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

Experiencia de seis anos na reconstrução microvascular de retalho libre de neoplasias de cabeça y pescoço

Santiago Olguín Joseau[1,2,3], Ariel Arias[1,2], Juan Carlos Sánchez[1,2], Pablo Valle[1,2], Agustín Garzón[2], Emiliano Peretti[1,2], Luis Guzmán[1], Marcelo Ruggieri[1,2].

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 trae aparejado secuelas funcionales, anatómicas y estéticas que otorgan 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.

1- Hospital Privado Universitario de Córdoba. Córdoba, Argentina
2- Hospital Raúl A Ferreyra. Córdoba, Argentina.
3- ORCID: https://orcid.org/0000-0001-5539-0905. E-mail de contacto: santiaolguin@gmail.com

Recibido: 2020-07-21 **Aceptado:** 2020-09-16

DOI: http://dx.doi.org/10.31053/1853.0605.v78.n4.29523

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 neoplasm 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%, dehiscence of 29% and flap loss of 9.7%. Surgical site infection was independently associated with prolonged surgical time (Odds ratio [OR]=1.12, IC95%=1.02-1.34, 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 morbimortalidad 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 operados por neoplasia de cabeza y cuello con reconstrucción con colgajo libre 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 se realizó con colgajo radial en 76% y de peroné 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%, dehiscencia del 31% y pérdida del colgajo del 10%. La infección de sitio quirúrgico se asoció independientemente con tiempo quirúrgico prolongado (Odds ratio [OR]=1,12; IC95%=1,02-1,34; p=0,03) e 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 con 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.

Resumo:

Introdução: A reconstrução microvascular do 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 ressecção de malignidades de cabeça e pescoço com reconstrução de retalho microvascular. **Métodos:** Foram incluídos pacientes submetidos à cirurgia para neoplasia de cabeça e pescoço com reconstrução de retalho livre microvascular entre 2014-2020. As complicações foram estudadas aos 30 dias. Fatores associados independentemente à complicação 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 fíbula 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%, infecção do local cirúrgico de 10%, deiscência de 31% e perda de retalho de 10%. A infecção do sítio cirúrgico foi associada independentemente ao tempo cirúrgico prolongado (Odds ratio [OR]=1,12; IC95%=1,02-1,34; p=0,03) e índice de massa corporal maior que 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-myocutaneous 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

Variables	Flap
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).

Neoadjuvant therapy was performed in 14% (n=4) and in all of them chemotherapy was used. Prior resection was present in 26% (n=8). Mean surgical time was 420 minutes (SD=105). Location of tumor and staging is shown in Table 2.

Table N° 2: Surgery and Staging

Variables	Flap
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).

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	1
Reintervention	
Dehiscence	7
Surgical site infection	2

ICU (Intensive Care Unit)

Flap complications were of 35% (n=11). Reintervention was of 29% (n=9), surgical site infection of 9% (n=3), dehiscence of 29% (n=9) 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).

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)
Differentiation	
Well	25% (6)
Moderate	63% (15)
Poor	12% (3)

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° 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
Alocoholism	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)	056	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			Flaps loss		
	OR	IC95%	p	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 12-47%[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 30-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%[3,8,12]. Pastars[17] 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]. Kemmnerdnakta[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%)[3,7-9,11-5,17,18]. 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 III), alcoholism, diabetes, preoperative radiotherapy, surgical expertise, mandibulectomy, existence of an oral-neck defect and surgical time[3,14,19-25]. 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 Benatar[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[3,14,19,20]. 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.

Conflicto de interés:
Ninguno

Fuentes de apoyo:
La presente investigación no contó con fuentes de financiación.

Originalidad:
Este artículo es original y no ha sido enviado para su publicación a otro medio de difusión científica en forma completa ni parcialmente.

Cesión de derechos:
Los participantes de este trabajo ceden el derecho de autor a la Universidad Nacional de Córdoba para publicar en la RFCM y realizar las traducciones necesarias.

Contribución de los autores:
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.

REFERENCES

1- Balasubramanian D, Thankappan K, Kuriakose MA, Duraisamy S, Sharan R, Mathew J, Sharma M, Iyer S. Reconstructive indications of simultaneous double free flaps in the head and neck: a case series and literature review. Microsurgery. 2012 Sep;32(6):423-30. doi: 10.1002/micr.21963.

2- Kim L, King T, Agulnik M. Head and neck cancer: changing epidemiology and public health implications. Oncology (Williston Park). 2010 Sep;24(10):915-9, 924.

3- Kamnerdnakta S, Boochangkool N. Five-Year Review Outcome of Microvascular Free Flap in Siriraj Hospital. J Med Assoc Thai. 2015 Oct;98(10):985-92.

4- American Cancer Society. Cancer facts and figures 2003. Alabama. 2003 Available from: https://adph.org/ascr/assets/AlaCancerFactsFigures2003.pdf.

5- Kademani D. Oral cancer. Mayo Clin Proc. 2007 Jul;82(7):878-87. doi: 10.4065/82.7.878. Erratum in: Mayo Clin Proc. 2007 Aug;82(8):1017.

6- de Vicente JC, Rodríguez-Santamarta T, Rosado P, Peña I, de Villalaín L. Survival after free flap reconstruction in patients with advanced oral squamous cell carcinoma. J Oral Maxillofac Surg. 2012 Feb;70(2):453-9. doi: 10.1016/j.joms.2011.02.020.

7- Kesting MR, Hölzle F, Wales C, Steinstraesser L, Wagenpfeil S, Mücke T, Rohleder NH, Wolff KD, Hasler RJ. Microsurgical reconstruction of the oral cavity with free flaps from the anterolateral thigh and the radial forearm: a comparison of perioperative data from 161 cases. Ann Surg Oncol. 2011 Jul;18(7):1988-94. doi: 10.1245/s10434-011-1584-8.

8- Wong CH, Wei FC. Microsurgical free flap in head and neck reconstruction. Head Neck. 2010 Sep;32(9):1236-45. doi: 10.1002/hed.21284.

9- Schusterman MA, Miller MJ, Reece GP, Kroll SS, Marchi M, Goepfert H. A single center's experience with 308 free flaps for repair of head and neck cancer defects. Plast Reconstr Surg. 1994 Mar;93(3):472-8; discussion 479-80.

10- van Gijn DR, D'Souza J, King W, Bater M. Free Flap Head and Neck Reconstruction with an Emphasis on Postoperative Care. Facial Plast Surg. 2018 Dec;34(6):597-604. doi: 10.1055/s-0038-1676076.

11- Suh JD, Sercarz JA, Abemayor E, Calcaterra TC, Rawnsley JD, Alam D, Blackwell KE. Analysis of outcome and complications in 400 cases of microvascular head and neck reconstruction. Arch Otolaryngol Head Neck Surg. 2004 Aug;130(8):962-6. doi: 10.1001/archotol.130.8.962.

12- Zhao EH, Nishimori K, Brady J, Siddiqui SH, Eloy JA, Baredes S, Park RCW. Analysis of Risk Factors for Unplanned Reoperation Following Free Flap Surgery of the Head and Neck. Laryngoscope. 2018 Dec;128(12):2790-2795. doi: 10.1002/lary.27417.

13- Hoffman GR, Islam S, Eisenberg RL. Microvascular reconstruction of the mouth, jaws, and face: experience of an Australian oral and maxillofacial surgery unit. J Oral Maxillofac Surg. 2012 May;70(5):e371-7. doi: 10.1016/j.joms.2012.01.016.

14- Eckardt A, Meyer A, Laas U, Hausamen JE. Reconstruction of defects in the head and neck with free flaps: 20 years experience. Br J Oral Maxillofac Surg. 2007 Jan;45(1):11-5. doi: 10.1016/j.bjoms.2005.12.012.

15- Haughey BH, Wilson E, Kluwe L, Piccirillo J, Fredrickson J, Sessions D, Spector G. Free flap reconstruction of the head and neck: analysis of 241 cases. Otolaryngol Head Neck Surg. 2001 Jul;125(1):10-7. doi: 10.1067/mhn.2001.116788.

16- Shestak KC, Jones NF, Wu W, Johnson JT, Myers EN. Effect of advanced age and medical disease on the outcome of microvascular reconstruction for head and neck defects. Head Neck. 1992 Jan-Feb;14(1):14-8. doi: 10.1002/hed.2880140104.

17- Pastars K, Zarins J, Tars J, Ivanova A, Skagers A. Microsurgical reconstruction of oral defects with free flaps for patients with oral cancer: an 8 year experience with 153 consecutive cases. Stomatologija. 2018;20(2):39-42.

18- Al-Dam A, Zrnc TA, Hanken H, Riecke B, Eichhorn W, Nourwali I, Smeets R, Blessmann M, Heiland M, Gröbe A. Outcome of microvascular free flaps in a high-volume training centre. J Craniomaxillofac Surg. 2014 Oct;42(7):1178-83. doi: 10.1016/j.jcms.2014.02.005.

19- Kruse AL, Luebbers HT, Grätz KW, Obwegeser JA. Factors influencing survival of free-flap in reconstruction for cancer of the head and neck: a literature review. Microsurgery. 2010;30(3):242-8. doi: 10.1002/micr.20758.

20- Lin SC, Chang TS, Yang KC, Lin YS, Lin YH. Factors contributing to surgical site infection in patients with oral cancer undergoing microvascular free flap reconstruction. Eur Arch Otorhinolaryngol. 2018 Aug;275(8):2101-2108. doi: 10.1007/s00405-018-5035-z.

21- Zhou W, Zhang WB, Yu Y, Wang Y, Mao C, Guo CB, Yu GY, Peng X. Risk factors for free flap failure: a retrospective analysis of 881 free flaps for head and neck defect reconstruction. Int J Oral Maxillofac Surg. 2017 Aug;46(8):941-945. doi: 10.1016/j.ijom.2017.03.023.

22- Benatar MJ, Dassonville O, Chamorey E, Poissonnet G, Ettaiche M, Pierre CS, Benezery K, Hechema R, Demard F, Santini J, Bozec A. Impact of preoperative radiotherapy on head and neck free flap reconstruction: a report on 429 cases. J Plast Reconstr Aesthet Surg. 2013 Apr;66(4):478-82. doi: 10.1016/j.bjps.2012.12.019.

23- Ishimaru M, Ono S, Suzuki S, Matsui H, Fushimi K, Yasunaga H. Risk Factors for Free Flap Failure in 2,846 Patients With Head and Neck Cancer: A National Database Study in Japan. J Oral Maxillofac Surg. 2016 Jun;74(6):1265-70. doi: 10.1016/j.joms.2016.01.009.

24- Farquhar DR, Masood MM, Pappa AK, Patel SN, Hackman ATG. Predictors of Adverse Outcomes in Free Flap Reconstruction: A Single-Institution Experience. Otolaryngol Head Neck Surg. 2018 Dec;159(6):973-980. doi: 10.1177/0194599818787801.

25- Mücke T, Ritschl LM, Roth M, Güll FD, Rau A, Grill S, Kesting MR, Wolff KD, Loeffelbein DJ. Predictors of free flap loss in the head and neck region: A four-year retrospective study with 451 microvascular transplants at a single centre. J Craniomaxillofac Surg. 2016 Sep;44(9):1292-8. doi: 10.1016/j.jcms.2016.04.029.