CHEST

Original Research

RESPIRATORY CARE

Atelectasis as a Cause of Postoperative Fever

Where Is the Clinical Evidence?

Michael N. Mavros, MD; George C. Velmahos, MD, PhD; and Matthew E. Falagas, MD, DSc

Background: **Atelectasis is considered to be the most common cause of early postoperative fever (EPF) but the existing evidence is contradictory. We sought to determine if atelectasis is associated with EPF by analyzing the relevant published evidence.**
Methods: **We performed a systematic search in PubMed and Scopus databases to identify studies examining the association between atelectasis and EPF.**
Results: **A total of eight studies, including 998 cardiac, abdominal, and maxillofacial surgery patients, were eligible for analysis. Only two studies specifically examined our question, and six additional articles reported sufficient data to be included. Only one study reported a significant association between postoperative atelectasis and fever, whereas the remaining studies indicated no such association. The performance of EPF as a diagnostic test for atelectasis was also assessed, and EPF performed poorly (pooled diagnostic OR, 1.40; 95% CI, 0.92-2.12). The significant heterogeneity among the studies precluded a formal metaanalysis.**
Conclusion: **The available evidence regarding the association of atelectasis and fever is scarce. We found no clinical evidence supporting the concept that atelectasis is associated with EPF. More so, there is no clear evidence that atelectasis causes fever at all. Large studies are needed to precisely evaluate the contribution of atelectasis in EPF.** ***CHEST 2011; 140(2):418–424***

Abbreviations: CXR = chest radiograph; DOR = diagnostic OR; EPF = early postoperative fever; NPV = negative predictive value; POD = postoperative day; PPV = positive predictive value

Early postoperative fever (EPF) is a common sequel of various procedures.[1] It may be attributed to infectious or noninfectious causes, usually in accordance with its temporal association to the operation. Empirically, infectious causes are considered mainly for fever presenting later than 48 h after surgery, whereas EPF is most commonly attributed to noninfectious causes.[2] Moreover, noninfectious causes appear to cause fevers of <38.9°C (102°F), whereas a higher temperature should raise concern for infectious causes.[3] Often, the cause of fever is not identified despite the rigorous efforts of the clinicians.[4-6]

Atelectasis is also a common finding in the postoperative setting, with an incidence of up to 90%.[7] It has also been argued that atelectasis accounts for 90% of postoperative respiratory system complications,[8] and that respiratory complications compose the largest single cause of morbidity and prolonged hospitalization after major surgery.[9]

Most surgical textbooks have adopted the concept that atelectasis is the most common cause of EPF,[10-12] some claiming that atelectasis "is responsible for over 90% of febrile episodes during that period" (the first 48 h after operation).[10] On the other hand,

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Affiliations: From the Alfa Institute of Biomedical Sciences (Drs Mavros and Falagas), Athens, Greece; the Division of Trauma, Emergency Surgery, and Surgical Critical Care (Dr Velmahos), Massachusetts General Hospital and Harvard Medical School, Boston, MA; the Department of Medicine (Dr Falagas), Henry Dunant Hospital, Athens, Greece; and the Department of Medicine (Dr Falagas), Tufts University School of Medicine, Boston, MA.
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Correspondence to: Matthew E. Falagas, MD, DSc, Alfa Institute of Biomedical Sciences (AIBS), 9 Neapoleos St, 151 23 Marousi, Athens, Greece; e-mail: m.falagas@aibs.gr

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several investigators strongly deny the fact that atelectasis is a major cause of EPF, describing it as "common textbook dogma,"[13] or "misconception."[14,15] In this context, we aimed to evaluate the available evidence and address a fundamental question: Is atelectasis a major cause of EPF?

Materials and Methods

Data Sources

A systematic review of the literature was performed on PubMed and Scopus databases, up to January 2011. There was no limitation on the year of publication. The primary search was conducted with the following pattern: ("atelectasis" or "atelectatic") and ("fever" or "febrile" or "pyrexia") and ("postoperative" or "surgery" or "surgical" or "operation"). Secondary searches included the terms "respiratory complications" and "temperature." We also sought to find potentially useful studies in the references of the relevant articles, considering any study written in English, French, German, Spanish, Italian, and Greek.

Study Selection

One investigator (M. N. M.) searched the literature and examined relevant studies for potential inclusion in this review. To be considered eligible, a study should report data on operated patients, including the incidence of atelectasis and fever, as well as their potential coexistence in patients. We considered all patient populations, except for the patients who had undergone lung surgery, taking into account that such patients may suffer from other local complications (clinical or subclinical) that may influence the emergence of atelectasis and/or fever. Studies reporting on fewer than five patients with postoperative atelectasis or fever were excluded. Moreover, unpublished studies reported as abstracts in conferences were not included in this review.[16]

Data Extraction

We extracted data regarding the design (prospective or retrospective, blinding, randomization) and the methodology of the study, the population characteristics (type of surgery, number of participants), the incidence of unexplained postoperative fever and properly diagnosed atelectasis, and their coexistence in operated patients. We also extracted data regarding the interventions that some studies applied to reduce the incidence of postoperative atelectasis and the outcomes of those interventions.

Definitions

EPF is conventionally defined as an axillary temperature of $\geq$38°C (100.4°F) up to 48 h after the operation, which seems equivalent to a rectal temperature of $\geq$38.5°C (101.3°F).[5,17-19] Investigators' definitions of EPF were accepted for all included studies. Atelectasis, on the other hand, is usually diagnosed by clinical, laboratory, or radiologic criteria; yet, the existing evidence suggests that a diagnosis based on a chest radiograph (CXR) or CT scan is preferable.[20-25] Therefore, studies in which atelectasis was diagnosed without the use of imaging modalities were excluded.

Statistical Methods

The statistical analyses were performed with SPSS 17.0 (SPSS Inc; Chicago, Illinois) and Review Manager (RevMan), version 5.0 (the Nordic Cochrane Centre, the Cochrane Collaboration; Copenhagen, Denmark) software. Comparison of dichotomous variables was made by χ^2 tests, when applicable. For the studies reporting data on the crude daily occurrence of atelectasis and fever in consecutive days, we also used Pearson correlation analysis. Diagnostic OR (DOR) was calculated for each study using the formula (TP/FN)/(FP/TN), where T is true, F is false, P is positive, N is negative, and the pooled DOR was estimated using the random effects model.[26] Statistical heterogeneity between studies was assessed with a χ^2 test ($P < .10$ indicated significant heterogeneity). Statistical significance was set at $P < .05$.

Results

Our primary search yielded 369 articles; eventually, eight studies were considered eligible (Fig 1). All studies were prospective in design and four were blind (the investigators who examined the CXR or CT scan were blinded). Four studies were interventional (three were randomized), and four were observational (Table 1). In all studies, atelectasis was diagnosed partly or solely by radiologic criteria (CXR in six, spiral chest CT scan in one, both in one study). Fever was defined as a temperature of $\geq$38°C (100.4°F) in three of the studies (other cutoff points were 37.8°C and 37.5°C in two studies; one study examined the mean temperature of the patients and two studies did not report the temperature cutoff point). The included studies enrolled a total of 998 postoperative patients (681 in observational and 317 in interventional studies). Most patients had undergone cardiac surgery (564 patients), and others had undergone abdominal (370 patients) or maxillofacial surgery (64 patients).

Seven out of eight studies suggested no statistically significant association between atelectasis and early postoperative fever. Two out of eight studies provided data on fever and atelectasis for each of the three first postoperative days (POD),[27,28] and another two studies reported the incidence of fever during the first two or four PODs but only assessed for atelectasis once.[29,30] One study evaluated the patients for atelectasis and fever on POD 1 only,[31] another one did not report the time point of patient assessment,[32] and two studies evaluated the impact of an intervention on both postoperative atelectasis and fever.[33,34]

Five studies reported data eligible for extraction and synthesis.[27,29-32] Despite the considerable heterogeneity in the definition of fever, the time point of fever and atelectasis assessment, and the subjectivity of radiologic findings, we synthesized these data with the methodology of meta-analysis. The pooled DOR of EPF for the diagnosis of postoperative atelectasis was 1.4 (95% CI, 0.92-2.12) (Fig 2). This should be interpreted with caution because of the major limitations stated above. We also calculated the sensitivity, specificity, positive predictive value (PPV), negative

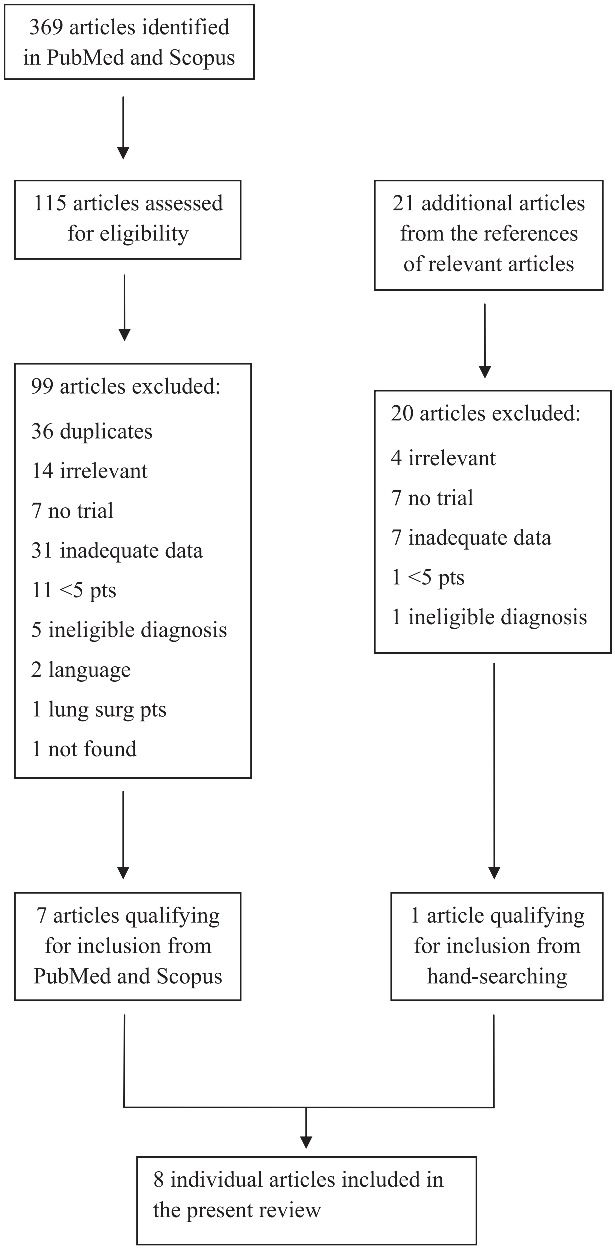

FIGURE 1. Flow diagram describing the selection process for our review. pts = patients.

predictive value (NPV), and accuracy of EPF (as a diagnostic test) for the detection of atelectasis. Sensitivity ranged from 13% to 47%, specificity from 41% to 87%, PPV from 22% to 66%, NPV from 45% to 77%, and accuracy from 43% to 72% (Table 2).

Only one study reported a significant association between EPF and atelectasis.[29] In this study, the investigators prospectively evaluated the incidence of fever each of the first four postoperative days, as well as atelectasis on POD 4. Whereas no association was found between EPF on each POD and atelectasis ($P > .05$) on POD 4, there was a significant association between EPF on any of POD 1 to 2 and atelectasis

Table 1—*Characteristics and Outcomes of Reviewed Studies*

Study/Year	Population Characteristics	Study Design	Fever Assessment	Atelectasis Diagnosis	Fever Occurrence	Confirmed Atelectasis
Engoren[27]/1995	Cardiac surgery, 100 pts	B, non-R	≥38 (bladder) POD 1-3	CXR POD 1-3	POD 1: 37/100 POD 2: 21/100 POD 3: 17/100	POD 1: 43/100 POD 2: 69/100 POD 3: 78/99
Iverson et al[28]/1978	Cardiac surgery, 145 pts	R, non-B	>37.8 POD 1-3	CXR POD 1-3	POD 1: 102/145 (70%) POD 2: 97/145 (67%) POD 3: 73/145 (50%)	POD 1: 47/145 (32%) POD 2: 65/145 (45%) POD 3: 76/145 (52%)
Roberts et al[29]/1988	Abdominal surgery, 270 pts (elective)	B, non-R	≥38 (oral) POD 1-4	CXR POD 4	POD 1-2: 72 pts atelectasis and fever, 82 pts atelectasis without fever, 37 pts fever without atelectasis, 79 pts without atelectasis/fever	
Pérez-Aispuro et al[30]/1991	Abdominal surgery, 100 pts (elective)	B, non-R	NR definition POD 1-2	CXR POD 2	4 pts atelectasis and fever, 27 pts atelectasis without fever, 14 pts fever without atelectasis, 55 pts without atelectasis/fever	
Afranian-Farnad et al[31]/2002	Maxillofacial surgery, 64 pts	Non-B, non-R	NR definition POD 1	CXR and CT scan POD 1	5 pts atelectasis and fever, 12 pts atelectasis without fever, 6 pts fever without atelectasis, 41 pts without atelectasis/fever	
Lim et al[32]/2003	Cardiac surgery, 211 pts	Non-B, non-R	>37.5 NR	CXR NR	86 pts atelectasis and fever, 61 pts atelectasis without fever, 35 pts fever without atelectasis, 35 pts without atelectasis/fever	
Chulay et al[33]/1982	Cardiac surgery, ICU, 35 pts (elective)	B, R (RCT)	>38 (in hours) POD 1-3	CXR POD 1-3	POD 2: 10.4 ± 7.0 vs 14.8 ± 6.4 POD 3: 3.1 ± 4.7 vs 13.9 ± 7.3	72% vs 68%, NR which day(s)
Westerdahl et al[34]/2005	Cardiac surgery, 73 pts (elective)	B, R (RCT)	Mean temperature POD 1-4	Spiral CT scan POD 4	37.5 ± 0.3°C vs 37.6 ± 0.4°C	1.2 ± 0.8 vs 2.2 ± 2.8 (mean ± SD of an atelectasis scale)

All studies were prospective. B = blind; CXR = chest radiograph; NR = not reported; POD = postoperative day; pts = patients; R = randomized; RCT = randomized controlled trial.

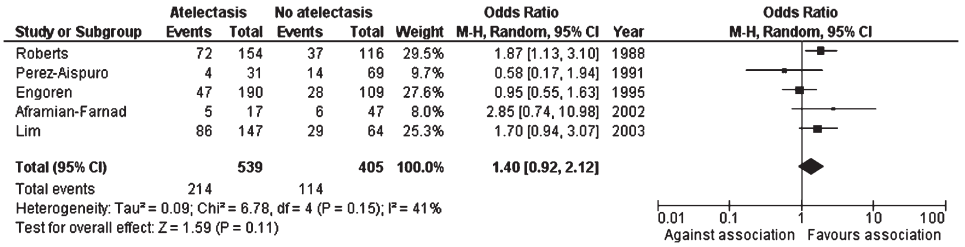

FIGURE 2. Diagnostic OR (DOR) of early postoperative fever (EPF) for the diagnosis of atelectasis (EPF is evaluated as a diagnostic test for atelectasis; gold standard is considered the radiologic diagnosis). The figure should be interpreted with caution because of the heterogeneity of the studies. Vertical line = "no discrimination" point between the patients with or without atelectasis; squares = DOR; horizontal lines = 95% CI; diamond = pooled DOR. df = degrees of freedom; M-H = Mantel-Haenszel.

on POD 4 ($P = .02$). However, even in the latest scenario, EPF performed poorly as a diagnostic test (sensitivity, 26%; specificity, 75%; accuracy, 43%).

Only two of the included studies directly addressed our question.[27,30] The prospective study by Engoren[27] specifically examined the potential association of EPF with atelectasis. The author performed multiple analyses and concluded that "atelectasis and fever are independent of each other" and that febrile patients were as likely to have as not to have atelectasis. In contrast, although the authors of the Spanish study refrained from performing any analysis, using their data we calculated a P value of .54, implying no association between atelectasis and fever.[30] In both studies, EPF performed poorly as a diagnostic test (sensitivity, 13%-26%; specificity, 75%-80%; accuracy, 43%-59%). This was also the pattern for the rest of the included studies (Table 2).

Discussion

Our findings suggest that the popular belief of atelectasis being the most common cause of EPF is not supported by the existing clinical evidence. Moreover, the perception that atelectasis is a cause of fever at all has yet to be proven. In this context, cases of EPF traditionally attributed to atelectasis may in fact be associated with the physiologic response of the human body to tissue injury derived by an operation and the overall perioperative stress.[14,35,36]

In fact, our review only indirectly assesses whether atelectasis is a major cause of EPF. All eligible studies reported a potential association between atelectasis and EPF; no study actually examined the potential for causation (ie, that atelectasis is the cause of EPF). To do so, one should examine the Bradford-Hill criteria, which constitute of strength of association, consistency, specificity, temporal relationship, biologic gradient, biologic plausibility, coherence, reversibility, and analogy.[37] However, since the first criterion (association) is not met according to the existing evidence, one can presume the absence of a causal relationship.

The study of Roberts et al,[29] which has been highly cited by authors advocating that EPF is unrelated to atelectasis, may have been misinterpreted, at least in part. Several researchers commented on this study that it "fail(s) to show correlation between body temperature and atelectasis,"[36] there is "poor correlation between fever and atelectasis,"[15] and that the "association…was no better than chance."[27] However, using their own data, we calculated a P value of .02, suggesting a significant association between postoperative fever (48 h) and atelectasis (POD 4). This was the only study suggesting such an association.

In another study, enrolling 151 abdominal surgery patients, Schlenker and Hubay[38] concluded that fever on POD 1 was correlated with auscultatory findings of atelectasis ($P < .01$). The authors claim that "a good correlation was found between the auscultatory and roentgenographic evidence for atelectasis"; however, out of 16 patients with an auscultatory diagnosis of mild atelectasis who received a CXR, only nine had radiographic abnormalities, including but not confined to atelectasis. Furthermore, out of 34 patients with auscultatory evidence of severe atelectasis who received a CXR, 21 had abnormal findings: five had plate-like atelectasis, 11 a homogeneous density, and five a pleural effusion. Taking those findings into account, it appears that radiographic modalities are preferable to auscultation alone for the diagnosis of atelectasis and do not allow for any conclusions with regard to the association of atelectasis with fever.

Lansing and Jamieson[39,40] and Shields[41] have investigated the pathogenesis of fever in atelectasis in animal models. Lansing and Jamieson[39] observed that after placing cotton plugs in the left main bronchus of 30 dogs, the animals became febrile within 12 h; however, there was evidence of infection distal to the plug in almost all animals. Antibiotics resolved

Table 2—*Diagnostic Assessment and End Points of Reviewed Studies*

Study/Year	DOR (95% CI)	Sens, %	Spec, %	PPV, %	NPV, %	Acc, %	Authors' Conclusion	Our Findings and Comments
Engoren[27]/1995	0.95 (0.55-1.63)	26	75	25	75	43	No difference of atelectasis between febrile and nonfebrile. Fever and atelectasis are independent of each other.	EPF was not correlated with atelectasis ($r = -0.997$, $P = .052$). The most reliable/relevant study of those reviewed.
Iverson et al[28]/1978	NA	NA	NA	NA	NA	NA	NA	EPF was not correlated with atelectasis ($r = -0.850$, $P = .35$). Pts were randomized in three groups (IPPB, IS, blow bottles) to assess for differences in postoperative atelectasis; cumulative data presented here.
Roberts et al[29]/1988	1.87 (1.13-3.10)	47	68	66	49	56	Fever is not an accurate diagnostic test for the detection of atelectasis.	EPF (POD 1-2) was associated with atelectasis ($P = .02$). However, fever in POD 1 or POD 2 was not associated with atelectasis ($P = .27$ and 0.12, respectively). Fever performs poorly as a diagnostic test for atelectasis.
Pérez-Aispuro et al[30]/1991	0.58 (0.17-1.94)	13	80	22	67	59	Atelectasis is not the most common cause of EPF.	EPF was not associated with atelectasis ($P = .54$). Scarce data were reported, no analysis was performed, and fever was not defined.
Aframian-Farnad et al[31]/2002	2.85 (0.74-10.98)	29	87	45	77	72	There was no significant difference of EPF in patients with vs without atelectasis.	EPF was not associated with atelectasis ($P = .15$). Pts were enrolled in two groups (MMF, non-MMF) to assess for differences in postoperative atelectasis; cumulative data presented here. Fever was not defined.
Lim et al[32]/2003	1.70 (0.94-3.07)	45	41	55	45	57	Atelectasis may contribute to the development of postoperative fever (although there was no significant difference of fever in patients with vs without atelectasis).	Postoperative fever was not associated with atelectasis ($P = .08$). Not reported when atelectasis and fever were assessed. Although temperature was assessed via various routes, a common cutoff point is reported.
Chulay et al[33]/1982	NA	NA	NA	NA	NA	NA	NA	There was no association between postoperative fever and atelectasis. Pts were randomized in two groups (early mobilization, control subjects) to assess for differences in postoperative atelectasis. Although EPF was significantly higher in control subjects (POD 2: $P < .05$; POD 3: $P < .001$), atelectasis was slightly lower in control subjects.
Westerdahl et al[34]/2005	NA	NA	NA	NA	NA	NA	NA	There was no association between postoperative fever and atelectasis. Pts were randomized in two groups (deep-breathing exercises, control subjects) to assess for differences in postoperative atelectasis. There was no difference in temperature, but significant difference in atelectasis ($P < .05$).

Acc = accuracy; DOR = diagnostic OR; EPF = early postoperative fever; IPPB = intermittent positive-pressure breathing; IS = incentive spirometry; MMF = maxillo-mandibular fixation; NA = not applicable; NPV = negative predictive value; PPV = positive predictive value; r = Pearson correlation coefficient; Sens = sensitivity; Spec = specificity. See Table 1 legend for expansion of other abbreviations.

the fever but not the atelectasis, whereas removal of the plug cured both fever and atelectasis. The authors reproduced the experiment in dogs and cats and confirmed the findings.[40] Shields[41] ligated the right middle lobe of dogs and injected pneumococci in one group. The injected group had radiographic evidence of pneumonia, whereas the noninjected group showed evidence of atelectasis. Interestingly, neither of the groups developed fever.

It has been proposed that fever may be attributed to microatelectasis, undetectable by radiographs.[42] Lindberg et al[43] reported that out of 13 patients, only one had evidence of atelectasis in CXR, whereas the CT scan showed atelectasis in 12 of them. However, only one patient (out of 13) was febrile. Therefore, microatelectasis diagnosed by CT scan, with normal CXR, does not seem to be accompanied by fever; however, data on this setting are scarce.

It is also possible that EPF is indeed associated with atelectasis, which becomes evident in radiographs a few days after the operation. In this case, the majority of the cases of EPF may be attributed to other causes (eg, perioperative stress), and the rest of them might show temporal association with the emergence of atelectasis. This hypothesis might explain the findings of some of the included studies.[27-29]

It appears that stress derived by surgery is significant enough to increase the patient's IL-6 levels and thermostatic setpoint. In their study, Wortel et al[35] observed that in 19 patients undergoing pancreaticoduodenectomy, there was an early postoperative increase in portal and peripheral IL-6 levels, which correlated logarithmically with peak body temperature. In addition, Frank et al[36] studied 271 vascular, abdominal, and thoracic surgery patients and reported that there was an increase of $1.4°C \pm 0.8°C$ in their temperature in the early postoperative period, with the peak occurring 11.1 ± 5.8 h after surgery. This increase in temperature was also associated with an enhanced IL-6 response.

Our review is limited by the heterogeneity of the studies, which did not allow for a formal metaanalysis. In particular, only two of the studies specifically examined our question, whereas most of the studies had different end points but reported enough data to be included in our review. In addition, only three out of eight studies set the cutoff point for fever at 38°C (100.4°F) but without reporting how the temperature was measured (oral, rectal, bladder, and so forth), whereas the CXRs/CT scans were obtained at various time points (from the first to the fourth POD). Moreover, although radiologic modalities seem preferable for the diagnosis of atelectasis, there is no gold standard yet. Last, we only evaluated studies reporting the word "atelectasis" in the abstract or the keywords; it is possible that we may have missed studies reporting relevant data because of that limitation in the search process.

Our findings have important implications for clinical practice. EPF should not be a priori attributed to atelectasis. Moreover, patients may not need atelectasis-related interventions, such as incentive spirometers or other measures (ie, intermittent positive pressure breathing, deep breathing exercises under supervision, and so forth), solely because of the presence of fever. Despite the lack of proven benefit of these interventions after upper abdominal surgery[44] and coronary artery bypass grafting[45] and their association with increased cost, they currently constitute common practice. In addition, although this fever is usually benign and requires no additional measures to resolve, the surgeon should keep in mind the possibility of another process causing fever. Some advocate that EPF should not be evaluated at all for the sake of cost-effectiveness.[5] Furthermore, atelectasis may be present in afebrile patients as well.

In conclusion, there is no clinical evidence suggesting that atelectasis is a major cause of EPF. The rather limited evidence implies that atelectasis may be not associated with fever at all. Consequently, EPF may be caused by the stress of operation and the increase in circulating pyrogenic cytokines in the absence of infection. Large studies are needed to precisely evaluate the contribution of atelectasis in EPF.

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