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Long-Acting Lipoglycopeptides in Orthopedic and Cardiovascular Device-Associated Infections: Outcomes According to Source-Control Strategy in a Multicenter Day-Hospital Cohort

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Abstract

Background: Long-acting lipoglycopeptides (LALs) can simplify prolonged anti-Gram-positive therapy, but evidence in infections involving orthopedic or cardiovascular prosthetic material remains limited, particularly in relation to surgical source control. Methods: We performed a post hoc secondary analysis of a previously published multicenter day-hospital cohort. Adults with orthopedic or cardiovascular prosthetic material and a deep-seated or device-associated infection treated with at least one dose of dalbavancin and/or oritavancin between January 2020 and December 2025 were included; patients with an unrelated acute bacterial skin and skin-structure infection were excluded. Clinical outcomes were examined according to eventual device management (retention versus removal; total versus partial explantation). Results: Forty-six patients were included; median age was 72.3 years (IQR 60.4–79.1) and median Charlson Comorbidity Index was 4 (IQR 2.2–6.0). Prosthetic joint infection accounted for 25/46 cases (54.3%). Forty-five patients received a dalbavancin-containing regimen and 31/46 (67.4%) received LAL monotherapy. Clinical success at last available follow-up was 87.0% (40/46; exact 95% CI 73.7–95.1). Among the 40 patients with a classified source-control strategy and an infection involving the recorded device, success was 88.9% with retention (16/18) and 86.4% with removal (19/22); the exact conditional

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odds ratio was 1.26 (95% CI 0.13–16.79; Fisher $p = 1.000$). After removal, success was 89.5% after total explantation (17/19) and 66.7% after partial removal (2/3). C-reactive protein fell from 3.65 to 0.91 mg/dL ($p < 0.001$). Adverse drug events were mild and infrequent (2/40). Conclusions: In this post hoc, uncontrolled device-focused analysis, LAL-based day-hospital management was feasible with favorable observed outcomes. The source-control comparison was imprecise and cannot support superiority of retention or removal; it should be interpreted as descriptive and hypothesis-generating. Follow-up duration was not standardized, so durable cure could not be assessed.

Keywords: long-acting lipoglycopeptides; dalbavancin; oritavancin; prosthetic joint infection; device-associated infection; source control; suppressive antibiotic therapy; day hospital; OPAT

1. Introduction

Infections involving prosthetic joints, osteosynthesis hardware, prosthetic valves, cardiac implantable electronic devices, and vascular grafts are among the most difficult Gram-positive infections to manage. Successful treatment commonly requires prolonged antimicrobial therapy integrated with an individualized source-control strategy. In prosthetic joint infection, options range from debridement and implant retention to one- or two-stage exchange or resection; in cardiovascular device infection, complete hardware removal is frequently central to curative management when feasible [1,2].

When definitive removal is not feasible because of operative risk, mechanical considerations, or patient preference, selected patients may receive prolonged or suppressive antimicrobial strategies, although the evidence base is largely observational and highly dependent on case selection [3]. Conventional outpatient parenteral antimicrobial therapy (OPAT) can reduce hospitalization, but daily infusions and long-term vascular access remain burdensome and expose patients to line-related complications [4].

Dalbavancin and oritavancin have prolonged terminal half-lives that allow infrequent parenteral dosing. Although regulatory approval is primarily for acute bacterial skin and skin-structure infections (ABSSSIs), both agents are increasingly used off-label for osteoarticular, endovascular, and other deep-seated Gram-positive infections, particularly as consolidation therapy or as the parenteral component of longer outpatient regimens [5–9].

We previously reported a multicenter day-hospital cohort of 160 patients treated with LALs, describing overall effectiveness, safety, treatment-selection patterns, and modeled resource implications [10]. That report included descriptive prosthetic-device data but did not evaluate outcomes according to device retention versus removal. The present secondary analysis focuses specifically on patients with orthopedic or cardiovascular prosthetic material and asks a distinct clinical question: how were LALs used alongside real-world source-control strategies, and what outcomes were observed under retention, total explantation, or partial removal? The analysis is explicitly descriptive and hypothesis-generating rather than comparative.

2. Results

2.1. Cohort Characteristics

Forty-six patients met the inclusion criteria. Median age at first LAL administration was 72.3 years (IQR 60.4–79.1), median CCI was 4.0 (IQR 2.2–6.0), and 26 patients (56.5%) were male. Hypertension (60.9%), cardiac disease (47.8%), and diabetes mellitus (28.3%) were the most frequent comorbidities (Table 1).

Table 1. Demographic, clinical, infection, device, and treatment characteristics overall and according to known source-control strategy.

Characteristic	Overall (N = 46)	Retention (n = 22)	Removal (n = 22)	*p* Value
Age at first LAL administration, years—median (IQR)	72.3 (60.4–79.1)	75.2 (56.6–79.6)	67.5 (63.8–74.3)	0.430
Male sex, n (%)	26 (56.5)	13 (59.1)	11 (50.0)	0.763
Charlson Comorbidity Index—median (IQR)	4.0 (2.2–6.0)	4.0 (1.3–7.8)	4.0 (3.0–6.0)	1.000
Hypertension, n (%)	28 (60.9)	13 (59.1)	13 (59.1)	1.000
Cardiac disease, n (%)	22 (47.8)	10 (45.5)	11 (50.0)	1.000
Diabetes mellitus, n (%)	13 (28.3)	6 (27.3)	7 (31.8)	1.000
COPD, n (%)	5 (10.9)	3 (13.6)	2 (9.1)	1.000
Neurological disease, n (%)	5 (10.9)	2 (9.1)	2 (9.1)	1.000
Active malignancy, n (%)	5 (10.9)	2 (9.1)	3 (13.6)	1.000
Primary indication, n (%)				0.121
Prosthetic joint infection	25 (54.3)	10 (45.5)	15 (68.2)	-
Osteomyelitis involving hardware	9 (19.6)	4 (18.2)	5 (22.7)	-
Spondylodiscitis	5 (10.9)	4 (18.2)	0 (0.0)	-
Endocarditis	4 (8.7)	2 (9.1)	2 (9.1)	-
Prosthetic cardiac infection	3 (6.5)	2 (9.1)	0 (0.0)	-
Device type, n (%)				
Orthopedic	37 (80.4)	16 (72.7)	20 (90.9)	0.240
Cardiovascular	10 (21.7)	7 (31.8)	2 (9.1)	0.132
Care pathway, n (%)				
De novo	25 (54.3)	13 (59.1)	11 (50.0)	0.763
Step-down	21 (45.7)	9 (40.9)	11 (50.0)	0.763
LAL exposure, n (%)				
Dalbavancin-containing	45 (97.8)	21 (95.5)	22 (100)	1.000
Oritavancin-containing	2 (4.3)	1 (4.5)	1 (4.5)	1.000
Oritavancin only	1 (2.2)	1 (4.5)	0 (0.0)	1.000
Treatment strategy, n (%)				
Monotherapy	31 (67.4)	16 (72.7)	14 (63.6)	0.747
Combination therapy	15 (32.6)	6 (27.3)	8 (36.4)	0.747
Number of LAL administrations—median (IQR)	2 (2–3)	2 (2–2)	2 (2–3)	0.424
First-to-last administration interval, days—median (IQR)	8 (7–14)	7 (6–14)	8 (7–14)	0.721
TDM performed, n (%)	4 (8.7)	0 (0.0)	4 (18.2)	0.108

Notes: The overall column includes two patients with unclassified source-control status; retention-versus-removal comparisons use the 44 classified patients. Device-type and LAL-exposure categories are not mutually exclusive. *p* values are exploratory and unadjusted: Fisher's exact test for binary categorical variables, Fisher–Freeman–Halton exact test for the overall primary-indication distribution, and Mann–Whitney U test for continuous variables. Lack of statistical significance should not be interpreted as equivalence or balance. The retention column includes four patients with spondylodiscitis in whom device involvement was not established; they are excluded from the outcome comparison (Table 2). Abbreviations: LAL, long-acting lipoglycopeptide; IQR, interquartile range; COPD, chronic obstructive pulmonary disease; TDM, therapeutic drug monitoring.

Table 2. Clinical success according to source-control strategy.

Source-Control Strategy	n	Clinical Success, n (%)	Exact 95% CI
Device retention	18	16 (88.9)	65.3–98.6
Device removal	22	19 (86.4)	65.1–97.1
Total explantation	19	17 (89.5)	66.9–98.7
Partial removal	3	2 (66.7)	9.4–99.2
Unclassified source-control status	1	0 (0.0)	0.0–97.5
Spondylodiscitis, device involvement not established (excluded from comparison)	5	5 (100)	47.8–100

Note: Retention versus removal: exact conditional OR for clinical success 1.26 (95% CI 0.13–16.79); Fisher's exact $p = 1.000$. Clinical success refers to the last available follow-up. Patients with spondylodiscitis, in whom device involvement was not established, are excluded from the comparison; including them in the retention group gives an exact conditional OR of 1.56 (95% CI 0.16–20.66). Abbreviations: CI, confidence interval; OR, odds ratio.

2.2. Infection, Device, Treatment, and Source-Control Characteristics

Prosthetic joint infection was the leading indication (25/46, 54.3%), followed by osteomyelitis involving hardware (9/46, 19.6%), spondylodiscitis (5/46, 10.9%), endocarditis (4/46, 8.7%), and prosthetic cardiac infection (3/46, 6.5%). Thirty-seven patients had orthopedic material and ten had cardiovascular devices; one patient had both. The most common recorded orthopedic sites were the knee (n = 15) and hip (n = 8); the most common cardiovascular sites were the cardiac chambers (n = 5) and aorta (n = 4). Among the four patients with endocarditis, the recorded cardiovascular device was intracardiac in three and its site was not specified in one, who also carried hip and knee prostheses; among the three patients with prosthetic cardiac infection, the device was aortic in two and intracardiac in one.

A dalbavancin-containing regimen was used in 45/46 patients; one patient received oritavancin alone and one of the dalbavancin-treated patients also received oritavancin. The median number of LAL administrations was 2 (IQR 2–3), and the median recorded interval from first to last administration was 8 days (IQR 7–14). Dosing was not protocolized; the initial dalbavancin dose was 1500 mg in 43/45 dalbavancin-treated patients and 1000 mg in two; eight received a single dose, 24 received two administrations (two 1500 mg doses in 22, given 6–8 days apart in 19), and 13 received three or more. Both oritavancin-treated patients received 1200 mg. Doses of companion agents were not recorded in a standardized form. Thirty-one patients (67.4%) received LAL monotherapy. Among patients receiving combination therapy, recorded companion agents included doxycycline (n = 4), rifampicin (n = 3), cotrimoxazole (n = 3), levofloxacin (n = 2), fosfomycin (n = 2), ciprofloxacin (n = 1), and delafloxacin (n = 1); some patients received more than one companion agent.

Source-control status was classified in 44/46 patients: 22 underwent device retention and 22 underwent removal. Among the 22 removals, 19 were total explantations and three were partial removals. A removal date was available for 21 patients; in 6/21, removal occurred after the first LAL dose, underscoring that source-control category was not uniformly determined before LAL initiation. In the five patients with spondylodiscitis, no spinal instrumentation was recorded: the recorded device was extra-vertebral in three (bilateral shoulder prostheses, a femoral device, and an intracardiac device) and its site was not recorded in two. Because device involvement, and therefore a source-control decision for an infected device, could not be established in these patients, they were retained in the descriptive cohort but excluded from the source-control comparison, which therefore included 40 patients (18 retention, 22 removal).

2.3. Microbiology

Microbiological status was available for 43 patients; 35/43 (81.4%) had a positive culture and 8/43 (18.6%) were culture-negative. Staphylococci predominated. *Staphylococcus aureus* was identified in 22 patients (17 methicillin-susceptible and 5 methicillin-resistant), and coagulase-negative staphylococci in 11 (*Staphylococcus epidermidis* n = 7, including 4 methicillin-resistant isolates; *S. hominis* n = 2; *S. haemolyticus* n = 1; *S. sciuri* n = 1). *Streptococcus mitis* was isolated in one patient, and *Enterococcus faecalis* was recorded as a co-isolate in one patient. In one additional culture-positive patient, no organism was recorded at species level in the archived extract. Overall, nine patients had methicillin-resistant staphylococci.

2.4. Clinical Outcomes and Source Control

After reconciliation with the final parent-study outcome adjudication, clinical success at last available follow-up was observed in 40/46 patients (87.0%; exact 95% CI 73.7–95.1). Success by indication was 88.0% for prosthetic joint infection (22/25), 88.9% for osteomyelitis involving hardware (8/9), 100% for spondylodiscitis (5/5), 75.0% for endocarditis (3/4), and 66.7% for prosthetic cardiac infection (2/3). By device type, success was 89.2% among patients with orthopedic material (33/37) and 80.0% among patients with cardiovascular devices (8/10); the patient with both device types is represented in both device-specific denominators.

The two known source-control groups were equal in size but differed descriptively in case mix (Table 1). The retention group in Table 1 includes the four patients with spondylodiscitis described above. Retention included a larger proportion of cardiovascular devices and more spondylodiscitis, whereas removal included more prosthetic joint infection and all four patients who underwent TDM. None of the exploratory between-group tests reached conventional statistical significance, but the cohort was too small for non-significance to establish balance. These directional differences reinforce the likelihood of treatment-selection bias and confounding by indication.

Among the 40 patients included in the source-control comparison, clinical success was 88.9% with device retention (16/18) and 86.4% with device removal (19/22). The exact conditional OR for success with retention versus removal was 1.26 (95% CI 0.13–16.79), and Fisher's exact p value was 1.000. The very wide CI is compatible with substantial benefit or harm and precludes a comparative interpretation. Among patients undergoing removal, success was 89.5% after total explantation (17/19) and 66.7% after partial removal (2/3); the partial-removal subgroup was too small for meaningful inference. The patient with an unclassified source-control status had clinical failure, and all five patients with spondylodiscitis achieved clinical success. In a sensitivity analysis including the four patients with spondylodiscitis in the retention group, results were similar (retention 20/22, 90.9%; removal 19/22, 86.4%; exact conditional OR 1.56, 95% CI 0.16–20.66; Fisher $p = 1.000$).

2.5. Laboratory Response, Safety, and Readmission

Among 36 patients with paired CRP measurements, median CRP decreased from 3.65 mg/dL at baseline to 0.91 mg/dL at end of therapy (Wilcoxon $p < 0.001$). In 33 patients with paired creatinine values, median serum creatinine increased modestly from 0.77 to 0.83 mg/dL (Wilcoxon $p = 0.008$); the median within-patient change was 0.05 mg/dL (IQR 0.00–0.16), and no patient required new dialysis. This small laboratory shift should be interpreted cautiously given the limited paired sample and absence of protocolized safety surveillance.

Adverse-event data were available for 40 patients. Two mild events (5.0%) were recorded, with no serious adverse drug event, treatment discontinuation, or drug-related

death. Thirty-day readmission data were available for 41 patients; one patient was readmitted within 30 days (2.4%), and no additional readmission was recorded between days 31 and 60 in the available data.

3. Discussion

This post hoc device-focused analysis suggests that long-acting lipoglycopeptides can be incorporated into day-hospital pathways for complex orthopedic and cardiovascular device-associated infections with favorable observed outcomes. The cohort was elderly and comorbid, most infections involved prosthetic joints or other orthopedic hardware, and staphylococci dominated the microbiology. Treatment was overwhelmingly dalbavancin-based and typically required only a small number of administrations, illustrating the logistical appeal of LALs for consolidation or outpatient continuation of therapy [5–9,11].

The central finding is not that one source-control strategy was superior to another, but that favorable short-term clinical outcomes were observed across heterogeneous management pathways. Success was 88.9% with retention and 86.4% with removal; the exact confidence interval around the retention-versus-removal OR was extremely wide and the Fisher test was non-significant. These data therefore do not support retaining infected hardware when guideline-based removal is otherwise indicated [1,2]. Rather, they show that in carefully selected patients—including patients managed with retention because surgery was not feasible or not chosen—a LAL-based outpatient strategy can be operationally feasible.

The descriptive differences between the retention and removal groups are clinically important. Retention included more cardiovascular-device patients and spondylodiscitis, whereas removal included more prosthetic joint infection and somewhat more combination therapy; TDM was performed only in the removal group. In addition, four patients with spondylodiscitis had been classified as retention although involvement of their device was not established; they were therefore excluded from the outcome comparison. These differences did not reach conventional statistical significance in exploratory unadjusted tests, but the study was underpowered to demonstrate balance. In addition, source control was not a fixed baseline exposure: among patients with a recorded removal date, six explantations occurred after the first LAL administration. Any crude comparison is therefore vulnerable not only to confounding by indication but also to time-dependent classification and reverse causality. The present data should be viewed as a description of real-world treatment trajectories, not an effectiveness comparison of surgical strategies.

The high observed success in retained-device patients is compatible with the growing use of prolonged or suppressive antibiotic strategies when definitive surgery is not possible, but suppressive therapy is inherently a selected-patient approach rather than an alternative to appropriate source control [3]. Long-acting agents may be attractive in this setting because they maintain Gram-positive exposure while reducing the need for daily intravenous access. The frequent use of doxycycline, rifampicin, cotrimoxazole, fluoroquinolones, or fosfomycin as companion agents in this cohort reflects the individualized and frequently prolonged nature of treatment.

The results are also consistent with observational experience using dalbavancin in bone, joint, and other complex Gram-positive infections and with reports showing that LALs can facilitate early discharge or outpatient treatment [6–9,11]. Nevertheless, off-label dosing remains heterogeneous, and the evidence supporting LALs in prosthetic and endovascular infections is substantially weaker than the randomized-trial evidence available for approved skin and soft-tissue indications. In this cohort, the most frequent regimen (two 1500 mg doses one week apart, 19/45 dalbavancin-treated patients) corresponds to the schedule supported by pharmacokinetic data on bone and articular tissue exposure and evaluated in a randomized trial in osteomyelitis [12,13]; however, that trial excluded patients with

prosthetic material at the infection site or concomitant endocarditis, so it supports the dosing rationale rather than providing direct evidence in device-associated infection; repeated-dose oritavancin regimens for deep-seated infections remain less well defined [8]. The present study therefore adds pragmatic information about implementation rather than establishing efficacy relative to standard intravenous therapy.

Safety findings were reassuring: recorded adverse events were infrequent, and no patient required new dialysis. However, paired creatinine values showed a small statistically significant increase in this subgroup, despite the absence of an overall renal signal in the parent cohort [10]. The magnitude of change was modest, and the finding may reflect clinical complexity, concomitant treatments, or sampling variability; it should not be interpreted as evidence of a nephrotoxic effect without a comparator and protocolized monitoring.

The 30- and 60-day readmission rates should likewise be interpreted as early healthcare-utilization measures rather than as sufficient follow-up for relapse in prosthetic or endovascular infection. Durable infection control may require substantially longer observation, which could not be standardized across centers in this retrospective dataset.

This study has several limitations. First, it is a retrospective post hoc secondary analysis of a previously published single-arm cohort, and all patients overlap with the parent report [10]. The research question is distinct—device-focused management and source control—but the analysis remains subject to the limitations of the parent dataset. Second, the sample is small, there are few failures, and no adjusted comparison of source-control strategies is credible. Third, source-control decisions and their timing were not protocolized, and removal sometimes occurred after LAL initiation. Fourth, dosing, companion therapy, and follow-up were individualized across centers; follow-up after LAL completion was not recorded as a standardized variable, so its duration cannot be summarized and the primary endpoint reflects clinical status at the last available assessment; late relapse, which is particularly relevant after device retention, may therefore be underestimated. Moreover, because 15/46 patients (32.6%) received companion antimicrobials and no LAL-free comparator was available, clinical success cannot be attributed to the LAL component alone, and the respective contributions of the LAL, companion agents, and source control cannot be disentangled. Fifth, systematic radiological follow-up (including modality-specific reassessment such as echocardiography, PET/CT, CT, or MRI when clinically applicable) was not captured in a standardized analyzable form, and radiologic response could not be evaluated. Sixth, outcome counts required reconciliation with the final adjudication used in the published parent study, while source-control variables derived from the archived patient-level device extract. Seventh, the clinical-success definition was author-defined and adjudicated in the parent study; it has not been formally validated and does not directly correspond to consensus outcome definitions for periprosthetic joint infection [14,15]. Eighth, infection categories were inherited from the parent study and device involvement was not separately adjudicated; no spinal instrumentation was recorded in the five patients with spondylodiscitis, who were therefore excluded from the source-control comparison, and in endocarditis a cardiovascular device was recorded in all four patients, but its direct involvement could not be confirmed in every case. In addition, patients came from five centers, one of which contributed 19/46 patients (41.3%), so center-level practice patterns may have influenced the observed outcomes. Finally, adverse-event and laboratory data were incomplete and collected through routine care rather than systematic active surveillance.

4. Materials and Methods

4.1. Study Design, Parent Cohort, and Population

This was a post hoc secondary analysis of a retrospective, multicenter observational study conducted across nine Italian infectious-diseases centers between 1 January 2020 and

31 December 2025. The parent cohort included 160 adults who received at least one LAL administration in a day-hospital setting; its design and overall results have been published previously [10].

The parent database contained 52 unique patients with orthopedic and/or cardiovascular prosthetic material (43 orthopedic devices and 10 cardiovascular devices; one patient had both) (Figure 1). Six patients whose primary indication was an acute bacterial skin and skin-structure infection (ABSSSI) unrelated to the implanted device were excluded. The resulting device-focused cohort comprised 46 patients belonging to one of two groups. The first group included 41 patients with a device-associated infection, that is, an infection involving the implanted device or its anatomical site: prosthetic joint infection (n = 25), osteomyelitis involving orthopedic hardware (n = 9), infective endocarditis in patients carrying a cardiovascular device (n = 4), and prosthetic cardiac infection (n = 3). The second group included five patients with a deep-seated infection (spondylodiscitis) in the presence of prosthetic material not shown to be related to the infected site: the device was extra-vertebral in three (bilateral shoulder prostheses, a femoral device, and an intracardiac device) and its site was not recorded in two, and no spinal instrumentation was recorded in any of them. Patients in the second group were retained in the descriptive analyses but excluded from the source-control comparison. The cardiovascular devices recorded in patients with endocarditis and prosthetic cardiac infection are detailed in Section 2.2. These 46 patients were treated at five of the participating centers, located in Catania, Messina, and Sassari (Supplementary Table S1); the remaining centers had no patients meeting the inclusion criteria of this analysis.

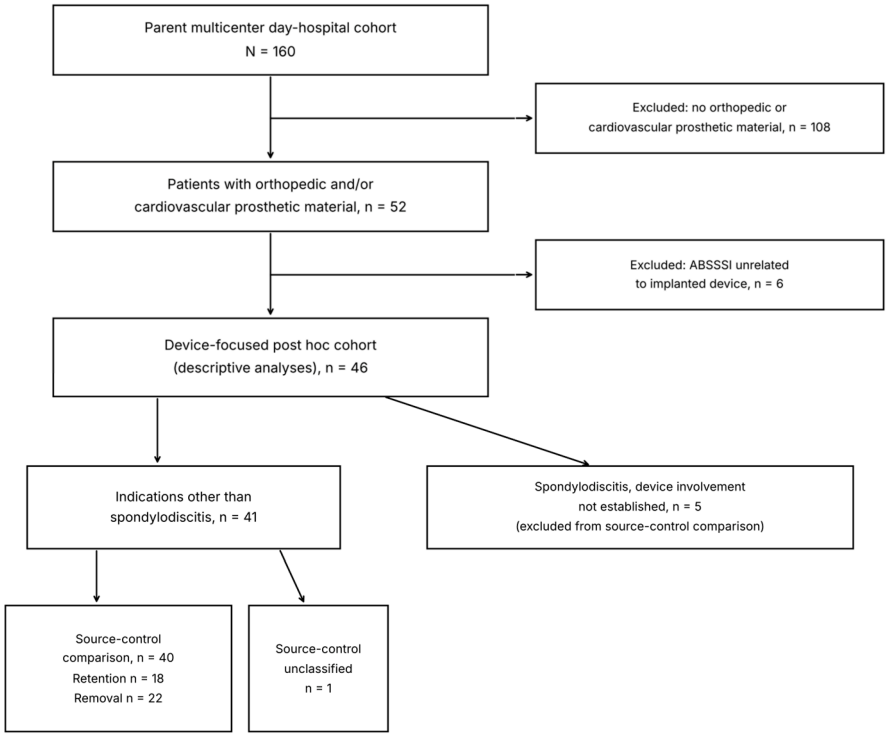


Figure 1. Study flow from the published parent cohort to the device-focused post hoc analysis. ABSSSI, acute bacterial skin and skin-structure infection.

The study was approved by the Ethics Committee Catania 2 (protocol no. 101/CECT2; 18 April 2023), was conducted in accordance with the Declaration of Helsinki, and had a waiver of informed consent because of its retrospective design.

4.2. Variables, Definitions, and Source-Control Classification

Patient-level variables were obtained from the anonymized study database and included demographics, comorbidities, Charlson Comorbidity Index (CCI), infection syndrome, device type and anatomical site, microbiology, day-hospital pathway, LAL agent and number of administrations, concomitant antimicrobial therapy, therapeutic drug monitoring (TDM), laboratory values, adverse drug events, and readmissions. Age was calculated at the first recorded LAL administration. Primary infection categories followed the final parent-study classification. In this classification, endocarditis denoted infective endocarditis in a patient carrying a cardiovascular device (devices listed in Section 2.2), whereas prosthetic cardiac infection denoted infection of a cardiac implantable electronic device or vascular graft without a diagnosis of endocarditis [10].

Diagnostic syndromes were not re-adjudicated for this post hoc analysis. They were inherited from the final parent-study classification, for which syndrome-specific diagnostic definitions were described in the parent article and its Supplementary Methods [10]. The present centralized extract did not contain a complete, standardized patient-level record of all diagnostic imaging findings, and radiologic response was therefore not analyzed as an outcome.

The care pathway was classified as de novo when LAL treatment began without a preceding inpatient admission for the index infection, or as step-down when it followed inpatient therapy. LAL monotherapy indicated no concomitant systemic antimicrobial; combination therapy indicated at least one concomitant agent.

Source control was classified according to the eventual management of the relevant prosthetic material: device retention, device removal, or unclassified when the archived source-control field was unavailable. Removal was further categorized as total explantation or partial removal. Importantly, this variable describes the management course rather than a randomized or fixed baseline exposure. Among patients with removal and an available removal date, some explantations occurred after the first LAL administration; source-control comparisons are therefore descriptive and are not interpreted causally.

4.3. Outcomes and Data Reconciliation

The primary endpoint was clinical success at the last available follow-up, corresponding to the final adjudicated clinical outcome used in the parent study. In the parent report, clinical success was defined as clinical cure at final follow-up after completion of LAL therapy without the need for additional antibiotics or unplanned surgery for the index infection; clinical failure included persistence or worsening requiring additional antimicrobial therapy or unplanned surgery, relapse, or infection-related death [10]. Because the archived extract also contained concomitant and post-LAL antibiotic fields whose clinical intent could not always be distinguished retrospectively, this secondary analysis used the adjudicated outcome variable rather than re-deriving outcome algorithmically from those fields. Outcome counts were reconciled against the final published parent-study adjudication, which was treated as authoritative when the archived subgroup extract differed from the final report [10].

Secondary endpoints were change in C-reactive protein (CRP) and serum creatinine from baseline to end of therapy, adverse drug events, and 30- and 60-day readmission. The 30- and 60-day readmission measures were prespecified healthcare-utilization endpoints rather than measures of durable infection cure. Follow-up timing for the final adjudicated clinical outcome was determined by routine clinical practice and was not available as a uniform analyzable duration across centers; consequently, the duration of follow-up could not be summarized, as the date of the last follow-up visit was not recorded in the study

database. End of therapy was the reference time point for laboratory endpoints only, not for the clinical outcome.

4.4. Statistical Analysis

Categorical variables are reported as counts and percentages and continuous variables as medians with interquartile ranges (IQR). Binomial proportions are accompanied by Clopper-Pearson exact 95% confidence intervals (CI). The retention-versus-removal outcome comparison used Fisher's exact test and an exact conditional maximum-likelihood odds ratio (OR) with an exact 95% CI. Exploratory comparisons of patient characteristics between the known retention and removal groups used Fisher's exact test for binary categorical variables, a Fisher–Freeman–Halton exact test for the multi-category infection-syndrome distribution, and the Mann–Whitney U test for continuous variables. No adjustment for multiple comparisons was made; these p values are provided only to describe case-mix differences and are not interpreted as evidence of baseline balance or causal effects. Paired CRP and creatinine measurements were compared using the Wilcoxon signed-rank test. The retention-versus-removal comparison was restricted to patients with a classified source-control strategy and an infection involving the recorded device (n = 40); a sensitivity analysis repeated it including the patients with spondylodiscitis classified as retention (n = 44). Because the cohort was small and the number of failures was limited, no multivariable modeling was performed. All source-control comparisons are exploratory. Analyses were performed on available cases; no imputation of missing data was undertaken.

5. Conclusions

In this multicenter real-world device-focused cohort, long-acting lipoglycopeptides delivered through day-hospital pathways were feasible for selected orthopedic and cardiovascular device-associated Gram-positive infections, with an observed clinical success rate of 87.0% at the last available follow-up. Similar crude success proportions were observed with retention and removal, but the comparison was markedly underpowered, confounded by treatment selection, and affected by non-uniform timing of source control. Because follow-up was not standardized, durable infection control could not be assessed. These data support further prospective evaluation of LAL-based consolidation and suppressive strategies in device-associated infection; they do not establish equivalence or superiority of any source-control approach.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/antibiotics15111150/s1, File S1: STROBE Statement; Table S1: Participating centers.

Author Contributions: A.M. and E.V.R. contributed equally to this work. A.M., E.V.R., G.P., B.C. (Bruno Cacopardo) and G.N. conceived and designed the study. A.G.G., A.D.V., A.A., N.G., A.F., B.B., E.P., P.I., B.C. (Bianca Catania), A.B., L.S., C.I. (Chiara Iaria), G.M., C.I. (Carmelo Iacobello), R.M., S.S. and F.P. contributed to patient identification and data acquisition. A.M., E.V.R. and G.P. curated the dataset and performed the analyses. A.M. drafted the manuscript. All authors interpreted the data, critically revised the manuscript, approved the final version, and agree to be accountable for all aspects of the work. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement: Informed consent was waived due to the retrospective nature of the research.

Data Availability Statement: The data presented in this study are available on request from the corresponding author due to legal and ethical reasons.

Conflicts of Interest: The authors declare no conflicts of interest.

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