RESEARCH ARTICLE

DOI: 10.4274/ijca.2023.47955
Int J Cardiovasc Acad 2023;9(4):82-87

Assessment of the Extent of Myocardial Injury in Patients Undergoing Transvenous Implantation of a Pacemaker Using Cardiac Troponin I as a Marker of Structural Heart Damage and Its Relation to Different Sites of RV Implantation

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Abstract

Background and Aim: This study aimed to evaluate the degree of myocardial injury that occurs after transvenous pacemaker implantation using cardiac troponin I (cTnI) as a myocardial injury marker and the relationship between the number of screws, different sites of right ventricle (RV) lead implantation, and myocardial injury.

Materials and Methods: Fifty patients at Ain Shams University Hospitals who underwent transvenous implantation of single- or dual-chamber permanent pacemakers were included in the study. According to the site of RV lead implantation, the study population was divided into 2 equal groups, 25 patients each. In the first group, the RV lead was implanted in the RV apex and in the other group, the RV lead was implanted in the RV septum.

Results: In all patients, the cTnI level was elevated after pacemaker implantation, showing a significant relationship between transvenous pacemaker implantation and the incidence of myocardial injury. Comparing the RV apical pacing group with the RV septal pacing group, a greater rise in cTnI was recognized in the septal RV pacing group, indicating a significant relationship between the site of RV lead implantation and the degree of myocardial injury being more in the RV septum than in the RV apex. Moreover, the higher the number of attempts of screwing the lead in different RV sites caused more rise in cTnI, denoting a significant relationship between the number of screwing attempts and the extent of myocardial injury.

Conclusion: Transvenous pacemaker implantation is associated with an increased incidence of myocardial injury, and septal RV lead implantation is associated with a higher degree of myocardial injury than apical RV lead implantation. In addition, a higher number of screwing attempts of the RV lead into the myocardium is associated with a higher degree of myocardial injury.

Keywords: Apical RV pacing, septal RV pacing, myocardial injury, pacemaker implantation

To cite this article: Ali MM, Damanhoury HM, Badran HA, Fakhry EE. Assessment of the Extent of Myocardial Injury in Patients Undergoing Transvenous Implantation of a Pacemaker Using Cardiac Troponin I as a Marker of Structural Heart Damage and Its Relation to Different Sites of RV Implantation. Int J Cardiovasc Acad 2023;9(4):82-87

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Received: 10.06.2023
Revised: 04.09.2023
Accepted: 18.09.2023
Published Online: 07.12.2023

***Only the abstract was previously presented at the conference of our university as an obligatory step to register the manuscript in our university.**

INTRODUCTION

Myocardial injury is defined as an elevation of cardiac troponin (cTn) with at least one value above the 99th percentile upper reference limit. It is considered acute if there is a rise and/or fall in cTn values[1]. Cardiac troponin I (cTnI) is a part of the cardiac contractile apparatus, the troponin-tropomyosin complex. It is a very sensitive laboratory marker of myocardial cell necrosis and a gold standard measurement for detecting myocardial injury. Elevated cTnI levels may be associated with a variety of clinical conditions such as myocardial infarction, acute pulmonary edema, ventricular tachycardia, shock, and acute renal impairment[2]. Transvenous insertion of endocardial pacemaker leads is accompanied by cTnI elevation, representing myocardial damage secondary to the direct myocardial trauma elicited by pacing leads[3]. The right ventricular (RV) apex was previously the preferred site for RV lead placement because of its ease of implantation and low risk of lead dislodgement. With the development of active fixation leads, alternative RV pacing sites have been explored, including the RV outflow tract, RV septum, His bundle, and left bundle area. Pacing from these sites is thought to be more physiological, engaging the Purkinje fibers earlier than apical pacing, thus reducing the electric and mechanical dyssynchrony associated with RV apical pacing[4]. In this study, we aimed to evaluate the degree of myocardial injury using cTnI in patients undergoing permanent pacemaker implantation and its relation to different sites of RV lead implantation and the number of RV lead screwing attempts into the RV myocardium.

MATERIALS AND METHODS

This study was approved by the Ain Shams University Faculty of Medicine Research Ethics Committee (no: MS 252/2020, date: 01.04.2020), and all patients signed an informed written consent for participation in the study in accordance with the Declaration of Helsinki. Fifty patients undergoing transvenous implantation of single- or dual-chamber permanent pacemakers were included in the study. According to the site of RV lead implantation, the study population was divided into 2 equal groups, 25 patients each. In the first group, the RV lead was implanted in the RV apex and in the other group, the RV lead was implanted in the RV septum. The study protocol was approved by the scientific and ethical committees. The study included patients above 18 years old, undergoing implantation of single or dual chamber permanent pacemakers with normal pre-procedural cTn values. Those patients were excluded from the study: Patients with previously implanted permanent pacemaker and undergoing re-implantation for any reason, patients with recent active cardiac condition such as myocardial infarction, acute pulmonary edema, cardiogenic shock, and ventricular tachycardia within one month prior to pacemaker implantation, and patients with any form of active infection were excluded from the study. All patients were subjected to 1) Full history taking including age, sex, presence of cardiovascular risk factors such as smoking, hypertension, diabetes mellitus, family history of premature cardiovascular disease, presence or absence of chronic kidney disease, and past history of implantation of a permanent pacemaker. 2) Resting 12 leads surface electrocardiogram: Twelve leads surface electrocardiogram was performed in all patients before and after the procedure. 3) Fluoroscopy data: Fluoroscopy findings of the implantation procedure were obtained to assess the site of implantation of the RV lead and the number of attempts of lead screwing. The lead position was also confirmed via fluoroscopy. 4) Measurement of cTn level: Blood samples for cTnI (using VIDAS® TNHS kit) using were obtained before the procedure and 12 h after the procedure with normal reference ranged from (0-34) pg/mL. Peri-procedural myocardial injury was diagnosed in the presence of elevated cTn values with at least one value above the 99th percentile upper reference limit. 5) Echocardiography: Echocardiography was performed in all patients before the procedure, which showed normal left ventricle (LV) and RV functions and dimensions.

Statistical analysis

Revised data were collected and entered for analysis using the Statistical Package for Social Science (IBM SPSS) version 23. Parametric quantitative data are presented as mean, standard deviation, and range, whereas non-parametric quantitative data are presented as median and interquartile range. Numbers and percentages are used to present qualitative variables. Comparing groups with qualitative data was done using chi-square test, but when the expected count in any cell was less than 5, Fisher's exact test was used. Comparing groups with parametric quantitative data was done by using independent t-test, while comparing groups with non-parametric quantitative data was done by using Mann-Whitney U test. Comparing two paired groups with non-parametric quantitative data was done by Wilcoxon test. The correlation between two quantitative variables in the same group was assessed using Spearman correlation coefficients. The confidence interval was set to 95% and the margin of error accepted was set to 5%; thus, the *P*-value was interpreted as follows: *P*-value >0.05 was non-significant, *P*-value <0.05 was significant, and *P*-value <0.01 was highly significant.

RESULTS

The current study included 50 individuals. All patients underwent pacemaker implantation. Troponin I levels were measured for all patients both before and 12 h after the intervention. The study population was divided equally into two groups: (group A) 25 patients (50.0%) with the RV lead implanted into the RV apex and (group B) 25 patients (50.0%)

with the RV lead implanted into the septum. Their age ranged from 39 to 75 years, with a mean age of 59.56 ± 8.53 years. Among the two groups, there were 39 males (78.0%) and 11 females (22.0%). Regarding smoking habits, 26 patients (52.0%) were smokers and 24 patients (48.0%) were non-smokers.

Regarding diabetic status, 18 patients (36.0%) were non-diabetic (HbA1C less than 6.5% according to definition of Diabetes Mellitus by American Diabetes Association) and 32 patients (64.0%) were diabetic.[5] Regarding hypertension, 19 patients (38.0%) were non-hypertensive and 31 patients (62.0%) were hypertensive (Table 1). The median number of screws was 2 (1-3) for all patients (Table 2). Twenty patients in group A and 20 patients in group B received dual chamber pacemaker implantation, whereas only five patients in each group received single chamber pacemaker implantation, with no statistically significant difference between the 2 groups (*P*-value: 1). There was no significant relationship between age (*P*-value: 0.233), sex (*P*-value: 0.806), smoking history (*P*-value: 0.353), diabetic status (*P*-value: 0.991), hypertension (*P*-value: 0.701), and incidence of myocardial injury (Table 3, 4). Regarding the relationship between demographic data and post-procedural increase in troponin level in folds, there were no statistically significant differences regarding sex, smoking, presence of diabetes and hypertension, and the increase in troponin level (Table 5). There were no statistically significant differences between age and pre- and postprocedural troponin levels (Table 6). Regarding the relationship between permanent pacemaker implantation and post-procedural rise in troponin level, the median troponin level in the whole study group before implantation was 8 pg/mL (3-10) while median troponin level after implantation was 128 pg/mL (43-227) with a median increase fold of 20.19 (12.25-29.94). Therefore, there was a statistically significant relationship between pacemaker implantation and incidence of myocardial injury (*P*-value >0.001) (Table 7). Regarding the relationship between the two groups regarding myocardial injury in the apex group, the median troponin level before implantation was 3 pg/mL (2-8), while in the septum group it was 9 pg/mL (7-10). In the apex group, the median troponin level after implantation was 43 pg/mL (20-115) with a median increase fold 12 (9.7-21.5), whereas in the septum group, it was 204 pg/mL (135-365) with a median increase fold of 21 (20-30.42). There was a statistically significant difference between the two groups regarding the extent of myocardial injury, which was higher in the septum RV lead implantation group (Table 8, 9) (*P*-value: <0.0001). There was a statistically significant relationship between the number of attempts to screw the RV lead and the degree of myocardial injury (*P*-value: <0.0001) (Table 10) (Figure 1). Multivariate analysis showed no statistically significant correlation between age, sex, hypertension, smoking, diabetes, and the rise in troponin fold in both groups.

Table 1: Demographic data

		Number	%
Sex	Female	11	22.0%
	Male	39	78.0%
Smoker	Non-smoker	24	48.0%
	Smoker	26	52.0%
Diabetic	No	18	36.0%
	Yes	32	64.0%
Hypertensive	No	19	38.0%
	Yes	31	62.0%

Table 2: Number of screwing

Number of screwing	Median (IQR)	2 (1-3)
	Range	1-5

IQR: Interquartile range

DISCUSSION

In this study, 50 patients were scheduled for permanent pacemaker implantation. Troponin I levels were measured in all patients both before the procedure and 12 h after the procedure. They were divided into two equal groups, apical and septal, according to the site of RV lead implantation.

In the current study, there was a statistically significant relationship between the site of RV lead implantation and the degree of myocardial injury. Troponin I was higher in the septal group than in the apical group (*P*-value: <0.0001), which may represent deeper implantation of the RV lead in the septal group. Troponin I elevation was higher with an increased number of attempts to screw the RV lead into the myocardium

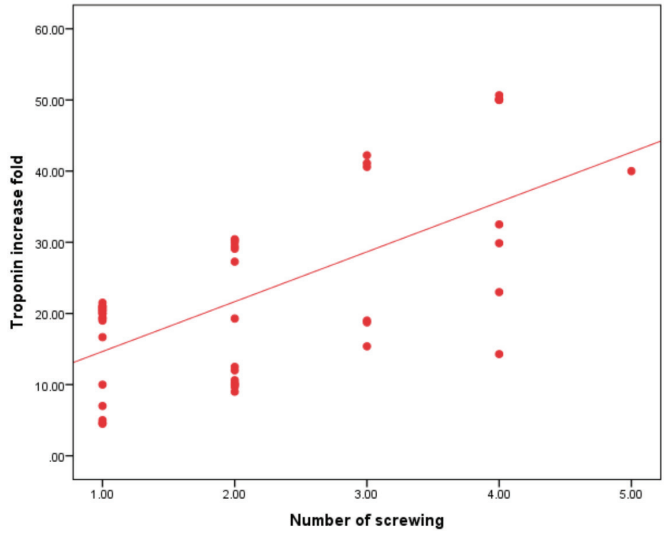

Figure 1: Correlation between number of screwing and troponin increase fold

Table 3: Relationship between demographic data and pre-procedural troponin level

		Troponin before (pg/mL)		*P*-value	Significance
		Median (IQR)	Range		
Sex	Female	7 (2-9)	2-10	0.396	NS
	Male	8 (4-10)	0-13		
Smoker	Non-smoker	7 (2-9)	0-12	0.125	NS
	Smoker	8 (5-10)	0-13		
Diabetic	No	6 (2-8)	0-10	0.062	NS
	Yes	8.5 (5-10)	0-13		
Hypertensive	No	8 (4-10)	0-13	0.265	NS
	Yes	7 (2-9)	0-12		

IQR: Interquartile range, *P*-value >0.05: Non-significant; *P*-value <0.05: Significant; *P*-value <0.01: Highly significant

Table 4: Relationship between demographic data and post-procedural troponin level

		Troponin after (pg/mL)		*P*-value	Significance
		Median (IQR)	Range		
Sex	Female	135 (43-190)	18-380	0.870	NS
	Male	120 (41-239)	5-501		
Smoker	Non-smoker	110 (34-169)	5-500	0.137	NS
	Smoker	175 (65-300)	11-501		
Diabetic	No	117.5 (20-152)	11-500	0.127	NS
	Yes	162.5 (65-282.5)	5-501		
Hypertensive	No	163 (45-303)	11-501	0.294	NS
	Yes	105 (37-225)	5-500		

IQR: Interquartile range, NS: Non-significant, *P*-value >0.05: NS; *P*-value <0.05: Significant; *P*-value <0.01: Highly significant

Table 5: Relationship between demographic data and post-procedural increase fold of troponin level

		Troponin increase fold		*P*-value	Significance
		Median (IQR)	Range		
Sex	Female	20 (10-41.11)	9-50.67	0.806	NS
	Male	20.38 (12.5-29.88)	4.5-50.1		
Smoker	Non-smoker	19.29 (10.63-23)	4.5-50.67	0.353	NS
	Smoker	20.8 (16.67-30)	4.63-50.1		
Diabetic	No	20 (12-30.3)	5-50.67	0.991	NS
	Yes	20.4 (12.5-29.88)	4.5-50.1		
Hypertensive	No	20.19 (15.38-30.3)	4.5-50.1	0.701	NS
	Yes	20.2 (10.63-29.88)	4.63-50.67		

IQR: Interquartile range, *P*-value >0.05; NS: Non-significant; *P*-value <0.05: Significant; *P*-value <0.01: Highly significant

Table 6: Relationship between age and pre, post procedural troponin level

	Troponin					
	Before		After		Increase fold	
	R	*P*-value	r	*P*-value	r	*P*-value
Age	0.097	0.501	0.020	0.888	-0.176	0.233

P-value >0.05: Non-significant; *P*-value <0.05: Significant; *P*-value <0.01: Highly significant

(*P*-value: <0.0001). Of note, there was a statistically significant relationship between pacemaker implantation in all patients regardless of the site of implantation of the RV lead and the incidence of myocardial injury (*P*-value <0.001).

In 2011, Nikolaou et al.[6] studied the effect of implantation of an endocardial permanent pacemaker on myocardial injury using cTnI. During a period of 3 years, 283 patients underwent pacemaker implantation. A normal level of cTnI before pacemaker implantation was required as an inclusion criterion. six hours after the procedure, cTnI was measured in all patients. Elevated cTnI levels were found in 167 patients (59%, 95% CI: 0.53-0.64). There was no clinical evidence of an acute coronary syndrome before or during pacemaker implantation; moreover, coronary angiography showed no significant coronary lesions. They concluded that cTnI elevations following pacemaker implantation may exceed levels that correspond to minimal myocardial damage[6].

Regarding the active fixation of the RV lead into the myocardium and the number of attempts of screwing to achieve the best pacing thresholds, Saxonhouse et al.[7] in 2005 studied whether active fixation leads cause myocardial injury at the time of implantation, indicated by the current of injury that may result in an acute rise in pacing thresholds. Sixty-five patients undergoing pacemaker implantation with active fixation leads were included in this study. The current of injury was defined as the duration of the intracardiac electrogram (EGM) and the amplitude of ST-segment elevation. Pacing parameters were measured up to 10 min after lead fixation. Ninety-six active fixation leads were included in the study, and 76 leads had current of injury. From baseline to the time of lead fixation, the duration of the EGM in ventricular leads increased from 150 +/- 31 ms to 200 +/- 25 ms (*P*-value <0.001), and the ST-segment elevation increased from 1.5 +/- 0.2 mV to 10.0 +/- 2.0 mV (*P*-value <0.001), followed by improvement in pacing thresholds from 1.5 +/- 0.4 V to 0.8 +/- 0.3 V (*P*-value <0.001) at 10 min. Atrial leads with an evident current of injury had

Table 7: Relationship between permanent pacemaker implantation and pre, post-procedural troponin level

		Troponin (pg/mL)
Before	Mean ± SD	6.76±3.66
	Median (IQR)	8 (3-10)
	Range	0-13
After	Mean ± SD	163.94±137.64
	Median (IQR)	128 (43-227)
	Range	5-501
Increase fold	Mean ± SD	50.67±22.68
	Median (IQR)	20.19 (12.25-29.94)
	Range	4.50-50.67
Mean difference	Mean ± SD	157.15±19.10
Wilcoxon signed-rank test		6.154
P-value		<0.001 (HS)

IQR: Interquartile range, SD: Standard deviation, *P*-value >0.05: Non-significant; *P*-value <0.05: Significant; *P*-value <0.01: HS: Highly significant

Table 8: Relationship between site of RV lead implantation and post-procedural troponin level

		Troponin after (pg/mL)		*P*-value	Significance
		Median (IQR)	Range		
Site of RV lead	Apex	43 (20-115)	5-239	<0.0001	HS
	Septum	204 (135-365)	104-501		

IQR: Interquartile range, HS: Highly significant, *P*-value >0.05: Non-significant; *P*-value <0.05: Significant; *P*-value <0.01: HS

Table 9: Relationship between site of RV lead implantation and post-procedural increase fold of troponin

		Troponin increase fold		*P*-value	Significance
		Median (IQR)	Range		
All patients		20.19 (12.25-29.94)	4.50-50.67		
Site of RV lead	Apex	12 (9.7-21.5)	4.50-50.67	<0.0001	HS
	Septum	21 (20-30.42)	16.67-50.10		

IQR: Interquartile range, HS: Highly significant, *P*-value >0.05: Non-significant; *P*-value <0.05: Significant; *P*-value <0.01: HS

Table 10: Correlation between number of attempts of screwing and pre, post procedural troponin level

	Troponin					
	Before		After		Increase fold	
	R	*P*-value	r	*P*-value	R	*P*-value
Number of screwing	0.127	0.380	0.374**	0.007	0.497**	<0.0001

**We evaluate the correlation between the number of attempts to screw the right ventricular lead into the right ventricle and the troponin fold increase after pacemaker implantation, so that the values before and after implantation and their fold increase were correlated with the number of screw attempts

almost similar results. Of the 20 leads with no current of injury, 5 were acutely dislodged and 15 had elevated pacing thresholds in 10 min, necessitating lead repositioning. They concluded that the presence of a current of injury indicates that within 10 min of lead implantation, the pacing threshold will be in an acceptable range even if the initial pacing threshold was elevated. However, without a current of injury, lead fixation is inadequate and must be repositioned. Therefore, they demonstrated that active fixation of the RV lead causes myocardial injury at the time of implantation represented in the current of injury, and without adequate current of injury, the lead must be repositioned until adequate current of injury is achieved[7]. Our results were concordant with the results of this study, but we used cTnI as the biomarker of myocardial injury, which showed a significant increase with increasing number of attempts to lead into the myocardium (*P*-value: <0.0001).

Chen et al.[8] demonstrated that implantation of pacemakers was associated with cTn T elevation in 55.6% of the patients 6 h after the procedure, but this was related to complications and adverse cardiac outcomes at 1 year follow-up. They also showed that gender, NT-pro-BNP at baseline, left ventricle EF, eGFR, and fluoroscopy time were independent predictors of cTn T elevation.[8]

Study limitation

This study was a single-center study with a limited number of patients. We recommend having a larger-scale multi-center study with long-term follow-up. The clinical significance of troponin elevation after pacemaker implantation is unknown, and a follow-up study is needed to assess the clinical significance.

CONCLUSION

Permanent pacemaker implantation is associated with an increased incidence of myocardial injury, and septal RV lead implantation is associated with a higher extent of myocardial injury than apical RV lead implantation.

Increasing the amount of screws during active fixation attempts is associated with a higher degree of myocardial injury.

Although the clinical significance of myocardial injury after pacemaker implantation is unknown, a follow-up study is needed to assess its clinical significance.

Ethics

Ethics Committee Approval: This study was approved by the Ain Shams University Faculty of Medicine Research Ethics Committee (no: MS 252/2020, date: 01.04.2020)

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.E.F., Concept: H.M.D., Design: H.A.B., Data Collection or Processing: M.M.A., H.A.B., E.E.F., Analysis or Interpretation: H.A.B., E.E.F., Literature Search: E.E.F., Writing: E.E.F.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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