stents (DES).

TABLE III.—*In-hospital outcomes according to treatment group.*

Variable	DES (N.=133)	Both (N.=99)	BMS (N.=197)	Overall (N.=429)	P
Major adverse cardiac events† N. (%)	3 (2.2)	13 (13.1)	25 (12.7)	41 (9.5)	0.0026
Death N. (%)	0 (0)	0 (0)	5 (2.5)	5 (1.2)	0.0508
Myocardial infarction N. (%)	3 (2.2)	13 (13.1)	20 (10.1)	36 (8.4)	0.0060
Coronary bypass grafting N. (%)	0 (0)	1 (1.0)	0 (0)	1 (0.2)	0.1881
Re-PCI N. (%)	0 (0)	1 (1.0)	3 (1.5)	4 (0.9)	0.3675
Stroke N. (%)	0 (0)	0 (0)	2 (1.0)	2 (0.5)	0.3063

*Defined as combined treatment with bare-metal stents (BMS) and drug eluting stents (DES); †Defined as cardiac death, myocardial infarction, target vessel revascularization percutaneous coronary intervention (PCI) or coronary bypass grafting.

stents had a significantly higher cardiac (P=0.03) and non cardiovascular mortality (P=0.01), data to be read together with their older age at the time of index procedure (P<0.01) and longer follow-up duration (P<0.01).

Further differences were assessed in the number of angiographic follow-up procedures (P<0.01), percutaneous TVR (P<0.01) and percutaneous non TVR (P<0.01) performed in the drug-eluating stent group versus the bare-metal stent counterpart.

We adjudicated 9 (2.1%) definite stent thromboses: 4 (0.9%) occurred within 30 days from index procedures (early), and 5 (1.2%) occurred following this period (late or very ate). Of note, no difference in incidence of definite, probable and possible stent thrombosis was detected among stent type groups (P=0.09, P=0.88 and P=0.55 respectively). Finally, subgroup analysis showed a higher frequency of all causae death (22.6% vs 9.8%, P<0.01) and MI (13.8% vs 6.4%, P<0.01) for insulin requiring diabetics compared to non insulin requiring patients. (**Figures 1-5**) allow to follow the assignment of study population to all possible outcomes, particularly to follow the real sequence of revascularization events.

Specifically, following the index procedure the first event was a percutaneous TVR in 30.1% (129) (95% CI: 25.9-34.6), bypass grafting in 2.1% (9) (95%CI:1.1-3-9), and percutaneous non TVR in 65% (28) (95%CI:4.6-9.3), with following-up showing 42.2% (181) (95% CI:37.6-46.9) of patients alive without repeat revascularizations, 11.2% (48) (95% CI: 8.5-14.5) dead without repeat revascularizations, 7.9% (34) (95% CI:5.7-10.9) untraceable (figure 1). Among 129 patients undergoing percutaneous TVR as first event, 21.7% (28) (95% CI: 15.5-29.6) underwent a further percutaneous TVR, 0.8% (1) (95% CI:0.1-4-3) experienced bypass as second final event, 1.5% (2) (95% CI: 0.4-5.5) underwent a percutaneous non-TVR followed in one case (0.8%) (95% CI:0.1-4.3) by a third identical event (**Figure 2**). Subjects free from further revascularizations were 65.1% (84) (95% CI: 56-72.8) living were 65.1% (84) (95% CI: 6.6-17.4) deceased.

In the group undergoing percutaneous TVR as second event, a third percutaneous TVR was performed in 25.0% (7) (95% CI: 12.7-43.4) of patients, 7.1% (2) (95% CI: 2.0-22.6) of them underwent a fourth percutaneous TVR, and 17.8% (5) (95% CI: 7.9-35.6) were alive without further interventions (**Figure 3**). In only one case (3.6%) (95% CI: 0.6-17.7) the third event was surgical revascularization, whereas another patient (3.6%) (95% CI:0.6-17.7) underwent percutaneous non-TVR with a subsequent fourth analogous event. Surviving patients without events were 60.7% (17) (95% CI: 42.4-76.4), and deceased without revascularization 7.1% (2) (95% CI: 2.0-22.6).

During the follow-up 28 subjects underwent only percutaneous revascularizations of epicardial vessels different from the target vessel: 10.7% (3) (95% CI: 3.7-27.2) of them needed a second percutaneous non-TVR, and 3.6% (1) (95% CI: 0.6-17.7) a third percutaneous non-TVR (**Figure 4**). Of the remaining patients 82.1% (23) (95% CI: 64.4-92.1) were alive without revascularization, 7.1% (2) (95% CI: 2.0-22.6) died without events.

Surgical revascularization occurred as a first event following index revascularization in 2.1% (9) of cases

(Figure 5). Among them one patient (11.1%) (95% CI: 2.0-43.5) had a second and a third event, both percutaneous TVR. In another one (11.1%) (95% CI: 2.0-43.5) percutaneous non-TVR was performed as second event. No second event. No second bypass grafting took place and one patient (11.1%) (95% CI: 2.0-43.5) deceased without other revascularizations, whereas 6 (66.6%) (95% CI: 35.4-87.9) were alive without further events.

Discussion

The main findings of this study, appraising the problem of recurrent events in diabetics undergoing percutaneous revascularization, are as follows: 1) repeat target vessel and non-target vessel revascularization occur frequently in this patient population, but can be managed in a safe and successful fashion by means of repeat PCI in most cases; 2) the sequence of revascularization events may be very complex in a minority of subjects, thus the treatment of any new adverse event should be individualized and clinically driven, but also based on coronary anatomy and addressed to the particular stage of diabetic disease; 3) careful clinical fol-

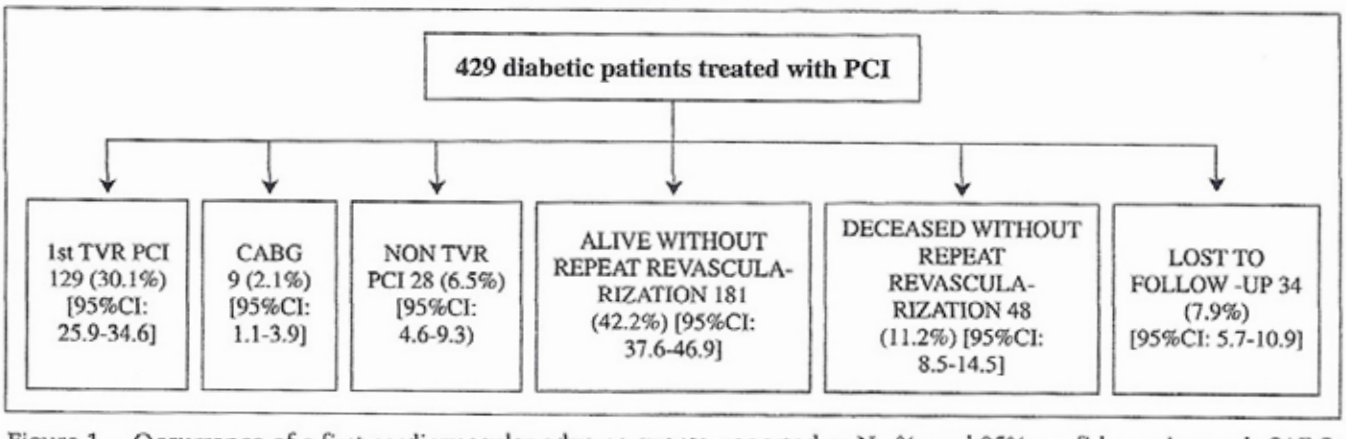

Figure 1.—Occurrence of a first cardiovascular adverse events, reported as N., %, and 95% confidence interval. CABG: coronary artery bypass grafting; NON TVR PCI: non target vessel revascularization percutaneous coronary intervention; TVR PCI: target vessel revascularization percutaneous coronary intervention.

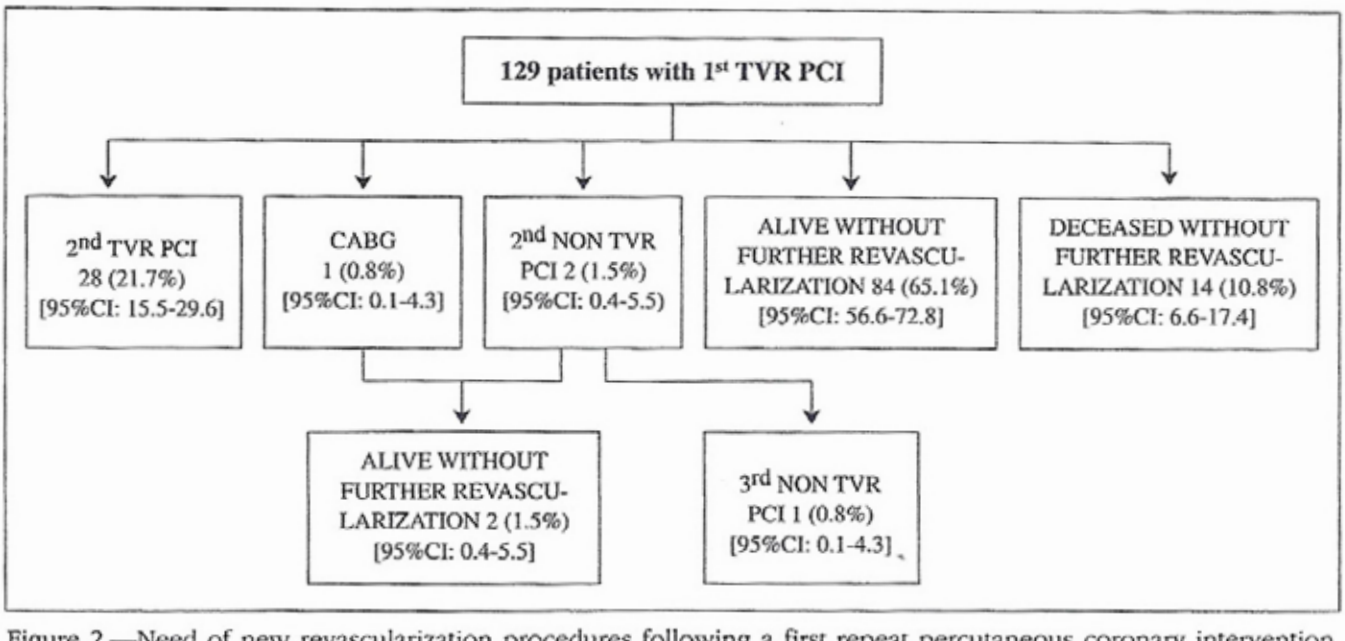

Figure 2.—Need of new revascularization procedures following a first repeat percutaneous coronary intervention, reported as N., %, and 95% confidence interval. CABG: coronary artery bypass grafting; NON TVR PCI: non target vessel revascularization percutaneous coronary intervention; TVR PCI: target vessel revascularization percutaneous coronary intervention.

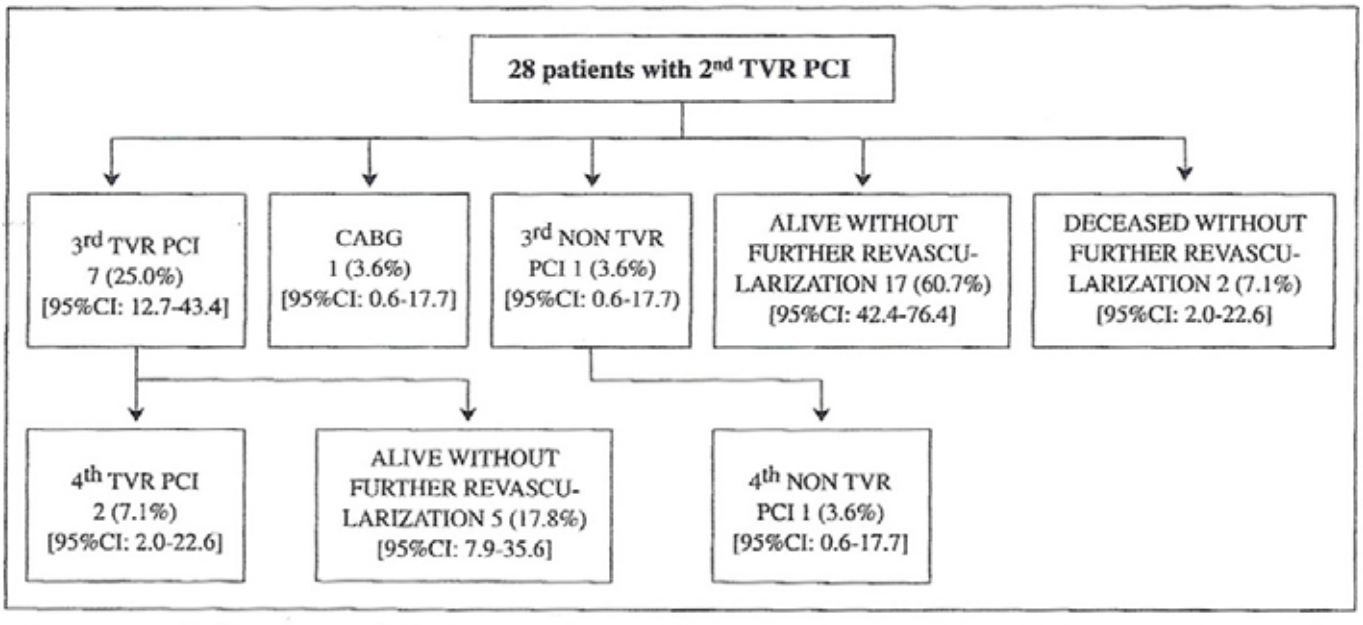

Figure 3.—Need of new revascularization procedures following a second repeat percutaneous coronary intervention, reported as N., %, and 95% confidence interval. CABG: coronary artery bypass grafting; NON TVR PCI: non target vessel revascularization percutaneous coronary intervention; TVR PCI: target vessel revascularization percutaneous coronary intervention.

low-up and maximal medical therapy remain pivotal in these patients, who can experience adverse events even several months or years following the index procedure and despite long periods of well being and freedom from angina or ischemia.

Diabetes mellitus is a recognised major risk factor for cardiovascular morbidity and mortality[12] and an independent predictor of restenosis after coronary stenting.[10] Several studies on the pathophysiology of diabetic coronary heart disease only partially explained the excess risk of adverse events by means of frequent comorbidities, conferring a crucial role to dysmetabolic features of diabetics condition itself and systemic inflammation.[2,11]

Unselected diabetics have a cardiovascular risk profile higher than patients enrolled in clinical trials. Their

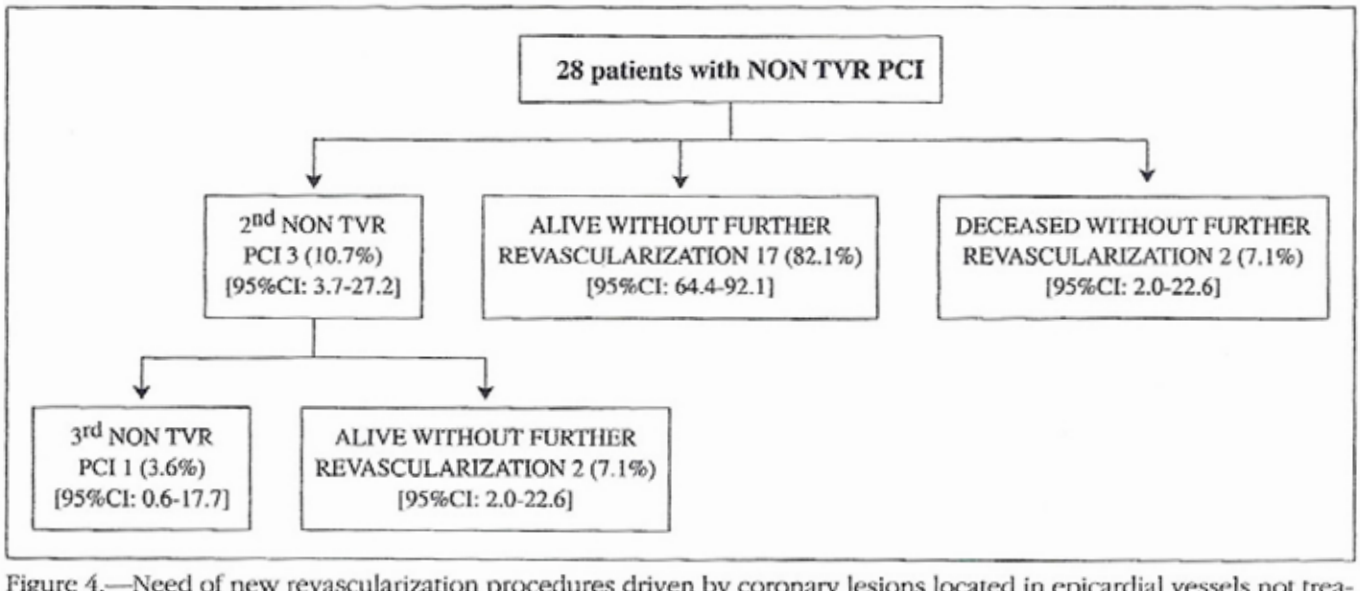

Figure 4.—Need of new revascularization procedures driven by coronary lesions located in epicardial vessels not treated during the index PCI, reported as N., %, and 95% confidence interval. CABG: coronary artery bypass grafting; NON TVR PCI: non target vessel revascularization percutaneous coronary intervention; TVR PCI: target vessel revascularization percutaneous coronary intervention.

clinical and angiographic complexity may be the plausible explanation for the relatively poor short and long term outcomes reported in this study.

Notwithstanding the rather complete revascularization obtained with the index procedure and secondary prevention medical care at discharge, more than one third of patients underwent a percutaneous or surgical re-intervention. Both in-stent restenosis and disease progression led to multiple subsequent revascularization, with no single sequence of interventions yielding complete freedom from adverse events.

Our study is unlike to randomized trials or observational studies comparing performance of drug-eluating and bare-metal stents. Instead, we examined safety and efficacy end points long after the occurrence of first adverse events. We thus obtained detailed information on the influence of diabetes on the response of these patients to percutaneous revascularization. Considerable recurrences of intervention for myocardial ischemia emerged at three-year follow-up, a long period to explore device properties, but brief when related to diabetes disease duration. The phenomenon evaluated in our analysis may thus assume greater proportions in the whole history of disease of diabetics.

Further studies based on the present design should investigate a more homogeneous population with a longer follow-up. Nonetheless, coronary revascularization maintain a prominent role in managing the heavy burden of coronary disease in diabetics, and the percutaneous approach is likely to extend its applications thanks to growing evidence for safety and efficacy of drug-eluting stents. This observational study, the first to examine the risk of recurrent averse events, adds new important information to our knowledge of coronary stenting in real-world diabetics. A randomized clinical trial clearly appears unsuited to explore an objective as complex as multiple repeat revascularizations.

Selection bias should not be a major internal study limitation because losses to follow-up were 7.9% an acceptable number given the all-comers population and the long term clinical follow-up. We cannot however exclude that primary outcome measures could be underestimated since only symptoms lead to repeat interventions and no systematic angiographic control nor testing for silent ischemia was planned.

Conclusion

In conclusion, this study, originally reporting on the risk of recurrent repeat revascularization events among diabetics treated with PCI, shows that repeat target vessel and non target vessel revascularization occurs frequently in this patient population, but can be managed in most cases in a safe and successful manner by means of repeat percutaneous intervention.

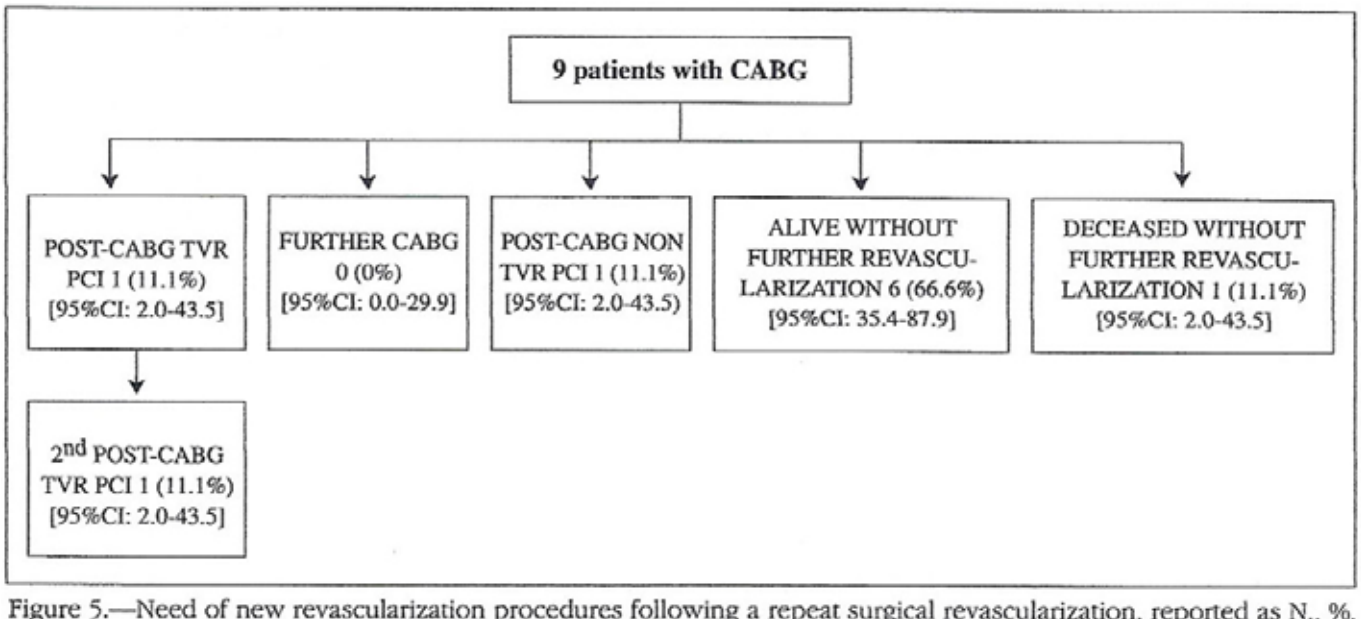

Figure 5.—Need of new revascularization procedures following a repeat surgical revascularization, reported as N., %, and 95% confidence interval. CABG: coronary artery bypass grafting; NON TVR PCI: non target vessel revascularization percutaneous coronary intervention; TVR PCI: target vessel revascularization percutaneous coronary intervention.

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Diabetes and coronary artery disease: Scary duo of the developing world

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Summary

Abstract: For many years, diabetes mellitus (DM) has been known to be an independent risk factor for atherosclerosis. However in recent years, better understanding of the relations between DM and cardiovasculary system, and especially the accumulating epidemiological evidence caused DM to be referred as "cardivascular disease equivalent" in risk evaluation. Indeed, morbidity and mortality risk related with coronary artery disease in diabetic patients is 2 - 3-fold higher than normal population. Diabetics without a history of previous myocardial infarction and non-diabetics with a history of previous myocardial infarction show similar mortality characteristics. Coronary artery disease is the primary cause of death in adult DM patients. Moreover, when acute coronary syndrome is developed in diabetic patients, both in-hospital and long-term mortality rates are higher than non-diabetics.

Keywords: Diabetes mellitus, atherosclerosis, coronary artery disease.

Introduction

Another important subject is that macrovascular complications induced by diabetes may develop years before emergence of overt diabetes. Epidemiological studies have revealed that the frequency of type 2 diabetes increases with age both in males and females. The incidence of coronary artery disease also increases with age, therefore one should take into account the fact that possibility of co-existence of these two illnesses in elderly would be high. With the aging society, the importance of this duo regarding community health will gradually increase.

While the information regarding coronary artery disease in diabetics has been known for a long time, data regarding the glucometabolic regulation in patients with coronary artery disease started to draw attention rather recently. For example, "Euro-Heart Survey on Diabetes and the Heart" have shown that 20% of the coronary artery patients have apparent diabetes, 30% of them have impaired glucose tolerance test, and 5% of them have impaired fasting glucose. Recently performed GAMI trial showed that the glucose tolerance test performed before discharge of the patients who had acute myocardial infarction, reveals previously unknown glucometabolic disorder in up to 30% of the patient, and more importantly long-term prognosis is worse in the group with impaired glucose tolerance.

Diabetes and coronary artery disease: Pathophysiological considerations

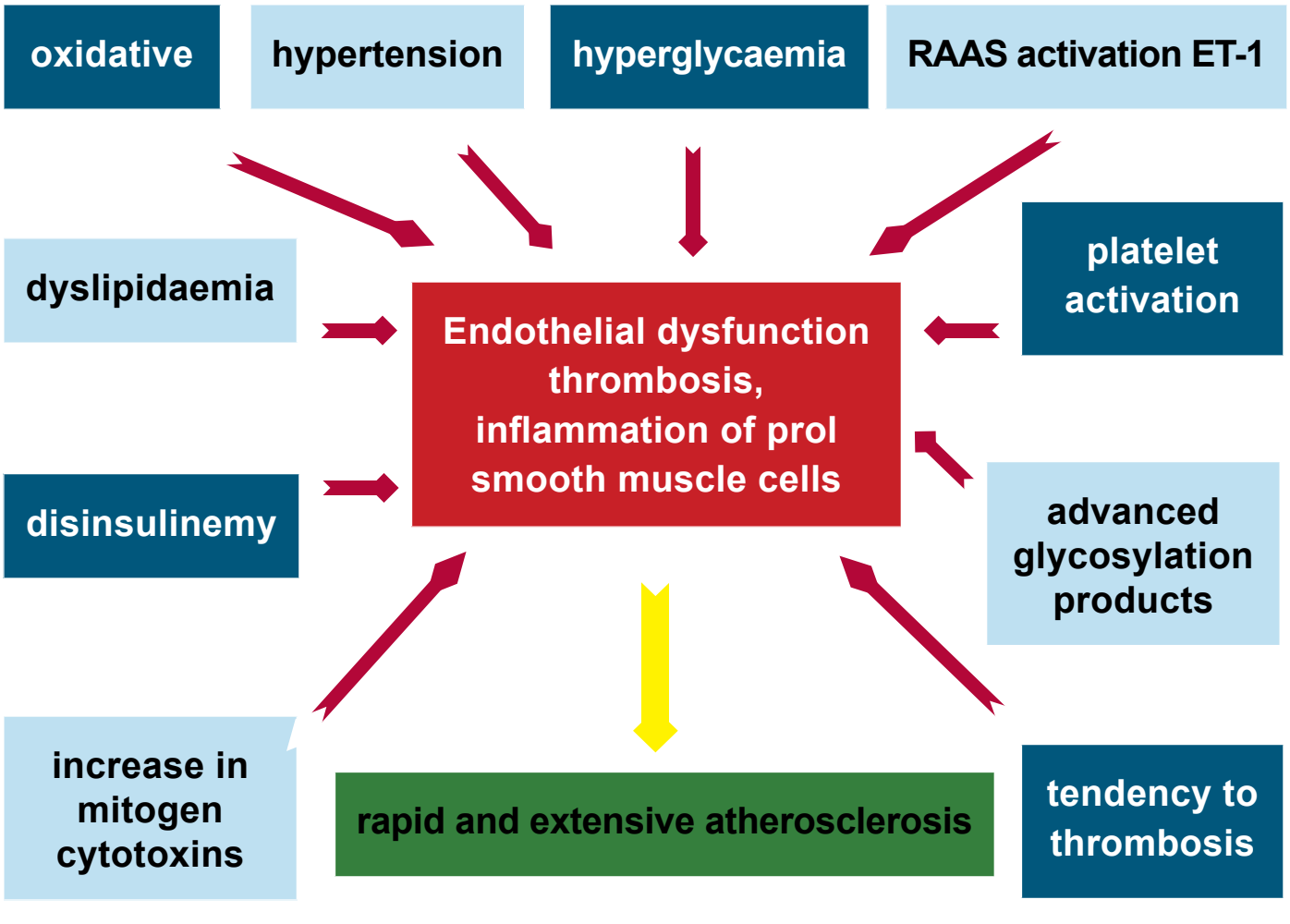
There is no doubt that risk factors such as hypertension, dyslipidemia, etc. co-existing with DM have a contribution to the development of atherosclerotic heart disease. However hyperglycemia on its own probably also has an important contribution to pathophysiology. Hyperglycemia results in production of free oxygen radical directly, and indirectly by increasing free fatty acid load. And this is known as the initiator of a process triggering many adverse the metabolic pathway, increasing vascular permeability, decreasing fibrinolytic activity and triggering inflammation.

On the other hand, there is also evidence showing that the activity of renin-angiotensin aldosterone system (RAAS) is increased in diabetic patients. These evidences led RAAS blockers to be used for treatment, and prevention of cardiovascular complications, and thus RAAS became a treatment target. Therefore now in our day, ACE inhibitors and/or angiotension receptor blockers are considered as the essential elements of the current therapy in diabetic patients.

In fact the adverse effects of diabetes on cardiovascular system are much more complicated. In **Figure 1**, the adverse effects of DM on cardiovascular system are shown. As observed, in addition to hyperglycemia and RAAS activation, there are many negative factors predisposing diabetic patient to the rapid and generalized development of atherosclerosis. New investigations have focused on the pathogenetical relations between diabetes, inflammation, atherosclerosis and atherothrombosis.

In diabetic coronary artery disease patients, multiple vessel disease, left main coronary artery disease,

Figure 1. The adverse effects of DM on cardiovascular system



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involvement of multiple vessel segments and distal lesions are seen frequently. Furthermore, diabetic atherosclerotic lesions mostly exert unstable plaque characteristis as a result of decreased collagen production, increased degradation, increased matrix metalloprotein activity and increased cytokines.

Glycemic control and coronary artery disease

The glycemia margin for the onset of atherosclerosis and cardiovascular disease in diabetics, has been tried to be explained for many years. Several trials have shown that post-prandial glycemia is an independent risk factor for cardiovascular disease. On the other hand there is evidence showing that the risk of cardiovascular event increases with the elevating fasting blood glucose levels.

While it remains controversial, in light of the available evidence, current opinion is that effective glycemic control is beneficial for prevention of cardivovascular events both type I and type II diabetics. HbA1c is the gold standard method for the monitorization and evaluation of glycemic control. The fact that each 1% increment in HbA1c may cause up to 20% increase in the risk of cardiovascular event, is highly significant.

Significant decreases in mortality have been shown after establishing good glycemic control also in patients in intensive care unit due to acute coronary syndrome. The decreased risk of mortality has been associated with the elimination of toxic effects due to acute hyperglycemia which suddenly emerges in critical patients by establishing a good glycemic control, and the direct beneficial effects of insulin treatment in critical patients.

Practical approach recommendations for diabetic patients are as follows:

1. Diabetic patients should be closely monitored and investigated for coronary artery disease.

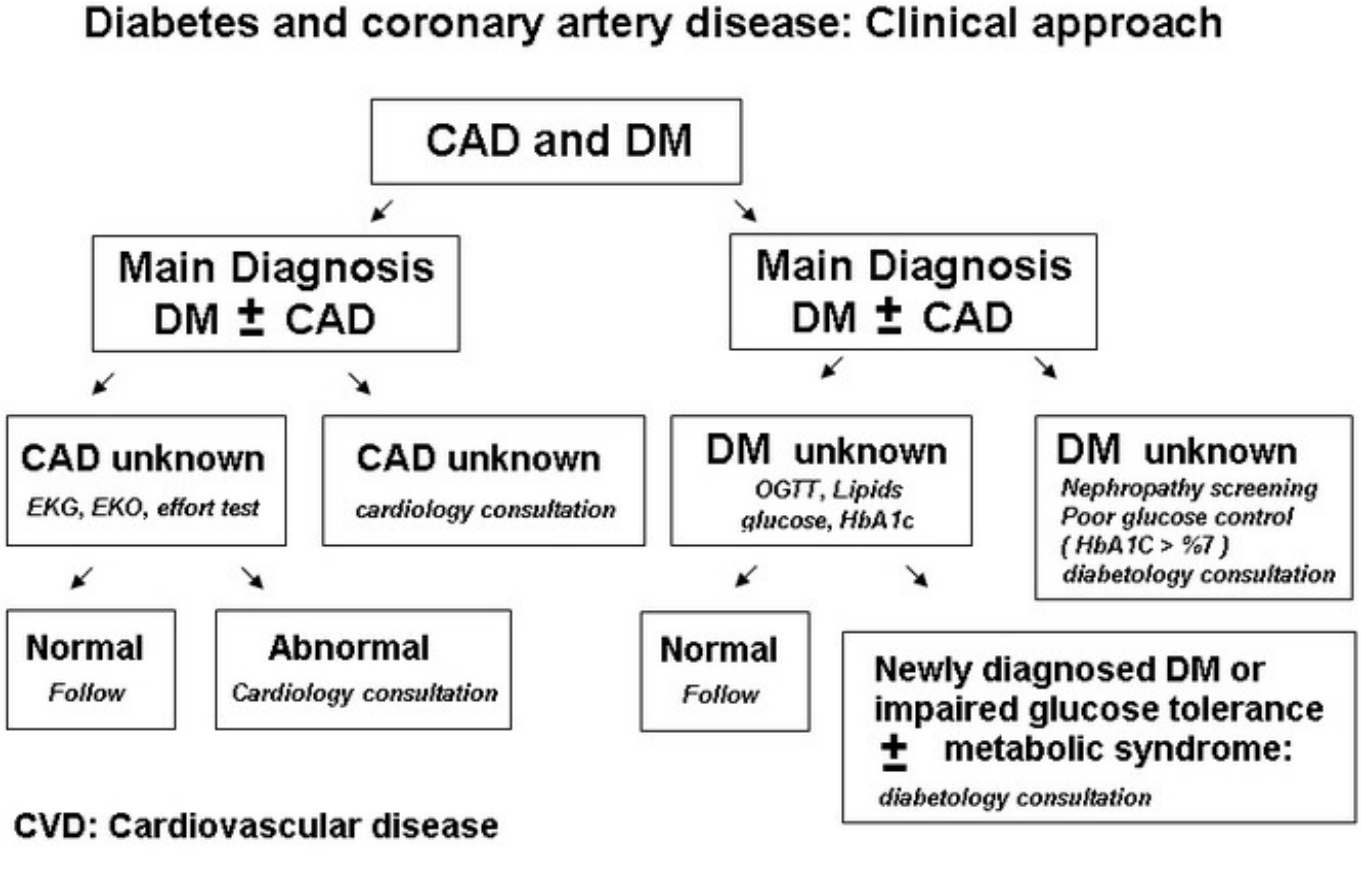
2. Concomitant risk factors (e.g., hypertension, dyslipidemia) should be detected and corrected.

3. Effective blood glucose control should be established.

4. Antithrombotic medications (aspirin, clopidogrel)

5. RAAS blockers should be given.

Risk assessment should be performed rapidly in diabetic patients having acute coronary syndrome. Fibrinolytic treatment indications in acute myocardial infarction



are similar to non-diabetics. If possible, early coronary angiography and mechanical revascularization should be preferred in diabetics. Strict blood glucose control is considered to be beneficial in acute myocardial infarction (AMI). Beta receptor blocking medications decrease morbidity and mortality in diabetics having acute coronary syndrome. Aspirin should be given in doses and indications similar to non-diabetics. However, in diabetics having acute coronary syndrome, addition of clopidogrel to aspirin should be considered. Adding ACE inhibitors to treatment in patients with diabetes and cardiovascular disease, has been shown to reduce cardiovascular events. Treatment targets in patients with diabetes and coronary artery disease are shown in **Table I**.

It is still controversial to choose coronary bypass or percutaneous coronary intervention in multiple vessel revascularization in diabetic coronary artery patients. Trials featuring surgery, are usually related with pre-stent period. Initial studies performed with stents have shown that while the mortality rates are similar, there are more revascularization procedures involved although less than before in percutaneous coronary intervention. While the use of drug-eluting stents in diabetic patients is still controversial, the tendency is towards using the drug-eluting stents in diabetic patients.

Conclusion

Diabetes and coronary artery disease are like two sides of the same coin: Today, diabetes is considered to be coronary artery disease equivalent. Many coronary cardiac patients have diabetes. One should expect that the frequency of co-existence of these duo will increase with the aging population.

As the cardiovascular complications of diabetes occur in a very wide glycemia range, prevention, early diagnosis and control of diabetes is highly important for prevention of the development of cardiovascular complications. Therefore, investigating and monitoring the diabetic patients for possible cardiovascular disease is as vitally important as evaluating the coronary cardiac patients for diabetes.

BLOOD PRESSURE 130/80 mmHg Renal impairment and 125/75 mmHg Proteinuria >1 g/24 h
STRICT BLOOD GLUCOSE CONTROL HbA1C < 6.5% / FBG < 108 mg/dL Post-prandial < 135 mg/dL T2 DM 135-160 mg/dL T1 DM
LIPID PROFILE mg/dL Total cholesterol < 175 / LDL-C < 70 HDL E > 40 / K > 46 Triglyceride > 150 / TC/HDL
Smoking cessation Mandatory Regular physical exercise >30-45 min/day Weight control BMI (kg/m2) <25 10% weight loss if overweight Waist circumference <94 in males (cm) <80 in females

Table 1. ***Recommended treatment targets for patients with diabetes and coronary artery disease***

(Modified based on the European Society of Cardiology Cardiovascular Prevention Guidelines)

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On-pump beating heart mitral valve replacement with protection of the mitral leaflets in poor ventricle patients with end stage severe mitral regurgitation

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Summary

Abstract: Mitral valve replacement (MVR) in patients with severe mitral regurgitation and poor ventricle has a high mortality and morbidity. For such patients if mitral valve repair is not possible MVR can be performed with partial or complete protection of the mitral leaflets. Herein we report 2 patients with severe mitral regurgitation and poor ventricle (EF 20%– 25%). MVR was performed by complete protection of the both anterior and posterior mitral leaflets and using the on-pump beating heart technique.Levosemindan was administered to one of the patients on induction of anesthesia. Weaning from cardiopulpunary bypass was uneventful for the both patients. The postoperative course of the 2 patients was uneventful and they were discharged on the 5th and 6th days.

Keywords: Heart valve surgey, levosemindan, cardiopulmonary bypass.

Introduction

Mitral valve surgery by using CPB in the functioning heart provides advantages in protecting cardiac functions especially in patients with reduced ventricle function, and its use recently is increasing. In patients with limited cardiac reserves, substantial morbidity and mortality increase is seen in the operations performed with arrest. Cardiac functions might be better protected with CPB guidance in the functioning heart in patients with reduced ventricle function. As cardioplegia solution is not given in the mitral valve surgery performed with CPB guidance in the functioning heart, the patient will be protected from myocardial reperfusion injury, and coronary perfusion continues. Thereby, normal cardiac physiology can be maintained with normothermic coronary perfusion.(1)

Protection of functions and geometry of left ventricle by the performed cardiac surgery is highly important. In this regard, protection of subvalvular apparatus is also highly important. Protection of subvalvular ap-

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paratus has been reported to decrease early-period mortality-morbidity and to improve the long-term survival and functional capacity.[2,3]

Levosimendan is a novel positive inotrope drug which can increase contractility without increasing intracellular calcium level and oxygen consumption, and which can be used in postoperative patients who have difficulties in getting out of CPB with decompensated cardiac failure.[4] We also used prophylactic Levosimendan to facilitate getting out of CPB in one of these patients.

Case Report 1

60-Year-old male patients admitted to our clinic with the complaints of shortness of breath, palpitation, getting tired quickly and chest pain. The patient had these complaints for nearly ten years, and as their severity increased recently; he undergone an echocardiography (EKO) in an external center, and grade 3-4 mitral regurgitation was detected. The patient had no known history, and he had inguinal hernia comorbidity. In the physical examination, blood pressure was 110/70mmHg, pulse was 80/min and arrhythmic. He had 5/6 systolic murmur in apex with auscultation. He had rales in the bilateral basal parts of the lungs with auscultation. The patient's NYHA functional capacity was III. Cardiac rhythm was in atrial fibrillation in electrocardiogram. In the telecardiogram, he had mild loading findings in basal zones of bilateral lungs, and cardiomegaly.

In EKO, he had grade 3-4 eccentric severe mitral regurgitation, ejection fraction: 25%, left ventricular end diastolic diameter: 7.0 cm, left ventricular end systolic diameter: 6.5 cm, left atrium: 6.7 cm, and diffuse hypokinetic areas were present in left and right ventricles. Also pulmonary arterial pressure of the patient with grade 2 tricuspid regurgitation was measured to be 50 mmHg. In the coronary angiography, coronary arteries were assessed to be normal. No pathology was detected in the patient's routine blood work-up.

When the patient was taken for operation with these findings, in addition to anesthesia induction, Levosimendan was initiated as 12 microgram/kg/min bolus, followed by 24-hour-infusion at 0.1microgram/kg/min. Following median sternotomy, standard aorto-bicaval cannulation was performed. CPB was initiated, cooling was not performed and cross-clamp was not put. In the normothermic functioning heart, mitral valve was reached with left atriotomy when patient was in upside-down position and aortic vent was at maximum vent. Anterior leaflet was thickened, fibrotic, and had prolapse, posterior leaflet was fibrotic and not suitable for repair. MVR was performed with 27 no St. Jude medical mechanical valve with individual pledgeted sutures by protecting the whole subvalvular apparatus (anterior and posterior leaflets were freed, and then fixed to annulus with pledgeted sutures to provide orifice, and ventricle geometry was preserved by protecting chordas).

Left atriotomy was closed, deairing was performed, cardiopulmonary bypass was ended without problems with 5 mcg dopamine and levosimendan infusion. Decannulation was completed without problems, and the patient's operation was completed without any complication. The patient's CPB duration was 80min, and operation duration was 160min. There was no problem during postoperative follow-up. He woke-up at the postoperative 3rd hour, no cerebrovascular event occurred, and he was extubated in the 15th hour. The patient was hemodynamically stable during intensive care follow-ups. He was taken into normal ward on postoperative day 1. As there was no problem in the routine work-up during postoperative period, and the patient was discharged with recovery at post-op. day 5.

Case Report 2

63-Year-old female patient was admitted with severe shortness of breath and palpitation on exertion. The patient's NYHA functional capacity was III. In the examination, blood pressure was 130/60mmHg, pulse was 92/min and arrhythmic. She had 4/6 systolic murmur in apex with auscultation. The patient's NYHA functional capacity was III. In the telecardiogram, he had mild loading findings in basal zones of bilateral lungs, and cardiomegaly. She had hypertension, and atrial fibrillation rhythm on electrocardiogram. When EKO findings were evaluated; 6.8 CM, LVESD: 5.8 CM, EF: 29%, 3O Mitral Regurgitation, CPAB: 34 mmHG, left atrium was dilated, posterior mitral valve systolic movement was limited, and it was in global hypokinesia form with more significance on inferior part.

Again, left atriotomy was performed in the functioning heart after standard procedure. Venous bleeding was observed. Subvalvular apparatus was prolonged, got thinner and not suitable for repair. 27 no ST. JUDE MEDICAL metal valve replacement and secundum ASD primary repair was performed with protection of anterior and posterior leaflets. CPB was ended without problems. CPB duration was 91 min. The patient was extubated without problems at the 14th postoperative hour, and discharged with recovery on postoperative day 6.

Discussion

Levosimendan is a novel positive inotrope drug which can increase contractility without increasing intracellular calcium level and oxygen consumption, and which can be used in postoperative patients who have difficulties in getting out of CPB with decompensated cardiac failure. The primary mechanism of action of levosimendan in increasing contractility, is based on its effect of increasing the sensitivity of cardiac troponin-C to cytoplasmic calcium.[4] During this inotropic effect, the most important aspect is the non-increasing intracellular calcium level; therefore the important side effects of adrenergic inotropes such as cardiac myositis dysfunction and arrhythmia due to increase in intracellular calcium. Diastolic relaxation is not impaired with levosimendan, and both preload and afterload of the heart are decreased as well. This process occurs by not increasing the oxygen consumption of the myocardium. Levosimendan also has an anti-ischemic effect due to its dilating effect on coronary arteries.[4,5]

Cardiac functions might be better protected with CPB guidance in the functioning heart in patients with reduced ventricle function. As cardioplegia solution is not given in the mitral valve surgery performed with CPB guidance in the functioning heart, the patient will be protected from myocardial reperfusion injury, and coronary perfusion continues. Cardiac physiology is maintained thanks to normothermia.[1,6] After the recognition of the favorable effect of preserving posterior leaflet on left ventricle functions in postoperative period, the applications for complete protection of mitral valve apparatus, continue to be performed.

The role of mitral valve apparatus is not only limited with valvular functions, it also has an important place in left ventricular functions. Results of the limited number of clinical trials performed, consistently show that protection of valve apparatus protects or improves the left ventricular functions even though different techniques are used.[7-11] In addition to the sudden afterload increase occurring after mitral valve replacement, many authors reported that the continuity impairment in annular-chordal-papillary-muscular-left ventricle wall as a result of removal of chordal structures, contributes to left ventricle dysfunction in early postoperative period. These authors also associate the better hemodynamic outcomes and low mortality obtained after the application of repair techniques in mitral regurgitation with the preservation of annular-papillary-ventricular continuity with these techniques.[8-9]

In patients with chronic mitral regurgitation, the most important cause of left ventricle dysfunction after replacement is considered to be the tension on left ventricle wall as a result of sudden afterload increase which occurs after valve replacement with the elimination of low-impedance flow to left atrium in mitral regurgitation. Left ventricle has an absolute need for continuation of chordal tension and the supportive effects in the area on which the papillary muscles are holding on to resist this sudden development of afterload.

Left ventricle can protect its contractile functions by preserving especially its diastolic sizes and ideal geometry during contraction, and by preventing the increase in cavitary pressure.[9-11] In these cases, mitral orifice was extended by cutting the anterior leaflet from 2-3 mm distance and fixing it to annulus with pledgeted sutures without harm to chordal links. Extra valvular tissue was trimmed. Posterior leaflet kept as it was.

Here, especially preserving the anterior leaflet as complete may also cause obstruction in left ventricle

outlet with the systolic forward movement of the anterior leaflet tissue. Therefore and ideal orifice should be provided. The second possible problem is the prosthetic valve dysfunction due to adverse interaction between the protected papillary muscle and its chordas and the prosthetic valve. In conclusion, we think that reconstructive surgery is appropriate for rheumatic mitral valve patients with pure mitral regurgitation or hemodynamically considerable mitral regurgitation, and in patients not suitable for reconstructive surgery, as an alternative mitral valve surgery with complete surgical protection of subvalvular apparatus is appropriate.

Mitral valve surgery by using cardiopulmonary bypass in the functioning heart is technically easy to use and may have less complications compared to conventional methods.[1]

For this patient, and in cases with low EF and high-risk of cardiac surgery, we obtained a good outcome by utilizing the effects of levosimendan and thinking that we had better protection of cardiac functions in the functioning heart Still, further experiences will contribute to our understanding on this subject.

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– Guidance for clinicians. An International Benchmarking Study. http://www.who.int/topics/surgery/ accessed: 29/09/2002.

Tables and Figures

Legends should take place on the top of the page for tables, and bottom of the page for figures and placed on separate pages. Explain all nonstandard abbreviations in footnotes.

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