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Medical versus Surgical Management of Native Joint Septic Arthritis in Adults:
A Retrospective Comparison of Outcomes within the VA CT Medical System

A Thesis Submitted to the
Yale University School of Medicine
in Partial Fulfillment of the Requirements for the
Degree of Doctor of Medicine

By

Ian Thomas McConnell

2017

Abstract

Objective: Septic arthritis is a medical emergency with significant associated morbidity and mortality that requires joint drainage in addition to antibiotic therapy. Closed-needle aspiration and surgery (via arthrotomy or arthroscopy) are the standard approaches to joint drainage, though little data exists regarding treatment outcomes with each approach. We compared long-term outcomes for adult patients with septic arthritis of a native joint based on whether they received a ‘medical’ or ‘surgical’ approach to joint drainage.

Methods: We retrospectively reviewed all chart records for patients diagnosed with septic arthritis at the West Haven VA Medical Center between January 2006 and December 2015. Treatment outcomes were recorded at one year post-diagnosis.

Results: Sixty-two patients were diagnosed with native joint septic arthritis during the study period, 19 who were managed medically and 43 surgically. There was no significant difference in demographic variables, risk factors, clinical presentation, laboratory parameters, or duration of antibiotic therapy between the two groups. 81% of medically-managed patients and 82% of surgically-managed patients achieved a full recovery within 12 months. Overall mortality was 3.2%, and both patients who died were managed surgically. There were no significant predictors of poor treatment outcome aside from Black race.

Conclusion: Our findings suggest that medical management of septic arthritis with closed-needle aspiration is non-inferior to surgical management in terms of both morbidity and mortality. Given the small sample size, a prospective randomized control trial is needed to guide definitive recommendations on the best form of joint drainage.

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I would like to sincerely thank Dr. Shaili Gupta for her guidance, mentorship, support, and good humor throughout the execution of this project. I must also thank her and Dr Juergen Holleck for their assistance with data collection and validation that enabled this analysis. I would be remiss not to acknowledge the Office of Student Research at the Yale School of Medicine for their guidance throughout the process of designing and completing a major scholarly project.

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I. Introduction

Septic arthritis has long been recognized as a medical emergency with significant associated morbidity and mortality. Mortality estimates range from 4-13% in native joint infections, with rates as high as 20% observed in prosthetic joints. [1-9] Of patients surviving an episode of septic arthritis, roughly one-third experience functionally impairing joint deterioration as a result. [2, 3, 5, 9] The incidence of septic arthritis is estimated to be 4-12 per 100,000 person-years among the general population. [7, 9-12] Several studies have shown particularly vulnerable populations, such as those with pre-existing joint disease [13] and socioeconomically marginalized groups such as IV drug users in Northern Europe [4] and the Aboriginal people of Australia [7], to have much higher rates of infection. There is further evidence that the incidence of septic arthritis is rising due to an increase in the number of iatrogenic infections [10, 12] and the demographic reality of an ageing population. [14] Given its considerable associated morbidity and mortality, any patient suspected of having an infected joint requires immediate hospitalization for assessment, supportive care, and prompt treatment as necessary. [15]

Morbidity associated with septic arthritis is typically due to irreversible joint damage likely caused by a combination of bacterial virulence factors, the host inflammatory response, and some measure of tissue ischemia. [16] Tarkowski's work with model murine systems of *S. aureus* septic arthritis has suggested that certain virulence factors play a major role in promoting joint damage. [17] Further work by his group has highlighted the importance of the host immune response. They have identified TNF-alpha, IL-1, and IL-10 as potential protective factors in mediating septic arthritis, while

showing an association between increased IL-4 activity and higher incidence of and mortality from septic arthritis. [18-21] Others have identified tissue ischemia as a third potential mechanism of joint injury, related to the avascularity of cartilage and its dependence on the diffusion of oxygen and nutrients from the synovium. Stevens et al suggested that the accumulation of purulent exudate and the resulting increased intraarticular pressure may eventually cause tamponade of synovial blood flow and subsequent cartilage anoxia. [22]

The cumulative effect of these mechanisms is rapid destruction of the cartilage extracellular matrix which, due to the poor regenerative capacity of adult articular cartilage, can result in long-term joint dysfunction. In rabbit models, studies have demonstrated a greater than 20% loss of proteoglycans from cartilage extracellular matrix within 2 days of *E. coli* inoculation and nearly 40% loss of type II collagen within three weeks. [23, 24] A 2003 study comparing the use of low-dose intravenous dexamethasone therapy in conjunction with antibiotic therapy versus antibiotic therapy alone further highlighted the importance of the host immune response as a mediator of joint damage. This double blind, randomized, placebo-controlled trial in 123 children showed that the addition of dexamethasone to conventional antimicrobial therapy reduced clinical duration of septic arthritis and decreased the extent of joint damage and dysfunction. [25] While similar studies have not been carried out in adults, the role of host immune system in causing the long-term sequelae of septic arthritis is increasingly clear.

Given our understanding of the swift and destructive course of septic arthritis based on its pathogenesis, prompt diagnosis and treatment are essential. [26] Septic arthritis remains, however, a challenging diagnosis. In adults it continues to be ultimately a

clinical determination, as the gold standard of culturing bacteria from an infected joint can take days or may not be possible at all in the setting of prior antibiotic use. [27]

Newman identified three primary means of diagnosing septic arthritis: a) positive culture from joint fluid or tissue, b) positive culture from another source (blood, urine, etc.) with signs and symptoms of an infected joint, or c) no organism cultured anywhere but with histologic or radiologic evidence of infection or turbid fluid aspirated from a joint in the right clinical setting. [28] In one study of 242 instances of septic arthritis in a single UK district over a 10-year period, the authors found that 70% of cases were associated with a positive joint culture, 13% with a positive culture from another source, and 16% with joint aspiration of sterile pus in the setting of prior antibiotic use. [9]

In considering the inherent delay of awaiting culture results and our understanding that roughly one-third of joint cultures in patients with septic arthritis will be negative, several researchers have assessed the capacity of different aspects of the patient history, physical examination, and laboratory testing to contribute to the diagnosis or exclusion of septic arthritis. A 1995 prospective observational study from a rheumatology clinic evaluated risk factors for septic arthritis among 37 patients with septic arthritis as compared to 4,870 patients without septic arthritis. In a multivariate analysis, the authors found a significant association between several features of the history and physical exam and a diagnosis of septic arthritis: age >79, history of diabetes mellitus, history of rheumatoid arthritis, history of joint surgery, presence of hip or knee prosthesis, and the presence of skin infection over the affected joint. [13] Goldenberg's early study of outcomes in septic arthritis noted the elevation of ESR in all but one of his cases, suggesting the possibility of ESR having some discriminatory value in diagnosis. [3]

More recent systematic reviews have called into question the diagnostic utility of most traditional clinical, history, or laboratory findings in changing the pre-test probability of septic arthritis. The 2007 systematic review by Margaretten et al examined 14 studies that included a total of 653 patients presenting with a potentially septic peripheral monoarticular arthritis. [29] While the “classic” presentation of septic arthritis is the febrile patient with a hot, swollen, erythematous, and painful joint, their review found limited evidence to suggest that any clinical feature is significantly specific for septic arthritis. They also concluded that neither the absence of a fever nor a normal serum white cell count, ESR or CRP could reliably exclude the diagnosis of septic arthritis. They did find, however, that higher white cell counts in the synovial fluid and presence of more than 90% neutrophils in the synovial fluid increased the likelihood of septic arthritis. For synovial white cell counts, the likelihood ratios were 0.32, 2.9, 7.7, and 28.0 respectively for levels of $<25,000/\text{mm}^3$, $> 25,000/\text{mm}^3$, $>50,000/\text{mm}^3$, and $>100,000/\text{mm}^3$. The likelihood ratio for neutrophils comprising $>90\%$ of synovial white cell count was 3.4.

A similar 2011 review identified having a history of joint surgery [LR =6.9] and the presence of a skin infection overlying a prosthetic joint [LR=15.0] as the only features from the history and physical to significantly alter the pre-test probability for septic arthritis. [30] The authors found that serum WBC, ESR, and CRP were not useful in the acute diagnosis of joint infection. They did, however, affirm the diagnostic value of synovial fluid white cell count, with likelihood ratios of 0.33, 1.06, 3.59 and infinity respectively for levels of $<25,000/\text{mm}^3$, $25-50,000/\text{mm}^3$, $50-100,000/\text{mm}^3$, and $>100,000/\text{mm}^3$. A 2016 study of 458 knee aspirates (with 22 confirmed as septic

arthritis based on synovial fluid culture) largely supported the findings of the two review mentioned. [31] Their analysis indicated that patient baseline characteristics, a history of fever, and serum lab parameters were not reliable predictors of septic arthritis. They also concurred that synovial white cell count was a significant predictor of joint infection, with the highest combined sensitivity and specificity coming at a level greater than 64,000 (40% sensitive, 90% specific; LR = 2.8). This study did not, however, find the percentage of neutrophils in synovial white cell count to be a significant predictor of joint infection.

Finally, several studies of septic arthritis have examined the value of x-ray, CT, MRI, and bone scans in discriminating septic from other forms of acute arthritis. While these radiologic studies have proven effective at identifying effusions, diagnosing osteomyelitis, and assessing the presence and extent of inflammation and tissue damage, they have been unable to distinguish between infective and other causes of acute inflammatory arthritis. [14]

In summary, with few aspects of the history and physical exam meaningfully contributing to the diagnosis or exclusion of septic arthritis, and with little help provided by serum lab tests or radiography, clinicians are largely left to use their clinical judgment and white cell counts from joint aspiration in order to make the timely diagnosis of joint infection while awaiting culture results. At worst, when opting for a conservative approach, clinicians may end up unnecessarily beginning empiric antibiotics in order to potentially prevent rapid joint damage and severe functional deterioration.

Amidst such diagnostic uncertainty, professional societies have largely avoided prescribing definitive recommendations for the diagnosis and management of the

potential septic joint. While the IDSA has published guidelines for the diagnosis and management of prosthetic joint infections [32] and is currently developing guidelines for the management of joint infections in children, they have remained notably silent on how to handle the infected native joint in adults. The UK took an initial step forward in 2006 with the release of their *Guidelines for management of the hot swollen joint in adults*, jointly developed by the British Society for Rheumatology, British Orthopaedic Association, and Royal College of General Practitioners. [15] In it, the authors lay out a clear protocol for working up potential septic arthritis which includes mandatory aspiration of synovial fluid for Gram stain, culture, cell count, and microscopy prior to initiation of antibiotics. They highlight that blood cultures should be collected, as well as laboratory assessment of ESR and CRP at baseline in order to monitor ongoing response to treatment (not for diagnosis, notably). The guidelines reinforce that x-rays and MRI are of no benefit in diagnosing septic arthritis, at the same time acknowledging that radiographs may show chondrocalcinosis and that MRI is most sensitive in detecting osteomyelitis if there is clinical suspicion.

On the issue of management, the UK guidelines become notably vaguer given the paucity of clinical data upon which to guide treatment. They indicate that there is no evidence upon which to advise optimal duration of IV or PO antibiotics, while noting the traditional approach of 6 weeks duration. The guidelines make clear that “septic joints should be aspirated to dryness as often as required” but make no recommendation as to the relative effectiveness of closed-needle aspiration versus an arthroscopic surgical approach, making an equivocal recommendation that leaves the choice up to the provider.

Interestingly, the authors do note some special consideration for management of the infected hip, stating that “urgent open debridement is often necessary.”

The question of how best to drain a septic joint is of paramount importance in light of our understanding of the disease pathogenesis being a combination of bacterial virulence, host inflammatory response, and tissues ischemia secondary to increased intra-articular pressure. Removal of pus from the closed joint space is essential for multiple reasons: a) to increase the effectiveness of antibiotics and speed bacterial clearance, b) to enable release of cytokines that contribute to joint destruction, and c) to decrease the elevated intra-articular pressure. As noted in the UK guidelines, pus removal can be accomplished by either serial closed-needle aspiration or by surgical drainage via arthroscopy or open arthrotomy. Manadan et al, in their 2004 review of evidence comparing the effectiveness of closed-needle aspiration versus surgical lavage, detailed the practical advantages of each approach: “With surgical lavage, direct visualization permits debridement and lysis of adhesions, and high-volume lavage of the joint is possible; proponents of the surgical approach contend that lavage is necessary to adequately remove purulent material from the infected joint and thus protect the articular cartilage from rapid destruction. Conversely, surgical lavage is an invasive procedure, exposes the patient to the risks of anesthesia, and is a one-time procedure that cannot accommodate ongoing purulent synovial effusions. In contrast to surgical lavage, daily arthrocentesis is noninvasive and can be performed repeatedly until the infection is cleared.” [33] Manadan’s review ultimately concluded that, based upon the limited available literature, outcomes of patients treated with daily arthrocentesis were at least

comparable with surgical lavage. The authors were unable, however, to comment regarding the superiority of either approach due to the limited data available.

The equivocal recommendation in the UK guidelines regarding the optimal approach to joint drainage reflects the near total lack of outcomes data on the management of septic arthritis in this regard. Only one study prior to Manadan's 2004 review directly compared outcomes of daily arthrocentesis versus surgical lavage, and only two additional such studies have been published since. In the original 1975 retrospective study by Goldenberg et al, the authors compared outcomes among 59 patients hospitalized for septic arthritis who presented over an 8-year period. For inclusion in the study, patients had to present within 14 days of joint symptom onset and have a positive synovial fluid culture. Cases of gonococcal arthritis were excluded, and 12 of the 59 patients were children. After consideration of polyarticular septic arthritis, a total of 73 affected joints were included in the analysis. All patients received appropriate antibiotics, with 55 joints managed via serial closed-needle aspiration and 18 via open arthrotomy. Patients were followed via clinic records for a brief period, with 80% having a follow-up period of at least three months. This study found that patients treated medically with arthrocentesis had a higher rate of full recovery (67% vs. 42%), lower rate of poor outcome (21% vs. 53%), and higher rate of death (12% vs 5%) than patients treated surgically with open arthrotomy. The authors noted, however, that these differences were not statistically significant, and they also noted that the increased percentage of hip infections in the surgical group (22% vs. 2%) contributed to the differential outcome because of the universally poorer outcomes associated with infected

hip joints. With these caveats, the authors concluded that “needle drainage appeared in general to be the preferable initial mode of treatment” of the septic joint. [3]

A second study directly comparing outcomes of medical versus surgical management in septic joints did not come until 2009 when Ravindran et al retrospectively analyzed outcomes from 50 adult patients hospitalized at a UK academic center over a 6-year period. Of the 51 episodes of septic arthritis, 32 were managed medically with serial arthrocentesis and 19 surgically with arthroscopy or arthrotomy. All episodes were monoarticular and included only cases of native joints with a positive synovial fluid culture. Patients were followed until time of discharge. As in the Goldenberg study, the authors observed better outcomes among the medically managed group though again did not reach the level of statistical significance. Among medically treated patients, 69% achieved full recovery as compared to 53% of the surgically treated patients ($p=0.24$). When comparing knee infections only, they observed 71% full recovery with medical management ($n=24$) and 38% for surgical management ($n=13$) while nearly achieving statistical significance ($p=0.05$). They did note a slightly increased length of stay for patients treated medically (16.5 vs 15 days). Based on these findings, the authors concluded that surgical treatment is not superior to medical treatment in draining pus as part of septic joint management.[8]

A recent retrospective study from a university hospital in Spain analyzed data from 186 hospitalized patients with septic arthritis over a 9-year period. The study authors included only adults with native joint infections that had positive synovial fluid cultures. Their analysis compared rates of treatment failure—defined as death, admission to ICU, readmission for septic arthritis, or need for surgery after 72 hours of initial

treatment—between patients managed with closed-needle aspiration (n = 154) versus surgical drainage (n= 32). The authors found that the type of joint drainage appeared to depend primarily on which service the patient was admitted to. Their analysis showed that rates of treatment failure did not differ significantly between patients managed with early surgery versus conservative management (53.1% vs 37.0%, $p = 0.09$). They did note, however, as in the Goldenberg study, that the surgical group had a higher percentage of hip infections that were differentially associated with treatment failure. [34]

Other studies have analyzed joint drainage technique as a predictor of poor outcome without directly comparing outcomes with medical versus surgical management. In another UK study of 242 hospitalized patients with septic arthritis that included children and prosthetic joints, multivariate analysis demonstrated an association between arthroscopy and arthrotomy with increased morbidity (OR 1.72, 3.74 respectively) but decreased mortality (OR 0.44, 0.16 respectively). The associations with arthrotomy achieved statistical significance. Other factors that were positively and significantly associated with increased morbidity included history of diabetes mellitus, age >65, and infections with *Streptococcus* or other Gram-positive organisms aside from *S. aureus*. [9]

A 1996 study of 135 patients in the Northern Territory of Australia, which also included children and prosthetic joints, found that surgical lavage as compared to closed-needle aspiration was associated with lower rates of requiring a repeat procedure and shorter length of stay. [7]

Finally, a 1986 UK study of 74 cases of septic arthritis (including children) concluded, without presenting any of the accompanying data, that there was no difference in outcome with surgical drainage, noting that surgical drainage was actually associated with higher rates of complications and permanent immobility. [1]

Considered together, these studies directly and indirectly comparing the effectiveness of medical versus surgical management of septic arthritis present an inconclusive picture regarding how best to drain an infected joint. While all three studies that directly compared outcomes showed better patient outcomes with closed-needle aspiration, all of the studies were retrospective and none achieved statistical significance due to small sample sizes. This lack of sufficient evidence to inform recommendations accounts for the absence of clear management guidelines. Perhaps no observation speaks better to the nature of this clinical “no-man’s land” than the incredible practice variation seen across all of these small studies. It is obvious that practitioners are suffering from insufficient evidence to inform their practice, as during the same time period only 17% of patients in a Spanish academic center underwent surgical drainage [34] as compared to 94% in a West Texas hospital. [6] A 2011 web-survey of rheumatologists (n=74) and orthopedic surgeons (n=77) further reinforces this notion. While the authors were surprised to find relative agreement between the two specialties in terms of how they believe drainage of a septic joint should be performed (77% of rheumatologists and 66% of orthopedic surgeons recommended surgical joint drainage), less than one quarter of each specialty cited published guidance as their main evidence base in treating septic arthritis. [35]

In summary, septic arthritis is a medical emergency with significant associated morbidity and mortality that must be diagnosed clinically while awaiting synovial fluid cultures. Timely drainage of a septic joint is essential to improve antibiotic effectiveness, enable release of cytokines destructive to articular cartilage, and decrease intra-articular pressure that can hasten tissue ischemia and joint damage. Current guidelines equivocally recommend use of either closed-needle aspiration or surgical drainage (via

either arthroscopy or arthrotomy) to achieve pus removal. Existing data provides insufficient evidence to indicate superiority of either the medical or surgical approach to joint drainage, though limited retrospective studies suggest that medical management is at least non-inferior. Given the severe functional deterioration and mortality associated with poor treatment outcomes, more data is needed on outcomes of medical versus surgical management of the septic joint in order to inform the development of definitive treatment guidelines.

II. Statement of Purpose

The primary purpose of this research is to compare outcomes of patients with septic arthritis at the West Haven VA Connecticut Medical Center, based on whether they were managed medically with joint drainage via closed-needle aspiration or surgically with joint drainage via arthroscopy or arthrotomy. Our hypothesis is that there will be no significant difference in mortality or functional deterioration attributable to septic arthritis between these groups at one year post-diagnosis. In addition, we intend to assess risk factors that may be associated with poor outcomes for these patients.

Secondary aims of this study include description of the presentation and diagnosis of septic arthritis within our unique setting. Specific questions to address include:

- What clinical features and laboratory parameters are associated with the diagnosis of septic arthritis?
- On what basis are patients diagnosed with septic arthritis?
- What joints are most commonly infected?

- What organisms most commonly cause septic arthritis?

We will also examine whether there are significant differences in presentation (clinical features, joint involved, organism, etc.) between medically- and surgically-managed patients in regards to the factors above that may help explain clinical decision-making as to which joint drainage technique is employed. Our hypothesis is that there will be significant differences in the presentation of medically- vs. surgically-managed patients.

III. Methods

Design and setting

This hospital-based retrospective chart review was conducted at the West Haven VA Connecticut Medical Center (VACT; West Haven, CT). All episodes of septic arthritis occurring among patients over a ten-year period (January 1, 2006 to December 31, 2015) were identified. By design, all patients at the West Haven VA are adults. Patients with infection of a prosthetic joint were excluded from this study given that guidelines for the diagnosis and management of prosthetic joint infections are already well-established. Patients with implanted hardware overlying or adjacent to the infected joint were also excluded as these few patients were uniformly treated with surgical removal of the hardware and had distinct underlying risk factors for joint infection not relevant to management a typical native joint infection. This study also excluded septic arthritis associated with Lyme disease or gonococcal infection, as clear guidelines also exist for management of these infections.

This study was designed in accordance with the ethical standards of the VACT Ethics Committee and approved by its Institutional Review Board. As a retrospective study, patient care was not influenced as part of study execution. No written informed consent to participation was necessary.

Case definition

All included cases met one of Newman's diagnostic criteria for septic arthritis [28]: (A) positive culture from an affected joint (synovial fluid or tissue), (B) positive culture from another site in a patient with clinical features of septic arthritis, and (C) negative cultures but clinical features and purulent joint fluid consistent with septic arthritis in a patient having undergone prior antibiotic therapy. No cases were included based on histologic or radiologic evidence of septic arthritis alone. All organisms were isolated and identified by the West Haven VA microbiology laboratory utilizing conventional biochemical assays.

Ascertainment

Two methods were used to retrospectively identify potential cases of septic arthritis diagnosed between January 1, 2006 and December 31, 2015. First, an exhaustive list of ICD codes related to septic arthritis, joint infection, arthrocentesis, arthroscopy and arthrotomy for an infected joint, and pyogenic arthritis were used to search all hospital records over this period. Second, a list of all positive synovial fluid cultures was obtained from the microbiology laboratory as a cross-check to ensure that as many cases as possible of septic arthritis were captured, given that it is a relatively uncommon diagnosis.

Data collection

For all potential cases of septic arthritis, all patient records from the course of their admission or treatment were reviewed with data extracted on the joint location, joint type (native vs. prosthetic), results of diagnostic joint aspirations (including culture, cell counts, and microscopy), results of all other cultures done, and history of antibiotic use. Based on this data and the clinical presentation as documented by the medical team, all cases of native joint septic arthritis were identified. For all definite cases of septic arthritis meeting inclusion criteria, a structured data extraction tool was used to review records from the date of presentation to at least one year post-diagnosis. In addition to the variables mentioned above, other items extracted included the following: race, gender, history of diabetes mellitus, history of joint disease, history of joint surgery, HIV status, history of IV drug use, use of immunosuppressive medications, factors precipitating diagnosis, joint functional status prior to infection, involvement of other joints, presence of fever/joint pain/swelling/erythema/limited range of motion, joint function at time of presentation, serum WBC/ESR/CRP, number of times joint was aspirated, use of antibiotics prior to diagnostic aspiration, type of surgical procedure (if done), radiographic studies done, type and duration of antibiotics given, type of disposition, joint function upon discharge and at follow-up visits up to one-year post-discharge, and date/cause of death. If patients did not have a recorded follow-up visit between 9 to 12 months post-discharge, subsequent visits were reviewed until finding the next visit with documentation of function of the affected joint.

Treatment and outcome coding

All episodes of septic arthritis were coded as receiving ‘medical’ or ‘surgical’ management based on the method of joint drainage used over the course of their treatment. Patients were classified as receiving ‘surgical’ management if they went to the operating room for joint drainage at any point during their admission. ‘Surgical’ patients were then further classified as being treated with either arthroscopy or arthrotomy based on review of surgical notes. All other episodes were classified as receiving ‘medical’ management.

The number of closed-needle joint aspirations was counted to include only those done prior to surgery for those who went to the operating room for surgical drainage. For the few patients with multiple joints involved, our analysis only included treatment of the joint of primary complaint.

As noted above, the medical records of all included patients were reviewed for at least one year following the diagnosis of septic arthritis. Using a combination of notes from providers in Medicine, Orthopedics, Rheumatology, Infectious Disease, Kinesiotherapy, Physical Therapy, and Primary Care, specific documentation was made regarding function of the affected joint at 1-2 months, 3-9 months, and 12 months post-diagnosis. Specific attention was paid to documentation of pain, swelling, range of motion, and any changes in function from the patient’s baseline prior to infection. An episode was recorded as ‘Full Recovery’ if the patient did not have any deterioration in joint function from baseline at 12 months post-discharge. An episode was recorded as a ‘Poor Outcome’ if the patient met one of the following criteria at 12 months post-discharge: a) experienced any deterioration in joint function, b) failed to clear the organism from the joint based on aspirations done post-treatment, c) experienced

recurrent infection within the same joint within 12 months post-diagnosis after having a documented culture-negative joint aspiration, d) treatment required full or partial amputation, or e) the patient died as a result of their joint infection. If a patient did not have any documented visits at 12 months post-diagnosis or beyond with no documentation of death, they were classified as “Lost-to-follow-up” and therefore excluded from the final outcomes analysis. Patients with a date of death documented in the medical chart within 12 months post-discharge were recorded as such. Records were thoroughly reviewed to determine if the cause of death could be reasonably attributed to complications related to septic arthritis.

Statistical Analysis

All statistical analysis was performed using SAS software (version 9.4). All analyses were stratified by type of management (‘medical’ versus ‘surgical’), with aggregate findings for the entire sample also shown. Categorical variables are reported as the frequency and percentage. Continuous variables are reported as the mean and standard deviation with any missing variables noted. For comparison between the two management groups, all tests were two-sided with a designated significance threshold of $p < 0.05$. For categorical variables, the two groups were compared using a Fisher’s exact test. For continuous variables, the two groups were compared using either the Student’s t -test or Mann-Whitney U-test.

A univariate logistic regression model was used to analyze risk factors associated with a ‘Poor Outcome’ and those associated with ‘death attributable to septic arthritis’, again for each treatment group and the sample overall. The following risk factors were analyzed as part of this analysis: type of management, age > 65, age > 80, gender, race,

joint location, infecting organism, use of immunosuppressive medications, history of DM, HIV status, history of IVDU, history of joint disease or joint surgery, factors precipitating infection, serum WBC and ESR at presentation, time from presentation to operating room, duration of antibiotics, and type of disposition.

Attribution

All chart review and data collection was completed by the present author along with Dr. Shaili Gupta and Dr. Juergen Holleck, both Assistant Professors at the Yale School of Medicine. The data collection tool was designed and managed by the present author. All final coding regarding treatment outcomes at 12 months post-discharge was done by Dr. Shaili Gupta, who is also the adviser and Principle Investigator on this project. All statistical analysis was completed by the present author.

IV. Results

Case ascertainment

A total of 366 distinct episodes of potential septic arthritis were identified over the study period from an initial medical record search using ICD codes related to septic arthritis. Subsequent search of positive synovial fluid cultures from the microbiology lab incorporated an additional 85 unique cases. Of the total 451 potential episodes of septic arthritis, 333 were excluded as cases of septic arthritis after thorough chart review. The most common alternative diagnoses were crystal arthropathy, degenerative joint disease, and septic bursitis. Of the 118 episodes confirmed to be septic arthritis, 48 were found to involve prosthetic joints and therefore excluded from further analysis. Within the 70

confirmed episodes of native joint septic arthritis, three cases of Lyme arthritis and five cases involving overlying or adjacent implanted hardware were excluded. There were no identified cases of gonococcal arthritis. The final sample, therefore, comprised 62 adult patients with septic arthritis meeting inclusion criteria.

Management of joint drainage and antibiotic therapy

All but 2 of the 62 patients included in the study were hospitalized for at least one night; the two non-hospitalized patients were managed medically as outpatients. Attempts to aspirate the affected joint were made in all but 2 of the 62 cases of septic arthritis. The two non-aspirated joints were both small and deemed to require surgical intervention regardless of the aspiration findings based upon the clinical picture and patient history. Intraoperative cultures confirmed the diagnosis of septic arthritis in both cases.

Forty-three of the 62 patients (69%) were managed surgically, with the remaining 19 cases managed conservatively with antibiotics and closed-needle aspiration alone. Of the surgically-managed patients, arthroscopy was the employed method of joint drainage in 18 cases (42% of all surgical cases) with the remaining 25 drained via open arthrotomy. Medically-managed patients had the affected joint aspirated, on average, 2.42 times over the course of their treatment, while surgically-managed patients had an average of 2.44 joint aspirations done prior to having the joint surgically drained in the operating room. On average, surgically-managed patients went to the operating room 2.3 days after their initial joint aspiration (n=40). The average length of stay for surgically-managed patients was 19.8 days, as compared to 16.1 days for medically-managed patients ($p=0.53$)

All episodes of septic arthritis were initially treated with broad-spectrum intravenous antibiotics, save the single case of fungal infection that was treated with oral fluconazole. Following initial empiric therapy all patients were narrowed to appropriately targeted antibiotics, when possible, based on culture results. Medically-managed patients received, on average, 37.6 total days of antibiotic therapy and 28.8 days of intravenous antibiotics, less than the average of 54.0 days and 48.1 days respectively for surgically-managed patients. These differences in duration of antibiotic therapy were not, however, statistically significant ($p=0.13$, $p=0.06$).

Patient characteristics

The average age of our sample presenting with septic arthritis was 67.4 years old, with no significant difference between the two treatment groups. 95% of patients were male, consistent with the gender breakdown of the general population treated in the VA system. 89% of patients were white, the rest black, with no significant difference between the two treatment groups. In terms of risk factors for acquiring septic arthritis, 43% of the sample had diabetes mellitus (DM), 26% insulin-dependent DM, 11% had a history of intravenous drug use (IVDU), 21% were on immunosuppressive pharmacotherapy at the time of diagnosis of septic arthritis, and 43% had pre-existing joint disease (RA, DJD, gout, etc.) of the infected joint. There was no significant difference in the prevalence of any of these conditions between the medically- and surgically-managed groups. Only 1 of 62 patients was HIV-positive, and only one had a history of septic arthritis.

Table 1. Patient demographics, risk factors, and treatment details; overall and by type of mgmt

Characteristics	Total (n = 62)	Medical (n = 19)	Surgical (n = 43)	P-value
Age	67.4	66.4	67.9	0.72
Sex (male : female)	59:3	18:1	41:2	1.0
Race				
White	55 (89%)	17 (89%)	38 (88%)	1.0
Black	7 (11%)	2 (11%)	5 (12%)	1.0
Risk factors				
Diabetes mellitus	27 (43%)	6 (32%)	22 (51%)	0.18
Insulin-dependent DM	16 (26%)	2 (11%)	14 (33%)	0.11
HIV	1 (1.6%)	1 (5.3%)	0 (0%)	0.31
IVDU	7 (11%)	2 (11%)	5 (12%)	1.0
Immunosuppressive meds	13 (21%)	5 (26%)	8 (19%)	0.51
Pre-existing joint disease	27 (43%)	7 (37%)	20 (47%)	0.58
Hx of septic arthritis	1 (1.6%)	1 (5.3%)	0 (0%)	0.31
Hx of surgery on joint	2 (3.2%)	1 (5.3%)	1 (2.3%)	1.0
Treatment				
# of joint aspirations (not including OR)	2.44	2.42	2.44	0.99
Length of stay (days)	18.8	16.1	19.8	0.53
Total days of antibiotics	48.0	37.6	52.7	0.13
Days of IV Antibiotics	41.3	28.8	47.0	0.06

Pathogens and joints involved

Overall, 56% of patients had *S. aureus* isolated from cultures of joint fluid, joint tissue, or blood. Of these, 32% were infected with MRSA. After *Staphylococcus*, *Streptococcus* was the next most common isolated pathogen at 11% of the overall sample. Gram-negative organisms were isolated in only 8% of patients. No organism

was isolated in 6 patients (10%) who had recently been treated with antibiotics at the time of diagnosis. There was no significant difference in the prevalence of organisms isolated between patients managed medically versus surgically.

Table 2. Type of organism isolated; overall and by type of management

Organism	Total (n = 62)	Medical (n = 19)	Surgical (n = 43)	P-value
S. aureus	35 (56%)	9 (47%)	26 (60%)	0.41
MSSA	24 (39%)	5 (26%)	19 (44%)	0.26
MRSA	11 (18%)	4 (21%)	7 (16%)	0.72
Coagulase-neg Staph	2 (3%)	1 (5%)	1 (2%)	1.0
Streptococcus	7 (11%)	2 (11%)	5 (12%)	1.0
Other Gram-positive	5 (8%)	3 (16%)	2 (5%)	0.31
Gram-negative	5 (8%)	2 (11%)	3 (7%)	0.98
No organism isolated	6 (10%)	2 (11%)	4 (9%)	1.0

In terms of joint location, knees were most commonly infected, accounting for 45% of the study sample. The shoulder was next most common at 23%, representing 11% of medically-managed patients and 28% of surgically-managed ones. There were two total hip infections, representing only 3% of the overall sample. There were four wrist infections, all of which were treated medically, and four infections of the small joints of the hands and feet which were all treated surgically. The only significant difference between the two treatment groups was observed in wrist infections, which were significantly over-represented in the medical group. As for involvement of multiple joints, 16% of medically-managed patients presented with polyarthrititis, similar to the rate of 14% among surgically-managed patients.

Table 3. Location of infected joint; overall and by type of management

Joint	Total (n = 62)	Medical (n = 19)	Surgical (n = 43)	P-value
Knee	28 (45%)	8 (42%)	20 (47%)	0.79
Shoulder	14 (23%)	2 (11%)	12 (28%)	0.19
Ankle	5 (8%)	1 (5%)	4 (9%)	1.0
Small Joints	4 (6%)	-	4 (9%)	0.30
Wrist	4 (6%)	4 (21%)	-	0.01
Elbow	4 (6%)	3 (16%)	1 (2%)	0.08
Hip	2 (3%)	1 (5%)	1 (2%)	1.0
Sternoclavicular	1 (2%)	-	1 (2%)	1.0

Presentation and diagnosis

Based on chart review from their initial presentation, all 62 patients with septic arthritis reported experiencing pain in the affected joint. 94% endorsed having limited range of motion and 90% reported a history of swelling. On exam, 47% were found to have erythema of the affected joint. Only 24% of presents were found to be febrile (>37.0 C) at the time of presentation. In terms of factors potentially precipitating the development of septic arthritis, no contributing factor could be identified in 55% of patients. 18% reported a history of trauma to the joint, 10% reported a penetrating injury, and 6% presented with infection adjacent to the joint in the form of cellulitis or osteomyelitis.

Table 4. Prevalence of factors precipitating septic arthritis

Precipitating Factor	Number of Patients (n = 62)
Adjacent infection	4 (6%)
Penetrating Injury	6 (10%)
Known Bacteremia	7 (11%)
Trauma	11 (18%)
Spontaneous (no factor identified)	34 (55%)

Following Newman's schema for the diagnosis of septic arthritis, 85% of patients were diagnosed based on isolation of an organism from synovial fluid or, as in some of cases managed surgically, from synovial tissue. An additional 5% of patients had an organism cultured from the blood in the presence of symptoms suggestive of septic arthritis. As mentioned above, in 6 patients (10%) no organism was ever isolated, though all of these patients had recently been on antibiotic therapy and had purulent fluid aspirated from the affected joint.

Table 5. Basis for diagnosis of septic arthritis

Source	Number of Patients (n = 62)
Synovial fluid culture	48 (77%)
Synovial tissue culture	5 (8%)
Blood culture	3 (5%)
No organism isolated	5 (10%)

As for lab parameters collected at time of presentation, the overall average synovial white blood cell count (WBC) was 114,427/mm³. The average synovial WBC was slightly higher in the medically-managed group (126,437/mm³ vs. 109,966/mm³), though this difference was not statistically significant ($p=0.55$). Synovial WBC was not determined for 14 of the 62 patients, most commonly due to insufficient fluid collected during aspiration. Of the 48 patients who did have a synovial WBC determined, 15% had a synovial WBC less than 25,000/mm³ and an additional 15% had a synovial WBC between 25,000/mm³ and 50,000/mm³. The average percentage of neutrophils within the synovial WBC was 89.7%, with no significant difference between the two treatment groups. The average serum WBC at presentation was 11.3 (+/- 5.5), also with no significant difference between treatment groups. There was insufficient data for analysis of baseline CRP values. The average baseline ESR among the medically-treated group

was 59.4 (+/29.7), which was significantly lower than the average of 85.6 (+/22.5) among the surgical group ($p < 0.01$).

Table 6. Distribution of synovial WBC

Synovial WBC Range (count per mm ³)	Number of Patients (n = 48)
< 25,000	7 (15%)
25,000 - 49,999	7 (15%)
50,000 - 99,999	11 (23%)
> 100,000	23 (48%)

Treatment outcomes

Overall, 7 of 62 patients died by the end of the 12-month follow-up period (11%), 4 of whom died prior to discharge (6.5%). Only 2 of the deaths, however, were attributable to septic arthritis, corresponding to an overall mortality rate of 3.2% from septic arthritis. The other two deaths that occurred prior to discharge were due to respiratory failure secondary to aspiration pneumonitis and cardiac arrest. Both patients who died from septic arthritis were managed surgically, resulting in a mortality rate of 4.7% for the surgically-managed group as compared to 0% for the medically-managed group. This mortality difference is not, however, statistically significant ($p = 0.57$).

Across the entire sample, 7 patients were excluded from the final 12-month outcome analysis: two who were lost-to-follow-up (one from each treatment group), and five who died from causes unrelated to septic arthritis before the follow-up period was over. Of the remaining 55 patients with outcomes determined, 10 experienced a Poor outcome: 3 in the medical group and 7 in the surgical group. As mentioned above, two of these patients in the surgical group died from complications attributable to septic arthritis. Three experienced significant deterioration in joint function as a result of their infection. Three had recurrent septic arthritis of the same joint within one year, and one failed to

clear the infection within one year. One additional patient had to have their finger amputated as result of the infection.

Table 7. Patient outcomes at 1-year; overall and by type of management

Outcomes	Total (n = 62)	Medical (n = 19)	Surgical (n = 43)	P-value
<i>Outcome Determined</i>	55 (89%)	16 (84%)	39 (91%)	0.67
Full Recovery	45 (73%)	13 (68%)	32 (74%)	0.76
Poor Outcome	10 (16%)	3 (16%)	7 (17%)	1.0
<i>No Outcome Determined</i>	7 (11%)	3 (16%)	4 (9%)	0.67
Died during follow-up period	5 (8%)	2 (11%)	3 (7%)	0.98
Lost-to-follow-up	2 (3%)	1 (5%)	1 (2%)	1.0

When considering only patients with an outcome determined (n=55), 13 of 16 medical patients (81%) and 32 of 39 surgical patients (82%) had achieved full recovery in joint function at one year from their diagnosis of septic arthritis. This small difference in outcome was not statistically significant ($p=1.0$).

Univariate logistic regression showed no significant association between nearly all of the analyzed variables and having a Poor treatment outcome. No predisposing risk factors or elements of the patient's history conferred increased likelihood of failing to achieve a full recovery. Neither the location of the affected joint nor the type of causative organism were associated with greater likelihood of a Poor outcome. Nor were any aspects of treatment, such as type of joint drainage, number of days to the operating room, or duration of antibiotics significant in this analysis. The only factor that did increase odds of a Poor outcome was being Black, which had an associated odds ratio of 9.5 (95% CI 1.3 -65.4).

Table 8. Odds ratios for having a ‘Poor’ Outcome at 1-year

Variable	Odds Ratio	95% Confidence Interval
Surgical management	0.95	0.2 - 4.2
Age > 65	0.70	0.1 - 2.8
Age > 80	1.16	0.2 - 6.5
Race		
White	1	Ref
Black	9.2	1.3 - 65.4
Gender	<i>*no ‘poor’ outcomes among women; unable to do analysis</i>	
Diabetes mellitus	0.70	0.2 – 2.8
History of IVDU	4.4	0.8 – 24.0
History of joint disease	1.4	0.3 – 5.4
On immunosuppressive medications	3.1	0.7 – 13.5
Contributing factor		
Spontaneous	1	Ref
Trauma	2.1	0.4 – 10.8
Bacteremia	0.8	0.1 – 8.2
Penetrating injury	1.2	0.1 – 13.1
Adjacent infection	<i>*no ‘poor’ outcomes; unable to do analysis</i>	
Joint location		
Knee	1	Ref
Hip	3.80	0.2 – 72.0
Shoulder	0.69	0.1 - 4.2
Small Joints	1.90	0.1 - 25.5
Wrist	1.27	0.1 – 14.9
<i>*No ‘poor’ outcomes among ankle, elbow, or sternoclavicular joint infections</i>	-	-
Organism		
MSSA	1	Ref

MRSA	0.67	0.1 – 4.1
Serum WBC	1.00	0.9 – 1.1
Serum ESR	1.00	0.97 - 1.03
Days to operating room	1.05	0.95 – 1.14
Total days of antibiotics	1.00	0.98 – 1.02
Days of IV antibiotics	1.00	0.98 – 1.02

In terms of discharge outcomes, 3 of 62 patients died prior to discharge and one was referred to home hospice. Of the remaining 58 patients, 67% of medically-managed patients were sent to a short-term rehabilitation facility or sent home with home physical therapy services, as compared to 70% of surgically-managed patients requiring short-term rehab or home physical therapy services ($p=1.0$).

V. Discussion

Prior to the discovery of modern antibiotics and their adoption in treating septic arthritis, practitioners had little choice but to surgically drain purulent joints and hope for the best. In current practice, even with administration of highly effective intravenous antibiotic therapy, joint drainage remains an essential part of managing the infected joint by helping to mitigate the destructive mechanisms of bacterial virulence, host immune response, and tissue ischemia secondary to elevated intra-articular pressures. Although rheumatologists and orthopedists have been draining infected joints surgically and via closed-needle aspiration alongside antibiotic therapy for decades now, there is strikingly little published data regarding which approach to joint drainage yields the best outcomes. Our retrospective study of 62 cases of septic arthritis at the West Haven VA Medical

Center has tried to help fill that gap by comparing treatment outcomes for patients managed medically with antibiotics and close-needle aspiration against those managed surgically with antibiotics and some form of surgical drainage.

Before discussing the outcomes observed, we should first comment briefly upon the general presentation of septic arthritis among our unique study population at the VA which was older, more predominantly male, and had a greater burden of chronic disease (as measured by the percentage of patients with diabetes mellitus) than populations from other similar studies. [3, 8, 34] First, the predominance of knee infections among our population (45%) was in line with nearly all other studies of septic arthritis, which have consistently identified the knee as the most commonly affected native joint. [1, 3, 7, 8] The relative frequency of infections in other joints varies from study to study, and our distribution was notable for a higher relative incidence of shoulder infections and lower relative incidence of hip infections. Our findings on the relative frequency of causative organisms was also consistent with broader literature identifying *S. aureus* as the most common infectious agent in native joint septic arthritis, followed by *Streptococcus* species. [36] The prevalence of MRSA within *S. aureus* joint infections (32%) was also comparable to the rate found (41%) in another recent U.S. hospital study. [6]

Our study supports previous findings showing elevated average serum WBC, serum ESR, and synovial WBC among those diagnosed with septic arthritis, although we cannot comment regarding their relative specificity given our study design. It is important to note, however, that, as found in prior studies, the sensitivity of synovial WBC for diagnosing septic arthritis is very poor at lower levels. In our study, 30% of patients diagnosed with septic arthritis would have been missed had a synovial WBC

threshold of 50,000 cell per mm³ been used alone for diagnosis. Our study findings also reinforce the observation from the review by Margaretten et al that the absence of fever should not be considered at all when ruling out septic arthritis, as only 24% of our study population was febrile at the time of presentation.

One notable difference between our study and the three others that have directly compared medical versus surgical management of septic arthritis was our decision to also include cases of septic arthritis without a positive synovial fluid or tissue culture, or so-called ‘culture-negative’ cases. 15% of our sample did not have a positive joint culture, and prior studies have shown that nearly one-quarter of cases of septic arthritis will have a negative synovial fluid culture. [37] Gupta et al in their comparison of cases of culture-positive versus culture-negative septic arthritis found that the two groups had similar demographics, risk factors, and outcomes, suggesting the importance of treating culture-negative cases of septic arthritis no different from culture-positive ones. [27] Given the prevalence of culture-negative septic arthritis and the similar outcomes observed, we see our inclusion of culture-negative cases as a relative strength of our study design by capturing the full spectrum of cases that practitioners must treat.

In terms of treatment outcomes, our overall mortality rate attributable to septic arthritis of 3.2% is just below the low-end of the mortality range of 4-13% for native joint infections documented in prior studies. [1-9] The lower rate may be partly due to differences in attributing the cause of death, as we were particularly diligent in reviewing all records of the 7 total patients who died during the study period in order to determine if their death was related to joint infection. It is possible that prior studies were less strict in their mortality attributions. Of course, the lower mortality rate may also simply represent

normal variance to be expected across studies with such small sample sizes. As for morbidity, our observed rate of ‘Full Recovery’ (82%) was greater than the rates documented in the Ravindran (63%) and Goldenberg (71%) studies. [3, 8] This may be attributable to the fact that our final outcome was determined a full 12-months after diagnosis, while the outcomes for those studies were documented only at the time of discharge and up to 3 months post-discharge, thus giving our study population more time to recover and rehabilitate. We had relatively few patients where an outcome could not be determined, and, as they were proportionally split between the two treatment groups, are unlikely to have significantly affected our results.

In comparing outcomes between the two treatment groups, it is remarkable that medically- and surgically-managed patients achieved ‘Full Recovery’ at near identical rates (81% vs. 82%). While the mortality rate due to septic arthritis was higher among the surgical group (4.7% vs 0%), with only 2 deaths in the entire sample it is hard to attribute this difference to more than chance. Our findings are in slight contrast to the prior studies mentioned which showed better outcomes with medical management, though not at the level of statistical significance. [3, 8, 34] It is possible, as noted by Goldenberg and Ravindran in their papers, that the disproportionate inclusion of hip infections with notably poorer outcomes into their surgical treatment groups skewed their results in favor of the medical groups. Both authors also point out though, that outcomes were still better among their medical groups even when hip infections were excluded.

There are a few potential explanations for the improved outcomes among surgical patients in our study as compared to prior studies. It is interesting to note that in our study 69% of patients were treated surgically, while only 30% and 37% of patients in the

Goldenberg and Ravindran studies underwent surgical joint drainage. It is possible that surgeons within the VA CT medical system are more accustomed to draining septic joints, which may contribute to their realizing better outcomes. It is perhaps more likely that the relatively better outcomes among our surgical patients was due to the longer follow-up period. It is quite possible that some of the surgically-managed patients in the prior studies would have achieved full recovery had they been followed for 12 months rather than for a few weeks or months at most. Given that the healthcare system should generally be more focused on longer-term outcomes, we see our longer follow-up period as a strength of this study contributing to the overall validity of our results.

It is important when comparing the outcomes of the medical and surgical treatment groups in our study to highlight that there were no major differences of statistical significance between the two groups. Our ingoing hypothesis was that surgical management would be reserved for certain types of joint infections—based on either the joint or organism involved—or for patients who were relatively ‘healthier’ and better positioned to tolerate surgery. This appears, however, to not be the case. As shown in Table 1, there were no significant differences in demographics or historical risk factors between medically- and surgically-treated patients. In fact, surgically-treated patients had higher rates of diabetes mellitus and pre-existing joint disease, suggesting that surgery was not systematically reserved for ‘healthier’ patients. As for the impact of the type of joint infected, there does appear to be some preference towards treating shoulders and small joints surgically while generally avoiding surgery in elbow and wrist infections. Only the difference in management of wrist infections, however, achieved statistical significance. The type of organism involved also did not appear to affect

clinical decision-making regarding drainage technique, though this may be less surprising given that the determination to proceed with surgery must often be made before culture results are available. The main point here is that while a majority of patients were treated surgically, there were no measurably divergent variables when comparing the two groups that would have undermined the validity of results through explicit selection bias.

Our study also had a few notable weaknesses that have generally plagued other outcome studies of septic arthritis. First, it is obvious that the strength of our results suffered from the small sample size inherent to studying a diagnosis as uncommon as septic arthritis. Despite reviewing all records over 10 years from a large VA hospital, we were only able to identify 62 cases of native joint septic arthritis. There are very few studies of septic arthritis with sample sizes larger than 100. As a result, it was obviously difficult to achieve statistical significance when comparing outcomes and risk factors between two small treatment groups. It is quite possible that there were significant differences between the two groups that our study was simply not powered to detect.

Perhaps the larger weakness of our study came in its retrospective, non-randomized design. As a retrospective study, we had to rely on the quality of the existing records in documenting often subjective or nuanced variables such as range of motion and pain. Without a standard tool for prospective data collection, we were sometimes unable to collect all of the data we would have liked for each individual case. For example, there was large variation in provider documentation of key aspects of the physical exam. The bigger issue with an observational study with two distinct treatment groups is of course the problem of selection bias. While our groups do not appear strikingly different based on the statistical analysis completed, it is impossible for us to

know what factors affected the decision to pursue medical or surgical management for each case. It is plausible that surgical intervention was used for cases that were deemed to be ‘worst’ or ‘most aggressive’, while one might also argue that the surgical patients had better underlying health based on factors not considered in our analysis. Without prospective randomization, and particularly with a sample size, it is impossible to say that our results were not affected by implicit or explicit selection bias.

To conclude, this study was designed to add to the limited body of evidence regarding the relative superiority of closed-needle aspiration versus surgical drainage in the management of septic arthritis. In that aim we have succeeded, by demonstrating among our sample that medically- and surgically-managed patients achieved full recovery at one year at near identical rates. Our results support prior findings that medical management is, at a minimum, non-inferior to surgical joint drainage in managing septic arthritis. Our study suffered, however, from the same problems of small sample size and selection bias that limited the impact of previous studies. Unfortunately, more than 40 years after Goldenberg’s seminal paper on this topic, his equivocal framing of this issue still rings true: “The place of surgery in the treatment of septic arthritis is debatable.” [3] It is clear that advancing our understanding of this topic—to the point of providing a definitive recommendation in favor of medical or surgical management—will require the design and execution of a randomized control trial. Given the low incidence of septic arthritis, this would require coordination across multiple centers for several years with involvement of the many specialties involved in the care of septic joints. Ideally, this would be powered to enable analysis at the level of the joint, given the differences in management by joint seen in prior studies. In the meantime, a meta-

analysis consolidating the results of all the small retrospective studies to-date would provide a valuable summation of our current understanding and may bolster our ability to derive at least some provisional conclusions regarding the best way forward.

VI. References

1. Cooper, C. and M.I. Cawley, *Bacterial arthritis in an English health district: a 10 year review*. *Ann Rheum Dis*, 1986. **45**(6): p. 458-63.
2. Ferrand, J., et al., *Morbimortality in adult patients with septic arthritis: a three-year hospital-based study*. *BMC Infect Dis*, 2016. **16**: p. 239.
3. Goldenberg, D.L., et al., *Treatment of septic arthritis: comparison of needle aspiration and surgery as initial modes of joint drainage*. *Arthritis Rheum*, 1975. **18**(1): p. 83-90.
4. Gupta, M.N., R.D. Sturrock, and M. Field, *A prospective 2-year study of 75 patients with adult-onset septic arthritis*. *Rheumatology (Oxford)*, 2001. **40**(1): p. 24-30.
5. Kaandorp, C.J., et al., *The outcome of bacterial arthritis: a prospective community-based study*. *Arthritis Rheum*, 1997. **40**(5): p. 884-92.
6. Lim, S.Y., D. Pannikath, and K. Nugent, *A retrospective study of septic arthritis in a tertiary hospital in West Texas with high rates of methicillin-resistant Staphylococcus aureus infection*. *Rheumatol Int*, 2015. **35**(7): p. 1251-6.
7. Morgan, D.S., et al., *An 18 year clinical review of septic arthritis from tropical Australia*. *Epidemiol Infect*, 1996. **117**(3): p. 423-8.
8. Ravindran, V., I. Logan, and B.E. Bourke, *Medical vs surgical treatment for the native joint in septic arthritis: a 6-year, single UK academic centre experience*. *Rheumatology (Oxford)*, 2009. **48**(10): p. 1320-2.
9. Weston, V.C., et al., *Clinical features and outcome of septic arthritis in a single UK Health District 1982-1991*. *Ann Rheum Dis*, 1999. **58**(4): p. 214-9.
10. Geirsson, A.J., S. Statkevicius, and A. Vikingsson, *Septic arthritis in Iceland 1990-2002: increasing incidence due to iatrogenic infections*. *Ann Rheum Dis*, 2008. **67**(5): p. 638-43.
11. Kaandorp, C.J., et al., *Incidence and sources of native and prosthetic joint infection: a community based prospective survey*. *Ann Rheum Dis*, 1997. **56**(8): p. 470-5.
12. Kennedy, N., et al., *Native Joint Septic Arthritis: Epidemiology, Clinical Features, and Microbiological Causes in a New Zealand Population*. *J Rheumatol*, 2015. **42**(12): p. 2392-7.
13. Kaandorp, C.J., et al., *Risk factors for septic arthritis in patients with joint disease. A prospective study*. *Arthritis Rheum*, 1995. **38**(12): p. 1819-25.
14. Mathews, C.J., et al., *Bacterial septic arthritis in adults*. *Lancet*, 2010. **375**(9717): p. 846-55.
15. Coakley, G., et al., *BSR & BHPR, BOA, RCGP and BSAC guidelines for management of the hot swollen joint in adults*. *Rheumatology (Oxford)*, 2006. **45**(8): p. 1039-41.
16. Ross, J.J., *Septic arthritis*. *Infect Dis Clin North Am*, 2005. **19**(4): p. 799-817.
17. Tarkowski, A., et al., *Model systems: modeling human staphylococcal arthritis and sepsis in the mouse*. *Trends Microbiol*, 2001. **9**(7): p. 321-6.
18. Gjerdtsson, I., O.H. Hultgren, and A. Tarkowski, *Interleukin-10 ameliorates the outcome of Staphylococcus aureus arthritis by promoting bacterial clearance*. *Clin Exp Immunol*, 2002. **130**(3): p. 409-14.
19. Hultgren, O., et al., *TNF/lymphotoxin-alpha double-mutant mice resist septic arthritis but display increased mortality in response to Staphylococcus aureus*. *J Immunol*, 1998. **161**(11): p. 5937-42.
20. Hultgren, O., M. Kopf, and A. Tarkowski, *Outcome of Staphylococcus aureus-triggered sepsis and arthritis in IL-4-deficient mice depends on the genetic background of the host*. *Eur J Immunol*, 1999. **29**(8): p. 2400-5.

21. Hultgren, O.H., L. Svensson, and A. Tarkowski, *Critical role of signaling through IL-1 receptor for development of arthritis and sepsis during Staphylococcus aureus infection*. J Immunol, 2002. **168**(10): p. 5207-12.
22. Stevens, C.R., et al., *Hypoxia and inflammatory synovitis: observations and speculation*. Ann Rheum Dis, 1991. **50**(2): p. 124-32.
23. Smith, R.L., T.C. Merchant, and D.J. Schurman, *In vitro cartilage degradation by Escherichia coli and Staphylococcus aureus*. Arthritis Rheum, 1982. **25**(4): p. 441-6.
24. Smith, R.L. and D.J. Schurman, *Comparison of cartilage destruction between infectious and adjuvant arthritis*. J Orthop Res, 1983. **1**(2): p. 136-43.
25. Odio, C.M., et al., *Double blind, randomized, placebo-controlled study of dexamethasone therapy for hematogenous septic arthritis in children*. Pediatr Infect Dis J, 2003. **22**(10): p. 883-8.
26. Horowitz, D.L., et al., *Approach to septic arthritis*. Am Fam Physician, 2011. **84**(6): p. 653-60.
27. Gupta, M.N., R.D. Sturrock, and M. Field, *Prospective comparative study of patients with culture proven and high suspicion of adult onset septic arthritis*. Ann Rheum Dis, 2003. **62**(4): p. 327-31.
28. Newman, J.H., *Review of septic arthritis throughout the antibiotic era*. Ann Rheum Dis, 1976. **35**(3): p. 198-205.
29. Margaretten, M.E., et al., *Does this adult patient have septic arthritis?* JAMA, 2007. **297**(13): p. 1478-88.
30. Carpenter, C.R., et al., *Evidence-based diagnostics: adult septic arthritis*. Acad Emerg Med, 2011. **18**(8): p. 781-96.
31. Borzio, R., et al., *Predictors of Septic Arthritis in the Adult Population*. Orthopedics, 2016. **39**(4): p. e657-63.
32. Dauchy, F.A., et al., *Infectious Diseases Society of America guidelines for the diagnosis and management of prosthetic joint infection: what is the correct duration of antibiotic treatment?* Clin Infect Dis, 2013. **57**(1): p. 160-1.
33. Manadan, A.M. and J.A. Block, *Daily needle aspiration versus surgical lavage for the treatment of bacterial septic arthritis in adults*. Am J Ther, 2004. **11**(5): p. 412-5.
34. Maneiro, J.R., et al., *Predictors of treatment failure and mortality in native septic arthritis*. Clin Rheumatol, 2015. **34**(11): p. 1961-7.
35. Butt, U., et al., *What are we doing about septic arthritis? A survey of UK-based rheumatologists and orthopedic surgeons*. Clin Rheumatol, 2011. **30**(5): p. 707-10.
36. Sharff, K.A., E.P. Richards, and J.M. Townes, *Clinical management of septic arthritis*. Curr Rheumatol Rep, 2013. **15**(6): p. 332.
37. Krey, P.R. and D.A. Bailen, *Synovial fluid leukocytosis. A study of extremes*. Am J Med, 1979. **67**(3): p. 436-42.