

Original Research

Marked Troponin Elevation After Implantation of a Permanent Antibradycardia Pacemaker

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Introduction: Transvenous insertion of endocardial leads for permanent pacing is often accompanied by minor myocardial damage, detected thanks to the high sensitivity of cardiac troponins. It is unknown whether higher troponin levels, commensurate with more severe myocardial damage, can be encountered after implantation procedures.

Methods: Over a 3-year period, 283 patients underwent an implantation of a full antibradycardia pacemaker system (pulse generator plus leads). Patients were required to have normal levels of cardiac troponin I (CTN-I) on a venous blood sample taken immediately prior to elective pacemaker insertion. Post implantation CTN-I levels were measured in all patients 6 hours after the procedure. Repeated samples were taken if high CTN-I levels were found at 6 hours.

Results: Elevated CTN-I levels were found in 167 patients (59%, 95% CI: 0.53-0.64), but only 5 of them (1.8%, 95% CI=0.8 to 4.1%) had peak CTN-I levels far exceeding the range of minimal myocardial damage (i.e. CTN-I >1.5 ng/ml). Implantation of the devices was successful in all patients and we did not observe any complications. None had clinical evidence of an acute coronary event before or during the pacemaker implantation procedure and coronary angiography revealed no significant lesions in the coronary arteries.

Conclusions: CTN-I elevations after pacemaker implantation may far exceed levels corresponding to minimal myocardial damage. This should be a matter of concern, especially if an early discharge is planned after pacemaker implantation.

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In general, elevated cardiac troponin (I and T) levels are consistent with the diagnosis of acute coronary syndrome and haemodynamically relevant coronary artery stenosis. However, they may also point to minor myocardial injury in other circumstances (pathological, traumatic, or concerning interventional cardiology).^{1,2}

Transvenous insertion of endocardial leads for permanent pacing is accompanied by troponin elevation compatible with myocardial damage, secondary to the direct myocardial trauma elicited by pacing leads or to other associated clinical conditions. Published data from oth-

ers^{3,4} and from our institution⁵ mostly report troponin elevations within or very close to the range of "minimal myocardial damage". In a previous study of ours, all cardiac troponin-I (CTN-I) elevations occurred within 6 h from implantation.⁵ Most patients had peak CTN-I levels compatible with minimal myocardial damage, while none exceeded 3 ng/ml. It is now routine practice in our institution to measure CTN-I levels at 6 hours post implantation.

It is unknown whether higher troponin levels, commensurate with more severe myocardial damage, can be encountered after implantation procedures.

Methods

The study population consisted of 283 patients in whom a full permanent pacemaker system (pulse generator plus electrodes) was implanted during the course of a 3-year period. All patients gave written informed consent to the procedure. The study protocol was approved by the local scientific committee for human research. Decisions about the indication and the appropriate mode of permanent pacing were made, and pacemaker implantation performed, by the physicians who were ordinarily involved in patient care in all patients. Forty-nine VVI, 227 DDD, and 7 VDD pacemaker systems were used. All ventricular electrodes were fixed passively using passive fixation tines. Atrial active fixation electrodes with an extendable screw were implanted in 193 patients. Demographics and clinical data are summarised in Table 1.

We excluded patients with evidence of acute ischaemic insult, renal failure, CTN-I levels above normal at baseline, and those who underwent electrophysiological testing, coronary angiography, or percutaneous coronary intervention within 24 hours before pacemaker implantation.

Blood for the evaluation of cardiac markers was taken from a peripheral vein before and 6 hours after the end of the procedure. Repeated samples were taken if high CTN-I levels (>0.1 ng/ml) were found at 6 hours. For measurement of CTN-I we used a fluorometric enzyme immunoassay (Centaur[®], Bayer). The upper reference limits for CTN-I, defined as the 95% cut-off by nonparametric analysis, are 0.1 ng/ml. CTNI values that exceed 1.5 ng/ml indicate myocardial necrosis compatible with acute myocardial infarction, while CTN-I levels between 0.1 and 1.5 ng/ml

represent smaller amounts of necrosis that we refer to here as “minimal myocardial damage”.

Results

Of the total patient population of the study, 167 had elevated CTN-I levels (59%, 95% confidence interval, CI: 0.53-0.64) but only 5 of them (1.8%, 95% CI: 0.8 to 4.1%) had peak CTN-I levels far exceeding the range of minimal myocardial damage (CTN-I >1.5 ng/ml), raising clinical concern regarding the differential diagnosis of acute myocardial infarction. The characteristics of the 5 patients with markedly elevated troponin levels after pacemaker implantation are summarised in Table 2.

All 5 patients were referred for symptoms that occurred >16 hours before admission to our hospital. None had renal failure, history of coronary artery disease or clinical evidence of myocardial ischaemia, including elevated CTN-I levels at baseline. Chest pain was absent in all 5 cases and no electrocardiographic evidence of myocardial ischaemia was found. Furthermore, none had haemodynamic instability manifested as marked increases in rate-pressure product or a fall in blood pressure before, during, or after implantation. The implantation procedure was relatively easy and uncomplicated for these patients and the CTN-I elevations were detected by routine screening, which is now performed 6 hours after the procedure. No significant variations of CK, CK-MB, creatinine and haemoglobin were observed during the hospital stay before or after implantation. Echocardiography revealed no wall motion abnormalities in any patient and all had a 4-6 day in-hospital follow up without notable complications. All patients underwent a coronary arteriography within a week from implantation, which revealed normal coronary arteries and no wall-motion abnormalities on the left ventriculogram.

Table 1. Demographics and characteristics of patients

Age (years)	75.9 \pm 8.9
Sex:	
Male	162 (57.2%)
Female	121 (42.8%)
Indication:	
Complete heart block	78 (27.6%)
2nd degree heart block	41 (14.5%)
Sick sinus syndrome	94 (33.2%)
Carotid sinus syndrome	31 (10.9%)
Bradyarrhythmia - atrial fibrillation	30 (10.6%)
Other	9 (3.2%)
Pacing mode:	
DDDR	227 (80.2%)
VVIR	49 (17.3%)
VDDR	7 (2.5%)
Fluoroscopy time (min)	6.5 \pm 4.2

Discussion

It seems unlikely that these CTN-I elevations are related to myocardial ischaemia. All patients had normal coronary arteries and no clinical evidence suggestive of ischaemia. In such cases, silent ischaemia should be considered as a possible cause of CTN-I elevation only if major haemodynamic derangements occur. Marked blood pressure fall, or elevation of the rate-pressure product, might disturb the myocardial oxygen supply-demand balance and cause myocardial damage. All patients, however, were stable at present.

Table 2. Characteristics of patients with markedly elevated troponin levels after pacemaker implantation.

Variable	Patient-1	Patient-2	Patient-3	Patient-4	Patient-5
Age (years)	71	74	82	77	69
Sex	Male	Male	Female	Female	Male
Indication	AF + CHB	CHB	CHB	CHB	CHB
Pacing mode	VVIR	DDDR	VDDR	DDDR	DDDR
Atrial electrode	(-)	Screw-in Biotronik SeloxSR53	(-)	Passive St Jude Med Isoflex1642T	Screw-in St Jude Med Tendril1782T
Maximum diameter (mm)	(-)	2.6	(-)	2	2
Atrial threshold (V)	(-)	0.8	(-)	0.7	0.5
P-wave (mV)	(-)	3.2	3.2	2.8	1.9
Ventricular electrode	Passive Biotronik SeloxST60	Passive Biotronik SeloxST60	Passive Biotronik Solox65/13	Passive St Jude Med Isoflex1646T	Passive St Jude Med Isoflex1646T
Maximum diameter (mm)	2.2	2.2	2.7	2.1	2.1
Ventricular threshold (V)	0.4	0.3	0.2	0.4	0.4
R-wave (mV)	13	15	11.1	14.3	12.5
Peak CTN-I (ng/ml)	31.7	7.74	7.57	5.51	8.11
Radiation time (min)	2.5	6.3	5	3	6.4

AF – atrial fibrillation; CHB – complete heart block; CTN-I – cardiac troponin-I.

tation and thereafter and had normal CTN-I levels at baseline. Unfortunately, in these patients, the electrocardiogram had a low diagnostic value in detecting ischaemia, due to paced rhythms.

Pulmonary embolism after pacemaker lead implantation⁶ is a highly unlikely cause of CTN-I elevation in our patients. CTN-I elevations of this magnitude are not common in patients with pulmonary embolism.⁷ Moreover, even minimal CTN-I elevation during the course of pulmonary embolism signals the presence of severe embolism with a high risk for adverse events. Our patients were in apparently good clinical condition without evidence of respiratory or haemodynamic distress after pacemaker implantation.

It is therefore more likely that the CTN-I elevations were associated with the electrode placement. In our previous relevant study,⁵ all CTN-I elevations occurred within 6 hours from implantation and peak CTN-I levels did not exceed 3 ng/ml. We now report patients with CTN-I values far exceeding these levels.

Transvenous insertion of endocardial pacemaker leads is followed by a sequence of cardiac histopathological changes, starting with acute inflammation and leading eventually to the formation of fibrous connective tissue scar.⁸⁻¹⁰ The myocardium is involved in the inflammatory process, with infiltration of the interstitium by inflammatory cells and degeneration of myocardial cells.^{10,11} This inflammatory reaction has been attributed to both the physical and immunologi-

cal presence of the lead.^{12,13} It has been demonstrated that maximum electrode diameter and the number of implanted electrodes were significant predictors of the peak CTN-I levels after pacemaker system implantation.⁵ Thicker endocardial electrodes for VDD pacing could be associated with higher troponin elevations, but among 5 patients with marked CTN-I, a VDD pacemaker system was used in only 1 case.

CTN-I release could also have been caused by the atrial active fixation electrodes that were used in 2 patients. Although active fixation leads are more traumatic and have been implicated even in myocardial perforation or pericardial effusion,¹⁴ no such complications were observed in our patients. Moreover, marked CTN-I elevation was observed in 2 cases with DDD and in 1 case with VVI pacemaker system implantation, where passive fixation electrodes were used. It seems that the diameter of the implanted electrodes alone could not be an explanation for the marked CTN-I elevation in these patients. As no unusual difficulties were encountered during lead implantations, it seems impossible that these procedures were more traumatic than average, suggesting that this marked CTN-I elevation rather reflects an exaggerated response to lead placement.

However, CTN-I increase, apart from its fundamental role in patients with myocardial ischaemia, is associated with a worse prognosis in hospitalised patients and its release could play a prognostic role for clinically relevant events.^{15,16} As previously demon-

strated, troponin levels are independently associated with short- and long-term mortality, even after adjustment for severity of disease.¹⁷

An increasing number of implant procedures are performed on an outpatient basis and in some cases patients are discharged during the same day. Despite the fact that the clinical course of the 5 patients who showed high post-implantation troponin levels was uneventful, we think that the risk of any complications in these patients, as well as the required length of in-hospital follow up should be assessed in larger scale trials. Until then, every effort should be made to detect and exclude them from early discharge policies. Since electrocardiograms fail to provide clear information, because of the alterations in ventricular depolarisation after pacemaker implantation, a CTN-I measurement should be made at 6 h post implant and, if it is positive for damage, a second sample at 24 hours should be analysed. This would suffice, as CTN-I levels in these patients tend to peak relatively early, probably as a result of the unobstructed myocardial blood flow and quick CTN-I washout from the damaged myocardium.

Conclusion

CTN-I elevations after pacemaker implantation may far exceed levels corresponding to minimal myocardial damage. This should be a matter of concern, especially if an early discharge is planned after pacemaker implantation.

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