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MAJOR ARTICLE

Clinical Characteristics, Etiology, and Initial Management Strategy of Newly Diagnosed Periprosthetic Joint Infection: A Multicenter, Prospective Observational Cohort Study of 783 Patients

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Background. Periprosthetic joint infection (PJI) is a devastating complication of joint replacement surgery. Most observational studies of PJI are retrospective or single-center, and reported management approaches and outcomes vary widely. We hypothesized that there would be substantial heterogeneity in PJI management and that most PJIs would present as late acute infections occurring as a consequence of bloodstream infections.

Methods. The Prosthetic joint Infection in Australia and New Zealand, Observational (PIANO) study is a prospective study at 27 hospitals. From July 2014 through December 2017, we enrolled all adults with a newly diagnosed PJI of a large joint. We collected data on demographics, microbiology, and surgical and antibiotic management over the first 3 months postpresentation.

Results. We enrolled 783 patients (427 knee, 323 hip, 25 shoulder, 6 elbow, and 2 ankle). The mode of presentation was late acute (>30 days postimplantation and <7 days of symptoms; 351, 45%), followed by early (≤30 days postimplantation; 196, 25%) and chronic (>30 days postimplantation with ≥30 days of symptoms; 148, 19%). Debridement, antibiotics, irrigation, and implant retention constituted the commonest initial management approach (565, 72%), but debridement was moderate or less in 142 (25%) and the polyethylene liner was not exchanged in 104 (23%).

Conclusions. In contrast to most studies, late acute infection was the most common mode of presentation, likely reflecting hematogenous seeding. Management was heterogeneous, reflecting the poor evidence base and the need for randomized controlled trials.

Keywords. arthroplasty infection; artificial joint infection; periprosthetic jo int infection.

Periprosthetic joint infection (PJI) is a devastating complication of joint arthroplasty, resulting in pain, suffering, impaired mobility, prolonged hospitalization, broad-spectrum antibiotic therapy, and societal and economic costs [1–3].

Although arthroplasty revision operations performed for infection have progressively increased [4], estimates from arthroplasty registry data or infection control surveillance may underestimate the true incidence of PJI [5, 6]. Unlike early postoperative or chronic low-grade infections, these data sources do not reliably capture late acute PJI (LA-PJI), which may not be

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managed with revision arthroplasty, or may present after surveillance activities are complete and might account for these underestimates. Treatment success rates for PJI vary widely [7] and are likely to be dependent on a number of patient, microbiological, and treatment factors. There are few randomized controlled trials to guide management, and most studies are retrospective [8, 9]. Reported prospective studies are small or reported from single centers with specialized PJI expertise. To date, no multicenter prospective observational study has been sufficiently large to describe contemporary clinical characteristics, etiology, and management across diverse regions and clinical settings, or to link treatment outcomes in terms of initial management, surgical methods, or antibiotic therapy.

To fill this knowledge gap, we established the Prosthetic joint Infection in Australia and New Zealand (NZ), Observational (PIANO) study. We hypothesized that across different hospital settings from the private and public sectors, late acute PJI would comprise a larger proportion of the PJI burden than had been reported previously and that there would be heterogeneity in initial management approaches that deviated from international guidelines [10, 11]. Here we report the baseline and initial follow-up data to 90 days after diagnosis. Extended follow-up and 2-year outcome data are still being collected.

METHODS

Study Sites and Ethical Approval

The PIANO study is a prospective, binational, multicenter observational cohort study conducted at 27 hospitals in Australia and New Zealand, identified through the Australasian Society for Infectious Diseases Clinical Research Network. Ethical approvals were obtained from each site, and the study was registered (ANZCTR12615001357549). All participants provided written informed consent.

Participants

Participants were prospectively identified and enrolled after referral from orthopedic and infectious diseases/microbiology teams at each institution. Adult patients (>18 years old) with a newly identified PJI of a large joint (hip, knee, shoulder, elbow, wrist, or ankle) were eligible when diagnosed according to the presence of at least 1 of the following: (i) presence of sinus tract in communication with the prosthesis; (ii) increased leukocyte count or neutrophil percentage in preoperative synovial fluid aspirate (synovial fluid white blood cell count >1700 cells/μL or neutrophil percentage >65%); (iii) visible pus around the prosthesis at operation without alternative explanation; iv) acute inflammation as reported by the clinical pathologist on examination of periprosthetic tissue (≥5 neutrophils per high-power field); (v) ≥2 preoperative or intraoperative cultures (blood, synovial fluid, periprosthetic tissue, or sonication fluid) that yielded the same organism (indistinguishable based on common laboratory tests including genus and species identification or common antibiogram); or (vi) pure growth of *Staphylococcus aureus*, β-hemolytic streptococci, or pathogenic aerobic gram-negative rod from a single synovial fluid or intraoperative tissue/fluid specimen. These diagnostic criteria for PJI reflected international guidelines at the time the study was designed.

Patients were excluded if they were not likely to be accessible by telephone for follow-up or presented with complications from a PJI diagnosed before the study period. All laboratories used traditional culture-based methods on blood cultures, synovial fluid, periprosthetic joint tissue, or explanted prosthesis components.

Data Management and Statistical Analysis

Data were collected at baseline and 3 months and entered into a purpose-built web-based database. The statistical program R was used for statistical analyses [12]. Continuous data are presented as median and interquartile range (IQR), and comparisons between groups were by nonparametric tests. Comparisons between categorical variables were analyzed with a chi-square test.

Definitions

We defined early PJI as the date of diagnosis occurring ≤30 days after the original arthroplasty operation. Late acute PJI (LA-PJI) was defined as occurring >30 days from implantation, but with a duration of symptoms ≤7 days and no evidence of a sinus overlying the joint. Patients with a late-onset infection (>30 days from implantation) and a prolonged duration of symptoms (>30 days) at the time of diagnosis or the presence of a sinus were considered to be late chronic PJI. Patients with late-onset PJI, a duration of symptoms between 8 and 30 days, and without the presence of a sinus were considered to have late indeterminate infections. The remainder were considered late unclassifiable PJI. If the exact date of arthroplasty implantation was not available, it was estimated to be the first day of the nearest month or the year that the patient recalled having the operation.

We also categorized patients according to whether they were culture negative (no organisms isolated from microbiological samples), monomicrobial (1 clinically significant organism isolated), or polymicrobial (>1 clinically significant organism). The initial surgical management was categorized as (i) debridement, antibiotics, irrigation, and implant retention (DAIR), (ii) 2-stage exchange arthroplasty, (iii) single-stage exchange arthroplasty, (iv) suppressive antibiotics alone, (v) excision arthroplasty, or (vi) no clear plan identified. The degree of operative debridement was classified as minor (lavage with minimal debridement), extensive (synovectomy, removal of all

periprosthetic pus, infected tissue, and loose cement), or moderate (more than minimal but less than extensive).

RESULTS

Baseline Characteristics

From July 2014 to December 31, 2017, 783 patients were enrolled into the PIANO study (Figure 1). The median (IQR, range) age and body mass index (BMI) were 69 years (62–77, 28–99) and 31 kg/m^2 (27–37, 16–57), respectively. Male gender (57.0%) and right-sided PJIs (55.7%) were more common. The most commonly affected joint was the knee (427, 54.5%), followed by hip (323, 41.3%), shoulder (25, 3.2%]), elbow (6, 0.8%), and ankle (2, 0.3%). The most common comorbidities included diabetes mellitus (172, 22.1%) and ischemic heart disease (131, 16.8%) (Table 1). After adjustment for multiple comparisons, none of the comorbidities were associated with the type of PJI. Sixteen (2.1%) deaths occurred within the first 90 days after diagnosis of PJI.

Classification of PJI, Based on Time From Implantation and Duration of Symptoms

Late acute PJI accounted for 351 (44.8%) episodes. Early PJI occurred in 196 patients (25.0%) and late chronic infections in 148 (18.9%) patients. The remainder had late infections, with duration of symptoms between 8 and 30 days (55, 7.0%), or unspecified duration of symptoms (32, 4.1%) (Figure 2A and B, Table 1). When late indeterminate groups were excluded, LA-PJI accounted for nearly half of all classifiable PJI. The affected joint according to prosthesis age is shown (Figure 2E and F). When comparing PJI in hips and knees, infections of knee prostheses accounted for a higher proportion of PJI

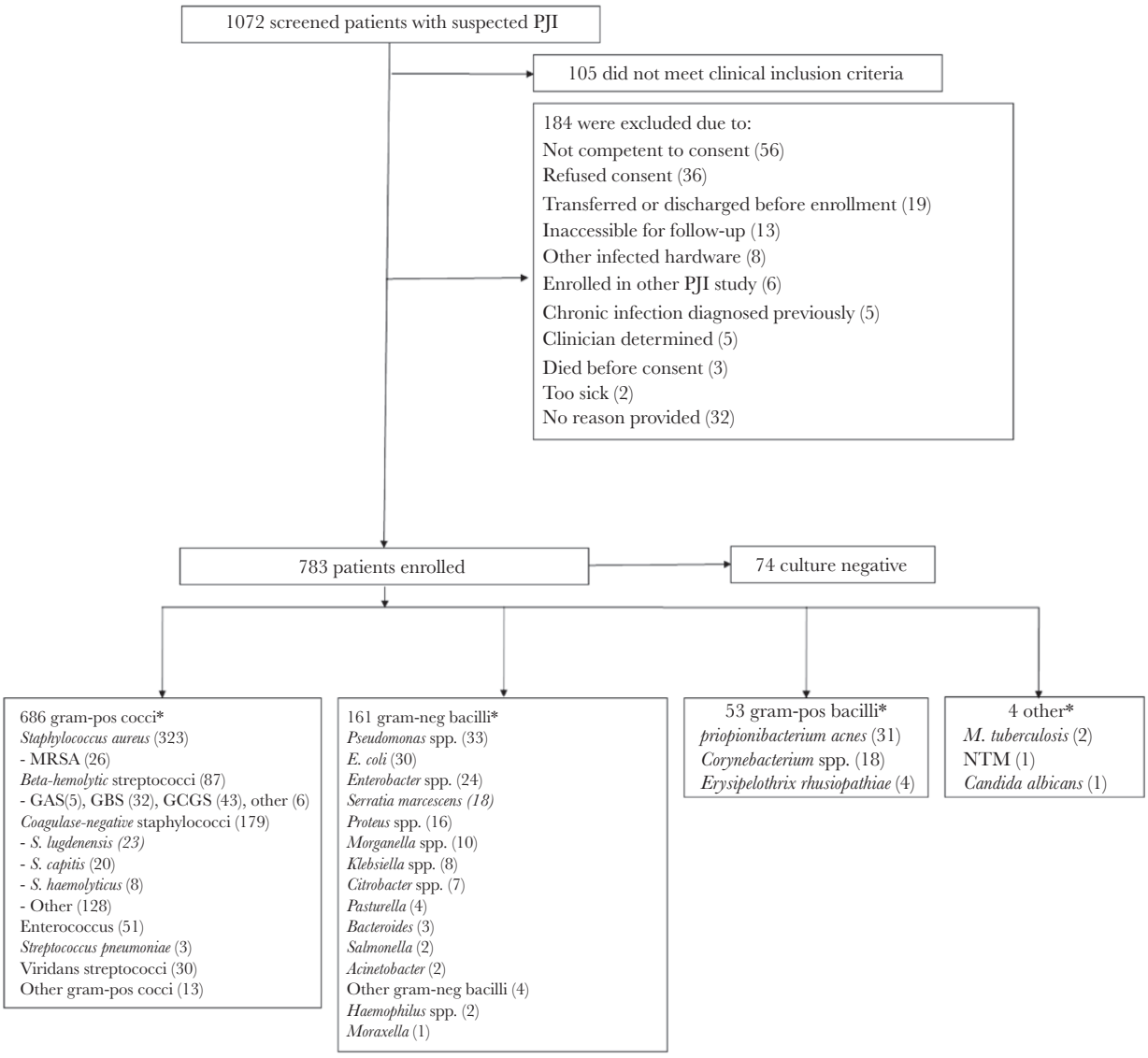

Figure 1. Flowchart of study and microbiological causes of periprosthetic infection. Abbreviations: GAS, Group A Streptococcus; GBS, Group B Streptococcus; GCGS, Group C/G Streptococcus; MRSA, methicillin-resistant *Staphylococcus aureus*; NTM, Non tuberculous mycobacterium; PJI, periprosthetic joint infection.

Table 1. Clinical Characteristics, Laboratory Findings, and Initial Management Strategy of Patients With Periprosthetic Joint Infection According to Infection Type

Characteristic	Late Acute (n = 351)	Early (n = 196)	Chronic (n = 148)	Late (Duration 8–30 d) (n = 55)	Late (Unspecified) (n = 32)	*P*
Age, y	70 (62–78)	68 (61–76)	69 (62–77)	72 (68–76)	69 (55–77)	.03
Gender						
Male	217 (61.8)	108 (55.1)	72 (48.6)	33 (60.0)	19 (59.4)	.09
Female	134 (38.2)	88 (44.9)	76 (51.4)	22 (40.0)	13 (40.6)	
Body mass index, kg/m^2	31 (27–36)	33 (28–38)	31 (26–37)	31 (27–36)	29 (25–32)	.03
Comorbidities	(Y)	(Y)	(Y)	(Y)	(Y)	
Diabetes	92 (26.2)	35 (17.8)	26 (17.5)	12 (21.8)	7 (21.9)	.13
Rheumatoid arthritis	31 (8.8)	8 (4.1)	10 (6.7)	7 (12.7)	3 (9.4)	.15
Chronic renal impairment	33 (9.4)	8 (4.1)	15 (10.1)	5 (9.1)	2 (6.2)	.19
End-stage renal failure	2 (0.5)	0 (0.0)	3 (2.0)	0 (0.0)	0 (0.0)	.18
Cirrhosis	4 (1.1)	3 (1.5)	1 (0.7)	0 (0.0)	1 (3.1)	.69
Malignancy	15 (4.2)	3 (1.5)	12 (8.1)	3 (5.4)	1 (3.1)	.06
Congestive cardiac failure	27 (7.7)	7 (3.6)	5 (3.4)	6 (10.9)	1 (3.1)	.07
Ischaemic heart disease	75 (21.3)	20 (10.2)	22 (14.8)	8 (14.5)	6 (18.7)	.02
Corticosteroid use	29 (8.2)	17 (8.7)	13 (8.9)	6 (10.9)	1 (3.1)	.77
Immunosuppressed	24 (6.8)	7 (3.6)	10 (6.7)	4 (7.3)	0 (0.0)	.29
Active orders limiting life-sustaining treatment	3 (0.8)	1 (0.5)	3 (2.0)	0 (0.0)	0 (0.0)	.52
Joint affected						
Knee	244 (69.5)	72 (36.7)	69 (46.6)	26 (47.3)	12 (37.5)	
Hip	97 (27.6)	116 (59.2)	72 (48.6)	26 (47.3)	15 (46.9)	
Shoulder	8 (2.3)	5 (2.6)	4 (2.7)	3 (5.4)	5 (15.6)	<.0001
Elbow	2 (0.6)	2 (1.0)	2 (1.4)	0 (0.0)	0 (0.0)	
Ankle	0 (0)	1 (0.5)	1 (0.7)	0 (0.0)	0 (0.0)	
Side						
Right	189 (53.8)	118 (60.2)	75 (50.7)	33 (60.0)	20 (62.5)	.32
Left	162 (46.2)	78 (39.8)	73 (49.3)	22 (40.0)	12 (37.5)	
Time from implant to diagnosis, d	952 (203–2814)	17 (12–22)	458 (104–1430)	434 (90–2334)	1434 (333–3176)	<.0001
Indication for original implant						
Primary	287 (81.8)	162 (82.7)	118 (79.7)	39 (70.9)	21 (65.6)	
Infection	20 (5.7)	3 (1.5)	6 (4.1)	3 (5.5)	3 (9.4)	.02
Other/unknown	44 (12.5)	31 (15.8)	24 (16.2)	13 (23.6)	8 (25.0)	
Duration of symptoms, d	2 (1–5)	4 (1–7)	55 (11–144)	14 (10–19)	NA	<.0001
Clinical findings on admission	(Y)	(Y)	(Y)	(Y)	(Y)	
Fever	203 (57.8)	60 (30.6)	23 (15.5)	21 (38.2)	2 (6.2)	<.0001
Local inflammation	282 (80.3)	168 (85.7)	108 (72.9)	47 (85.4)	17 (53.1)	<.0001
Shock	27 (7.7)	5 (2.5)	1 (0.6)	3 (5.4)	1 (3.1)	.006
Sinus	6 (1.7)	46 (23.4)	71 (47.9)	0 (0.0)	6 (18.7)	<.0001
Laboratory findings						
Leukocyte count, $\times 10^9$/L	13.0 (9.7–16.3)	11.3 (8.8–14.1)	9.6 (7.6–11.8)	9.7 (7.4–13.5)	10.8 (7.4–14.8)	<.0001
Neutrophil count, $\times 10^9$/L	10.6 (7.5–14.0)	8.4 (6.6–11.3)	6.6 (5.3–9.3)	7.1 (5.1–9.9)	7.8 (5.0–11.9)	<.0001
C-reactive protein, mg/L	230 (135–320)	130 (57–229)	80 (40–169)	132 (56–251)	106 (39–189)	<.0001
Creatinine, μmol/L	90 (69–120)	76 (63–94)	79 (65–98)	83 (73–115)	83 (65–95)	<.0001
Albumin, g/L	30 (26–36)	30 (25–34)	32 (28–36)	29 (24–33)	31 (27–37)	.02
No. of organisms isolated						
Culture-negative (0 organisms)	30 (8.5)	18 (9.2)	15 (10.1)	4 (7.3)	7 (21.9)	
Monomicrobial (1 organism)	285 (81.2)	97 (49.5)	104 (70.3)	37 (67.3)	18 (56.2)	<.0001
Polymicrobial (≥2 organisms)	36 (10.3)	81 (41.3)	29 (19.6)	14 (25.4)	7 (21.9)	
Microbial etiology[1]						
Staphylococcus aureus	179 (51.0)	79 (40.3)	40 (27.0)	15 (27.2)	9 (28.1)	<.0001
MRSA	8 (2.2)	7 (3.5)	8 (5.4)	2 (3.6)	1 (3.1)	.52
Coagulase-negative staphylococci	46 (13.1)	59 (30.1)	49 (33.1)	15 (27.2)	9 (28.1)	<.0001
β-hemolytic streptococci	58 (16.5)	17 (8.6)	3 (2.0)	8 (14.5)	1 (3.1)	<.0001
Enterococci	8 (2.2)	32 (16.3)	8 (5.4)	3 (5.4)	0 (0.0)	<.0001
Enterobacteriaciae	15 (4.2)	24 (12.2)	7 (4.7)	6 (10.9)	1 (3.1)	.003

Table 1. Continued

Characteristic	Late Acute (n = 351)	Early (n = 196)	Chronic (n = 148)	Late (Duration 8–30 d) (n = 55)	Late (Unspecified) (n = 32)	*P*
ESCAPPM group	4 (1.1)	27 (13.7)	16 (10.8)	7 (12.7)	1 (3.1)	<.0001
Initial management strategy (d7)						
DAIR	247 (70.4)	160 (81.6)	66 (44.6)	37 (67.3)	10 (31.3)	
Two-stage revision	56 (15.9)	19 (9.7)	51 (34.5)	8 (14.5)	12 (37.5)	
Single-stage revision	9 (2.6)	7 (3.6)	8 (5.4)	3 (5.5)	8 (25.0)	<.0001
Antibiotic suppression	27 (7.7)	7 (3.6)	13 (8.8)	5 (9.1)	1 (3.1)	
Excision arthroplasty	2 (0.6)	1 (0.5)	3 (2.0)	0 (0.0)	1 (3.1)	
No clear plan	10 (2.8)	2 (1.0)	7 (4.7)	2 (3.6)	0 (0.0)	

Data are No. (%) for categorical variables and median (interquartile range) for continuous variables. Denominators are those in row 1, unless otherwise stated.

Abbreviations: DAIR, debridement, antibiotics, irrigation and implant retention; ESCAPPM, organisms with inducible, chomosomally mediated β-lactamase activity including *Enterobacter* spp., *Serratia* spp., *Citrobacter freundii*, *Aeromonas* spp., *Proteus vulgaris, Providentia* spp., and *Morganella morganii*; MRSA, methicillin-resistant *Staphylococcus aureus*.

in LA-PJI (71%) compared with early PJI (38%; $P < .0001$) and chronic PJI (49%; $P < .0001$). Other clinical and laboratory characteristics according to classification of PJI type are shown (Table 1).

Microbiology

Monomicrobial PJI accounted for 542 (69.2%) infections, whereas polymicrobial and culture-negative PJI accounted for 167 (21.3%) and 74 (9.5%) infections, respectively. The presence of monomicrobial, polymicrobial, and culture-negative infections according to prosthesis age is shown in Figure 2C and D. After excluding culture-negative infections, polymicrobial infections were less common than monomicrobial infections in patients with LA-PJI (11.2%) than with either early (46.5%; $P < .0001$) or late (21.8%; $P = .003$) PJI. Patients with polymicrobial infections had a higher BMI than those with monomicrobial infections (34 vs 31 kg/m^2; $P = .002$). Across the whole cohort, *Staphylococcus aureus* was the most common pathogen and was present in 323 (41.2%) patients with PJI.

There were significant differences between the organisms identified in monomicrobial and polymicrobial PJI. Enterobacteriaceae, coagulase-negative staphylococci (CoNS), enterococcus, and AmpC β-lactamase-producing gram-negative organisms were more commonly identified in polymicrobial infections ($P < .0001$). There were also significant differences in the micro-organisms isolated between PJI classifications and according to the age of the prosthesis (Figure 3, Table 1). For patients with early PJI, enterococci and gram-negative organisms predominated ($P < .0001$ for all comparisons) (Table 1). For chronic infections, CoNS were significantly more common ($P < .0001$) (Table 1). *S. aureus* and β-hemolytic streptococci (BHS) were significantly more common in LA-PJI than in early or late chronic PJI ($P < .0001$ for both comparisons) (Table 1). One hundred fifty (43%) with LA-PJI had positive blood cultures on admission.

Initial Management Strategy at Day 7

The most common initial management strategy was DAIR, reported in 520 episodes (66.4%), then 2-stage revision (146, 18.6%), 1-stage revision (36, 4.6%), antibiotic suppression (53, 6.7%), excision arthroplasty (7, 0.9%), and "no clear plan" (21, 2.7%) (Table 2). The median (IQR) time from implantation to diagnosis for patients managed with DAIR was 154 (23–1426) days, whereas the median duration of symptoms for this group of patients was 4 (1–8) days. This surgical approach was undertaken as the primary management strategy in LA-PJI (247, 70.3%), early PJI (160, 81.6%), and chronic PJI (66, 44.6%). Of patients managed with DAIR, 50 (9.6%) and 37 (7.1%) had documented symptoms for ≥21 or ≥30 days, respectively.

Actual Operative Management in the First 90 Days

Excluding those patients for whom there was no clear plan, 55 patients were managed with a different approach than that planned within the first 7 days. This included 17 in the DAIR group and 35 in the revision groups (Table 2). Only 7 participants did not receive any surgical management.

Debridement, Irrigation, Antibiotics, and Implant Retention

Of the 520 patients for whom debridement was the initial management strategy, 131 (25.2%) patients had 2 episodes, 32 (6.2%) had 3 episodes, and 9 (1.7%) had 4 episodes of operative debridement. Of the total of 565 DAIR procedures where details of the most senior operator was recorded, 157 (27.8%) were performed by a registrar (surgeon in training). Arthroscopic washouts were undertaken on 36 (6.5%) occasions. The reported extent of the debridement was only minimal or moderate in 18 (4.2%) and 124 (29.2%), respectively, with the remainder coded as extensive (283, 66.6%). The liner was not exchanged in 104 (23.4 %) patients (Table 2).

Two-Stage Revision

Details regarding the first stage of a 2-stage revision procedure were available for 178 patients. An articulating spacer

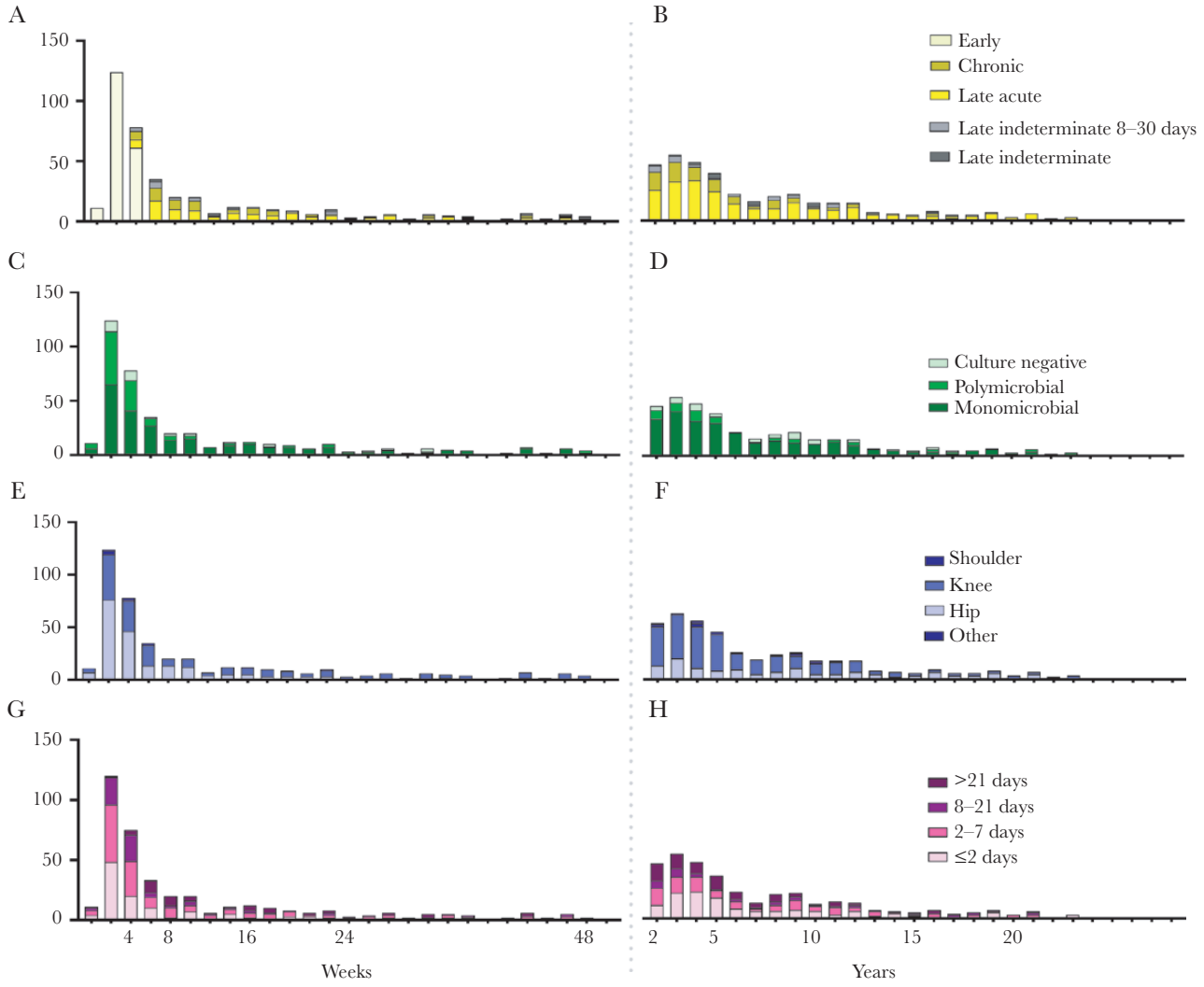

Figure 2. Duration of time from arthroplasty implantation to diagnosis according to classification of periprosthetic joint infection (A and B), the presence of polymicrobial vs monomicrobial infection infection (C, D), joint involved (E, F), and duration of symptoms (G, H).

was used in 111 (62.4%) patients, and a nonarticulating spacer, other implant, or nothing was inserted into the joint space in 57 (32.0%), 8 (4.5%), and 2 (1.1%) patients, respectively.

Intra-articular antibiotics were used in 156 (87.6%) patients. The most common intra-articular antibiotic delivery method was through an antibiotic impregnated cement spacer in 126 patients. Of 151 patients for whom an intra-articular antibiotic was recorded, vancomycin was the most commonly used (128, 84.8%), followed by gentamicin (47, 31.1%).

In 41 (27.9%) patients, systemic antibiotics were continued until re-implantation. For the remaining 106 patients, antibiotics were ceased a median (IQR) of 33 (20–46) days before the second stage.

Antibiotic Therapy

Empiric parenteral antibiotics were used in 614 (82.2%) cases. Vancomycin was the most commonly prescribed empiric agent (279, 45.4%), followed by cefazolin (244, 39.7%), flucloxacillin (194, 31.6%), piperacillin-tazobactam (59, 9.6%), and ceftriaxone (39, 6.4%). Only 26.9% (165) of patients received adequate gram-negative cover in their empiric antibiotic regimen.

The median (IQR) total duration of parenteral antibiotics, including empiric and directed therapy prescribed within the first 90 days, was 42 (35–48) days (Figure 4). Of 404 patients with gram-positive infection who had a DAIR procedure, the majority (52.8%) started oral antibiotics during the parenteral course. Rifampicin and fusidic acid were used in 209 (56.8%) and 43 (11.7%) patients, respectively (rifampicin use is described in Table 3).

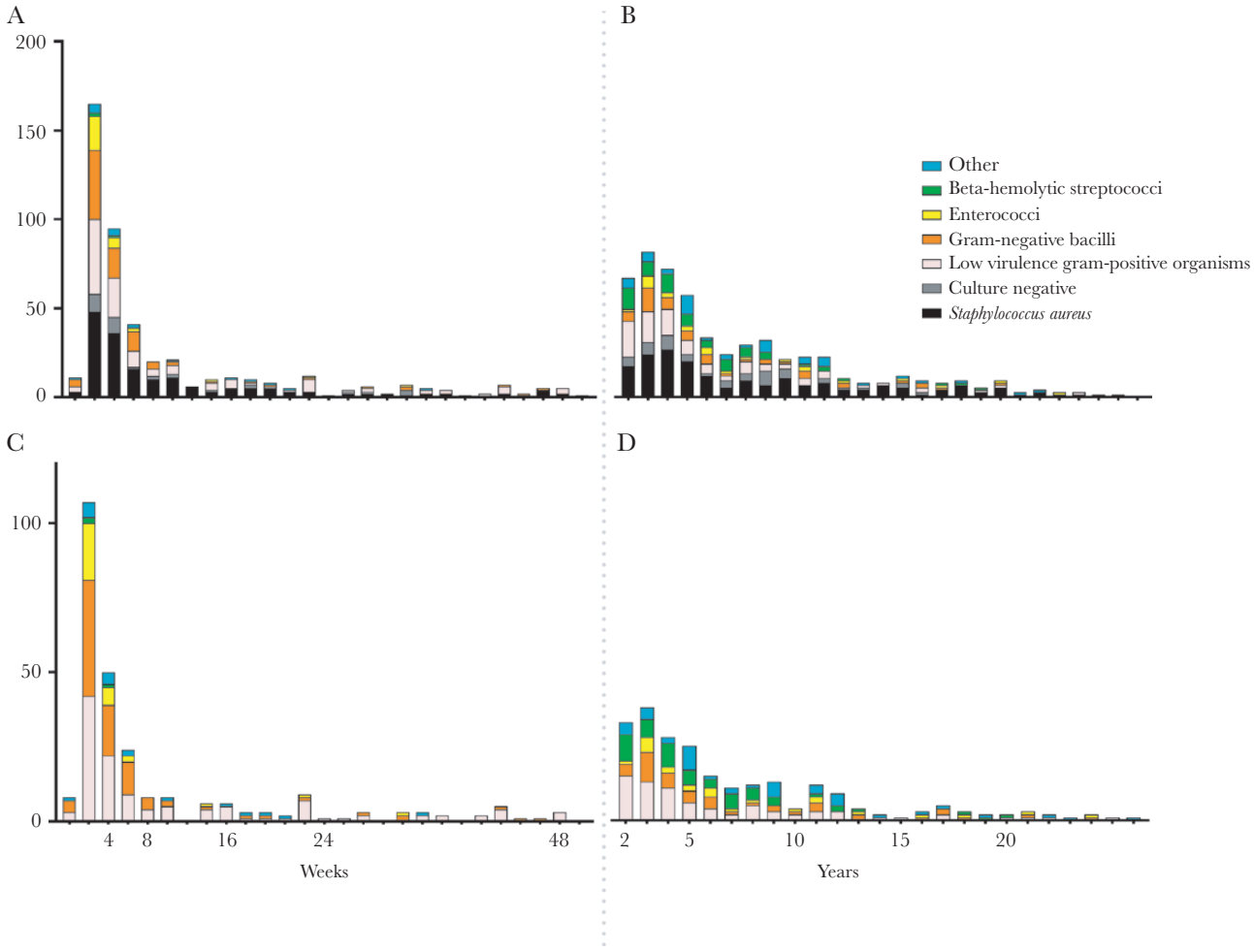

Figure 3. Duration of time from arthroplasty implantation to diagnosis according to causative organisms isolated. Panels A and B show all organisms cultured. Panels C and D depict non-*Staphylococcus aureus* isolates.

At least 1 adverse event occurred with parenteral antibiotic therapy in 143 (18.2%) patients, resulting in a change of therapy in 104 patients. Adverse events were most commonly allergic reaction (32) and acute kidney injury (28). Peripherally inserted central catheter (PICC)-associated complications occurred in 14 patients.

DISCUSSION

Key Findings

This large prospective study provides a contemporary description of the clinical characteristics, etiology, and management strategies of patients presenting to Australian and New Zealand hospitals with a newly diagnosed PJI. Nearly half of classifiable cases were LA-PJI, with early postoperative and chronic infections each accounting for one-quarter or less of the presentations. There was substantial heterogeneity in the surgical and antibiotic management, reflecting the lack of high-quality evidence from randomized trials to guide these decisions.

These data reveal broad patterns in the presentation of PJI that could have important implications for empiric antibiotic management. Although *Staphylococcus aureus* is the most common pathogen across all groups, early PJIs occur more commonly in obese individuals following hip arthroplasty and were often caused by polymicrobial infections, with a high proportion due to gram-negative organisms and/or enterococci, which are not always covered by empiric antibiotic regimens. By contrast, LA-PJIs present more commonly in knee arthroplasties, have higher C-reactive protein concentrations, higher proportion of patients reporting fever and a higher proportion of patients with *S. aureus* and BHS isolated.

Many patients treated with DAIR did not receive debridement that would be considered adequate [13, 14] due to a lack of liner exchange, use of arthroscopic debridement, or the failure to remove all infected material. Furthermore, 45% of those with chronic PJI were treated with DAIR, despite 2-stage revision being recommended. Outcome data at 24 months are still being collated, and it will be important to compare outcomes according to adequacy of surgical debridement and concordance of management with published guidelines.

Table 2. Surgical Management Approaches of Periprosthetic Infections Used Within the First 90 Days According to Initial Management Strategy at Day 7

Surgical Details	Initial Management at 7 d, No. (%)						Total
	DAIR (n = 520)	2-Stage Revision (n = 146)	Single-Stage Revision (n = 36)	Suppression (n = 53)	Excision (n = 7)	No Clear Plan (n = 21)	
Surgical management at 90 d							
DAIR	486	22	6	8	1	6	529
2-stage	62	114	1	1	0	1	179
Single-stage	13	11	32	1	0	2	59
Suppression	16	4	1	40	0	7	68
Excision	8	12	1	1	6	3	31
Did not get initial management	17	21	3	13	1	NA	55
No. of surgical management approaches within the first 90 d							
0	0	0	0	6	0	1	7
1	422	109	27	43	7	16	624
2	77	24	7	4	0	1	112
3	3	2	0	0	0	0	6
Characteristics of DAIR							
No. of trips to theater							
≥2	131	5	3	2	0	1	142
≥3	32	2	2	2	0	0	38
4	9	1	1	0	0	0	11
Debridement extent							
Extensive	283	9	2	3	0	3	300
Moderate	124	10	4	4	1	0	143
Minimal	18	2	0	0	0	1	21
Most senior operator in theater							
Registrar	157 (27.8)	9 (34.6)	4 (33.3)	3 (30)	0 (0)	2 (40)	175 (28.3)
Consultant	408 (73.2)	17 (65.4)	8 (66.7)	7 (70)	1 (100)	3 (60)	444 (71.7)
Arthroscopic washout, yes	36 (6.5)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	38 (6.3)
Liner exchanged, yes	340 (76.6)	12 (52.2)	4 (66.7)	4 (50)	0 (100)	5 (100)	365 (74.9)

Abbreviation: DAIR, debridement, antibiotics, irrigation, and implant retention.

There was also substantial variation in the approach to 2-stage revision. In most patients, there was a substantial delay before the second stage, even though this practice has been shown not to be necessary [15, 16].

Comparison With the Literature

Such a high proportion of LA-PJI is striking. Few prospective studies have reported the proportion of LA-PJI among all presentations with a newly diagnosed PJI. Our data are consistent with a prospective study of osteoarticular infections where hematogenous spread was thought to be the route of acquisition for 25 of 58 (43%) infections associated with prosthetic material [17] and a large, single-center retrospective study demonstrating that 35% were acute hematogenous PJI [11]. By contrast, these data are discordant with Spanish data, reporting acute haematogenous (AH) PJI in 11.6% of presentations [18], and a recent French single-centre study where 10.4% of PJIs were classified as AH-PJI [19]. It should be noted that our definitions for LA-PJI, which were based on duration from implantation (>30 days) [10, 11] and a short duration of symptoms [11, 20] are comparable to those in other studies and are generally synonymous with the definitions of AH-PJI. To improve the specificity of the LA-PJI diagnosis, we also included the absence of a sinus to the skin overlying the joint, as this feature is pathognomonic for chronic late PJI and should usually be managed accordingly. The higher proportion of LA-PJI and lower proportion of chronic PJI in our data compared with the literature in general may be explained by the diverse settings of our study that included a range of hospital types and sizes and only included a recent, new diagnosis of PJI in the index arthroplasty. This contrasts with specialized units with an interest in complex osteoarticular infections, which may be more likely to have a highly selected case mix, with an over-representation of late chronic infections [11] and relapsed PJI, and correspondingly lower proportions of LA-PJI.

A potential explanation is that in a setting where the incidence of arthroplasty is increasing [4], early postoperative PJIs might be expected to rise at a proportional rate. But as the cumulative prevalence of people living with a joint replacement increases, the population at risk of LA-PJI due to BSI will increase at a greater rate.

The observed variability in the management approach of PJI is likely to reflect the poor evidence base for current treatment recommendations; the 2012 Infectious Diseases Society of

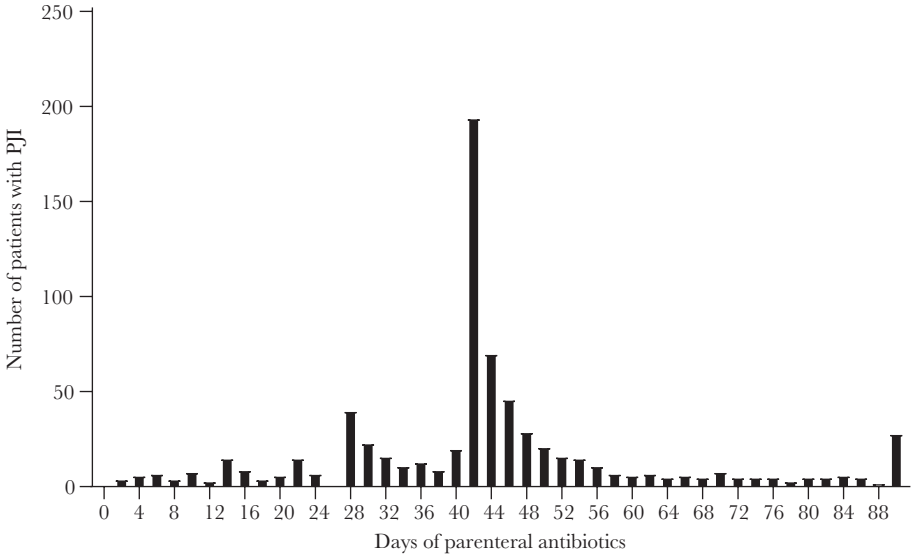

Figure 4. Duration of parenteral antibiotics in patients with periprosthetic joint infection. Abbreviation: PJI, periprosthetic joint infection.

America guidelines were based on poor (level C) or moderate (level B) evidence and evidence types 2 and 3 (observational data and expert opinion) [21, 22].

Strengths and Limitations

The PIANO cohort is one of the few truly prospective, multicenter, multiregional studies of PJI in the literature. This allows an accurate representation of the clinical presentation, microbiology, and treatment in typical hospital settings, not just specialized units. Because of the inclusion of multiple sites from all Australian states and New Zealand, it is likely that these findings are generalizable across Australia and New Zealand as well as in other similar high-income countries. Despite our definitions of PJI being consistent with the literature [11], the definition of LA-PJI may have misclassified some patients with "chronic" PJI with a short duration of symptoms, and other settings consider PJI occurring up 90 days from implantation to be "early" PJI.

Table 3. Use of Rifampicin for Periprosthetic Joint Infections Caused by Gram-Positive Organisms Managed With Debridement and Implant Retention According to Microbiological Species

	No.	Rifampicin, No. (%)
Staphylococcus aureus	216	161 (74.5)
Methicillin-resistant *Staphylococcus aureus*	20	15 (75)
β-hemolytic streptococci	67	21 (31.3)
Coagulase-negative staphylococci	39	20 (51.3)
Enterococci	39	6 (18.2)
Erisipelothrix rhusiopathiae	3	0 (0)
Granulicetella spp.	2	1 (50)
Milleri streptococci	5	2 (40)
Corynebacterium spp.	15	8 (53.3)
Streptococcus pneumoniae	3	1 (33.3)
Propionibacterium spp.	9	5 (55.6)
Viridans streptococci	15	5 (33.3)
Total	368	209 (56.8)

CONCLUSIONS

We have confirmed our initial hypotheses that LA-PJI is the most common mode of presentation, likely as a result of acute hematogenous seeding, and that there is substantial heterogeneity in surgical and antibiotic management of PJIs. This has important implications for prevention efforts (eg, early identification and prevention of BSI) and identification of gaps in the current evidence (eg, optimal debridement strategy for a DAIR procedure, the use of rifampicin in PJI, and the duration of antibiotic therapy). The PIANO cohort will allow analysis of the relationship between practice variations and outcome and will serve as a platform to build future interventional studies.

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