European Review for Medical and Pharmacological Sciences 2021; 25: 5228-5234

Lymphatic drainage map of the head and neck skin squamous cell carcinoma detected by sentinel lymph node biopsy

I. JANKOVIĆ[1,2], P. KOVAČEVIĆ[1,2], D. JANKOVIĆ[3], G. STEVANOVIĆ[1,2], S. MOMČILOVIĆ[1,2]

[1]Clinic of Plastic and Reconstructive Surgery, Clinical Center Niš, Niš, Serbia
[2]Department of Plastic Surgery, Faculty of Medicine, University of Niš, Niš, Serbia
[3]Department of Internal Medicine, Health Center Aleksinac, Aleksinac, Serbia

Abstract. – OBJECTIVE: Squamous cell carcinoma of the skin often affects the scalp and neck region and has a potential for complex lymphatic metastases. The aim of this study was to examine the pattern of lymphatic drainage that would enable better insight and prediction of lymphatic metastasis of head and neck squamous cell carcinoma (HNSCC) in relation to the anatomical localization of the primary process.

PATIENTS AND METHODS: A prospective analysis included 64 patients who underwent sentinel lymph node (SLN) biopsy. The biopsy was performed in patients with high-risk cutaneous head and neck squamous cell carcinoma between 2006 and 2010.

RESULTS: SLNs in tumors of the forehead, temporal region, lateral cheek, and auricle were found in the cervical region at level II and parotid lymph nodes ($p<0.001$). In tumors of the nose, periorbital region, and postauricular tumors, SLNs were found in parotid lymph nodes ($p<0.001$), in tumors of the medial cheek in level I cervical lymph nodes and parotid lymph nodes ($p=0.003$). In tumors of the neck, SLNs were detected in the cervical region at level IV, whereas in tumors of the posterior scalp they were found in the occipital region ($p<0.001$).

CONCLUSIONS: The results of SLN biopsy in high-risk cutaneous HNSCCs show the regularity of metastasis based on which a lymphatic drainage map can be constructed and thus potential metastatic sites depending on the primary tumor localization predicted.

Key Words:
Sentinel lymph node biopsy, Head and neck, Squamous cell carcinoma, Skin.

Introduction

Non-melanoma skin cancer is one of the most common malignancies in white patients[1,2]. Squamous cell carcinoma accounts for an average of 20% of all cases of non-melanoma cancers[3] and is most commonly localized in the head and neck region[4]. According to available data from the literature, the cutaneous form of squamous cell carcinoma metastasizes in about 0.3% to 16% of cases[5]. However, it is considered that this percentage is significantly greater in high-risk patients (11-47.3%)[5-8]. This type of carcinoma characteristically spreads to local lymph nodes first, and then, metastasizes to distant tissues and organs[6,9-11]. It has been proven that squamous cell carcinoma of the skin, primarily localized in the head and neck region, metastasizes locally to lymph nodes of the parotid region, as well as to lymph nodes of the neck[12]. Population analyzes estimate that the mortality rate of this type of carcinoma is around 0.7%[13]. Many cases of local metastases in lymph nodes are potentially curable. However, a small number of patients, unfortunately, suffer a fatal outcome despite treatment. The five-year survival rate among patients with operable, metastatic, cutaneous squamous cell carcinoma of the head and neck region amounts to 70-75%[14]. Given the fact that the presence of metastases in regional lymph nodes is a key prognostic indicator for survival in patients with squamous cell carcinoma, special attention should be paid to the prevention of nodal disease during treatment[15].

Sentinel lymph node biopsy (SLNB) plays a significant role in the treatment of high-risk cutaneous squamous cell carcinomas without clinical or radiological evidence of the metastatic disease[16-18]. Early identification of micrometastases could enable a selective and timely inclusion of high-risk patients in more aggressive treatment protocols, as well as scheduling more frequent follow-ups by physicians, thereby potentially improving the survival rate[16,17]. To date, an accurate

Corresponding Author: Dimitrije Janković, MD; e-mail: dimitrije.jankovic@apotekanis.co.rs

map of metastasis of cutaneous forms of squamous cell carcinoma of the head and neck region has not been formed. SLNB is a minimally invasive method that examines the presence of metastases in the nodal basin[16].

On the other hand, in patients with a parotid gland-affected tumor process and a clinically negative cervical region, optimal treatment remains controversial[19]. Furthermore, determining the presence of metastases in clinically negative lymph nodes of the neck remains a challenge[20]. Elective nodal treatment is appropriate in a significant number of subclinical metastases in lymph nodes of the neck[12,21]. In addition, in patients undergoing neck dissection, it is necessary to perform the dissection up to the level of lymph nodes considered most likely to be affected by the tumor process[19].

Our hypothesis is that metastases may vary regarding the anatomical localization of the primary tumor process, as well as that an appropriate map of lymphatic drainage of the head and neck skin may enable the prediction of potential metastases. Therefore, the aim of this study was to correlate the primary localization of cutaneous squamous cell carcinoma of the head and neck region with the localization of the sentinel lymph node (SLN).

Patients and Methods

This prospective study included 64 high-risk patients with cutaneous squamous cell carcinoma of the head and neck and clinically negative lymph nodes subjected to SLNB between 2006 and 2010 at the Clinic for Plastic, Reconstructive and Aesthetic Surgery of the Clinical Center in Niš, Serbia. Patients were selected based on the presence of high metastatic risk defined by the criteria published in the literature[22].

The study included patients whose biopsy indicated the presence of squamous cell carcinoma of the skin in the head and neck region. Furthermore, following clinical and ultrasonographic examinations, no enlarged lymph nodes or signs of potential metastatic disease were detected in any of the included patients. Patients in whom the presence of metastases was detected during the above examinations were excluded from the study.

Control follow-ups and ultrasonographic examinations of lymph nodes were performed every 3 months after the surgical intervention. In case we were not able to come to a follow-up at the scheduled time, information was collected from medical records and *via* telephone interviews. The study was approved by the Ethics Committee of the Faculty of Medicine of the University in Niš, and the written consent was obtained from all participants in the study.

The primary malignant process on the skin is divided into 12 different anatomical areas: anterior scalp, posterior scalp, retroauricular region, periorbital region, temporal region, frontal region, medial cheek, lateral cheek, nose, auricle, chin, and neck (Figure 1). Primary squamous cell carcinoma of the lips was excluded from the study given that the lips anatomically belong to the oral cavity.

Lymphoscintigraphy was performed after injecting 30-50 MBq of Technetium-99m radiolabeled nanocolloid at the tumor site. Following all valid guidelines[22], after 3-18 hours, surgical excision of the primary tumor with wide margins and SLN was performed, followed by SLNB using a manual gamma camera for SLN detection.

The excision of the primary lesion was made immediately before SLNB to prevent the "shine through" phenomenon. Radiolocalization was combined with the intradermal injection of vital blue dye at the primary site of the tumor at the onset of the surgical procedure. Tissue cross-sections 3 mm-thick of biopsied SLNs were em-

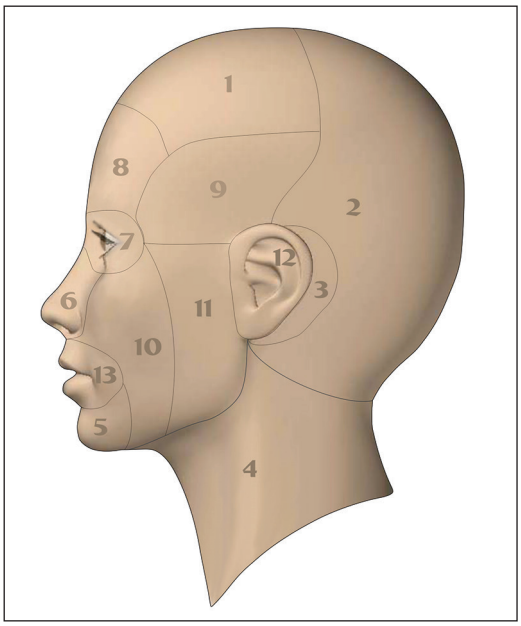

Figure 1. Anatomical regions of the head and neck region used in this study. 1, Anterior scalp; 2, Posterior scalp; 3, Postauricular; 4, Neck; 5, Chinn; 6, Nose; 7, Periorbital; 8, Forehead; 9, Temple; 10, Medial cheek; 11, Lateral cheek; 12, Pina; 13, Lips/perioral.

Table I. Distribution of SLN localization and location of primary tumor.

	SLN localization						Total	
Primary site	Level I	Level II	Level III	Level IV	Occipital	Parotid	Count	%
Anterior scalp	0	2	0	0	0	0	2	2.7
Posterior scalp	0	0	0	0	6	0	6	8.1
Postauricular	0	0	0	0	0	2	2	2.7
Neck	0	0	1	5	0	0	6	8.1
Chinn	2	2	0	0	0	0	4	5.4
Nose	0	0	0	0	0	2	2	2.7
Periorbital	0	0	0	0	0	2	2	2.7
Forehead	0	8	0	0	0	2	10	13.5
Temple	0	4	0	0	0	2	6	8.1
Medial cheek	4	0	0	0	0	2	6	8.1
Lateral cheek	0	10	0	0	0	2	12	16.2
Pinna	0	7	0	0	0	9	16	21.6
Total	6	33	1	5	6	23	74	100.0

bedded into paraffin blocks. Thereafter, ten 5 **μm**-thick sections were obtained from each preparation and examined microscopically using hematoxylin-eosin and immunohistochemical staining for cytokeratins AE1 and AE3. Finally, lymphatic drainage patterns were analyzed. The anatomical localization of the tumor was correlated with lymphatic drainage to levels I, II, III, IV, V, occipital and parotid lymph nodes. The external jugular lymph nodes, located in the immediate vicinity of *v. jugularis externa*, as well as lymph nodes in the region of the anterior border of the sternocleidomastoid muscle, were specially considered through level II. Superficial parotid lymph nodes were considered within the same region.

The StatCalc program and Fisher's exact test were used for the statistical analysis of the obtained data, while results were interpreted as statistically significant for probability values not greater than 0.05 ($p<0.05$).

Results

The study included 64 patients, 40 males and 24 females. The mean age of the patients was 71.5±7.9 (ranging from 58 to 84 years). The overall follow-up averaged at 9.2 years (ranging from 7-11 years). SLNB was performed under general anesthesia in 46 patients, whereas in 18 patients this procedure was accomplished under local anesthesia and analgesia. The patients were discharged from the clinic on the second day after the surgery.

In patients in whom the presence of micrometastases in SLN was not proven after the biopsy,

Table II. Distribution of SLN localization by location of primary tumor.

Localization	Lymph nodes	*p*-value
Forehead, temple, lateral cheek, the auricle	Level II + parotid 44/56	<0.001
Nose, periorbital region, postauricular	Parotid 6/23	<0.001
Medial cheek	Level I + parotid 6/29	0.003
Chin	Level I + level II 4/39	0.115
Neck	Level IV 5/5	<0.001
Anterior scalp	Level II 2/33	0.195
Posterior scalp	Occipital	<0.001

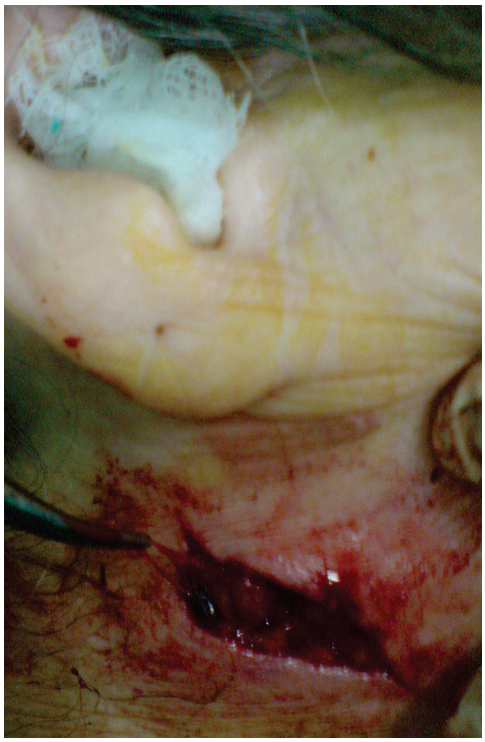

Figure 2. External jugular node.

there was no subsequent development of metastases at the level of other lymph nodes.

Lymphoscintigraphy identified 122 SLNs in 64 treated patients (on average 1.91 lymph nodes per patient, ranging from 1 to 4). In 10 patients, SLNs were localized at two levels. The anatomical distribution of primary sites and the distribution of lymphatic drainage in accordance with the localization of the primary tumor are shown in Table I. A large number of tumors were localized on the auricle (21.6%). Level II was the most common localization of SLNs, in as many as 44.6% of patients. Regarding 33 SLNs localized at level II, drainage into external jugular nodes was detected in 24 (72.7%) (Figure 2). Drainage into parotid lymph nodes amounted to 31.1%, and all SLNs were from the superficial parotid group. Level I and occipital lymph nodes had a lower rate of drainage (8.1%).

Drainage into level III was detected in 1.4% of cases. There were no localized SLNs at level V. In general, in 71.6% of cases, drainage was into superficial lymph nodes, followed by 24% into external jugular nodes, 23% into superficial parotid, and 6% into occipital lymph nodes.

The data were analyzed to examine whether the localization of the primary tumor affects the probability of drainage nodes at certain levels of the neck and parotid region. There was a statistically significant correlation between tumor localization and drainage in certain groups of lymph nodes. In patients who had a primary tumor on the frontal region, temporal region, lateral cheek, and the auricle, SLNs were found at level II and parotid lymph nodes ($p<0.001$). On the other hand, in tumors of the nose, periorbital region and postauricular region, SLNs were found in parotid lymph nodes ($p<0.001$), while in tumors of the medial cheek, SLNs were detected at level I and parotid lymph nodes ($p<0.003$). Finally, in tumors localized on the neck, SLNs were found at level IV ($p<0.001$), while in tumors of the posterior scalp SLNs were detected in occipital region ($p<0.001$). In patients with tumors localized on the chin, SLNs were found at levels I and II ($p=0.115$), whereas in tumors localized on the anterior scalp, they were found at level II ($p=0.195$), but there was no statistically significant difference between tumor localization and drainage in these regions (Table II and Figure 3).

Among the 64 patients with clinically negative lymph nodes who underwent SLNB at our clinic, 14 patients (21.9%) had histologically positive SLNs. The distribution of metastases regarding the localization of the primary tumor is illustrated in Figure 4.

Our study reported three small complications, such as the appearance of seroma (two cases in

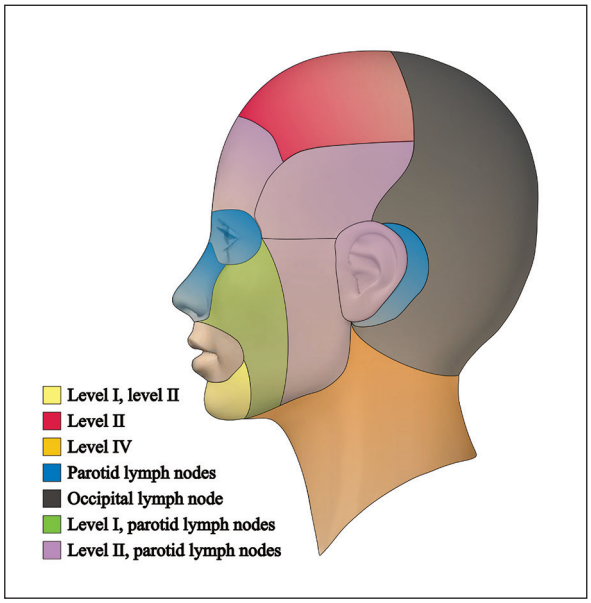

Figure 3. Distribution of SLNs regarding the localization of primary tumor.

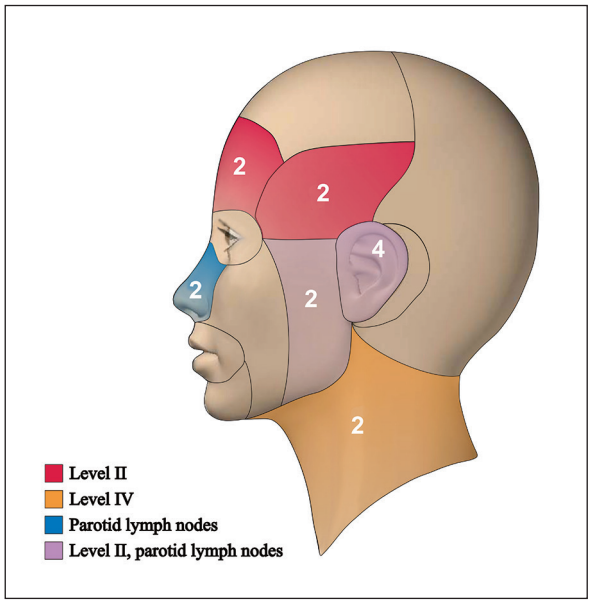

Figure 4. Distribution of metastases regarding the localization of the primary tumor.

which a lymph node of the parotid region was biopsied and one case in which a biopsy of level II lymph nodes was performed), which did not require further surgical treatment. No other complications were reported.

Discussion

The incidence of the cutaneous form of squamous cell carcinoma is on the increase[23]. Studies[24,25] conducted in Australia have shown that an average of 5-6% of squamous cell carcinomas metastasize. The incidence of metastases in high-risk squamous cell carcinoma patients undergoing SLNB ranges between 12.5% and 44.4%[17]. The results of our study have shown that 21.9% of patients had histologically positive SLNs. Therefore, the construction of lymphatic drainage patterns of the head and neck skin in relation to the primary anatomical localization of malignancy could potentially be of great importance in the treatment of patients. Several studies[26,27] conducted at Royal Prince Alfred Hospital have also tackled this issue and pointed out that SLNB should be considered for high-risk tumors and should be evaluated individually for each patient with squamous cell carcinoma, while for patients with cutaneous malignant melanomas of the head and neck, tumors metastasized to clinically predicted nodal groups in 92% of patients.

Sentinel lymph node biopsy has become the standard in the assessment of clinically negative lymph nodes in patients with malignant melanoma[21,28,29]. On the other hand, the use of SLNB in cutaneous forms of squamous cell carcinoma is still in the initial study phase, with only a few studies conducted on a small number of patients[7,30-35].

Several studies[5,36,37] have described levels of neck region involvement in patients with squamous cell carcinoma of the head and neck, and the results are based on the material obtained after neck dissections. To date, there are no studies that have analyzed lymphatic drainage according to the data obtained by SLNB in high-risk patients with squamous cell carcinoma of the head and neck. The authors of the conducted studies on the cutaneous form of squamous cell carcinoma recommend neither regional lymph node dissection nor SLNB, suggesting that this disease is quite common, and that the frequency of lymph node involvement is relatively small[21].

Once squamous cell carcinoma metastases appear, the overall survival rate is only 34.4%[6] which highlights the crucial importance of early diagnosis and treatment of this disease.

A high incidence of lymphatic drainage into level II in this study is consistent with the findings of previous studies[5,19,21,37].

The data on the involvement of superficial lymph nodes is scarce, especially in the area of *v. jugularis externa*. Lymph nodes in this region, being mostly solitary, are not located at a certain, specific level, but represent a frequent place for metastatic spread of the primary skin cancer[21]. Vauterin et al[21] drew special attention to these nodes and recommend their removal by any lymphadenectomy for skin carcinoma, including squamous cell carcinoma and melanoma. Chu and Osguthrope[37] also highlighted the involvement of external jugular and occipital lymph nodes. In our study, lymphatic drainage was mainly into the superficial lymph nodes - in external jugular nodes, superficial parotid, and occipital lymph nodes. In addition, lymphatic drainage of cutaneous squamous cell carcinomas has been shown to be predictable regarding the anatomical localization. Therefore, this study provided further understanding of the lymphatic drainage map of the head and neck in patients with squamous cell carcinoma of the abovementioned regions.

In clinical practice, SLNB can be a challenge for the surgeon. When performing in the cervical region, this diagnostic procedure is particularly

complex for an inexperienced surgeon due to the presence of large blood vessels and nerves. In addition, in some cases, atypical localization of the sentinel lymph node is also possible. Finally, due to the limited space between tumor area and SLN in the head and neck region, radiolocalization can be difficult due to diffuse radiation or signal superposition[26].

Early treatment of patients with the confirmed nodal disease could lead to a reduction in the number of fatal outcomes in association with squamous cell carcinoma[16].

Conclusions

The lymphatic drainage map is useful for predicting potential metastatic sites based on the primary location of the tumor. With the knowledge of the lymphatic drainage map, it is recommended to perform a thorough clinical examination of lymph nodes of the head and neck region where lymph is drained from the area of the primary tumor, given that it enables early diagnosis and appropriate treatment of patients with present metastases.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

1) Leiter U, Keim U, Garbe C. Epidemiology of Skin Cancer: Update 2019. Adv Exp Med Biol 2020; 1268: 123-139.
2) Stang A, Lamport T, Uhlemann T, Trocchi P. Skin cancer mortality in Germany before and after the post-communist transition. Int J Dermatol 2009; 48: 363-370.
3) Waldman A, Schmults C. Cutaneous Squamous Cell Carcinoma. Hematol Oncol Clin North Am 2019; 33: 1-12.
4) Alam M, Ratner D. Cutaneous squamous-cell carcinoma. N Engl J Med 2001; 344: 975-983.
5) Mooney CP, Martin RCW, Dirven R, Ashford BG, Shannon K, Ngo Q, Wykes J, Davies S, Gao K, Ch'ng S, Low TH, Gupta R, Clark JR. Sentinel node biopsy in 105 high-risk cutaneous SCCs of the head and neck: results of a multicenter prospective study. Ann Surg Oncol 2019; 26: 4481-4488.
6) Rowe DE, Carroll RJ, Day CL Jr. Prognostic factors for local recurrence, metastasis, and survival rates in squamous cell carcinoma of the skin, ear, and lip. J Am Acad Dermatol 1992; 26: 976-990.
7) Nouri K, Rivas MP, Pedroso F, Bhatia R, Civantos F. Sentinel lymph node biopsy for high-risk cutaneous squamous cell carcinoma of the head and neck. Arch Dermatol 2004; 140: 1284.
8) Cherpelis BS, Marcusen C, Lang PG. Prognostic factors for metastasis in squamous cell carcinoma of the skin. Dermatol Surg 2002; 28: 268-273.
9) Thompson AK, Kelley BF, Prokop LJ, Murad MH, Baum CL. Risk factors for cutaneous squamous cell carcinoma recurrence, metastasis, and disease-specific death: a systematic review and meta-analysis. JAMA Dermatol 2016; 152: 419-428.
10) Bander TS, Nehal KS, Lee EH. Cutaneous squamous cell carcinoma: updates in staging and management. Dermatol Clin 2019; 37: 241-251.
11) Barriera-Silvestrini P, Knackstedt T. In reference to prognostic value of tumor staging: predicting nodal metastases in cutaneous squamous cell carcinoma. Laryngoscope 2021; 131: E443.
12) Veness MJ. Porceddu S. Palme CE. Morgan GJ. Cutaneous head and neck squamous cell carcinoma metastatic to parotid and cervical lymph nodes. Head Neck 2007; 29: 621-631.
13) Lewis KG, Weinstock MA. Trends in nonmelanoma skin cancer mortality rates in the United States, 1969 through 2000. J Invest Dermatol 2007; 127: 2323-2327.
14) Veness MJ, Palme CE. Morgan GJ. High-risk cutaneous squamous cell carcinoma of the head and neck. Cancer 2006; 106: 2389-2396.
15) O'Brien CJ, McNeil EN, McMahon JD, Pathak I, Lauer CS, Jackson MA. Significance of clinical stage, extent of surgery, and pathologic findings in metastatic cutaneous squamous carcinoma of the parotid gland. Head Neck 2002; 24: 417-422.
16) Ross AS, Schmults CD. Sentinel lymph node biopsy in cutaneous squamous cell carcinoma: a systematic review of the english literature. Dermatol Surg 2006; 32: 1309-1321.
17) Renzi C, Caggiati A, Mannooranparampil TJ, Passarelli F, Tartaglione G, Pennasilico GM, Cecconi S, Potenza C, Pasquini P. Sentinel lymph node biopsy for high-risk cutaneous squamous cell carcinoma: case series and review of the literature. Eur J Surg Oncol 2007; 33: 364-369.
18) Sahn RE, Lang PG. Sentinel lymph node biopsy for high-risk nonmelanoma skin cancers. Dermatol Surg 2007; 33: 1-8.
19) Ebrahimi A, Moncrieff MD, Clark JR, Shannon KF, Gao K, Milross CG, O'Brien CJ. Predicting the pattern of regional metastases from cutaneous squamous cell carcinoma of the head and neck based on location of the primary. Head Neck 2010; 32: 1288-1294.
20) Bumpous J. Metastatic cutaneous squamous cell carcinoma to the parotid and cervical lymph nodes: treatment and outcomes. Curr Opin Otolaryngol Head Neck Surg 2009; 17: 122-125.
21) Vauterin TJ, Veness MJ, Morgan GJ, Poulsen MG, O'Brien CJ. Patterns of lymph node spread of cu-

taneous squamous cell carcinoma of the head and neck. Head Neck 2006; 28: 785-791.

22) Miller SJ, Alam M, Andersen J, Berg D, Bichakjian CK, Bowen G, Cheney RT, Glass F, Grekin RC, Grichnik JM, Kessinger A, Lee NY, Lessin S, Lydiatt DD, Margolis LW, Michalski J, Nehal KS, Nghiem P, Oseroff AR, Rosenberg EW, Shaha AR, Siegle RJ, Urist MM, National Comprehensive Cancer Network. Basal cell and squamous cell skin cancers. J Natl Compr Cane Netw 2007; 5: 506-529.

23) Eisemann N, Waldmann A, Geller AC, Weinstock MA, Volkmer B, Greinert R, Breitbart EW, Katalinic A. Non-melanoma skin cancer incidence and impact of skin cancer screening on incidence. J Invest Dermatol 2014; 134: 43-50.

24) Czarnecki D, Staples M, Mar A, Giles G, Meehan C. Metastases from squamous cell carcinoma of the skin in southern Australia. Dermatology 1994; 189: 52-54.

25) Veness MJ. High-risk cutaneous squamous cell carcinoma of the head and neck. J Biomed Biotechnol 2007; 2007: 80572.

26) Kofler L, Kolfer K, Schulz C, Breuninger H, Hafner HM. Sentinel lymph node biopsy for high-thickness cutaneous squamous cell carcinoma. Arch Dermatol Res 2021; 313: 119-126

27) Pathak I, O'Brien CJ, Petersen-Schaeffer K, McNeil EB, McMahon J, Quinn MJ, Thompson JF, McCarthy WH. Do nodal metastases from cutaneous melanoma of the head and neck follow a clinically predictable pattern? Head Neck 2001; 29: 785-790.

28) Živojinov M, Lakić T, Ilić-Sabo J, Trivunić Dajko S, Ivanov D, Živojinov S. Malignant melanoma metastasis in the ileum - two case reports. Vojnosanit Pregl 2020; 77: 344-348.

29) Vidal M, Vidal-Sicart S, Torres F, Ruiz DM, Paredes P, Pons F. Correlation between theoretical anatomical patterns of lymphatic drainage and lymphoscintigraphy findings during sentinel node detection in head and neck melanomas. Eur J Nucl Med Mol Imaging 2016; 43: 626-634.

30) Reschly MJ, Messina J, Zaulyanov L, Cruse W, Fenske N. Utility of sentinel lymphadenectomy in the management of patients with high risk cutaneous squamous cell carcinoma. Dermatol Surg 2003; 29: 135-140.

31) Wagner JD, Evdokimow DZ, Weisberger E, Moore D, Chuang TY, Wenck S, Coleman JJ 3rd. Sentinel node biopsy for high-risk nonmelanoma cutaneous malignancy. Arch Dermatol 2004; 140: 75-79.

32) Michl C, Starz H, Bachter D, Baida BR. Clinical and laboratory investigations Sentinel lymphonodectomy in nonmelanoma skin malignancies. Br J Dermatol 2003; 149: 763-769.

33) Altinyollar H, Berberoglu U, Celen O. Lymphatic mapping and sentinel lymph node biopsy in squamous cell carcinoma of the lower lip. Eur J Surg Oncol 2002; 28: 72-74.

34) Lhote R, Lambert J, Lejeune J, Gottlieb J, Badaoui A, Battistella M, Roux J, Pages C, Vercellino L, Vilmer C, Le Maignan C, Escande C, MBarek B, Bagot M, Lebbé C, Basset-Seguin N. Sentinel Lymph Node Biopsy in Cutaneous Squamous Cell Carcinoma Series of 37 Cases and Systematic Review of the Literature. Acta Derm Venereol 2018; 98: 671-676.

35) Tejera-Vaquerizo A, Garcia-Doval I, Llombart B, Canueto J, Martorell- Calatayud A, Descalzo-Gallego MA, Sanmartin O. Systematic review of the prevalence of nodal metastases and the prognostic utility of sentinellymph node biopsy in cutaneous squamous cell carcinoma. J Dermatol 2018; 45: 781-790.

36) Netterville JL, Sinard RJ, Bryant GL, Burkey BB. Delayed regional metastasis from midfacial squamous carcinomas. Head Neck 1998; 20: 328-333.

37) Chu A, Osguthorpe JD. Nonmelanoma cutaneous malignancy with regional metastasis. Otolaryngol Head Neck Surg 2003; 128: 663-673..