Parental influence on intracerebral hemorrhage onset in hereditary Dutch-type cerebral amyloid angiopathy

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ORIGINAL RESEARCH

Defibrillation Threshold Testing After ICD Implantation in Patients with Chronic Kidney Disease

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ABSTRACT

***Introduction*:** Routine defibrillation threshold (DFT) testing at the time of implantable cardioverter-defibrillator (ICD) implantation is no longer recommended because testing did not improve shock efficacy or reduce arrhythmic death. However, patients with severe chronic kidney disease (CKD) were not included in these trials and might benefit from DFT testing. International guidelines shed no light on the subject of the effect of kidney function on DFT testing in patients with CKD.

***Methods*:** In this retrospective study, we aimed to identify the success and safety of DFT in patients with CKD stages 1–5 (ages 55–80 years) undergoing primary transvenous ICD implantation.

***Results*:** A total of 451 patients were stratified into three groups based on kidney function: group 1 with CKD stage 1–2 ($n=294$), group 2 with CKD stage 3–4 ($n=90$), and group 3 with CKD stage 5 ($n=67$). Ventricular fibrillation was induced 827 times. The median number of threshold testing per patient was two (interquartile range 1–2; range 1–7). No evidence of between CKD-group differences in ICD defibrillation success rates could be found when using all patient attempts, regardless of correction for energy levels ($p=0.262$). DFT-related complications occurred in 16 patients (3.5%), predominantly hypoxemia due to hypoventilation (1.6%) and atrial arrhythmias. Five patients (1.1%) underwent ICD or lead revision following abnormal DFT test results.

***Conclusions*:** We did not demonstrate a correlation between CKD and increased DFT or an increased rate of inadequate defibrillation safety margin. DFT testing is feasible with a low risk of serious complications in patients with moderate and advanced CKD when clinically deemed necessary. DFT testing is not routinely required in patients with (advanced) CKD.

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Keywords: Implantable cardioverter-defibrillator; End-stage kidney disease; Chronic kidney disease; Dialysis; Defibrillation threshold testing; Defibrillation efficacy testing; Ventricular fibrillation conversion testing

Key Summary Points

Why carry out this study?

Routine defibrillation threshold (DFT) testing at the time of implantable cardioverter-defibrillator (ICD) implantation is no longer recommended because testing did not improve shock efficacy or reduce arrhythmic death.

However, patients with severely impaired kidney function were not included in these trials and might benefit from DFT testing. International guidelines shed no light on the subject of the effect of kidney function on the DFT testing in patients with chronic kidney disease (CKD).

We aimed to identify the effect of impaired kidney function on the DFT in patients undergoing primary transvenous ICD implantation using a random effect logistic model. Furthermore, we assessed the safety of DFT testing.

What was learned from the study?

Kidney function did not affect the DFT in this population. DFT testing is feasible with a low risk of serious complications in patients with moderate and advanced CKD, when clinically deemed necessary. DFT testing is not routinely required in patients with (advanced) CKD.

INTRODUCTION

Defibrillation threshold (DFT) testing, defined as the minimum energy required to successfully terminate ventricular fibrillation (VF) at the time of transvenous left-sided implantable cardioverter-defibrillators (ICD), is no longer routinely recommended [1]. However, perioperative assessment of ICD function can reveal VF undersensing or a high DFT, which may result in immediate ICD generator or lead revision. Routine DFT testing at the time of ICD implantation is generally well tolerated but does not improve shock efficacy or reduce arrhythmic death [2, 3]. The number needed to test is approximately 500 ICD recipients in order to prevent one death [4]. However, DFT can still be considered in selected patient subgroups in which a high DFT could be expected. For example, right-sided ICD implantation is associated with a higher DFT [5]. In patients on dialysis, a transvenous ICD device is often implanted in the right pectoral region, contralateral to a dialysis shunt in order to prevent symptoms of central vein stenosis [6]. Also, kidney dialysis is identified as a predictor of an inadequate defibrillation safety margin (DSM) [7]. International guidelines for managing ventricular arrhythmias and ICD therapy shed no light on the subject of DFT testing in patients on dialysis because patients on dialysis are systematically excluded from landmark ICD trials [8–11]. Also, DFT testing was evidently less frequently performed in patients with chronic kidney disease (CKD) due to a perceived higher risk of complications [12]. Our study group demonstrated earlier that prophylactic ICD implantation in patients on dialysis without a class I indication for ICD (e.g., history of sudden cardiac arrest or history of ventricular arrhythmias) did not reduce the rate of sudden cardiac death (SCD) or all-cause mortality, which remained high [13]. By conducting this retrospective analysis, we aimed to clarify several questions: (1) Is there a relationship between eGFR and the result of the intraoperative DFT, and (2) Is DFT safe in patients with (advanced) CKD?

METHODS

The data that support the findings of this study are available from the corresponding author upon request. This study was approved and informed consent was waived by the local ethics committee of Leiden University Medical Center

(LUMC, 2022-015). This study was conducted in accordance with the Helsinki Declaration.

We retrospectively assessed the electronic hospital records of all patients with an age of 55–80 years, with left ventricular ejection fraction (LVEF) ≥ 30%, that underwent an initial single- or dual-chamber, high-output transvenous ICD implantation at Leiden University Medical Center in the period from July 2007 to February 2018. After implantation, an intraoperative DFT was performed with the patient under conscious sedation (using midazolam and fentanyl) with the induction of VF. The definition of DFT is the minimum energy required to successfully terminate VF. Various methods were used over time to determine DFT at the time of ICD implant, as described by Hayase et al. [1]. Hospital records were scrutinized to assess perioperative DFT. All patients who underwent ICD replacement were excluded from this analysis because ICD replacement is associated with a higher incidence of failed shock during DFT [12]. Also, in case of unknown LVEF within 12 months preceding ICD implantation or absent or unknown DFT, patients were excluded, and the reason for omitting DFT was assessed. We then stratified the patients into three groups according to kidney function: group A were patients with normal kidney function or CKD stage 1–2 (e.g., eGFR > 60 ml/min/1.73 m^2): group B consisted of patients with CKD stage 3 and 4 (e.g., eGFR 15–59 ml/min/1.73 m^2), and lastly, group C included patients undergoing dialysis or eGFR < 15 ml/min/1.73 m^2. The urine albumin-to-creatinine ratio was not taken into account for CKD stratification because these values were limited available due to the retrospective nature of this study. The group with eGFR < 15 ml/min/1.73 m^2 consisted mainly of patients from the treatment group of the ICD2 study (98.5%) [13]. These patients treated with chronic dialysis had a LVEF ≥ 35% and no history of ventricular arrhythmias or cardiac arrest. Thus, these patients had no indication for an ICD according to the current guidelines regarding managing patients with ventricular arrhythmias and the prevention of SCD [8]. Patient characteristics such as age, sex, medical history, comorbidity, ICD indication, and serum laboratory examination were recorded (Table 1).

DSM testing is defined as the lowest successful energy tested. An inadequate DSM is defined as a < 10 J difference between the lowest successful energy tested during DSM testing and the maximum output of that specific ICD generator, as the maximum output may vary based on manufacturer and model. The endpoints included inadequate DSM, no failed shocks, one and two successful shocks ≥ 10 J below maximum device output, a single failed shock at < 21 J, 2–5 failed shocks at ≥ 21 J, and, lastly, adverse events after DFT test.

In addition, to compare rates of successful defibrillation between CKD groups across multiple within-patient attempts, a logistic regression model with patient-specific random effect was used, correcting for CKD group. The random-effect logistic was fit both with and without adjustment for energy levels of each corresponding attempt. A linear mixed-effect model was used to compare energy levels between CKD groups, using patient-specific random effects to account for multiple attempts within patients.

RESULTS

In the period July 2007 until February 2018, a total of 978 patients (aged 55–80 years) underwent single- or dual-chamber transvenous ICD implantation at Leiden University Medical Center. Of these, 527 patients (53.9%) were excluded from analysis because of the following reasons: ICD replacement ($n = 267$), LVEF < 30% ($n = 143$), DFT was not performed ($n = 103$) or other reasons ($n = 14$) (Fig. 1). Following publication of the SIMPLE trial, from October 2016 onwards, DFT was omitted from the standard operation protocol (51.5%). Other reasons for the omission of DFT included atrial fibrillation without oral anticoagulation therapy (15.5%), hyperkalemia (6.8%), hypokalemia (1.0%), or unknown serum potassium on the day of implantation (1.9%), high-risk sedation (2.9%), unsuccessful sedation with midazolam (1.0%), or unsuccessful induction of VF (1.0%). Also, reasons for not conducting intraoperative DFT testing were patient/physician preference, where

Table 1 Patient characteristics

	Group 1[a] ***n*** **= 294** **65.2%**	**Group 2**[b] ***n*** **= 90** **20.0%**	**Group 3**[c] ***n*** **= 67** **14.9%**	***p*** **value**
Age, years; median (IQR)	66 (60–72)	71 (65–74)	66 (62–74)	< 0.001
Sex, male; *n* (%)	246 (83.7)	66 (73.3)	56 (83.6)	0.078
Body mass index, kg/m^2; mean (SD)	26.4 (3.6)	27.5 (4.1)	28.0 (5.0)	0.004
Heart rate, bpm; mean (SD)	67 (14)	69 (22)	69 (12)	0.624
Systolic blood pressure, mmHg; mean (SD)	132 (21)	127 (20)	141 (22)	< 0.001
Diastolic blood pressure, mmHg; mean (SD)	75 (12)	73 (13)	75 (11)	0.251
Medical history; *n* (%)				
Atrial fibrillation/flutter	54 (18.4)	30 (33.3)	15 (22.4)	0.011
Coronary artery disease	180 (61.2)	67 (74.4)	22 (32.8)	< 0.001
Cerebrovascular disease	34 (11.6)	8 (8.9)	10 (14.9)	0.503
Chronic lung disease	22 (7.5)	11 (12.2)	15 (22.4)	0.001
Diabetes mellitus	44 (15.0)	29 (32.2)	20 (29.9)	< 0.001
Hypertension	119 (40.5)	48 (53.3)	54 (80.6)	< 0.001
Hypercholesterolemia	62 (21.1)	28 (31.1)	34 (50.7)	< 0.001
Medication; *n* (%)				
Beta-blocker[d]	164 (55.8)	55 (61.1)	38 (56.7)	0.670
Sotalol	38 (12.9)	9 (10.0)	3 (4.5)	0.130
Amiodaron	14 (4.8)	16 (17.8)	1 (1.5)	< 0.001
Antihypertensive drugs	219 (74.5)	78 (86.7)	45 (67.2)	0.012
Statin	189 (64.3)	69 (76.7)	38 (56.7)	0.024
Coumarin	86 (29.3)	40 (44.4)	10 (14.9)	< 0.001
Platelet aggregation inhibitor	157 (53.4)	43 (47.8)	34 (50.7)	0.633
Diuretics	102 (34.7)	73 (81.1)	42 (62.7)	< 0.001
Serum laboratory; mean (SD)				
Hemoglobin, mmol/l	8.3 (1.1)	7.9 (1.2)	7.5 (0.7)	< 0.001
Sodium, mmol/l	140 (3)	140 (3)	140 (3)	0.542
Potassium, mmol/l	4.4 (0.4)	4.5 (0.5)	4.5 (0.6)	0.008
Creatinine, µmol/l	82 (15)	136 (40)	630 (222)	< 0.001
Urea, mmol/l	6.7 (1.9)	11.6 (5.2)	21.9(23.2)	< 0.001
Echocardiography, left ventricular function; *n* (%)				< 0.001

Table 1 continued

	Group 1[a] *n* = 294 65.2%	Group 2[b] *n* = 90 20.0%	Group 3[c] *n* = 67 14.9%	*p* value
Normal (≥ 50%)	74 (25.2)	12 (13.3)	53 (79.1)	< 0.001
Mild dysfunction (40–49%)	97 (33.0)	30 (33.3)	12 (17.9)	0.046
Moderate dysfunction (30–39%)	123 (41.8)	48 (53.3)	2 (3.0)	< 0.001
Electrocardiogram; *n* (%)				
Left bundle branch block	21 (7.2)	11 (12.2)	0	0.013
Right bundle branch block	42 (14.3)	19 (21.1)	3 (4.5)	0.013

CKD chronic kidney disease, *eGFR* estimated glomerular filtration rate (ml/min/1.73 m^2), *IQR* interquartile range, *SD* standard deviation

[a]Group 1: eGFR > 60 ml/min/1.73 m^2, CKD stage 1–2 or normal kidney function

[b]Group 2: eGFR 15–59 ml/min/1.73 m^2, CKD stage 3–4

[c]Group 3: eGFR < 15 ml/min/1.73 m^2, CKD stage 5

[d]Not included sotalol

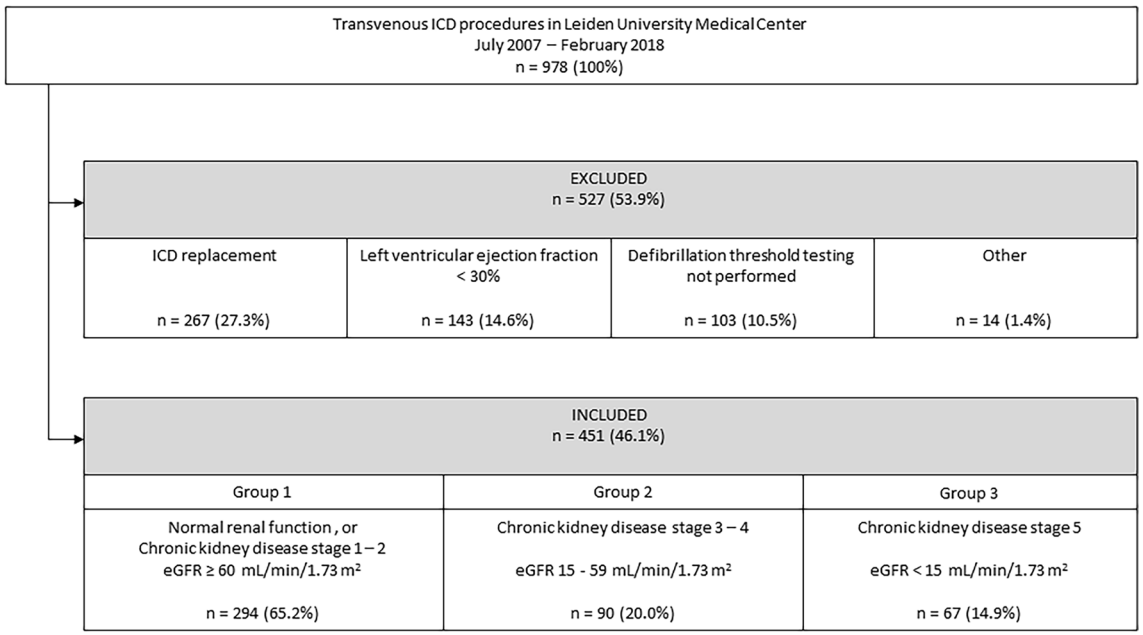

Fig. 1 Trial flow chart. *eGFR* estimated glomerular filtration rate (ml/min/1.73 m^2); *ICD* implantable cardioverter-defibrillators

DFT was considered unnecessary or unsafe (17.5%).

In total, 451 patients (46.1%) were included in analysis, stratified into three groups according to kidney function: group 1 with eGFR ≥ 60 ml/min/1.73 m^2, $n = 294$ (65.2%); group 2 with eGFR 15–59 ml/min/1.73 m^2, $n = 90$ (20.0%), and group 3 with eGFR < 15 ml/min/1.73 m^2, $n = 67$ (14.9%) (Fig. 1). The baseline characteristics are described in Table 1. The patients with an eGFR ≥ 15 ml/min/1.73 m^2 received an ICD for primary prevention in 173 out of 384 cases (45.1%), and the remaining patients received an ICD for secondary prevention (211/384; 54.9%). In groups 1 and 2, the ICD was most commonly implanted in the left pectoral region (98.6% and 97.8%, respectively). However, in group 3 the predominant ICD implantation site was the right pectoral region in 47 out of 67 patients (70.1%), $p < 0.001$. ICD implantation procedure time in patients with an eGFR ≥ 60 ml/min/1.73 m^2 was 5–10 min shorter compared to patients with an eGFR < 59 ml/min/1.73 m^2 ($p = 0.017$) (Table 2).

Almost all patients (444/451; 98.4%) received a dual-chamber ICD. The mean duration of the ICD implantation procedure was 68 min ± 27 (standard deviation, SD). VF was induced 827 times in the context of DFT testing. The predominant method of DFT testing was the *safety margin method* ($n = 254$; 56.3%), followed by *single successful defibrillation* ($n = 124$; 27.5%), *step-up method* ($n = 69$; 15.3%), and the *step-down method* ($n = 4$; 0.9%). The median (interquartile range, IQR) number of threshold tests per patient was two (IQR 1–2; range 1–7). The median lowest energy tested that defibrillates was 15 J (IQR 14 J–20 J) in group 1 and group 2. In group 3, the lowest energy tested was 20 J (median, IQR 15 J–20 J).

The first defibrillation conversion efficacy was 86.1% (253 out of 294 defibrillation attempts) in group 1, 83.3% (75 out of 90) in group 2, and 88.1% (59 out of 67) in group 3 ($p = 0.705$). An inadequate DSM (≤ 10 J below the maximum output of the ICD) occurred in ten out of 451 patients, of which 3/294 patients (1.0%) in group 1, in 4/90 patients (4.4%) in group 2, and in 3/67 patients (4.5%) in group 3 ($p = 0.067$). The median (IQR) shock impedance in group 1 was 63 Ω (48–74 Ω), 60 Ω (46–75 Ω) in group 2, and 72 Ω (52–79 Ω) in group 3 ($P_{\text{group 1 vs. group 2}} = 0.501$, $P_{\text{group 1 vs. group 3}} = 0.018$, $P_{\text{group 2 vs. group 3}} = 0.019$). The median (IQR) shock impedance in the patients with adequate DSM ($n = 441$, 97.8%) was 63 Ω (IQR 48–67 Ω) versus 63 Ω (IQR 59–67 Ω) in the patients with an inadequate DSM ($n = 10$, 2.2%), $p = 0.768$. Regarding the endpoints of inadequate DSM, no failed shocks ($p = 0.278$), one successful shock ≥ 10 J below maximum device output ($p = 0.553$), two successful shocks ≥ 10 J below maximum device output ($p = 0.683$), a single failed shock at < 21 J ($p = 0.236$), 2–5 failed shocks at ≥ 21 J ($p = 0.591$), there were no differences between the three groups. The results are shown in Table 2. In total, 15 patients (3.3%) received ≥ 4 defibrillation shocks via ICD. Nine patients, equally distributed among the three groups, received external defibrillation following failed or ineffective ICD shock ($p = 0.097$) (Table 2). The mean shock impedance in the patients who received external defibrillation was 60 Ω ± 15 Ω (SD) versus 63 Ω ± 16 Ω (SD) in the patients who did not receive a rescue shock ($p = 0.678$). DFT-related complications occurred in 15 patients (3.3%): nine patients with hypoxemia due to hypoventilation after sedation (2.0%), five patients with atrial fibrillation or atrial flutter (1.1%), and one patient with acute heart failure (0.2%). The rate of DFT-related complications was 3.0% (nine out of 294) in group 1, 3.3% (three out of 90) in group 2, and 4.5% (three out of 67) in group 3 ($p = 0.324$). Six patients (1.3%) underwent ICD or lead revision following abnormal DFT test results (Table 2). The DFT test characteristics by ICD implantation site (left versus right pectoral) in patients with CKD stage 5 (group 3) are depicted in Table 3. Our study includes 67 patients on chronic dialysis, with 47 ICD implants in the right pectoral region and 20 in the left pectoral region. There are no significant differences between patients receiving an ICD on the left versus the right pectoral region. No evidence of between CKD-group differences in success rates could be found when using all patient attempts (random effect logistic model), both after correction for energy levels ($p = 0.262$) or without correction ($p = 0.239$). There is evidence of different energy levels between CKD groups (mixed model, mean shock energy group 1: 17.5 J; group 2: 17.6 J, group 3: 19.5 J, $p < 0.001$). This

Table 2 ICD and defibrillation threshold testing[a] characteristics

	Group 1[b] *n* = 294 65.2%	Group 2[c] *n* = 90 20.0%	Group 3[d] *n* = 67 14.9%	*p* value
ICD indication; *n* (%)				
Primary prevention; *n* (%)	127 (43.2)	46 (51.1)	66 (98.5)	< 0.001
Left pectoral ICD implantation site	290 (98.6)	88 (97.8)	20 (29.9)	< 0.001
Implantation procedure time, minutes; mean (SD)	65 (27)	74 (30)	70 (21)	0.017
Right ventricular lead impedance, Ω; median (IQR)	63 (48–74)	60 (46–75)	72 (52–79)	0.043
Method of DFT testing				
Single successful shock; *n* (%)[d]	79 (26.9)	23 (25.6)	22 (32.8)	0.553
Safety margin method; *n* (%)	167 (56.8)	52 (57.8)	35 (52.2)	0.758
Step-up method; *n* (%)	45 (15.3)	15 (16.7)	9 (13.4)	0.874
Step-down method; *n* (%)	3 (1.0)	0	1 (1.5)	0.564
First defibrillation conversion efficacy; *n* (%)	253 (86.1)	75 (83.3)	59 (88.1)	0.705
No failed shocks during DFT; *n* (%)	247 (84.0)	69 (76.7)	56 (83.6)	0.278
Single successful shock; *n* (%)[a]	79 (26.9)	23 (25.6)	22 (32.8)	0.553
Two successful shocks; *n* (%)[a]	200 (68.0)	63 (70.0)	40 (59.7)	0.683
Three successful shocks; *n* (%)[a]	0	1 (1.1)	0	0.044
Single failed shock at < 21 J; *n* (%)	46 (15.6)	21 (23.3)	16.4	0.236
2–5 failed shocks at ≥ 21 J; *n* (%)	2 (0.7)	2 (2.2)	1 (1.5)	0.591
Ventricular fibrillation induction; *n* (%)				0.223
One	79 (26.9)	23 (25.6)	22 (32.8)	
Two	178 (60.5)	46 (51.1)	37 (55.2)	
Three	30 (10.2)	15 (16.7)	6 (9.0)	
Four	2 (0.7)	3 (3.3)	2 (3.0)	
Five	4 (1.4)	1 (1.1)	0	
Six	1 (0.3)	1 (1.1)	0	
Seven	0	1 (1.1)	0	
Inadequate defibrillation safety margin; *n* (%)	3 (1.0)	4 (4.4)	3 (4.5)	0.058
External defibrillation; *n* (%)	3 (1.0)	3 (3.3)	3 (4.5)	0.097
Adverse event after DFT test; *n* (%)	9 (3.0)	3 (3.3)	3 (4.5)	0.324
ICD system revision following abnormal DFT test; *n* (%)	3 (1.0%)	3 (3.3%)	0	0.144

ICD implantable cardioverter device, *DFT* defibrillation threshold, *CKD* chronic kidney disease, *eGFR* estimated glomerular filtration rate (ml/min/1.73 m^2), *IQR* interquartile range, *SD* standard deviation

[a] ≥ 10 J below maximum ICD output

[b] Group 1: eGFR > 60 ml/min/1.73 m^2, CKD stage 1–2 or normal kidney function

[c] Group 2: eGFR 15–59 ml/min/1.73 m^2, CKD stage 3–4

[d] Group 3: eGFR < 15 ml/min/1.73 m^2, CKD stage 5

Table 3 Defibrillation threshold test characteristics by ICD implantation site (left versus right pectoral) in patients with chronic kidney disease stage 5 (group 3)

	Pectoral ICD implantation site			*p* value
	Left, *n* (%) *N* = 20	**Right, *n* (%) *N* = 47**	**Total, *n* (%) *N* = 67**	
First shock efficacy	18 (90.0)	41 (87.2)	59 (88.1)	0.749
No failed shocks during DFT testing; *n* (%)	18 (90.0)	38 (80.9)	56 (83.6)	0.355
Adequate safety margin	19 (95.0)	45 (95.7)	64 (95.5)	0.893
Single successful shock[a]	6 (30.0)	16 (34.0)	22 (32.8)	0.747
Two successful shocks[a]				
Yes	13 (65.0)	27 (57.4)	40 (59.7)	
No	1 (5.0)	4 (8.5)	5 (7.5)	0.804
Single failed shock at < 21 J				
Yes	2 (10.0)	9 (19.1)	11 (16.4)	
No	18 (90.0)	38 (80.9)	56 (83.6)	0.355
2–5 failed shocks at ≥ 21 J				
Yes	1 (5.0)	0	1 (1.5)	
No	13 (65.0)	31 (66.0)	44 (65.7)	0.298
External shock after unsuccessful ICD shock	2 (10.0)	1 (2.1)	3 (4.5)	0.154
DFT testing-related complications	2 (10.0)	1 (2.1)	3 (4.5)	0.074

ICD implantable cardioverter device, *DFT* defibrillation threshold

difference in energy levels is considered inconsequential in daily clinical practice.

DISCUSSION

In this study, we assessed the impact of kidney function on the DFT in patients receiving an initial transvenous ICD. We found no evidence of differences in defibrillation success rates among the three groups, stratified according to kidney function namely: CKD stage 1–2 (e.g., eGFR > 60 ml/min/1.73 m^2), CKD stage 3 and 4 (e.g., eGFR 15–59 ml/min/1.73 m^2), and CKD stage 5 patients undergoing dialysis or eGFR < 15 ml/min/1.73 m^2. We also found that the first shock conversion efficacy was similar in the three groups, irrespective of kidney function. In ten out of 451 patients (2.2%), an adequate DSM was not achieved, which is in agreement with the general literature [1]. Furthermore, we demonstrated trends in which the need for external defibrillation after a failed ICD shock, and the rate of an inadequate DSM occurred more frequently as kidney function declined, although the difference was nonsignificant, respectively ($p = 0.097$ and $p = 0.058$). ICD or lead revision following abnormal DFT test results occurred in six out of 451 patients (1.3%). Life-threatening adverse events related to intraoperative DFT testing occurred in one out of 451 patients (0.2%). There were no cases of mortality in our study.

The benefits of testing defibrillation efficacy are early detection of ICD or right ventricular lead failure, generally with a low incidence of procedure-related serious adverse events. Furthermore, submaximal programmed shock

energy can lead to extended ICD battery longevity. Also, submaximal programmed energy has the advantage that ICD charging time is reduced. Currently, there is no class I recommendation for DFT testing in transvenous ICDs [14]. Although routine DFT is not performed, DFT can be performed in selected patients on indication, such as subcutaneous ICD implantation (class I indication), right pectoral transvenous ICD implantation, or ICD pulse generator change (class IIa), or at the discretion of the implanting physician [14]. Kolb et al. found a number needed to defibrillation test 500 ICD recipients in order to prevent one death [4]. Healy et al. concluded that omitting DFT results in a cost reduction of approximately $800 Canadian dollars [12].

Patients treated with chronic dialysis have several unique characteristics. It is an understudied group with respect to the subject of ICD therapy due to systematic exclusion from landmark trials. Our purpose was to provide insight into this vulnerable group. The patients with an eGFR < 15 ml/min/1.73 m^2 in this study are derived from the ICD2 trial cohort [13]. The CKD stage 5 patients undergoing dialysis in our study are unique because they were recipients of an ICD in the context of a trial without having a class I indication for ICD implantation, as opposed to the other included patients in the current study.

A high shock impedance (> 100 Ω) is associated with a higher chance of DFT testing failure but is a poor predictor of successful defibrillation [15]. Acute impedance increases post-implantation can be due to an erroneous connection of the shock lead to the pulse generator, a pneumothorax, or lead displacement. In our population, only two patients had a shock lead impedance > 100 Ω (107 Ω and 113 Ω). These two patients were both patients in group 1 (eGFR ≥ 60 ml/min/1.73 m^2) and had an adequate DSM. In our study, shock impedance was similar between patients with and without adequate DSM. However, in this analysis only ten patients had an inadequate DSM.

Literature concerning the correlation between kidney function and DFT outcomes is scarce. Intraoperative DFT testing is more likely to be omitted in patients with chronic kidney failure, which is probably due to a perceived higher risk of perioperative complications [12]. Shih et al. found that lower age, male gender, severe left ventricular dysfunction, secondary prevention, and amiodaron use are identified as independent predictors of high DFT (EF-SAGA) [16]. In this study, kidney function was not assessed. Hsu et al. identified dialysis treatment as a predictor of inadequate DSM [7]. The authors developed a risk score in order to predict inadequate DSM by evaluating inadequate DSM among 132,477 ICD implantations, of which 3992 patients were on dialysis. In total, 617 patients (15.5%) on dialysis had inadequate DSM. In our analysis, inadequate DSM occurred in only 4.5% of dialysis patients. Healey et al. concluded that routine DFT testing at the time of ICD implantation is generally well tolerated but does not improve shock efficacy or reduce arrhythmic death (SIMPLE trial) [2]. However, the outcomes of the SIMPLE trial cannot be extrapolated 1-to-1 on patients with CKD, especially not on the dialysis population, as the dialysis population undergoes relatively frequent right-sided ICD implantations, and this was an exclusion criterion in the important and well-designed SIMPLE trial. To the best of our knowledge, we have the largest population of patients with right-sided transvenous ICD implantation. Our study includes 67 patients on chronic dialysis, with 47 (70.1%) ICD implants in the right pectoral region, and 20 in the left pectoral region. It is true that the numbers are small; however, we feel that it does reflect that there are no significant differences between patients receiving an ICD on the left versus the right pectoral region with regard to the outcomes of DFT test characteristics (Table 3).

Bansch et al. assessed the first shock efficacy for all true ventricular tachycardia and VF during a 22.8-month follow-up in patients with an ICD programmed to deliver shocks at 40 J, and 1:1 randomized to undergo DFT testing or not (NORDIC ICD trial) [3]. The authors concluded that not performing intra-operative DFT was non-inferior. Also, there were fewer procedure-related serious adverse events within 30 days in the non-DFT-tested group as compared to the DFT-tested group (respectively, 13.9% vs. 17.6%). The NORDIC ICD trial included patients

with left-sided ICD implants. Furthermore, patients with terminal kidney insufficiency were excluded. In our current study, we included patients with (terminal) kidney insufficiency ($n=67$). Wase et al. found a trend that significant CKD in ICD recipients was related to overall survival, arrhythmic death, and high DFT's [17]. In total, 95 patients were included in this analysis of which 12 had ESKD. Also, only two patients received right-sided ICD implantation. Furthermore, in this study, no description was available concerning DFT procedure.

Our study has limitations. Inherent to conducting a retrospective study, there was a limited amount of missing data (Supplementary Table 3). Because of the retrospective design of this study, there was no uniform protocol for DFT. However, this is consistent with daily practice, as the method used for DFT testing depends on the operator's choice, with no single method having been shown to be superior (e.g., step-down method, step-up method, safety margin method, binary method). Furthermore, during the course of our study, new ICD systems and leads have been developed. A total of 20 different ICD types, 17 types of right ventricular leads, and 13 types of atrial leads were used in our population (Supplementary Tables 1 and 2).

Evidently, due to the inclusion criteria used, differences at baseline between the three groups could be expected. For example, the patients not on dialysis mostly received left-sided ICD implants, as opposed to patients on dialysis, which received right-sided implants in 70.1% of the cases. The patients with an eGFR < 15 ml/min/1.73 m^2 had a significantly better left ventricular ejection fraction, as opposed to patients with an eGFR ≥ 15 ml/min/1.73 m^2, which is inherent to the study design. Also, differences in comorbidity, medication use, and serum lab values can also be explained by this. Statistical correction for these differences (logistic regression model) did not change the results.

Several drugs can affect the DFT, including sotalol (decreases DFT) and amiodarone (increases DFT) [18]. In our study, in patients with CKD stage 5 (group 3), amiodarone use was lower as compared to groups 1 and 2 ($p<0.001$), and sotalol use was lower as compared to groups 1 and 2 (p value is insignificant). The difference is explained by the fact that the patients in group 1 and group 2 had an indication for an ICD because of impaired LVEF or sudden cardiac arrest due to ventricular arrhythmia. The use of sotalol or amiodaron may have influenced DFT in our study, as amiodaron use was higher in group 2 compared to groups 1 and 3 (Table 1). In our study, we did not find a higher rate of inadequate DSM in group 2, as compared to groups 1 and 3, which suggests that the impact of more amiodaron use on DFT in group 2 was minimal.

CONCLUSIONS

In this study, we did not demonstrate a correlation between CKD and increased DFT or an increased rate of inadequate DSM. DFT testing in patients on dialysis seems feasible when deemed necessary or desirable. The benefits of a DFT test, i.e., early recognition of ICD system dysfunction and the complications of DFT testing, are both low in patients with CKD. Regarding DFT, we found no differences in patients with CKD stage 5 who underwent right-sided ICD implantation compared with patients with CKD stage 5 with left-sided ICD. Withholding DFT testing in dialysis patients or in patients with right-sided ICD implantation could be considered.

Author Contributions. J. Wouter Jukema, Bart Mertens, Joris I. Rotmans, and Rohit J. Timal contributed to the study design. Rohit J. Timal contributed to the collection of data. Bart Mertens and Rohit J. Timal performed the data analyses. Rohit J. Timal wrote the first draft of the manuscript. Marianne Bootsma, J. Wouter Jukema, Bart Mertens, Lano Osman, Ton J. Rabelink, Joris I. Rotmans, and Martin J. Schalij provided critical revisions to the manuscript before seeing and approving the final version. J. Wouter Jukema, Bart Mertens, Joris I. Rotmans, and Rohit J. Timal had full access to all the data in the study and takes responsibility for the

integrity of the data and the accuracy of the data analysis.

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Data Availability. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of Interest. J. Wouter Jukema is an Editorial Board member of Cardiology and Therapy. J. Wouter Jukema was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions. Marianne Bootsma, Bart Mertens, Joris I. Rotmans, Lano Osman, Ton J. Rabelink, Martin J. Schalij, and Rohit J. Timal have nothing to disclose.

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REFERENCES

1. Hayase J, Do DH, Boyle NG. Defibrillation threshold testing: current status. Arrhythm Electrophysiol Rev. 2018;7(4):288–93.

2. Healey JS, Hohnloser SH, Glikson M, et al. Cardioverter defibrillator implantation without induction of ventricular fibrillation: a single-blind, non-inferiority, randomised controlled trial (SIMPLE). Lancet (London, England). 2015;385(9970):785–91.

3. Bansch D, Bonnemeier H, Brandt J, et al. The NO Regular Defibrillation testing In Cardioverter Defibrillator Implantation (NORDIC ICD) trial: concept and design of a randomized, controlled trial of intra-operative defibrillation testing during de novo defibrillator implantation. Europace Eur Pacing Arrhythm Cardiac Electrophysiol J Work Groups Cardiac Pacing Arrhythm Cardiac Cell Electrophysiol Eur Soc Cardiol. 2015;17(1):142–7.

4. Kolb C, Tzeis S, Zrenner B. Defibrillation threshold testing: tradition or necessity? Pacing Clin Electrophysiol PACE. 2009;32(5):570–2 (**discussion 572**).

5. Friedman PA, Rasmussen MJ, Grice S, Trusty J, Glikson M, Stanton MS. Defibrillation thresholds are increased by right-sided implantation of totally transvenous implantable cardioverter defibrillators. Pacing Clin Electrophysiol PACE. 1999;22(8):1186–92.

6. Saad TF, Ahmed W, Davis K, Jurkovitz C. Cardiovascular implantable electronic devices in hemodialysis patients: prevalence and implications for arteriovenous hemodialysis access interventions. Semin Dial. 2015;28(1):94–100.

7. Hsu JC, Marcus GM, Al-Khatib SM, et al. Predictors of an inadequate defibrillation safety margin at ICD implantation: insights from the National Cardiovascular Data Registry. J Am Coll Cardiol. 2014;64(3):256–64.

8. Priori SG, Blomstrom-Lundqvist C, Mazzanti A, et al. 2015 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology

(ESC)endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). Europace Eur Pacing Arrhythm Cardiac Electrophysiol J Work Groups Cardiac Pacing Arrhythm Cardiac Cell Electrophysiol Eur Soc Cardiol. 2015;17(11):1601–87.

9. Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Eur Heart J. 2022;43(40):3997–4126.

10. Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. New Engl J Med. 1996;335(26):1933–40.

11. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. New Engl J Med. 1997;337(22):1576–1583.

12. Healey JS, Dorian P, Mitchell LB, et al. Canadian Registry of ICD Implant Testing procedures (CREDIT): current practice, risks, and costs of intraoperative defibrillation testing. J Cardiovasc Electrophysiol. 2010;21(2):177–82.

13. Jukema JW, Timal RJ, Rotmans JI, et al. Prophylactic use of implantable cardioverter-defibrillators in the prevention of sudden cardiac death in dialysis patients. Circulation. 2019;139(23):2628–38.

14. Wilkoff BL, Fauchier L, Stiles MK, et al. 2015 HRS/EHRA/APHRS/SOLAECE expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. Heart Rhythm. 2016;13(2):e50-86.

15. Sticherling C, Ellenbogen KA, Burri H. Stepping back for good reasons: a reappraisal of the DF-1 connector for defibrillator leads. Europace 2024;26:1–4

16. Shih MJ, Kakodkar SA, Kaid Y, et al. Reassessing risk factors for high defibrillation threshold: the EF-SAGA risk score and implications for device testing. Pacing Clin Electrophysiol PACE. 2016;39(5):483–9.

17. Wase A, Basit A, Nazir R, et al. Impact of chronic kidney disease upon survival among implantable cardioverter-defibrillator recipients. J Interv Cardiac Electrophysiol Int J Arrhythm Pacing. 2004;11(3):199–204.

18. Hohnloser SH, Dorian P, Roberts R, et al. Effect of amiodarone and sotalol on ventricular defibrillation threshold: the optimal pharmacological therapy in cardioverter defibrillator patients (OPTIC) trial. Circulation. 2006;114(2):104–9.