

Safety and Efficacy of Direct Physician Office-Based Infusion Center (POIC) Admissions for Antibiotic Treatment of Osteomyelitis (OSTEO) and Complicated Skin and Skin Structure Infections (cSSSI)

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Abstract

Background: POICs provide an alternate treatment site for patients with severe infections. Avoiding hospital admission has numerous benefits that include reduction of nosocomial infection risk and adverse events. The study purpose was to evaluate outcomes of POIC-initiated intravenous antibiotics (IVAB) for the treatment of serious infections, including OSTEO and cSSSI in patients without immediate prior hospitalization.

Methods: We conducted a retrospective database and chart review of all adult patients receiving IVAB in 2008. Patients without immediate prior hospitalization, defined as 72 hours prior and diagnosed with either OSTEO or cSSSI were evaluated. The primary outcome was clinical success rate, defined as cure + improving, with secondary outcome of adverse events (AEs).

Results: Of 248 patients reviewed, 89 (35%) were directly admitted to the POIC for IVAB without prior hospitalization. 24 patients (28%) had OSTEO and 65 (72%) cSSSI. For both diagnoses, the overall success rate (cure + improving) was 96% (79% + 17%). Success rate for OSTEO was 100% and for cSSSI was 94%. Mean age was 52 (range 20-80); mean weight was 99kg, with 48% males. Diabetes was present in 41 patients (46%) and renal disease in 21 (24%). Predominant site of infection was the foot. Methicillin-resistant *Staphylococcus aureus* (MRSA) was the most commonly reported pathogen (37%) overall. Vancomycin was the most used antibiotic. AEs were reported in 19 patients (21%), 17 (19%) mild and 2 (2%) serious. All resolved or were treated without sequelae. One catheter-related infection was reported in 2146 total IVAB treatment days. POIC therapy resulted in large cost-savings per day compared to hospitalization for the area.

Conclusions: Treatment of patients with IVAB in an Infectious Disease POIC without prior hospitalization appears to be safe and effective for OSTEO and cSSSI. Further prospective studies can confirm these findings.

Introduction

With the increase in hospital acquired infections and rising associated costs, treatment of patients requiring IVAB without requiring hospitalization poses significant merit. This study was designed to assess the safety and efficacy of IVAB for cSSSI and osteomyelitis when the therapy is initiated in a POIC.

Methods

- Retrospective database and chart review of Infectious Disease Associates (IDA) POIC patients.
- Electronic reporting form used to record demographic, clinical, and safety data.

Inclusion Criteria

- IVAB initiated in the IDA POIC between January 1 and December 31, 2008.
- Receipt of POIC-provided IVAB for a minimum of 48 hours.
- Age 18 years and older.
- One of the following documented diagnoses.
 - Osteomyelitis (with and without hardware).
 - Complicated skin and skin structure infections.
 - Deep soft tissue infection, major abscess, surgical wounds, diabetic infections/ulcers, necrotizing fasciitis, infections with underlying vascular insufficiency, gastrointestinal or urogenital site infections, traumatic wounds, and animal bites.
- POIC-initiated treatment, defined as no inpatient hospitalization within 72 hours of receiving IVAB in the POIC.

Demographic Data

- Age, gender, weight, ethnicity.
- Concurrent disease states: diabetes, renal failure, immunosuppression.

Clinical Data

- Infection diagnosis.
- IVAB name, dose, duration of therapy.
- Oral antibiotic use (pre-POIC and concurrent).
- Culture results, pre-POIC and during POIC treatment.
- Daily POIC cost compared to HCUP national data⁴
- Adverse events:
 - Mild: Resolution with or without discontinuation of IVAB, use of medication or short term treatment allowed.
 - Serious: Results in IVAB-related hospital admission and/or permanent change in patient status and/or requires IVAB discontinuation to prevent patient status change.
- IVAB efficacy at time of POIC discharge:
 - Cure: Clinical signs/symptoms resolved, and/or no additional antibiotic therapy needed, and/or negative culture at end of therapy.
 - Improved: Partial resolution of clinical signs/symptoms, and/or additional antibiotic therapy necessary.
 - Failed: Resistant, worsening, or new clinical signs/symptoms, recurrence of same infection within 90 days, and/or the need to change antibiotic therapy, and/or hospital admission due to worsening infection.
- Success rate defined as (Cure + Improved)/(total # of patients).
- Adverse event rate defined as (Mild + Serious events)/(total # of patients).

Data Analysis

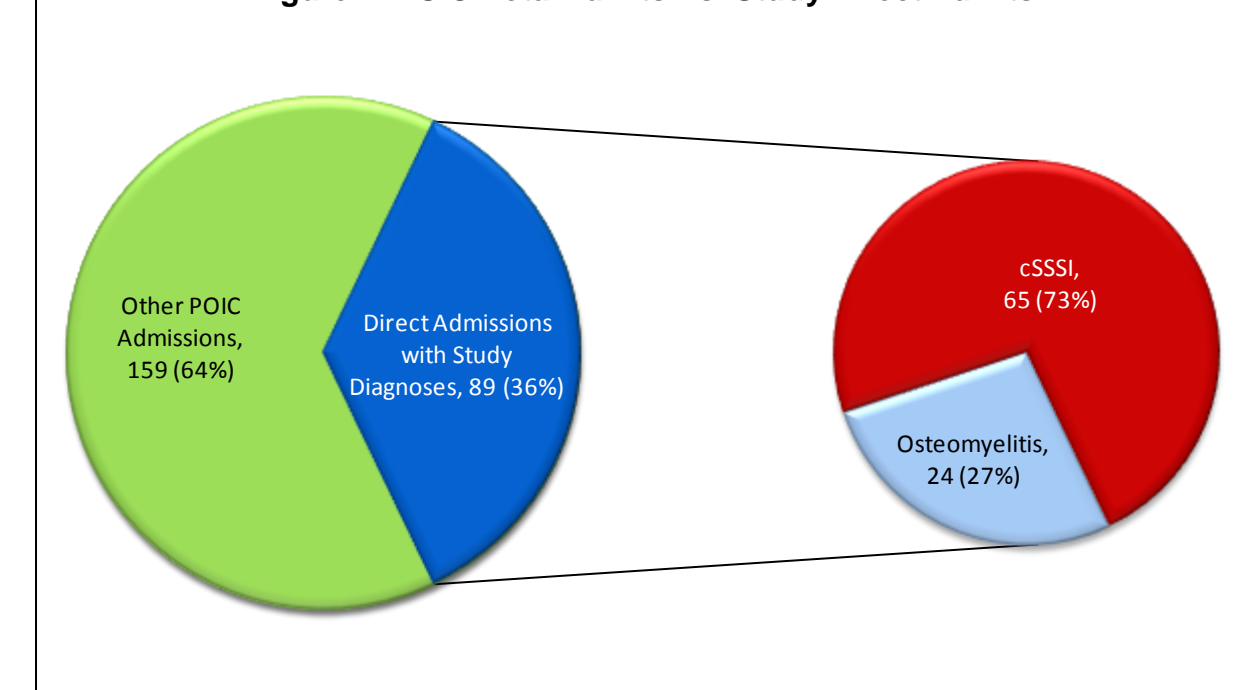
- Descriptive statistics (mean, standard deviation, min/max) were used for demographic data.
- Percentages were used for efficacy and safety data.

Results

Patient Demographics and Characteristics:

- The POIC treated 248 patients 2008 with IVAB. Of these, 89 (36%) had treatment initiated in the POIC, meeting study criteria.
- 46% of patients had diabetes, while 62% had one or more high-risk comorbidities.

Figure 1: POIC Total Admits vs. Study Direct Admits



Characteristic (n=89)	No. (%)	Range
Gender		
Female	46 (52%)	
Male	43 (48%)	
Mean Age (years)	52±13	(20-80)
Mean Weight (kg)	99±30	(36.8-181.8)
Ethnicity		
Caucasian	53 (59%)	
African American	30 (34%)	
Other	6 (7%)	
Comorbidities		
Diabetes	41 (46%)	
Chronic Kidney Disease	21 (24%)	
Immune Disorders (non-HIV)	12 (13%)	
Immunosuppressive Drugs	10 (11%)	
Comorbidities Per Patient		
None	34 (39%)	
One	28 (31%)	
Two	25 (28%)	
Third	2 (2%)	

Types of Infection:

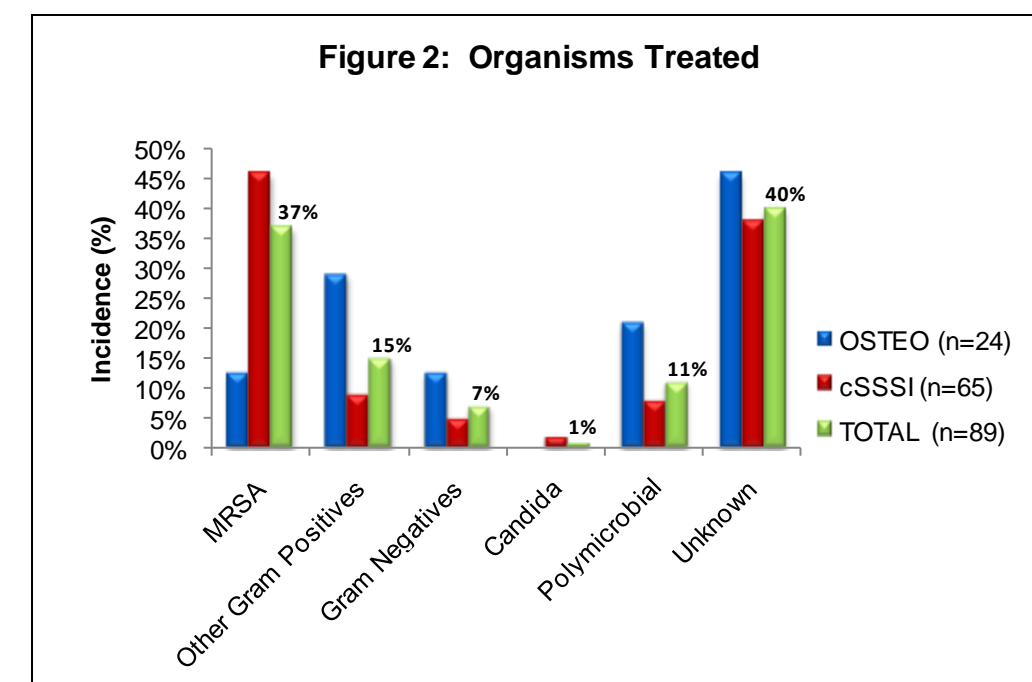
Diagnosis	No. (%) (n=65)
Complicated Cellulitis	27 (42)
Major Abscesses	13 (20)
Surgical Wounds	9 (14)
Animal Bites	8 (12)
Diabetic Foot Infections	4 (6)
Ulcers	3 (5)
Deep Incisional Wounds	1 (1)

Location	Foot	Lower Leg	Toe	Multi-Site	Abdomen	Ankle	Arm	Chest	Finger	Knee	Spine	Other*
OSTEO	11	n/a	8	2	n/a	1	n/a	n/a	n/a	n/a	2	n/a
cSSSI	14	12	2	5	5	3	4	4	4	4	n/a	9
TOTAL	25	12	10	7	5	4	4	4	4	3	2	9

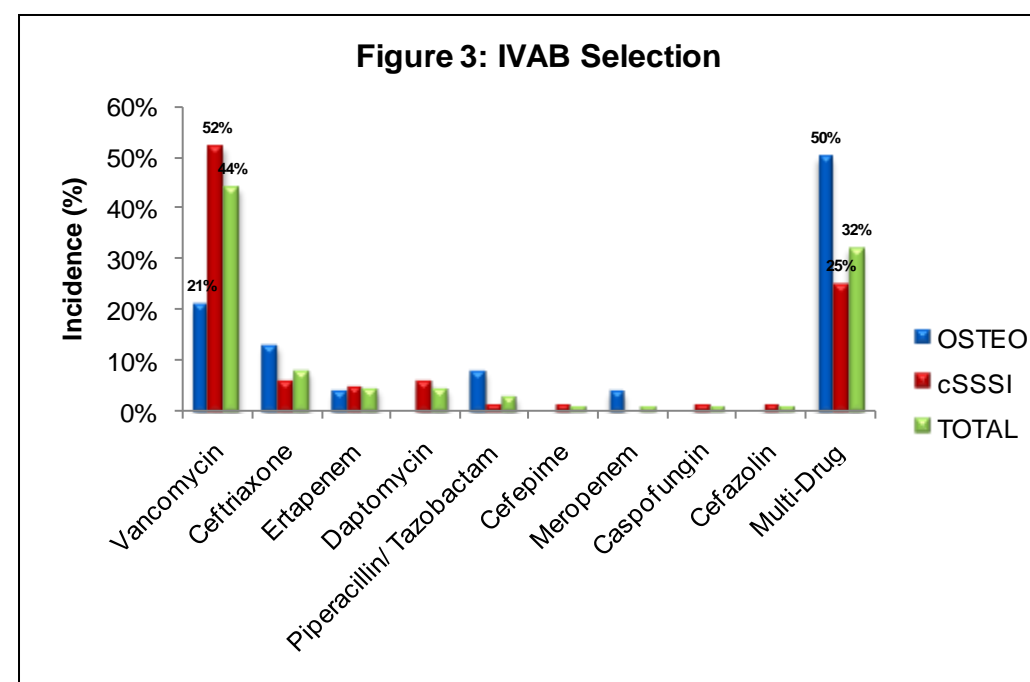
*Other includes: ear, face, back, thigh, buttocks, genitals, and head

- cSSSI: Complicated cellulitis (42%) was the most common skin infection, followed by major abscess (20%).
- OSTEO: Only one patient had hardware present.

Drug Therapy:



- 51 total patients (57%) failed oral antibiotics prior to POIC admit.
- Across both diagnoses, MRSA was the most common pathogen (33 total patients, 37%); positive cultures were obtained in the POIC for 23 of these patients (26%).
- Dual IVAB therapy was frequent (32% overall; 50% OSTEO, 25% cSSSI); vancomycin + cefepime was the most used dual regimen.
- Mean duration of IVAB therapy was 33.4 days for OSTEO and 20.6 days for cSSSI.
- Drug doses were all within recommended guidelines. OSTEO patients receiving daptomycin had mean dose of 6mg/kg/day; cSSSI patient doses ranged between 4mg/kg and 6mg/kg.
- 27 patients (30%) received concurrent oral therapy; (9 OSTEO, 18 cSSSI); metronidazole was most common, (6,9) followed by a fluoroquinolone (3,5), clindamycin (1,3) and others (1,2).
- Costs of POIC-initiated care averaged \$314 per day for OSTEO and \$212 per day for cSSSI, which is significantly less than average hospital daily costs, which range from \$1,225 to \$3,442 per day.

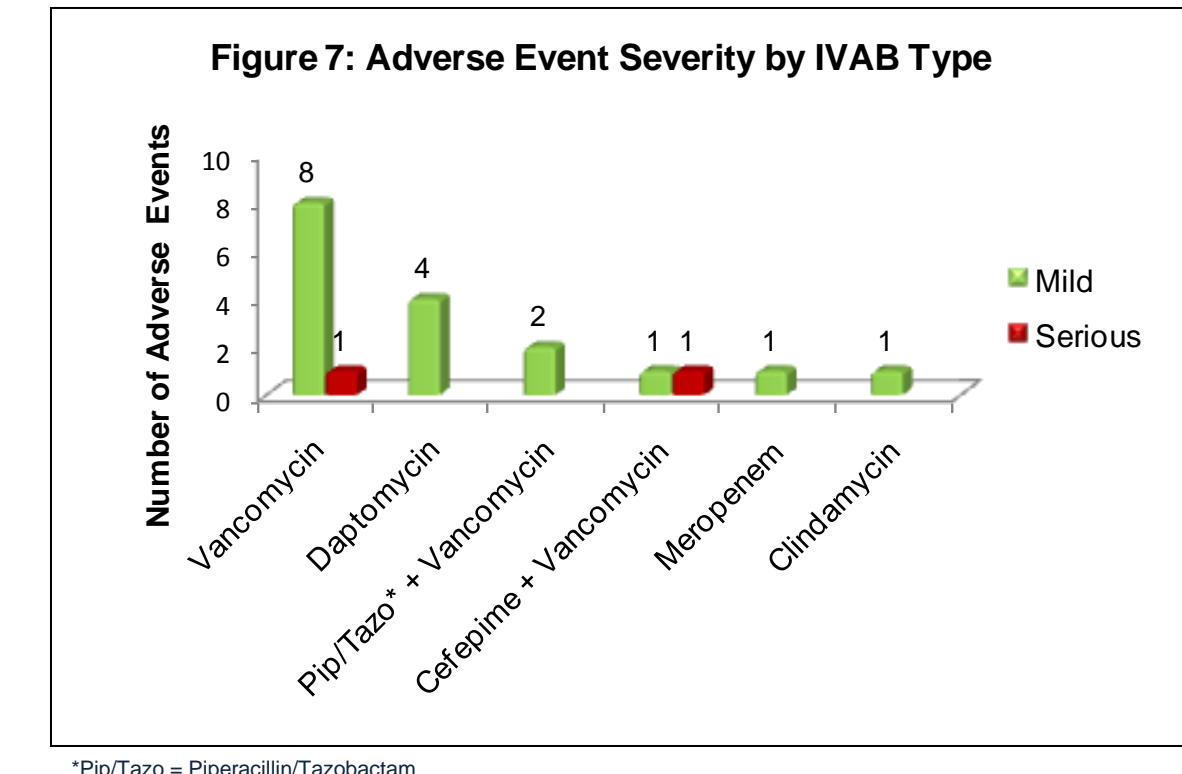


Safety:

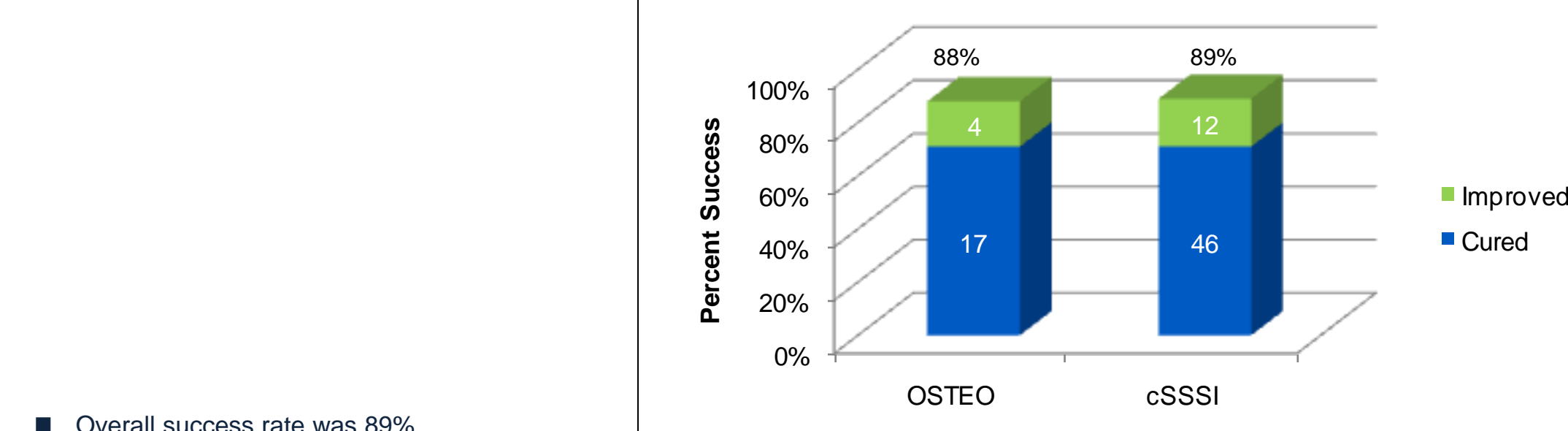
Adverse Event	No. (%)	Relevant IVAB	Serious	Outcome	Drug Changed
OSTEO: n=24					
CPK Increase*	3 (13)	Daptomycin	No	Resolved	No (2), Yes (1)
		Meropenem	No	Resolved	No
Diarrhea	2 (8)	Vancomycin + Piperacillin/Tazobactam	No	Resolved	No
Genital Yeast	1 (4)	Vancomycin, Cefepime	No	Resolved	No
Rash	2 (8)	Vancomycin	Yes	Resolved	Yes
		Vancomycin + Cefepime	Yes	Resolved	Yes
Total	8 (33)				
cSSSI: n=65					
Diarrhea	1 (2)	Clindamycin	No	Resolved	Yes
Itching	5 (8)	Vancomycin	No	Resolved	No
		Vancomycin + Piperacillin/Tazobactam	No	Resolved	No
Rash	2 (3)	Daptomycin	No	Resolved	No
		Vancomycin	No	Resolved	Yes
Renal Insufficiency†	1 (2)	Vancomycin	No	Resolved	No
Vomiting	1 (2)	Vancomycin	No	Unknown	Yes
Total	11 (17)				

*Creatine Phosphokinase (CPK)
†Serum creatinine rise of 0.5 mg/dl

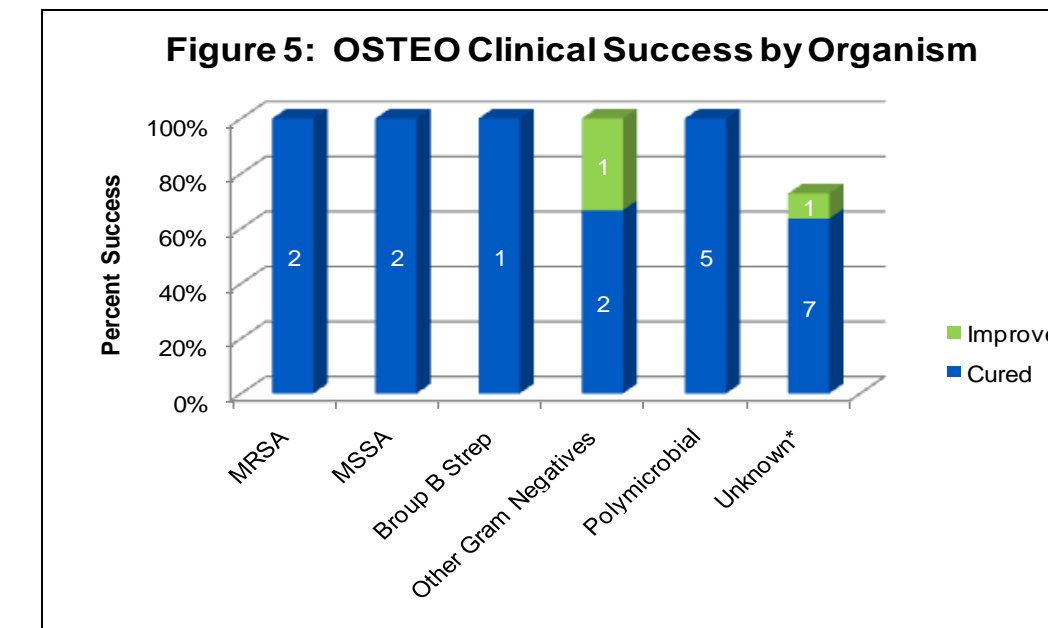
- Overall adverse event (AE) rate was 21%; serious adverse event rate was 2%.
- No AEs resulted in hospitalization.
- All AEs (except one unknown) resolved without sequelae prior to POIC discharge.
- The majority of AEs involved itching and rash (allergic-type reactions).
- Vancomycin was the IVAB most commonly used in patients with AEs (68%).
- One catheter-related infection occurred out of 2,146 total IVAB treatment catheter days (catheter-infection rate <0.01%).



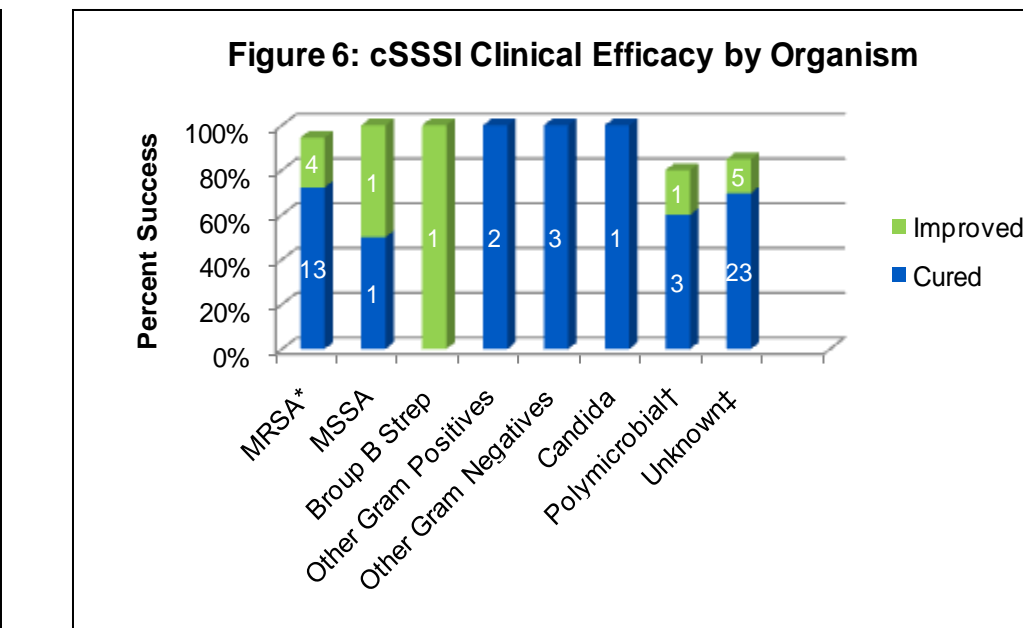
Clinical Outcomes:



- Overall success rate was 89%.
- Success rate upon discharge (cure + improving) was 96% (100% for OSTEO, 94% for cSSSI). Patients were then evaluated and considered failed if there was recurrence of infection within 90 days (OSTEO - 3 failures, cSSSI - 3 additional failures).
- 88% OSTEO patients received successful IVAB therapy in the POIC (71% cured, 17% improving at time of POIC discharge).
- Three OSTEO patients failed therapy (3 had recurrence of infection, 1 required surgical intervention)
 - In the 3 OSTEO failures, all had significant co-morbidities (1-diabetes, 2-diabetes + renal disease)
- 89% of cSSSI patients received successful IVAB therapy in the POIC (71% cured, 18% improving at time of discharge).
- Seven cSSSI patients failed therapy by protocol definition (3-wound infections, 2-complicated foot infections, 2-lower leg infections)
 - 3 patients had recurrence of infections, 3 others required surgical intervention following POIC discharge; (1-abdominal wound, 1-foot, 1-lower leg infection)
 - 2 patients had MRSA infections and 3 had significant co-morbidities (1-renal disease, 2-diabetes)



*1,3 patients failed who had unknown organisms



*1 patient failed who had identified MRSA.
†3 patients failed in the polymicrobial category (1-wound, 2 complicated foot infections).
‡2 patients failed whose organisms were unknown.

Discussion

- In 2008, 35% of POIC admissions for IVAB were patients with osteomyelitis or cSSSI without immediate prior hospitalization.
- Methicillin-resistant *S.aureus* was the most common pathogen. The majority of patients had failed oral antimicrobial therapy and had one or more significant comorbidities.
- Outcomes were affected by co-morbidities, particularly diabetes.
- POIC therapy was appropriate, efficacious and cost-effective for both osteomyelitis and cSSSI patients.
- Adverse event rates were low and comparable to other retrospective studies.^{1,2}
- There were no long term sequelae for any AE, including the two serious events.
- Catheter-related infection rate was extremely low, well below national norms and reported studies.³
- Limitations: Surgical interventions were not evaluated, continued success after study period was not evaluated, data was retrospective and lacked control group

Conclusion

- Patients requiring intravenous antibiotics for serious infections, including OSTEO and cSSSI can be treated entirely in a physician-operated infusion center
- IVAB in this setting for treatment of OSTEO and cSSSI appears to be both safe, efficacious and cost-effective. Patients with significant co-morbidities may require additional intervention.
- Treatment in a non-inpatient setting could reduce morbidity and mortality with absence of nosocomial infections.
- Further studies, including a prospective trial and follow-up data could confirm these findings.

References

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