



Evaluation of postoperative fever after surgical correction of neuromuscular scoliosis: implication on management

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Abstract

Background Scoliosis is a common deformity in patients with neuromuscular disorders which usually necessitates surgical correction. Patients with neuromuscular scoliosis are characterized by increased incidence of associated medical co-morbidities and higher postoperative complication rate; therefore, these patients are often managed with a wide multidisciplinary care team. Postoperative fever is a frequent complication after surgery which is often routinely investigated using different workup tests to rule out infection. These tests lack clear evidence on how they impact the patient care and are associated with increased cost and burden on the health system.

Objective The objective of our study was to evaluate the incidence of postoperative fever after surgical correction of neuromuscular scoliosis and evaluate the clinical usefulness of fever diagnostic workup.

Methods Demographic and clinical data on patients who underwent neuromuscular scoliosis corrective surgery between March 1, 2014 and February 28, 2017 were reviewed at a single institution. The occurrence of postoperative fever (defined by body temperature $\geq 38^{\circ}\text{C}$ during the 1st week after surgery) was characterized by maximum temperature (T_{max}), postoperative day of occurrence (POD), and frequency as described by either single or multiple temperature spikes. The diagnostic tests performed for the assessment of postoperative fever were reviewed. The cost per health effect was calculated by dividing the total costs of performed fever workup tests by the number of tests that resulted in change of the patient care.

Results Seventy-six patients (47 females and 29 males) were identified. Cerebral palsy was the most common aetiology in 40 patients (52.6%). The mean age at surgery was 13.5 years (range 3–18 years). The operative time was 490.34 ± 127.21 min. The intraoperative blood loss was 912.3 ± 627.8 cc. The hospital stay was 9.79 ± 5.3 days and the intensive care unit (ICU) stay was 3.26 ± 3.7 days. Wound drains were used in 71 patients for a period of 3.6 ± 2.3 days. Urinary catheters were used for a period of 3.6 ± 1.8 days. Forty-nine patients (64.5%) developed postoperative fever with a temperature of $38.7^{\circ} \pm 0.45^{\circ}$ (range 38.10° – 39.9°). The most frequent POD for occurrence of fever was the 2nd day in 22 patients (44.9%). The frequency of fever was in the form of multiple temperature spikes in 32 patients (65.3%) or in the form of a single spike in 17 patients (34.7%). There were a total of 20 positive tests out of 132 performed fever workup tests (15.2%). These included nine positive urine analysis ($n = 32$), five positive urine cultures ($n = 28$), one positive blood culture ($n = 23$), and two positive chest X-ray ($n = 24$). The occurrence of postoperative fever was statistically correlated with the operative time and increased hospital stay and ICU days. The most common identified cause of infection was urinary tract infection in 11 patients followed by respiratory tract infection in four patients and wound infection in one patient. The calculated cost per health effect was \$3763.

Conclusion Sixty-four percent of patients who underwent surgical correction of neuromuscular scoliosis developed postoperative fever. Postoperative fever was sign of infection in 32.7% of patients and urinary tract infection was the most frequent finding. Only 15.2% of fever diagnostic workup tests were positive. Diagnostic urine tests account for 70% of the positive diagnostic workup. The routine use of blood cultures for the assessment of postoperative fever in such population should be avoided due to the low rate of positive tests and the associated high cost.

Keywords Deformity · Neuromuscular disorders · Postoperative complications · Hyperpyrexia

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Introduction

The incidence of scoliosis in children with neuromuscular disorders has been reported to be as high as 90% [1]. Neuromuscular scoliosis is characterized by complex progressive spinal deformity that continues to increase even after skeletal maturity and it is usually refractory to conservative orthotic treatment. Such progressive spinal deformity is usually associated with pelvic obliquity which adversely affects the sitting balance and may result in pulmonary restriction [2]. Therefore, surgery is often recommended to correct the functional disability, improve pulmonary function, and enhance the quality of life in these patients. However, surgical treatment of neuromuscular scoliosis has been associated with high complication rates and prolonged hospital stay [3]. The reported complications include neurological compromise, severe blood loss, pulmonary complications, infection, and pseudoarthrosis with implant failure [4]. Because patients with neuromuscular scoliosis often have greater medical co-morbidities as compared to their idiopathic counterparts, they are often managed postoperatively by the orthopaedic service along with a broad multidisciplinary team including pediatric medicine, pulmonary, and critical care medicine. Therefore, it is important to have some agreement among the team members with regard to the expectations of postoperative course.

Postoperative fever is described as an increased body temperature greater than 38 °C and considered a common event that might complicate the postoperative course [5]. The occurrence of postoperative fever is usually anticipated as a normal inflammatory response to the tissue surgical trauma resulting from release of cytokines such as interleukins 1 and 6, tumor necrosis factor- α , and interferon- γ which affect the thermoregulatory mechanism at the hypothalamus [6]. Therefore, postoperative fever is usually considered a benign and self-limiting condition particularly in the first 48 h [5]. However, postoperative fever may also be a manifestation of a complication such as urinary tract infection, pneumonia, and wound infection.

Variable approaches exist with regard to the management of postoperative fever among the different members of the multidisciplinary team caring for these patients. The medical service providers tend to follow the rationale of routinely performing extensive laboratory and radiological diagnostic workup tests for the assessment of postoperative fever to rule out infection. However, it seems that in postoperative patients, such workup often does not result in a change in patient care. Furthermore, these tests increase the care cost and the burden on the care team and patient's family [7]. Surgeons, on the other hand, tend to not routinely order such tests and focus mainly on the

surgical site infection as being the major source of concern in the postoperative period. Since these neuromuscular patients are often co-managed after surgery with a broad multidisciplinary team, it is important to have a more uniform and perhaps evidence-based approach for the management of postoperative fever.

To the best of our knowledge, the literature is limited with regard to the frequency, underlying aetiology, and characteristics of postoperative fever after surgical correction of neuromuscular scoliosis. There is also lack of evidence-based clinical practice guidelines for the use of the variable diagnostic workup tests in the setting of postoperative fever. The objective of our study was to evaluate the incidence and characteristics of postoperative fever after surgical correction of neuromuscular scoliosis and evaluate the clinical usefulness of the fever diagnostic workup tests.

Patients and methods

After approval by the institutional review board, retrospective review of patient medical records was performed to identify patients who underwent surgical correction of neuromuscular scoliosis at a single institution over a 36-month period from March 1, 2014 to February 28, 2017. Patients with preoperative infection, previous surgery, pre-existing immunodeficiency, and patients who were regularly receiving antibiotics before the surgery were excluded. Demographic and perioperative data including sex, age, associated neuromuscular disorder, surgical procedure, amount of blood loss, operative time, hospital and intensive care unit stay, and inpatient complications were retrieved.

The patients' charts were inspected for the occurrence of postoperative fever which was defined by an increased body temperature greater than 38 °C in the first 7 days after the surgery. Postoperative fever was further described by recording the maximum registered temperature (T-max), postoperative day of occurrence (POD), and the characteristic fever pattern as defined by either being a single isolated fever spike or multiple fever spikes.

Diagnostic tests performed to assess postoperative fever were collected including, but not limited to: urinalysis and urine culture, blood culture, and chest radiograph. A diagnostic test was considered positive depending on the presence of specific parameters such as: (1) urine analysis was considered positive upon detection of greater than five white blood cells and/or leukocyte esterase or nitrite; (2) urine culture was defined positive if more than 1000 colony-forming units/ml had been detected; (3) blood culture collected at the time of fever spike was defined positive if the culture had demonstrated noncontaminant bacterial growth; and (4) chest radiograph was defined positive if consolidation representing pneumonia was detected.

In addition to our interest in the characteristics of postoperative fever and the performed diagnostic workup tests, we were also interested in the cost of the diagnostic tests performed for the assessment of postoperative fever and number of positive tests which actually resulted in a change of the patient care. The estimated cost per health effect was determined by dividing the total costs of the performed diagnostic tests by the number of tests that resulted in a change of the treatment plan [8].

Data were presented as mean \pm standard deviation. Statistical analysis of the association between the development of postoperative fever and wound infection was performed using binary logistic regression test. The correlation between the occurrence of postoperative fever and hospital stay, ICU days, intraoperative blood loss, operative time, duration of use of surgical drain (i.e., hemovac drain), and duration of urinary catheter use was studied using Spearman's rho test. The likelihood of having a positive diagnostic workup test in relation with T-max, POD, and fever frequency was studied using multinomial logistic regression test with confidence interval was set at 95%. The correlation between the performance of a diagnostic workup and the length of hospital stay was studied using Spearman's rho test. The association between the development of wound infection and both the operative time and the duration of use of surgical drain was studied using Spearman's rho test. Any difference was considered statistically significant if *P* value was less than 0.05.

Results

Seventy-six patients were included in our study. The mean age at the time of surgery was 13.5 years (range 3–18 years). There were 47 female and 29 male patients. All patients had neuromuscular scoliosis with different associated neuromuscular conditions (Table 1) and cerebral palsy was the most common aetiology (52.6%). All patients underwent surgical treatment of scoliosis including posterior spinal fusion and instrumentation from the upper thoracic vertebrae down to the pelvis in 71 patients (93.4%) or placement of vertical expandable prosthetic titanium rib (VEPTR) from T2 to the pelvis in 5 patients (6.6%).

The operative time was 490.34 ± 127.21 min (range 299–924 min). The intraoperative blood loss was 912.3 ± 627.8 cc (range 40–3000 cc). The hospital stay was 9.79 ± 5.3 days (range 4–33 days) and the intensive care unit (ICU) stay was 3.26 ± 3.7 days (range 0–20 days). Inpatient complications were reported in 31 patients (40.8%) which included respiratory failure in 18 patients, hypovolemic shock in 6 patients, seizures in 3 patients, paralytic ileus in one patient, disseminated intravascular coagulopathy in one patient, syndrome of inappropriate secretion of antidiuretic hormone in one patient, and frontal bone fracture with cerebrospinal fluid leakage from the halo pin site in one patient. Wound drains were used in 71 patients for a period of 3.6 ± 2.3 days (range 2–15 days). Urinary catheters were used for a period of 3.6 ± 1.8 days (range 2–10 days).

Table 1 Associated neuromuscular conditions in our study population

Diagnosis	Number of patients	Percentage (%)
Cerebral palsy	40	52.6
Rett syndrome	8	10.5
Duchenne muscular dystrophy	6	7.9
Chromosome abnormality (1q21.1 duplication, 1p36 deletion, trisomy 8, trisomy 18, partial monosomy 11q and partial trisomy 17q)	5	6.6
Chiari malformation	3	3.9
Congenital myopathy	3	3.9
Myelomeningocele	2	2.6
Adrenoleukodystrophy	1	1.3
Ullrich muscular dystrophy	1	1.3
Facioscapulohumeral muscular dystrophy	1	1.3
Congenital neuropathy	1	1.3
Transverse myelitis	1	1.3
Posttraumatic paraplegia	1	1.3
Neurofibromatosis	1	1.3
Syringomyelia	1	1.3
Arthrogryposis	1	1.3
Joubert syndrome	1	1.3

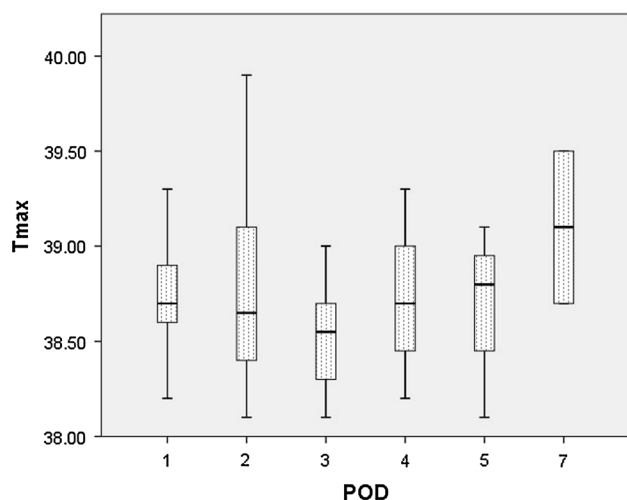


Fig. 1 Characteristics of postoperative fever with regard to the maximum registered temperature (T-max) and postoperative day of occurrence (POD)

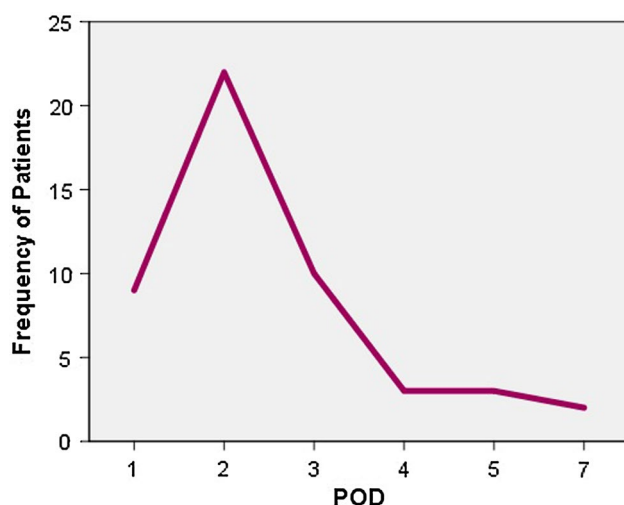


Fig. 2 Distribution of postoperative fever in relation with the postoperative day of occurrence (POD)

Forty-nine patients (64.5%) developed postoperative fever with T-max of $38.7^\circ \pm 0.45^\circ$ (range 38.10° – 39.9°) (Fig. 1). The most frequent POD for occurrence of fever was the 2nd day in 22 patients (44.9%) (Fig. 2). The frequency of fever was in the form of multiple temperature spikes in 32 patients (65.3%) or in the form of single spike in 17 patients (34.7%).

132 diagnostic tests were performed for the evaluation of postoperative fever in 39 patients (79.6%). Of 132 tests (Table 2), there were a total of 20 positive tests (15.2% of total tests ordered; $n = 20/132$). Tests resulted in a change of the patient care in 16 patients by changing the patient drug treatment. The total cost of the fever workup diagnostic tests was \$60,208. The cost per health effect was calculated

(\$60,208/16) to be \$3763. The specific cost of blood cultures was calculated and was found to be \$18,165 which accounted for 30.2% of the total costs of the performed diagnostic workup tests.

Abnormal chest X-ray findings were reported in 18 patients including atelectasis in 15 patients, pleural effusion in 5 patients, pneumothorax in 2 patients, and bronchiectasis in one patient. Late wound infection was detected after hospital discharge in eight patients (11.9%) by clinical examination demonstrating wound dehiscence and drainage then confirmed with surgical wound cultures. Five of these patients with wound infection had postoperative fever with a mean T-max of 38.7° (range 38.2° – 39.4°), whereas the other three patients did not develop any postoperative fever. The association between the development of postoperative fever and wound infection was tested using binary logistic regression and it was found to be statistically insignificant ($P = 0.9$). It was also found that the development of wound infection was not statistically associated with either the operative time ($P = 0.3$) or the duration of use of surgical drain ($P = 0.5$) using Spearman's rho test.

The correlation between the occurrence of postoperative fever and the intraoperative blood loss was studied using Spearman's rho test and it was found to be statistically insignificant ($P = 0.2$). However, the occurrence of postoperative fever was statistically correlated with the operative time ($P = 0.02$) using Spearman's rho test (Fig. 3). The occurrence of postoperative fever was statistically associated with increased hospital stay and ICU days using Spearman's rho test with P value equals 0.0001 and 0.001, respectively (Table 3). Furthermore, patients who underwent fever diagnostic workup had a statistically significant prolonged hospital stay in comparison with who did not have such workup using Spearman's rho test ($P = 0.03$). Interestingly, no statistically significant difference was detected between patients with positive diagnostic workup and those with negative workup with regard to the length of hospital stay using Mann–Whitney test ($P = 0.5$).

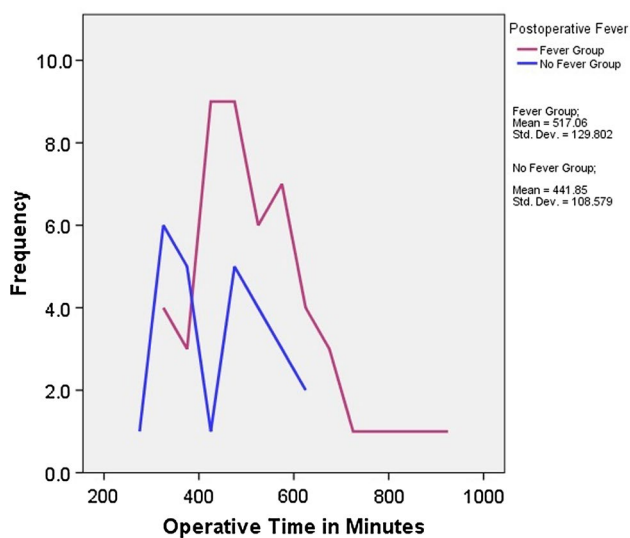
Neither the duration of use of surgical wound drain nor the duration of urinary catheter use was statistically correlated with the occurrence of postoperative fever using Spearman's rho test with P value equals 0.18 and 0.15, respectively. No statistically significant association was detected using multinomial logistic regression between the positive diagnostic workup and the fever characteristics: T-max (Fig. 4), POD (Fig. 5), and fever frequency with confidence interval set at 95% (P value equals 0.4, 0.9, and 0.5, respectively).

Discussion

The reported complication rate after surgical treatment of neuromuscular scoliosis ranges from 44 to 62% [9]. Although the development of postoperative fever seems to

Table 2 Diagnostic tests done for the assessment of postoperative fever in our study group

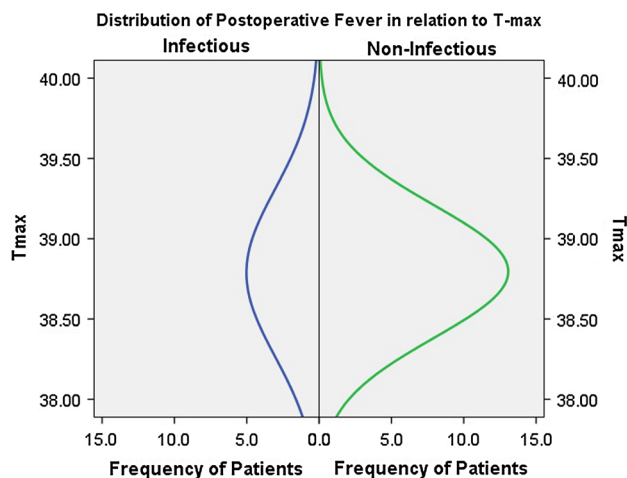
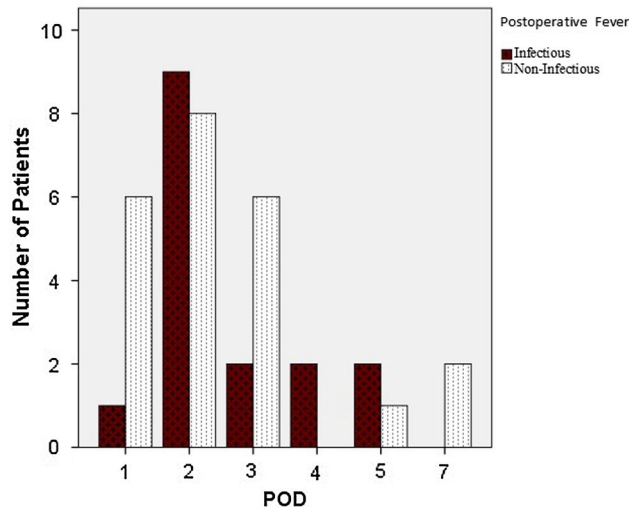
	Total number of tests	Number of positive tests	Comments
Urine analysis	32	9	
Urine culture	28	5	Positive for <i>Escherichia coli</i> (<i>E. coli</i>) in 3 patients Positive for both <i>E. coli</i> and <i>proteus mirabilis</i> in 2 patients
Blood culture	23	1	Positive for <i>serratia marcescens</i> and coagulase negative staphylococcus
Chest X-ray	24	2	
Wound culture	2	1	Positive for <i>pseudomonas aeruginosa</i> , <i>morganella morganii</i> , and <i>E. coli</i>
Bronchoalveolar culture	5	2	Positive for <i>haemophilus influenza</i> (beta lactamase negative) and <i>staphylococcus aureus</i> in one patient Positive for <i>pseudomonas aeruginosa</i> in one patient
Nasal wash respiratory virus panel PCR for influenza A&B and respiratory syncytial virus	4	0	
Adenovirus PCR	3	0	
Human metapneumovirus PCR	2	0	
Parainfluenza virus type 1,2,3 PCR	2	0	
Sputum culture	1	0	
Clostridium difficile toxin PCR	1	0	
Pleural fluid culture	1	0	
Cerebrospinal fluid culture with gram stain	1	0	
Quantiferon (R) tuberculosis	1	0	
Tracheal aspirate culture	1	0	
Histoplasma antigen serum	1	0	
Total	132	20	

**Fig. 3** Diagrammatic presentation of the difference between the patients who developed postoperative fever (fever group) and those who did not develop postoperative fever (no fever group) in relation with the operative time

be a common event after such complex surgery, the literature is limited with regard to the incidence or significance of postoperative fever after surgical correction of neuromuscular scoliosis. The reported incidence of postoperative fever after spine surgery in normal population ranged from 14% [10] to 19.9% [11]. In our study, the incidence of postoperative fever after surgical treatment of neuromuscular scoliosis was 64.5%. The greater prevalence of postoperative fever among our population may be related to wide exposure and greater levels of spinal instrumentation needed to correct such complex neuromuscular deformity with subsequent increased tissue damage as result of surgical trauma. A number of risk factors related to the development of postoperative fever after spine surgery had been previously identified in the literature including posterior approach with anterior corpectomy and graft reconstruction, long operative time, and increased surgical levels [11]. The occurrence of postoperative fever was also more prevalent in other surgical procedures with large surgical tissue injury such as trauma and tumor spinal surgery as compared to degenerative spinal surgery [11]. Our results concerning surgical factors that may predict the development of postoperative fever are consistent with these previous studies as our entire population was neuromuscular scoliosis which commonly included

Table 3 Length of hospital and intensive care unit stay in patients with and without postoperative fever

		Minimum	Maximum	Mean	SD
Hospital stay (days)	Patients with postoperative fever group	5	33	11.28	5.99
	Patients without postoperative fever group	4	13	7.07	1.89
ICU stay (Days)	Patients with postoperative fever group	0	20	4.14	4.17
	Patients without postoperative fever group	0	5	1.66	1.75

**Fig. 4** Distribution of infectious and non-infectious postoperative fever in relation with the maximum registered temperature (T max)**Fig. 5** Distribution of infectious and non-infectious postoperative fever in relation with postoperative day of occurrence (POD)

large surgical levels from the upper thoracic spine down to the pelvis. In addition, we found that the occurrence of postoperative fever was statistically correlated with the duration of surgery. Neither the duration of use of surgical drain, the duration of urinary catheter, nor intraoperative blood loss were predictive of postoperative fever.

The timing of the occurrence of postoperative fever has been used traditionally to predict the presence of underlying infection. Early postoperative fever developed in the first 72 h after surgery is believed to be of non-infectious aetiology, while fever occurring after the third postoperative is thought to be more concerning for underlying surgical site infection [5, 12]. This approach may lead the care team to start an empirical antibiotic for presumptive infection if fever developed after the third postoperative day. However, other previous reports in the orthopaedic literature have shown that non-infectious fever might still develop after the third postoperative day [11] and it is also difficult to differentiate between a normal postoperative systemic inflammatory reaction and infection even up to the seventh postoperative day [13]. However, these studies were performed in non-neuromuscular patients and did not include patients who underwent spinal deformity surgery. This leaves a gap in the knowledge base for these specific types of patients and provides equipoise for the current study. In our study, postoperative fever that developed in the 1st week after surgery was associated with underlying source of infection in 16 patients (32.6%), while the previous reports in the literature showed an identified source of infection for postoperative fever after spine surgery ranging from 7.7% [11] to 20% [10]. The most frequent source of infection among our study population was urinary tract infection in 11 patients (22.4%) followed by respiratory tract infection in 4 patients (8.2%) and acute wound infection in one patient (2%). There were no cases of sepsis or bacteremia. We did not find any statistically significant difference between patients with non-infectious postoperative fever and those with infectious fever in regard to the postoperative day of occurrence. Fever of non-infectious origin was noted to develop even after the third postoperative fever, while infectious postoperative fever was surprisingly detected in the first 2 days after surgery. Therefore, our findings did not support the belief that early postoperative fever is usually benign, while late postoperative fever should be considered a sign of infection. We believe that clinical assessment should be the main factor to decide if further assessment is needed or not regardless of the timing of postoperative fever.

The literature is also mixed with regard to the relationship between the number of fever spikes or the degree of fever and the likelihood of infection. Some have suggested that postoperative temperature greater than 39° and multiple

fever spikes are more likely to have an infectious origin [14]. Others have demonstrated that T-max greater than 39° and multiple spikes should not be used as a predictor of infectious postoperative fever [10]. Our study agreed with the later in that we did not detect any association between the recorded T-max or number of fever spikes and the underlying aetiology of postoperative fever.

Higher rates of wound infection have been reported after surgical correction of neuromuscular scoliosis in comparison with the idiopathic counterpart ranging from 10.91% [4] to 24.3% [3]. Non-ambulation, cognitive impairment, malnourishment, large Cobb angles, increased blood loss, prolonged hospitalization, respiratory problems, and allograft use have been identified as a potential risk factors for wound infection [3, 4]. In our study population, late wound infection, which developed after discharge from the hospital, was identified in eight patients (11.9%); however, only five of the eight patients had postoperative fever. Regression analysis showed that the occurrence of wound infection was not statistically correlated with development of postoperative fever.

In our population, there were a total of 20 positive fever diagnostic workup tests out of 132 tests (15.2%). Therefore, 84.8% of the ordered workup tests were negative and did not result in a change in the patient care. This resulted in a calculated cost per health effect of \$3763. Moreover, patients who underwent the diagnostic workup for postoperative fever had a prolonged hospital stay in comparison with those who did not undergo this workup and interestingly, the prolonged hospital stay was not statistically different between the patients with underlying infectious source and those with non-infectious fever, and therefore, the increased hospital stay was related to the diagnostic workup performance rather than to underlying infectious source in patients with postoperative fever. This adds additional indirect cost of the routinely performed diagnostic workup that is difficult to be estimated and would further increase the economic burden on the health system without any impact in the patient care. This begs the question of whether it is beneficial and cost effective to order routine diagnostic tests in response to postoperative fever in such patients. There is no evidence-based rationale for using the different fever diagnostic workup tests to identify a potential infectious cause of fever and previous reports in the literature have also questioned their value. Freischlag and Busuttill [7] found in a retrospective review of 464 patients who underwent abdominal surgeries that routine ordering of fever workup tests is not cost effective, because they did not affect the outcome of the majority of patients and they would instead be a source of increased cost which was calculated to be \$19,738. Similarly, de la Torre et al. [15] showed that in 676 patients who underwent laparotomy, only 69 fever workup tests were positive

out of 520 performed tests (13.2%) and the total cost of the performed fever workup was \$48,432. Beside the surgical and gynecological studies, similar findings have been demonstrated in the orthopaedic literature. Ward et al. [14] showed that in 1100 patients who underwent total hip and knee arthroplasty, only 35 diagnostic workup tests out of 236 performed tests (14.8%) were positive and the total cost of the performed workup was \$73,878. In addition, they estimated the cost per change in patient management to be \$8209. All these reports had agreed that the diagnostic workup used for the assessment of postoperative fever has low clinical yield and limited impact on the patient care in addition to the increased total cost.

One specific test that is performed regularly in the setting of routine workup of postoperative fever is blood culture. Blood culture represents an integral part of the diagnostic workup for postoperative fever and it is considered the ideal test for the detection of bacteremia. However, its clinical yield in the postoperative setting is limited [16, 17]. Bindelglass and Pellegrino [16] had shown that only two blood cultures were positive among all blood cultures that were drawn from 100 febrile patients after total joint arthroplasty and interestingly, they found that neither of the two patients with positive blood culture had developed any signs of infection after 6-month follow-up. They also estimated an annual expenditure of \$8300 because of the routine use of blood culture in the setting of postoperative fever in addition to the indirect uncalculated cost of delayed hospital discharge. Similarly, Fanning et al. [17] had found that blood cultures which were obtained from 77 febrile patients after gynecological surgery were all negative. In our population, all blood cultures drawn from 23 febrile patients were negative and only one was positive. These findings are consistent with those in the literature. Therefore, we agree that the use of blood culture as a part of the postoperative fever workup in such population is not helpful for the detection of bacteremia and it is not recommended.

Conclusion

Sixty-four percent of patients developed postoperative fever after surgical correction of neuromuscular scoliosis. Postoperative fever was a sign of infection in 32.7% of patients and urinary tract infection was the most frequent finding (22.4%). Only 15.2% of diagnostic tests for workup of fever were positive in our population. Diagnostic urine tests account for 70% of the positive diagnostic workup. The routine use of blood cultures in the evaluation of postoperative fever in neuromuscular scoliosis surgery patients should be avoided due to the low rate of positive tests and the associated high cost.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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