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Surgical site infection in adults undergoing major non-cardiac surgery and its association with anemia, severe bleeding and intraoperative transfusion: A preliminary report from a prospective registry

Infección de sitio operatorio en adultos llevados a cirugía mayor no cardiaca y su relación con anemia, sangrado mayor y transfusión intraoperatoria: Informe preliminar de un registro prospectivo

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What do we know about this problem?

· Surgical site infection is an important quality indicator and a permanent source of concern for health systems because of its association with morbidity and mortality, high cost of care and bed occupancy.
· Identification of preventable perioperative factors could point to those high-risk individuals who might benefit from optimization.

What is the contribution of this study?

· Preoperative anemia, major bleeding and intraoperative transfusions work as independent risk markers for surgical site infection in major non-cardiac surgery.
· Institutions must implement strategies to identify and treat preoperative anemia and to prevent major bleeding.
· Future models of risk interaction for this adverse event must include these factors.

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Abstract

Introduction

Surgical site infection (SSI) is among the most common healthcare-related infections. Given their greater morbidity and surgical complexity, patients undergoing major surgery are exposed to a high risk of SSI.

Objective

To determine the incidence of SSI in adult patients undergoing major elective non-cardiac surgery, and to identify risk factors associated with its occurrence within the first 30 days after surgery.

Methods

An analytical study was designed on the basis of a prospective institutional registry. Clinical and laboratory variables associated with perioperative management were recorded. An active search was conducted in order to find SSI episodes, renal failure and multiple organ dysfunction during the first 30 days after surgery. Adjusted logistic regression was done to identify potential associations between risk factors and the development of SSI.

Results

Overall, 1501 patients were included. The incidence of SSI during the first 30 days after surgery was 6.72% (95% CI 5.57-8.11). ASA III, abdominal surgery and longer procedures were more frequent in the SSI group. Association with the occurrence of SSI was documented for preoperative hemoglobin levels (adjusted OR 0.79 [95% CI 0.72-0.88], p = 0.04), intraoperative transfusion (adjusted OR 2,47 [95% CI 1.16-5.27], p = 0.02) and major blood loss (adjusted OR 3.80 [95% CI 1.63-8.88], p = 0.04).

Conclusion

Preoperative hemoglobin level, intraoperative transfusion and major bleeding are independent risk factors associated with the occurrence of SSI in adult patients undergoing major elective non-cardiac surgery.

Keywords

Surgical site infection; risk factors; major surgery; anemia; major bleeding.

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¿Qué sabemos acerca de este problema?

· La infección de sitio operatorio es un importante marcador de calidad y una permanente preocupación para los sistemas de salud, debido a su asociación con morbimortalidad, altos costos en la atención y ocupación hospitalaria.
· Identificar factores perioperatorios prevenibles podría ayudar a identificar sujetos de alto riesgo con oportunidad de ser optimizados.

¿Qué aporta este estudio de nuevo?

· La anemia preoperatoria, el sangrado mayor y las transfusiones intraoperatorias funcionan como marcadores de riesgo independientes para infección de sitio operatorio en cirugía mayor no cardiaca.
· Las instituciones deben implementar estrategias para identificar y tratar la anemia preoperatoria y prevenir el sangrado mayor.
· Los futuros modelos de interacción de riesgo para este evento adverso deben incluir estos factores

Resumen

Introducción

La infección del sitio operatorio (ISO) ocupa los primeros lugares entre las infecciones asociadas a la atención en salud. Con una mayor morbilidad y complejidad quirúrgica, los pacientes de cirugía mayor están expuestos a un alto riesgo de ISO.

Objetivo

Determinar la incidencia de ISO en pacientes adultos sometidos a cirugía mayor electiva no cardiaca e identificar factores de riesgo relacionados con su aparición durante los primeros 30 días postoperatorios.

Métodos

Se diseñó un estudio analítico a partir de un registro institucional prospectivo. Se registraron variables clínicas y de laboratorio relacionadas con el manejo perioperatorio. Se realizó una búsqueda activa de episodios de ISO, sepsis, falla renal y disfunción multiorgánica durante los primeros 30 días postoperatorios. Las potenciales asociaciones entre factores de riesgo y el desarrollo de ISO fueron identificadas mediante regresión logística ajustada.

Resultados

Se incluyeron 1.501 pacientes. La incidencia de ISO durante los 30 días postoperatorios fue de 6,72 % [IC 95 % 5,57-8,11). El estado ASA III, la cirugía abdominal y los procedimientos de duración prolongada fueron más frecuentes en el grupo ISO. Se documentó asociación con la ocurrencia de ISO para los niveles de hemoglobina preoperatoria (OR ajustado 0,79 [IC 95 % 0,72-0,88], p = 0,04), transfusión intraoperatoria (OR ajustado 2,47 [IC 95 % 1,16-5,27], p = 0,02) y sangrado mayor intraoperatorio (OR ajustado 3,80 [IC 95 % 1,63-8,88], p = 0,04).

Conclusiones

El nivel de hemoglobina preoperatoria, la transfusión intraoperatoria y el sangrado mayor son factores de riesgo asociados de forma independiente a la ocurrencia de ISO en pacientes adultos llevados a cirugía mayor electiva no cardiaca.

Palabras clave

Infección de sitio operatorio; factores de riesgo; cirugía mayor; anemia; sangrado mayor.

INTRODUCTION

Healthcare-associated infections (HAIs) represent one of the biggest problems for patients and healthcare institutions (increased length of stay, re-interventions, use of antimicrobial agents) (1,2). According to the report of the Colombian Ministry of Health and Social Protection, surgical site infection (SSI) in the adult population is classified as the second most frequent HAI after catheter-associated urinary tract infections, and it is one of the most important indicators included in the healthcare quality observatory (3). The Global Guidelines on Prevention of Surgical Site Infections recently published by the WHO contain 29 perioperative interventions that can help to reduce the occurrence of SSI and avoid the development of multiresistant microorganisms (4).

The diagnosis of SSI may involve three clinical conditions: 1) evidence of erythema, edema, local heat and pain, with or without purulent discharge from the incision site; 2) a positive culture of the discharge material or tissue obtained aseptically from the incision; 3) the presence of an abscess or varying degrees of tissue compromise (superficial incisional, deep incisional and organ-space) (5,6). However, diagnosing SSI in the mediate postoperative period may be difficult because, in many cases, length of stay is too short (at least 90% of cases become more evident after the first 21 days following the surgical procedure) (7).

The various scales used for SSI prediction are limited due to the many factors that come into play and the characteristics of the

population they are applied. This study was designed to determine the incidence of SSI in adult patients undergoing major non-cardiac surgery, and to identify potential risk factors associated with its development within the first 30 days following the surgical procedure.

METHODS

This study followed the recommendations contained in the STROBE guidelines (Strengthening the Reporting of Observational studies in Epidemiology) for reporting observational studies (8). The report was created from a prospective institutional registry of major non-cardiac surgery, and it was approved by the ethics committee (RAMP registry, FVL Medical Research Ethics Committee; Protocol # 871). The study included patients over 18 years of age taken to major non-cardiac elective surgery in a Level IV institution between August 2015 and March 2019.

Registry data were entered by independent staff trained in data extraction from electronic medical records (SAP, Net Weaver GUI for Windows Business Software, Germany). The main inclusion criteria were defined as subjects undergoing non-contaminated elective procedures, with a risk of hemodynamic instability and major bleeding (blood loss of more than 20% of the blood volume), or who required hospitalization during at least 24 hours for postoperative care. Patients with active infections or who were receiving a course of antibiotics before surgery, subjects taken to transplant surgery, or records that lacked more than 10% of the data were excluded from the analysis. All subjects were assessed on a daily basis during the first hospitalization week (or up until discharge, if it happened first). In-hospital visits or weekly telephone calls were made after the first week until the end of the 30-day period.

The prospective registry included a total of 109 variables ranked in accordance with the following categories: demographics, preoperative characteristic, type of procedure, intraoperative management, fluid and transfusion therapy during the first 24 hours, and associated events during anesthesia induction, during the procedure and during the stay in the post-anesthetic care unit (PACU). Postoperative events in this analysis included SSI defined as any superficial, deep or surgery-related implant material infection, sepsis (systemic inflammatory response syndrome associated with suspected or proven infectious focus), renal dysfunction (serum creatinine increase of ≥ 0.3 mg/dL [≥ 26.5 µmol/L] or ≥ 1.5 times the preoperative value), and multiple organ dysfunction syndrome (MODS) (potentially reversible dysfunction of two or more organ systems) during the first week, and 7 to 30 days thereafter. These data were stored in a pre-designed electronic database (BD Clinic FVL-CIC, Cali, Colombia) for later analysis.

The main outcome for this analysis was SSI within the first 30 days after surgery. Results are expressed as medians (inter-quartile ranges) for continuous variables and as proportions for categorical variables. For initial comparisons, individuals were classified according to the presence or absence of this event. Statistical comparisons for categorical variables were carried out using the X2, and the Mann-Whitney U test was used for continuous variables after non-normality verification using the Shapiro-Wilks test. Risk associations with the main outcome were determined by means of the odds ratio (OR) calculations with their respective 95% confidence intervals (95% CI).

Logistic regression was used to build a multivariate model and the potential risk factors with a significance lower than or equal to 0.2 in the bivariate analysis were selected. To arrive at a most parsimonious model as possible, variables with a statistical significance greater than 0.05 in the initial model were removed. Risk estimates for potential associated factors were adjusted for the effect of age, gender and ASA classification variables. Adjusted ORs and their respective 95% CI are described. All descriptive and analytical analyses were carried out using the SPSS 10.0 software package for windows (IBM Products). A p value < 0.05 was considered significant.

RESULTS

Overall, 1501 patients were included in this analysis, and the incidence of SSI was 6.72% [95% CI 5.57-8.11). Of the sample analyzed, 77% were subjects taken to abdominal, head/neck, and limb surgery. The frequency of SSI was significantly higher among patients ASAIII or more (38.6% vs. 23.4%; p = 0,01), patients undergoing abdominal surgery (49.5% vs. 30.4%; p = 0.003) and longer procedures [180 (100-285) vs. 130 (90-190) min; p = 0.001] (Table 1). The 3-day incidence of sepsis, MODS and renal dysfunction was significantly higher in the SSI group when compared to the control group (p = 0.001) (Table 2).

The adjusted multivariate logistic regression model for SSI showed a significant association with preoperative hemoglobin levels (adjusted OR 0.79 [95% CI 0.72-0.88], p = 0.04), intraoperative transfusions (adjusted OR 2.47 [95% CI 1.16-5.27], p = 0.02) and major intraoperative bleeding (adjusted OR 3.80 [95% CI 1.63-8.88], p = 0.04) (Table 3). The risk model showed a progressively increased possibility of SSI with preoperative hemoglobin levels of less than 11 g/dL (Figure 1).

TABLE 1. Demographic and clinical characteristics.

Characteristics	Overall	Surgical site infection (n = 101)	No surgical site infection (n = 1,400)	*p* value
Age, years, median (IQR)	60 (44-70)	63 (48-73)	59 (44-70)	0.04
Gender,% Female Male	63.4 36.6	55.5 44.5	63.9 36.1	0.09
Diabetes mellitus, %	6.3	7.3	5.4	0.18
Chronic steroid use, %	2.7	3.8	1.6	0.07
Preoperative Hb, (g/dL)	13.1 (12.0-14.2))	12.3 (10.0-13.5)	13.2 (12.0-14.3)	0.24
Creatinine, mg/dL	0.8 (0.7-1.0)	0.8 (0.6-1.0)	0.81 (0.7-1.0)	0.48
Blood glucose, mg/dL	96.0 (89-106)	100 (93-111)	96 (91-106)	0.72
ASA status, % Class I Class II Class III Class IV	17.5 58.2 23.1 1.3	11.9 49.5 38.6 0	17.9 58.8 22 1.4	0.01
Anatomic area, % Central nervous system Head and neck Chest Abdomen Spine Limbs	 6.9 25.3 5.8 31.6 9.9 20.5	 4 15.8 5.9 49.5 9.9 14.9	 7.1 26 5.8 30.4 9.9 20.9	0.003
Operative time, min	130 (90-195)	180 (100-285)	130 (90-190)	0.001
General anesthesia, %	91.6	97	91.2	0.06
TIVA, %	5	5.9	13	0.04
NAA,%	14.9	14.9	15	0.9

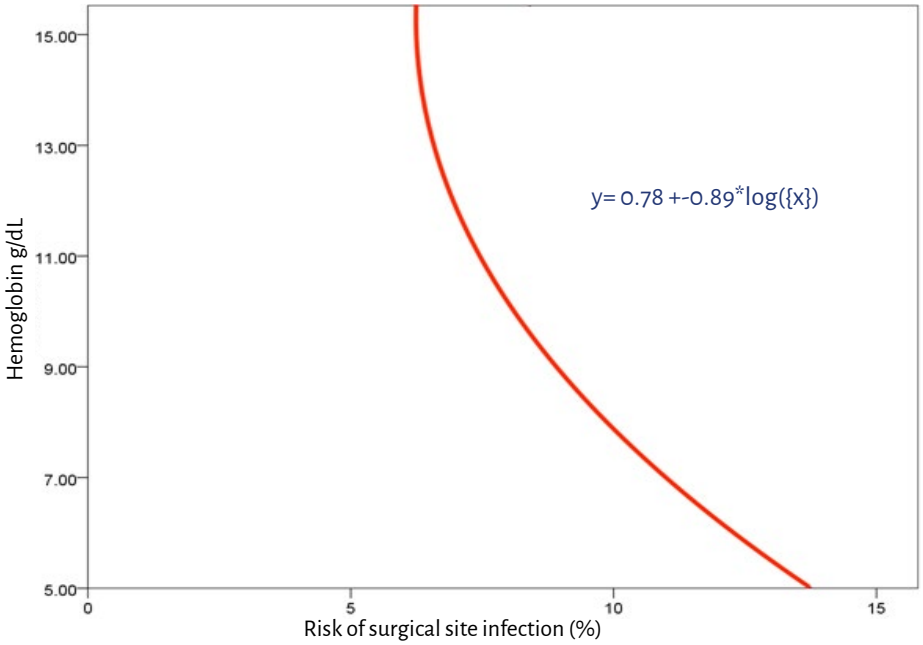
ASA: American Society of Anesthesiologist, Hb: hemoglobin, IQR: interquartile range, NAA: neuroaxial anesthesia, TIVA: total intravenous anesthesia. Data expressed as medians and interquartile ranges.
SOURCE: Authors.

TABLE 2. Surgical site infection and other secondary outcomes.

Outcomes	Overall* (95% CI)	Surgical site infection (n = 101)	No surgical site infection (n = 1,400)	*p* value
SSI	6.7 (5.6-8.1)	100	0	-
POP major blood loss**, %	2.8 (2.2-3.5)	3.1	2.7	0.08
Renal dysfunction, %	2.2 (1.6-3.1)	7.9	1.8	0.001
Sepsis, %	3.1 (2.4-4.2)	20.8	0.7	0.001
MOD,%	0.7 (0.4-1.3)	5.9	0.4	0.001

*Data expressed as proportions. SSI: surgical site infection.**Bleeding greater than 20% of the blood volume calculated for ideal weight. MOD: multiple organ dysfunction, POP: postoperative, SIS: Surgical site infection.
SOURCE: Authors.

FIGURE 1. Association between preoperative hemoglobin levels and surgical site infection (SSI) in major non-cardiac surgery. Logistic regression model adjusted by age, gender and preoperative ASA status for the cumulative incidence of SSI according to hemoglobin values (g/dL).



SOURCE: Authors.

TABLE 3. Adjusted model (age, gender and ASA) for surgical site infection risk

Variable	OR [95% CI]	*p* value
Tolerance to exercise < 4 MET	1.14 [0.41-3.21]	0.80
Intraoperative dexamethasone	0.89 [0.51-1.56]	0.69
Neuroaxial block	1.36 [0.71-2.63]	0.36
Occasional hypotension*	1.36 [0.84-2.89]	0.36
Major intraoperative bleeding (> 20% of blood volume)	3.80 [1.63-8.88]	0.04*
Intraoperative blood product transfusions**	2.47 [1.16-5.27]	0.02*
Sustained hypotension^	0.93 [0.58-1.51]	0.78
Intraoperative hypothermia (< 36 °C)	1.05 [0.33-3.36]	0.93
Hemoglobin, increase of 0.1 g/dL	0.79 [0.72-0.88]	0.04*
Creatinine, increase of 0.01 mg/dL	0.79 [0.72-0.88]	0.09
Blood glucose, increase of 1 mg/dL	1.001 [0.99-1.01]	0.75
Thyroid stimulating hormone, increase of 0.001 UI/dL	1.00 [0.99-1.01]	0.92

MET: metabolic equivalent at rest (3.5 mL O2/kg/min) , OR: Odds ratio.*Intraoperative recording of ≤ 2 isolated episodes of mean arterial pressure < 60 mmHg. ** Intraoperative transfusion of ≥ 1 unit of any blood product. ^Intraoperative recording of > 2 isolated episodes or sustained mean arterial pressure < 60 mmHg.

SOURCE: Authors.

DISCUSSION

HAIs are a strong indicator of healthcare quality. There is no doubt that SSI plays a significant role among this group of complications. This preliminary report of a prospective registry built in a Level IV Colombian hospital shows an incidence of SSI of 6.72% in adult patients undergoing major non-cardiac surgery during the first 30 days after the surgical intervention. Adjusted regression models found a significant association between low preoperative hemoglobin levels, intraoperative blood product transfusions and major bleeding and the possibility of SSI occurrence.

The incidence of SSI described in high income countries ranges between 2 and 5% (9). The incidence of SSI described in our paper is consistent with the WHO report on SSI for low and middle income countries (4). Our findings differ from others reported in recent local publications that point to considerably lower rates of SSI. In their work, Molina et al. (10) described an incidence of 1.8%, while the figure reported in a case control study was 1.1% (11). As potential explanations for these differences we may argue that the subjects in our study underwent major surgery, including more complex types of procedures than would usually be performed in conventional elective outpatient surgery services. Likewise, the probability of comorbidities, events and intraoperative complications would be especially frequent, increasing the risk for postoperative complications. We also believe that, given the prospective nature of the registry and the clear definition of the event of interest, underrecording in this study may have been lower than usual.

Among the risk factors associated with SSI occurrence, the most prevalent are those related to inadequate wound healing (smoking (12), old age (13), obesity, malnutrition (14), diabetes (15), immunosuppressive therapy (16)). Others, such as major bleeding, emergent

surgeries, operative time and type of anesthesia have also been described (17). Regarding the latter, studies have shown that patients receiving local anesthesia had a significantly lower incidence of SSIs as compared to those receiving general anesthesia, in cases in which a local approach could have been employed (18). It has been suggested that general anesthesia could be associated with greater changes in tissue perfusion, temperature and immune-mediated pharmacological effects (19).

In terms of potential explanations for the findings in this study, it may be that preoperative anemia is at the root of a higher probability of microcirculatory defects and poor intraoperative oxygen delivery. This could overexpose areas at risk of ischemia and inadequate healing later on. In this regard, a nested cohort study by Bartoszko et al. (20) actually showed an association between preoperative anemia (serum hemoglobin < 12.0 g/dL) and the development of respiratory failure, renal damage and surgical site infection, although it could not demonstrate an association with abnormal oxygen delivery. Likewise, Chenni Ji et al., in a case control study, found that low preoperative hemoglobin (< 11 g/dL) worked as an independent risk factor associated with SSI (17). In a study of 24,912 thyroid cancer patients, Burton et al. (21) had similar findings, showing an association between hematocrit levels (< 36% in non-pregnant women and < 39% in men) and postoperative infectious complications.

Just as this work and other studies in different surgical scenarios show (22), there is a direct relationship between major bleeding and a higher risk of SSI, among other adverse events. On the one hand, significant blood losses give rise to shock episodes of varying duration, leading to loss of endothelial integrity and perpetuating ischemia phenomena despite "sufficient" volume replacement with fluids and blood products. On the other hand, it may be that these patients with major bleeding may have been exposed to high blood product volumes, as shown by our final regression model. As far as this is concerned, prior publications have shown that perioperative transfusion of blood concentrates is associated with a higher risk of infection (up to 9%) for every unit of blood that is transfused (23,24). The findings of this study suggest that structured strategies such as the patient blood management (PBM) policy, could indirectly reduce SSI rates by intervening different preoperative conditions that increase transfusion exposure as is the case with anemia; and also the use at different levels of strategies designed to reduce bleeding (25).

Several scales are available for predicting the risk of developing SSI (26). One of these was developed by the National Nosocomial Infection Surveillance (NNIS) system that includes 3 factors (ASA III score, contaminated or dirty wound, and the duration of the procedure > 75th percentile) that allow to predict a risk of infection of 1%, 3%, 7% and 15%, according to the presence of 0, 1, 2 or 3 factors, respectively (27). A recent publication described the Surgical Site Infection Risk Score (SSIRS), a new model that helps determine the 30-day risk of SSI with better discrimination power than the NNIOS scale. According to the inherent SSI risk, it assigns codes to procedures (CPT3 Score), clinical conditions (smoking, higher body mass index, peripheral vascular disease, metastatic cancer, use of steroids and preoperative sepsis), and surgical factors (hospitalized patient or emergency, ASA III, more than one procedure during surgery, and prolonged operative time) (28). Like these, most predictive models for SSI share the duration of the surgery as an independent risk factor, as was the case in our study.

This is one of the most comprehensive reports concerning major non-cardiac surgery in Latin America. It is worth noting that because of its prospective nature and the predesigned database, it is less prone to the loss of information. However, there are limitations in these types of reports, in particular as relates to selection bias, given the systematic differences between the characteristics of the subjects selected for the study and those of the non-selected individuals. Inter-observer variability may also have negatively influenced the results considering the possibility that two individuals may perceive the same event differently, despite an attempt at minimizing measurement errors by means of the accurate definition of each variable or outcome. Finally, there is a probability that not all cases which met the inclusion criteria during the study period were recorded, given limitations in the ability to recruit all subjects with inclusion criteria, or failure to identify them.

In conclusion, this work shows that low hemoglobin levels, intraoperative transfusion and major intraoperative bleeding act as independent risk factors for the development of SSI within the first 30 days following major elective non-cardiac surgery in adult individuals. Surgical teams wishing to achieve an efficient reduction in the risk of this postoperative adverse event must focus on group strategies designed to work directly on preoperative optimization of hemoglobin levels, and must also revisit their practices for the prevention of perioperative blood losses. Likewise, studies of adequate quality are needed in order to show the true impact of these interventions on the occurrence of SSI and other postoperative infectious events.

ETHICAL CONSIDERATIONS

Human and animal protection

This research is in compliance with the World Health Organization (WHO) international regulations applicable to biomedical research, contained in the Declaration of Helsinki. It also abides by Resolution 8430 of 1993 of the Colombian Ministry of Health. According to the risk categories established, this research was considered free of risk, given its documentary nature.

Data confidentiality

The researchers ensured protection of the subjects in the study as well as privacy of

patient information through anonymity and strict confidentiality of the data entered in the data collection form, thus ensuring information confidentiality.

Right to privacy and informed consent.

No biological, psychological or social exposures different from those required for the surgical procedures were assigned to the patients. For that reason, the Ethics Committee decided to forgo the informed consent.

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Conflict of interest

The authors have no conflict of interest to disclose.

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Authors' contributions

FA: Study planning and methodological execution, interpretation of the results, drafting and editing of the final manuscript.
DAC: Patient entry in the database, statistical analysis, interpretation of the results, participation in the preparation of the manuscript.
JDBA: Patient entry in the database, participation in the preparation of the manuscript.
MQD: Interpretation of the results and participation in the discussion. Review and approval of the final manuscript.

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