



## **STEADIED Study : S-ICD in Patients with CKD/ESRD**



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## COI Disclosure

*Name of First Author: Jongmin Hwang*

The authors have no financial conflicts of interest  
to disclose concerning the presentation



# Sudden cardiac death in ESRD patients

- Patients with end-stage renal disease (ESRD) requiring renal replacement therapy have a 14-fold increased risk of death compared with the general population.
- with the largest category of cause-specific death believed to be attributable to cardiovascular disease
- To date, no therapy has been shown to be effective in reducing this mortality.



# Sudden cardiac death in ESRD patients

- Several landmark trials have identified high-risk patients who are eligible for implantable cardioverter-defibrillator (ICD) implantation for primary or secondary prevention of sudden cardiac death (SCD).
- However, ESRD patients were systematically excluded from these trials, irrespective of their left ventricular ejection fraction (LV EF).



# Sudden cardiac death in ESRD patients

- Literature concerning ICD therapy in ESRD patients is scarce, comprising studies with conflicting results and small sample size.



# Sudden cardiac death in ESRD patients

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## Effect of Renal Function on Survival After Implantable Cardioverter Defibrillator Placement

Casey S. Hager, MD   • Sunil Jain, MD • Jeffrey Blackwell, MD • Benjamin Culp, MD • Juhee Song, PhD • Christopher D. Chiles, MD

DOI: <https://doi.org/10.1016/j.amjcard.2010.06.058>



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Implantable cardioverter defibrillators (ICDs) are effective at reducing arrhythmic death in patients with left ventricular dysfunction, but few studies have investigated the outcomes after ICD implantation in patients with chronic kidney disease (CKD). We conducted a 2-center retrospective study of 958 patients who had undergone ICD placement for primary prevention from the 2000 to 2006. The patients were stratified into 5 groups according to the CKD stage (stage 1, glomerular filtration [GFR] 90 to 120 ml/min; stage 2, GFR 60 to 89 ml/min; stage 3, GFR 30 to 59 ml/min; stage 4, GFR 15 to 29 ml/min; and stage 5, GFR 0 to 14 ml/min). The primary end point was death at 1 year. Of the 958 patients included in our analysis, 73 (7.6%) had died at 1 year. The mortality rate at 1 year increased with worsening CKD (1.8%, 5.3%, 9.0%, 22%, and 38% for stage 1 to 5, respectively,  $p < 0.0001$  for group). CKD was an independent predictor of mortality; hazard ratio 1.0, 1.075 (95% confidence interval 0.578 to 2.0), 1.372 (95% confidence interval 0.736 to 2.556), 3.092 (95% confidence interval 1.52 to 6.29), and 10.15 (95% confidence interval 4.25 to 24.23) for stage 1 to 5, respectively ( $p < 0.0001$  for group). Patients with CKD and left ventricular dysfunction have a poor prognosis despite ICD placement. The 1-year mortality increased as the renal function decreased. In conclusion, physicians should be cognizant of the prognosis when considering whether an ICD should be implanted in patients with CKD.



# Sudden cardiac death in ESRD patients

## Implantable Cardioverter-Defibrillators for Primary Prevention of Sudden Cardiac Death in CKD: A Meta-analysis of Patient-Level Data From 3 Randomized Trials

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**Background:** The benefit of a primary prevention implantable cardioverter-defibrillator (ICD) among patients with chronic kidney disease is uncertain.

**Study Design:** Meta-analysis of patient-level data from randomized controlled trials.

**Setting & Population:** Patients with symptomatic heart failure and left ventricular ejection fraction < 35%.

**Selection Criteria for Studies:** From 7 available randomized controlled studies with patient-level data, we selected studies with available data for important covariates. Studies without patient-level data for baseline estimated glomerular filtration rate (eGFR) were excluded.

**Intervention:** Primary prevention ICD versus usual care effect modification by eGFR.

**Outcomes:** Mortality, rehospitalizations, and effect modification by eGFR.

**Results:** We included data from the Multicenter Automatic Defibrillator Implantation Trial I (MADIT-I), MADIT-II, and the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). 2,867 patients were included; 36.3% had eGFR < 60 mL/min/1.73 m<sup>2</sup>. Kaplan-Meier estimate of the probability of death during follow-up was 43.3% for 1,334 patients receiving usual care and 35.8% for 1,533 ICD recipients. After adjustment for baseline differences, there was evidence that the survival benefit of ICDs in comparison to usual care depends on eGFR (posterior probability for null interaction  $P < 0.001$ ). The ICD was associated with survival benefit for patients with eGFR  $\geq 60$  mL/min/1.73 m<sup>2</sup> (adjusted HR, 0.49; 95% posterior credible interval, 0.24-0.95), but not for patients with eGFR < 60 mL/min/1.73 m<sup>2</sup> (adjusted HR, 0.80; 95% posterior credible interval, 0.40-1.53). eGFR did not modify the association between the ICD and rehospitalizations.

**Limitations:** Few patients with eGFR < 30 mL/min/1.73 m<sup>2</sup> were available. Differences in trial-to-trial measurement techniques may lead to residual confounding.

**Conclusions:** Reductions in baseline eGFR decrease the survival benefit associated with the ICD. These findings should be confirmed by additional studies specifically targeting patients with varying eGFRs.

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# Sudden cardiac death in ESRD patients

## Clinical characteristics and in-hospital outcome of patients with end-stage renal disease on dialysis referred for implantable cardioverter-defibrillator implantation

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**BACKGROUND** Little is known about the clinical profile of end-stage renal disease (ESRD) patients who undergo implantable cardioverter-defibrillator (ICD) implantation.

**OBJECTIVE** This study sought to analyze the risk profile of ESRD patients admitted for ICD implantation.

**METHODS** Patients undergoing first-time device implantation in National Cardiovascular Data Registry/ICD registry from 01/01/06 to 12/31/07 were analyzed (n = 164,069). Patients with ESRD (defined as those requiring dialysis) were compared with patients without ESRD. Primary outcome was in-hospital complications. Because length of hospital stay for ESRD patients was significantly longer (8 vs. 4 days), complications within 2 days of ICD implantation were also examined. The proportion of patients meeting approved indications for ICD implantation was evaluated.

**RESULTS** ESRD patients (n = 6,851, 4.4%) had higher rates of comorbid medical conditions, major complications, and total complications, and were less likely to receive an ICD for primary prevention. ESRD patients who received ICD implantation for primary prevention were more likely to meet trial criteria. ESRD

patients were less likely to receive beta-blockers and angiotensin inhibitors ( $P < .0001$ ). Unadjusted in-hospital mortality was almost 5-fold among patients with ESRD (1.9% vs. 0.4%,  $P < .0001$ ). Multivariable analysis confirmed that ESRD was independently associated with total in-hospital complications (odds ratio [OR] = 1.38, 95% confidence interval: 1.23 to 1.54,  $P < .0001$ ), and total complications at 2 days (OR = 1.20, 95% confidence interval: 1.05 to 1.36,  $P = .006$ ).

**CONCLUSION** ESRD patients presenting for ICD implantation are sicker, and have higher rates of in-hospital complications even when accounting for overall longer length of hospital stay. Strategies to decrease complications among ESRD patients who undergo ICD implantation need exploration.

**KEYWORDS** Dialysis; Renal failure; Defibrillator

**ABBREVIATIONS** CI = confidence interval; ESRD = end-stage renal disease; ICD = implantable cardioverter-defibrillator; NCDR = National Cardiovascular Data Registry; OR = odds ratio

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# Sudden cardiac death in ESRD patients

## Clinical Presentation and Outcomes of Cardiovascular Implantable Electronic Device Infections in Hemodialysis Patients

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### Abstract

**Background**—Infection is a serious complication of cardiovascular implantable electronic device (CIED) implantation. Kidney failure is as an independent risk factor for CIED infection and associated mortality. The presence of multiple comorbid conditions may contribute to varied clinical presentations and poor outcomes in hemodialysis (HD)–dependent patients with cardiac device infection.



# Sudden cardiac death in ESRD patients

- Therefore, the potential value of prophylactic transvenous ICD implantation in patients undergoing dialysis is unknown and questionable.
  - ✓ It is unclear whether ICD implantation offers a survival advantage or whether competing risks from comorbidities and device-related complications negatively affect outcome, mitigating any benefit.



# Sudden cardiac death in ESRD patients

## Outcomes of subcutaneous implantable cardioverter-defibrillator implantation in patients on hemodialysis

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### Abstract

**Background** Subcutaneous implantable cardioverter-defibrillator (S-ICD) provides potential benefits in patients on hemodialysis (HD) by reducing the risk of blood stream infection and preserving vascular access sites. We evaluated the safety and efficacy of S-ICD in patients with end-stage renal disease (ESRD) on HD.

**Methods** All consecutive patients implanted with S-ICD between October 2012 and April 2015 at our high-volume center were included in this retrospective, single-center study. Baseline demographics, procedural details, and short- as well as long-term outcomes were compared between patients on HD and not on HD.

**Results** A total of 86 S-ICDs were implanted at our institution during the study period. Eighteen (21 %) patients were on HD at the time of implant. HD patients were more likely to be implanted for secondary prevention. There was no statistically significant difference in procedural complications between the two groups. HD patients had a longer duration hospital stay after implant ( $3.6 \pm 5.14$  vs.  $1.69 \pm 2.29$  days,  $p = 0.021$ ). During a mean follow-up of  $205 \pm 208$  days in the HD cohort and  $242 \pm 238$  days in the non-HD cohort ( $p = 0.268$ ), there was no device or blood stream infection in the HD group, compared

with five device infections in the non-HD group. The incidence of inappropriate shocks was similar in both groups. All appropriate shocks were successful in terminating ventricular tachyarrhythmias in both groups. Patients on hemodialysis had worse inpatient as well as long-term mortality after S-ICD implant, compared with non-HD patients.

**Conclusions** Our study demonstrates the safety and efficacy of S-ICD in patients on HD. Despite representing a sicker patient population, HD patients implanted with S-ICD had similar procedural outcomes and inappropriate shocks. There was no device or blood stream-related infection in HD patients. All appropriate shocks for ventricular arrhythmias in HD patients were successful.

**Keywords** Subcutaneous implantable cardioverter-defibrillator · Implantable cardioverter-defibrillator · End-stage renal disease · Hemodialysis

### 1 Introduction

Implantable cardioverter-defibrillators (ICDs) have been im-



# Sudden cardiac death in ESRD patients

- Thus, it is reasonable to assume that the survival benefit of the ICD may be offset by an increased risk of endovascular infection associated with transvenous hardware, particularly in patients on hemodialysis who are at significantly increased risk of bacteremia.
- To date, no randomized clinical trials have been performed in this area. Furthermore, this group of patients was excluded from most ICD trials despite that the prevalence of LV dysfunction in dialysis patients is reported as high as 14%.



# Sudden cardiac death in ESRD patients

- The subcutaneous ICD (S-ICD) offers a potentially attractive alternative to the transvenous ICD in patients on dialysis by providing protection from SCD without the need for transvenous hardware, thus limiting the risk of endovascular infection.
- The limited data are available whether S-ICD implantation for primary prevention in patients with end stage of renal disease (ESRD) on hemodialysis and reduced LVEF is effective and beneficial.



# Study objective

- The aim of the present study is to determine whether S-ICD implantation for primary prevention in patients with ESRD on dialysis and reduced LVEF is effective on treatment of life-threatening arrhythmia.



# Study Design

- Prospective, multicenter, observational registry study
- Primary endpoint
  - ✓ incidence of appropriate S-ICD treatment
- Secondary endpoint
  - ✓ death from any cause, arrhythmic death, cardiac death, non-cardiac death, incidence of inappropriate shocks, implant related complications





# Sample size

- Previous meta-analysis showed that in patients with ischemic heart disease and transvenous ICD implantation for the primary prevention, the appropriate shocks were identified in 7.8%.
- A recent small retrospective study reported 18% of annual shock rate of S-ICD implanted in ESRD patients on dialysis.
- We will validate if the efficacy (appropriate shock) of S- ICD could reach as high as 18% in a large number of patients.
- When the power is 80%, and the significance level is 0.05, the required number of subjects is 70.
- Considering the dropout rate of 10%, the number of patients required to achieve the purpose of this study is 77.



# Study Procedure

- We will prospectively enroll ESRD patients on dialysis who indicated for ICD implantation for the primary prevention of SCD according to current guideline.
- The decision to implant ICD will be made by the operator's discretion and patient's preference. The patients who decided to have S-ICD implanted will be enrolled.
- Boston Scientific S-ICD® system will be used
- Patients were followed at least 12 months after enrollment



# Current study status

## 1. Study Overview

- 연구 대상 : 좌심실 기능 부전을 동반한 만성 신질환 3-5 기 환자이면서 Primary prevention ICD indication 에 해당하는 자
- 목표 대상자수 : 77 명
- 연구 디자인: 다기관, 비중재 관찰연구, 12 개월 follow up
- 선정/제외기준

\* 다른 Registry 에 참여 중인 환자도 중복 등록이 가능합니다\*

선정기준	제외기준
① 19 세 이상 성인환자	① 임상연구에 취약한 피험자(KGCP 에 따름)
② 만성 신질환 3 기~5 기 인환자	② 피하 삽입형 제세동기 가능 선별에서 부적격인자
③ 좌심실 구혈률이 35%이하인 환자	③ 심정지를 경험하고 소생한 환자
④ 현재 진료지침 권고사항에 따라 급사의 일차적 예방을 위해 피하삽입형 제세동기 삽입 받은 환자	④ 심실 빈맥의 병력이 있는 환자
	⑤ 인공심장 박동기나 경정맥 제세동기를 갖고 있는 환자
	⑥ 기대여명이 1 년 이내인 환자
	⑦ 신장 이식이 예정되어 있는 환자



# Current study status

2. Status: Activated site **10sites**, Enrolled patient: **28 patients(36%)/Target 77**

Site Name	PI	Site Activation	Enrollment	Ongoing	Completed
계명대학교 동산병원	한성욱	2020-09-25	2	2	0
세브란스병원	정보영	2020-12-29	8	4	4
서울대학교병원	최의근	2021-02-09	3	1	2
삼성서울병원	박승정	2021-01-28	10	5	5
서울아산병원	조민수	2021-01-07	1	0	1
분당서울대병원	오일영	2021-02-17	2	0	2
경북대병원	배명환	2021-04-21	1	1	0
대구가톨릭대학교병원	이영수	2021-05-25	0	0	0
세종병원	박상원	2021-05-18	0	0	0
동아대병원	박종성	2022-04-25	1	0	1



# Notice

- We are conducting a concurrent registry study where we register patients who refuse ICD implantation and opt for medical treatment alone.
- The study started at 2020.9 but only 28 patients were enrolled.
- Suspected causes of delayed patient enrollment
  - ✓ Can be divided into physician factors and patient factors.
  - ✓ Physicians may be concerned about the poor prognosis of patients with CKD5 on dialysis and the as-yet-unestablished role of primary prevention ICDs.
  - ✓ Patients on dialysis often tend to be reluctant towards procedural treatments and resistant to information from health care providers (esp. implantation for primary prevention).



# Thank you for your attention~!

- While it is a challenging topic, it is our mission to never cease our efforts toward evidence-based medicine.

