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OBSERVATIONAL STUDY

Transient reduction in ejection fraction following aortic valve replacement for aortic regurgitation

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ABSTRACT

BACKGROUND: In patients following aortic valve replacement (AVR) for aortic regurgitation, a transient reduction in ejection fraction (TREF) sometimes occurs in the postoperative period without a clear remediable cause, which leads to a spontaneous improvement without the need for a specific treatment.

OBJECTIVE: To study the incidence and risk factors of TREF following AVR for aortic regurgitation.

METHODS: We designed a single-centre retrospective observational study. A total of 164 patients were enrolled in the study: 82 in the regurgitation group and 82 in the stenosis group. Data were obtained from international registries and patient documentation.

RESULTS: There were statistically significant differences in TREF between the regurgitation and stenosis groups (9.76 % and 0 %, respectively, p = 0.004). There was zero hospital mortality in both regurgitation and stenosis groups. The presence of TREF had no impact on long-term survival.

CONCLUSION: Our results show that transient reduction in ejection fraction is a relatively common phenomenon following aortic valve replacement for aortic regurgitation and that in our study population it had no effect on short- and long-term survival *(Tab. 2, Fig. 1, Ref. 15)*. Text in PDF *www.elis.sk*

KEY WORDS: transient reduction in ejection fraction, aortic valve replacement, aortic regurgitation.

What is new?

- To our knowledge this is the first study investigating the incidence and long-term mortality of patients with transient reduction of ejection fraction after aortic valve replacement for aortic regurgitation on a larger population.
- Transient reduction in ejection fraction (TREF) subsequent to aortic valve replacement for aortic regurgitation is relatively common.
- TREF does not require specific treatment and does not affect short and long-term survival.

Introduction

Severe aortic regurgitation (AR) causes a volume overload of the left ventricle and may lead to hemodynamic deterioration especially in the setting of acute AR (1 ,2).

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Although the exact prevalence of AR among adult population is not known, in clinical practice we encounter these patients relatively often (3, 4).

Aortic valve replacement is a well-established therapeutic option for treatment of severe aortic regurgitation in symptomatic or asymptomatic patients with either ventricular dilatation or reduced function (5, 6).

In this group of patients, we sometimes encounter a transient reduction in ejection fraction in the postoperative period without a clear remediable cause, leading to spontaneous improvement without the need for a specific treatment. Although in experience, this phenomenon is relatively common there are only limited data available in the literature describing its incidence or explaining the pathophysiological basis (2, 7).

Methods

Study population

We designed a single-centre retrospective study analysing patients from cardiosurgical registry *(https://www.nczisk.sk)* operated at the National Institute of Cardiovascular Diseases in Bratislava, Slovakia in the period between 2010 and 2021. The population consisted of two study groups, namely group of patients after isolated aortic valve replacement for isolated aortic regurgitation consisting of 82 patients (regurgitation group), and a matched group of patients after isolated aortic valve replacement for iso-

Tab. 1. Comparison of stenosis and regurgitation groups.

	Aortic regurgitation (n = 82)	Aortic stenosis (n = 82)	p
Patient history			
Age (years)	52.34±14.06	52.43±13.94	0.99
Male gender (%)	80.5	81.7	0.84
Weight (kg)	85.44±19.09	81.71±12.58	0.14
Height (cm)	176.29±10.31	173.49±7.8	0.051
BMI (kg/m2)	27.28±4.83	27.18±4.16	0.89
NYHA	2.38 (median 2)	2.2 (median 2)	0.36
CCS	0.65 (median 0)	1.1 (median 1)	0.06
History of PCI	0	0	–
Previous Cardiac Surgery (%)	2.44	4.88	0.41
Smoking >3 cigarettes/day (%)	2.44	3.66	0.65
Diabetes (%)	12.2	15.85	0.5
Hypertension (%)	75.1	69.51	0.382
Dyslipidaemia (%)	45.12	57.32	0.118
Hepatopathy (%)	9.76	6.1	0.386
Serum creatinine >200 μmol/l (%)	1.22	1.22	1
COPD/emphysema (%)	4.88	8.54	0.349
Asthma (%)	1.22	3.66	0.311
TIA history (%)	2.44	0	0.155
Cerebral atherosclerosis (%)	0	1.22	0.316
Atrial fibrillation pre-OP (%)	1.22	0	0.316
Pacemaker pre-OP (%)	2.44	0	0.155
Echocardiography			
Ejection fraction (%)	52.4±8.53	56.04±8.19	0.006
Aortic regurgitation (%)	100	0	–
Aortic stenosis (%)	0	100	–
Mitral stenosis (%)	0	0	–
Mitral regurgitation			0.368
1st degree (%)	29.27	21.95	
2nd degree (%)	3.66	7.32	
Tricuspid regurgitation			0.123
1st degree (%)	18.29	15.85	
2nd degree (%)	4.88	0	
3rd degree (%)	1.22	0	
Operation data			
Urgent operation (%)	17.07	2.44	0.002
Type of prosthesis			0.749
mechanical	62.2	59.76	
biological	37.8	40.24	
Prosthesis size (mm)	24.76 (Mdn = 25)	23.02 (Mdn = 23)	<0.001
CPB time (min)	59.43±26.4	65.61±25	0.012
Cross-clamp time (min)	47.28±21.23	52.06±15.68	0.001
Blood cardioplegia (%)	60.98	45.12	0.034
Transfusion on CPB (nr.)			
Red blood cells	0.59±1.19	0.34±0.77	0.279
Fresh frozen plasma	0.29±1.11	0.05±0.31	0.05
Postoperative course – ICU			
Total blood loss (%)			0.08
0–500 ml	58.54	70.73	
501–1000 ml	32.93	26.83	
>1001 ml	7.32	1.22	
Intubation time (%)			0.22
<8 h	34.15	37.81	
8–12 h	32.93	30.49	
12–24 h	24.39	30.49	
24–48 h	4.88	0	
>48 h	3.66	1.22	

lated aortic stenosis consisting of 82 patients (stenosis group).

The inclusion criteria for the regurgitation group were as follows: age > 17 years, isolated aortic valve replacement, and isolated aortic regurgitation. The exclusion criteria for the regurgitation group were as follows: other concomitant procedure, aortic stenosis, and coronary artery disease.

The inclusion criteria for the stenosis group were as follows: age > 17 years, isolated aortic valve replacement, and isolated aortic stenosis. The exclusion criteria for the stenosis group were as follows: other concomitant procedure, aortic regurgitation, and coronary artery disease. The AR and non-AR groups were matched according to parameters as follows: age, gender, and BMI.

Transient reduction in ejection fraction (TREF) was defined as a postoperative decrease in left ventricular ejection fraction by ≥ 10 % with subsequent normalisation.

For further analysis, the regurgitation group was divided into two subgroups based on the presence of TREF, particularly TREF subgroup consisting of 8 patients and non-TREF subgroup consisting of 79 patients. Three patients were excluded due to unavailability of follow-up echocardiographic and mortality data. Mean follow-up durations in TREF and non-TREF subgroups were 5.5 ± 2.8 years and 5.1 ± 3.58, respectively.

The study was approved by the Ethics Committee of the National Cardiovascular Institute, Bratislava, Slovakia.

Data collection

Baseline clinical data were obtained from cardiosurgical registry (https://www.nczisk.sk). Additional follow-up postoperative and echocardiographic data were obtained from patient documentation. Mortality data were obtained upon request from The Health Care Surveillance Authority registry (https://www.udzs-sk.sk/en).

Statistical methods

Continuous variables are presented as sample means and standard deviations. Normality of data was tested using a Shapiro–Wilk test. Paired or unpaired Student t-test and Mann–Whitney test were used to compare continuous variables as appropri-

Tab. 1.

	Aortic regurgitation (n = 82)	Aortic stenosis (n = 82)	p
Postoperative course – ICU			
Therapy (%)			
Inotropes	53.66	51.22	0.754
CPR	1.22	0	0.316
Tracheostomy	0	1.22	0.316
Electrical cardioversion	2.44	1.22	0.56
Pacemaker implantation	1.22	1.22	1
Haemodialysis/ultrafiltration	4.88	1.22	0.367
Length of stay (h)	100.45	91	0.848
Surgical revision (%)			
Requiring CPB	2.44	0	0.155
Without CPB	14.63	7.32	0.211
TIA or stroke (%)	0	2.44	0.155
Wound infection (%)	2.44	0	0.155
Urine tract infection (%)	3.66	3.66	1
Sepsis (%)	1.22	0	0.316
Bronchopneumonia (%)	2.44	0	0.155
GIT complications (%)	1.22	0	0.316
Fibrillation/flutter (%)	18.29	13.42	0.392
Other arrhythmias (%)	10.98	10.98	1
Other complications (%)	4.88	3.66	0.699
Hospital mortality (%)	0	0	-
TREF (%)	9.76	0	0.004

BMI – body mass index, NYHA – New York Heart Association functional classification, CCS – Canadian Cardiovascular Society score, PCI – percutaneous coronary intervention, COPD – chronic obstructive pulmonary disease, TIA – transient ischaemic attack, CPB – cardiopulmonary bypass, CPR – cardiopulmonary resuscitation, TREF – transient reduction in ejection fraction

ate. Categorical variables were analysed using contingency tables and Chi squared test. p values < 0.05 were considered statistically significant.

Data were analysed using StatsDirect statistical software version 3.2.10 (http://www.statsdirect.com) and JASP statistical software JASP Team (2021). JASP (0.14.1) [Computer software].

Results

Baseline characteristics

A total of 164 patients were enrolled in the study: 82 in the regurgitation group and 82 in the stenosis group. Patient characteristics are presented in Table 1. There were statistically significant differences between the regurgitation and stenosis groups in ejection fraction (52.4 ± 8.53 vs 56.04 ± 8.19 (%), respectively; p = 0.006), urgency of operation (17.07 % vs 2.44 %, respectively; p = 0.002), prosthesis size (24.76 (Mdn = 25) vs 23.02 (Mdn = 23) [mm], respectively; p < 0.001); cardiopulmonary bypass time (CPB) (59.43 ± 26.4 vs 65.61 ± 25 (min), respectively; p = 0.012), Cross-clamp time (47.28 ± 21.23 vs 52.06 ± 15.68 (min), respectively; p = 0.001), use of blood cardioplegia (60.98 % vs 45.12 %, respectively; p = 0.0034), transfusions of fresh frozen plasma during CPB (0.29 ± 1.11 vs 0.05 ± 0.031 [units], respectively; p = 0.05) and incidence of TREF (9.76 % vs 0 %, respectively; p = 0.004).

Regurgitation group was divided into two subgroups: TREF consisting of 8 patients and non-TREF subgroup consisting of 71 patients. Patient characteristics are presented in Table 2. There were statistically significant differences between the TREF and non-TREF subgroups in mitral regurgitation (1st degree 75 % vs 23.94 %, respectively and 2nd degree 0 % vs 4.23 %, respectively; p = 0.016), total blood loss (0–500 ml: 25 % vs 63.38 %, respectively; 501–1000 ml: 50 % vs 29.58 %, respectively; > 1001 ml: 25 % vs 5.63 %; respectively; p = 0.045), cardiopulmonary resuscitation in postoperative period (12.5 % vs 0 %, respectively; p = 0.003).

Maximal decrease in ejection fraction was observed in average on postoperative day 6.75 ± 3.73.

Normalisation of ejection fraction was observed in average after 11.57 ± 7.04 days after maximal decrease.

There was zero hospital mortality in both regurgitation and stenosis groups.

The presence of TREF had no impact on long-term survival (0%), mean follow-up was 5.5 ± 2.8 years in TREF, 11.27 % (4.23 % cardiac), mean follow-up 5.1 ± 3.58 years in non-TREF, Log-rank p = 0.307) (Fig. 1).

Discussion

In our study population, transient reduction in ejection fraction following aortic valve replacement occurred only in patients operated for aortic regurgitation. The incidence of TREF was 9.75

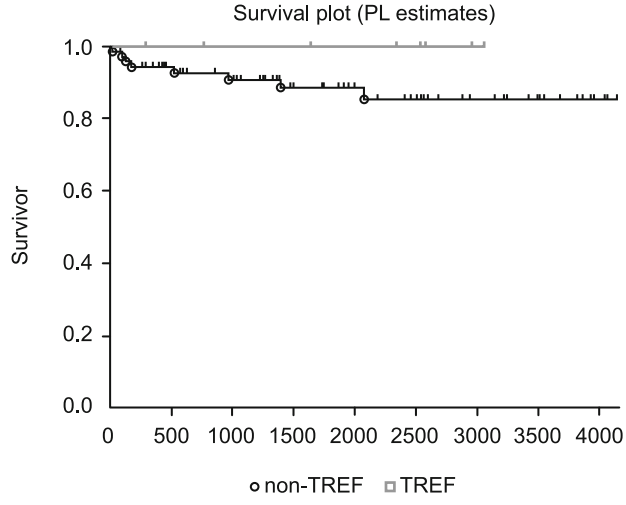

Fig. 1. Kaplan-Meier plot comparing survival of TREF and non-TREF subgroups.

Tab. 2. Comparison of TREF and non-TREF subgroups.

	TREF (n = 8)	Non-TREF (n = 71)	p
Patient history			
Age (years)	54.38±11.76	52.24±14.26	0.801
Male gender (%)	83.1	75	0.57
Weight (kg)	79±21.14	86.1±19.23	0.33
Height (cm)	175.29±11.99	176.41±10.29	0.719
BMI (kg/m2)	25.44±4.81	27.46±4.87	0.354
NYHA	2.25 (median 2)	2.37 (median 2)	0.909
CCS	0.67 (median 0)	0.75 (median 0.5)	0.839
History of PCI	0	0	–
Previous Cardiac Surgery (%)	0	2.82	0.631
Smoking >3 cigarettes/day (%)	0	1.41	0.736
Diabetes (%)	0	11.29	0.317
Hypertension (%)	62.5	77.47	0.948
Dyslipidaemia (%)	37.5	47.89	0.577
Hepatopathy (%)	0	8.45	0.392
Serum creatinine >200 µmol/l (%)	0	1.41	0.736
COPD/emphysema (%)	0	4.23	0.553
Asthma (%)	0	1.41	0.736
TIA history (%)	0	2.82	0.631
Cerebral atherosclerosis (%)	0	0	–
Atrial fibrillation pre-OP (%)	0	1.41	0.736
Pacemaker pre-OP (%)	0	2.82	0.631
Echocardiography			
Ejection fraction (%)	48.13±8.84	52.77±8.55	0.124
Aortic regurgitation (%)	100	100	–
Aortic stenosis (%)	0	0	–
Mitral stenosis (%)	0	0	–
Mitral regurgitation			0.016
1st degree (%)	75	23.94	
2nd degree (%)	0	4.23	
Tricuspid regurgitation			0.579
1st degree (%)	37.5	16.9	
2nd degree (%)	0	4.23	
3rd degree (%)	0	1.41	
Operation data			
Urgent operation (%)	25	16.9	0.57
Type of prosthesis			0.469
mechanical	75	61.97	
biological	25	38.03	
Prosthesis size (mm)	24.63 (Mdn = 27)	24.78 (Mdn = 25)	0.88
CPB time (min)	64.86±28.58	59.07±26.82	0.581
Cross-clamp time (min)	51±22	47.01±21.69	0.536
Blood cardioplegia (%)	62.5	63.38	0.921
Transfusion on CPB (nr.)			
Red blood cells	0.028±0.237	0	–
Fresh frozen plasma	0.028±0.237	0	–
Postoperative course – ICU			
Total blood loss (%)			0.045
0–500 ml	25	63.38	
501–1000 ml	50	29.58	
> 1001 ml	25	5.63	
Intubation time (%)			0.533
<8 h	25	36.62	
8–12 h	25	32.39	
12–24 h	25	23.94	
24–48 h	12.5	4.23	
>48 h	12.5	2.82	

% in the regurgitation group and 0 % in the stenosis group. Patients with coronary artery disease were excluded to rule out the possible effect of insufficient myocardial protection (8). To avoid a drop in the number of patients in the study population, the matching based on age, gender and BMI was limited, which resulted in several statistically significant differences between the study groups. These differences are in line with the distinct risk profiles of patients suffering from aortic regurgitation and stenosis (9). Urgent operations, mainly due to infective endocarditis, were more common in the regurgitation group, which also explains more frequent transfusions of fresh frozen plasma during CPB. Differences in total CPB and cross-clamp time are expectedly longer in the setting of aortic stenosis due the more technically demanding valve excision and need for annular decalcification. A more flexible non-degenerate annulus and more frequent annular dilatations in the setting of aortic regurgitation explain the difference in the prosthesis sizes. Several studies demonstrate superior myocardial protection of blood cardioplegia as compared to crystalloid (10, 11), potentially explaining the difference in postoperative LV function. However, the use of blood cardioplegia was significantly more common in the regurgitation group. A study by Dubroff et al (7) suggested that the depression of systolic function may be due to altered loading conditions, myocardial depression secondary to ischaemic arrest during surgery and/or by anaesthesia, or by reversal of the prolonged effects of long-term volume overload. The anaesthetic management in terms of medication used, dosing, or postoperative care did not differ between the two groups. Furthermore, the impact of ischaemia was arguably more significant in the stenosis group due to longer CPB and cross-clamp times, less frequent use of blood cardioplegia and possibly worse myocardial protection in the setting of myocardial hypertrophy (12, 13). We thus hypothesise that this transient depression reflects mainly the time necessary for the reversal of compensation mechanisms developed during volume overload and that particularly the sudden drop in ventricular preload does not allow for an effective involvement of extended myocardial fibres.

Tab. 2.

	TREF (n = 8)	Non-TREF (n = 71)	p
Therapy (%)			
Inotropes	37.5	56.34	0.310
CPR	12.5	0	0.003
Tracheostomy	0	0	–
Electrical cardioversion	0	1.41	0.736
Pacemaker implantation	0	1.41	0.736
Haemodialysis/ultrafiltration	0	2.82	0.631
Length of stay (h)	128±115.71	98.24±57.77	0.839
Surgical revision (%)			0.334
Requiring CPB	0	2.82	
Without CPB	50	11.27	
TIA or stroke (%)	0	0	–
Wound infection (%)	0	2.82	0.631
Urine tract infection (%)	0	4.23	0.553
Sepsis (%)	0	1.41	0.736
Bronchopneumonia (%)	12.5	1.41	0.058
GIT complications (%)	0	1.41	0.736
Fibrillation/flutter (%)	12.5	19.72	0.622
Other arrhythmias (%)	25	9.86	0.201
Other complications (%)	0	5.63	0.491
Hospital mortality (%)	0	0	–

BMI – body mass index, NYHA – New York Heart Association functional classification, CCS – Canadian Cardiovascular Society score, PCI – percutaneous coronary intervention, COPD – chronic obstructive pulmonary disease, TIA – transient ischaemic attack, CPB – cardiopulmonary bypass, CPR – cardiopulmonary resuscitation, TREF – transient reduction in ejection fraction

To investigate potential risk factors for the development of TREF we further analysed the regurgitation group. Three patients with reduction of EF by > 10 % postoperatively were excluded due to unavailable follow-up post discharge. Two patients died of non-cardiac causes (trauma and complications related to alcohol abuse) and one patient discontinued their ambulatory visits.

There was a significant difference in mitral regurgitation between the two groups. It can be argued that in the setting of combined mitral and aortic regurgitations antegrade cardioplegia administration (which is the preferred method of administration at our institution) may lead to inadequate myocardial protection. The information about cardioplegia administration was missing/incomplete in four patients, however, in four patients it was specified that cardioplegia was administered via direct ostial coronary cannulation.

Total blood loss was significantly higher in the TREF subgroup. We assume that reduced oxygen supply and compensatory sympathetic response (15) in the setting of acute bleeding might have contributed to the depression of ventricular function following sudden haemodynamic alterations following valvular replacement.

One patient in the TREF subgroup was resuscitated in early postoperative period. Echocardiography showed ejection fraction to be reduced to 15–20 % with global hypokinesis. Selective coronarography was performed to rule out coronary occlusion by prosthetic valve, revealing coronary spasm of the right coronary artery (RCA). The event was concluded as a consequence of coronary spasm treated by local administration of calcium channel blockers.

However, no wall-motion abnormalities were present, hypokinesia was global, not limited to the area supplied by RCA and the the coronary spasm could have been catheter-induced (15).

Following this episode, the hospital course was otherwise uneventful, and the patient was discharged to ambulatory care with normalisation of ejection fraction to the preoperative value.

There was no significant difference in both hospital and long-term mortality between the two groups suggesting a benign nature of this phenomenon. However, these patients pose both diagnostic and therapeutic challenge. On one hand, unnecessary invasive examinations or heart failure treatment are associated with their own adverse effects. On the other hand, missing important remediable causes such as coronary obstruction might lead to serious, potentially life-threatening complications.

We believe that our results encourage further research on incidence, potential risk factors and diagnostic approach allowing exact identification of TREF.

Study limitations

Our study has several limitations. The study is observational and retrospective. The study population is relatively small, especially that of the TREF subgroup, not allowing sufficient identification and analysis of risk factors. Lastly, follow-up included only mortality and echocardiography.

Conclusion

Our results show that transient reduction in ejection fraction is a relatively common phenomenon following aortic valve replacement for aortic regurgitation as well as that in our study population it had no effect on short- and long-term survival.

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