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Head and Neck Non-Melanoma Skin Malignancies and Surgical Margins in Patients Over 75 Years of Age. Which Approach to use? Further Experience and Observations

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2. Key words

1. Abstract

Non-Melanoma Skin Malignancies (NMSM) mostly occur in the elderly population which has been significantly increasing in numbers for the past two decades or more. The related health, economic and social costs have increased as well. The issues of handling these frail patients and the on-going care required for them have become more and more urgent. Skin malignancies, typically the basal and squamous cell carcinomas (cBCC and cSCC) are low risk tumors with a good prognosis in more than 90 % of the cases. The Authors already published the encouraging preliminary results of a highly-conservative, minimally-invasive approach, in patients over 75 years of age, where a strategy based on a single surgical excision followed by watchful follow-ups was adopted, even in cases that the histologic examination resulted in close or involved margins.

After three additional years of collection and analysis of such cases, the Authors' conservative approach appears to be further validated and advisable.

3. Introduction

The aging populations and the decreased natality in western countries has become an increasingly significant phenomenon over the last twenty years or more [1], which has required changes in the management of several areas such as work organization and health provision. The elderly population typically struggles with chronic diseases and requires less aggressive treatments in conjunction with dedicated nursing and intensive long-term care-giving. The concept of the "frail patient" has developed and the health systems are continuously making adjustments to deal with this challenging segment of the population.

Non-Melanoma Skin Cancers (NMSC) are keratinocytic-epithelial tumors. They represent the most common human malignancy and account for 80% of all skin cancers. Cutaneous basal cell carcinoma (cBCC: 70 %) and cutaneous squamous cell carcinoma (cSCC: 20%) are the most important histologic types, both epidemiologically and clinically [2]. The incidence of NMSC progresses with age and poses specific issues regarding the invasiveness of the therapeutic procedures [3].

In 2018, the Authors published a paper where the outcome of a surgical approach consisting of a single excision and follow up was analyzed [4]. Based on their daily patient experience, in the majority of the cases, where the surgical margins were close or even positive, the patient did not develop a persistence and/or a recurrence of the disease. Thus, the Authors adopted a strategy of strictly following those patients without any early surgical revisions, based on the low risk of recurrence and the probability of resolving the problem with a delayed, yet still conservative operation. They also followed the cases with clear margins to quantify the risk of local recurrence, despite the histologic negativity, or the growth of new neoplasms. The data reported in the previous paper seemed to validate this strategy.

Over a three-year-period, new patients were treated and observed and the follow-ups on patients from the previous study were prolonged and included. The complete patient data from both groups, seems to confirm once again the validity of this tissue-sparing philosophy of treatment for such pathologies. The up-dated results will be hereby detailed and discussed.

4. Materials and Methods

At the ENT Outpatient and Day Surgery Service of the "A. Murri" Hospital in Fermo, Italy, the patients with suspected head and neck skin cancers are referred by their general practitioners, dermatologists or general surgeons. In this facility, the patients are operated on under local anesthesia, with the anesthetist always on call. Minor cases are treated on an outpatient basis, while major cases,

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when a reconstruction is needed, are operated on in the operating room, both under local and general anesthesia. After the operation, the patients are followed on an outpatient basis and, upon receipt of the histologic report, further or additional treatment is taken into consideration. As reported in the introduction, particularly in patients over 75 years of age, in nearly all of the cases with close or involved margins up to 1 mm, the standard procedure is a watchful follow up without an immediate surgical revision.

The Authors reviewed the cases of the previous paper (years 2002 to 2016), considering only patients that were alive as of December 2016. For these cases, the follow up interval was extended to December 2019, if the patient was still alive, or ended upon the date of death. In addition, a new group of patients, operated on between January 2017 to December 2019 were also included.

The whole series consists of 94 patients, a total of 65 patients up to December 2016 and an additional 29 patients from January 2017 through December 2019. Of these 94 patients, a group of 86 cases was first analyzed, consisting of 47 cBCC, 36 cSCC, and 3 concomitant cBCC and cSCC (cB-S). In this last small subgroup (cB-S), the presence of the two histologic types in a single lesion, or two or more concomitant cBCC and cSCC in different head and neck sites were observed. The epidemiological analysis of these first 86 patients is shown in Table 1, while the clinical and pathological aspects are summarized in Table 2. Among these 86 patients, 6 cases underwent an early revision (Table 3) to find out if residual disease still existed or if there was just scar tissue. A second group of 8 patients was then considered (Table 4), in whom several surgical excisions were performed over time. Following the various operations, the recurrences at the sites of a previous surgery were differentiated from new localizations. It was also reported if the histologic types were the same or differed.

Table 1: Epidemiologic data

	N. cases	SEX M	SEX F	AGE GROUP (years) 75-80	81-85	86-90	>90	FOLLOW UP (years) <2 NED	<2 AwD	<2 DoD	2-4 NED	2-4 AwD	2-4 DoD	5-10 NED	5-10 AwD	5-10 DoD	>10 NED	>10 AwD	>10 DoD
BCC CLEAR	21	14	7	6	8	6	1	2			9			6			4		
BCC CLOSE	10	8	2	4	5	1		3			5			1			1		
BCC POSITIVE	16	11	5	5	3	7	1	4			9	1		1			1		
	47	33	14	15	16	14	2	9			23	1		8			6		
SCC CLEAR	20	16	4	8	7	4	1	9			6			3			2		
SCC CLOSE	6	5	1	3	1	1	1	5			1								
SCC POSITIVE	10	9	1	6	2	1	1	4			5					1			
	36	30	6	17	10	6	3	18			12			3		1	2		
B-S CLEAR	2		2	1	1			1						1					
B-S POSITIVE	1	1				1					1								
	3	1	2	1	1	1		1			1			1					
	86																		

Legends: NED: Non Evidence of Disease; AwD Alive with Disease; DoD: Dead of Disease

Table 2: Pathological data

	N. cases	SEX M	SEX F	SITE nose	ear	other	MORPHOLOY nodular	ulcerated	GRADING well diff	mod diff	poorly diff	SIZE cm) <1	1-2	>2	THICKNESS(mm) <2.5	2.5-5	>5	MARGIN INVOVED lat	deep	both	NECK +
BCC CLEAR	21	14	7	7	10	4	10	11				11	9	1							
BCC CLOSE	10	8	2	3	7		4	6				2	8					5	3	2	
BCC POSITIVE	16	11	5	5	10	1	7	9				10	5	1				9	2	5	
	47	33	14	15	27	5	21	26				23	22	2				14	5	7	
SQUAMO CLEAR	20	16	4	3	15	2			13	4	3	6	8	6	13	5	2				
SQUAMO CLOSE	6	5	1		5	1			3	3		2	2	2	3	2	1	3	2	1	
SQUAMO POSITIVE	10	9	1		8	2			6	2	2	3	5	2	3	4	3	3	4	3	
	36	30	6	3	28	5			22	9	5	11	15	10	19	11	6	6	6	4	
B-S CLEAR	2		2	1	1		1	1	1	1		1	1		2						
B-S POSITIVE	1	1			1		1		1				1			1			1		
	3	1	2	2	1		2	1	2	1		1	2		3						
	86																				

Table 3: Recurrence followed by early revision

	N. cases	SEX M	F	AGE GROUP (years) 75-80	81-85	86-90	>90	REV neg	pos	2nd Rev pos	neg	FOLLOW UP (years) <2 NED	<2 AwD	<2 DoD	2-4 NED	2-4 AwD	2-4 DoD	5-10 NED	5-10 AwD	5-10 DoD	>10 NED	>10 AwD	>10 DoD
BCC pos	2	1	1	1		1		1	1			1									1		
SCC pos	4	3	1	3				2	2		1	1			2								

Legends: NED: Non Evidence of Disease; AwD Alive with Disease; DoD: Dead of Disease

Table 4: Recurrent/Multiple NMSC

Case 1: B. L. m (January 6, 1932) – 2003, July: BCC right cheek, OK → NED → 2007, November: BCC left cheek, OK → NED → 2010, November: BCC right cheek, OK; BCC right inferior lid, OK → NED → 2013, July: BCC nose, lateral and deep margin + → NED → 2017, October: BCC right cheek, lateral margin + → NED at December 2017 examination → lost to follow up → December 2019: AwD (information from his GP: the patient has multiple recurrences but refuses further treatment).

Case 2: M. F. m (Dec 5, 1941) – 2009, November: BCC left ear, lateral margin + → NED → 2012, April: BCC left ear, OK → 2014, March: BCC left ear deep margin + → NED → 2016, October: BBC left ear, lateral margin +; BCC right ear, lateral margin + → NED → 2017, December: BCC nose, OK → NED → 2018, December: BCC left ear, lateral and deep margin + → December 2019 NED.

Case 3: O. A. f (July 15, 1926) – 2012, November: BCC right ear, lateral margin + → NED → 2016, September: BCC right ear, lateral margin close → NED → 2017, December: BCC right ear, deep margin close → December 2019 NED.

Case 4: M. A. m (February 16, 1928) – 2012, June: BCC right ear, lateral margin + → NED → 2017, October: BCC nose, OK; BCC right ear, lateral margin + → December 2019 NED.

Case 5: F. A. m (November 9, 1934) – 2015, February: BCC left ear, OK → NED → 2016, October: BBC left ear, lateral margin + → 2017, January: BCC right ear, lateral margin + → NED → 2018, April: BCC left ear, lateral margin + → NED → 2018, July: BCC neck, OK → December 2019: NED.

Case 6: S. M. m (January 1, 1933) – 2015, June: SCC scalp, OK → NED → 2016, June: SCC left cheek , OK; BCC right ear, deep margin + → December 2019, DwD (information from his GP: dead for cardiac attack. He had skin recurrences).

Case 7: C. S. m (July 16, 1932) – 2015, September: SCC left ear, lateral and deep margin + → NED → 2016, September: BCC left nose, OK; SCC left nasolabial fold, lateral margin + → early revision, no residual tumor → NED → 2017, March: BCC nose, lateral margin +; BCC thorax, OK; → 2017, August: BCC right ear, OK → 2017, October: BCC right shoulder, OK → NED → 2017, November: BCC sternum, OK → 2018, January: SCC left ear, lateral margin +; Concomitant focus of BCC → early revision: SCC, lateral margin + → NED → 2018, July: BCC left nose, lateral margin + → early revision, BCC, OK → 2019, March: BCC left wrist, lateral margin + → December 2019, NED.

Case 8: T. G. m (July 11, 1933) – 2016, May: SCC left ear, lateral and deep margin + → NED → 2019, April: ? recurrence left ear: keratosis + ca in situ → Dec 2019 NED.

In regards to cBCC, cSCC and cB-S (86 patients), the epidemiological parameters taken into consideration were sex, age groups and number of years of follow up. Relating to the clinical and pathologic aspects, the site of the disease was limited to nose, ear and other localizations.

For cBCC, the histologic morphology and the size of the lesions were also recorded. Despite the WHO histologic classification [5] into lower risk cBCC (nodular, superficial, pigmented, infundibulocystic, fibroepithelial) and higher risk histologic types (basosquamous carcinoma, sclerosing/morphoeic, infiltrating, BCC with sarcomatoid differentiation, micro-nodular) the Authors clinically divided the cBCC, as they did in their previous paper, into nodular and ulcerated forms, according to the major division their pathologists usually report. The presence and the level of infiltration was also recorded. In regards to the size of the lesion, three groups were considered: less than 1 cm, between 1 and 2 cm and more than 2 cm.

For cSCC, the grading (well, moderately and poorly differentiated) and the thickness (< 2,5 mm, 2,5-5 mm and > 5 mm) were taken into account.

For both cBCC and cSCC, the surgical margins were considered as "close" when a residual strip of 1 mm or less of healthy tissue was observed and reported by the pathologist around (lateral margin) and underneath (deep margin) the surgical specimen.

Finally, for cSCC, evidence of nodal involvement or distant metastasis were reported.

5. RESULTS (Tabs. 1, 2 ,3 and 4)

cBCC with clear margins (BCC CLEAR)

- 21 patients, 14 males and 7 females. Median age was 84 years with MAD* = 4. The range was between 76 and 94 years of age.

- In 7/21 cases the nose was affected, in 10/21 cases the ear was affected, and in 4/21 cases other head and neck sites were affected.

- 10/21 cases were of nodular type (4/10 cases were with dermal infiltration) and 11/21 cases were ulcerated (8/11 cases with dermal infiltration).

- The size (the mean diameter) was less than 1 cm in 11/21 cases, between 1 and 2 cm in 9/21 cases, and more than 2 cm in 1/21 cases.

- No patient had any recurrence during the follow up period. 4 patients were NED after more than ten years, 6 were NED after more than five years, 9 were NED after more than 2 years and the remaining 2 had follow ups lasting less than two years.

cBCC with close margins (BCC CLOSE)

- 10 patients, 8 males and 2 females. Median age was 80.5 years with MAD = 2. The range was between 75 and 87 years of age.

- Ear was involved in 7/10 cases and the nose was involved in 3/10 cases.

- 4/10 cases were of nodular type (2/4 with dermal infiltration) and 6/10 cases were ulcerated (6/6 cases were with dermal infiltration).

- The size (the mean diameter) was less than 1 cm in 2/10 cases, and between 1 and 2 cm in 8/10 cases.

- No patient had any recurrence during the follow up period. 1 patient was NED after more than ten years, 1 was NED after more than five years, 5 were NED after more than 2 years and the remaining 3 had follow ups lasting less than two years.

*MAD (median absolute deviation) measures the dispersion of the sample around the median value.

cBCC with positive margins (BCC POSITIVE)

- 16 patients, 11 males and 5 females. Median age was 85.50 with MAD = 3.5. The range was between 75 and 98 years of age.

- The ear was involved in 10/16 cases, the nose was involved in 5/16 cases, and in 1/16 the right temporal skin was involved.

- 7/16 cases were of the nodular type (3/7 cases with dermal infiltration) and 9/16 cases were ulcerated (7/9 cases with dermal infiltration).

- 10/16 cases were smaller than 1 cm, 5/16 cases were between 1 and 2 cm and 1/16 cases was greater than 2 cm.

- Only 2/16 cases had a recurrence during the follow up period (see after). At the December 2019 examination, 1 patient was NED after more than ten years, 1 patient was NED after more than five years, 9 patients were NED after more than 2 years, 1 patient was alive with disease (AwD) and the remaining 4 patients were NED, with a follow up lasting less than two years.

- In regards to the 2/16 cases with recurrence, one patient was a male, born in 1933, who was operated on by the Authors in 2015 for an infiltrative, ulcerated cBCC of the nose with involvement of the lateral margin. This patient belonged to the series of the Authors' previous paper (4) and was NED at the December 2016 follow up control. After that time, he developed a recurrence in the same area and was treated by a different dermatologist. At the December 2019 interview, he was alive and free of disease. The second patient with a recurrence was a lady, born in 1928, operated on for a nodular, infiltrative cBCC of the nose in April 2017. At the December 2019 interview she was alive, in relatively good general condition with a small, clinically non-invasive recurrence that was judged to not be worth surgical revision.

- The recurrence rate was then 2/16 (12.5 %).

- Among the 16 cBCCs with positive margins, two cases underwent early surgical revision. (Tab. 3). One case (nodular, non-infiltrative cBCC) showed no residual tumor, while in the other case, (ulcerated, infiltrative), the same histologic type was found in the surgical revision specimen, with clear margins. Both the patients were NED and alive on December 2019.

cSCC with clear margins (SCC CLEAR)

- 20 patients, 16 males and 4 females. Median age was 81.5 years, with MAD = 3. The range was between 76 and 93 years of age.

- The ear was the most frequently affected site (15/20 cases). There were 3/20 cases involving the nose and only 2/20 affecting other locations, one cheek and one lip.

- The prevalent histologic type was the well differentiated one (13/20 cases). The size was less than 1 cm in 6/20 cases, between 1 and 2 cm in 8/20 cases and > 2 cm in the remaining 6/20 cases.

- In 13/20 cases the tumor thickness was less than 2.5 mm, in 5/20 patients it was between 2.5 and 5 mm, and in the remaining 2/20 cases it was more than 5 mm.

- None of the 20 patients had a recurrence of skin cancer. 2/20 cases were followed for more than ten years, 3/20 cases for more than five years, 6/20 had a follow up for longer than two years, and the remaining 4/20 cases were followed for less than two years.

cSCC with close margins (SCC CLOSE)

- 6 patients, 5 males and 1 female. Median age was 81.50 years with MAD =3.5. The range was between 78 and 92 years of age.

- 5/6 cases were located in the ear while the remaining 1/6 was in the neck.

- 3/6 cases were of the well differentiated histologic type while 3/6 cases were mildly differentiated.

- 2/6 cases were smaller than 2 cm in size, 2/6 cases were within 1 and 2 cm, and 2/6 cases were larger than 2 cm.

- The thickness was less than 2.5 mm in 3/6 patients, between 2.5 and 5 mm in 2/6 cases and more than 5 mm in 1/6 patients.

- In 3/6 cases the close margin was the lateral, in 2/6 cases the close margin was the deep one and in 1/6 patients both the lateral and the deep margins were close.

- No recurrence was observed in any of the cases. 1/6 cases was followed for more than two years and 5/6 cases were followed for less than two years.

cSSC with positive margins (SCC POSITIVE)

- 10 patients, 9 males and 1 female. Median age was 79 years with MAD = 3.5. The range was between 75 to 93 years of age.

- In 8/10 cases the malignancy was in the ear, in 1/10 cases the cheek was affected and in 1/10 cases the tumor was located in the inferior lip.

- In 6/10 cases the histologic type was well differentiated, in 2/10 cases mildly differentiated and in 2/10 cases poorly differentiated.

- The size was between 1 and 2 cm in 5/10 patients, less than 1 cm in 3/10 cases, and more than 2 cm in 2 cases.

- In 3/10 cases tumor thickness was less than 2.5 mm, in 4/10 cases it was between 2.5 and 5 mm, and in the remaining 3/10 cases it was more than 5 mm.

- In 4/10 cases the deep margin was involved, in 3/10 cases the lateral margin was involved, and in 3/10 cases both margins were involved (lateral and deep).

- In December 2019, 5/10 casese were NED after as longer than two years and 4/10 cases, were NED after less than two years of follow ups.

- A patient (male, born in 1925), operated on in the year 2010 (well differentiated cSCC of the inferior lip, with muscular infiltration, lateral margin positive, and deep margin close) was NED up until 2017. In 2018, he developed a slow-growing recurrence at the site of the previous operation, but he was not operated on again due to his age and general condition. He died in 2019, for a pneumonitis due to a probable lung metastasis.

- The recurrence rate was then 1/10 (10 %).

- No lymph node involvement nor distant metastases were encountered.

- Four cases underwent early surgical revisions (Table 3). One case (male, born in 1942), operated on in March 2017, was a poorly differentiated cSCC, 6 mm thin, infiltrating the dermis. The revision carried out one month later showed a residual tumor, 7 mm thick and infiltrating the cartilage. This surgical revision was radical and the patient had no further recurrence and was NED at the December 2019 examination. The second case (male, born in 1939), was operated on in April 2017, for a moderately differentiated cSCC of the left ear. The deep margin turned out positive, he underwent surgical revision one month later, and no residual tumor was found. The patient showed no recurrence and was alive and NED at the December 2019 examination. The third patient (male, born in 1943), was operated on in February 2019 for a well differentiated, ulcerated cSCC of the right ear, with the deep margin positive. The one-month-later surgical revision showed a residual focus of SSC in situ of the Bowen type, with clear margins. In July 2019, he underwent a further surgical revision, at another institution, with no evidence of a residual tumor. At the December 2019 examination he was well and NED. Lastly, the fourth case refers to a male born in 1941 who underwent, in April 2019, an excision of a moderately differentiated cSCC of the left ear. The tumor was 3 mm thick with dermal infiltration and a lateral margin was positive. A wait and see policy was planned. On July 2019, a skin lesion on his left cheek became evident and was judged to be worth removing. In the same surgical session, a revision of the scar in the left

ear was also performed. The lesion of the cheek turned out to be a moderately differentiated cSCC with dermal infiltration, completely excised. At the left ear no residual tumor was found. The patient was NED in Dec 2019.

Concomitant cBCC and c SCC (cB-S)

- 2 patients with clear margins. One (female, born in 1930) was operated on in September 2012, and she turned out to have an ulcerated, non-infiltrative cBCC of the nose, and a lesion in the right temple, where the pathologist found a nodular, non-infiltrative cBCC with an adjacent well differentiated superficial cSCC. The second patient (female born in 1939), was operated on in January 2019, and had a nodular, infiltrative cBCC in her left ear and a moderately differentiated cSCC in the left pre-tragal area. Both the patients were alive and NED at December 2019 examination.

- 1 patient with positive margins (male, born in 1927). He was operated on in December 2014, and two lesions were excised. At the level of the nose, a 6 mm infiltrative well differentiated cSCC and a contiguous nodular infiltrative cBCC were found. Both the components were excised with the lateral and the deep margins involved (positive). In the left cheek, a well differentiated, in situ and infiltrative cSCC was encountered, involving the lateral margin. The patient was followed, as usual, and twelve months later (December 2015) a moderately differentiated, 3 mm-thick, infiltrative SCC was completely excised from the neck. The scar in the nose was also revised and a residual, superficial cBCC was found, reaching a lateral margin. From that time, the patient was regularly followed and, at the December 2017 examination, he was alive and NED. The patient died in 2019 for gastric cancer without any recurrence of the skin malignancies.

Patient with subsequent cBCC and/or cSCC (Table 4)

- 8 patients (7 males and 1 female), 4/8 with patient history of more than five years and 3/8 followed for more than four years. In 5/8 patients there was a recurrent cBCC both at the same site as well as in different locations. 2/3 patients who had a cSCC, also developed a cBCC. In regards to the outcome, 1/8 patients is still alive after sixteen years with recurrences he refused to further treat. 1/8 died after four years for other causes, but also with evidence of recurrences of skin tumors. The remaining 6/8 patients were alive and NED at the December 2019 examination.

6. Discussion

As well documented, NMSCs depend on several risk factors, including race, age, gender, sun-sensitive phenotypes, amount of sun- exposure, immunodepression and photosensitizing drugs.

cBCC is two-fold more frequent in males than in females [6]. Light-skinned people have a 10-20 times higher probability to develop a cancer than dark-skinned people, even when living in the same geographic area. The amount of UV radiation exposure is another important risk factor and fair-skinned people who live at lower latitudes are the most prone to develop a cBCC. More than 50 % of cBCC cases occur in people older than 50 years of age. 10 to 50 years seem to be necessary to the sun-exposure to cause skin cells to transform into malignant. Sun-burns in childhood or youth, together with work related sun-exposure, like in farmers and fishermen, are other credited risk-factors. The head and neck regions account for more than 60% of sBCCs, with the nose being the most affected area (on average 30% of cases), followed by cheek, forehead, eyelids, ear and preauricular region (around 8% of cases). The neck is involved in nearly 10 % of the cases.

When a patient develops a cBCC, the risk of developing further cBCCs is ten-fold higher than in the general population. Treatment of cBCCs includes surgical and non-surgical therapies. Surgical therapies include standard surgical excision with or without reconstruction, Mohs micrographic surgery, electrodissection and curettage, laser surgery and cryosurgery. Non-surgical treatments are topical medical treatments, photodynamic therapy, radiotherapy, chemotherapy and treatment with biologic drugs. Considering that surgery is the main treatment modality, its accuracy and cure-rate is related to several factors that led a European Interdisciplinary Group (7) to distinguish between "easy-to-treat" and "difficult-to-treat" cBCCs. This difficulty of treatment depends on: the size and/or location; the well or poorly defined borders; multiple prior recurrences; previous treatments, both surgical and non-surgical; patient's reluctance to accept the consequences of surgery; and the patient's comorbidities interfering with surgery. This last consideration is crucial in evaluating older patients, where less invasive treatments, with no reconstruction required, minimal drug load, local anesthesia and minimum amount of time for execution are highly advisable.

Recurrence after surgery varies from 2% to 8% at 5 years [8] and, again, increases with tumor size, poorly defined margins, aggressive histological subtype and previous recurrences. In regards to the margins, that is the amount of clinically free tissue to be left around the lesion, current guidelines [9] suggest a range of peripheral (lateral) margins between 2 mm and 5 mm in low-risk tumors and between 5 mm and 15 mm in high-risk lesions. The size of the tumor seems to be the most important risk factor, with 2 cm being the cut-off. For the deep margins, an excision down to the fat is advised and in head and neck localizations reaching the fascia, the pericondrium and the periosteum is also recommended. The most recent literature [7] still acknowledges the lack of consensus about what to do in the case of close margins, if an early surgical revision or a watchful follow up. The frequency of one or more margins found to be involved by the pathologist, ranges between 4.7 and 24% of the excised cBCCs and is thought to be influenced by surgical experience, anatomical site, histologic subtype and the excision of multiple lesions during a single procedure [10]. In cases of positive margins, risk of recurrence varies between 26% and 41% in a period of two to five years and again depends on the histologic type, with the morphoeic variant being the most aggressive. When an early surgical revision is performed, a residual tumor is found in only 50% of the cases. Nevertheless, in these cases, with residual tumor cells, the risk of developing a new cBCC increases to more than 50%, with the maximum chance of a new development occurring when both the lateral and the deep margins are involved [11]. In regards to the close margins, the Authors found a single report [12] with the outcome of the cases where the amount of healthy tissue around the tumor was within 1mm (close margin in the Authors' grouping). In this paper, a recurrence rate of 1.2 % for histologic margins of ≥ 0.5 mm is reported while for histologic margins of < 0.5 mm the recurrence rate rises to 12 %. In the Authors' experience, over a series of 47 cBCCs in people over 75 years of age, the Authors had 21 clear margins (45 %), 10 close margins (21 %) and 16 positive (involved) margins (34 %). These figures are worse than the ones available in the literature, which range between 4.7% and 24% (see before). One might imply this is due to a too-conservative, sub-optimal surgical technique. Conversely, in the Authors' opinion this is worth-paying-a-price for, in order to avoid major surgeries with consequently longer surgical times, longer healing durations, greater aesthetic disfigurements, and with potential functional problems. In fact, when looking at the percentages of recurrences in the Authors' series, they are negligible and the possibility of surgical recuperation is high and mild. Neither a patient of the cBCC-clear-group, nor of the cBBC-close-group had a recurrence, while in only 2/16 of the cBBC-positive-group the tumors recurred. Thus, the percentage of recurrence in the whole group of cBCCs (2/47) is 4.5 %, while the risk of recurrence for the close margin group, in this Authors' series, is zero, and for the positive margins at the first surgical excision is 12.5 % (2/16). All of these figures are lower than the percentages of recurrences reported in the literature both for the radical surgical excision (under 10 %), for the close margins (up to 12 %), and for the positive margins (up to 40 %). Moreover, the two patients who recurred did not develop further tumors after the recurrence was excised. Even though the numbers are too limited, the literature data of a ten-fold-higher risk of recurrence after a previous cBCC excision are not confirmed in this study. The low rate of recurrence, for the limited and low-risk cBCC, allows a conservative approach for the great majority of the BCCs, in every age group. This is much more important when dealing with older and possibly more frail patients. The figure of a 12.5 % risk of recurrence, even lower than what was expected, in the Authors' opinion confirms that following

a tissue-sparing philosophy in this age group doesn't significantly affect the outcome and is therefore worth pursuing. Furthermore, it might validate the idea that the oncologic progression slows down in the elderly.

In addition, and based on the Authors' experience, it seems there is a different category of patients who are (genetically ?) prone to develop subsequent cutaneous malignancies, both in the same area and in different ones, of different histologic types (cBCC and cSCC), and despite the previous excisions having been radical (Table 4). It is important to note that even in this group of patients, especially if elderly, minor surgeries and/or multiple minor surgeries that are minimally invasive are preferred by the Authors and recommended for this segment of patients. This is due to the possibility of a still easy surgical salvage, in case of tumor recurrence or new malignancies, and to the patient tolerance for such mild surgical procedures.

Finally, the results achieved with a limited, standard surgical excision, allows the avoidance of Mosh surgery, which is 10-fold more effective but takes longer, is more invasive, is more expensive and is not always available [13].

cSCC has traditionally accounted for 20% of skin cancers, but recent surveys found its incidence has greatly increased [14]. In the European countries the yearly incidence is up to 95/100,000 for males and up to 65/100,000 for females, while in Australia the incidence increases are up to 500/100,000 for males and up to nearly 300/100,000 for females [15]. As for the cBCC, the most important risk factors are sun exposure, age, male sex, fair skin, ultraviolet radiation, immunosuppression, human papillomavirus, chronic scarring conditions, familial cancer syndromes, and environmental exposures. Genic mutations are also found to be important predisposing factors. From the histologic point of view [16], besides the common cSCC there are several subtypes, with progressive malignity: Keratoacanthoma, Verrucous, Clear cell, Acantholytic, Spindle-cell, Adenosquamous and other rare variants. The grade of cell differentiation is directly correlated to the risk of local recurrence and nodal/metastatic spread. The presence of desmoplasia is another negative prognostic factor. Tumor location, diameter, depth and cellular differentiation determine the rate of recurrence, as well as perineural invasion and distant metastasis. In a recent review of the literature, Genders and Co. [17] found a pooled, incomplete excision risk estimate of 13% with a range between 0.4% and 35.7%. Risk factors included tumor depth and size, type of operator (general surgeon or specialist), head and neck localization and former incomplete excision. These data correspond to those reported by Elliot and Co. [18], who found, on histological examination following excision, 9% of cases with positive margins and 17% of cases with close margins. In patients with positive margins, 52.6% went on to have surgical re-excision, and residual tu-

mors were found in 31.7% of the original patients with positive margins. Interestingly, in patients with close margins, 13.6% underwent re-excision, but no residual tumors were found in any of them. In early stages, local recurrence occurs in 3–8% of the cases and loco-regional lymph node and/or metastatic spread occurs in 1.9–10% of the cases, with mortality rates of 2–5% for all cSCCs. The risk of recurrence after excision depends again on the size of the lesion and the histologic grade. Lesions larger than 2 cm recur at a rate of 15.7% while poorly differentiated lesions recur at a rate of 25%, as opposed to well-differentiated lesions, which recur at a rate of 11.8% [19]. Moreover, in head and neck patients with locally advanced or regionally metastatic disease, the 5-year recurrence rate may be as high as 63%, with a resulting 5-year overall survival rate estimated between 44% and 71% [20]. Local recurrence influences the risk of regional and distant metastases, which is also increased by the size of the lesion > 2 cm, depth of invasion > 2 mm, poor histologic differentiation, perineural invasion, acantholysis, infiltrative strands (budding) of tumor and lesions from existing scars. Tumors smaller than 2 cm in diameter have been associated with a 9.1% rate of metastasis, whereas those larger than 2 cm in diameter have a metastatic rate of up to 30.3%. A tumor depth of less than 2 mm rarely metastasizes; lesions with a depth of invasion of 2-4 mm have a metastasis rate of 6.7%. Perineural invasion has been estimated to occur in up to 7% of people with cutaneous SCC. The prognosis in such cases is worse, with a risk of metastasis up to 47%. Positive lymph nodes increase the risk of recurrence and significantly decreases the overall survival rate.

The series hereby analyzed consists of 36 cSCC cases. 20/36 cases had clear margins (55 %), 6/36 cases had close margins (17 %) and 10/36 cases had positive margins (28 %). Again, these figures fall within the ranges reported in the literature, even though they appear worse than those reported by Elliot and Co. [18]. In the Authors' opinion the approach is the same as for cBCC, in that it is an acceptable risk because the recurrence percentage in the Authors' series is 1/10 (10 %), which is just higher than those reported in the literature for the early-stage tumors. Moreover, no patient had positive lymph nodes and/or distant metastases, and among the four cases where an early revision was carried out, two had no residual tumor, two were positive and only one was revised again with no residual disease. All the patients were alive and NED at the end of the follow up.

Once again, when dealing with elderly patients, it seems that they should be handled with a more conservative approach even in the cases of cSCC. For this histologic type too, a standard, tissue-sparing surgery seems adequate, without the necessity of the more precise, but cumbersome and expensive micrographic surgery.

For the group of patients who develop multiple, subsequent cSCCs, with or without intercurrent cBCCs (Table 4), the considerations

are the same as previously stated. These patients probably belong to a particular, maybe genetically predisposed group, but the risk of uncontrollable recurrences remains low and they may undergo the same conservative and minimally invasive approach, even with repeated but mild surgical procedures.

7. Conclusion

Treating the elderly is a challenging task that entails facing age-caused-fragility, comorbidities, difficulty in managing and significant care-giving. In western countries, the aging population has increased in the last twenty years and age-dependent cutaneous malignancies now represent an important health and economic burden. Limited therapeutic approaches, with minimal invasiveness and yet still positive cure rates are thus worth pursuing, in order to save the elderly's global health and at the same time contain social and economic costs and impacts. Based on the acquired experience, the Authors further recommend their policy of treating NMSM of people over 75 years of age via a single, limited, surgical excision with a watchful follow up.

8. Aknowledgments

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