Six-year experience of microvascular free-flap reconstruction of head and neck neoplasms

Experiencia de seis años en reconstrucción con colgajo libre microvascular en neoplasias de cabeza y cuello

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Las neoplasias de cabeza y cuello abarcan lesiones de pequeño tamaño hasta lesiones que pueden comprometer en gran proporción el área afectada. La resección de lesiones de gran tamaño traía aparejado secuelas funcionales, anatómicas y estéticas que otorgaban al paciente una alta morbilidad. En estos pacientes se debe considerar la mejor opción disponible para la reconstrucción luego de la resección. Es aquí donde el colgajo libre microvascular tiene un rol importante ya que es un procedimiento complejo que se realiza en centros especializados. No contamos en nuestra población con datos referentes a este tipo de reconstrucción por lo que resulta importante conocer los resultados y detectar que factores favorecen a presentar complicaciones con el colgajo.

Conceptos clave:
La reconstrucción con colgajo microvascular en neoplasias de cabeza y cuello es un procedimiento complejo que se realiza en centros especializados. No contamos en nuestra población con datos referentes a este tema por lo que resulta importante conocer los resultados y detectar que factores favorecen a presentar complicaciones con el colgajo.

Abstract:
Introduction: Microvascular free-flap reconstruction is one of the treatment options after large resection of head and neck neoplasms. The objectives of this study are to identify short-term outcomes and risk factors for flap complication in patients who underwent neoplasms resection of head and neck with microvascular free-flap reconstruction. Methods: Retrospective study of patients who underwent surgery for head and neck neoplasms with microvascular free-flap reconstruction between January 2014-2020. Complications were studied at 30-days follow-up and divided into medical and flap complications. Factors independently associated with flap complication were analyzed. Results: We included 31 patients (15 men). The mean age was 60 years. Reconstruction was performed with radial-forearm flap in 74% (n=23) and with free-fibula flap in 26% (n=8). Mean surgical time was 420 minutes. Median hospital length of stay was 7 days. Medical complications were of 23%. Minor complications were of 35% and major of 32%. There was no mortality in 30-days follow-up. Flap complications were of 35%. Reintervention was of 29%, surgical site infection of 9.7%, site dehiscence of 31% and paresthesia of 10%. Site infection was independently associated with prolonged surgical time (Odds ratio [OR]=1.62; p=0.03) and body mass index equal to or greater than 30 (OR=1.28, IC95%=1.03-1.62; p=0.03) while flap loss was associated with prolonged surgical time (OR=7.24, IC95%=1.4-73.1; p=0.01). Conclusion: Microsurgical free-flap reconstruction should be considered in our population in patients with large head and neck neoplasms. Preoperative assessment of the risk of postoperative complications is essential before selecting patients for this surgery.

Keywords: head and neck neoplasms; free tissue flaps; microsurgery; postoperative complications; risk factors.

Resumen:
Introducción: La reconstrucción con colgajo libre microvascular es una de las opciones disponibles luego de grandes resecciones de neoplasias de cabeza y cuello. Los objetivos de este estudio son identificar la morbitomortalidad postoperatoria y los factores de riesgo para complicación de colgajo en pacientes sometidos a resección de neoplasias de cabeza y cuello con reconstrucción con colgajo microvascular. Métodos: Se incluyeron pacientes con neoplasias de cabeza y cuello con reconstrucción con colgajo microvascular entre 2014-2020. Las complicaciones se estudiaron a 30 días. Se analizaron los factores asociados independientemente con complicación de colgajo. Resultados: Se incluyeron 31 pacientes. La edad media fue de 60 años. La reconstrucción con colgajo radial fue en 76% (n=23) y el colgajo fibular en 24%. La mediana de tiempo quirúrgico fue 420 minutos. La mediana de estadía hospitalaria fue 7 días. Las complicaciones médicas fueron del 24%. No hubo mortalidad en el seguimiento a 30 días. Las complicaciones del colgajo fueron del 38%. La reintervención fue del 31%, infección del sitio quirúrgico del 10%, desincisión del 31% y parestesias del 10%. La infección del sitio quirúrgico se asoció independientemente con tiempo quirúrgico prolongado (Odds ratio [OR]=1.62; IC95%=1.03-1.62; p=0.03) y índice de masa corporal mayor a 30 (OR=1.28, IC95%=1.03-1.62; p=0.03) mientras que la pérdida del colgajo se asoció a tiempo quirúrgico prolongado (OR=7.24, IC95%=1.4-73.1; p=0.01). Conclusión: La reconstrucción con colgajo libre microquirúrgico debe ser considerada una de las opciones de tratamiento en nuestra población en pacientes con grandes neoplasias de cabeza y cuello.

Palabras clave: neoplasias de cabeza y cuello; colgajos libres; microcirugía; complicaciones postoperatorias; factores de riesgo.

Resumen:
Introducción: A reconstrucción microvascular del retalho livre é uma das opções disponíveis após grandes ressecções de neoplasias de cabeça e pescoço. Os objetivos deste estudo são identificar a morbimortalidade pós-operatória e os fatores de risco para complicações do retalho em pacientes submetidos à reseção de malignidades de cabeça e pescoço com reconstrução de retalho microvascular. Métodos: Foram incluídos pacientes submetidos à cirurgia para neoplasias de cabeça e pescoço com reconstrução de retalho livre microvascular entre 2014-2020. As complicações foram estudadas aos 30 dias. Fatores associados independentemente à complicaçãod do retalho foram analisados. Resultados: 31 pacientes foram incluídos. A idade média foi de 60 anos. A reconstrução foi realizada com retalho radial em 76% e retalho de fibula em 24%. O tempo cirúrgico médio foi de 420 minutos. O tempo médio de internação foi de 7 dias. As complicações médicas foram de 24%. Não houve mortalidade no seguimento de 30 dias. As complicações do retalho foram de 38%. A reoperação foi de 31%, infeção do local cirúrgico de 10%, desincisão de 31% e perda de retalho de 10%. A infeção do sítio cirúrgico foi associada independentemente ao tempo cirúrgico prolongado (Odds ratio [OR]=1.62; IC95%=1.03-1.62; p=0.03) e Índice de massa corporal maior a 30 (OR=1.28; IC95%=1.03-1.62; p=0.03) enquanto a perda do retalho foi associada ao tempo cirúrgico prolongado (OR=7.24; IC95%=1.4-73.1; p=0.01). Conclusão: A reconstrução com retalho microcirúrgico livre deve ser considerada uma das opções de tratamento em nossa população em pacientes com grandes neoplasias de cabeça e pescoço.

Palavras-chave: neoplasias de cabeça e pescoço; retalhos de tecido livre; microcirurgia; complicações pós-operatórias; fatores de risco.
INTRODUCTION

Approximately 90% of head and neck neoplasms belong to squamous cell carcinoma, affecting 300,000 patients a year. One of the options for surgical reconstruction after large resections is microvascular free flap[1-6].

As for soft tissue flap, radial forearm (RF) flap and anterolateral thigh flap are the most frequently used in the reconstruction of head and neck tumors. The RF flap has the advantages of easy dissection, long vascular pedicle that allows anastomosis without tension and low morbidity of the donor site[7-9].

With respect to osteo-myo-cutaneous flap free fibula (FF) is the one chosen in our service. Bone and myocutaneous component can be extracted in a single flap that allows the grafting of both tissues simultaneously. Bone is of exceptional quality allowing multiple segmental osteotomies to mold the flap and reproduce the bone structure to be reconstructed[8-10].

The objectives of this study are to identify short-term outcomes and risk factors for flap complication in patients who underwent neoplasms resection of head and neck with microvascular free flap reconstruction.

METHODS

We performed a retrospective study including patients who underwent surgery for head and neck neoplasm with microvascular free flap reconstruction between January 2014 and January 2020. We included patients with head and neck neoplasms in which resection with microsurgical free flap reconstruction was performed regardless of loco-regional extension and prior resection.

Demographics, surgical indication, surgery and surgical time were analyzed. Complications were studied at 30-days follow-up and classified in minor (clinical management, without need of reintervention or intensive care unit admission) and major (surgical management or need of intensive care unit admission) complications. Mortality, hospital length of stay, reintervention and need for transfusions were analyzed. Flap complications included surgical site infection, dehiscence and flap loss.

Variables with a p<0.05 on the univariate analysis were included to the multivariate analysis. Factors independently associated with flap complication (surgical site infection, dehiscence and flap loss) were analyzed.

This study was performed in accordance with Helsinki Declaration of 1975 as revised in 1983. No experiments were performed on humans or animals. Protocols of our work center were followed on the publication of patient data.

Qualitative variables were analyzed with chi-square test while quantitative variables were analyzed with the Student T test. We identified the variables independently associated with flap complication from the multivariate analysis. For statistical analysis, the IBM SPSS Statistics 25 program was used.

RESULTS

We included 31 patients (15 men). The mean age was 60 years (Standard deviation [SD]=13). Reconstruction was performed with RF flap in 74% (n=23) and with FF flap in 26% (n=8). Demographic variables are presented in Table 1.

| Table N° 1: Demographics | Flap |
|--------------------------|------|
| **Variables**            |      |
| Sex                      |      |
| Male                     | 48% (15) |
| Female                   | 52% (16) |
| ASA                      |      |
| 2                        | 68% (21) |
| 3                        | 32% (10) |
| BMI (mean and SD)        | 28 (6) |
| Neoadjuvant therapy      | 13% (4) |
| Hypertension             | 48% (15) |
| Renal disease            | 3% (1) |
| Diabetes                 | 16% (5) |
| Heart disease            | 13% (4) |
| Alcoholism               | 32% (10) |
| Smoking                  | 24% (13) |

ASA (American Society of Anesthesiologists), BMI (Body mass index), SD (Standard Deviation).

Table N° 2: Surgery and Staging

| Table N° 2: Surgery and Staging | Flap |
|---------------------------------|------|
| **Variables**                   |      |
| Primary sites                   |      |
| Floor of mouth                  | 19% (6) |
| Tongue                          | 23% (7) |
| Retromolar trigone              | 16% (5) |
| Mandible                        | 13% (4) |
| Gingiva                         | 10% (3) |
| Buccal mucosa                   | 13% (4) |
| Oropharynx                      | 3% (1) |
| Scalp                           | 3% (1) |
| T Stage                         |      |
| T1                               | 29% (7) |
| T2                               | 38% (9) |
| T3                               | 25% (6) |
| T4                               | 8% (2) |
| N Stage                         |      |
| N0                               | 64% (14) |
| N1                               | 18% (4) |
| N2                               | 13% (3) |
| N3                               | 5% (1) |
| Stage                            |      |
| I                                | 15% (4) |
| II                               | 33% (9) |
| III                              | 37% (10) |
| IV                               | 15% (4) |
Median hospital length of stay was 7 days (SD=11). Medical complications were of 23% (n=7). Minor complications were of 19% (n=6) and major of 35% (n=11). Transfusions were required in 26% (n=8). There was no mortality in 30-days postoperative follow-up (Table 3).

Flap complications were of 35% (n=11). Reintervention was of 29% (n=9), surgical site infection of 9% (n=3), dehiscence of 29% (n=8) and flap loss of 9.7% (n=3). All cases of flap loss were on FF flap group. The most frequent tumor was squamous carcinoma (80%) followed by ameloblastoma (10%). Surgical margins were clear in 94%.

Biopsy results are shown in Table 4. Adjuvant therapy was performed in 58% (n=18), chemotherapy on 26% (n=8) and radiotherapy on 52% (n=16).

Univariate analysis was performed for flap complication, surgical site infection, dehiscence and flap loss and the results are shown on Table 5. Multivariate analysis showed that surgical site infection was independently associated with surgical procedure greater than 8 hours and body mass index equal to or greater than 30 while flap loss was associated with surgical procedure greater than 8 hours. No statistical differences were found with the rest of the variables analyzed (Table 6).

### Table N° 3. Complications

| Complication                      | % & (n) |
|-----------------------------------|---------|
| Minor (Without reintervention or ICU) | 19% (6) |
| Surgical site infection           | 1       |
| Dehiscence                        | 3       |
| Cervical fistula                  | 1       |
| Donor site infection              | 1       |
| Major (Reintervention or ICU)     | 35% (11)|
| Mechanical ventilation            |         |
| Respiratory distress              | 1       |
| Septic shock                      |         |
| Reintervention                    | 7       |
| Dehiscence                        |         |
| Surgical site infection           | 2       |

(ICI: Intensive Care Unit)

### Table N° 4. Biopsy

| Variables          | Flap       |
|--------------------|------------|
|                    | Squamous carcinoma | 80% (24) |
|                    | Radio-induced carcinoma | 3.3% (1) |
|                    | Fibrohistiocitoma | 6.7% (2) |
|                    | Ameloblastoma | 10% (3) |
|                    | Odontogenic myxofibroma | 3.4% (1) |

### Table N° 5: Univariate analysis

| Variables          | Flap complication | Dehiscence | SSI | Flap loss |
|--------------------|-------------------|------------|-----|-----------|
|                    | - | + | p   | - | + | p   | - | + | p   | - | + | p   |
| Age over 60 years  | 54% (6) | 46% (5) | 0.8  | 55% (5) | 45% (4) | 0.95 | 33% (1) | 67% (2) | 0.57 | 67% (2) | 33% (1) | 0.66 |
| BMI > 30           | 64% (7) | 36% (4) | 0.5  | 67% (6) | 33% (3) | 0.73 | - | 100% (3) | 0.05 | 33% (1) | 67% (2) | 0.66 |
| Smoking            | 54% (6) | 46% (5) | 0.76 | 55% (5) | 45% (4) | 0.85 | 100% (3) | - | 0.24 | 67% (2) | 33% (1) | 0.75 |
| Alcoholism         | 64% (7) | 36% (4) | 0.7  | 67% (6) | 33% (3) | 0.93 | 100% (3) | - | 0.53 | 67% (2) | 33% (1) | 0.96 |
| Diabetes           | 100% (11) | - | 0.07 | 100% (9) | - | 0.26 | 100% (3) | - | 0.42 | 100% (3) | - | 0.42 |
| Previous radiotherapy | 82% (9) | 18% (2) | 0.6  | 78% (7) | 22% (2) | 0.56 | 67% (2) | 33% (1) | 0.34 | 67% (2) | 33% (1) | 0.34 |
| Surgical time > 8 hours | 82% (9) | 18% (2) | 0.26 | 78% (7) | 22% (2) | 0.67 | - | 100% (3) | 0.04 | - | 100% (3) | 0.04 |
| Previous intervention | 72% (8) | 28% (3) | 0.8  | 78% (7) | 22% (2) | 0.77 | 33% (1) | 67% (2) | 0.15 | 67% (2) | 33% (1) | 0.75 |

BMI (Body mass index), SSI (Surgical site infection)

### Table N° 6: Multivariate analysis

| Variables          | SSI OR | IC95% | p   | Flaps loss OR | IC95% | p   |
|--------------------|--------|-------|-----|---------------|-------|-----|
| Age over 60 years  | 0.99   | 0.65-15.4 | 0.98 | 54.8 | 0.001-278 | 0.54 |
| BMI > 30           | 1.28   | 1.03-1.62 | 0.03 | 0.35 | 0.01-192 | 0.74 |
| Previous radiotherapy | 0.42   | 0.16-11.59 | 0.61 | 0.49 | 0.01-74 | 0.41 |
| Surgical time > 8 hours | 1.12   | 1.02-1.34 | 0.03 | 7.24 | 1.4-73.1 | 0.01 |
| Previous intervention | 0.17   | 0.09-3.18 | 0.23 | 0.71 | 0.01-490 | 0.92 |

BMI (Body mass index), SSI (Surgical site infection)
DISCUSSION

Microvascular free flap reconstruction allows anatomical and functional structures to be restored after large resections for head and neck tumors[2,3]. In this study we analyzed short-term outcomes and risk factors for flap complication.

Regarding to medical complications, similar results were published in other series that mention between 2-47%[3,7,11,12]. Kamnerdnakta[3] et al presented his experience in 5 years and observed 27.5% of medical complications while Suh[11] et al in 399 patients presented 20.6%. Despite the fact that the 23% of medical complications presented in our series is within the previously mentioned, this high number could be explained since we present an elderly population with many comorbidities exposed to large surgeries. On the other hand, we do not have mortality in 50-day postoperative follow-up. Hoffman[13] et al in his experience with 107 patients presented 2.8% mortality similar to other series[11,12,14-16]. We presented a flap complication of 35%. Kamnerdnakta[3] et al reported 49.7% while Zhao[12] et al in an analysis of 1796 patients observed 44.2%. Haughey[15] on the other hand, observed 29% in 241 patients, a percentage lower than published by other series. Reintervention was needed in 29% of patients on our study. Variable results are presented so far which mention a reintervention between 5-25%[3,8,13]. Pastars[16] demonstrated his 8-year experience with 153 consecutive cases where he presented a 15% reintervention. We present our initial experience on microsurgical free flap reconstruction on head and neck neoplasms so it is expected that results may be higher than published in other series.

We divided flap complications into dehiscence, surgical site infection and flap loss. Results published by other authors regarding flap dehiscence are varied and range between 5-20%[3,12,13,15]. Kamnerdnakta[3] presented 20% flap dehiscence while Zhao[12] 5.7%. As regards surgical site infection, large series mention between 2-31%[3,9,11,12]. We observed a 9.7% flap loss, at the higher limit recommended by other series (2-10%)[3,9,11,16]. One of the cases lost was due to venous thrombosis in the immediate postoperative period with need of reintervention and revascularization, which finally had to be extracted due to necrosis. Another case was lost due to infection and dehiscence. The third case was an alcoholic and smoking patient who presented an episode of hemorrhage with the need of reintervention that finally presented flap dehiscence and necrosis.

When comparing our results with big series we found that we present a similar number of flap complications. When analyzing by type of complications dehiscence and flap loss are within the higher limits recommended. As mentioned before, these results are expected since it is our initial experience on this subject. Moreover, it should be considered that head and neck patients usually present many comorbidities that may predispose to complications.

Multiple risk factors for flap complications have been reported, among them stand out preoperative status, age over 60 years, smoking, ASA (II and Ill), alcoholism, diabetes, preoperative radiotherapy, surgical expertise, mandiblectomy, existence of an oral-neck defect and surgical time[3,13,19-20]. Preoperative radiotherapy has been described as one of the main determinants of the outcomes on head and neck microvascular reconstruction in some series. Zhou[21] found that it was a risk factor for flap failure while Benatari[22] found that it was a risk factor for cervical fistula and surgical site infection. In our study we found no difference on those patients who received radiotherapy when analyzing flap complications.

On the other hand, surgical procedure greater than 8 hours was independently associated with surgical site infection and flap loss in our series. Longer operative time reflected the higher complexity of surgery as well as greater extent of destruction, thereby increasing the risk of wound exposure to a micro bacterial environment[14,20]. In addition, surgical site infection could be related with dehiscence and the consequent flap loss. Ishimaru[23] found in a retrospective study of 2846 patients that flap loss was related with duration of anesthesia longer than 18 hours compared with 12 hours in contrast with our study in which prolonged surgical time were surgeries longer than 8 hours.

Obesity was also related to surgical site infection in our study. Head and neck neoplasms presents on patients which generally have many comorbidities that may predispose to complications. As mentioned before, many risk factors for flap complication have been reported so far, many of them related with obesity[3,14,19]. A proper and critical preoperative assessment of the risk of postoperative complications is essential before such patients are selected for extensive oncological and reconstructive surgery[14].

This study has limitations. These includes its retrospective, non-randomized design that presents a small number of cases. However, we believe it demonstrates the safety of microvascular flap reconstruction on head and neck neoplasms in short-term outcomes. Microsurgical free flap reconstruction should be considered one of the treatment options in our population in patients with large head and neck neoplasms since our short-term outcomes are similar to large series. However, a proper preoperative assessment of the risk of postoperative complications is essential before selecting patients for this type of surgery.

Limitaciones de responsabilidad:
La responsabilidad de este trabajo es exclusivamente de los autores.

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Todos los autores han participado en la concepción del diseño, recolección de la información y elaboración del manuscrito, haciéndose públicamente responsables de su contenido y aprobando su versión final.

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