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A prospective randomised trial of isolated pathogens of surgical site infections (SSI)

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HIGHLIGHTS

- Seven main pathogens were isolated from patients with SSIs: *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Pseudomonas aeruginosa, Bacteroides fragilis, Staphylococcus aureus* and *Enterococcus faecalis.*
- SSI incidence was 4,3% (31 patients out of a whole of 715 patients).
- Potentially contaminated are all scheduled operations of the GI tract and SSIs appear in this classification with an incidence of 7–8%.
- All patients participating in our study underwent scheduled operations of the upper or lower digestive system, considered potentially contaminated as stated.

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ABSTRACT

Background: Every surgical wound is colonized by bacteria, but only a small percentage displays symptoms of infection. The distribution of pathogens isolated in surgical site infections has not significantly changed over the last decades. Staph. Aureus, Coag(-) Staphylococci, Enterococcus spp and *E. Coli* are the main strains appearing. In addition, a continuously rising proportion of surgical site infections caused by resistant bacterial species (MRSA, *C. Albicans*) has been reported.

Methods: This prospective and randomized clinical study was performed in the 1st Surgical Clinic of Sismanoglion General Hospital of Athens, from February 2009 to February 2015. Patients undergoing elective surgery in the upper or lower digestive system were randomized to receive antimicrobial treatment as chemoprophylaxis. Each patient filled a special monitoring form, recording epidemiological data, surgery related information, surgical site infections (deep and superficial), as well as postoperative morbidity (urinary and respiratory infections included).

The monitoring of patients was carried by multiple visits on a daily basis during their hospitalization and continued after they were discharged via phone to postoperative day 30.

Results: Our overall SSI incidence was 4,3% (31patients out of a whole of 715 patients). Specifically, the incidence of SSIs for scheduled surgery of the upper GI tract was 2,2% (11 out of 500 patients) and for the lower GI tract was 9,3% (20 out of 215 patients). Seven main pathogens were isolated from patients with SSIs: *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Pseudomonas aeruginosa, Bacteroides fragilis, Staphylococcus aureus* and *Enterococcus faecalis*. Their growth rates were respectively: *S. Aureus* (17,3%), *E. faecalis* (19,5%), *P. aeruginosa* (10,5%), *B. Fragilis* (13,4%) *E. coli* (20,4%), *Enterobacter cloacae* (9,1%) and *K. Pneumoniae* (9,8%). In addition, all the SSIs were found to be multimicrobial. Several studies have already revealed that patient characteristics and coexisting morbidities such as obesity, smoking, heart or renal failure, pre-existing localized infections and patients' age (especially if age exceeds 65) seem to be independent prognostic factors for surgical field infections. Additionally, classification of the surgical wound, surgical operation complexity, preoperative hospitalization, prolongation of surgical time and need for transfusions have been proved to differentiate the incidence of SSIs.

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Conclusions: In conclusion, surgical site infections are important complications affecting the healthcare services, the cost of hospitalization and the patient himself. Future thorough studies are expected to reveal much more data, regarding predisposing and precautionary patient and hospital characteristics.

1. Introduction

Every surgical wound is colonized by bacteria, but only a small percentage displays symptoms of infection. When a wound is contaminated by more than 10^5 microorganisms per gram of tissue the risk of infection augments. Surgical site infection is the third most common hospital-acquired infection (HAI) with a quota reaching 14–16% and the first between surgical patients. Around two thirds of the SSIs are limited in the surgical wound area and only 30% regards organs and anatomical spaces that were accessed during the procedure.

The distribution of pathogens isolated in surgical site infections has not significantly changed over the last decades. Staph. Aureus, Coag (-) Staphylococci, Enterococcus spp and *E. Coli* are the main strains appearing [1]. In addition, a continuously rising proportion of surgical site infections caused by resistant bacterial species (MRSA, *C. Albicans*) has been reported. This ratio reflects the increase of immunosupressed and critically ill patients as well as antibiotics misuse [2,3].

In the majority of SSIs the source of pathogens is normal skin, mucosa and bowel microbiota. Prosthetic implants can also become sources of bacteria proliferation. Other external sources are the surgical staff, the surgical room and every machine and instrument used during the procedure.

Surgical site infections can also be caused by unusual pathogens such as Rhizopus Orizae, C. Perfrigens, Rhodococcus Bronchialis, Nocardia Farcinica, Legionella Pneumophilla, Legionella Dumoffil and Pseudomonas Multivorans. Whenever an unusual strain causes an SSI, it is mandatory that an extended research is carried, questing the source of the pathogen [4–6].

In particular types of interventions several factors may be associated with increased risk of surgical site infection colonization [7,8] diabetes [9], smoking [10,11], systemic use of steroids [12], obesity (>20% of ideal BW), age [13–15], malnutrition [16,17] perioperative blood transfusion and its derivatives [18,19].

Microorganisms may contain or produce toxins that improve their ability to cause damage to the host cells or tissues. For example, many gram (-) bacteria produce endotoxins which cause secretion of cytokines. These substances can trigger the syndrome of systemic inflammatory reaction and may in some cases lead to multiple organ dysfunction and failure [18,19]. A variety of microorganisms including gram (+) bacteria, such as coagulase negative staphylococci produce glycocalyx which provides natural protection from phagocytes and prevents binding or penetration of antimicrobial agents.

In order to reduce surgical site infections several researchers suggest the use of preoperative chemoprevention [20,21]. Preoperative antibiotic administration should be done closely to the skin incision time. The start of the antibiotic administration within 60 min before the incision is under consensus. The start 120 min before the incision affecting the rate of surgical field infections [20,21]. Especially the administration of cefuroxime 30–60 min before skin incision may minimize surgical infections [22,23].

According to literature higher percentages of SSIs are encountered in gastrointestinal procedures (5,3–10,6% for small intestine, 4,3–10,5% for colon, 2,8–12,3% for stomach and 2,8–10,2% for billiary system) [20–23].

The purpose of this study was to evaluate and record the surgical site infection (SSI) in elective procedures of the upper digestive such as laparoscopic cholecystectomy comparing the administration of single dose chemoprotection against three doses in surgical field infection rate.

2. Materials and methods

2.1. Study design

This prospective and randomized clinical study was performed in the 1st Surgical Clinic of Sismanoglion General Hospital of Athens, from February 2009 to February 2015. The study protocol was approved by the Scientific Council of the Sismanoglion Hospital and written consents were received from all patients included in this study.

Patients undergoing elective surgery in the upper or lower digestive system were randomized to receive antimicrobial treatment as chemoprophylaxis. The administration of antibiotics was performed preoperatively and within 60 min prior to the surgical incision. Repeated dose was administered intraoperatively whereas the procedure lasted more than 3 h and/or if blood loss exceeded 300 ml.

The study excluded patients with preoperative hospitalization longer than 15 days, patients undergoing urgent surgery because of obstruction, bleeding or inflammation of the gastrointestinal (GI) tract and patients with active infections and systemic antibiotic administration.

2.2. Antibiotic treatment

Cefuroxime (1,5 gr) was provided, in 1 or 3 doses depending on randomization, for upper GI interventions, while ticarcilline - clavulanate (5,2 gr) was selected for chemoprophylaxis of lower GI surgery. In addition, patients undergoing scheduled colectomy underwent mechanical bowel cleaning without oral antibiotics intake.

In case of known and certified beta-lactams hypersensitivity, aztreoname (2gr) was alternatively administered, combined with metronidazole (1gr) for lower GI tract, 1 or 3 doses on randomization basis. In cases of previous antibiotics intake, patients were randomized according to their medication with penicillin, ampicillin, amoxicillin-clavulanate, aminoglycosides, cephalosporins, cefaclor, cefprozil, cotrimoxazol or quinolones.

Each patient filled a special monitoring form, recording epidemiological data, surgery related information, surgical site infections (deep and superficial), as well as postoperative morbidity (urinary and respiratory infections included).

The monitoring of patients was carried by multiple visits on a daily basis during their hospitalization and continued after they were discharged via phone to postoperative day 30.

3. Results

In this study, seven main pathogens were isolated from patients

with SSIs: *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Pseudomonas aeruginosa, Bacteroides fragilis, Staphylococcus aureus* and *Enterococcus faecalis*. Their growth rates were respectively: *S. Aureus* (17,3%), *E. faecalis* (19,5%), *P. aeruginosa* (10,5%), *B. Fragilis* (13,4%) *E. coli* (20,4%), *Enterobacter cloacae* (9,1%) and *K. Pneumoniae* (9,8%). In addition, all the SSIs were found to be multimicrobial.

Among the 92 isolated strains of pathogens, 34 strains were isolated from surgical infections of the upper digestive system and 58 strains were isolated from surgical infections of the lower digestive tract.

31 patients were diagnosed with SSIs out of a total of 715 patients, which is translated to a percentage of 4,3%. More specifically, the percentage of surgical infections for the upper digestive system was 2.2% (11 out of 500 patients) and for the lower digestive system 9.3% (20 out of 215 patients). The proportion of SSIs for the upper digestive system is among the lowest according to literature.

Patients with surgical infections had a statistically significant higher age ($p < 0.001$). Patients with severe concomitant diseases and ASA> 3 (severity of the underlying disease; rating of the American Society for Anesthesiology) revealed a significantly increased risk of infections of the surgical field. Patients exhibiting SSIs were found having at least one severe co-morbid disease ($p < 0.001$).

Patients with diabetes presented more frequently with SSIs ($p = 0.014$) with the relative risk in patients without diabetes being remarkably lower (RR: 0.415, 95% CI: 0.2–0.846).

Patients with respiratory failure are predisposed to surgical field infections ($p = 0.01$) and the relative risk in patients without respiratory failure was significantly lower (RR: 0.38, 95% CI: 0.18–0.81).

Additionally, patients with heart failure revealed surgical infections more frequently ($p = 0.006$), while the relative risk in patients without heart failure was also very low (RR: 0.37, 95% CI: 0.18–0.77).

Contrariwise, no statistically significant differences were found between subgroups receiving steroids ($p = 1$), radiation therapy ($p = 0.2$), or patients with renal failure ($p = 1$), atrial fibrillation ($p = 0.33$), thyroid diseases ($p = 0.63$) or hypertension ($p = 1$) (Table 1).

Concerning obesity, it has been proved that adipose tissue is a poor blood perfused tissue with low oxygen concentration. As a result, obese people tend to have an increased SSI occurrence. Moreover, surgical operations in obese patients are more complex and lengthy. While the risk of surgical site infections in obese patients has been studied in cardiac surgery, neurosurgery and gynecology, it has not yet been widely studied in general surgery. In our study, no statistically significant differences were found between obese and non-obese subgroups ($p = 0.16$). This can be explained by the fact that obese patients were more frequently treated for upper GI diseases ($p = 0.002$) and especially underwent laparoscopic cholecystectomy with short preoperative hospitalization and duration of surgery (Table 2).

4. Discussion

The surgical site infection (SSI) is the third most frequent hospital infection, approaching 16% of all hospital-acquired infections. It is also the most frequent infection among surgical patients, making up 38% of all infections. Most of the SSIs are limited in the surgical wound while the rest are located in organs or anatomic sites which have been accessed during the operation.

77% of total death rate in patients with surgical field infections could be associated with this condition and 93% of these patients faced severe infections of organs or anatomical sites accessed during operation.

Previous studies have estimated that patients with SSIs remain in hospital for 7.3–10 days increased hospitalization costs up to 3.152 US dollars per patient. Broex et al. estimate that the cost of surgical field infections is almost double compared to the cost of hospital treatment for patients without an SSI [22,23]. However, there are fluctuations of the estimated costs of surgical field infections, ranging from $ 400 per patient per day for limited superficial infections to $ 63,135 for invasive infections [24,25]. The simple wound suppuration increases the hospitalization for almost 10 days, leading to a proportional increase of the total treatment cost [26]. In a study about the surgical field infections after lower GI tract operations, the cost of home care after hospital discharge reached $ 6200 per patient [27,28].

The optimum frequency of SSIs has not yet been determined. As the duration of hospitalization is often short, the patients' monitoring outside the hospital is very important if we want to achieve

Table 1
Pivot Tables of Coexisting diseases.

		N	Morbidity (%)	Percentage % on patient
Coexisting disease	Diabetes Mellitus	133	17.9%	27.4%
	Respiratory Insufficiency	97	13.1%	20.0%
	Corticoid administration	6	0.8%	1.2%
	Radiotherapy	5	0.7%	1.0%
	Renal Failure	9	1.2%	1.9%
	Respiratory Insufficiency	108	14.5%	22.3%
	Obese	92	12.4%	19.0%
	Atrial fibrillation	9	1.2%	1.9%
	Thyroid disease	28	3.8%	5.8%
	Hypertension	27	3.6%	5.6%
	Other	229	30.8%	47.2%
Total		743	100.0%	153.2%

	Number of Coexisting diseases			
	Frequency	Percentage %	Percentage% of valid	Cumulative Percentage%
0	229	32.0	32.2	32.2
1	285	39.9	40.0	72.2
2	142	19.9	19.9	92.1
3	52	7.3	7.3	99.4
4	4	0.6	0.6	100.0
Total	712	99.6	100.0	
Incomplete prices	3	0.4		
Total	715	100.0		

Table 2
Pivot Table of surgical diseases.

		N	Percentage of Diseases	Percentage of Patients
Diseases	Gallstone	472	64.9%	66.0%
	Right Colon Cancer	61	8.4%	8.5%
	Left Colon Cancer	62	8.5%	8.7%
	Rectal cancer	72	9.9%	10.1%
	Stomach cancer	19	2.6%	2.7%
	Uterine cancer	18	2.5%	2.5%
	Pyloric stenosis	1	0.1%	0.1%
	Splenomegaly	1	0.1%	0.1%
	Biliary cancer	1	0.1%	0.1%
	Gallbladder polyps	20	2.8%	2.0%
Total		727	100.0%	

accurate rates [27,28]. At least two studies have shown that most SSIs are evident within the first 21 postoperative days [29,30]. In this study the monitoring of patients was completed in 30 days after surgery by telephone communication and interview.

Nowadays there are several methods for post-operative monitoring used by various hospitals. Those include direct examination of the surgical wound and monitoring of patients via mail or telephone communication [31,32].

One study revealed that patients can hardly appreciate their surgical wounds for possible infection (52% specificity, 26% positive predictive value) [33], indicating that the data collected from patient questionnaires could be less worthy in extracting specific frequencies of SSIs. Currently the chosen methods necessarily reflect the individual characteristics of each hospital, defined by the range of interventions, staff resources and data collection [32,33]. According to literature there are only few prospective randomized studies to assess the contribution of risk factors for surgical field infections. However, related data from statistical models may be very important [32,33].

Several studies have already revealed that patient characteristics and coexisting morbidities such as obesity, smoking, heart or respiratory failure, pre-existing localized infections and patients' age (especially if age exceeds 65) seem to be independent prognostic factors for surgical site infections [34–36].

The importance of patient's normal flora and its correlation with SSIs has been recognized decades ago. Whether or not a wound colonized by normal flora bacteria will become infected depends on the extension of contamination [37,38]. In order to better understand and facilitate these conditions, a classification of surgical operations and wounds as clean, potentially contaminated, contaminated and dirty has been established [38,39].

Potentially contaminated are all scheduled operations of the GI tract and SSIs appear an incidence of 7–8% caused by internal normal flora bacteria. The highest rates regarding potentially contaminated operations, were: for small intestine (5.3%–10.6%), for the colon (4.3%–10.5%), for gastric surgery (2.8%–12.3%) and for the billiary tree (2.8%–10.2%) [40].

All patients participating in our study underwent scheduled operations of the upper or lower digestive system, considered potentially contaminated as stated above [40]. Our overall SSI incidence was 4,3% (31patients out of a whole of 715 patients). Specifically, the incidence of SSIs for scheduled surgery of the upper GI tract was 2,2% (11 out of 500 patients) and for the lower GI tract was 9,3% (20 out of 215 patients). Regarding our upper GI surgery results, they are considered to be among the lowest based on Greek and international literature [40,41].

Additionally, classification of the surgical wound, surgical operation complexity, preoperative hospitalization, prolongation of surgical time and need for transfusions have been proved to differentiate the incidence of SSIs [41–43].

In conclusion, surgical site infections are important complications affecting the healthcare services, the cost of hospitalization and the patient himself. Future studies are expected to reveal much more data, regarding predisposing, precautionary patients and hospital characteristics.

Ethical approval

No ethics committee request was submitted.

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Author contribution

Konstantinos Alexiou, Argyrios Ioannidis, Maria Terzopoulou, Nikolaos Sikalias, Nikolaos Economou carried out and participate at the surgical excision and the manuscript demonstration. Konstantinos Alexiou, Ioannis Drikos participated in the design of the study and helped to draft the manuscript. All authors read and approved the final manuscript.

Conflicts of interest

All authors declare no conflicts of interest.

Guarantor

Konstantinos Alexiou.

Consent

Written informed consent was obtained from the patients for publication of this prospective randomized trial. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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List of abbreviations

SSI	Surgical Site infections
HAI	Hospital Acquired Infection
MRSA	Methicillin-resistant *Staphylococcus aureus*
GI	Gastro Intestinal

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