

Subcutaneous Implantable Cardioverter Defibrillators Implantation Without Defibrillation Threshold Testing: A Single Center Experience

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Abstract

Background: Subcutaneous implantable cardioverter defibrillator (S-ICD) system has been proven to be an effective therapy for prevention of sudden cardiac death (SCD) in selected patients. Although the Shockless IMPLant Evaluation (SIMPLE) trial has shown that defibrillation threshold (DFT) testing is not necessary for transvenous ICD (TV-ICD) systems, it is still recommended for S-ICD systems. We aimed to study the efficacy and safety of S-ICD implantation without DFT in our Heart Center with the comparison of S-ICD patients' outcome to those with a single chamber TV-ICD without DFT in the same period.

Methods: A retrospective analysis of patients underwent S-ICD without DFT from December 2014 to May 2016 with the comparison to single chamber TV-ICD patients implanted during the same period.

Results: Thirty consecutive patients (23 males (76.7%); mean age 41 ± 13 years; mean left ventricular ejection fraction $30 \pm 12\%$) received a S-ICD for primary (25 patients, 83.3%) or secondary prevention (five patients, 16.7%) of SCD. During a mean follow-up of 710.6 ± 190 days, three patients received 38 appropriate ICD shocks (90.5%), and two patients received four inappropriate shocks (9.5%). There were two mortalities (6.7%): one cardiac and one non-cardiac. When compared to 30 consecutive who received a single chamber TV-ICD during the same period, there was no significant difference in mortality.

Conclusions: Implantation of S-ICD using intermuscular approach without DFT seems to be safe and effective. Data from large S-ICD registries with long-term follow-up, and preferably randomized controlled studies, are needed to confirm this finding.

Keywords: Subcutaneous implantable cardioverter defibrillators; Defibrillation threshold testing; Shocks; Complications; Transvenous implantable cardioverter defibrillator

Introduction

Sudden cardiac death (SCD) is a leading cause of death worldwide. The introduction of the implantable cardioverter defibrillator (ICD) into clinical practice over the past 25 years has provided a life-saving therapy for primary and secondary prevention of SCD [1-4]. The subcutaneous ICD (S-ICD) is a relatively new technology that does not require vascular access or permanent intravascular defibrillator leads. It is developed to overcome the limitations and complications associated with traditional transvenous ICDs (TV-ICDs) such as venous thrombosis, cardiac perforation, lead fracture, and lead-related infective endocarditis. The S-ICD is approved for primary and secondary prevention of SCD based on clinical studies that demonstrated successful conversion of ventricular tachyarrhythmias with acceptably low rates of complications [5-7]. It is recommended for individuals who meet conventional ICD implantation criteria but do not have an indication for permanent pacing or cardiac resynchronization therapy, and not known to have recurrent ventricular tachycardia (VT) with expected good response to antitachycardia pacing (ATP), or preexisting unipolar pacemaker leads [7].

The term defibrillation threshold (DFT) testing refers to the minimum shock strength that defibrillates the heart [8]. A threshold below a specific value has been used as an acceptable criterion for device implantation [9, 10]. The clinical measurement of DFT has only fair reproducibility and represents an estimate of a point on the patient's defibrillation probability of success curve. A variety of methods have been used to determine DFT [11]. With the improved technology available in current ICD devices, the need for DFT has come under question [12].

The potential benefits of DFT include confirmation of system integrity and reliable sensing, discovery of high DFTs needing system modification, increased assurance that successful defibrillation of VF should occur after the patient is discharged, allow programming lower first shock energies, and guarantee of a safety margin for testing after addition of medications that may increase DFT, such as amiodarone [12].

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On the other hand, there are potential adverse effects or procedural complications related to DFT. The risks of DFT at the time of implantation could lead to a circulatory arrest and hypoperfusion related to VF itself. Other risks may also be related to the shocks alone or to the anesthetic drugs that are required for DFT. In one study, it was estimated that three of 19,067 (0.016%) deaths were related to DFT testing [13].

The use of S-ICD is rapidly increasing in the United States, and the early adoption of this technology has been associated with a low complication rate and high rate of successful DFT testing despite use in patients with a high number of comorbidities [14]. Compared to TV-ICD, early S-ICD use was associated with a high rate of successful defibrillation for ventricular fibrillation (VF) during DFT testing [14]. Among 2,791 patients with S-ICD who underwent DFT testing, 2,588 (92.7%), 2,629 (94.2%), 2,635 (94.4%), and 2,784 (99.7%) were successfully defibrillated with ≤ 65 , ≤ 70 , ≤ 75 , and ≤ 80 Joule (J), respectively [14].

In a matched cohort of S-ICD and TV-ICD patients (mostly dual-chamber devices), complication rates were similar. However, the S-ICD effectively reduced lead-related complications at the cost of non-lead-related complications. Both appropriate and inappropriate shock rates were similar [15]. The results of Shockless IMPLant Evaluation (SIMPLE) trial, which is a single-blinded, randomized, multicenter non-inferiority trial, showed that routine DFT at the time of TV-ICD implantation did not improve shock efficacy or reduce arrhythmic death [10]. This is not the case with S-ICD [16]. As a matter of fact, in a recent study looking at intraoperative DFT of S-ICD systems in 98 patients with the first shock of 65 J, the intraoperative DFT was successful in 74 patients (75%), successful test with reversed shock polarity in 14 (15%), successful test after lead repositioning in one (1%), successful test after pulse generator repositioning in five (5%), and safety margin < 10 J in four (4%) [17].

Current guidelines recommend DFT at the time of S-ICD implantation, based on the absence of evidence suggesting that it is safe to forgo DFT testing and concerns regarding increased defibrillation energy requirements compared to TV-ICDs [18].

To our knowledge, there are currently no data describing the use of the S-ICD without DFT, so we sought to 1) describe our experience with S-ICD implantation without DFT with evaluation of safety and efficacy of this approach and 2) compare outcomes of these patients to the outcomes of similar patients who received a traditional TV-ICD without DFT during the same period.

Materials and Methods

Study population

The data of 30 consecutive patients who underwent S-ICD systems implantation without DFT between December 2014 and May 2016, in the Heart Center at King Faisal Specialist Hospital & Research Center, were retrospectively analyzed. The DFT was not performed due to high risk at the time of implantation with severe comorbidities in five patients or patient's request not have DFT when the treating physician felt that S-

ICD was the best option for the patient, e.g. patients with end-stage renal disease (ESRD) or congenital heart disease in the other patients. The corresponding group consists of 30 patients implanted with a single chamber TV-ICD implantation without DFT during the same period.

Data collection

Data collection was performed at regular intervals by reviewing medical records for baseline characteristics, implantation data, and follow-up data on clinical outcomes, complications, and device therapy delivery. The survival status of patients was retrieved from electronic records.

Definitions

Primary prevention of SCD refers to use of ICDs in individuals who are at risk for, but have not yet had, an episode of sustained VT, VF, or cardiac arrest.

Secondary prevention refers to an indication for an ICD exclusively for patients who have survived one or more cardiac arrests or sustained VT [19].

Three-incision technique for inserting S-ICD

The conventional S-ICD implantation technique involves electrode and device implantation by three incisions - one for the lateral pocket and two parasternal incisions [20].

Two-incision technique

The parasternal part of the S-ICD electrode is positioned using a standard 11-Fr peel-away sheath avoiding the superior parasternal incision [21].

The generator-related complication was generator malfunction.

The lead-related complications included the following situations: dislodgement defined as X-ray-confirmed dislodgement of the lead combined with significant changes in sensing/pacing performance, failure to capture at practical device output with no visible change in the lead position or considerable impedance rise, loose set screw at the ICD connector, lead insulation defect, and lead fracture defined as changes in impedance with changes in sensing/pacing performance (intermittent or permanent) which could be optionally confirmed by X-ray study. Suboptimal and abnormal findings in the device analysis were defined as threshold > 2 Volts (V) at 0.5 ms, right atrial (RA) lead impedance $> 1,500 \Omega$, right ventricular (RV) lead impedance $> 2,000 \Omega$, left ventricular (LV) lead impedance $> 1,500 \Omega$, RV coil $> 200 \Omega$, supraventricular (SVC) coil $> 200 \Omega$, R-wave < 5 mV, and P-wave < 0.5 mV [22].

Appropriate therapy consisted of device therapy with ATP and/or shocks for VT or VF. Inappropriate therapy consisted of ATP and/or shocks for heart rhythms other than VT or VF.

Procedure

Screening ECG test was performed in two postures (lying down and sitting) for all patients with at least one of the three sensing configurations acceptable in both postures. Two patients failed screening test and underwent TV-ICD implantation.

The procedure was performed in the electrophysiology laboratory under standard sterile conditions and general anesthesia. The left arm was abducted to 60°, and then a dummy of the S-ICD and lead were secured on the patient's chest by adhesive plaster. The positioning of both was guided by anatomical landmarks, as suggested by the manufacturer user's manual [21], with the pocket at the fifth intercostal space between the mid and anterior axillary lines and the lead 1 - 2 cm to the left of the sternal midline. The position of the lead and S-ICD relative to the heart silhouette was checked by a brief fluoroscopy. Finally, the S-ICD position was drawn onto the chest with a demographic marker pen, as well as the incision line for the pocket creation along the chest Langer's lines. Following sterile draping, an incision was made along the predefined Langer's lines to create the device pocket. Subcutaneous dissection was carried out using an electrosurgical cutting and coagulation device, parallel to the incision, down to the fascia overlying the latissimus dorsi. Intermuscular implantation places the S-ICD device (Cameron Health, SQ RX model 1010 or Boston Scientific, Emblem MRI S-ICD model A219) in the virtual space between the latissimus dorsi and serratus anterior muscles. The pocket was formed over the serratus anterior muscular fascia and beneath the latissimus dorsi muscle by detaching the fibrous tissue between the muscles [22]. The single lead for sensing and defibrillation (Cameron Health Model 3010 Q-TRAK or Emblem S-ICD Electrode model 3401) electrodes positioning was performed following the three- or two-incision techniques [20, 21] based on the implanting physician preference. The lead was connected to the generator, and the latter was placed in the pocket. Device analysis was performed to make sure that at least two sensing vectors were acceptable. Non-absorbable sutures were inserted through the connector block suture portal, and a suture knot was tied to anchor the S-ICD to the latissimus dorsi muscle [22].

On the first post-procedure day, the device was analyzed with the patient lying down, standing up and with a short walking distance to choose the best vector.

ICD programming and follow-up

The conditional shock zone and shock zone were programmed at 190 - 200 and 220 beats per minute, respectively. The patients were followed up initially after 2 months of ICD implant then every 6 months.

Statistical analysis

Statistical analysis was performed using the SPSS version 20.0 software (IBM Corp., Armonk, NY, USA). Categorical vari-

ables were presented in frequency, and differences between the groups were compared with the Chi-square test. Data were presented in mean \pm standard deviation for normally distributed variables or median and interquartile ranges for abnormally distributed variables. Normally distributed variables were compared using independent sample *t*-test. Spearman's correlation analysis was performed to show the relationships between continuous variables. A two-tailed P-value of < 0.05 was considered statistically significant [23]. Kaplan-Meier time-to-event analyses were conducted with censoring of subjects at their last known status.

Ethical consideration

This study conformed to the Declaration of Helsinki and its later amendments and was approved by our institution Research Ethics Committee.

Results

The patients' baseline characteristics are summarized in Table 1. Thirty patients, 23 males (76.7%), age 16 - 64 years with a mean age of 41 ± 13 years, received S-ICD for primary prevention in 25 (83.3%) and secondary prevention in five patients (16.67%). The indication for ICD implantation was ischemic cardiomyopathy in 11 patients (36.7%), non-ischemic cardiomyopathy in 10 patients (33.3%), inherited arrhythmia disorders in four patients (13.3%), and congenital heart disease in five patients (16.7%). The follow-up period was 122 - 1,034 days (mean 710.6 ± 190 days). Thirteen patients (34.3%) had S-ICD implantation with two-incisions and 17 patients (56.7%) with three-incision technique. Two patients (6.7%) had wound infection which was treated with antibiotics; one patient (3.3%) had a hematoma which was treated conservatively.

During the follow-up, one patient died 22 months after S-ICD implantation due to advanced heart failure. He had ESRD and ischemic cardiomyopathy, and he was on the combined heart and renal transplant list. He had multiple successful shocks for VF episodes. Another patient died with malignancy that was diagnosed 4 months after S-ICD implantation. Four patients received 38 appropriate ICD shocks (90.5%), and two patients received four inappropriate shocks (9.5%). The first patients with inappropriate shock had congenital heart disease with right bundle branch block and had three inappropriate ICD shocks due to T wave over sensing with physical activity. The change of sensing vector from primary to alternative vector resolved the problem. The second patient also had one shock for T wave oversensing 18 months post-S-ICD implant, and it was corrected with reprogramming of the sensing vector.

When compared to 30 consecutive patients (24 males (80%); mean age 50 ± 13.8 years; mean left ventricular ejection fraction $28 \pm 9.5\%$) who received a single chamber TV-ICD during the same period, there was no significant difference in mortality. The indication for ICD implantation was

Table 1. Baseline Clinical Characteristics of the S-ICD and TV-ICD Patients

Patient characteristics	S-ICD, N (%)	TV-ICD, N (%)	P value
Mean age (years)	41.03	50.33	0.009
Male (%)	23 (76.7%)	24 (80%)	0.754
Mean LVEF (%)	30.50	28.17	0.405
Primary prevention	25 (83%)	26 (86.7%)	0.718
Diagnosis			
Ischemic heart disease	11 (36.7%)	14 (46.7%)	0.432
Non-ischemic cardiomyopathy	10 (33.3%)	14 (46.7%)	0.292
Genetic (inherited) arrhythmia disease	4 (13.3%)	2 (6.7%)	0.389
Congenital heart disease	5 (16.7%)	0 (0%)	0.020
Diabetes	6 (20%)	16 (53.3%)	0.007
Hypertension	7(23.3%)	16 (53.3%)	0.017
Myocardial infarction	10 (33.3%)	10 (33.3%)	1.000
CABG	5 (16.7%)	6 (20%)	0.739
Atrial fibrillation	3 (10%)	7 (23.3%)	0.166
Renal function			
Good (eGFR > 60 mL/min)	26 (86.7%)	20 (66.7%)	0.067
Moderate (eGFR 30 - 60 mL/min)	3 (10%)	8 (26.7%)	0.095
Poor (eGFR < 30 mL/min)	1 (3.3%)	2 (6.7%)	0.554
NYHA functional class			
I	16 (53.3%)	4 (13.3%)	0.001
II	10 (33.3%)	20 (66.7%)	0.010
III	4 (13.3%)	5 (16.7%)	0.718
IV	0 (0.0%)	1 (3.3%)	0.313

CABG: coronary artery bypass surgery; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; N: number; NYHA: New York Heart Association; S-ICD: subcutaneous implantable cardioverter defibrillators; TV-ICD: transvenous implantable cardioverter defibrillators.

ischemic cardiomyopathy in 14 (46.7%), non-ischemic cardiomyopathy in 14 (46.7%), and inherited arrhythmia disorders in two (6.7%). There were no patients with congenital heart disease. Two patients (6.7%) had a hematoma, which was treated conservatively, and three patients (10%) needed a second procedure for lead-related problems due to lead dislodgment (one patient), poor sensing and capture with microperforation (one patient) and small R wave with T wave oversensing (one patient). The follow-up period was 195 - 972 days (mean 632 ± 156 days). Four patients received 40 appropriate shocks, and one patient received 12 inappropriate shocks. Two patients received 37 appropriate ATP therapies, and one patient received one inappropriate ATP therapy. Overall, the appropriate TV-ICD therapy was 85.6%, and inappropriate therapy 14.4%.

Discussion

This study suggests that S-ICD implantation without DFT is safe and effective. The outcome was favorable and comparable to TV-ICD. This will be discussed further below regarding the

following.

Mortality

Over an average follow-up of 2 years, the overall mortality in the S-ICD group was 6.7% and cardiovascular mortality was 3.3%. This is comparable to what has been reported in the pooled analysis of the IDE study and EFFORTLESS registry with an annual mortality rate of 1.6% and 2-year mortality rate of 3.2% [24]. The cardiovascular mortality was similar in the TV-ICD group (Fig. 1). Although the TV-ICD patients were relatively older and had more risk factors for coronary artery disease, the S-ICD group included five patients with complex congenital heart disease and another five patients with prior TV-ICD lead-related infection or fracture. The percentage of secondary prevention cases was not significantly different, 16.7% in S-ICD group and 13.3% in the TV-ICD group.

The SCD-Heft study enrolled a mixed population of ischemic and non-ischemic cardiomyopathies and found a risk of death at 2 years in the intervention group of approximately 11-12% [25]. However, low annual mortality rates of 5% [26,

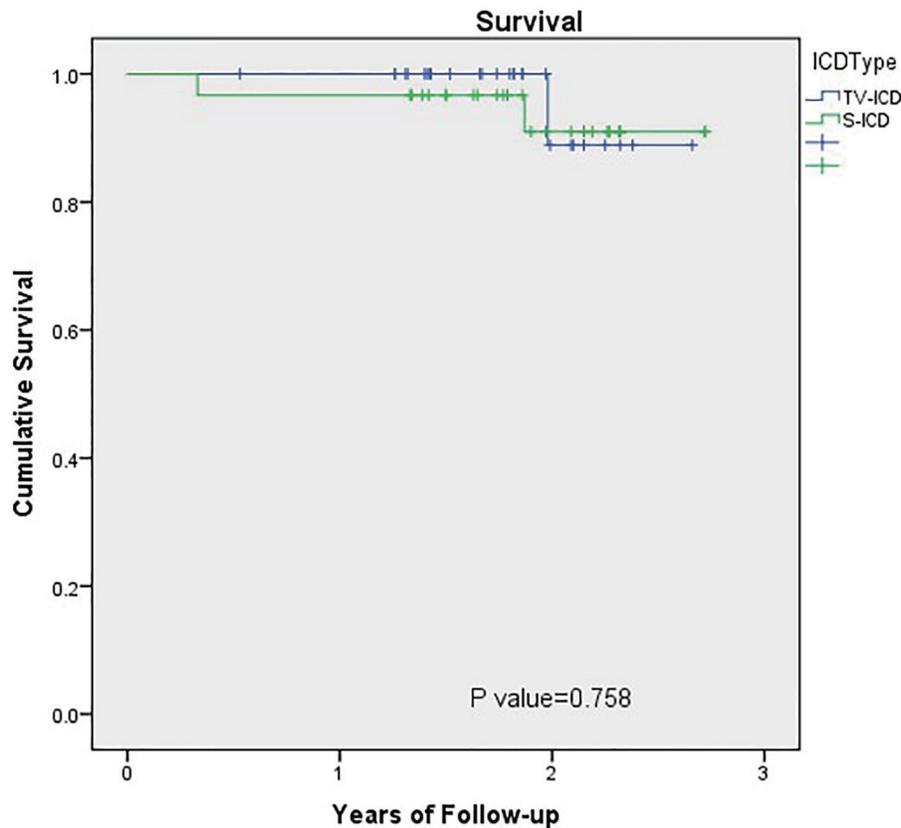


Figure 1. Outcomes comparison of S-ICD and TV-ICD: survival. Kaplan-Meier plot of survival in the S-ICD and TV-ICD patients. S-ICD: subcutaneous implantable cardioverter defibrillators; TV-ICD: transvenous implantable cardioverter defibrillators.

27] and annual appropriate shock rates of 4-5% [26] have been reported. This is likely secondary to improvements of pharmaceutical and interventional treatment options for coronary artery disease and heart failure [26].

Appropriate S-ICD therapy efficacy

The S-ICD was effective in terminating all the 42 VT/VF episodes from the first shock. There were no VT/VF episodes that were not detected correctly. The appropriate shocks were 90.5% of all delivered therapies. For the TV-ICD group, the appropriate TV-ICD therapy (ATP or shock) was 85.6%, and inappropriate therapy was 14.4%. Previous S-ICD studies showed success at the conversion of clinical VT/VF with first shock ranging from 57.9% to 100% [6, 24, 28-31] and from more than one shock from 96.4% to 100% [6, 24, 28-33]. In the recent TV-ICD studies, annual appropriate shock rates were 4-5% [26].

Inappropriate S-ICD therapy

Inappropriate therapy occurred in 9.5% of the S-ICD group and 14.4% in the TV-ICD group. The incidence of inappropriate shocks was 5-16% in previous S-ICD studies [6, 24, 28-33]. The cause of inappropriate shock in S-ICD was T-

wave oversensing, which is the leading cause of inappropriate shocks in previous S-ICD studies (about 85% of inappropriate shocks were due to T-wave oversensing) [6, 28].

Device-related complications

The S-ICD device-related complications were less compared to TV-ICD but not statically significant (Fig. 2). This is consistent with what has been reported before [15]. In the EFFORTLESS registry, the peri-operative complication-free rate in the first 30 days post-implant was 97% (15 system-related complications occurred in 14 patients) [24]. The documented system or implantation-related complication-free rate was 94% at 360 days post-implantation [24]. Infection is one of the main complications associated with the S-ICD system. The rate of infection of the generator pocket ranges from 2% to 10% in clinical trials, and it may lead to the explanation of the S-ICD system in 1.3-4% of the patients [6, 24, 28-33].

Limitations of the study

The present study is a single-center experience of S-ICD systems without DFT in a small sample size compared with previous multicenter trials with TV-ICD systems. It has the limitation

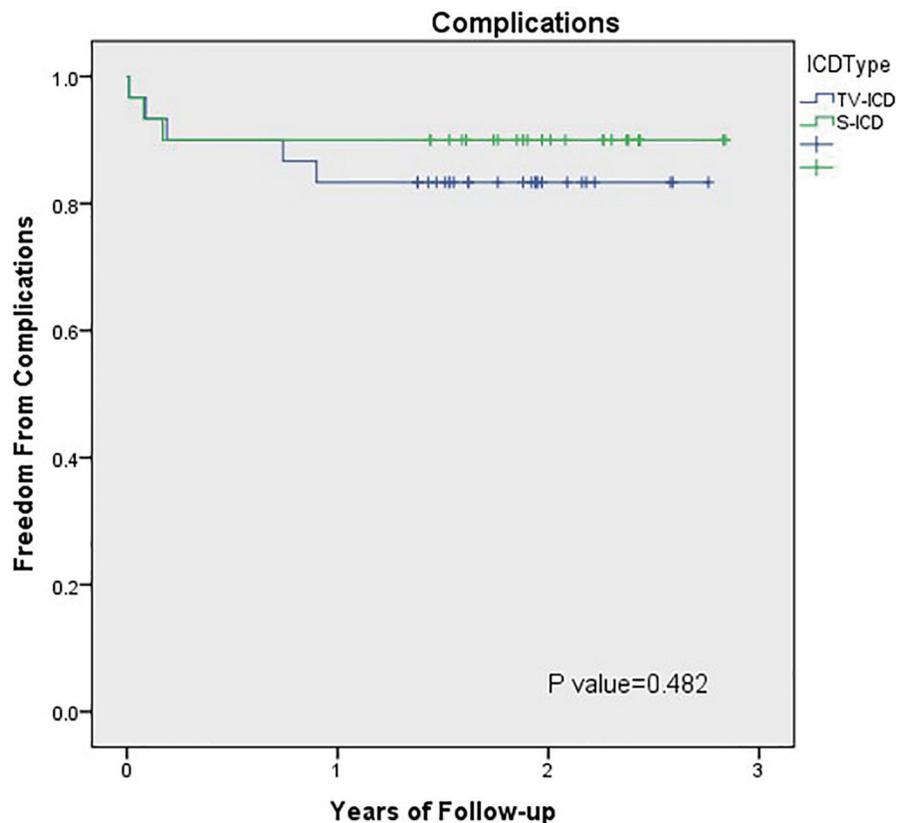


Figure 2. Outcomes comparison of S-ICD and TV-ICD therapy: device-related complications. Kaplan-Meier plot of device-related complications in the S-ICD and TV-ICD patients. S-ICD: subcutaneous implantable cardioverter defibrillators; TV-ICD: transvenous implantable cardioverter defibrillators.

of the retrospective design. All patients in this study underwent S-ICD implantation using intermuscular implantation technique, so the results of this study may not apply to patients who have the S-ICD device implanted using other techniques. Of note, the previous study utilizing the same intermuscular pocket technique showed a successful DFT in all the 14 involved patients [22].

Conclusions

Implantation of S-ICD with intermuscular approach without DFT seems to be safe and effective. Data from large S-ICD registries with long-term follow-up and ideally randomized controlled studies are needed to confirm this result.

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Conflict of Interest

The authors declare that there is no conflict of interest.

Author Contributions

All authors certify that he or she has participated sufficiently in the intellectual content, the analysis of data. Each author has reviewed the final version of the manuscript and approves it for publication.

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