The Significance of Fever Following Cholecystectomy

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Background. Family physicians are often called upon to evaluate a patient with fever that occurs following a surgical procedure. While fever is a common postoperative event, it can have various prognostic implications.
Methods. The incidence and significance of postoperative fever was studied in a relatively healthy group of patients who had undergone cholecystectomy. Risk factors for infection as well as the incidence of infection were recorded.
Results. The overall rate of infection was 5.7%. In comparing the epidemiologic, operative, and laboratory data of patients with fever with those without fever, the only statistical difference noted was a greater incidence of fever in men ($P < .01$). As the sole diagnostic criterion for determining the presence of infection, fever was of little value. Other clinical findings proved to be more discriminating markers for infection.
Conclusions. Postoperative fever in a cholecystectomy patient by itself is not suggestive of infection. Clinical findings remain the primary diagnostic guide to distinguishing those patients who require further evaluation.
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Postoperative fever is not an uncommon clinical event; however, its usefulness in differentiating between serious infection and other less threatening conditions in the postoperative surgical patient is unclear. Previous studies in this area have pointed to the wide variability in both the incidence of postoperative fever and its reliability as an indicator of infection.[1,2] While this may in part be explained by the varied criteria used to define postoperative fever, many studies have incorporated a variety of surgical cases that may not be directly comparable to one another.[1–8] The goal of our investigation was to narrow the study of postsurgical fever to a group of patients who had undergone a common single abdominal procedure, namely, cholecystectomy.

Methods and Materials

Consecutive case records of patients who underwent cholecystectomy between January 1983 and January 1988 at University Medical Center (Tucson, Ariz) were reviewed. The following data were collected: age, sex, co-morbid conditions (diabetes mellitus, obesity,[9] underlying pulmonary disease), American Society of Anesthesiologists risk assessment,[10] preoperative laboratory data (complete blood count with differential, blood urea nitrogen, aspartate aminotransaminase, alkaline phosphatase, total bilirubin, amylase), presentation at time of surgery (acute or elective), perioperative use of antibiotics, length of surgery, common bile duct exploration, and estimated intraoperative blood loss. Patients who had infection or fever before surgery were excluded from the study.

The maximum oral temperature postoperatively and the time of its occurrence were noted for all patients. Fever was defined as an oral temperature of ≥38.4°C (101.1°F) or ≥38.0°C (100.4°F) on two consecutive measurements taken at least 4 hours apart. This definition of fever was well within the range of previous investigations[1–5] and is the one commonly used at our institution. Rectal temperatures were corrected (−0.56°C [−1°F]) to conform with oral measurements.[11,12]

The postoperative course of all patients was reviewed for evidence of significant clinical symptoms or signs of infection. Postoperative laboratory data recorded for all patients were those noted closest to the time of either fever onset or maximum temperature. The presence of infection was identified when symptoms, physical findings, laboratory studies, culture results, and radiographic evidence that had been documented fulfilled guidelines for infection established by the Centers for

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Table 1. Clinical Findings, Diagnostic Tests Ordered, and Source of Infection in Patients with Documented Postoperative Infections (n = 10)

Age (y)	Sex	Fever	Clinical Findings	Diagnostic Test	Findings
77	F	Yes	Chills, emesis, right upper quadrant pain	Blood culture Bile culture	No growth *Escherichia coli*, *Enterobacter cloacae*
72	M	Yes	Decreased breath sounds, right-sided crepitations	Sputum culture Chest radiographs	*Streptococcus viridans* *Hemophilus influenzae*, right lower lung infiltrate
52	M	No	Erythema, tenderness	Wound culture	*Enterobacter cloacae*
45	M	No	Right upper quadrant pain, chills	Bile culture	*Escherichia coli* *Calcoacetis freundii* *Pseudomonas aeruginosa* *Acinetobacter lwoffii*
64	F	No	Dysuria, polyuria	Urine culture	*Escherichia coli*
44	F	No	Dysuria	Urine culture	*Escherichia coli*
33	F	No	Dysuria	Urine culture	*Escherichia coli*
32	F	No	Dysuria	Urine culture	*Escherichia coli*
22	F	No	Dysuria	Urine culture	*Escherichia coli*
22	F	No	Dysuria	Urine culture	*Streptococcus pyogenes*, group D

**Fever was defined as a temperature ≥38.4°C (101.1°F), or ≥38.0°C (100.4°F) on two consecutive measurements taken 4 hours apart.*

Disease Control.[13] Urinary tract infection was defined as greater than 100,000 colony-forming units in the presence of clinical symptoms such as dysuria. Biliary tract infection was defined by right upper quadrant pain, elevated white blood count or fever, and growth of bacteria in a bile specimen. Wound infection was defined as erythema surrounding the wound, tenderness, and a wound culture positive for bacteria. Pneumonia was defined by a productive cough, findings on auscultation, a positive sputum culture, and evidence of infiltration on a chest radiograph.

Statistical testing was performed using chi-square analysis and Fisher's exact test. A probability of less than 1 in 20 ($\alpha = .05$) was considered significant.

Results

Of the 195 patients whose charts were reviewed, 19 patients were found to have had evidence of infection or fever before surgery and were removed from further evaluation. The remaining 176 cases included 144 women and 32 men with a mean age of 44 years. Twenty-eight (16%) patients were found to meet the criteria defining postoperative fever. In 23 of the 28 cases, no additional clinical evidence of infection had been found; therefore, no specific laboratory investigation had been carried out. The remaining 5 patients in this group had various diagnostic tests performed as part of a fever evaluation, but an actual infection was documented in only 2 of these patients (Table 1).

The other 148 patients did not have temperatures high enough to be defined as fever. Eight cases of infection had been identified in these patients based on specific clinical and diagnostic findings (Table 1). The incidence of infection was 7.1% for patients with postoperative fever, 5.4% for those without fever, and 5.7% for the population as a whole. The patient characteristics, clinical findings, and source of infection are listed in Table 1. Of note, six of eight infections seen in afebrile patients were urinary tract infections. All six patients complained of dysuria, prompting diagnostic evaluations. One episode of wound infection occurred in this group. The other infection was in a 45-year-old man who, after a common duct exploration, complained of right upper quadrant pain and chills. A bile culture contained four different species of bacteria as noted in Table 1.

In comparing patients who had postoperative fever (n = 28) with those who did not (n = 148), the only variable of significance was with respect to sex, namely an

Table 2. A Comparison of 176 Cholecystectomy Patients With and Without Postoperative Fever

Variable	Patients With Fever (n = 28)	Patients Without Fever (n = 148)
Epidemiologic characteristics		
Age (y)	48	43
Sex (% female)*	61	85
ASA risk assessment ≥3 (%)	14	16
Diabetes (%)	12	11
Obesity (%)	44	48
Pulmonary risk (%)	12	11
Preoperative laboratory values		
White blood count ($\times 10^9$/L)	9.2 (±14)	9.4 (±4.0)
PMN leukocytes (%)	65 (±14)	64 (±10)
Bands (%)	3 (±3)	3 (±2)
Blood urea nitrogen (μmol/L)†	4.20 (±1.95)	4.25 (±1.80)
Aspartate aminotransferase (U/L)	26 (±12)	43 (±28)
Alkaline phosphatase (U/L)	80 (±28)	96 (±45)
Bilirubin (μmol/L)‡	8 (±6)	10 (±6)
Amylase (U/L)	47 (±22)	47 (±23)
Characteristics of operation		
Emergent (%)	68	47
Antibiotic use (%)	93	84
Length of surgery (h)	2.1 (±0.9)	1.8 (±0.8)
Common duct exploration (%)	11	15
Blood loss (mL)	152 (±104)	153 (±86)
Postoperative laboratory values		
White blood count ($\times 10^9$/L)	12.9 (±6.6)	12.4 (±4.5)
PMN leukocytes (%)	70 (±9)	71 (±20)
Bands (%)	8 (±6)	5 (±5)
Blood urea nitrogen (μmol/L)†	2.55 (±1.85)	2.55 (±1.80)
Aspartate aminotransferase (U/L)	56 (±35)	62 (±46)
Alkaline phosphatase (U/L)	90 (±46)	128 (±69)
Bilirubin (μmol/L)‡	16 (±8)	24 (±14)
Postoperative temperature		
Maximum temperature (°C)	38.5 (±0.3)	37.5 (±0.3)
Onset after surgery (h)	30 (±25)	33 (±23)
Duration (h)	12 (±10)	—

$\chi^2 = 10.9$, $P < .01$. All other differences in variables between patients with fever and patients without fever were not significant.
†The preoperative values for blood urea nitrogen (BUN) in conventional units were 11.7 mg/dL (±5.5 mg/dL) for patients with fever and 11.9 (±5.0) for patients without fever. The postoperative values for BUN were 7.2 mg/dL (±5.2 mg/dL) for patients with fever and 7.1 (±5.1) for patients without fever.
‡The preoperative values for bilirubin in conventional units were 0.5 mg/dL (±0.4 mg/dL) for patients with fever and 0.6 mg/dL (±0.4 mg/dL) in patients without fever. The postoperative values for bilirubin were 0.9 mg/dL (±0.5 mg/dL) in patients with fever and 1.4 mg/dL (±0.8 mg/dL) in patients without fever.
ASA denotes American Society of Anesthesiologists; PMN, polymorphonuclear.

increased incidence of postoperative fever in men as compared with women ($P < .01$). No significant difference was noted with regard to the remaining preoperative laboratory values, operative characteristics, or postoperative laboratory values (Table 2).

As the sole diagnostic test for postoperative infection, fever was of little value. Clinical features showed greater discriminatory power as markers for documented infection. In patients with postoperative fever, the imposition of clinical features as a second diagnostic characteristic increased the accuracy of diagnosis.

Discussion

The incidence of infection in the patient with postoperative fever varies widely.[1–5] Our study showed that fever in an otherwise uncompromised cholecystectomy patient is often inconsequential. Yet infection does occur, as evidenced by an incidence of 5.7% in this study population and a documented incidence of 6.1% in an investigation of 696 cholecystectomy patients.[14] With regard to our data, men were found to have a significantly greater incidence of postoperative fever, though most documented infections were in women. This may be due, however, to multiple comparisons. Previous studies have shown no specific criteria for identifying which patients are more likely to develop postoperative fever.[1,15] In cholecystectomy patients, risks for postoperative infection have been identified as increased age,[16,17] obesity,[18,19] diabetes mellitus,[17] and common duct exploration.[18]

Noninfectious or "benign" postoperative fever has been characterized as occurring within the first 48 hours after surgery.[1,3,14,20,21] This was seen in the majority of our febrile patients (76%) who had fevers not associated with infection occurring within the first 48 hours. Beyond these findings, attempts to quantify distinctions in fever characteristics have not met with great success.[3,22,23] As several authors have concluded, there is no fever curve pathognomonic for the presence of infection.[24–26]

Previous studies have found no substantial differences in the laboratory values of postoperative patients with fever but without infection and postoperative patients with proven infection.[25,27] Furthermore, no significant differences in either preoperative or postoperative data were found between the two groups of patients in our study (Table 2).

In our study, there was a lack of correlation between fever and infection. Perhaps a more important finding was the reliability of clinical findings in distinguishing infection. In comparison with fever, findings from the clinical history and examination were more predictive of infection. Without other suspect clinical findings, postoperative fever by itself does not suggest infection. Some authors have suggested that in patients with postoperative fever it is more important to assess the patient than the temperature chart.[5,21,27] Our study gives some justification to this approach in a selected group of patients undergoing a common surgical procedure.

The last finding is particularly relevant in light of the trend toward routine fever evaluation. One recent study[27] concerning the cost-effectiveness of diagnostic tests ordered on the basis of fever indicated that only 29% of test results were of value. Another investigator[15]

has shown similarly low yields of 7% and 14%, respectively, for cultures and radiographs when carried out indiscriminately. In our own study, only 3 of 12 tests were positive in patients evaluated for fever. In comparison, the focus of infection in each of the eight patients without fever was properly identified by one test directed by the clinical findings. This was also demonstrated by Freischlag and Busuttil,[27] who noted that the site of infection in 14 of 19 febrile patients could have been confirmed by one diagnostic test chosen on the basis of relevant historical and physical examination findings.

The cause of fever in the early postoperative period remains speculative. While a number of investigators cite atelectasis as a cause of postoperative fever, others have demonstrated an elevation in temperature following tissue trauma. A hypothesis that has been proposed is the activation of the inflammatory response by tissue injury.[5,21] In studies involving pediatric patients,[5,21–23] a common finding has been a greater incidence of postoperative fever unrelated to infection following orthopedic surgery, suggesting tissue injury as a cause of fever. Activation of the interleukin system following surgery has been noted by a number of investigators and has also been implicated as the cause of postoperative fever. Additionally, the remarkable similarity in our data of the early onset of maximum temperature postoperatively between our two groups implies that some degree of transient elevation in temperature is a normal physiological response. How the magnitude of temperature elevation and the degree of operative trauma are related is unclear.

Conclusions

The association of fever with infection is well known. However, fever by itself in the postoperative cholecystectomy patient is not synonymous with infection. That the febrile response is a common result that can be activated by several different physiological mechanisms serves only to highlight the difficulty of determining when it should be recognized as an indicator of infection. Physicians must look beyond the rise in temperature to other objective criteria to assess the condition of their postoperative patients. To that end, clinical findings remain the primary evidence for identifying those patients who require further evaluation and treatment.

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