Dejavniki tveganja za pojav okužbe po kraniotomiji: 10-letna retrospektivna kohortna študija

Risk factors for surgical site infection following craniotomy: a 10-year retrospective cohort study

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Izvleček

Namen: *Kraniotomija je osnovni nevrokirurški pristop, ki je povezan z zapleti, med katere spada okužba kirurške rane, za pojav katere so dejavniki tveganja še vedno nepopolno definirani. Namen raziskave je bil prepoznati dejavnike tveganja za pojav okužbe kirurške rane pri odraslih bolnikih, operiranih na Oddelku za nevrokirurgijo Univerzitetnega kliničnega centra v Mariboru.*

Metode: *Izvedli smo retrospektivno kohortno študijo, v kateri smo analizirali podatke za obdobje od januarja 2009 do avgusta 2019. Primerjali smo podatke bolnikov, ki so razvili okužbo kirurške rane, s podatki tistih, ki okužbe niso razvili. 66 bolnikov je razvilo okužbo kirurške rane, v kontrolno skupino smo naključno uvrstili 70 bolnikov brez omenjene rane. V raziskavo smo vključili*

Abstract

Purpose: *A craniotomy is a common surgical procedure with complications, including a surgical site infection after craniotomy (SSI-CRAN), for which risk factors are ill-defined. Therefore, we determined the risk factors for developing an SSI-CRAN in adult patients at a university hospital in Maribor.*

Methods: *A retrospective cohort study was conducted to compare patients with an SSI-CRAN (n=66) against a control group (n=70) from January 2009 to August 2019. We collected data from patients in who elective craniotomy had been performed and required surgical treatment for an infection.*

Results: *A total of 1192 patients underwent a craniotomy, of whom 66 (5.5%) developed an SSI-CRAN. The most common infections were osteom-*

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le bolnike, ki so po opravljeni elektivni kraniotomiji potrebovali kirurško zdravljenje okužene kirurške rane.

Rezultati: *Med 1192 bolniki, ki so v opazovanem obdobju imeli opravljeno kraniotomijo, je 66 (5,5 %) bolnikov razvilo okužbo kirurške rane. Najpogosteje je prišlo do razvoja osteomielitisa (66,7 %) in epiduralnega abscesa (63,6 %), najpogosteje izoliran povzročitelj pa je bil Propionibacterium acnes (54,5 %). V raziskavi so se kot dejavniki, povezani s pojavom okužbe kirurške rane, izkazali uporaba izdelka Surgicel® (p = 0,0019, Fisherjev natančni test), duralni nadomestki (p = 0,0028, Fisherjev natančni test), samolepilna dura (p = 0,0274, Fisherjev natančni test), zapiranje kože s šivi (p = 0,0001, Fisherjev natančni test), opravljena frontalna kraniotomija (p = 0,0328, Fisherjev natančni test) in pooperativno predpisovanje glukokortikoidov (p = 0,04, Fisherjev natančni test).*

Zaključek: *Z našo študijo smo prepoznali določene dejavnike tveganja, povezane s pojavi okužbe kirurške rane, ki jih lahko odpravimo in tako znižamo pojavnost tovrstnega operativnega zapleta oz. zaplet hitreje prepoznamo.*

yelitis (66.7%) and epidural abscesses (63.6%). The most frequent causative organism was Propionibacterium acnes (54.5%). Based on Fisher's exact test, the factors associated with an SSI-CRAN compared to the control group were use of Surgicel® (89.4% vs. 67.1%, p=0.0019), use of dural substitutes (53% vs. 27.1%, p=0.0028), use of adhesive dura (13.9% vs. 2.9%, p=0.0274), sutures used for skin closure (69.7% vs. 34.3%, p=0.0001), a frontal craniotomy (28.8% vs. 12.9%, p=0.0328), and postoperative administration of glucocorticosteroids (73.7% vs. 54.4%, p=0.04).

Conclusion: *We identified risk factors associated with SSIs-CRAN, for which alternatives exist that could reduce the incidence of SSIs-CRAN.*

INTRODUCTION

A craniotomy is a surgical procedure in which a portion of the skull (bone flap) is removed to expose the underlying structures of the central nervous system and adjacent anatomic structures. During surgery the bone flap is separated from the rest of the skull and returned to its original anatomic site upon completion of the surgery before the skin is sutured, which separates the craniotomy from the craniectomy. Postoperative complications of craniotomies include hematomas (intracerebral, subdural, and epidural), stroke, postoperative epileptic seizures, acute hydrocephalus, pneumocephalus, cerebral edema, osteomyelitis of the bone flap, and extradural abscess formation (1-4). Depending on the anatomic location of the pathologic process, which is the indication for surgery, different craniotomies allow the most optimal approach to the surgical site. Importantly, the approach allows for achieving the desired results (e.g., tumour removal) without additional

nerve damage (3,5). A surgical site infection after craniotomy (SSI-CRAN) is an infection that develops at the site of surgery and can be a superficial or deep incision, or an organ-space SSI. A superficial incision SSI is an infection of the skin and subcutaneous tissue. A deep incision SSI is an infection of the muscles and fascia. An organ-space SSI is an infection of any organ or tissue in the surgical field under the muscle layer (6). An SSI-CRAN is a severe complication that requires timely diagnosis and treatment because such infections are associated with a high morbidity rate and the increased cost of hospital treatment. The predicted incidence of SSIs-CRAN is 5%, but ranges between 1% and 11% depending on the risk factors (7,8). Several risk factors for an SSI-CRAN, such as previous radiotherapy, previous brain surgery, a postoperative cerebrospinal fluid (CSF) leak, duration of surgery > 4 h, a body mass index ≥40 kg/m2, preoperative glucocorticosteroid use, emergency surgery, intraoperative breach into the sinus, concomitant infection, CSF drainage, entry into the venous sinus, > 2 points on the American Society of Anesthesiologists (ASA) point score, male gender, an atraumatic cause of craniotomy, age 70+ years, absence of antibiotic prophylaxis, preoperative chemotherapy, use of dural substitutes, infratentorial or intraventricular tumour location, hospital admission > 1 day before craniotomy, and multiple failed attempts at wound closure (9-18). An SSI-CRAN is often detected after discharge from the hospital. The clinical presentation of an SSI-CRAN depends on the anatomic location. In patients with superficial SSIs, there are signs of cellulitis. Deep SSIs are usually recognised by the presence of an abscess. Organ-space SSIs may be clinically manifested as meningitis, ventriculitis, or osteomyelitis (6).

An SSI-CRAN represents a significant and concerning postoperative complication. Patients affected by an SSI-CRAN often need another operation for treatment, hospitalisation, long-term antimicrobial therapy, increased costs, and the treatment of their primary disease may be delayed. In this retrospective cohort study, we determined risk factors for the development of an SSI-CRAN in patients who underwent surgery in the Department of Neurosurgery at the University Medical Centre Maribor to reduce the number of patients developing an SSI-CRAN.

MATERIAL AND METHODS

Study design and patients

A retrospective cohort study was conducted in the Department of Neurosurgery at the University Medical Centre in Maribor. We included patients who were surgically treated for an SSI-CRAN between January 2009 and August 2019. The study included patients who developed an SSI-CRAN after an elective neurosurgical procedure. Patients who developed an SSI-CRAN after an emergency craniotomy (e.g., head and brain injury) were not included in the study. We also did not include patients who required only conservative therapy (e.g., antibiotic treatment). Considering the inclusion and exclusion criteria, there were 66 patients with SSIs-CRAN. We also included 70 randomly selected patients who did not develop an SSI-CRAN after the elective neurosurgical procedure, who served as the control group.

Data collection and statistical analysis

We retrospectively reviewed the medical records of the patients with SSIs-CRAN and the control group. We considered the potential risk factors for the development of an SSI-CRAN. We analysed patient factors, such as gender, age at first surgery, smoking status, diabetes, arterial hypertension, liver cirrhosis, chronic kidney disease, and chronic obstructive pulmonary disease, and factors in the first surgery or factors related to the first surgery, such as average duration of hospitalisation for the first craniotomy, glucocorticosteroid administration before surgery and in the postoperative period, use of electrodes to control intracranial pressure, intraoperative breach of the sinuses, occurrence of a postoperative CSF leak, radiotherapy before surgery, type of craniotomy performed, pathohistologic diagnosis, indication for surgery, surgical material used, presence of infection at the time of hospital discharge after the first craniotomy, oncologic therapy after the first craniotomy, and

revision of the craniotomy before the onset of infection. The Statistical Package for Social Sciences (SPSS) for Windows (version 25.0.0.1) was used for statistical analysis of the data. Fisher's exact test was used for statistical analysis of the descriptive variables, and a t-test for independent samples was used for analysis of numerical variables. Statistical significance was set at a $p < 0.05$. Due to the retrospective nature of this study, approval by the Ethics Committee was not required.

RESULTS

During the observation period (1 November 2009-17 October 2019), 1192 elective craniotomies were performed in the Department of Neurosurgery at the University Medical Centre Maribor. Among the 1192 patients, 66 developed an SSI-CRAN that required re-operation. Based on this data, the overall incidence of SSIs-CRAN was 5.5%. The average length of hospitalisation for the first surgical treatment of the SSI-CRAN was 26.37 days (SD=30.73 days) and the average time between the first craniotomy and the diagnosis of an SSI-CRAN was 58.6 days (SD=52.57 days). Propionibacterium acnes was the most frequently isolated bacterium (54.5%), followed by coagulase-negative staphylococci (45.5%), and Staphylococcus aureus (39.4 %). The most common Gram-negative bacterium was Enterobacter cloacae (9.1%). Other isolated pathogens occurred in < 10% of patients with an SSI-CRAN; fungi were isolated in 3% of the patients. In the current study gender was not a statistically significant risk factor for the development of an SSI-CRAN. There were 52.9% men in the control group and 47% in the group with an SSI-CRAN (p=0.6069). The mean age in the control and SSI-CRAN groups (56.85±11.55 and 59.42±11.36 years, respectively; p=0.1767) at the first surgery and the duration of hospitalization (14.29±17 and 14.34±14.14 days, respectively; p=0.9852) for the first surgery did not represent statistically significant risk factors. The mortality during hospitalization was statistically higher in the group with an SSI-CRAN than in the control group (2.9% and 13.6%, respectively; p=0.0274).
Table 1 shows that osteomyelitis (66.7%) alone or

Table 1. *Group of patients with SSI-CRAN*

Group with SSI-CRAN	n = number
Infection site	
Epidural abscess	63.6% (n=42)
Subdural abscess	10.6% (n=7)
Intracerebral abscess	19.7% (n=13)
Subcutaneous abscess	31.8% (n=21)
Osteomyelitis	66.7% (n=44)
The number of operations required to treat an SSI-CRAN	
1	74.2% (n=49)
2	16.7% (n=11)
3	7.6% (n=5)
4	1.5% (n=1)
Number of isolated pathogens in each patient	
Polymicrobial infection	56.1% (n=37)
Monomicrobial infection	42.4% (n=28)
Sterile sample	1.5% (n=1)
Isolated pathogens	
Gram-positive bacteria	81.8% (n=112)
Gram-negative bacteria	16.8% (n=23)
Fungi	3% (n=2)

with an epidural abscess (63.6%) and vice versa was/were the most common infection sites. We identified the site of infection using a description given during the operation because imaging diagnostics of intracranial infections are often not completely reliable. Patients often developed infections at > 2 sites, resulting in an overall total > 100%. In most patients with an SSI-CRAN, only 1 operation was required to treat the infection and 25.8% of patients required > 2 operations. A polymicrobial SSI-CRAN was the most common finding and a Gram-positive bacterium was isolated in most cases (81.8%).

In the current study we determined whether patient characteristics were risk factors for an SSI-CRAN. For the control and SSI-CRAN groups, data on smoking status and co-morbidities (arterial hypertension, diabetes mellitus, chronic kidney disease, liver cirrhosis, and chronic obstructive pulmonary disease [COPD]) were obtained from the medical records. Figure 1 shows that smoking status and selected associated diseases did not have a statistically significant association with a SSI-CRAN. We attempted to determine whether the type of craniotomy, and thus the anatomic location of the procedure, posed a risk factor for the subsequent development of an SSI-CRAN. Figure 2 shows that frontal craniotomy was associated with the onset of an SSI-CRAN ($p = 0.0328$). Also, a pterional craniotomy was performed more often in the control group ($p=0.038$). The surgical procedure, such as reduction of the tumour or excision of metastases, was not represent a risk factor for development of an SSI-CRAN. We also showed that the histopathologic diagnosis of the excised lesion was not a risk factor for an SSI-CRAN. Moreover, the development of an SSI-CRAN was not influenced by the origin of the removed lesion (e.g., primary brain tumour or metastasis).

Furthermore, we examined the effects of preoperative (green square), intraoperative (blue square), and postoperative (yellow square) factors on the occurrence of an SSI-CRAN. Preoperative administration of glucocorticosteroids and prior radiotherapy were

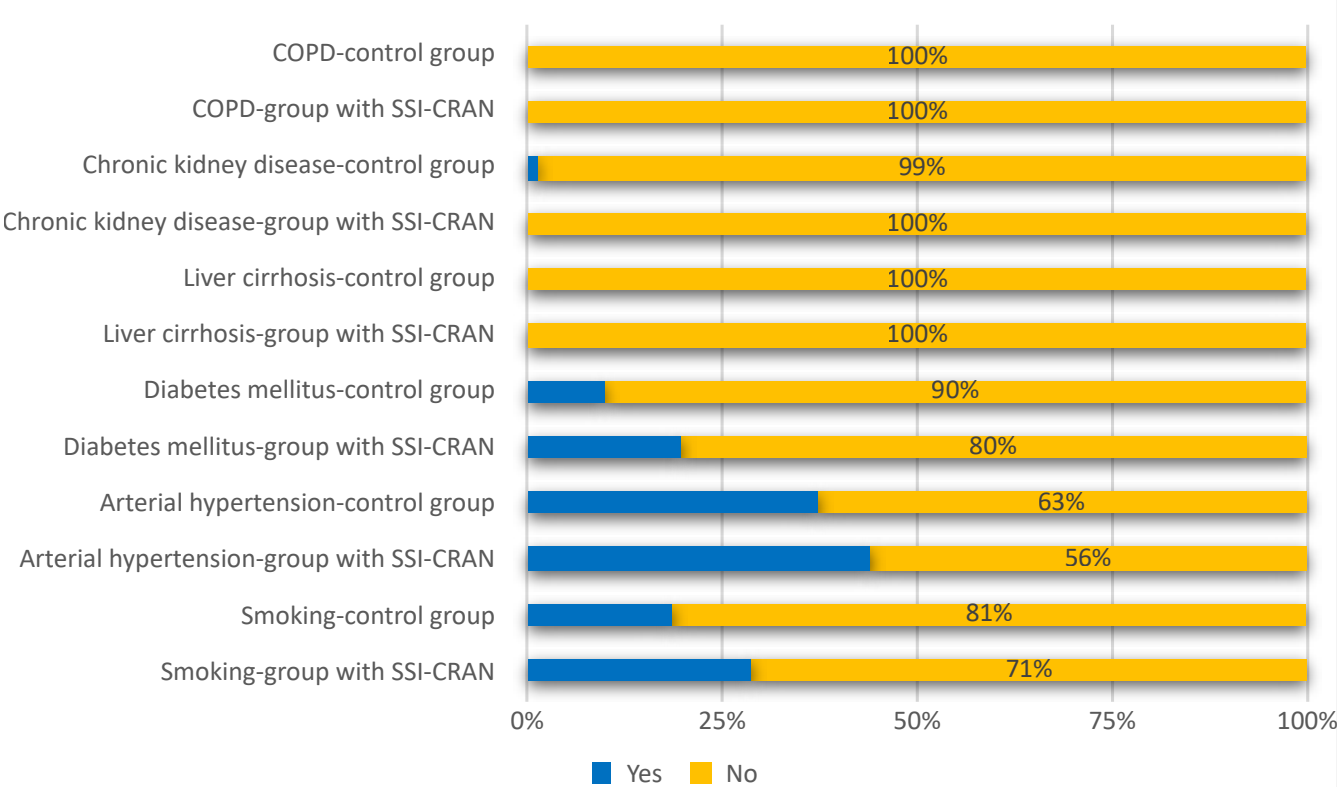

Figure 1. *Patients' factors.*

not risk factors for an SSI-CRAN. One patient in the control group and three patients in the group with an SSI-CRAN had an intraoperatively breached frontal sinus; however, intraoperative frontal sinus breach was not a risk factor for an SSI-CRAN nor was the use of electrodes to monitor intracranial pressure (ICP). Two patients from the control group had pneumonia at the time of hospital discharge and two patients from the SSI-CRAN group had lower urinary tract infections; however, infection at the time of hospital discharge was not a risk factor for an SSI-CRAN. Figure 3 shows that the prescription of glucocorticosteroids at the time of hospital discharge had a statistically significant association with the development of an SSI-CRAN (p=0.04). No patient characteristics during the postoperative period were risk factors for the development of an SSI-CRAN.

We then determined if any of the surgical materials used posed a risk for the subsequent development of an SSI-CRAN. Table 2 shows that the development of an SSI-CRAN was associated with the use of dural substitutes (p=0.0028), especially self-adhesive dura (p=0.0274); however, there were no statistically significant differences amongst other types of dural substitutes between the groups. In the group of patients who developed an SSI-CRAN the craniotomy wound was more frequently closed with sutures (p=0.0001), while the surgical wound was more frequently closed with staples in the control group (p=0.0001) and the dura was more frequently sutured (p=0.0001). There were no statistically significant differences between the groups with respect to the use of hemostatic agents; Surgicel® was more frequently used in the SSI-CRAN group (p=0.0019) and TachoComb® was more often used in the control group (=0.0241).

DISCUSSION

This retrospective cohort study of patients treated at Maribor University Hospital showed that the overall incidence of SSI-CRAN was 5.5%, which is in agreement with the 1%-11% incidence reported

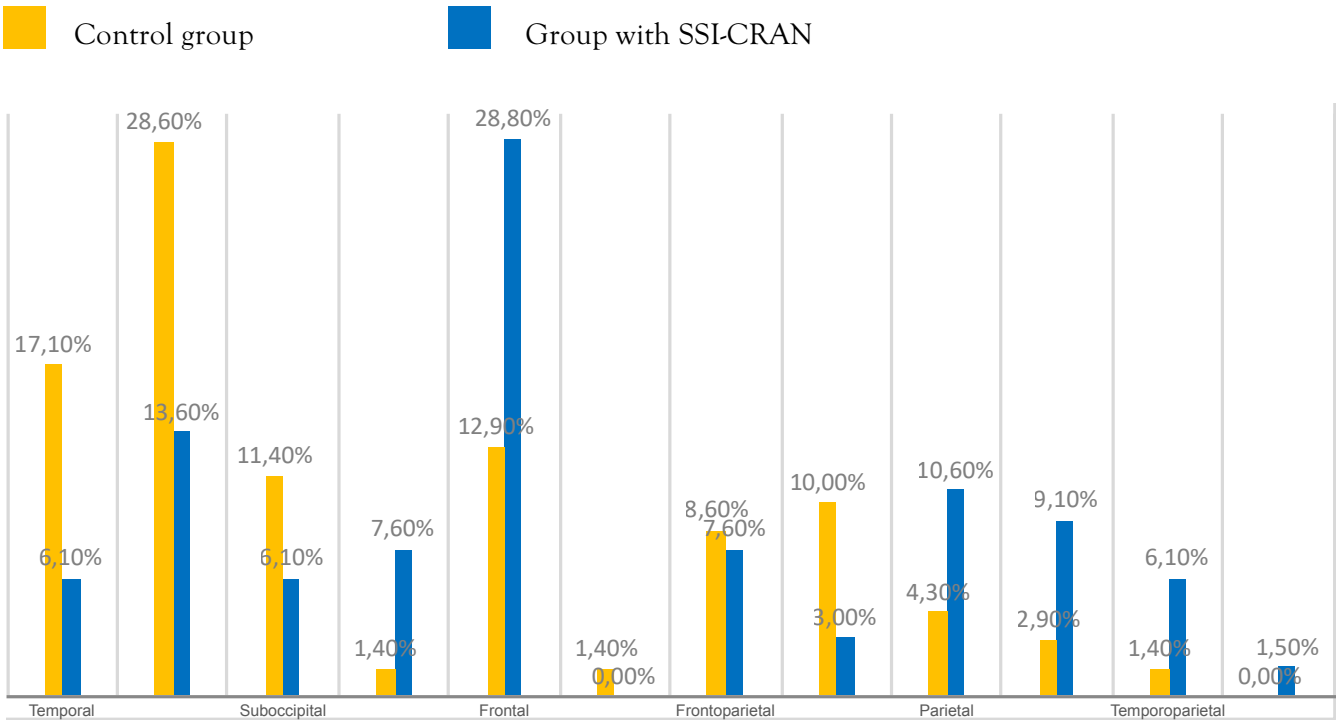

Figure 2. *Type of performed craniotomy.*

in other studies (1,8,19). Notably, a retrospective study reported a 0.5% incidence of SSI-CRAN over a 10-year period (7). It is possible that the incidence of SSI-CRAN in our patients was higher or that we operated sooner and allowed patients to continue with oncologic treatment as soon as possible. The average time of onset of an SSI-CRAN was 58.6 days (SD=52.57 days), which is longer than the 39 days (SD=54 days) in comparable studies (1). In another study, most SSIs-CRAN occurred within 2 weeks of surgery (9). In our study most patients with SSIs-CRAN were diagnosed after discharge from the hospital, which is similar to the results of related studies (20,21). The most prevalent SSIs were osteomyelitis (66.7%) and/or epidural abscesses (63.6%), as previously reported (7,20,22). In most cases, patients with an SSI-CRAN only required one surgery to treat the SSI (74.2%). In 56.1% of patients > 1 microorganism was isolated, with monomicrobial infections occurring in 42.4% of patients. Gram-positive bacteria were isolated in 81.8% of SSIs, which is in agreement with other studies (1,7,9,10,20,21). The most commonly isolated bacterium was Propionibacterium acnes (54.5%), followed by coagulase-negative staphylococci (45.5%) and Staphylococcus aureus (39.4%). The most commonly isolated bacterial genus was Staphylococcus (84.85%), as reported in previous studies (31,33). The most commonly isolated Gram-negative bacterium was Enterobacter cloacae (9.1%), as previously reported (1).

Smoking status, diabetes, arterial hypertension, liver cirrhosis, chronic kidney disease, and COPD were not shown to be risk factors for the development of SSI-CRAN. Likewise, gender and mean age at the time of first surgery were not risk factors for SSI-CRAN, which is comparable to data from other studies (1,7,19); however, a meta-analysis concluded that male gender was a risk factor for SSI-CRAN (23). In the current study there was no statistically significant difference in the mean duration of hospitalisation for the first craniotomy among the groups, while other researchers reported that hospitalisation after the first surgery was longer in the group of patients who subsequently developed an SSI-CRAN (19). In addition, we showed that hospitalization of patients with an SSI-CRAN was greater (26.37 days) than hospitalization for the first surgery (14.34 days).

The most common indication for the first craniotomy in both groups was removal of a primary brain tumour, as reported by others (1,7). Revision of the craniotomy was not shown to be a risk factor for an SSI-CRAN, which is in contrast to reports that concluded revision of a craniotomy to be a risk factor (8,20,23).

Preoperative administration of glucocorticosteroids and preoperative radiotherapy were not risk factors for the development of an SSI-CRAN; however, one study did conclude that preoperative chemotherapy and administration of glucocorticosteroids were risk factors for an SSI-CRAN (22). The use of electrodes to control intracranial pressure was also shown not to be a risk factor for an SSI-CRAN, in contrast to the findings in one study (9).

SSI-CRAN was more frequent in patients who underwent a frontal craniotomy (p=0.0328 [Fisher's exact test]), while intraoperative breach of the paranasal sinus was not a risk factor for an SSI-CRAN (p=0.3551 [Fisher's exact test]). Numerous studies have concluded that breach of the paranasal sinus is an important risk factor for an SSI-CRAN (24). The reason for this discrepancy is likely the small number of patients in our study where an intraoperative breach of the paranasal sinus was detected and documented in the medical records, both in the control (1.4% of patients) and SSI-CRAN groups (4.5% of patients). Considering that frontal craniotomy was a risk factor for SSI-CRAN, unlike breach of the paranasal sinus, it is possible that we overlooked some of the intraoperative breaches. We also found that pterional craniotomy was more frequently performed in the control group (p=0.038 [Fisher's exact test]); there were no statistically significant differences for the other types of craniotomies. We also did not demonstrate that the pathohistologic diagnosis of the removed lesion was a risk factor for the development of an SSI-CRAN based on a comparison of the two groups. In one study, the authors identified surgical treatment of extrinsic tumours as a risk factor for SSI-CRAN because such tumours require a more aggressive approach and are therefore associated with a more frequent occurrence of an SSI-CRAN (1).

The use of dural substitutes (p=0.0028 [Fisher's exact test]) was a risk factor for an SSI-CRAN. Of the types of dural substitutes, the self-adhesive dura (p=0.0274 [Fisher's exact test]) was more likely to be used in the group of patients who developed an SSI-CRAN. Likewise, other researchers have recognised the use of dural substitutes as a significant risk factor for an SSI-CRAN (10,19). A risk factor for the subsequent occurrence of an SSI-CRAN was closure of the skin with sutures versus staples (p=0.0001 [Fisher's exact test]), as reported in previous studies (25,26). We also found a study in which the use of staples was shown to be a risk factor for the occurrence of an SSI-CRAN (19). Taken together, we conclude that there is no convincing evidence regarding the safety of different materials with respect to the incidence of SSIs. The staples allow the wound to close faster, which may be one of the reasons for the lower incidence of SSIs. In addition, titanium staples are more inert than the materials used to make sutures (26). Moreover,

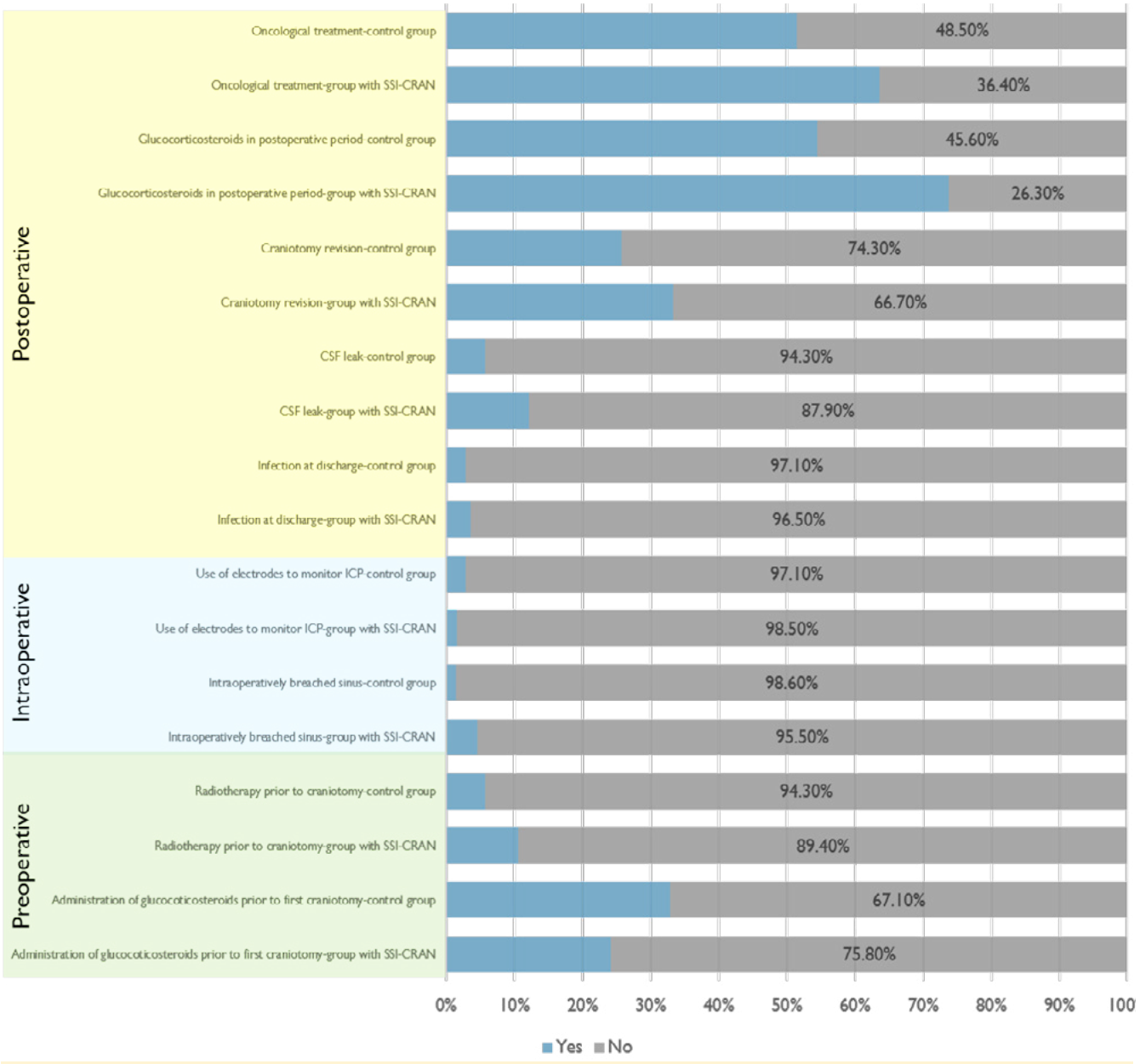

Figure 3. *Potential risk factors compared between the groups.*

when using sutures the risk of infection is increased by the development of a biofilm, which occurs more frequently when using multifilament sutures, but may also develop on the surface of monofilament sutures (1). There were no statistically significant differences between the two groups regarding the use of hemostatic agents. Surgicel® was more frequently used in the group of patients with an SSI-CRAN (p=0.0019 [Fisher's exact test]); no studies have reported similar findings. There was a statistically significant increase in the use of the hemostatic agent, TachoComb®, in the control group.

Referral to further oncologic treatment after the first craniotomy was not a risk factor for an SSI-CRAN. The data in other studies were not available regarding the number of patients commencing oncologic treatment after the first craniotomy (1,4,7). We did not demonstrate that a postoperative CSF leak was a risk factor for an SSI-CRAN, which may reflect the relatively small sample of patients in our study who developed CSF leaks postoperatively (4 patients in the control group and 8 patients in the SSI-CRAN group). Other studies have reported the occurrence of postoperative CSF leaks as a statistically significant risk factor for an SSI-CRAN (20,23). Infection at the time of discharge from the hospital after the first craniotomy was also not shown to be a risk factor. A review of the literature revealed one study that reported infection at the time of discharge from the hospital as a risk factor for an SSI-CRAN (23), but this was not the finding in most studies (1,4,7).

The administration of glucocorticosteroids in the early postoperative period was a risk factor for the development of an SSI-CRAN (p=0.04 [Fisher's exact test]). Glucocorticosteroids slow the wound healing process, increase the risk of wound dehiscence and subsequent infection, and also have immunosuppressive effects (27). Other researchers have also reported the use of glucocorticoids in the perioperative and early postoperative periods as a risk factor for an SSI-CRAN (17). In the SSI-CRAN group, death was statistically significantly more frequent during hospitalisation than in the control group (p=0.0274 [Fisher's exact test]). Similar findings have been reported other researchers (20).

Unlike other studies (1,8,19-21), a strength of our study was the 10-year observation period. In contrast, a weakness of in our study was the retrospective cohort design and a randomly selected control group because a case-control retrospective study with a large, carefully selected and balanced control group would have been a more suitable method with an increase in the statistical power of the result. An additional drawback of our study was the relatively small number of craniotomies performed over the entire period, and consequently, the small absolute number of patients who developed an SSI-CRAN compared to other studies, in which the number of patients varied between a few hundred and several thousand (1,7,19-21). A small sample was likely the reason that the intraoperative breach of the paranasal sinus and the postoperative appearance of the CSF leak were not considered a risk factor in our study, which is in contrast to other studies (20,23,34). Therefore, in the future, the results of our study should be verified in a larger group of patients with SSIs-CRAN at the national level. We intend to monitor the use of Surgicel® and TachoComb® in the future and the impact on the incidence of SSIs-CRAN as we are currently unable to explain these associations. Other factors (frontal craniotomy and administration of glucocorticosteroids in the postoperative period), which also appeared to be risk factors for an SSI-CRAN, cannot be changed, but it is important to recognize them nonetheless because this is the only way can we be more alert to patients with these risk factors and to recognize SSI-CRAN in a timely fashion.

UNITS AND ABBREVIATIONS

SSI-CRAN: Surgical site infection after craniotomy
CSF: cerebrospinal fluid
ASA: American Society of Anesthesiologists
SPSS: Statistical Package for Social Sciences
COPD: chronic obstructive pulmonary disease

Table 2. *The material used during the first craniotomy*

The material used during the first craniotomy	Control group (percentage, number of patients)	Group with SSI-CRAN (percentage, number of patients)	p-value
Hemostatic agents	120% (n=84)	133.3% (n=88)	p=1.0
Dural substitutes	27.1% (n=19)	53% (n=35)	p=0.0028
Dural suturing	95.7% (n=67)	71.2% (n=47)	p=0.0001
Fibrin sealant	65.7% (n=46)	78.8% (n=52)	p=0.1257
Drain located underneath the bone	32.9% (n=23)	31.8% (n=21)	p=1.0
CranioFix®	35.7% (n=25)	24.2% (n=16)	p=0.1907
Titanium bone plates and screws	57.1% (n=40)	72.7% (n=48)	p=0.0729
Skin suturing	34.3% (n=24)	69.7% (n=46)	p=0.0001
Skin stapling	65.7% (n=46)	30.3% (n=20)	p=0.0001
Drain located under galea	50% (n=35)	39.4% (n=26)	p=0.2315
Drain located epidurally	28.6% (n=20)	31.8% (n=21)	p=0.7117
Subcutaneous drain location	30% (n=21)	19.7% (n=13)	p=0.2343
Titanium mesh	0% (n=0)	6.1% (n=4)	p=0.0529
Bone cement	0% (n=0)	1.5% (n=1)	p=0.4853
Type of hemostatic agent			
Surgicel®	67.1% (n=47)	89.4% (n=59)	p=0.0019
TachoComb®	30% (n=21)	13.6% (n=9)	p=0.0241
TachoSil®	22.9% (n=16)	30.3% (n=20)	p=0.3389
Type of dural substitute			
Artificial dura	4.3% (n=3)	13.6% (n=9)	p=0.0714
Self-adhesive dura	2.9% (n=2)	13.6% (n=9)	p=0.0274
Bovine dura	2.9% (n=2)	0% (n=0)	p=0.4967
Bovine pericardium	1.4% (n=1)	1.5% (n=1)	p=1.0
Duraform®	2.9% (n=2)	3% (n=2)	p=1.0
Lyophilized dura	12.9% (n=9)	21.2% (n=14)	p=0.2534

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