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Mortality and Case Fatality Rates Associated With Surgical Site Infections: A Retrospective Surveillance Study

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(Article begins on next page)

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Mortality and case fatality rates associated with surgical site infections: a retrospective surveillance study

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3 **Mortality and case fatality rates associated with surgical site infections: a**
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6 **retrospective surveillance study**
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56 Surgical site infections; healthcare-associated infections; mortality; case fatality rate; surveillance;
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58 Italy.
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Abstract

Background. Surgical site infections (SSIs) have been associated with important increases in terms of costs, hospital stay, morbidity and mortality. We aimed to assess trends in SSIs monitored through 10 years of surveillance activities in our region, and to describe mortality attributable to SSIs in the two most frequently monitored surgical procedures: colorectal surgery and hip arthroplasty.

Methods. A retrospective cohort study was conducted among the 42 hospitals participating in the surveillance network of our region in Northern Italy. All colorectal and hip arthroplasty procedures performed between January 1st, 2010, and December 31st, 2019, and monitored through the surveillance system were included in the study. SSI rates, overall mortality, case fatality rates (CFR), and mortality attributable to SSIs were evaluated overall and by year of participation in the surveillance program.

Results. In total, 11,417 colon surgery and 20,804 hip arthroplasty procedures were included. Among colon surgery procedures, SSI rates decreased from 9.21% in 2010 to 5.7% in 2019. A significant decreasing trend was found for overall mortality (p 0.008), which progressively decreased from 4.96% in 2010 to 2.96% in 2019. Among hip arthroplasty procedures, no significant trend emerged for SSI and mortality rates. Considering the ten-year period, the CFR was 6.62% and 3.7% for SSIs following colon surgery and hip arthroplasty procedures respectively.

Conclusion. The impact of SSIs on the clinical outcomes of patients undergoing surgery highlight the importance of SSI surveillance.

~~Infection prevention and control activities, including surveillance, could have a positive effect in reducing the clinical and economic burden of SSIs.~~

Background

Healthcare associated infections (HAIs) are known to be associated with a significant burden for healthcare system worldwide.¹⁻⁴ In particular, surgical site infections (SSIs) are a frequent type of HAIs, and have been linked to important increases in terms of costs, hospital stay, morbidity and mortality.^{5,6} The economic burden is linked to the direct costs of hospitalization, such as the ones for diagnostic tests and treatment, but also to the prolonged hospital stay and eventually to a reoperation, if required.⁷ Moreover, Astagneau *et al.*⁸ previously described the associated burden in terms of mortality in patients with SSIs from 1997 to 1999, finding that 38% of deaths occurring among SSI patients were attributable to the infection itself, and identified SSIs as a significant predictor of mortality. A more recent study showed that crude mortality rates were higher in patients with SSIs for all the categories of surgery considered.⁹

SSIs are also considered to be among the most preventable HAIs.¹⁰⁻¹² An effective measure to reduce the incidence of SSIs are surveillance programs, as demonstrated by several previous reports.^{5,13-18} In this regard a robust methodology must be applied, standardizing definitions and data collection, and implementing a rigorous follow-up.¹⁰

In Italy, SSIs have been monitored through a national surveillance system for SSIs (Sistema Nazionale Sorveglianza Infezioni del Sito Chirurgico [SNICH])¹⁹ following the European centre for disease prevention and control (ECDC) HAI-SSI protocol for definitions, data collection and reporting methodology.²⁰ In the Piedmont region, in North-western Italy, surveillance through the national network began in 2008 and is ongoing, involving all public and some private hospitals in the region.^{5,21}

Considering the burden associated with SSIs in terms of mortality, it is worth exploring the issue. Therefore, the objective of this study was to update the findings of Astagneau *et al.*⁸ and give further insights into Italian epidemiology, assessing the trends through 10 years of surveillance activities, from 2010 to 2019, and describing mortality attributable to SSIs in the two most

frequently monitored surgical procedures: colorectal surgery and hip arthroplasty. In addition, this study aimed at identifying areas where quality improvement efforts should be focused.

Methods

Study design

A retrospective cohort study was conducted among the 42 hospitals participating in SNICH in Piedmont. All colorectal and hip arthroplasty procedures performed between January 1st, 2010, and December 31st, 2019, and monitored through the surveillance system were included in the study.

Data Collection

Data on included procedures were collected through SNICH, as previously reported in detail.^{5,22} Briefly, the surveillance system applies a national protocol based on the ECDC HAI-SSI network protocol.^{19,20} The participation in the network is voluntary and the surveillance is conducted for a minimum of six months each year, encouraging continuity. Demographic and clinical data are collected, including the occurrence of infection (within 30 days following the procedure for colorectal surgery, and 90 days for hip arthroplasty), and the state at discharge (alive or deceased in hospital). Post-discharge surveillance is performed through postoperative visits in the same hospital or through a standardized telephone interview.

Ethics

As stated in the SNICH protocol,¹⁹ the purposes of the program are surveillance of diseases and quality of care improvement, thus the written consent of patients involved or any other authorization from the Ethics Committee and/or the Protection Commissioner are not required. Additionally, the program is coordinated by public entities (National Centre for Disease Prevention and Control, Ministry of Health, Emilia-Romagna and Piedmont Regions). Patients are provided with an information sheet at admission to inform them about the hospital's participation in the

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3 surveillance program. All collected data are transferred anonymously to the regional coordinating
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5 center.

6 7 8 *Statistical analysis*

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11 Patient demographics were summarized using descriptive statistics. SSI rates, overall mortality,
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13 case fatality rates (CFR, *i.e.* number of deaths occurring among infected patients), and mortality
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15 attributable to SSIs (difference between mortality in patients with and without an SSI), were
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17 evaluated overall and by year of participation in the surveillance program. Pearson Chi-squared or
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19 Fisher exact tests were used to evaluate differences of distributions for the following categorical
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21 variables: gender, American Society of Anesthesiology (ASA) physical status score, infection risk
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23 index, elective or urgent/emergent procedure, and surgical technique (minimally invasive *vs.* open).
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25 Due to non-normal distribution at Shapiro-Wilk test, continuous variables were assessed using non-
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27 parametric Mann-Whitney U tests. Trends in SSI rates and overall mortality rates were calculated
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29 using Chi-squared tests for trends. Analyses were performed using IBM SPSS v.28.0.1 and setting
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31 two-tailed statistical significance at 0.05.
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40 **Results**

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43 In total, during the study period 11,417 colon surgery and 20,804 hip arthroplasty procedures were
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45 monitored in 27 and 35 hospitals, respectively. Descriptive characteristics of included patients,
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47 overall and comparing the first and final included years, are summarized in *Table 1*. Further detail
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49 on performed operations is provided in *Figures 1 and 2*. As shown in *Figure 1*, the proportion of
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51 partial colectomy procedures among all colon surgery procedures was around 80% throughout the
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53 study period. The proportion of revisional hip arthroplasty procedures progressively decreased from
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55 2010 to 2019 (*Figure 2*).
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3 Considering colon surgery procedures, a significant increase in the proportion of patients with an
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5 ASA score ≥ 3 was found comparing 2010 and 2019, however the proportion of minimally invasive
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7 procedures also increased significantly, reaching almost 50% in 2019. Pre-intervention and overall
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9 hospital length of stay (LOS) significantly decreased from 2010 to 2019.
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13 Considering hip arthroplasty procedures, significantly older patients underwent surgery in 2019
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15 compared to 2010. Comparing the same two years, there was a significant increase in the proportion
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17 of patients with ASA score ≥ 3 and urgent/emergent procedures. The distribution of infection risk
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19 index scores was also significantly different comparing 2019 to 2010, with a shift towards higher
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21 scores.
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25 *Tables 2 and 3* summarize considered outcomes: SSI rates, mortality rates, and CFR, per year.

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27 Overall, 936 and 297 SSIs occurred among patients undergoing colon surgery and hip arthroplasty
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29 procedures respectively, and a total number of 373 and 209 deaths were recorded. In total, 63.1% of
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31 SSIs occurred during the index hospital stay, whereas the rest occurred post-discharge. Median time
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33 to infection was 9 days (interquartile range, IQR 5 - 14) for SSIs after colon surgery procedures,
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35 and 20 (IQR 10 – 30.5) for SSIs after hip arthroplasty procedures.
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39 Among colon surgery procedures, SSI rates decreased from 9.21% in 2010 to 5.7% in 2019;
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41 however, no significant trend emerged (p 0.268). A significant decreasing trend was found for
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43 overall mortality (p 0.008), which progressively decreased from 4.96% in 2010 to 2.96% in 2019.
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45 Considering the ten-year period, the SSI rate was 8.2%, the overall mortality rate was 3.34% and
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47 the CFR was 6.62%.
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51 Among hip arthroplasty procedures, no significant trend emerged for SSI and mortality rates
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53 (respectively p 0.578 and p 0.253). Considering the ten-year period, the SSI rate was 1.43%, the
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55 overall mortality rate was 1% and the CFR was 3.7%.
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3 Among colon surgery procedures, 62 out of 373 deaths (16.62%) occurred among patients with an
4 SSI. Mortality among patients with and without infection was 6.62% and 2.97% respectively, with
5 an estimated attributable mortality of 3.65% for SSIs occurring following colon surgery procedures.
6
7 Among hip arthroplasty procedures, 11 out of 209 deaths (5.26%) occurred among patients with an
8 SSI. Mortality among patients with and without infection was 3.7% and 0.97% respectively, with an
9 estimated attributable mortality of 2.73% for SSIs occurring following hip arthroplasty procedures.
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11 Characteristics of deceased patients with vs. without SSI are reported in *Table 4*. As shown in the
12 table, the only significant differences emerged for overall LOS, which was higher among patients
13 developing SSI for both procedure categories.
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28 Discussion

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30 This study reports surveillance data collected over a ten-year period, including more than 30,000
31 procedures. The progressive increase in the number of both colon surgery and hip arthroplasty
32 procedures monitored is a first important result, which has led to an increased representativeness of
33 the surveillance system.
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40 Considering colon surgery, this study found a significant decreasing trend in overall mortality
41 during the ten-year period, even though the proportion of patients with ASA score ≥ 3 significantly
42 increased in 2019 compared to 2010. Further, a not significant, but progressive, reduction in SSI
43 rates of around 3.5% was observed, in line with previously described findings.⁵ SSI and mortality
44 rates following hip arthroplasty procedures also decreased non-significantly, probably due to having
45 reached a plateau in terms of preventable negative outcomes. This result is even more relevant when
46 considering that the continued widening of surveillance has resulted in the inclusion of older
47 patients as well as patients with greater clinical complexity, reflecting the demographic situation in
48 Italy.
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3 Comparing the procedure categories included in the study, the rate of SSIs after hip arthroplasty
4 was 4 times less frequent than after colon surgery procedures, and mortality following hip
5 arthroplasty was 50% lower than following colon surgery procedures. This result is consistent with
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10 studies describing variable mortality rates and incidence of SSI depending on the type of surgery
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12 considered.^{8,23}
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15 Previous studies have described a significant increase in mortality of patients with SSI.^{8,24} Based on
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17 the results of this study, we estimated an attributable mortality of around 4% for SSIs following
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19 colon surgery procedures and 3% for SSIs following hip arthroplasty procedures. Further, this study
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21 found a considerable increase in overall LOS in patients deceased with SSI in both types of surgery
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23 considered (median of 27.5 days for colon surgery and median of 41 days for hip arthroplasty), in
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25 accordance with previous findings of prolonged hospital LOS by about 7-11 days in patients with
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27 SSI, compared with patients without infection.²⁵ Therefore, our results support previous findings of
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29 increased economic burden associated with severe SSIs, in addition to the clinical burden in terms
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31 of increased morbidity and mortality.⁷
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36 SSIs are related to higher all-cause mortality rates, prolonged hospitalization, higher re-admission
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38 rates and increased costs for healthcare systems.^{7,23-24} On the other hand, standardized and
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40 continuous SSI surveillance has proven effective in reducing SSI rates, LOS, re-admissions and the
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42 negative impact on patients' quality of life,^{7,26-28} reducing related costs and improving the
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44 management of elective surgery waiting lists.^{29,30} According to our results, a significant reduction in
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46 both preoperative and overall LOS for colon surgery procedures and a reduction in overall LOS for
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48 hip arthroplasty procedures was found considering the ten-year period. Regarding colon surgery,
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50 these results are most likely ~~could be~~ due to thea significant increase in the proportion of minimally
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52 invasive approach, however ~~but could also be in part explained by~~ the reduction in SSI rates could
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54 also have contributed.
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3 The effectiveness of participation in surveillance networks in reducing SSI rates has been
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5 previously described in the literature.²⁶⁻²⁸ Moreover, the number of consecutive years of
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7 participation in surveillance networks has been associated with an increased impact in reducing SSI
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9 rates.⁵ Other factors such as improvements in infection prevention and control activities could have
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11 ~~contributed~~ contributed to decreasing SSI rates,²¹ in particular the adoption of a surgical bundle in
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13 our region has been associated with a positive impact of infection risk for both procedure
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15 categories.^{21,31} The 4-element bundle was introduced in 2012, and included the following evidence-
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17 based practices: preoperative showering, appropriate hair removal, antimicrobial prophylaxis (in
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19 terms of appropriate agent, timing, dose, and duration), and maintenance of intraoperative
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21 normothermia. The four elements of the bundle are established SSI prevention practices, however
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23 introducing the bundled intervention allowed to increase standardization and consistency of their
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25 implementation throughout our region, however surveillance activities could also have contributed, in
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27 turn positively affecting healthcare costs and healthcare organization, in particular in terms of
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29 optimization of the management of waiting lists for elective surgery.
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36 This study had several limitations. The most important limit was the lack of information on post-
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38 discharge deaths, due to surveillance design. As other studies have also pointed out, it would be
39
40 appropriate to monitor mortality longer after patient discharge,²³ or to be able to detect any SSI-
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42 related hospitalizations or deaths that have occurred post-discharge in other hospitals that are not part
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44 of the surveillance network. Based on the results shown in *Table 2*, we might assume worse clinical
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46 conditions of patients with SSI than those without, therefore further analysis with multistate models
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48 could be useful to avoid competing risk bias. Finally, we did not account for changing infection
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50 prevention and control activities over time or different implementation in participating hospitals.
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58 **Conclusions**

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3 Standardised data collection and participation in surveillance networks such as SNICH provide
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5 useful data for benchmarking purposes and allow to identify trends over time. The impact of SSIs
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7 on the clinical outcomes of patients undergoing surgery highlight the importance of SSI
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9 surveillance. ~~Infection prevention and control activities, including surveillance, could have a~~
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11 ~~positive effect in reducing the clinical and economic burden of SSIs.~~
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3 Conception and design: CV, CMZ; data collection: HSMAE, GP, ARC, NM; formal analysis: CV;
4
5 writing – original manuscript: CV, HSMAE, NM; writing – review and editing: CMZ; project
6
7 coordination: CMZ.
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12

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Tables

Table 1. Demographic and clinical characteristics of included patients, 2010-2019.

Characteristic	Colon surgery procedures (N=11,417)			Hip arthroplasty procedures (N=20,804)		
	Overall	2010 (N=836)	2019 (N=1490)	Overall	2010 (N=288)	2019 (N=3294)
Age, median (IQR)	72 (63 – 80)	72 (64 – 79)	72 (61 – 80)	75 (66 – 82)	70 (60 – 77)	74 (65 – 81)*
Male gender, n (%)	6137 (53.8)	437 (52.3)	819 (55)	8007 (38.5)	120 (41.7)	1350 (41)
ASA \geq 3, n (%)	5320 (46.6)	374 (44.7)	762 (51.1)*	8536 (41)	83 (28.8)	1452 (44.1)*
Infection risk index, n (%)						
0	2835 (24.8)	171 (20.5)	298 (20)	11026 (53)	138 (47.9)	1689 (51.3)*
1	5002 (43.8)	365 (43.7)	652 (43.8)	8167 (39.3)	97 (33.7)	1179 (35.8)*
2	2877 (25.2)	217 (26)	457 (30.7)	1015 (4.9)	8 (2.8)	365 (11.1)*
3	455 (4)	37 (4.4)	61 (4.1)	26 (0.1)	0	13 (0.4)*
Not applicable	248 (2.2)	46 (5.5)	22 (1.5)	570 (2.7)	45 (15.6)	48 (1.5)*
Minimally invasive	3606 (31.6)	176 (21.1)	730 (49)*	20688-116 (99.40.6)	288 (100) 0	3293 (100) 0

procedures, n (%)						
<u>Urgent/emergent</u> <u>procedures</u> <u>Non-</u> <u>elective</u> <u>procedures, n</u> (%)	2609 (22.9)	191 (22.8)	405 (27.2)	2630 (12.6)	18 (6.3)	559 (17)*
Pre-intervention LOS in days, median (IQR)	1 (1 – 2)	1 (1 – 1)	1 (0 – 1)*	1 (1 – 2)	1 (1 – 1)	1 (1 – 2)
Overall LOS in days, median (IQR)	10 (8 - 16)	12 (9 – 19)	9 (6 – 15)*	10 (8 – 14)	8 (7 – 11)	9 (7 – 13)*

*indicates statistical significance ($p < 0.05$). Differences between 2010 and 2019 values investigated using Pearson Chi-squared and Mann-Whitney U tests. ASA: American Society of Anesthesiologists physical status score; IQR: interquartile range; LOS: length of stay.

Table 2. Outcomes for patients undergoing colon surgery procedures, stratified by year.

Year	Total number of procedures	SSI rate (n, %)	OR (95% CI)	Mortality rate (n, %)*	OR (95% CI)	CFR (%)
2010	836	77 (9.21)	1	40 (4.96)	1	6.49
2011	394	40 (10.15)	1.11 (0.75 - 1.67)	12 (3.08)	0.61 (0.32 - 1.17)	5
2012	1326	152 (11.46)	1.28 (0.96 - 1.7)	55 (4.26)	0.85 (0.56 - 1.3)	7.89
2013	1251	96 (7.67)	0.82 (0.6 - 1.12)	24 (1.98)	0.39 (0.23 - 0.65)	1.04
2014	1070	101 (9.44)	1.03 (0.75 - 1.4)	34 (3.33)	0.66 (0.41 - 1.05)	6.93
2015	1082	111 (10.26)	1.13 (0.83 - 1.53)	29 (2.84)	0.56 (0.34 - 0.91)	4.50
2016	1153	72 (6.24)	0.66 (0.47 - 0.92)	35 (3.09)	0.61 (0.39 - 0.97)	5.56
2017	1120	83 (7.41)	0.79 (0.57 - 1.09)	43 (3.86)	0.77 (0.5 - 1.2)	9.64
2018	1695	119 (7.02)	0.74 (0.55 - 1)	57 (3.36)	0.67 (0.44 - 1.01)	10.92
2019	1490	85 (5.7)	0.6 (0.43 - 0.82)	44 (2.96)	0.59 (0.38 - 0.91)	5.88
<i>Total</i>	<i>11417</i>	<i>936 (8.2)</i>		<i>373 (3.34)</i>		<i>6.62</i>

*Not considering 252 procedures with missing status at discharge. CFR: case fatality rate; OR: odds ratio; SSI: surgical site infection.

Table 3. Outcomes for patients undergoing hip arthroplasty procedures, stratified by year.

Year	Total number of procedures	SSI rate (n, %)	OR (95% CI)	Mortality rate (n, %)*	OR (95% CI)	CFR (%)
2010	288	3 (1.04)	1	1 (0.35)	1	0
2011	386	5 (1.3)	1.25 (0.3-5.26)	2 (0.52)	1.5 (0.14 - 16.62)	0
2012	2046	59 (2.88)	2.82 (0.8784 to 9.0583)	17 (0.83)	2.44 (0.32 - 18.39)	5.08
2013	2232	38 (1.7)	1.65 (0.5046 to 5.3649)	20 (0.9)	2.6 (0.35 -19.42)	10.53
2014	2469	29 (1.17)	1.13 (0.3418 to 3.7301)	25 (1.02)	2.94 (0.4 - 21.75)	3.45
2015	2296	21 (0.91)	0.88 (0.2599 to 2.9584)	30 (1.32)	3.81 (0.52 - 28.07)	0
2016	2302	31 (1.35)	1.3 (0.3939 to 4.2690)	28 (1.23)	3.54 (0.48 - 26.13)	3.23
2017	2389	34 (1.42)	1.37 (0.4186 to 4.4943)	25 (1.05)	3.03 (0.41 - 22.44)	2.94
2018	3102	31 (1)	0.96 (0.2914 to 3.1563)	29 (0.93)	2.96 (0.4 - 21.82)	0
2019	3294	46 (1.4)	1.35 (0.4158 to 4.3532)	32 (0.97)	2.8 (0.38 -20.54)	2.17
<i>Total</i>	<i>20804</i>	<i>297 (1.43)</i>		<i>209 (1)</i>		<i>3.7</i>

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3 *Not considering 282 procedures with missing status at discharge. CFR: case fatality rate; OR: odds
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5 ratio; SSI: surgical site infection.
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Table 4. Characteristics of deceased patients with vs. without surgical site infection (SSI) following colon surgery and hip arthroplasty procedures, 2010-2019.

Characteristic	Colon surgery procedures		Hip arthroplasty procedures	
	Deceased patients without SSI (N=311)	Deceased patients with SSI (N=62)	Deceased patients without SSI (N=198)	Deceased patients with SSI (N=11)
Age, median (IQR)	80 (74 – 85.5)	79 (71.75 – 83)	86 (80.25 – 90)	83 (78 – 87)
Male gender, n (%)	163 (52.4)	31 (50)	96 (48.5)	5 (45.5)
ASA \geq 3, n (%)	266 (85.5)	60 (96.8)	158 (79.8)	10 (90.9)
Infection risk index				
0	17 (5.5)	2 (3.2)	29 (14.6)	1 (9.1)
1	88 (28.3)	16 (25.8)	150 (75.8)	9 (81.8)
2	164 (52.7)	36 (58.1)	10 (5.1)	1 (9.1)
3	30 (9.6)	8 (12.9)	0	0
Not applicable	12 (3.9)	0	9 (4.5)	0
Minimally invasive procedures, n (%)	36 (11.6)	4 (6.5)	198 (100)0	11 (100)0
Urgent/emergent Non-elective procedures, n (%)	191 (61.4)	37 (59.7)	65 (32.8)	3 (27.3)
Pre-intervention LOS in days, median (IQR)	1 (0 – 8)	2.5 (1 – 12)	2 (1 – 4)	3 (1 – 12)

Overall LOS in days, median (IQR)	16 (7 – 27)	27.5 (19.75 – 43.75)*	13 (7 – 21)	41 (34 – 64)*
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* indicates statistical significance ($p < 0.05$). Differences among patients deceased with vs. without

SSI investigated using Fisher's exact test and Mann-Whitney U test. ASA: American Society of

Anesthesiologists physical status score; IQR: interquartile range; LOS: length of stay.

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For Peer Review/NOT for Distribution

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3 **Figure 1.** Distribution of colon surgery operation types per year.
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15 **Figure 2.** Distribution of hip arthroplasty operation types per year.
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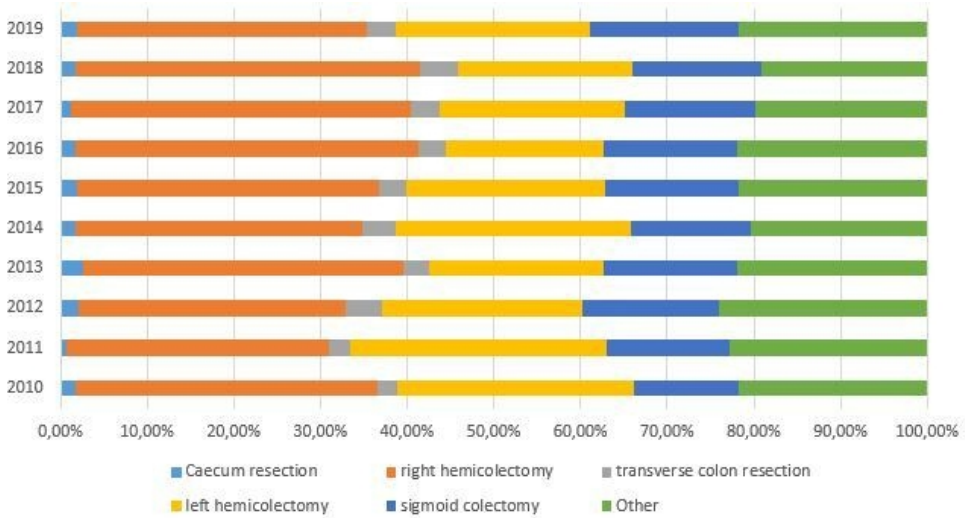


Figure 1. Distribution of colon surgery operation types per year.

55x29mm (300 x 300 DPI)

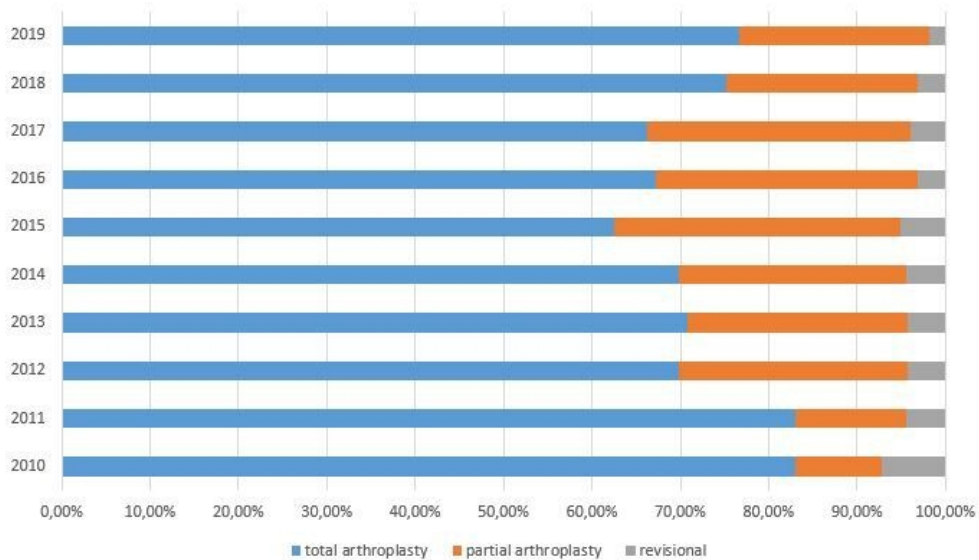


Figure 2. Distribution of hip arthroplasty operation types per year.

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