

Supplementary Online Content

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eFigure. Stratified Analysis of Indexed Infection Rate

eTable 1. Baseline Characteristics According to the Combination of Timing and Extent of Infections

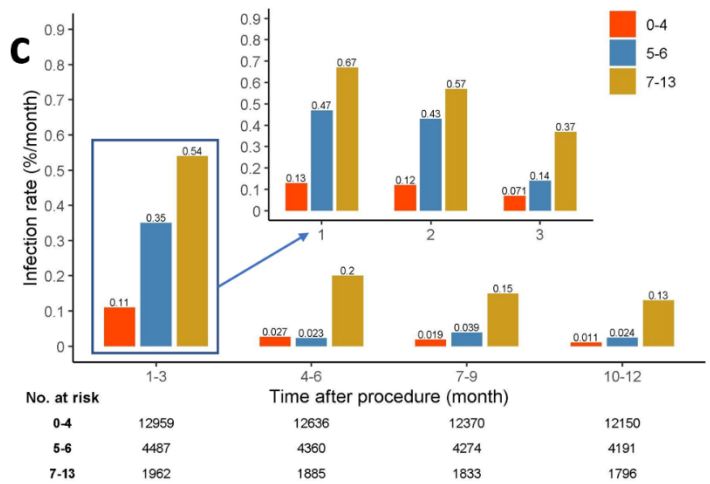
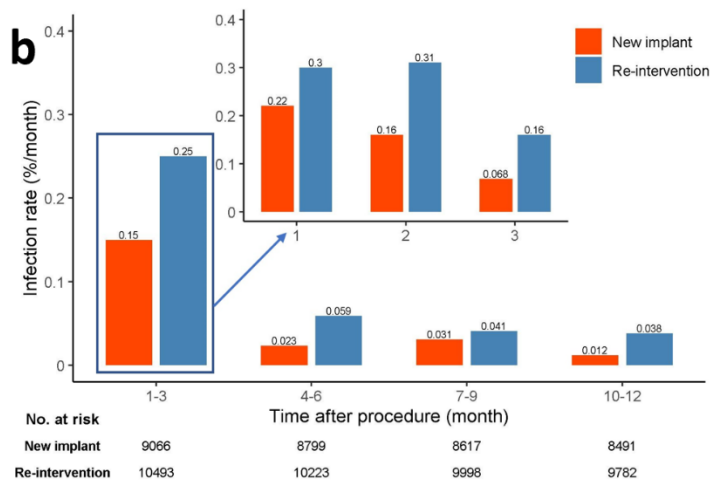
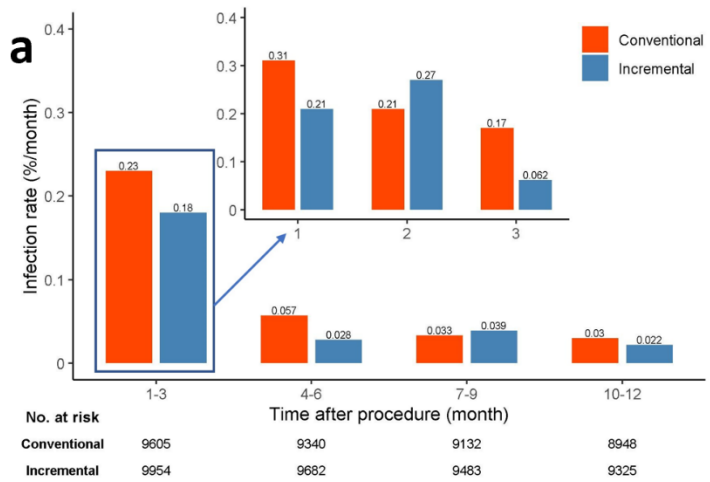
eTable 2. Microbiology of CIED Infections With Patient-Level and Organism-Level Data

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eTable 4. Outcome Data According to the Timing and Extent of Infection

This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure. Stratified Analysis of Indexed Infection Rate



Indexed infection rate stratified according to: **a)** conventional or incremental antimicrobial treatment; **b)** initial implant or re-intervention; and **c)** PADIT risk score

eTable 1. Baseline Characteristics According to the Combination of Timing and Extent of Infections

	Early localized (N=74)	Early systemic (N=45)	Delayed localized (N=35)	Delayed systemic (N=23)	P Value^a
<i>Demographics and history</i>					
Age	66.8±13.0	70.6±10.5	69.6±13.3	69.7±14.4	0.402
Female	18 (24.3)	13 (28.9)	7 (20.0)	7 (30.4)	0.758
Diabetes	16 (21.6)	17 (37.8)	12 (34.3)	10 (43.5)	0.119
History of heart failure	39 (52.7)	27 (60.0)	16 (45.7)	12 (52.2)	0.650
Renal insufficiency	15 (20.3)	12 (26.7)	7 (20.0)	7 (30.4)	0.673
Penicillin allergy	11 (14.9)	9 (20.0)	6 (17.1)	2 (8.7)	0.668
Immuno-compromised	3 (4.1)	2 (4.4)	1 (2.9)	1 (4.3)	>0.999
<i>Type of procedure</i>					
New PM	5 (6.8)	7 (15.6)	0 (0.0)	4 (17.4)	0.024
New ICD	9 (12.2)	6 (13.3)	1 (2.9)	2 (8.7)	0.393
PM generator replacement ^b	10 (13.5)	5 (11.1)	7 (20.0)	2 (8.7)	0.639
ICD generator replacement ^b	12 (16.2)	5 (11.1)	5 (14.3)	0 (0.0)	0.182
CRT generator replacement ^b	6 (8.1)	7 (15.6)	4 (11.4)	4 (17.4)	0.450
Revision ^b (pocket or lead)	32 (43.2)	10 (22.2)	15 (42.9)	6 (26.1)	0.068
New CRT-P	1 (1.4)	1 (2.2)	0 (0.0)	1 (4.3)	0.635
New CRT-D	5 (6.8)	6 (13.3)	4 (11.4)	5 (21.7)	0.219
<i>Duration of procedure</i>					
<1 hr	39 (52.7)	24 (53.3)	24 (68.6)	11 (47.8)	
1-1.5 hrs	18 (24.3)	13 (28.9)	7 (20.0)	7 (30.4)	
>1.5 - 2 hrs	9 (12.2)	3 (6.7)	2 (5.7)	2 (8.7)	
> 2 hrs	8 (10.8)	5 (11.1)	2 (5.7)	2 (8.7)	
Other procedure on pocket	19 (25.7)	9 (20.0)	16 (45.7)	5 (21.7)	0.056
<i>Number of other procedures</i>					
1 other procedure	13 (17.6)	4 (8.9)	8 (22.9)	2 (8.7)	
2 other procedures	5 (6.8)	4 (8.9)	6 (17.1)	2 (8.7)	
> 2 other procedures	1 (1.4)	1 (2.2)	2 (5.7)	1 (4.3)	
Incremental antibiotics	34 (45.9)	19 (42.2)	16 (45.7)	9 (39.1)	0.933

^a P value is from ANOVA test for continuous variables and Chi-square test or Monte Carlo estimates of Fisher's exact test for categorical variables

^b Replacement indicates generator change (when battery reaches elective replacement indicator or end of life); revision relates to interventions for device pocket (e.g. evacuation of significant hematoma) or lead (e.g. lead upgrade procedures or re-implantation of dislodged leads)

eTable 2. Microbiology of CIED Infections With Patient-Level and Organism-Level Data

2a

	Early localized (N=74)	Early systemic (N=45)	Delayed localized (N=35)	Delayed systemic (N=23)	P Value ^a
Microbiology of infections					
Monomicrobial infections	40/74 (54.1)	33/45 (73.3)	13/35 (37.1)	17/23 (73.9)	0.004
Polymicrobial infections	14/74 (18.9)	11/45 (24.4)	7/35 (20.0)	5/23 (21.7)	0.909
No pathogen identified	20/74 (27.0)	1/45 (2.2)	15/35 (42.9)	1/23 (4.3)	<0.001
Susceptibility of pathogens					
Main pathogen sensitive to cefazolin	30/47 (63.8)	32/40 (80.0)	9/12 (75.0)	14/20 (70.0)	0.413
Main pathogen sensitive to vancomycin	47/53 (88.7)	42/44 (95.5)	17/19 (89.5)	18/21 (85.7)	0.528
≥1 pathogen sensitive to cefazolin	31/46 (67.4)	35/40 (87.5)	12/14 (85.7)	14/20 (70.0)	0.114
≥1 pathogen sensitive to vancomycin	50/54 (92.6)	43/44 (97.7)	19/19 (100)	18/21 (85.7)	0.160
All pathogens sensitive to cefazolin	26/44 (59.1)	30/39 (76.9)	7/13 (53.8)	11/18 (61.1)	0.268
All pathogens sensitive to vancomycin	47/54 (87.0)	42/44 (95.5)	15/19 (78.9)	17/21 (81.0)	0.145

^a P value is from Kruskal-Wallis test for continuous variables and Chi-square test or Monte Carlo estimates of Fisher's exact test for categorical variables

2b

	Early localized (N=72) ^a	Early systemic (N=78) ^a	Delayed localized (N=28) ^a	Delayed systemic (N=31) ^a	P Value ^b
Gram-positive bacteria	63/72 (87.5)	75/78 (96.2)	24/28 (85.7)	26/31 (83.9)	0.31
Staphylococcus aureus	12/72 (16.7)	48/78 (61.5)	7/28 (25.0)	8/31 (25.8)	<0.001
Coagulase-negative Staphylococcus	38/72 (52.8)	21/78 (26.9)	11/28 (39.3)	12/31 (38.7)	0.05
Streptococcus pneumoniae	0/72 (0.0)	0/78 (0.0)	0/28 (0.0)	1/31 (3.2)	-
Enterococcus sp.	1/72 (1.4)	1/78 (1.3)	0/28 (0.0)	2/31 (6.5)	-
Viridans streptococci	1/72 (1.4)	2/78 (2.6)	0/28 (0.0)	2/31 (6.5)	-
Other streptococci	1/72 (1.4)	1/78 (1.3)	0/28 (0.0)	0/31 (0.0)	-
Propionibacterium sp.	8/72 (11.1)	1/78 (1.3)	3/28 (10.7)	0/31 (0.0)	-
Other gram-positive bacteria	2/72 (2.8)	1/78 (1.3)	3/28 (10.7)	1/31 (3.2)	-
Gram-negative bacteria	7/72 (9.7)	3/78 (3.8)	3/28 (10.7)	4/31 (12.9)	-
Escherichia coli	0/72 (0.0)	0/78 (0.0)	0/28 (0.0)	1/31 (3.2)	-
Klebsiella sp.	0/72 (0.0)	1/78 (1.3)	0/28 (0.0)	0/31 (0.0)	-
Serratia sp.	0/72 (0.0)	1/78 (1.3)	0/28 (0.0)	1/31 (3.2)	-
Enterobacter sp.	4/72 (5.6)	0/78 (0.0)	0/28 (0.0)	0/31 (0.0)	-
Other Enterobacteriaceae	1/72 (1.4)	0/78 (0.0)	0/28 (0.0)	0/31 (0.0)	-
Pseudomonas aeruginosa	1/72 (1.4)	1/78 (1.3)	1/28 (3.6)	2/31 (6.5)	-
Non-fermenting gram-negatives	0/72 (0.0)	0/78 (0.0)	2/28 (7.1)	0/31 (0.0)	-
Other gram-negatives	1/72 (1.4)	0/78 (0.0)	0/28 (0.0)	0/31 (0.0)	-
Other pathogens	2/72 (2.8)	0/78 (0.0)	1/28 (3.6)	1/31 (3.2)	-
Anaerobes (not Propionibacterium)	1/72 (1.4)	0/78 (0.0)	0/28 (0.0)	1/31 (3.2)	-
Candida albicans	1/72 (1.4)	0/78 (0.0)	1/28 (3.6)	0/31 (0.0)	-

^a Number of organisms does not match number of patients due to presence of CIED infections without identifiable pathogens and polymicrobial infections

^b P values were calculated for the variables with at least 20 cases using logistic mixed model to account for underlying correlation among microorganisms detected in the same patient

eTable 3. Outcome Data According to the Timing and Extent of Infection

	Early localized (N=74)	Early systemic (N=45)	Delayed localized (N=35)	Delayed systemic (N=23)	P Value
30-day mortality ^a , n/N(%)	0/74 (0.0)	4/45 (8.9)	3/34 (8.8)	5/23 (21.7)	<0.001
90-day mortality ^a , n/N(%)	2/74 (2.7)	4/45 (8.9)	3/34 (8.8)	5/23 (21.7)	0.024
Length of hospitalization	11.0 (7.0-15.0)	13.0 (7.0-32.0)	12.0 (6.0-22.0)	19.0 (6.0-30.0)	0.017
Stay in ICU/CCU	11 (14.9)	12 (26.7)	6 (17.1)	6 (26.1)	0.361
Length of stay	6.0 (1.0-11.0)	4.0 (2.0-7.0)	9.0 (2.0-12.0)	8.5 (5.0-12.0)	0.383
Surgical exploration or device explant	67 (90.5)	38 (84.4)	33 (94.3)	19 (82.6)	0.388
Duration of antibiotics	15.0 (10.0-24.0)	28.0 (17.0-42.0)	17.5 (10.0-34.0)	28.0 (14.0-49.0)	0.003

CCU, coronary care unit; ICU, intensive care unit.

Values are given as mean median (IQR) or n (%) unless otherwise indicated.

^a Included patients with at least 30 (or 90) days follow-up after infection unless patient died

eTable 4. Outcome Data According to the Timing and Extent of Infection**4a**

	All (N=177)	Early infection (N=119)	Late infection (N=58)	P value
30-day mortality*, n/N(%)	12/176 (6.8)	4/119 (3.4)	8/57 (14.0)	0.020
90-day mortality*, n/N(%)	14/176 (8.0)	6/119 (5.0)	8/57 (14.0)	0.07
Length of hospitalization	12.0 (7.0-21.0)	12.0 (7.0-18.0)	13.0 (6.0-23.0)	0.37
Stay in ICU/CCU, n(%)	35 (19.8)	23 (19.3)	12 (20.7)	0.83
Length of stay in ICU/CCU	5.0 (2.0-11.0)	4.0 (1.0-9.0)	9.0 (4.0-12.0)	0.10
Surgical exploration or device explant	157 (88.7)	105 (88.2)	52 (89.7)	0.78
Duration of antibiotics	20.0 (10.0-35.0)	20.0 (10.0-33.0)	20.0 (10.0-42.0)	0.37

4b

	All (N=177)	Systemic infection (N=68)	Local infection (N=109)	P value
30-day mortality*, n/N(%)	12/176 (6.8)	9/68 (13.2)	3/108 (2.8)	0.012
90-day mortality*, n/N(%)	14/176 (8.0)	9/68 (13.2)	5/108 (4.6)	0.040
Length of hospitalization	12.0 (7.0-21.0)	17.5 (7.0-31.0)	11.0 (7.0-17.0)	0.002
Stay in ICU/CCU, n(%)	35 (19.8)	18 (26.5)	17 (15.6)	0.08
Length of stay in ICU/CCU	5.0 (2.0-11.0)	5.0 (3.0-10.0)	7.0 (1.0-11.0)	0.96
Surgical exploration or device explant	157 (88.7)	57 (83.5)	100 (91.7)	0.11
Duration of antibiotics	20.0 (10.0-35.0)	28.0 (14.0-42.0)	15.0 (10.0-28.0)	<0.001